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INTERNATIONAL CONFERENCE

On

Ayurveda -Yoga-Nathpanth - 2025

From : 12-01-2025 to 14-01-2025

Organized by :

Mahayogi Gorakhnath University Gorakhpur

Gorakhpur, Uttar Pradesh, India

Convener and Issue Editor

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YOGI ADITYANATH

CHIEF MINISTER
UTTAR PRADESH

Lok Bhawan,
Lucknow - 226001

Date : 23 NOV 2024

Message

I am happy to know that Guru Gorakshnath Institute of Medical Sciences, Mahayogi Gorakhnath University, Gorakhpur is organising an International Conference On Ayurveda-Yoga-Nathpanth-2025' from 12th to 14th January, 2025 in Gorakhpur.

Our Civilization is one of the most ancient civilizations in the world. Ayurveda, Yoga and Nath panth are some of the glories of our civilizational heritage.

Ayurveda and Yoga are ancient India's gift to humanity. These are two interrelated branches of the same tree of great Vedic knowledge, which encompasses every aspect of human life. Ayurveda not only helps in treating diseases but also in preventing the occurrence of diseases. It provides an effective cure for many chronic diseases.

Yoga as an integral part of Ayurveda helps in maintaining well-being of body, mind and soul. Due to the efforts of Hon'ble Prime Minister. Shri Narendra Modi ji, it has attained global popularity and acceptance. Every year on 21st June, International Yoga Day is celebrated across the globe.

Nath panth school of Yoga and Rasa shastra have contributed greatly for the welfare of mankind. Mahayogi Guru Gorakhnath was a leading exponent of the spiritual order of Nath Yogis. He is considered as the main propagator of Hatha Yoga. Nath Yogis were able to refine their bodies and minds to attain a spiritually enlightened state.

Most of the Siddha Yogis belonging to the Nath order are also known as Rasa Siddhas. Yoga and the Nath Siddhas are closely linked. Much of the Yogic techniques and texts that are taught today can be attributed to the Nath Yogis.

I appreciate that the objective of this International Conference is to assess the therapeutic effects of Ayurveda, Yoga and the contribution of Nath panth in physical and mental wellbeing of the people. I am confident that this event would provide a suitable platform for understanding the Nath Philosophy as well as the various aspects of Yogic practices and Ayurveda.

My best wishes for the entire endeavour.

(Yogi Adityanath)

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Metabolomics Profiling of *Boerhavia diffusa* (*Punarnava*): High-Resolution Mass Spectrometry Unveils Hepatoprotective Metabolites

Research Article

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Abstract

Boerhavia diffusa (*Punarnava*), a highly valued medicinal plant in Ayurveda, has been traditionally used for its hepatoprotective properties. Despite its extensive use in treating liver disorders, the specific bioactive compounds and underlying mechanisms responsible for its hepatoprotective effects remain largely undefined. This study utilizes High-Resolution Mass Spectrometry (HRMS) to comprehensively analyse and profile the bioactive compounds in *Boerhavia diffusa*, aiming to uncover its hepatoprotective potential at the molecular level. The HRMS analysis revealed a diverse spectrum of phytochemicals many of which are associated with anti-inflammatory, antioxidant, and liver-regenerative activities. These compounds were further explored for their interactions with key hepatic pathways, particularly in mitigating oxidative stress, inhibiting inflammatory mediators, and regulating enzymes crucial for liver function and detoxification. The study further explores potential mechanisms of action of these phytochemicals through reviews of existing pharmacological data, proposing a multifaceted approach to liver protection that includes scavenging free radicals, reducing lipid peroxidation, and inhibiting pro-inflammatory cytokines. The findings underscore the potential of *Boerhavia diffusa* as a natural therapeutic agent for liver diseases, reinforcing its place in both traditional and modern medicine. These findings could facilitate the development of novel plant-based therapeutics aimed at liver health.

Keywords: High Resolution Mass Spectrometry Analysis, Hepatoprotective Activity, *Boerhavia diffusa*, *Punarnava,* Liver function.

Introduction

The liver is a vital organ essential for maintaining homeostasis, performing critical metabolic and physiological functions such as bile production, energy generation, vitamin storage, and the metabolism of carbohydrates, proteins, and fats. After intestinal absorption, nutrient-rich blood flows to the liver via the portal vein, which also carries various toxic substances, including ethanol, drugs, and toxins. This makes the liver particularly vulnerable to damage and toxicity. Many individuals suffer from liver conditions, including fatty liver, non-alcoholic steatosis, hepatitis A, B, or C, cirrhosis, and hepatocellular carcinoma (one of the leading causes of cancer-related deaths worldwide) (1) As the primary organ responsible for metabolism, the liver is especially prone to damage from drugs and chemicals. The impact of such damage can vary widely, from mild, asymptomatic increases in liver enzymes to severe, life-threatening fulminant hepatic failure (2). Despite significant advancements in hepatology in recent years, liver disorders are increasingly prevalent. Unfortunately, the available drugs for treating liver diseases are limited and often come with serious side effects. Given the adverse effects of synthetic medications, there is a growing interest in exploring the therapeutic potential of medicinal plants through systematic research approaches (3). *Boerhavia diffusa* (*Punarnava*) belongs to the family Nyctaginaceae, is a perennial creeping herb widely used in Ayurveda for its therapeutic properties. Known for its rejuvenating and detoxifying effects, it is primarily valued for its role in supporting liver and kidney health. *Punarnava* exhibits anti-inflammatory, diuretic, antioxidant, hepatoprotective, and immunomodulatory properties. Previous studies have shown that the root of *Boerhavia diffusa* exhibits significant hepatoprotective activity (4). Consequently, an attempt has been made to isolate the bioactive compounds responsible for the hepatoprotective effects of *Boerhavia diffusa* and to explore the mechanisms through which they exert their action.

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Materials and Method

Collection of Boerhavia diffusa

The raw material of *Boerhavia diffusa* used for analysis by High-Resolution Mass Spectrometry (HRMS) was sourced from a local herbal market in Varanasi, Uttar Pradesh. Subsequently, the *Boerhavia*

diffusa sample was authenticated by the Department of Dravyaguna (related to Ayurvedic Pharmacognosy) with the accession number DG/24-25/853. It was also validated by the Department of Botany with the Voucher Specimen No. Nyctagina. 2024/02

The study utilized *Boerhavia diffusa* root powder, methanol, distilled water, and Eppendorf tubes. A High-Resolution Accurate Mass Spectrometry system, specifically the Orbitrap Eclipse Tribrid Mass Spectrometer from Thermo Fisher Scientific, was employed. For the analysis of small molecules, the Dionex UltiMate 3000 RS UHPLC system was employed to conduct detailed phytochemical analysis (5).

Method employed for HRMS analysis

The sample preparation for HR-MS analysis started with the addition of individual optimized sample of *Boerhavia diffusa* [Root powder (100 mg)] with 1.5 ml solvent (Methanol:Water; 80:20) and homogenized using Eppendorf Thermo-mixer at 750 rpm for 30 min at 25°C. Then, the sample was centrifuged (3500 rpm/ 10 min/ 25 °C). The supernatant was filtered with a 0.22 µ PTEF syringe filter and 4 µl of the filtrate was used as injection volume on C18 RP-HPLC column (Hypersil GOLD™: Particle size 1.9µ, 2.1mm × 100mm)

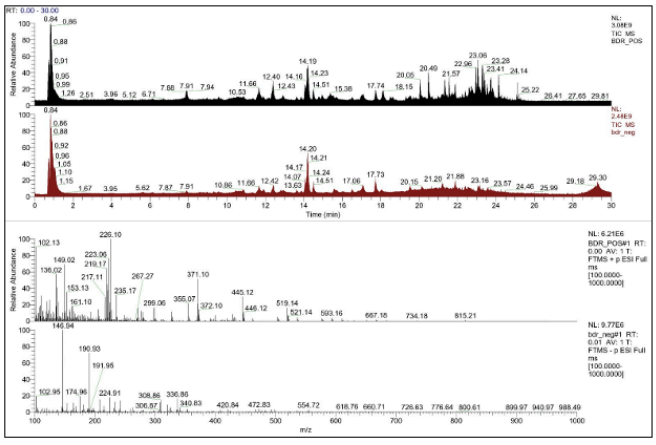
The Reversed-phase chromatographic separation start with a high aqueous phase (+0.1% formic acid) and ends on highly organic phase (MeOH+ 0.1% formic acid) typically 100% aqueous to 100% organic. The LC gradient parameters were 0-6 min 5% MeOH, 6-10 min 30% MeOH, 10-20 min 50% MeOH, 20-25 min 90% MeOH, 25-27 min 90% MeOH, and 27-30 min 5% with flow rate of 300 l/min and column oven temperature 40 °C. The optimised sample of *Boerhavia diffusa* was tested for metabolomics analysis. Thermo Fisher Scientific - High Resolution Accurate Mass Spectrometry System of the model "Orbitrap Eclipse Tribrid Mass Spectrometer coupled with Nano Liquid Chromatography and Ultra High-Pressure Liquid Chromatography" (Diones Ultimate 3000 RSLC) system, Heated Electro Spray Ionisation (HESI) source was used to fed the sample to the mass spectrometer post chromatographic separation. The Orbitrap analyser was utilized at 60,000 resolutions separately for positive/negative polarity with mass range (m/z) 100-1000, 35% RF Lens, 25% Normalized AGC Target keeping 2.0e5 as intensity threshold to perform MS-OT (Master scan). To obtain ddMS2 OT HCD the selection parameters were, Quadrupole isolation mode with 1.5 isolation window (m/z) HCD Activation type, 30, 45, 60HCD collision energy (%), 15000 Orbitrap Resolution, 20% Normalized AGC Target (6).

The raw data obtained from the mass analyser were performed through default parameters of "Compound discoverer 3.3.2.31" using online databases. The chosen workflow was the Natural Product Unknown ID, incorporating both online and local database searches. This untargeted food research ID workflow operates without statistics, focusing on the detection and identification of unknown compounds. It includes retention time alignment, unknown compound detection, and compound grouping across all samples. The workflow predicts elemental compositions for all identified compounds and filters out chemical background using blank samples. Compound identification is achieved through mzCloud (using ddMS2 and/or DIA), ChemSpider (based on exact mass or formula), and local database searches against mass lists (with or without retention time). Additionally, it conducts spectral similarity searches against mzCloud for compounds with ddMS2 and applies spectral distance scoring to matches from ChemSpider and mass lists (7).

Result

A Total Ion Chromatogram (TIC) represents the overall intensity of all ions detected over time and serves as an essential tool for analysing the composition of a sample. By providing a visual representation of the ions detected during chromatographic separation, the TIC allows for a detailed understanding of the various compounds present within the sample. The Total Ion Chromatogram of the components found in *Boerhavia diffusa* is illustrated in Figure 1, offering insights into its chemical profile.

Figure 1: Total ion chromatogram of the *Boerhavia diffusa*. It shows Total ion chromatogram obtained by UHPLC-HRAMS analysis of the *Boerhavia diffusa* (*Punarnava*) sample in positive and negative ion mode



The Standard Ion Chromatogram serves as a reference for the identification and quantification of ions within the tested sample. In the case of Boerhavia diffusa, the identified hepatoprotective metabolites were quantified and characterized according to their retention times and peak intensities, as depicted in Figure 2-7.

Mechanisms of Hepatoprotective action of bioactive metabolites derived from *Boerhavia diffusa*

In a comprehensive analysis utilizing High-Resolution Mass Spectrometry (HRMS), a total of 1,584 metabolites were identified from the *Boerhavia diffusa* sample. Among these, six specific compounds demonstrated notable hepatoprotective activity. The bioactive metabolites identified are as follows: 1) Citral; 2) Choline; 3) Betaine; 4) Itaconic acid; 5) Syringic

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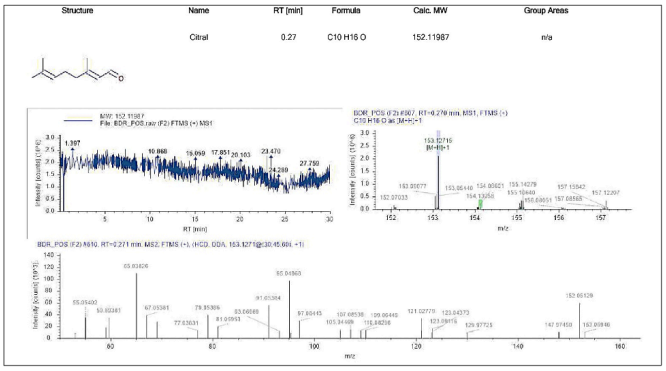
acid; and 6) Catechin. The specific mechanisms through which these metabolites confer liver protection are outlined in the references provided below.

Citral

Previous research investigated the effects of citral on acetaminophen (APAP)-induced liver toxicity in a murine model. To assess citral's hepatoprotective properties, liver function markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (γGT) were measured. Additionally, liver tissues were analysed for myeloperoxidase (MPO) activity, nitric oxide (NO) production, and through histological examination. Citral's impact on leukocyte migration and antioxidant activity was also evaluated in vitro. Pretreatment with citral significantly reduced ALT, AST, ALP, γGT, MPO activity, and NO production. Histological findings showed improvement in liver damage after citral pretreatment. Furthermore, citral inhibited neutrophil migration and demonstrated antioxidant properties, suggesting its protective role against APAP-induced liver toxicity (8). Citral has also demonstrated renoprotective and hepatoprotective properties in mice, attributed to its antioxidative and anti-inflammatory effects (9)(10). NAD(P)H quinone oxidoreductase 1 (NQO1) has been reported to shield cells from oxidative stress caused by reactive and harmful quinines (11). Another study found that rats treated with citral exhibited a significant decrease in hepatic testosterone 6β-hydroxylation and ethoxyresorufin O-de-ethylation activities. Furthermore, citral significantly increased the activity of NAD(P)H quinone oxidoreductase 1 (NQO1). Additionally, treatment with citral led to reduced lipid peroxidation and lower levels of reactive oxygen species in the liver. The study suggested that citral may alter the activities of drug-metabolizing enzymes and alleviate oxidative stress in the liver (12). Similarly, citral was shown to inhibit the expression of pro-inflammatory cytokines such as IL-6 and TNFα in LPS-stimulated hepatocytes by preventing lipopolysaccharide (LPS)-induced phosphorylation and nuclear translocation of NF-κB. Citral may function as a TLR4 antagonist, blocking LPS binding to the receptor and, consequently, counteracting the downstream effects of LPS/TLR4 signalling, including NF-κB activation and its target genes involved in the inflammatory response. Additionally, pretreatment with citral mitigated LPS-induced oxidative stress by reducing reactive oxygen species (ROS) levels. These findings support the hypothesis that citral acts as a TLR4 antagonist by inhibiting the TLR4 signalling cascade, rendering cells unresponsive to LPS-induced oxidative stress. Furthermore, citral was found to counteract the expression of epithelial–mesenchymal transition (EMT) markers in LPS-stimulated hepatocytes, emphasizing its potential to prevent the establishment of a fibrotic environment in the liver (13). The standard ion chromatogram is depicted in Figure 2.

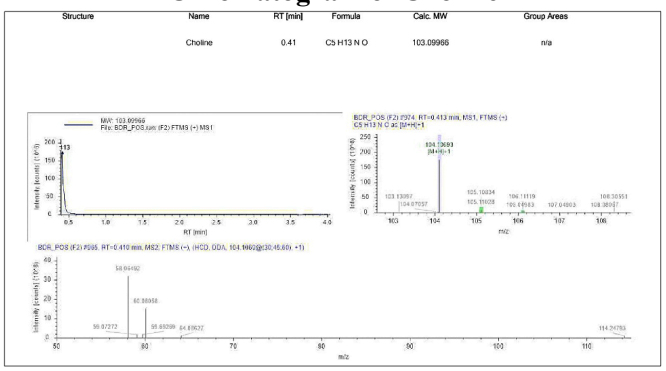
Figure 2: Illustrates the Standard Ion Chromatogram of Citral



Choline

The liver is the central organ for the metabolism of choline, methyl folate, methionine, and S-adenosylmethionine (SAM), and it is where most of the methylation reactions occur. It is particularly sensitive to the availability of dietary methyl donors like choline. When these nutrients are deficient, the liver becomes susceptible to damage, leading to fat accumulation (steatosis), hepatocyte death, fibrosis, and, ultimately, the development of carcinogenic foci. This underscores the critical importance of methyl donors in preserving liver function and preventing serious liver diseases (14). A study demonstrated that choline supplementation effectively prevented weight loss and liver function decline, while also reducing inflammation by normalizing hepatic cholesterol levels and metabolism. Choline supplementation increased hepatic phosphatidylcholine (PC) and phosphatidylethanolamine (PE) levels but did not affect triglyceride (TG) concentrations in phosphatidylethanolamine N-methyltransferase (PEMT)-deficient mice. By restoring cholesterol metabolism, choline supplementation improved liver function and prevented the progression to non-alcoholic steatohepatitis (NASH) and liver failure. Notably, choline supplementation significantly improved liver function by regulating markers related to macrophage activity, oxidative stress, and fibrosis. The findings suggest that choline supports liver health by maintaining cholesterol homeostasis (15). The standard ion chromatogram is depicted in Figure 3.

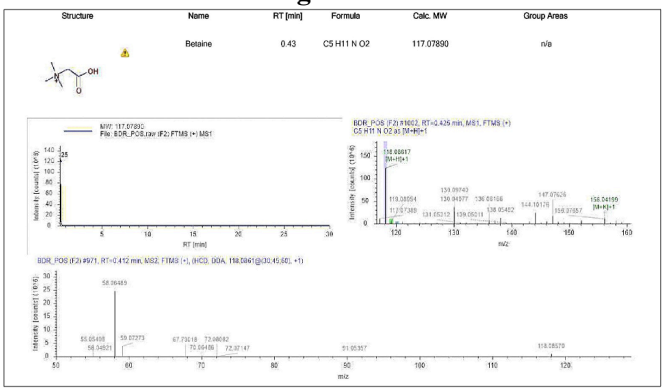
Figure 3: Illustrates the Standard Ion Chromatogram of Choline



Betaine

Betaine is recognised as a vital nutrient with protective properties, particularly for the liver. According to a study by, betaine demonstrated effectiveness in preventing liver damage induced by carbon tetrachloride. As a potent antioxidant, betaine has also been shown to positively influence redox balance during ischemia-reperfusion liver injury in rats. The administration of betaine as an antioxidant demonstrated significant protective effects on the liver, specifically by preventing necrosis. It reduced the production of inflammatory mediators and enhanced tissue repair by mitigating degenerative changes, with optimal protective outcomes observed at doses of 150 and 250 mg/kg (16). Betaine treatment has been reported to significantly reduce oxidative stress, lower cytochrome P450 (CYP450) activity, enhance glutathione transferase (GSH-T) activity, decrease caspase-3 activity, and reduce fibrotic markers, all contributing to improved liver function. Through its antioxidant properties, along with its ability to enhance liver detoxification and reduce apoptosis, betaine may help slow the progression of liver fibrosis and provide a protective effect against radiation-induced liver damage (17). The standard ion chromatogram is depicted in Figure 4.

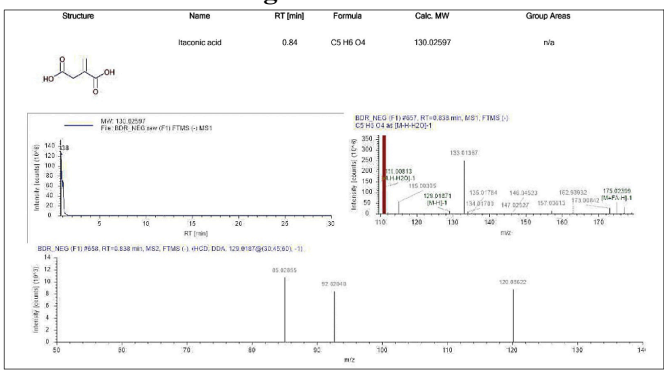
Figure 4: Illustrates the Standard Ion Chromatogram of Betaine



Itaconic acid

Itaconic acid is a metabolite generated by immune cells, particularly macrophages, during inflammation and can aid in reducing inflammation. It is reported that Itaconic acid blocks the activity of the NF-κB pathway, decreases the buildup of the transcription factor P-P65 in the nucleus, and diminishes the expression of inflammatory proteins linked to the downstream effects of the NF-κB pathway. As a result, it helps mitigate liver injury and inflammation during ischemia-reperfusion (18). Nrf2 is a transcription factor involved in intracellular signalling that helps protect organs from oxidative stress. Numerous studies have shown that a reduction in Nrf2 levels makes the liver more vulnerable to toxin-induced damage, providing strong evidence for Nrf2's role in liver protection. Furthermore, it has been established that activating Nrf2 can safeguard the liver from ischemia/reperfusion (I/R) injury in mice. Recent research has also highlighted that itaconate can stimulate Nrf2-driven signalling. Treatment with itaconic acid has been found to enhance the expression and nuclear translocation of Nrf2, as well as increase the activity of its downstream protective pathways (HO-1 and NQO1), in both mouse and primary human hepatocytes thus contributing to its hepatoprotective activity (19). The standard ion chromatogram is depicted in Figure 5.

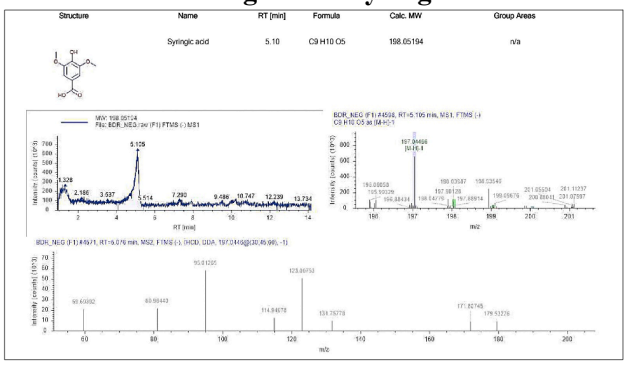
Figure 5: Illustrates the Standard Ion Chromatogram of Itaconic acid



Syringic acid

Syringic acid reduced the levels of transaminases and malondialdehyde in mice treated with CCl4. This compound exhibits 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity, suggesting that the reduction of reactive oxygen species (ROS) generation may be responsible for its hepatoprotective effect (20). Syringic acid has been shown to effectively inhibit the activation of cultured hepatic stellate cells, which play a crucial role in liver fibrogenesis. When administered, syringic acid reduced hepatic fibrosis in the context of chronic liver injury. A study examining the effects of syringic acid on acetaminophen (APAP)-induced hepatotoxicity in rats revealed that it significantly lowered markers of lipid peroxidation while increasing the activity of enzymatic antioxidants in the liver. These findings indicate that syringic acid offers substantial protection against APAP-induced liver damage in rats. Additionally, syringic acid demonstrates hepatoprotective effects against hepatic encephalopathy by reducing hepatotoxicity biomarkers. Its antioxidant and anti-inflammatory properties further contribute to its hepatoprotective actions (21). The standard ion chromatogram is depicted in Figure 6.

Figure 6: Illustrates the Standard Ion Chromatogram of Syringic acid



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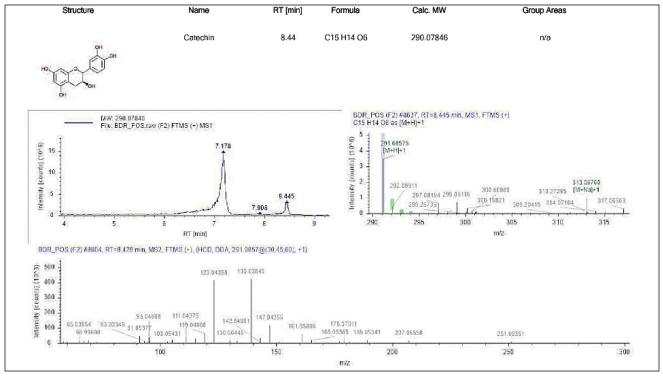
Catechin

Research demonstrated that catechin has a notable protective effect on the liver. This hepatoprotective effect may be attributed to its ability to scavenge free radicals and suppress cytokines. Treatment with catechin led to the restoration of levels of TNF-α, IL-1β, IL-6, and NO. Additionally, catechin effectively shielded hepatocytes from drug induced oxidative damage. It also restored antioxidant enzymes and biochemical markers, while lowering serum cytokine levels (22). The standard ion chromatogram is depicted in Figure 7.

Figure 7: Illustrates the Standard Ion Chromatogram of Catechin



Discussion

Hepatoprotection in Ayurveda refers to the safeguarding and restoration of liver health through the use of specific herbs and treatments. The liver or "*Yakrit*" is seen as an essential organ for digestion, metabolism, and detoxification. Ayurvedic hepatoprotective herbs help detoxify, rejuvenate, and protect the liver from damage caused by toxins, infections, and imbalances in bodily functions. *Punarnava*, botanically known as *Boerhavia diffusa*, belongs to the Nyctaginaceae family. It is renowned as one of the most effective diuretic herbs referenced in Ayurvedic texts. True to its name, which implies a capacity for rejuvenation, *Punarnava* is recognized for its revitalizing properties (23). Research has shown that the alcoholic extract of the *Boerhavia diffusa* plant is a potent and safe antihepatotoxic agent. When administered orally, the alcoholic extract of the entire plant demonstrated hepatoprotective effects against carbon tetrachloride-induced liver toxicity in rats and mice (24). As per *Bhavaprakasha Nighantu, Punarnava* exists in two primary varieties: *Rakta Punarnava* (*Boerhavia diffusa* Linn) and *Shweta Punarnava* (*Boerhavia verticillata* Poir) (25). In this study, the hydroalcoholic extract of the root of Rakta *Punarnava* (*Boerhavia diffusa*) was subjected to High-Resolution Mass Spectrometry (HRMS) analysis in order to obtain its metabolomic profile and unveil its hepatoprotective activity. The HRMS analysis of *Boerhavia diffusa* identified 1,584 bioactive metabolites. Notably, six of these compounds namely Citral, Choline, Betaine, Itaconic acid, Syringic acid, and Catechin have been recognized for their significant hepatoprotective properties.

Citral is reported to reduce myeloperoxidase activity, nitric oxide production, and neutrophil migration, indicating its hepatoprotective and antioxidant properties (8). Citral is also reported to significantly increase the NAD(P)H quinone oxidoreductase 1 (NQO1) activity. Additionally, citral decreased lipid peroxidation and reactive oxygen species levels as well, thus reducing the oxidative stress in the liver (12). Choline supplementation maintains cholesterol homeostasis to support liver health. It normalizes hepatic cholesterol levels and metabolism, reduces inflammation and improves liver function markers (15). Betaine has antioxidant and detoxifying properties. It can also reduce apoptosis. It decreases oxidative stress, lowers cytochrome P450 activity, enhances glutathione transferase activity, decreases caspase-3 activity, and reduces fibrotic markers, improving liver function (17). Itaconic acid is known to inhibit the NF-κB pathway 18 and activate Nrf2-driven signalling (19). Thus, contributing to its hepatoprotective activity. The liver protective effect of Syringic acid are likely due to its ability to lower reactive oxygen species (ROS) levels (20) and hepatotoxicity biomarkers. Its strong antioxidant and anti-inflammatory properties further enhance its liver-protective actions (21). The hepatoprotective effect of catechin may be attributed to its ability to neutralize free radicals and inhibit cytokine production (22). A summarized overview of the metabolites with identified hepatoprotective activity is presented in Table 1.

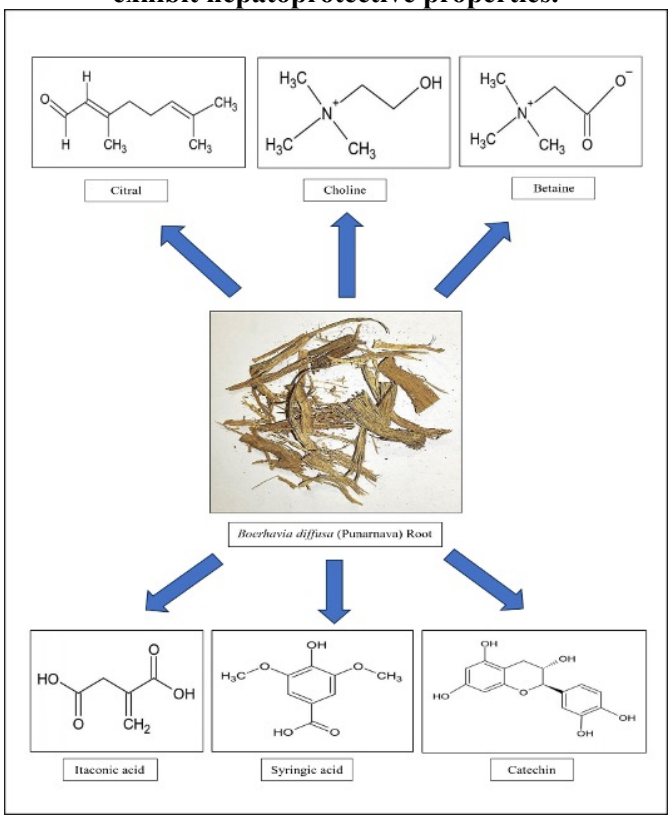
Table 1: Illustrates the details of the Metabolites isolated by HRMS. It shows the Chemical formula, Calculated Molecular Weight (MW), Retention Time (RT) values, Delta Mass and the Peak area under Negative (NEG) / Positive (POS) ion mode of the bioactive metabolites.

Bioactive Metabolite	Formula	Calc. MW	Retention Time (min)	Delta Mass (ppm)	Area NEG	Area POS
Citral	$C_{10}H_{16}O$	152.11987	0.269	-1.58	-	43770954.72
Choline	$C_5H_{13}NO$	103.09966	0.412	-0.55	-	323936836.84
Betaine	$C_5H_{11}NO_2$	117.0789	0.427	-0.7	-	352699468.42
Itaconic acid	$C_5H_6O_4$	130.02597	0.838	-4.92	444518852.76	-
Syringic acid	$C_9H_{10}O_5$	198.05194	5.102	-4.46	14486809.04	-
Catechin	$C_{15}H_{14}O_6$	290.07846	8.444	-2.01	-	19782377.47

The molecular structure of a metabolite is fundamental to its hepatoprotective activity, as it determines the interaction of the metabolite with liver enzymes, cellular membranes, and their key biochemical

pathways. Structural features like functional groups, polarity, and size influence antioxidant, anti-inflammatory, and detoxification effects, which are crucial for protecting liver cells from oxidative stress and inflammation. Additionally, certain structures aid in the regulation of apoptosis and cell regeneration. Synergistic interactions between metabolites, driven by their diverse structures, can enhance overall hepatoprotective efficacy. Therefore, the molecular structures of the active metabolites identified in *Boerhavia diffusa* are illustrated in Figure 8.

Figure 8: Shows the Molecular Structures of bioactive metabolites isolated from *Boerhavia diffusa*. This figure highlights the molecular structures of compounds identified through High-Resolution Mass Spectrometry analysis, which exhibit hepatoprotective properties.



This study primarily focuses on the identification and profiling of bioactive compounds through HRMS, with limited in vivo or clinical validation of the proposed mechanisms of action. While pharmacological data were reviewed, direct experimental evidence linking these phytochemicals to specific hepatic pathways in humans remains to be established. Additionally, variations in phytochemical composition due to environmental, seasonal, and geographical factors were not fully explored. Future studies should include in-depth pharmacokinetic analyses and clinical trials to substantiate these findings and assess the therapeutic efficacy and safety of *Boerhavia diffusa* in the treatment of liver disorders.

Conclusion

This study provides a detailed molecular profile of *Boerhavia diffusa* using High-Resolution Mass Spectrometry, identifying a diverse range of bioactive compounds with strong hepatoprotective potential. Six metabolites with hepatoprotective properties were identified. The hepatoprotective effects of *Boerhavia diffusa* are likely the result of the combined, synergistic actions of these metabolites. These compounds exhibit antioxidant, anti-inflammatory, and liver-regenerative properties, supporting the traditional use of *Boerhavia diffusa* in treating liver disorders. The proposed mechanisms, such as the reduction of oxidative stress, inhibition of pro-inflammatory cytokines, and regulation of liver detoxification pathways, present a multifaceted approach to liver protection. These findings reinforce the relevance of *Boerhavia diffusa* in both Ayurvedic and modern medicine, offering a scientific foundation for its use as a natural therapeutic agent in maintaining hepatic health. This study could serve as a critical step toward the development of plant-based treatments targeting liver health, offering new insights for future pharmacological applications.

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Anatomical study of shringataka marma using cadaveric dissection technique

Research Article

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Abstract

In *Ayurveda*, the concept of *Marma* describes 107 vital points in the body where *Prana*, or life force, resides. These points are crucial because injury to them can result in sudden pain or even death. Among these, the *Shringataka Marma* is located on the nose and falls under the category of *Urdhwajatrugat Marma* or *Sira Marma*. It measures about 8 cm. (which is equivalent to four *angula*) and in turn consists of four individual points. Injury to the *Shringataka Marma* is considered potentially fatal. In this study, the *Shringataka Marma* is analysed from the perspective of contemporary anatomy, comparing its location and associated components with insights from both *Ayurvedic* and modern medical literature. The aim is to explore the anatomical structures associated with the *Shringataka Marma* using the cadaveric dissection and also used to assess the relevance of ancient *Ayurvedic* concepts, such as those described by *Sushruta*, in the context of modern medical understanding.

Keywords: *Marma, Shringataka Marma*, Cadeveric Study, Cavernous Sinus, Intercavernous sinus.

Introduction

Ayurveda, a branch of medical science dedicated to maintaining the balance of body, mind, and soul for optimal health of the individual and it also holds profound influence over human life. The foundational concept of *Marma*, with its 107 vital points strategically located in the body, has been instrumental in advancing *Ayurvedic* understanding. Injury to these critical areas can profoundly diminish overall bodily energy or the vitality of specific organs or systems, thereby leads to potential fatalities.

Maharshi Sushruta, a pioneering figure in surgery, detailed a crucial aspect of *Marma* in the *Sharira Sthana* chapter of his *Sushruta Samhita*, titled "*Pratyeka Marma Nirdeshaniya Sharir*". He defined *Marma* as a physical entity whose vitality is intricately linked to the structures present within it. According to *Sushruta,* each *Marma* is a convergence point where muscle tissue (*Mansa*), blood vessels and nerves (*Sira*), ligaments, tendons, and nerve tissue (*Snayu*), bone tissue (*Asthi*), and joints (*Sandhi*) come together. (1)

According to *Acharya Sushruta*, *Marmas* are locations in the body where the three *doshas* (*Vata, Pitta*, and *Kapha*) and the three *Mahagunas* (*Satva, Raja*, and *Tama*) converge. These *doshas* represent the fundamental energies governing bodily functions, while the *Mahagunas* are considered supernatural forces influencing the mind and soul.(2)

Anatomically, *Marma* can be categorized into five types based on their structure and location. i.e, (3)

1. *Mansa Marma,*
2. *Sira Marma,*
3. *Snayu Marma,*
4. *Asthi Marma*
5. *Sandhi Marma*

Based on their susceptibility to traumatic impact and the prognosis outlined in *Ayurveda*, *Marma* points are classified into five types. i.e, (4)

1. *Sadhyapranhar Marma,*
2. *Kalantarpranhar Marma,*
3. *Vaikalyakara Marma,*
4. *Vishalyaghna Marma,*
5. *Rujakar Marma.*

Shringataka Marma:

The term "*Shringataka*" translates to "the place where four roads meet." (5)

Location	Intersection of veins between the nose (*ghrana*), ear passages (*shrota*), eyes (*Akshi*), and tongue (*jivha*) (6)
Number	Four (7)
Dimension	four *angula* (8)
Structural Anatomy	*Sira Marma* (9)
Prognostic Status	*Sadhyapranahar Marma* (10)
Injury Results	Serves as an extensive network providing nutrition to the tongue, ears, nose, and eyes. Injury to this vital point can result in instant death (11)

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Located in the nasal region, the *Shringataka Marma* is situated at the intersection of veins between the nose (*ghrana*), ear passages (*shrota*), eyes (*Akshi*), and tongue (*jivha*). This positioning classifies it as a *Sira Marma*. The *Shringataka Marma* plays a vital role in providing nourishment to these anatomical parts.

According to the teachings of the ancient scholars (*acharyas*), *Sadhyapranahar Marma* is a type of vital point in the body that, when injured, leads to immediate death.(12)

It has been noted that the *Shringataka Marma*. From a functional perspective, this *Marma* can be likened to a cavernous sinus. The location of the *Shringataka Marma* can be correlated with the area of the cavernous sinus and intercavernous sinus. Described as a cavernous nutrition network, this *Marma* provides nourishment to the tongue, ears, nose, and eyes. Conceptually, it can be understood as analogous to a cavernous sinus. The cavernous sinus receives venous blood from the brain, meninges, and skull bones, and contains cerebrospinal fluid (CSF). It connects with veins outside the skull via emissary veins. Occasionally, the central vein of the retina and the superior ophthalmic vein drain into the cavernous sinus.

The cavernous sinus drains into the facial vein through the superior ophthalmic veins. The facial vein, which is the largest vein in the face, collects blood from the mouth, nose, and ears. This anatomical arrangement clarifies the concept of "*Santarpan*" (nutrition) for the structures of the ear, nose, and mouth. According to *Ayurvedic* principles, any medication administered through the nasal route reaches the *Shringataka Marma*. From there, it uses the blood vessels (*Siras*) to nourish the structures of the ear, eye, nose, and throat. This process highlights how *Nasya* medication in *Ayurveda* is absorbed and distributed via the *Shringataka Marma*, influencing both local and systemic circulation.

The *Shringataka Marma* located on the brain's surface is associated with nerve centers. From this point, substances used in *Nasya* therapy disperse into various channels (*Strotasas*) comprising vessels and nerves, helping to eliminate imbalanced *Doshas* from the head region. These nerve cells and fibers play essential roles in functions such as speech, hearing, taste, smell, and vision.

According to Dr Avinash Lele, Supraorbital Artery, Frontal diploic vein, Superior Sagital Sinus, Occipito Frontalis muscle and Opthalmic nerve are considered as the important structures associated with the *Shringataka Marma*. (13)

According to Dr. Sandip Sahmrao Lanje, following structure can be considered under the area of *Shringataka Marma which are* Cavernous sinus, inter-cavernous sinuses, ophthalmic nerve and supra orbital artery.(14)

According to Dr. A. K. Pathak, the anatomical structures underlying the *Shringataka region* are Cavernous Sinus and Inter-cavernous Sinus.(15)

Modern Perspective(Practical anatomy) of *Shringataka Marma* the structures falling under the area of *Shringataka Marma* are Speech(motor) centres of the brain, Visual centres of the brain(sensory and psychic), Auditory centres of the brain, Gustatory centres of the brain and Olfactory centres of the brain. (16)

Materials and Methods

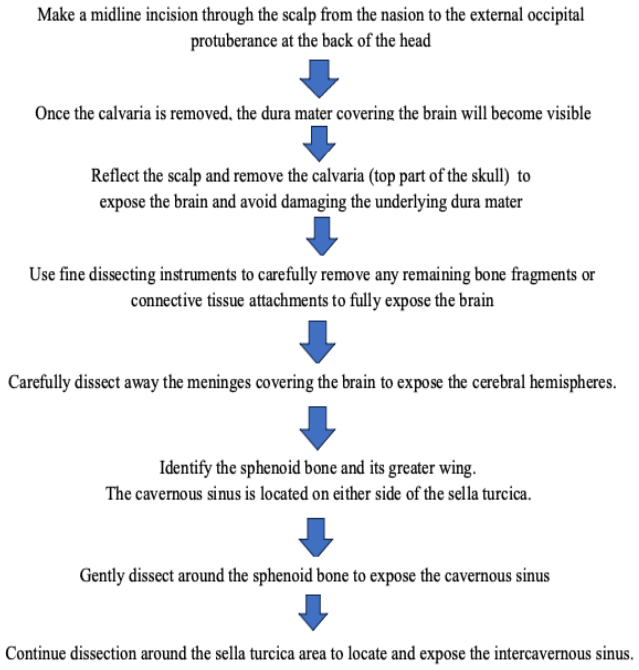
This article will gather information from primary *Ayurvedic* texts known as *Samhitas*, as well as modern anatomy books, national and international journals, and various databases.

Cadaveric Study

Methodology

- The anatomical analysis of the *Shringataka Marma is done* through studying relevant *Ayurvedic* and modern textbooks.
- Dissection of a selected female cadaver was conducted using a dissection kit over the region considered specific to the *Shringataka Marma* at the dissection hall of the Department of Rachana Sharir, Faculty of Ayurveda, Banaras Hindu University, Varanasi, Uttar Pradesh, India.
- The identification of the *Shringataka Marma* on the cadaver was based on findings from the literary study.
- The area around the *Shringataka Marma* point was marked according to proportions specified in the *Samhitas*.
- Detailed dissection focused on specific anatomical landmarks.
- Through precise dissection, structures related to the *Shringataka Marma*, including Cavernous Sinus and Inter-cavernous Sinus and their surrounding related structures like Occulomotor Nerve, Trochlear Nerve, Opthalmic Nerve, Maxillary Nerve, etc are identified.
- The findings from the dissection were interpreted in relation to *Ayurvedic* principles concerning the composition of the *Shringataka Marma* under the categories of *Mamsa*, Sira, Snayu, Asthi, and Sandhi.

Steps of Dissection (17)



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Dissected Anatomical Structures:

Fig 1: Cavernous Sinus **Fig 2: Right and Left Cavernous Sinus**

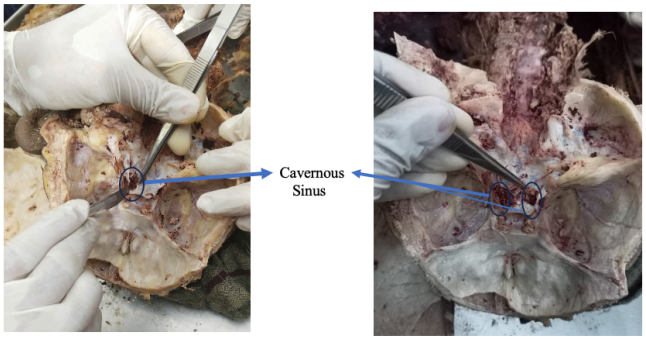


Figure 3: Important Structures related with Cavernous Sinus

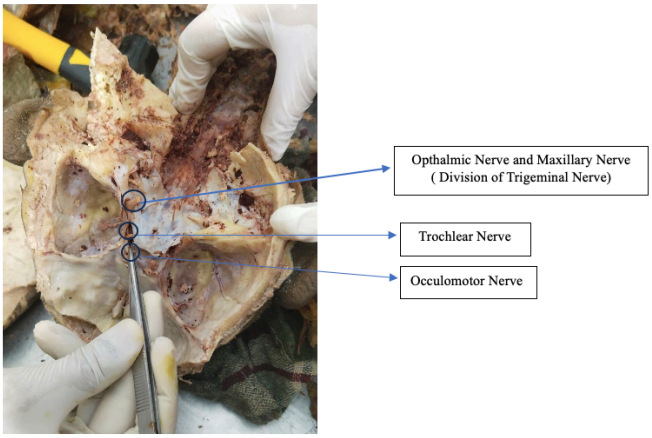
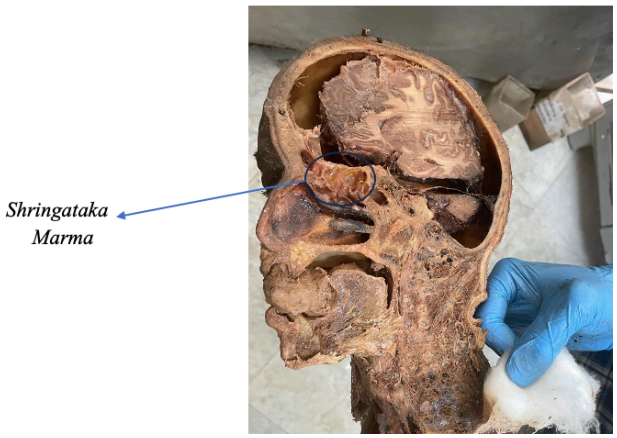


Figure 4: Shringataka Marma



Regional Anatomy of *Shringataka Marma* (18)

The cavernous sinus is located on each side of the sella turcica, above the sphenoid body which houses the sphenoid sinus. It consists of a network of very thin-walled veins extending from the petrous portion of the temporal bone at the apex posteriorly to the anterior superior orbital fissure. Venous blood from various sources such as the sphenoparietal sinus, superficial middle cerebral vein, and superior and inferior ophthalmic veins enters the cavernous sinus. These sinuses communicate with each other through intercavernous sinuses located anterior and posterior to the pituitary gland's stalk, and occasionally through veins below the pituitary gland. The pterygoid plexuses receive drainage from the posterior and inferior aspects of the cavernous sinuses via the superior and inferior petrosal sinuses as well as emissary veins. Inside each cavernous sinus lie the internal carotid artery and its smaller branches, surrounded by the abducent nerve (CN VI) and sympathetic nerve fibers of the carotid plexus. Embedded in the lateral wall of the sinus are the oculomotor (CN III), trochlear (CN IV), and two divisions of the trigeminal nerve (CN V). The cavernous sinus also serves as a site for heat exchange, cooling arterial blood as it passes through the sinus loaded with cooler venous blood returning from the body's periphery. In animals such as horses and cheetahs, the carotid artery takes a longer, more convoluted path through the cavernous sinuses during sprinting to aid in cooling blood before it enters the brain, although this mechanism is less significant in humans. Gravity and arterial pulsations within the cavernous sinus assist in the drainage of venous blood from the sinus.

Discussion

Upon anatomical and cadeveric analysis, the sites described by *Acharya Sushruta* converge at the junction of the cavernous and intercavernous sinuses near the base of the brain. *Sushruta* identifies the *Shringataka Marma* as the meeting point of four crucial veins—the nasal, auditory, optic, and lingual—within an area measuring four *angulas*. This precise location aligns with the anatomical convergence of the cavernous and intercavernous sinuses. The cavernous sinus is located on either side of the sella turcica and the intercavernous sinus is a small venous channel that connects the two cavernous sinuses across the midline. Due to its critical nature, this *Marma* is classified as a *Sadyah Pranhara Marma*, where injury can lead to immediate death, particularly if the cavernous sinus is ruptured.

Functionally, the *Shringataka Marma* corresponds closely with the cavernous sinus. It is surrounded by cranial nerves III, IV, and VI, which control eye movements, and cranial nerve V (Trigeminal nerve), responsible for sensory and motor functions of the face. The internal carotid artery passing through this region underscores its anatomical significance beneath the *Shringataka Marma*. The cavernous sinus, formed by the convergence of the superior and inferior ophthalmic sinuses along with the superior pterygoid sinus, has a triangular shape. Blows to the front or back of the head can transmit force to the cavernous sinus, potentially leading to complications such as cerebral hemorrhage or neurogenic consequences, with severe outcomes including death.

Conclusion

The *Shringataka Marma* is anatomically critical, located where the cavernous sinus and intercavernous sinus converge. Positioned at the junction of the tongue, nose, eyes, and ears on the soft palate, it sits approximately half an inch above the *sthapani* (forehead). This *Marma* regulates *Prana, Bodhaka*

Kapha (one of the subtypes of Kapha associated with taste), and the sense organ of taste. Described as a vast nutritional network, the *Shringataka Marma* provides nourishment to the tongue, ears, nose, and eyes. Injury to this *Marma* can result in severe hemorrhage and is therefore termed as a *Sadyah Pranahara Marma*, indicating its potential to cause immediate death.

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Mechanism of *Arkeshwara rasa* to combat hepatocellular carcinoma

Research Article

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Abstract

Background: Immunomodulatory treatments along with systemic and loco-regional methodology of treatment approach have reduced the incidence of Hepatocellular carcinoma (HCC) in recent observations. The phytomolecular applications have been seen to reverse the hepatic fibrosis aiding in regeneration of hepatocytes. The cytotoxicity of *Arkeshwara rasa* (AR) was investigated on HCC cell lines to observe the general signs of apoptosis. Methodology: The MTT (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) assay and Ethidium Bromide/Acridine orange Assay (EtBr/AO) were subjected on AR to know the cytotoxicity and the apoptotic results. Results: The IC_{50} of 37.14 µg/ml was exhibited by AR against Huh 7 cell lines and the (EtBr/ AO) Assay demonstrated the early and late apoptotic features in comparison with Untreated and Doxorubicin standard drug. Conclusion: AR on the basis of present evaluation against HCC cell lines and previous results on various other cell lines might be able to check the pathogenesis progression of HCC cells initiating the apoptotic features or reviving the vulnerable cell from further damage because of the phyto-constituents or mineral inclusions. These preliminary observations have to be again revalidated with reverse transcription, cDNA synthesis, western blotting, cell cycle analysis, etc.

Keywords: *HCC, AR, Rutin, Hesperidine, Kaempferol, Quercetin, MTT Assay, AO Assay*.

Introduction

Hepatocellular carcinoma (HCC) is addressed in the ICD 10 categorization, as the disease with rare incidence in United States and more in Asian countries. The prevalence of Hepatitis also follows such a pattern in Asian countries than the European regions revealing the chances of microbial resistance flaring up the world wide spread. (1) The infections and inflammations in the presence or absence of alcohol as in non- alcoholic cirrhotic conditions subsequently due to chronic nature also end as this carcinoma. (2)The HCC ranks as the sixth in overall cancer incidence, however stands fourth in the mortality turn over. (3) This data is a drop over from the incidence and death rate of 5th and 2nd positions, respectively. (4) This recent rise of survival rate from 18% to 43% has been concluded due to the systemic, immunomodulatory, loco-regional methodology of treatment approach.(5) The most effective treatment comprises the application of Orthotopic Liver Transplantation (OLT) and Marginal resections depending upon the spread and size of the tumor. Even though the asymptomatic phase and the late stage diagnosis delays the treatment aspects and leads to poor prognosis.(6) The multikinase inhibitor-Sorafenib faces the challenge of chemotherapeutic resistance and the main reason lies with ferroptosis phenomenon due to the drug. (7). The irreversible fibrotic change have been found to be generated from transforming growth factor (TGF)-β1 and the NF-κB cell signaling pathways. The same NF-κB protiens are the intermediates in the gut dysbiosis and the inflammatory routes, respectively. Therapies focusing the manipulation of dysbiosis are found benefitting the gut microbiome as well as the inflammatory routes. The Ayurvedic herbal medicine are found to positively dominate these regions like hindering the fibrogenesis, attenuating the oxidative stress and supporting the regeneration of hepatocytes. Here, the cytotoxicity features of an herb- mineral conjugation *Arkeshwara rasa* (AR) has been explored in the primary liver cell line, the Huh7. The same cell lines are seen permissive for the hepatitis viruses and are adopted for simulation studies. (8) The AR includes *Dwigun Kajjali (Parada/* Mercury*: Gandhaka/*Sulphur*=1:2 ratio)* and *Tamra bhasma/*Incinerated copper, in equal proportions. These two main ingredients are later levigated with ***Calotropis procera*** leaf juice, ***Plumbago zeylanica*** root decoction and the three myrobalans (*triphala*) decoction, each 12 times. The previous experimental studies done in AR had checked the cell viability assays on MDA-MB-231 and SW480 cell lines which represented an IC_{50} at 25.28 µg/ml (9) and 40.4 µg/ml, (10) respectively. Similar studies to elicit the anti-cancer activity with AR have been done by Md Nafiujjaman et al on MIA-PaCa-2 and KB cells. (11) Hence to find out the response of

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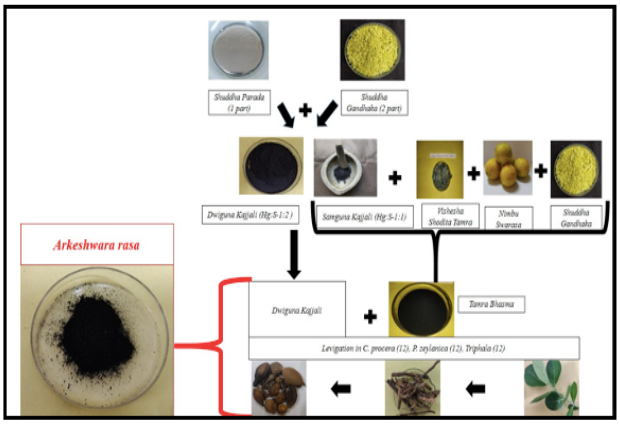
AR on Huh 7 cell lines, this work was propagated. The authors will also intricately explore the possibilities of embedded phytochemicals which have been analyzed in our previous study, (9) to combat HCC.

Material and methods

Processing

The analytical grade Mercury (CAS No:7438-87-6) (12), Sulphur (S094112) (13) and Copper turnings (CAS No:7440-50-8) (14) were subjected to *shodhana* procedures. The *shodith* Mercury and Sulphur were triturated for Kajjali preparation and S*hoditha Tamra* was processed towards *bhasma* preparation (15) and *Amritikaran* (16). This *Tamra bhasma* and *Dwigun Kajjali* were taken in equal proportion for the processing of AR in a modified version. These were levigated with *Calotropis procera* leaf juice, *Plumbago zeylanica* root decoction and *Triphala* decoction, each 12 times. (17) The herbal drugs were authenticated from NISCAIR (National Institute of Science Communication and Information Resources, Council of Scientific and Industrial Research, Ministry of Science and Technology, Government of India). The diagrammatical representation of AR has been done in the **Fig. 1**. The final AR was sent for sophisticated analyzes in different laboratories for characterization. This fine black powder was weighed and stored in air tight containers.

Fig.1: Diagrammatical representation of processing of *Arkeshwara rasa* (AR)



MTT ((3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) Assay of AR against Huh7 cell line

Huh 7 cells were purchased from N.C.C.S, Pune, India and the experimentation was carried at PBRI, Bhopal, India. The cells were treated with DMEM-high glucose media –(Cat no: AL149, Himedia) supplemented with 10 % FBS (#RM10432, Himedia) along with the 1% antibiotic-antimycotic solution in the atmosphere of 5% CO_2, 18-20% O_2 at 37^{0}C temperature in the CO_2 incubator. The 200µl cell suspension in 96-well plate was incubated by adding with the teat agent for 24 hrs. at 37°C in a 5% CO_2 atmosphere. The MTT dye (0.5mg/mL- #4060, Himedia) added plates were again incubated for 3 h at 37 °C in CO_2 incubator. These get used up by the viable cells transforming the yellow tetrazolium salt into purple blue formazan crystals. The formazan crystals after removing the medium were dissolved in dimethyl sulfoxide (DMSO-#PHR1309, Sigma) with incubation for 10 minutes and OD (Optical Density) at 540 nm measured with synergy H1 hybrid microplate reader. Accordingly, the dose–response graph was plotted between concentration of the drug and the inhibition rate. Cell viability percentage was calculated using the formula which forms the ratio between the Absorbance of Sample and Absorbance of Untreated cells × 100 (18).

Ethidium Bromide/Acridine Orange (EtBr/AO) assay of AR with Huh7 cell line

The EtBr/AO Assay is the colorimetric assay to define the apoptosis based on the reaction to Ethidium bromide (50µg/mL solution, Thermo Fischer, USA) and the Acridine orange (20µg/mL solution, Thermo Fischer, USA) on the Huh 7 cell line procured from the NCCS, Pune, India. The cells were cultured in the 12 well plates (Biolite-Thermo) in the concentration of the 2 ×105 cells/ 2 ml and used the cover slips with Poly L-ornithine solution (0.01% -#A-004-M, Sigma), followed by incubation for 24 hours. The cell culture medium used was DMEM- High Glucose media-(Cat No: 2120785, Gibco). The cells were incubated for another 24 hours with test and standard drug (Doxorubicin-#D1515, Sigma) and followed with D-PBS (#TL006, Himedia) wash. The well plates were again washed with D-PBS after removing the cover slips and stained with 200µl solution. These were again washed, mounted on the fluorescence microscope and emission checked with filter cube of Excitation 560/40 nm, Emission with 645/75 nm for EtBr. The Excitation of 470/40 nm and Emission of 525/50 nm for Acridine orange were used for evaluation results (19).

Results

The colorimetric MTT assay provided the half minimal inhibition of the cells at 37.14 µg/ml drug concentration. A decreasing linear pattern of cell viability were also observed with the results. The positive control cells attained the same in a concentration of 5ug/ml of standard Drug Doxorubicin. The formazan crystals and the crenate non-viable cells were identified in close observation. The AO assay in comparison with the control with the IC_{50} drug concentration exhibited the apoptosis features. The cytotoxicity of Doxorubicin standard was not achieved, although the early and late apoptotic features were clearly visible on the sample images. The images of the MTT Assay at different concentrations are expressed in the **Fig no: 2**. The MTT assay values and the respective cell viability are noted in the graphical pattern in **Fig no: 3**. The AO estimated cell line images are represented in the **Fig no: 4**. The **Table no: 1 & 2** represents the validated previous studies on the anti-cancer aspect in various cell lines with the ingredients of AR. This also includes the phytochemicals evaluated as per our previous LC/MS results on different aspects of liver pathogenesis.

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Figure 2: Representing the different concentration wise MTT assay with AR on Huh 7 cell line

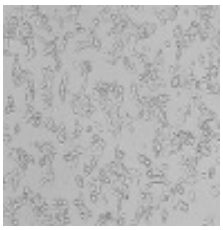
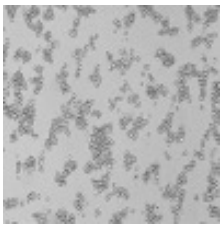
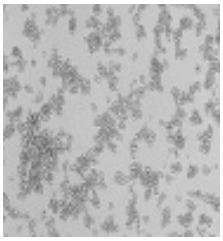
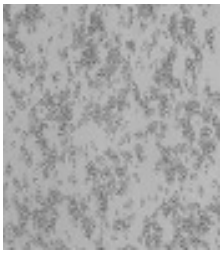
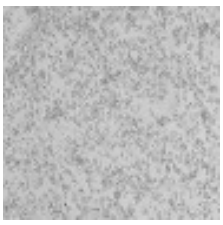
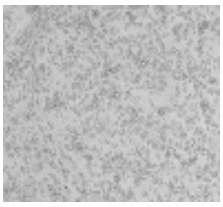
Untreated	STD	100µg/ml	50µg/ml	12µg/ml	6µg/ml
					

Figure 3: Different concentration mediated % of Cell viability of AR treated with Huh7 cells

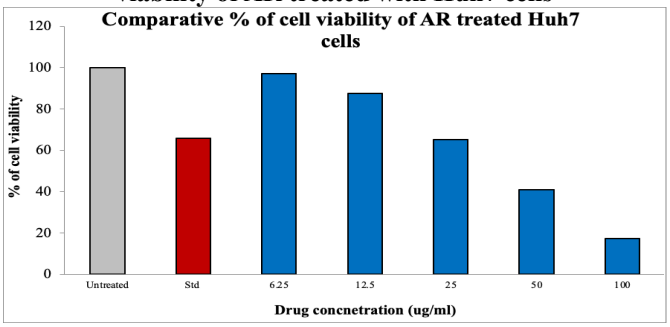


Fig no: 4 Acridine Orange assay with AR representing the VC- volatile cells, EA- Early apoptosis, LA- Late apoptosis in comparison with Untreated and Standard.

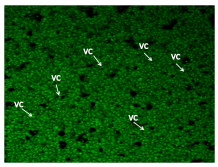
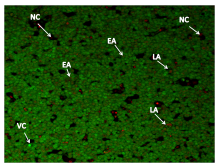
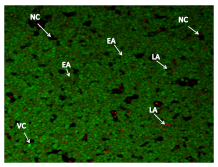
Untreated	STD	Huh 7 cell line with AR
		

Table 2: Hepatic cancer experimental studies with individual *Arkeshwara rasa* (AR) inclusions

AR inclusions	Experimental models	Experimental study details	Observed Results
1. *C. procera* ethanolic leaf extract (20)	Albino rats	Hepatitis B and Acetaminophen induced experiment for hepato-protective activity.	The increase levels of ALT, ALP and AST were brought to normal levels in the treated groups.
2. *Plumbago zeylanica* hexane fraction (21)	EAC cell –Swiss albino mice model	Flow cytometry and cyto toxicity assays	79.01% inhibition of EAC cells at 300mg/Kg. G_0/G1 phase arrest and the BCl_2 downstreaming.
3. *Plumbagin*(22)	HCC, Huh7, HepG2 cell lines	Genotoxicity, oxidative stress, Cell cycle analysis	G2/M phase arrest, γ-H2AX pertaining to DNA damage was increased, suppression p53 and
4. *Plumbago zeylanica* ethanolic root extract (23)	HeLa cancer cell line	MTT assay, wound healing activity, Cell cycle analysis	IC50-10.49 µg/ml, S phase cell cycle arrest
5. *Triphala* with diet (24)	Swiss albino mice	Benzo(a)pyrene induced forestomach papillomagenesis in	Reduced tumour incidences
6. *Triphala* extract (25)	HCC, HepG2, Hep3B	Cytotoxicity, Annexin V, Western blotting	Down regulated anti-apoptotic proteins and increased poly-ADP ribose polymerase cleavage

Table 3: Phytochemicals of AR in different hepatic carcinoma

AR – LC/MS - phytochemicals	Experimental models	Experimental study details	Observed results
1. Quercetin (26)	HCC cell line LM3 and nude mice tumor model	CCK8 assay, Cell cycle, colony formation, Transwell invasion assays	PCNA reduction ad Bax expression. S and G2/M phase
2. Hesperidine (27)	HepG2 cell line	Cell viability, Western blotting, electrophoresis	Absence of caspase activation and PARP cleavage, DNA fragmentation, paraptosis like cell death, activation of ERK1/2 pathway
3. Rutin(28)	HepG2 cells	Cell viability, flow cyto metry, Wound healing assay, Matrigel invasion assay	*IC*50 value of 52.7 µmol L–1, decrease CYP enzyme
4. Kaempferol (29)	Huh-7, Huh-1, HepG2, HepG2.2.15, SK-Hep-1, PLC/PRF/5, HLE, HLF, and Hep3B	Cell viability, cell cycle, mitochondrial apoptosis, wound healing , Western blotting, comparison with Doxorubicin(DOX)	Synergistic with DOX, metalloprotienases and AkT/mTOR down regulation

Discussion

AR was found to be in the tetrahedrite morphology with Copper, Sulphur, Antimony in the XRD peaks and EDAX levels coinciding with Fe, Mg, etc. (9) The FTIR data support the presence of O-H, N-H, S=O stretch vibrations and the finger print region were dominating with phenol (-OH) groups in the graph. (10) So the potential anticancer effects depend on the aggregate synergism of all the components of the AR. The derangements in copper metabolism can support the genesis of HCC and the role of copper cannot be avoided in the normal physiology being a trace element. The liver is also the storage hub of metabolized copper elements. Here, AR includes the *Tamra bhasma*/incinerated copper particles with herbal levigations which exhibits hepato-protective activity. A similar compound known as *Arogyavardhini vati* which also contains *Tamra bhasma* was found to be protective against CCl_4 induced liver toxicity. (30) *Roudra rasa* , a preparation experimented against different cell lines possess anti-cancer activity. (31) Similarly, AR was also found to be reversing the induced changes like vacuolations in the acute and sub-acute toxicity studies on Charles foster female rats. This toxicity study also pointed out the peak of hemoglobin (Hb) concentrations in treated groups than the control and the increase in concentration with escalated dose relates the proper copper metabolism for the maintenance of Hb. The similar rise of Packed Cell Volume (PCV) also coincides with Hb rise pointing out the fact that there was no hemolysis to substantiate the peak Hb level.

The ethanolic leaf extract of ***Calotropis procera*** when tested on HCT 116 and MCF-7 was found to cause apoptosis with cell cycle arrest at G2M phase and Sub-G1 phase respectively. There was loss of cell membrane asymmetry in MCF 7 (breast cancer) and HCT-116 (Colon cancer) cell lines when analyzed with Annexin V-FITC/PI. The same study also points out the dysregulation of cell death markers like Survivin, mTOR, p-mTOR, AKT, p-AKT and the inhibition of the cell cycle regulating proteins like CDK1, CDK4, CDK6 and cyclin B1. The alteration of mTOR and AKT levels suggest the disturbances of cellular proliferations (32) and the Cyclin Dependent Kinase inhibition are related to G1 phase arrest particularly in HCC cells. (33) In the PC-3 cells (prostate cancer), leaf extract was empowering the autophagy procedure which caused the upregulation of *p62, LC3B and Beclin-1* transcript proteins, which support the pre-apoptotic functions. (34) Whereas, the fractionated part of plant was found to exhibit anti-angiogenesis effect on HepG2 (Liver carcinoma) cell line. (35)

The ***Plumbago zeylanica***, root decoction was found to provide hepato-protective effect in paracetamol induced liver failure. (36) The plumbagin, the natural naphthoquinone content in the root extract can generate ROS species. This can produce double strand breaks in DNA triple negative breast cancer. In HepG2 cells, the p53 activation led to anti-proliferative effect. (23) The hepatocyte burden of lipids can be scraped out by Plumbago zeylanica extract. In the KEGG analysis network, the feed back of the plumbagin was found to influence the HCC via cell survival, proliferation, apoptosis, and angiogenesis hindrances. The cross talks between the cells were more focused on the *PI3K-Akt, mTOR* and *MAPK* signaling pathways. (37) This was similar to the Calotropis procera constituents as discussed above.

The inclusions of ***Terminalia chebula*** (38), ***Terminalia bellerica*** (39), ***Emblica officinalis*** (39) exerts hepato-protective activity in various methodologies. The chebulanic acid was found to preserve the hepatic enzymes against the CCl_4 toxicity. (40) The tannins in ***Terminalia bellerica*** can influence the immunomodulatory function with support to CD8+ T cell activities. (41) The methanolic extract of the fruit of ***Emblica officinalis*** was found to resist the carcinogenic activity against DEN (Diethyl nitrosoamine) and AAF (Acetylaminoflourine) induced tumour model in rats. (42) The combined effect was alone found to influence the caspases activation and downstreams the anti-apoptotic genes on pancreatic cell lines. (43)

The asymptomatic progression and advanced stage diagnosis of HCC might be the setback of the rhythmical orchestration of cross talks between different signal pathways. The expression of Galectin 3, the galactoside binding glycoprotein,(44) is found to be directed towards the immunosuppression by binding on to the tumor cells. This supports the maintenance of the TME (Tumor Micro Environment) by propagating the glycolysis and mitochondrial functions. Kaempferol (45) and Quercetin(46) was found to decrease this galactin 3 activating the ligand shield as to escape the receptors of natural killer cells. The same in AR might be presenting the tumor cells in surveillance of apoptosis mechanism as seen in our cytotoxicity assay. The progressive point of JAK/STAT 3 pathway is related to Gut dysbiosis in HBV (Hepatitis B Virus) and develop the HCC later. The hesperidine, neohesperidine, Rutin, Kaempferol, Resveratrol and Luteolin were found to produce the anti-proliferative action via this pathway(47) Moreover, the compounds isolated from the leaf extract of ***Calotropis procera*** like Ferulic acid are also present in the AR chromatographic expression because there was 12 times wet levigation with expressed leaf juice of the plant. (32) This Ferulic acid has been found to reverse the practically impossible fibrotic hepatic changes and the related oxidative stress in a mouse model. The ECM (Extracellular Matrix) rearrangement and deactivation of the HSC (Hepatic stellar cellular) functions are both connected towards the hepatocyte fibrosis. The fibrosis also happens due to the abundant ECM (Extracellular Matrix) deposition and the consequent scaring from diverse conditions including the viral infection to alcohol abuse, steatosis, oxidative stress, etc. Shortly, these fibrotic changes are repeated expression of inflammation and free radical internal milieu. (48)The reversible damage of fibrotic hepatocytes are seen vested along with the downstream transcription of NfkB proteins influenced with Ferulic acid. The further examination with Apoptosis Assay of AR might be producing the similar results due to the above mentioned phyto-constituents.

Immunotherapy has been found beneficial in improving the survival rate from 18% to 43% in recent

studies. The activations of macrophages and the production of NO from them has been seen with *Calotropis* water soluble latex extract. (49) Plumbagin was expressing the immunomodulatory functions by inhibiting the T-cell proliferation with cell cycle blockage as well as supported the viability of the lymphocytes. The NFkB activation was also inhibited by Plumbagin in the same study. (50) Whereas, Triphala manipulates the expression of different cytokines like IL4, IL2, IFN-γ by up and down regulations according to the oxidative stress.(51) The phenolic compounds in AR might also be able to protract the anti-microbial action due to the phenolic proportion with –OH(hydroxyl) groups ensuring the affinity towards the microbes. (52)

α-amylase, the hydrolyser of glycogen is secreted by salivary glands, pancreas and liver which floods out the glucose source to highly proliferated cells. Therefore, the inhibition of the same is well appreciated in both diabetic and Warburg effect prevailing in the cancer cells. Such an inhibition tendency is seen among ethanolic and aqueous extract of *Calotropis procera* leaf. (53) A conjugated presence of copper nano particles with *Plumbago zeylanica* processing were also revealing the same inhibitory activity. (54) As the obesity induced fatty liver changes also express a peak in alpha amylase activity, the same inhibitory potentials were elicited with *Triphala* and its constituents. (55) This effect might be also exhausting the hepatic cancer cells when α-glucosidase is inhibited from progressing against pathogenesis.

The advantage of precision medicine has been found beneficial in many recent works. They carry the essence of targeted delivery. Antimony encapsulated nano-spheres can form such carriers and so the presence of the same in AR might be precisely supporting the targeted delivery of herb- mineral conjugations. Also, the organo-sulphur compounds like GSH (Glutathione), ALA (Alpha Lipoic Acid), Allicin, etc were seen to reduce the damage associated with CCl_4 induced hepatic fibrosis and AR's EDAX point out the presence of Sulphur peaks in the compound.(56)

Ayurveda describes *yakrit*/liver as an organ and one of the *mula sthan* of *raktavaha srotas*. All the treatment aspects of *yakrit* are same as *pleeha*/spleen diseases. These factors also imply the disease management to be focused on the core immune related factors as CD4 cells, T cells, NK cells, etc. The etiological records point out the cause of gut dysbiosis as the consumption of too much salty, sourly, spicy foods which are known to cause *vidahi* (substances that produce burning sensations) and *abhishyanda* (*srothas* obstructing dravya) effect. The described formulations for *yakrit-pleeha vikara* like *Arka lavana, Chitrak grita*, etc constitute the AR ingredients.

Conclusion

AR in the Huh 7 cell line exhibited cytotoxicity and apoptotic features which need to be further examined with both in-vitro and in-vivo experiments. The previous studies and the LC/MS derived metabolites point out the specificity on downregulation of mTOR, NFkB protiens, levelling down of Galactosin, inhibition of amylase and glucosidase, supporting the CD8+ T cells, initiating the autophagy of macrophages, etc which all need to be further experimented. The tendency to infiltrate the neutrophils and maintain the intact copper metabolism has seen in the AR toxicity studies. These all suggest the presence of an ideal potency to combat the HCC related pathogenesis which needs to be confirmed with gene amplification, reverse transcription, cell cycle analysis, Western Blotting, etc.

Abbreviations

- HCC- Hepatocellular Carcinoma
- AR- *Arkeshwara Rasa*
- MTT Assay- (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) Assay
- EtBr/AO -Ethidium Bromide/Acridine orange Assay
- IC_{50}- Half maximal Inhibition Constant
- EAC cell- Ehrlich Ascites Carcinoma cell
- LC/MS- Liquid Chromatography Mass Spectrometry
- ECM – Extracellular Matrix
- NO- Nitric oxide

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Unlocking Antioxidant Potential in *Symplocos racemosa* Roxb. (*Lodhra*): A Phytochemical Exploration via High-Resolution Mass Spectrometry

Research Article

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Abstract

Symplocos racemosa Roxb., typically referred to as *Lodhra*, is a highly esteemed medicinal plant in traditional Indian medicine. Belonging to the Symplocaceae family, it is recognized for its wide-ranging therapeutic benefits, particularly in supporting dermatological health and fostering skin rejuvenation. This study delves into the phytochemical composition of S. racemosa by employing high-resolution mass spectrometry (HRMS) as a key analytical tool to assess its antioxidant potential. Antioxidants are bioactive compounds that mitigate oxidative stress by neutralizing free radicals that can cause cellular damage and contribute to ageing and disease progression. Oxidative stress is a major contributor to various chronic diseases, and antioxidants play a vital role in mitigating the damaging effects of reactive oxygen species (ROS). Identifying and characterizing potent antioxidant molecules within natural sources like *Lodhra* could open pathways to various therapeutic approaches. Renowned in traditional medicine for its multifaceted therapeutic properties, *Lodhra* was therefore systematically analyzed to elucidate its diverse array of bioactive compounds. HRMS facilitated the identification and characterisation of these metabolites, revealing a complex and rich biochemical profile. Through HRMS, seven metabolites namely Diselane, Catechin, Fraxetin, Eriodictyol, Coumarin, Panaxynol, and Ursolic acid have been identified to exhibit significant antioxidant activity. In vitro tests showed strong free radical scavenging activity, clearly linking certain phytochemicals to their antioxidant effectiveness. Previous in vitro tests demonstrated strong free radical scavenging activity of the isolated components, clearly justifying their antioxidant effects. The findings of this study highlight the significance of *Symplocos racemosa* as a potent source of natural antioxidants. The characterization of its bioactive compounds paves the way for further pharmacological research and possible development of antioxidant-based therapeutics from Ayurvedic resources.

Keywords: *Symplocos racemosa* Roxb., *Lodhra*, High-Resolution Mass Spectrometry, Oxidative stress, Antioxidant activity.

Introduction

Symplocos racemosa, commonly known as *Lodhra*, is a distinguished medicinal plant in traditional Indian medicine, particularly within the Ayurvedic system. It belongs to the Symplocaceae family, which comprises only the single genus Symplocos. This genus is prevalent in the tropical and subtropical regions of Asia, America, Australia, and Malaysia (1). *Lodhra* has been utilized for centuries for its numerous therapeutic properties, especially for its beneficial effects on skin health and overall vitality. The plant is characterized by its distinctive bark, which is often the primary source of its medicinal extracts. In Ayurveda, the astringent bark of S. racemosa is valued as a potent medicinal remedy for treating diverse ailments, including diarrhea, dysentery, ocular disorders, gum bleeding, menorrhagia, and other uterine issues (1). Rich in bioactive compounds, *S. racemosa* contains a variety of phytochemicals, which contribute to its notable antioxidant properties. These compounds play a crucial role in neutralizing free radicals and mitigating oxidative stress, a key factor in the development of various chronic diseases and skin ageing.

Oxidative stress is defined as a condition characterized by the overproduction of reactive oxygen species (ROS), resulting in damage to proteins, lipids, cell membranes, and, importantly, genetic material. Studies have established that oxidative stress is a critical contributor to numerous pathological conditions, especially in the context of neurological disorders, cancer and complication associated with diabetes (2). Furthermore, the ageing process can be linked to the harmful effects of free radicals, which contribute to DNA damage, lipid peroxidation, and protein oxidation (3). The cells generally respond to oxidative stress by activating compensatory mechanisms known as the antioxidant defense system. Among these, the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway plays a vital role in maintaining cellular homeostasis by promoting redox balance (4). Antioxidants can be either

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exogenous (natural or synthetic) or endogenous compounds that function to reduce or alleviate oxidative stress. (5). They prevent oxidation by functioning as reductants, chelating agents, and free radical scavengers, with a significant capacity to donate hydrogen. (6). A study revealed that the ethanolic extract of S. racemosa bark exhibit robust 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging activity, along with moderate scavenging effects against 1,1-diphenyl-2-picrylhydrazyl (DPPH), nitric oxide, and hydroxyl radicals, in comparison to the standard antioxidant ascorbic acid (7). Consequently, an effort has been undertaken to isolate the bioactive metabolites responsible for the antioxidant activity in *Symplocos racemosa* Roxb. (*Lodhra*) utilizing high-resolution mass spectrometry (HRMS).

Materials and Methods

Collection of *Lodhra*

The raw material of *Lodhra* for the analysis via High-Resolution Mass Spectrometry (HRMS) was procured from the local herbal drug market in Varanasi. Subsequently, it was authenticated in the Department of Botany, assigned Voucher Specimen No. Symploca. 2024/02.

Symplocos racemosa Roxb. (stem bark), methanol, distilled water, and Eppendorf tubes were utilized. The analysis was carried out with a High-Resolution Accurate Mass Spectrometry system, specifically the Orbitrap Eclipse Tribrid Mass Spectrometer developed by Thermo Fisher Scientific. For the characterization of small molecules, the Dionex UltiMate 3000 RSU HPLC system was employed for phytochemical evaluation (8).

Method employed for HRMS analysis

The sample preparation for HR-MS analysis began with the addition of 100 mg of the individual optimized sample of *Symplocos racemosa* Roxb. to 1.5 ml of solvent (Methanol:Water; 80:20), which was then homogenized using an Eppendorf Thermo-mixer at 750 rpm for 30 minutes at 25°C. Following this, the sample was centrifuged at 3500 rpm for 10 minutes at 25 °C. The supernatant was filtered through a 0.22 µ PTFE syringe filter, and 4 µl of the filtrate was used as the injection volume on a C18 RP-HPLC column (Hypersil GOLD™: Particle size 1.9 µ, dimensions 2.1 mm × 100 mm).

Reversed-phase chromatographic separation commenced with a highly aqueous phase (+0.1% formic acid) and transitioned to a predominantly organic phase (MeOH +0.1% formic acid), typically ranging from 100% aqueous to 100% organic. The gradient parameters for the liquid chromatography were as follows: 0-6 minutes at 5% methanol, 6-10 minutes at 30% methanol, 10-20 minutes at 50% methanol, 20-25 minutes at 90% methanol, and returning to 5% from 27 to 30 minutes. The flow rate was maintained at 300 l/min, and the column oven temperature was set at 40°C.

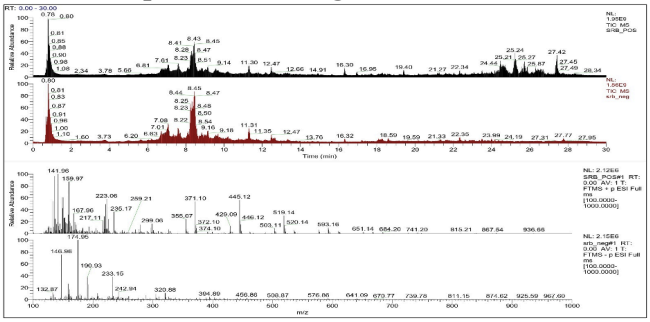
The optimized *Lodhra* sample underwent metabolomics analysis using a Thermo Fisher Scientific High-Resolution Accurate Mass Spectrometry System, specifically the Orbitrap Eclipse Tribrid Mass Spectrometer, in conjunction with Nano Liquid Chromatography and Ultra High-Pressure Liquid Chromatography (Dionex Ultimate 3000 RSLC). A Heated Electro Spray Ionization (HESI) source was employed to introduce the sample into the mass spectrometer following chromatographic separation. The Orbitrap analyzer operated at a resolution of 60,000 for both positive and negative polarities, covering a mass range (m/z) of 100-1000, with a 35% RF lens, a 25% Normalized Automatic Gain Control (AGC) target, and an intensity threshold set at 2.0e5 for the MS-OT (Master scan). For the ddMS2 OT HCD analysis, parameters included quadrupole isolation mode with a 1.5 m/z isolation window, HCD activation types with collision energies of 30%, 45%, and 60%, an Orbitrap resolution of 15,000, and a 20% Normalized AGC target (9).

The raw data from the mass analyser was processed using the default settings of "Compound Discoverer 3.3.2.31," in conjunction with online databases. The selected workflow, termed Natural Product Unknown ID, involved searches in both online and local databases. This untargeted food research workflow, which does not include statistical analysis, is designed to detect and identify unknown compounds. It aligns retention times, identifies these compounds, and groups them across all samples. The workflow also predicts elemental compositions for all compounds and reduces chemical background interference by utilizing blank samples. Compound identification is performed using mzCloud (with ddMS2 and/or DIA), ChemSpider (based on exact mass or formula), and local database searches against mass lists (exact mass, with or without retention time). Additionally, it conducts spectral similarity searches against mzCloud for compounds with ddMS2 and applies spectral distance scoring to matches identified in ChemSpider and the mass lists (10).

Results

A total ion chromatogram (TIC) is a graphical representation of the total ion count detected over time during a mass spectrometry analysis, showing all the ions generated from a sample. The total ion chromatogram of the compounds found in *Symplocos racemosa* Roxb. is shown in Figure 1.

Figure 1: Illustrates the total ion chromatogram of the compounds found in *Symplocos racemosa* Roxb. in positive and negative ion modes



A standard ion chromatogram (SIC) tracks the intensity of a specific ion or set of ions over time during a mass spectrometry analysis, providing detailed information about a particular compound in the sample.

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The metabolites identified in *S. racemosa* were quantified and characterized based on their retention times and peak intensities, as illustrated in Figure 2-8.

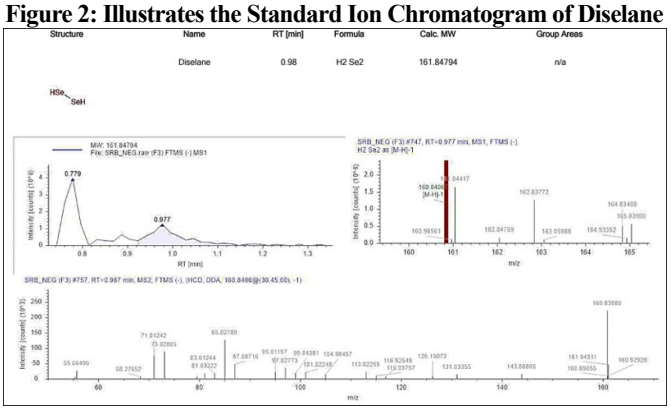
Antioxidant Activity of Bioactive Metabolites isolated from Symplocos racemosa

High-Resolution Mass Spectrometry (HRMS) identified 1,553 phytochemical constituents in *Symplocos racemosa*. Among these, the following compounds have been noted for their antioxidant properties: 1) Diselane, 2) Catechin, 3) Fraxetin, 4) Eriodictyol, 5) Coumarin, 6) Panaxynol, and 7) Ursolic acid, as supported by the references below.

1) Diselane

Studies revealed that the novel diselenides exhibited mimetic activity akin to glutathione peroxidase (GPx) and enhanced thioredoxin reductase (TrxR) activity in vitro. The GPx enzyme is essential for neutralizing the harmful or signaling effects of hydrogen and lipid peroxides. The observed GPx mimetic effect, coupled with the increased TrxR activity, is likely attributable to the generation of selenol groups, such as p-methyl-selenol and o-methoxy-selenol. The presence of diselanes /diselenides is expected to confer a more pronounced antioxidant effect, due to formation of these selenol groups, along with their GPx mimetic and elevated TrxR activities (11). Thioredoxin reductase (TrxR) is an enzyme that contains selenocysteine and plays a critical role in protecting cells from oxidative stress (12). Another study demonstrated that in mammals, GPx collaborates with superoxide dismutase and catalase to establish an enzymatic antioxidant system that diminishes reactive oxygen species (ROS) and curtails their toxicity. GPx predominantly utilizes glutathione (GSH) as a reducing agent to catalyze the conversion of hydrogen peroxide and organic peroxides into water or corresponding alcohols, respectively, thereby safeguarding cells from oxidative damage (13). The standard ion chromatogram is depicted in Figure 2.

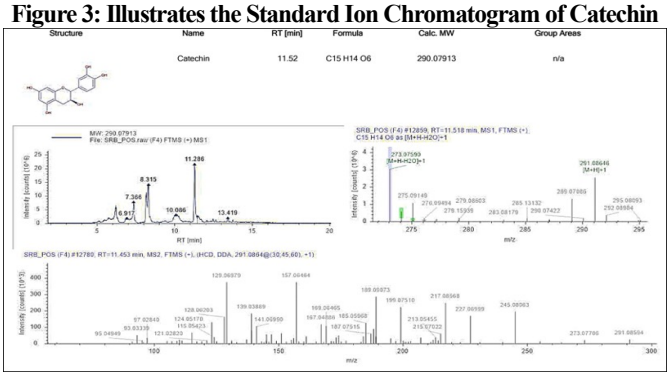
Figure 2: Illustrates the Standard Ion Chromatogram of Diselane



2) Catechins

Catechins are phytochemical compounds classified as secondary metabolites within the flavonoid family. Catechins protect keratinocytes primarily by mitigating damage caused by UVB radiation and reactive oxygen species (ROS) (14). As per Research articles, Catechin generates and eliminates free radicals via several pivotal direct and indirect antioxidant mechanisms. The direct mechanism entails the scavenging of reactive oxygen species (ROS), while the indirect mechanism enhances the activity of antioxidant enzymes and inhibits the pro-enzyme involved in oxidative stress. The phenolic hydroxyl groups in catechin play a critical role in ROS scavenging, indicating that an increased number of hydroxyl groups would enhance its antioxidant efficacy (15). The standard ion chromatogram is depicted in Figure 3.

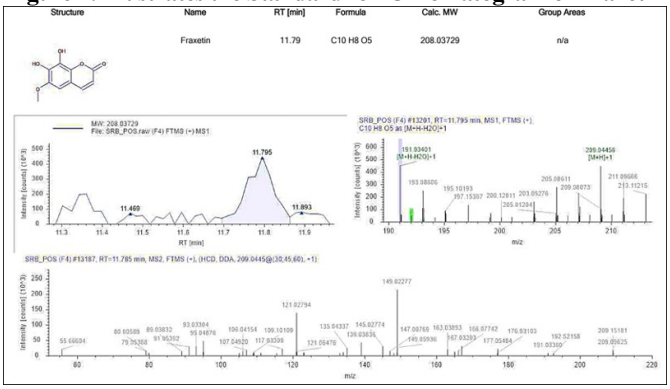
Figure 3: Illustrates the Standard Ion Chromatogram of Catechin



3) Fraxetin

Previous research suggests that the overall antioxidant activity mechanisms of fraxetin in aqueous media at physiological pH and lipid environments involve three primary reaction pathways: single electron transfer (SET), hydrogen transfer (HT), and radical adduct formation (RAF). In aqueous conditions, fraxetin interacts with peroxyl radicals through mechanisms based on its acid-base form. Specifically, neutral fraxetin predominantly engages via the HT mechanism, while its anionic form reacts primarily through the SET mechanism. Furthermore, our findings indicate that fraxetin exhibits remarkable scavenging activity against various free radicals under similar conditions, with the anion (HFR−) being the predominant contributor to its overall reactivity toward the examined peroxyl radicals. Consequently, the phenoxide anion emerges as the crucial species in the peroxyl radical scavenging capacity of fraxetin. Therefore, we can confidently assert that fraxetin is an exceptional and versatile antioxidant in aqueous media at physiological pH (16). The standard ion chromatogram is depicted in Figure 4.

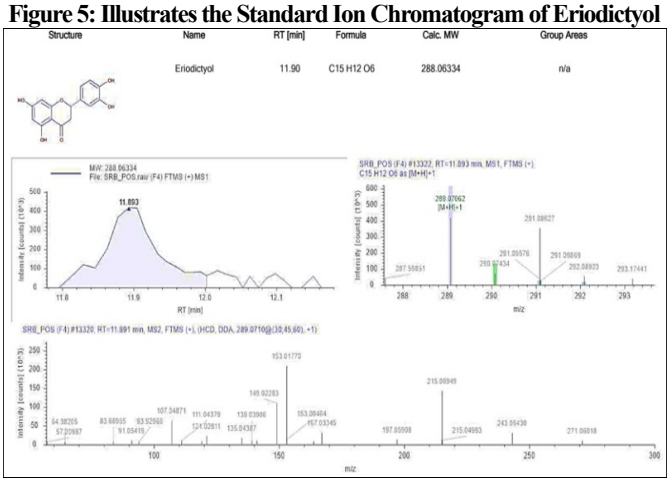
Figure 4: Illustrates the Standard Ion Chromatogram of Fraxetin



4) Eriodictyol

Studies demonstrated that Eriodictyol exerts its antioxidant effects on dermal fibroblasts in response to H_2O_2 through several mechanisms: (i) direct neutralization of reactive oxygen species; (ii) enhancement of H_2O_2-detoxifying enzyme activities, notably catalase (CAT) and glutathione peroxidase (GPx). CAT primarily detoxifies high concentrations of H_2O_2, while GPx is pivotal for eliminating low levels of H_2O_2; and (iii) induction of catalase and glutathione peroxidase 1 expression via activation of the Nrf2 signaling pathway. The nuclear factor erythroid 2-related factor 2 (Nrf2) pathway serves as a master regulator of redox homeostasis and the antioxidative response. Activation of this pathway promotes the upregulation of various cellular antioxidant defenses, including CAT and GPx1, thereby enhancing cellular resistance against oxidative stress. These findings underscore the potential utility of eriodictyol as an ingredient in skincare formulations for cosmeceutical and pharmaceutical applications (17). The standard ion chromatogram is depicted in Figure 5.

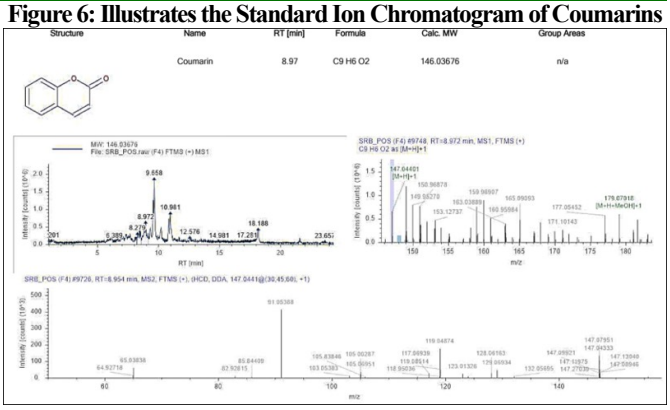
Figure 5: Illustrates the Standard Ion Chromatogram of Eriodictyol



5) Coumarins

Coumarins are recognized for their capacity to mitigate the generation of reactive oxygen species (ROS) and enhance their scavenging, thereby exhibiting significant antioxidant properties that protect against tissue damage. The underlying mechanisms of this antioxidant activity are multifaceted and likely attributable to their structural resemblance to flavonoids. Notably, the position and nature of substituents on the aromatic ring of coumarin molecules play a critical role in modulating their antioxidant efficacy. Specifically, the number of hydroxyl groups on the ring structure of coumarins is associated with their ability to suppress ROS. This relationship highlights the pivotal role of free radicals and ROS in the pathogenesis of complex diseases, indicating that coumarins may serve as valuable agents in alleviating oxidative stress (18). The standard ion chromatogram is depicted in Figure 6.

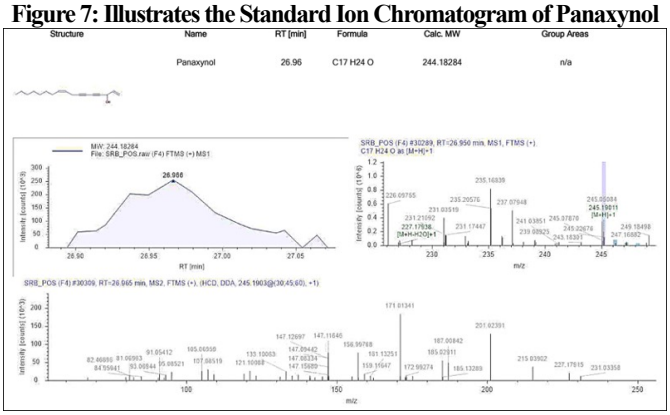
Figure 6: Illustrates the Standard Ion Chromatogram of Coumarins



6) Panaxynol

Research suggested that Panaxynol derived from plants exhibited considerable antioxidant activity by counteracting oxidative stress through the activation of the Kelch-like ECH-associated protein 1 (Keap1) and nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway, reducing lipid peroxidation (LPO) and its associated biomarkers, as well as the promotion of nitric oxide synthase 1 (NO1) and heme oxygenase (HO) activation (19). Panaxynol is reported to inhibit elevated levels of reactive oxygen species (ROS), thereby alleviating oxidative stress due to its inherent antioxidant properties (20). The standard ion chromatogram is depicted in Figure 7.

Figure 7: Illustrates the Standard Ion Chromatogram of Panaxynol



7) Ursolic acid

Ursolic acid has been found to significantly enhance levels of superoxide dismutase (SOD) and glutathione (GSH), while substantially decreasing malondialdehyde (MDA) levels in animal tissues. In vitro studies further indicate that ursolic acid notably increases GSH and reduces MDA levels. Therefore, it is reasonable to consider ursolic acid as a non-enzymatic antioxidant that reinforces both cellular and organismal antioxidant defenses, effectively mitigating oxidative stress. Regarding its antioxidant mechanisms, ursolic acid may function by scavenging free radicals. Additionally, ursolic acid has been shown to combat oxidative stress through the liver kinase B1 (LKB1)-activated protein kinase (AMPK) signaling pathway (21). The standard ion chromatogram is depicted in Figure 8.

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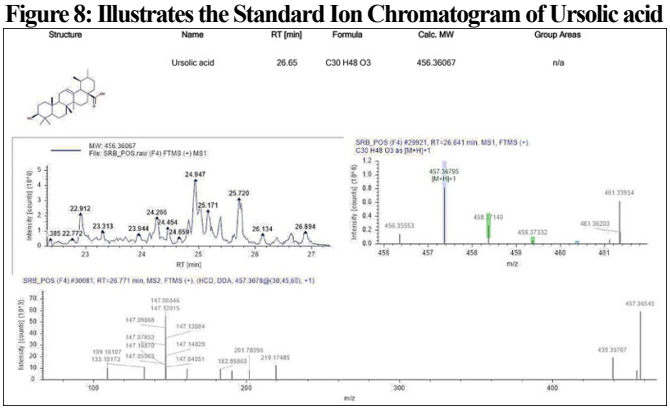
Figure 8: Illustrates the Standard Ion Chromatogram of Ursolic acid



Discussion

Antioxidant activity refers to the capacity of molecules to shield biomolecules from oxidative damage by neutralizing free radicals. It plays a crucial role in maintaining the body's redox balance and minimizing damage linked to various diseases. In Ayurveda, antioxidant properties align with balancing doshas and preventing *ama* (toxins). Several herbs act as *rasayanas*, rejuvenating and protecting tissues from oxidative damage, thereby enhancing vitality and longevity. *Symplocos racemosa* (*Lodhra*) demonstrates strong antioxidant properties, effectively neutralizing free radicals and safeguarding tissues from oxidative stress. It helps to reduce inflammation, supports skin health, and promotes cellular wellness. Traditionally used in Ayurveda, *Lodhra* aids in restoring balance and enhancing overall healing. Therefore, *Symplocos racemosa* was analyzed using High-Resolution Mass Spectrometry (HRMS) to identify the metabolites responsible for its antioxidant properties and understand their mechanisms. The analysis employed the Orbitrap Eclipse Tribrid Mass Spectrometer from Thermo Fisher Scientific for accurate and detailed results. Notably seven metabolites namely Diselane, Catechin, Fraxetin, Eriodictyol, Coumarin, Panaxynol, and Ursolic acid were identified to exhibit significant antioxidant activity.

Diselenides exhibit glutathione peroxidase (GPx)-like activity and enhance thioredoxin reductase (TrxR) activity, likely due to the generation of selenol groups. These properties are expected to provide a stronger antioxidant effect through GPx mimetic action and elevated TrxR activity (11). Catechin combats oxidative stress through both direct and indirect antioxidant mechanisms. Directly, it scavenges reactive oxygen species (ROS), while indirectly, it boosts antioxidant enzyme activity and inhibits pro-enzymes that contribute to oxidative stress (15). The antioxidant activity of Fraxetin in aqueous media at physiological pH and lipid environments follows three main pathways: single electron transfer (SET), hydrogen transfer (HT), and radical adduct formation (RAF). Its potent free radical scavenging ability is primarily attributed to the phenoxide anion, which plays a key role in neutralizing peroxyl radicals (16). Eriodictyol protects dermal fibroblasts from H_2O_2-induced oxidative stress by directly neutralizing reactive oxygen species (ROS) and boosting the activity of detoxifying enzymes, particularly catalase (CAT) and glutathione peroxidase (GPx) (17). Coumarins exhibit strong antioxidant properties by reducing the generation of reactive oxygen species (ROS) and enhancing their scavenging, thereby protecting tissues from damage. Their structural similarity to flavonoids and the presence of hydroxyl groups on the ring are key factors in their ROS-suppressing ability (18). Panaxynol demonstrates significant antioxidant activity by activating the Keap1-Nrf2 signaling pathway, reducing lipid peroxidation (LPO) and related biomarkers, while promoting nitric oxide synthase 1 (NO1) and heme oxygenase (HO) activation. This helps counter oxidative stress effectively (19). Ursolic acid exerts antioxidant effects by scavenging free radicals and combating oxidative stress through the activation of the liver kinase B1 (LKB1)-AMPK signaling pathway. These mechanisms contribute to its overall protective role against oxidative damage (21). A summarized overview about the details of the isolated components is shown in Table 1.

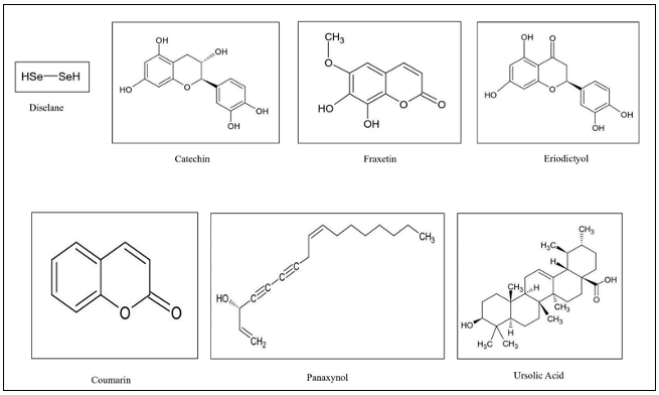
Table 1: Depicts the details of the Metabolites isolated by HRMS. It shows the Chemical formula, Calculated Molecular Weight (MW), Retention Time (RT) values, Delta Mass and the Peak area under Negative (NEG) / Positive (POS) ion mode of the bioactive metabolites

Bioactive Metabolite	Formula	Calc. MW	Retention Time (min)	Delta Mass (ppm)	Area NEG	Area POS
Diselane	H_2Se_2	161.84794	0.977	-4.63	5743307.77	-
Catechin	$C_{15}H_{14}O_6$	290.07913	11.524	0.33	-	39541920.22
Fraxetin	$C_{10}H_8O_5$	208.03729	11.789	0.56	-	2049729.26
Eriodictyol	$C_{15}H_{12}O_6$	288.06334	11.896	-0.16	-	2217013.03
Coumarin	$C_9H_6O_2$	146.03676	8.967	-0.16	-	10226194.93
Panaxynol	$C_{17}H_{24}O$	244.18284	26.958	0.51	-	1228056.59
Ursolic acid	$C_{30}H_{48}O_3$	456.36067	26.646	0.72	-	6512604.28

The molecular structure of antioxidants plays a key role in their effectiveness. Functional groups like hydroxyl and amine groups help scavenge free radicals, while conjugated systems and electron delocalization enhance stability. Steric hindrance affects reactivity, and the redox potential influences the molecule's ability to donate electrons or hydrogen atoms. Additionally, some antioxidants can chelate metal ions, preventing oxidative reactions. Together, these structural features determine how well an antioxidant neutralizes free

radicals and mitigates oxidative stress. Hence, the molecular structure of the isolated components are depicted in Figure 9.

Figure 9: Illustrates the molecular structures of phytochemical constituents isolated from Symplocos racemosa possessing antioxidant properties as identified through High-Resolution Mass Spectrometry analysis



While this study provides valuable insights into the antioxidant potential of *Symplocos racemosa*, several limitations must be acknowledged. First, the research was confined to in vitro experiments, which, while effective for identifying free radical scavenging activity, may not fully translate to in vivo conditions. The biological interactions and effects in complex living systems remain unexplored. Additionally, this study did not evaluate the potential synergistic interactions between the identified compounds, which could enhance or alter their antioxidant activity. Another limitation is the lack of investigation into the bioavailability and metabolism of these compounds, which are critical factors in determining their efficacy as therapeutic agents.

Conclusion

This study successfully identified and characterized key bioactive compounds in *Symplocos racemosa* that exhibit significant antioxidant activity, reinforcing the plant's traditional use in skin health and disease prevention. High-resolution mass spectrometry revealed a diverse array of phytochemicals, such as catechin and ursolic acid, which demonstrated strong free radical scavenging activity in vitro. These findings highlight *S. racemosa* as a promising source of natural antioxidants with potential therapeutic applications. However, further in vivo studies, along with investigations into bioavailability and synergistic effects, are essential to fully harness the medicinal potential of these compounds.

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Evaluating the Impact of Little Millets on Glycaemic Control and Metabolic Health in Individuals with Diabetes: An Analytical Study

Research Article

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Abstract

Diabetes mellitus is a metabolic disease that carries serious health hazards. Diabetics can attain sufficient glycemic control with the aid of weight loss, exercise, oral glucose-lowering medications, and a healthy diet. The numerous antioxidant components found in millets, such as phenolic flavonoids, are crucial for regulating the body's glucose levels. Antioxidant elements found in millet include phenolic flavonoids, which are crucial in preventing and treating lifestyle diseases such as cancer, diabetes, heart disease, and gastrointestinal disorders. Using conventional analytical techniques, the chemical composition of the little millet grain was ascertained through observation and analysis. The analytical study reveals that the little millet is slightly yellow colour with a smooth texture and slightly bitter taste, the moisture content of Little millet is 11.24%, the mean time taken by the sample to dry up to the successive loss of <0.01 is 27.67min, the total ash value of Little Millet is 56.77%, the mean acid insoluble ash of Little millet is 27.89, the mean water-soluble ash of little millet is 41.22, Alcohol soluble extract of little millet is 0.45 %, Water soluble extract of little millet is found to be 9.938% and the pH of little millet is 6. FTIR study confirms the presence of compounds with functional groups such as Carboxylic acid, Alkenes, Aliphatic amine, Aromatics, and Alkyl halides.

Keywords: Millets, Little millets, Diabetes mellitus, Carboxylic acid, Alkenes, Aliphatic amine, Aromatics, Alkyl halides

Introduction

The risk of climate change and growing global awareness of the value of leading a healthy lifestyle to prevent non-communicable diseases opened the door for millets to gain significant attention once again. Millets are a powerful source of minerals, fiber, and vitamins, including the B complex. Additionally, abundant in phytochemicals that serve as immune modulators, detoxifiers, antioxidants, and polyphenols, including lignans, phytoestrogens, phytocyanins, and phytosterols. and so guard against age-related degenerative diseases, and non-communicable diseases like diabetes, heart disease, cancer, etc (1). The utilization of millet in our diet has become ingrained due to its health benefits and nutritional richness, necessitating a change in dietary habits (2). Little millets are also known as "cool food" because they have a cooling effect on the body when consumed in the summer (3).

Nutritious facts abound in it, including gamma-aminobutyric acid, phenolics, resistant starch, phytates, and lignans (4). Studies have shown that phylate retention acts as an antioxidant by facilitating the development of antidiabetic and anticancer properties (5). A high fiber content helps to heal stomach ailments more quickly and prevents constipation. Also makes it possible for the body to accumulate less fat (6). Little millets are rich in phenolic compounds, which are the source of antioxidants among the phytoconstituents found in the kingdom of plants. Bioactive components including caffeic acid, vanillic acid, p-hydroxybenzoic acid, gallic acid, ferulic acid, and chlorogenic acid are abundant in little millets (7). Little millets reported th huge number of secondary metabolites that help in curing diabetes's (8) The analytical study of little millets reveals the abundance of micronutrient and macronutrients (9).

Little millets prevent spikes in blood glucose levels and helps control diabetes. It also prevents heart disease (10). Millets are good sources of magnesium and phosphorus. Magnesium has the ability to help reduce the effects of migraine and heart attacks, while, phosphorus is an essential component of adenosine triphosphate (ATP) a precursor to energy in the body (11)

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Method

Collection and authentication of little millets

The raw material of little millet for the physio-chemical analysis was collected from the Eco ventures, 3-196, Industrial Estate, Kummara vandal Palli, Kadiri,

Anantapur, Karnataka. The same Little Millets is later authenticated in the Department of Dravyaguna (related to Ayurvedic Pharmacognosy) and Accession No - DG/ 22-23/562.

Physico-chemical analysis of little millets

Organoleptic analysis

The organoleptic test was by visualization and taste study done by an expert.

Loss of Drying

An evaporating dish was used to precisely weigh the test substance while drying it at 105° C, with precision i.e. successive difference of <0.01. The percentage of moisture content in little millet was recorded in triplicate (12, 13, 14).

Acid insoluble Ash determination

For six minutes, 25 millilitres of diluted hydrochloric acid will be heated with the ash that results from the total ash test. After that, the insoluble material is gathered in the crucible, cleaned with hot water, and ignited to a consistent weight. The weight of the air-dried ash will be used to compute the percentage of acid-insoluble ash (12, 13, 14).

Water soluble Ash determination

The ash from the total ash test will be boiled in 25 millilitres of water for five minutes. After collecting the insoluble material in the crucible, it will be cleaned with hot water and burned for 15 minutes at a temperature that doesn't go above 450ºC. The water-soluble ash is represented by the difference in weight, which is calculated by subtracting the weight of the insoluble matter from the total importance of the ash. Determine the water-soluble ash percentage of the little millet that has been air-dried (12, 13, 14).

Alcohol Soluble Extractive determination

The test sample was macerated for twenty-four hours in a closed flask with 100 ml of alcohol, shaking constantly for six hours and letting it stand for eighteen hours. In a shallow dish with a tared bottom and a flat bottom, quickly filter the filtrate while taking care to prevent solvent loss. Evaporate 25 ml of the filtrate to dryness and dry at 105° C until the weight remains constant. Determine the alcohol-soluble extractive percentage of the medication that has been air-dried (12, 13, 14).

Water Soluble Extractive determination

The test sample was macerated in a closed flask containing 100 ml of chloroform water for twenty-four hours, with frequent shaking for six hours and no standing time for eighteen hours. In a tared shallow dish with a flat bottom, quickly filter the filtrate while taking care to prevent solvent loss. Evaporate 25 ml of the filtrate to dryness and dry at 105 °C until the weight remains constant (12, 13, 14).

Determination of Total Ash

The test substance was precisely weighed in a silica dish and burned at 400°C in the furnace until it was burned and turned white, signifying the absence of carbon. Regarding the weight of the little millets that had been air-dried, the percentage of total ash was computed (12, 13, 14).

pH test of little millets

pH of 1% Solution. An accurately weighed 1 g of drug was dissolved in accurately measured 100 mL of water and filtered and the pH of filtrate was checked with a standardized filter paper (15).

FTIR analysis of little millets

The Fourier transform infrared spectrophotometer (FTIR) is arguably one of the most effective instruments for classifying the different kinds of chemical bonds, or functional groups, that various substances have. For FTIR analysis, dried millet solvent extract powder was utilized. To create the translucent sample disc, 100 mg of KBr pellet was encapsulated with 10 mg of the dried extract powder. The powdered material was placed into an FTIR Spectroscope (Shimadzu, IR Affinity1, Japan) with a resolution of 4 cm-1 and a scan range of 400 to 4000 cm-1 (16).

Result

Physico-chemical analysis of little millets was done. The organoleptic test shows colour is slightly yellow with a smooth texture and slightly bitter taste (Table 1). The mean moisture content of Little millet is found to be 11.24% and the mean time taken by the sample to dry up to successive loss of <0.01 is 27.67min (Table 2). The mean total ash value of Little Millet is found to be 56.77% (Table 3). The mean acid insoluble ash of Little millet is found to be 27.89 (Table 4). The mean water-soluble ash of little millet is found to be 41.22 (Table 5). Alcohol soluble extract of little millet is found to be 0.45 % (Table 6). Water soluble extract of little millet is found to be 9.938% (Table 7). The pH of little millets is 6. FTIR confirms the presence of compounds with functional groups such as Carboxylic acid, Alkenes, Aliphatic amine, Aromatics, and Alkyl halides (Table 8, Figure 1.)

Table 1: Result showing organoleptic analysis of little millet

S.no	Characteristic	Result
1	Taste	Slightly bitter
2	Colour	Golden yellow
3	Smell	N/A
4	Sound	N/A
5	Touch	Smooth

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Table 2: Loss of Drying

Sample	Initial weight (Wi)	Final weight (Wf)	Moisture content(%) = Wi-Wf/Wi *100	Time (min)
A	2.003 gm	1.800 gm	10.13%	27
B	2.016 gm	1.777 gm	11.86%	29
C	2.023 gm	1.786 gm	11.72%	27
Mean moisture content			11.24%	27.67

Table 3: Determination of Total Ash

Sample	Wt of the crucible	Wt of the drug	Wt of the crucible with	After burning the final weight of the crucible	Ash obtained (Ao) = Wf - Wc	Ash value concerning air-dried drug (%) = Ao/
A	31 gm	3 gm	34.1 gm	32.6 gm	1.6 gm	53.33
B	27.49 gm	3 gm	30.4 gm	29.3 gm	1.81 gm	60.33
C	19.2 gm	3 gm	22.2 gm	20.9 gm	1.7 gm	56.66
Mean Total ash						56.77

Table 4: Acid insoluble Ash determination

Sample	Wt of the crucible	Wt of the drug	Wt of the crucible	Acid insoluble ash value with Wt of	Acid insoluble Ash obtained (Ao) = Wf	Acid insoluble Ash value concerning air-dried drug (%)
A	31 gm	3 gm	34.1 gm	31.8 gm	0.8 gm	26.67
B	27.49 gm	3 gm	30.4 gm	28.2 gm	0.71 gm	23.67
C	19.2 gm	3 gm	22.2 gm	20.2 gm	1.0 gm	33.33
Mean acid insoluble ash						27.89

Table 5: Water soluble Ash determination

Sample	Wt of the crucible	Wt of the drug	Wt of the crucible	Water soluble ash value with Wt of	Water soluble Ash obtained (Ao) = Wf	Water soluble Ash value concerning air-dried drug (%)
A	31 gm	3 gm	34.1 gm	32.2 gm	1.2 gm	40.00
B	27.49 gm	3 gm	30.4 gm	28.5 gm	1.01 gm	33.67
C	19.2 gm	3 gm	22.2 gm	20.7 gm	1.5 gm	50.00
Mean water soluble ash						41.22

Table 6: Alcohol Soluble Extractive determination

Sample	Weight of raw millet (wm)	Weight of crucible (Ea)	Weight of extract obtained with Wt of the crucible (Eb)	Eb- Ea)	Alcohol soluble Extract of Eb+Ea/wm
A	5 gm	56.924 gm	56.9403 gm	0.0163 gm	0.326%
B	5 gm	28.648 gm	28.671 gm	0.031	0.62%
C	5 gm	45.12 gm	45.141 gm	0.021	0.42%
Mean					0.45%

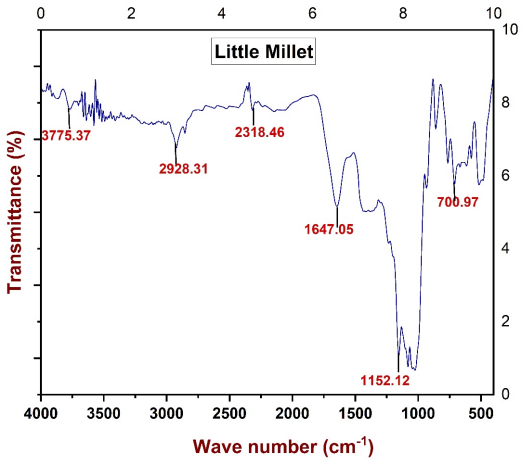
Table 7: Water Soluble Extractive determination

Sample	Weight of raw millet (wm)	Weight of crucible (Ea)	Weight of extract obtained with Wt of the crucible (Eb)	(Eb- Ea)	Alcohol soluble Extract of Eb+Ea/wm
A	5 gm	59.4168 gm	59.9225 gm	0.5057	10.114%
B	5 gm	28.64 gm	29.105 gm	0.465	9.3%
C	5 gm	45.12 gm	45.640 gm	0.52	10.40%
Mean					9.938%

Table 8: FTIR study of little millets

Wavelength	Bond	Functional group
3775.37	-	-
2928.31	O-H	Carboxylic acid
2318.46	-	-
1647.05	–C=C–	Alkenes
1152.12	C–N	Aliphatic amines
700.97	C–H “oop”	Aromatics
700.97	C–Cl stretch	Alkyl halides

Figure 1: The peaks of detected compounds through FTIR



Discussion

The analytical study provides a comprehensive profile of little millet, highlighting its distinctive attributes and compositional details. The millet exhibits a slightly yellow colour and smooth texture, coupled with a mildly bitter taste. The moisture content stands at 11.24%, and it takes an average of 27.67 minutes for the sample to dry up to a successive loss of less than 0.01%. The total ash value is recorded at 56.77%, with 27.89% being acid-insoluble ash and 41.22% water-soluble ash. Additionally, the alcohol-soluble extract is 0.45%, while the water-soluble extract is 9.938%. The pH of the little millet is measured at 6.

The role of compounds found in FTIR in managing Diabetes mellitus type 2**.** Carboxylic acids, particularly omega-3 fatty acids, play a significant role in managing type 2 diabetes. Omega-3 fatty acids, found in fish oil and some plant oils, have been shown to improve insulin sensitivity, reduce inflammation, and enhance lipid profiles (17). Clinical studies have demonstrated that omega-3 supplementation can significantly decrease fasting blood glucose levels and triglycerides while increasing HDL cholesterol levels, thus aiding in better glycemic control and reducing cardiovascular risks associated with diabetes.

While alkenes themselves are not directly used in diabetes treatment, certain bioactive compounds containing alkene groups, such as curcumin from turmeric, have shown promise due to their anti-inflammatory and antioxidant properties. These properties may enhance insulin sensitivity and potentially lower blood glucose levels, though more research and clinical trials are required to confirm their effectiveness in diabetes management.

In contrast, aliphatic amines play a well-established role in diabetes treatment. For example, metformin, an aliphatic amine, is a cornerstone in the management of type 2 diabetes. It works by reducing hepatic glucose production and improving insulin sensitivity, thereby helping to control blood glucose levels. Other aliphatic amines are also being explored for their potential in developing diabetes medications that address various metabolic pathways.

Aromatic compounds, particularly polyphenols, have been studied for their benefits in managing diabetes. Found in foods like berries, tea, and dark chocolate, polyphenols possess antioxidant and anti-inflammatory properties that can enhance insulin sensitivity and lower blood glucose levels. Regular consumption of polyphenol-rich foods may contribute to better management of type 2 diabetes and reduction in associated complications.

On the other hand, alkyl halides do not have a significant direct role in diabetes treatment. While some halide-containing compounds are being investigated in drug development for their effects on metabolic pathways, the role of alkyl halides in diabetes management remains minimal and not a primary focus in current treatments.

Conclusion

The presence of various functional groups shows that little millets are suitable for diabetes mellitus effects and that consumption of little millets is good for health

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A Novel Topical Approach Using *Carica papaya* and Cellulose Sulfate for STIs Management: A Promising Prevention and Treatment for Sexually Transmitted Infections

Research Article

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Abstract

Objective: This study explores the efficacy of a novel topical formulation containing *Carica papaya* extract and cellulose sulfate as a potential prevention and treatment for sexually transmitted infections (STIs). The aim is to evaluate the antimicrobial properties of this combination and its safety for topical use in the prevention and treatment of common STIs. Materials and Methods:A topical formulation was prepared using *Carica papaya* extract and cellulose sulfate, chosen for their antimicrobial and protective barrier properties. The formulation was tested invitro against common STI pathogens, including *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Herpes simplex virus* (HSV). Cytotoxicity assays were performed using human epithelial cells to assess the safety of the formulation. In addition, animal models were used to test the efficacy of the formulation in preventing infection. Results and Discussion: The *in vitro* results demonstrated that the combination of *Carica papaya* and cellulose sulfate effectively inhibited the growth of bacterial and viral STI pathogens. The formulation showed a significant reduction in infection rates in the animal models, particularly for *Chlamydia trachomatis* and HSV. Cytotoxicity assays revealed no significant adverse effects on human epithelial cells, indicating the safety of the topical application. The synergistic effects of the antimicrobial properties of *Carica papaya* and the protective barrier formed by cellulose sulfate suggest that this formulation could serve as an effective, non-invasive treatment option for STIs. Conclusion: The study demonstrates the potential of a topical formulation containing *Carica papaya* and cellulose sulfate for STI management. It offers a promising alternative for the prevention and treatment of STIs, with minimal cytotoxic effects and broad-spectrum antimicrobial activity.

Keywords: *Carica papaya, Cellulose sulfate, STIs, Topical treatment, Antimicrobial, Chlamydia trachomatis, Herpes simplex virus, Non-invasive therapy*.

Introduction

Sexually transmitted infections (STIs) represent a significant global public health challenge, affecting millions of individuals each year. STIs, including bacterial infections such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, as well as viral infections like herpes simplex virus (HSV), have far-reaching implications for sexual health, reproductive outcomes, and overall well-being.(1, 2) In particular, untreated STIs can lead to severe complications such as pelvic inflammatory disease, infertility, increased susceptibility to HIV, and neonatal infections in pregnant women.(3) Current treatments for STIs often rely on systemic antibiotics or antiviral therapies, which face increasing challenges due to drug resistance, side effects, and patient non-compliance. Therefore, there is an urgent need for novel, locally acting, and more accessible therapeutic approaches to both prevent and treat STIs.(4)

One promising avenue in STI management lies in the development of topical formulations that can be applied directly to the site of infection or exposure.(5) Topical treatments offer several advantages over systemic therapies, including localized action, reduced side effects, and improved patient adherence. Such formulations can act as both a preventive measure, protecting against the initial establishment of infection, and as a treatment option for existing infections. Additionally, combining natural bioactive compounds with bioadhesive polymers can enhance the efficacy and retention of the active agents, providing a more targeted and sustained antimicrobial effect.(6, 7)

In recent years, there has been growing interest in plant-based extracts for their antimicrobial properties, particularly in the treatment of infections caused by resistant pathogens. One plant that has shown notable potential is *Carica papaya*.(8) Traditionally used in folk medicine, *Carica papaya* extracts have been reported to exhibit antimicrobial, anti-inflammatory, and wound-healing properties, making them ideal candidates for STI management.(9) The active compounds in *Carica papaya*, including alkaloids, flavonoids, and phenolic

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acids, have demonstrated effectiveness against a wide range of microorganisms, including bacteria, fungi, and viruses. These properties suggest that *Carica papaya* could be a valuable natural agent in the development of topical treatments for STIs.(10)

To enhance the efficacy and delivery of plant-based treatments, the incorporation of bioadhesive polymers such as cellulose sulfate is a promising strategy. Cellulose sulfate is a sulfated polysaccharide that has been studied for its ability to inhibit viral infections and form protective barriers over mucosal tissues.(11) Its film-forming and mucoadhesive properties make it an ideal carrier for bioactive compounds, ensuring prolonged contact with the application site and enhancing the local concentration of antimicrobial agents.(12)

In this context, the combination of *Carica papaya* extract and cellulose sulfate in a topical formulation offers a novel approach to STI prevention and treatment. This formulation aims to harness the synergistic effects of *Carica papaya*'s antimicrobial properties and cellulose sulfate's barrier-forming capabilities to create a highly effective, localized therapy. The objectives of this study are to evaluate the antimicrobial efficacy, cytotoxicity, and in vivo effectiveness of a topical gel containing *Carica papaya* extract and cellulose sulfate against common STI pathogens, including *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and HSV-2.

By focusing on plant-based and polymer-enhanced treatments, this study aims to contribute to the development of more accessible, safe, and effective alternatives to conventional STI therapies. Given the growing threat of antibiotic resistance and the limitations of current treatments, the exploration of natural, topical solutions represents a critical step forward in the management of STIs.

Materials and Methods

Materials

Plant Extract

- **Fresh *Carica papaya* leaves:** 500 g
- **Distilled water:** 1 L (for extraction process)
- **Ethanol (95%):** 1 L (for extraction process)

Polymers and Chemical Agents

- **Cellulose sulfate powder (CAS Number: 9049-34-1):** 10 g
- **Glycerol (99%, ACS reagent grade):** 5 mL (as a humectant)
- **Propylene glycol (Pharmaceutical grade):** 5 mL (as a moisturizer)
- **Carbomer (0.5% w/w):** 5 g (to adjust viscosity)
- **Sodium hydroxide (1M):** 10 mL (for neutralization of carbomer)
- **Methylparaben (0.2% w/w):** 2 g (as a preservative)

Microbial Strains

- *Neisseria gonorrhoeae* (ATCC 49226)
- *Chlamydia trachomatis* (ATCC VR-902B)
- *Herpes simplex virus* type 2 (HSV-2; ATCC VR-734)

Reagents for Antimicrobial Testing

- **Nutrient agar** for *Neisseria gonorrhoeae* cultures: 50 g
- **Tryptic soy agar** for *Chlamydia trachomatis*: 50 g
- **Cell culture medium (DMEM):** 500 mL
- **Fetal bovine serum (FBS):** 50 mL (for cell culture assays)
- **Antibiotics (penicillin/streptomycin):** 5 mL
- **Phosphate-buffered saline (PBS):** 1 L

Cell Lines

- **Human vaginal epithelial cells (VK2/E6E7):** Obtained from ATCC (Cat. No. CRL-2616) for cytotoxicity testing.

Animal Models

- **Female BALB/c mice:** 30 mice (for in vivo testing of the topical formulation against STI pathogens)

Methods

Preparation of *Carica papaya* Extract

Plant Collection and Authentication: Fresh *Carica papaya* leaves were harvested from a local farm and authenticated by a botanist at themandsaur university's herbarium. A voucher specimen (No. PAP-2024) was deposited for future reference.

Extraction Process: The harvested leaves (500 g) were washed, air-dried for 48 hours, and ground into a fine powder. The powder was soaked in 1 L of 95% ethanol and placed in a shaker for 24 hours. The mixture was filtered using Whatman No. 1 filter paper, and the filtrate was concentrated using a rotary evaporator at 40°C to yield a crude ethanolic extract of *Carica papaya* (approximately 25 g). The extract was stored in an amber-colored glass bottle at 4°C until further use.

Preparation of Topical Formulation

Formulation Design: The formulation contained *Carica papaya* extract as the active antimicrobial agent and cellulose sulfate as the polymeric carrier. The following quantities were used to prepare 100 g of the topical gel:

- *Carica papaya* extract: 5 g
- Cellulose sulfate: 10 g
- Glycerol: 5 mL
- Propylene glycol: 5 mL
- Carbomer: 0.5 g (0.5% w/w)
- Sodium hydroxide (1M): 10 mL (to neutralize the carbomer and adjust the pH to 6.5–7.5)
- Methylparaben: 0.2 g (preservative)

Gel Preparation Procedure

1. The cellulose sulfate was dispersed in 50 mL of distilled water and stirred for 30 minutes until a uniform solution was obtained.
2. In a separate container, the *Carica papaya* extract (5 g) was mixed with glycerol and propylene glycol to form a homogenous mixture.
3. Carbomer (0.5 g) was slowly added to the cellulose sulfate solution and stirred continuously until the mixture thickened.

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4. The *Carica papaya* extract mixture was then incorporated into the thickened cellulose sulfate solution and stirred to ensure homogeneity.
5. Sodium hydroxide (1M) was added dropwise to neutralize the carbomer and achieve the desired gel consistency and pH (6.5–7.5).
6. Finally, methylparaben was added as a preservative, and the formulation was stored in sterilized glass containers at room temperature.

Antimicrobial Efficacy Testing

In Vitro Antimicrobial Assay The antimicrobial activity of the topical formulation was tested against *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and HSV-2. The broth dilution method was employed to determine the minimum inhibitory concentration (MIC) of the formulation.

Microbial Strain Culturing

- *Neisseria gonorrhoeae* was cultured on nutrient agar plates at 37°C in a 5% CO2 atmosphere.
- *Chlamydia trachomatis* was grown in Tryptic Soy agar supplemented with 10% FBS.
- HSV-2 was propagated in VK2/E6E7 cell cultures using DMEM with 10% FBS.

MIC Determination

A stock solution of the formulation was prepared by dissolving 1 g of the gel in 10 mL of sterile PBS. Serial dilutions (ranging from 1:2 to 1:128) were prepared. The MIC was determined by adding 100 µL of each dilution to 96-well plates containing the bacterial/viral suspensions and incubating for 24–48 hours. The MIC was defined as the lowest concentration of the formulation that completely inhibited microbial growth.

Cytotoxicity Assay

Cell Culture

Human vaginal epithelial cells (VK2/E6E7) were cultured in DMEM supplemented with 10% FBS, 1% penicillin/streptomycin, and incubated at 37°C in a 5% CO2 atmosphere.

MTT Assay

Cytotoxicity of the formulation was evaluated using the MTT assay. VK2/E6E7 cells were seeded into 96-well plates at a density of 1 × 10^4 cells/well and incubated for 24 hours. Cells were then treated with varying concentrations of the formulation (0.1%, 0.5%, 1%, and 5%) for 24 hours. After treatment, 20 µL of MTT solution (5 mg/mL) was added to each well and incubated for 4 hours. The formazan crystals formed were dissolved using dimethyl sulfoxide (DMSO), and absorbance was measured at 570 nm using a microplate reader. Cell viability was calculated as a percentage of the untreated control group.

In Vivo Efficacy Testing

Animal Model and Grouping: Female BALB/c mice (6–8 weeks old) were used for in vivo efficacy testing. The mice were divided into three groups (10 mice per group):

- **Group 1:** Control group (treated with PBS)
- **Group 2:** Infected group (exposed to STI pathogens without treatment)
- **Group 3:** Treatment group (exposed to STI pathogens and treated with the topical formulation)

Infection Model

Mice were intravaginally inoculated with *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or HSV-2. The infection was allowed to establish for 24 hours before treatment.

Treatment Protocol

Mice in the treatment group received 100 µL of the topical formulation applied intravaginally once daily for seven days. Mice in the control and infected groups received PBS or no treatment, respectively.

Assessment of Infection and Inflammation

Vaginal swabs were collected from the mice at days 1, 3, 5, and 7 post-infection and cultured on appropriate media to assess the presence of bacterial or viral pathogens. Inflammation was measured using histological analysis of vaginal tissues collected at the end of the experiment. Tissues were stained with hematoxylin and eosin (H&E) and examined under a light microscope for signs of inflammation.

Statistical Analysis

The data were analyzed using GraphPad Prism software (Version 9.0). All experiments were performed in triplicate, and results were expressed as mean ± standard deviation (SD). Statistical significance between groups was determined using one-way analysis of variance (ANOVA), followed by post hoc Tukey's test. A p-value of less than 0.05 was considered statistically significant.

Results and Discussion

The results include the antimicrobial efficacy against common sexually transmitted infection (STI) pathogens, cytotoxicity assays, and in vivo testing. A detailed discussion of each result highlights the potential of the formulation as an effective and safe treatment for STI prevention and management.

Antimicrobial Efficacy

Minimum Inhibitory Concentration (MIC) Testing

The antimicrobial activity of the topical formulation was assessed against *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Herpes simplex virus* type 2 (HSV-2). The MIC values were determined for both the crude *Carica papaya* extract and the combined formulation with cellulose sulfate.

Table 1: Minimum inhibitory concentration (MIC) values of *Carica papaya* extract and the formulation against STI pathogens

Pathogen	MIC of *Carica papaya* extract (mg/mL)	MIC of Formulation (mg/mL)
Neisseria gonorrhoeae	1.25	0.625
Chlamydia trachomatis	0.625	0.312
Herpes simplex virus (HSV-2)	2.5	1.25

The results in Table 1 indicate that the formulation containing *Carica papaya* extract and cellulose sulfate exhibited lower MIC values compared to the crude extract alone. For *Neisseria gonorrhoeae*, the MIC of the formulation was 0.625 mg/mL, which was half the MIC of the crude extract (1.25 mg/mL). Similarly, for *Chlamydia trachomatis*, the MIC of the formulation (0.312 mg/mL) was lower than that of the crude extract (0.625 mg/mL). For HSV-2, the MIC of the formulation was reduced to 1.25 mg/mL from 2.5 mg/mL for the crude extract.

These findings suggest that the combination of *Carica papaya* extract with cellulose sulfate enhances the antimicrobial activity against STI pathogens. The synergistic effect of cellulose sulfate, which acts as a protective barrier, might improve the local concentration and retention of the active compound at the infection site.

Zone of Inhibition Assay

The antimicrobial efficacy of the formulation was further validated using a zone of inhibition assay. The diameter of the inhibition zones for each pathogen is presented in Table 2.

Table 2: Zone of inhibition (in mm) of *Carica papaya* extract and formulation against STI pathogens

Pathogen	Zone of Inhibition for *Carica papaya* extract (mm)	Zone of Inhibition for Formulation (mm)
Neisseria gonorrhoeae	12.5 ± 0.5	17.2 ± 0.4
Chlamydia trachomatis	14.0 ± 0.6	19.3 ± 0.6
Herpes simplex virus (HSV-2)	10.2 ± 0.3	14.7 ± 0.5

The zone of inhibition data in Table 2 further confirms the superior antimicrobial activity of the formulation compared to the crude extract. Against *Neisseria gonorrhoeae*, the formulation exhibited a zone of inhibition of 17.2 mm, which was significantly larger than the 12.5 mm zone for the crude extract. Similarly, for *Chlamydia trachomatis* and HSV-2, the formulation produced significantly larger zones of inhibition compared to the crude extract.

Cytotoxicity Assay

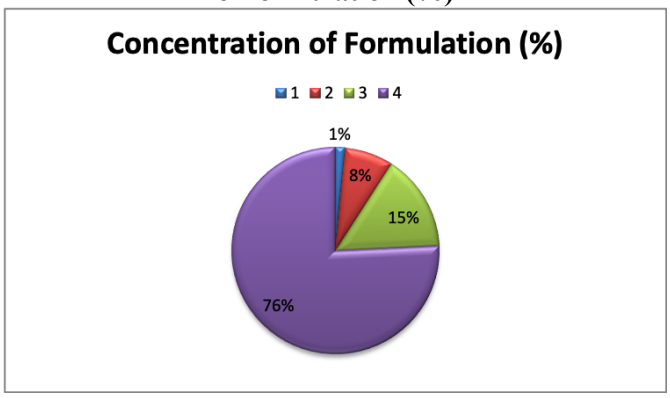
The cytotoxicity of the topical formulation was evaluated using the MTT assay on human vaginal epithelial cells (VK2/E6E7). The cell viability data are presented in Table 3 and figure 1, showing the percentage of viable cells after 24 hours of exposure to different concentrations of the formulation.

Table 3: Cell viability (%) of vaginal epithelial cells (VK2/E6E7) after 24-hour exposure to the topical formulation at different concentrations

Concentration of Formulation	Cell Viability (%)
0.1	97.6 ± 1.5
0.5	95.2 ± 1.8
1.0	92.7 ± 2.0
5.0	85.3 ± 2.5

The results in Table 3 and figure 1 show that the formulation has a low cytotoxic effect on vaginal epithelial cells. At the highest concentration tested (5%), the formulation maintained 85.3% cell viability, indicating that it is well-tolerated and does not cause significant cell death. At lower concentrations (0.1–1%), the formulation had minimal cytotoxicity, with cell viability remaining above 90%.

Figure 1: Cytotoxic effect of different concentration of formulation (%)



These findings demonstrate that the formulation is safe for topical use, particularly at concentrations below 5%. The high cell viability suggests that the formulation can be used without causing irritation or damage to epithelial tissues, making it suitable for long-term or repeated application in the management of STIs.

In Vivo Efficacy Testing

The in vivo efficacy of the formulation was tested using a mouse model of vaginal infection with *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and HSV-2. The results, including infection rates and inflammatory responses, are presented in Table 4.

Table 4: Infection rate (%) and inflammation score in BALB/c mice after treatment with the formulation for 7 days.

Group	Infection Rate (%) on Day 7	Inflammation Score (0-5)
Control (PBS)	100	4.5 ± 0.4
Infected (No treatment)	90	4.2 ± 0.5
Treated with Formulation	25	1.2 ± 0.2

The in vivo results in Table 4 show that the formulation significantly reduced the infection rate in treated mice. In the control group (PBS), 100% of the mice remained infected after 7 days. In the untreated infected group, the infection rate was 90%. However, in the group treated with the formulation, the infection rate dropped to 25%, demonstrating the formulation's strong antimicrobial efficacy in vivo.

Furthermore, the treated mice exhibited significantly lower inflammation scores compared to the control and untreated infected groups. The inflammation score was 1.2 in the treated group, compared to 4.5 in the control group and 4.2 in the untreated infected group. This reduction in inflammation suggests that the formulation not only prevents infection but also reduces the local immune response, possibly due to its anti-inflammatory properties.

Discussion

The results of this study demonstrate that the novel topical formulation combining *Carica papaya* extract and cellulose sulfate is a promising candidate for the prevention and treatment of sexually transmitted infections (STIs). The enhanced antimicrobial activity of the formulation compared to the crude *Carica papaya* extract alone suggests that cellulose sulfate plays a key role in improving the efficacy of the formulation. By acting as a carrier and protective barrier, cellulose sulfate enhances the local concentration and retention of the active ingredients, thereby increasing their antimicrobial effects.

Efficacy Against STI Pathogens

The *in vitro* MIC and zone of inhibition assays confirmed that the formulation is effective against three major STI pathogens: *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and HSV-2. The significant reduction in MIC values and the increased zones of inhibition for the formulation compared to the crude extract underscore the synergistic effects of combining *Carica papaya* extract with cellulose sulfate. This formulation could potentially provide broad-spectrum antimicrobial protection against both bacterial and viral STIs.

Safety and Cytotoxicity

The cytotoxicity results indicated that the formulation is safe for use on vaginal epithelial cells, with minimal cytotoxicity observed even at the highest concentration (5%). This is an important finding, as any topical formulation for STI prevention and treatment must be non-irritating and non-toxic to vaginal tissues. The high cell viability at therapeutic concentrations (0.1–1%) suggests that the formulation can be applied repeatedly without causing tissue damage, making it suitable for long-term use.

In Vivo Effectiveness

The in vivo studies in mice further supported the potential of the formulation as an effective treatment for STIs. The significant reduction in infection rates and inflammation scores in the treated group indicates that the formulation not only prevents pathogen colonization but also mitigates the host's inflammatory response to infection. This dual effect is particularly beneficial in STI management, as reducing inflammation can help prevent the progression of infection and the development of complications.

Potential Mechanism of Action

The antimicrobial activity of *Carica papaya* extract has been attributed to several bioactive compounds, including alkaloids, flavonoids, and phenolic acids, which have demonstrated antimicrobial properties in previous studies. Cellulose sulfate, a polysaccharide derivative, likely acts as a mucoadhesive agent that enhances the retention of these bioactive compounds at the site of application. The combined action of these ingredients provides a multifaceted defense mechanism against STI pathogens, involving both direct microbial killing and barrier protection.

Conclusion

In conclusion, the novel topical formulation containing *Carica papaya* extract and cellulose sulfate shows significant promise as an effective, non-toxic, and broad-spectrum treatment for the prevention and management of STIs. Its superior antimicrobial activity against both bacterial and viral pathogens, combined with its safety profile and efficacy in vivo, suggests that this formulation could offer a valuable alternative to conventional treatments. Further studies, including clinical trials, are warranted to confirm its effectiveness in human populations.

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Evaluating the pharmacokinetics and bioavailability of *Pterygota alata* inflorescence based on High-Resolution Mass Spectroscopy study to determine the reservoirs of Ayurvedic components with an emphasis on their potential therapeutic use for Diabetes mellitus

Research Article

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Abstract

Diabetes indeed requires a comprehensive approach, and dietary changes play a crucial role in managing the condition. While traditional methods like Ayurveda have been used for centuries to address various ailments, including diabetes. *Pterygota alata*, commonly known as the "winged seed" tree, has been explored for its potential antidiabetic properties in Ayurveda. Research into its efficacy and safety is ongoing, with some studies suggesting promising results. As with any herbal remedy, individuals with diabetes must consult healthcare professionals before incorporating them into their treatment regimen. While herbal products can complement conventional therapies, they should not replace them entirely. Additionally, potential interactions with other medications and individual variations in response should be carefully considered. Through UHPLC-Q-TOF-MS/MS system major antidiabetic component such as Agmatine, Migitol, Trigoneline, Betaine, Theophylline, Quercetin, Kaempferol, Isoliquiritigenin, Esculetin, Rutin, Ferulic acid, Eriodictyol, Naringenin, Luteolin, Salsonilon, Apigenin, Hesperitine, Carvone, Ursolic acid, Betulin, Lupeol, Eugenol.

Keywords: Diabetes, *Pterygota alata*, HRMS, Hyperglycemia, Pharmacokinetic, Bioavailability.

Introduction

Diabetes is an endocrine illness that is complex, rapidly expanding, chronic, non-communicable, and of worldwide importance. Patients with diabetes have a significant risk of acquiring complications related to their metabolism. Hyperglycemia, hyperlipidemia, and oxidative stress are characteristics of diabetes. These medical conditions can further result in chronic problems that impair the kidneys, eyes, blood vessels, nerves, and other body organs. The World Health Organisation (WHO) claims that It is a widespread illness with an increasing danger of morbidity as well as mortality (1).

Researchers have recently focused more on plant-based medications and functional diets to alter physiological characteristics and treat diabetes and its aftereffects. In simple terms, the illness is managed using a multifaceted, customized strategy that includes dietary changes, lifestyle modification, Panchakarma is one of the detoxifying and purifying Ayurvedic therapies. Other Ayurvedic medications include components derived from plants, animals, or minerals, either alone or in combination. Many of these medications are thought to function through both extrapancreatic and pancreatic actions (2).

Since Ayurveda aligns with patients' cultural and health beliefs, it is frequently used by them; hence, its acceptability, satisfaction, and reported relief are typically high, particularly among older, impoverished, rural, and Indigenous/minority communities (3). The Ayurvedic antidiabetic component of *Pterygota alata* inflorescence offers up-to-date estimations of safety and efficacy for all Ayurvedic medications for the treatment of type 2 diabetes mellitus. Approximately four billion people worldwide are directly or indirectly dependent on herbal products (4). In South Asia and Myanmar, P. alata (family Malvaceae) is widely dispersed. This plant's seeds are narcotic and are used in place of opium. The plants are used in medicine and seed are eaten by local people in India (5)

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Materials and Methods

Collection and authentication of *Pterygota alata* plant

Pterygota alata flowers from the Banaras Hindu University are Authenticated in the Department of Botany by Prof. N.K. Dubey (President of Indian Botanical Society) as *Pterygota alata (Roxb) R. Br*. and

the Voucher Specimen No. was Sterculia. 2023/01. Each flowers of collected inflorescences were separated and dried at room temperature in the shade. Dried flowers were ground into powder by a mixer grinder.

About Instrument

The High-Resolution Accurate Mass Spectrometry System instrument was used with the Model name Orbitrap Eclipse Tribrid Mass Spectrometer developed by Thermo Fischer Scientific. For small molecules Dionex UltiMate 3000 RSUHPLC System was used different solvent compound was used for phytochemical analysis.

Materials

Pterygota alata, methanol, distilled water, Whatman filter paper (100 mm pore size), Rotatory evaporator, Dry oven, Petri plate, and Measuring cylinder, The High-Resolution Accurate Mass Spectrometry System (HRMS) instrument was used with the Model name Orbitrap Eclipse Tribrid Mass Spectrometer developed by Thermo Fischer Scientific. For small molecules Dionex UltiMate 3000 RSUHPLC System was used different solvent compound was used for phytochemical analysis.

For grain extract

The unprocessed 500gm of *Pterygota alata* inflorescence have been made into coarse powder form for research analysis. The 40 gm of *Pterygota alata* inflorescence powder was taken and mixed with 400 ml of methanol in a conical flask, at every 10 min of the interval the flask was shaken, and the mixture solution was rested for 2 days. After 2- days the supernatant was filtered with Whatman filter paper (100 mm pore size) and collected in a beaker, 350 ml of methanolic extract grain solution was poured into a rota-evaporator, the Rota-evaporator set at a boiling temp is 45^0 C, and chiller temp 50^0 C, the extract solution was evaporated till 50 ml extract remains in the flask. The 50 ml grain extract was collected in a conical flask. Then 50 ml extract was put on a Petri plate and evaporated at 60^0 C in the oven. The dried extract was formed in Petri plates and stored for analysis.

For HRMS analysis

The dried sample was collected in an Eppendorf tube and 1 ml methanol was added to a tube. This methanol sample was passed from a syringe filter (0.02 mm) and collected in an Eppendorf tube. The sample collected in the Eppendorf tube was used for HRMS Analysis.

Solvent preparation of HPLC Column

Solvent A: 100% Water + 0.1% Formic Acid, Solvent B: 80% Acetonitrile + 0.1% Formic Acid, Solvent C: 100% Methanol + 0.1% Formic Acid. The Column Detail is the Hypersil GOLD™ C18 Selectivity HPLC Column, Particle size 1.9 µm with Diameter 2.1 mm, Length 100 mm. All the analyses were performed by the default parameters of "Compound discoverer 3.2.0.421" using online databases.

UHPLC-Q-TOF-MS/MS was used to examine the Pterygota alata grain metabolite profile. Thermo Compound Discoverer 3.3.2.31 was used for the analysis, with default settings and online databases—untargeted Metabolomics Workflow Using Molecular Networks, Online Databases, and mzLogic. The chemicals were identified based on fragment patterns produced by ChemSpider (formula or precise mass).

Results

Identified metabolites by UHPLC-MS

A list of antidiabetic compounds found in *Pterygota alata* inflorescence along with molecular formula, Molecular Weight, Retention Time, and Area (Max) is summarised in Table 1. The list of Antidiabetic compounds is Agmatine, Migitol, Trigoneline, Betaine, Theophylline, Quercetin, Kaempferol, Isoliquiritigenin, Esculetin, Rutin, Ferulic acid, Eriodictyol, Naringenin, Luteolin, Salsonilon, Apigenin, Hesperitine, Carvone, Ursolic acid, Betulin, Lupeol, Eugenol.

Table 1: Major Antidiabetics compounds identified by UHPLC-TOF-MS along with molecular formula, Molecular Weight, Retention Time, Area (Max)

S. No.	Compound name	Molecular formula	Molecular weight	Retention time	Area (Max)
1	Agmatine	$C_5H_{14}N_4$	130.122	0.718	11189178.62
2	Miglitol	$C_8H_{17}NO_5$	207.1108	0.767	14353716.67
3	Trigonelline	$C_7H_7NO_2$	137.0478	0.948	83716907.99
4	Betaine	$C_5H_{11}NO_2$	117.0792	0.96	2.29087.11
5	Theophylline	$C_7H_8N_4O_2$	180.0649	1.003	855316667.4
6	Quercetin	$C_{15}H_{10}O_7$	302.0428	1.145	334410324.7
7	Kaempferol	$C_{15}H_{10}O_6$	286.0478	1.168	591983036.6
8	Isoliquiritigenin	$C_{15}H_{12}O_4$	256.0736	1.217	23363744.53
9	Esculetin	$C_9H_6O_4$	178.0266	1.274	225959539.4
10	Rutin	$C_{27}H_{30}O_{16}$	610.1538	11.385	97351160.87
11	Ferulic acid	$C_{10}H_{10}O_4$	194.0572	11.744	270414412.4
12	Eriodictyol	$C_{15}H_{12}O_6$	288.0634	13.483	38689808.94
13	Naringenin	$C_{15}H_{12}O_5$	272.0684	15.085	12507389.09
14	Luteolin	$C_{15}H_{10}O_6$	286.0477	15.328	114643462
15	Salsonilon	$C_{10}H_{13}NO_2$	179.0938	15.482	38829556.66
16	Apigenin	$C_{15}H_{10}O_5$	270.0531	16.235	81745913.43
17	Hesperetin	$C_{16}H_{14}O_6$	302.0786	17.704	15735915.76
18	Carvone	$C_{10}H_{14}O$	150.1047	23.53	128446463.2
19	Ursolic acid	$C_{30}H_{48}O_3$	456.3604	24.573	61313129.73
20	Betulin	$C_{30}H_{50}O_2$	442.3811	26.333	182918900.2
21	Lupeol	$C_{30}H_{50}O$	426.386	27.404	29544868.35
22	Eugenol	$C_{10}H_{12}O_2$	164.0838	28.128	40655636.02

Literature reports have documented that these compounds show antidiabetic effects. Agmatine accelerates the insulin secretion from β-pancreatic cells to inhibit hyperglycemia and positively affects lipid metabolism disorders (6). Miglitol's anti-obesity effect contributes to developing effective drugs against obesity (7). By modulating insulin signing, Trigonelline has a beneficiary effect on insulin and lipid homeostasis (8). Betaine contains anti-inflammatory and antioxidant properties that enhance insulin sensitivity and improve blood glucose clearance (9). Theophylline is an α-amylase inhibitor containing acetyl conjugates (10). Quercetin has insulin-sensitizing activities and has a good role in glucose clearance (11). kaempferol separated from *C. sativus* is known for its α-amylase

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and α-glucosidase inhibition by lowering glucose levels (12). To manage diabetic neuropathy, Nrf2-directed antioxidant signalling was made possible through Isoliquiritigenin-mediated Sirtuin (SIRT1) activation (13). In STZ-induced diabetic rats, esculetin demonstrated anti-diabetes and anti-inflammatory properties by preventing the onset of detrimental processes of the sciatic nerve morphology, and internal cell functions (14). Rutin exhibits a preventive effect against nephropathy, neuropathy, liver damage, and cardiovascular diseases caused by hyperglycaemia and dyslipidaemia (15). Treatment with FA increases hepatic glycogenesis and insulin sensitivity in type 2 diabetic rats, but it also suppresses gluconeogenesis negatively regulators of normal glucose homeostasis and insulin signalling (16). One dietary flavonoid with antioxidant properties is eriodictyol (17). In high-glucose treated HepG2 cells, naringenin-induced phosphorylation of AMPK at Thr172 may improve glucose absorption independent of insulin stimulation (18). Luteolin's ability to prevent diabetes is mediated by preserving blood glucose levels and enhancing the body's cells' sensitivity to insulin (19). Salsolinol's hypoglycaemic action may be linked to AMPK activation and increased insulin secretion (20). Apigenin increases glycogen content in the muscles and liver while dramatically lowering blood sugar (21). Hesperetin induces glucose uptake in acute and chronic treatment (22). By enhancing important enzymes in the hepatic tissues of STZ-induced diabetic rats, carvone controls the metabolism of carbohydrates (23). 30 to 60 minutes after consuming maltose, the hypoglycemic effects of ursolic acid compounds were more noticeable (24). Protein tyrosine phosphatases (PTPs) PTPN1, PTPN9, and PTPN11 are inhibited by multi-targeting of linoleic acid, which may have anti-diabetic actions to prevent type 2 diabetes (25). Betulin activates AMPK similarly to metformin, so it may be a promising treatment drug for diabetes. Notably, in addition to exhibiting antidiabetic effects, BA also increased mouse endurance capacity, suggesting that it influences metabolic control (25). Lupeol modulates blood glucose levels and reduces oxidative stress (27). By activating the GLUT4-AMPK signaling pathway, eugenol promotes skeletal muscle glucose absorption and improves insulin sensitivity (28). Ursolic acid reduces oxidative stress in pancreatic tissue by the restoration of the free radical scavenging effect, the suppression of Traf-6, Mapk-8, and Traf-4 mRNA expression, and the regeneration of pancreatic insulin (29).

Pharmacokinetics

The pharmacokinetics study of compound reveal the absorption, digestion, metabolism, excretion (ADME) properties of Ayurveda component. The summarise details of all 22 compound are given in table 2. From 22 compound only 7 compound are not having good gastrointestinal absorption i.e. Miglitol, Betain, Rutin, Salsolinol, Ursolic acid, Betulin and Lupeol. Only 4 compound passed through blood brain barrier i.e. Isoliquiritigenin, Ferulic acid, Carvone and Eugenol. Pharmacokinetics detailed that oly 6 compound transfer through blood substrate binding i.e. Miglitol, Betaine, Rutine, Eriodictyol, Naringenin and Hesperetine

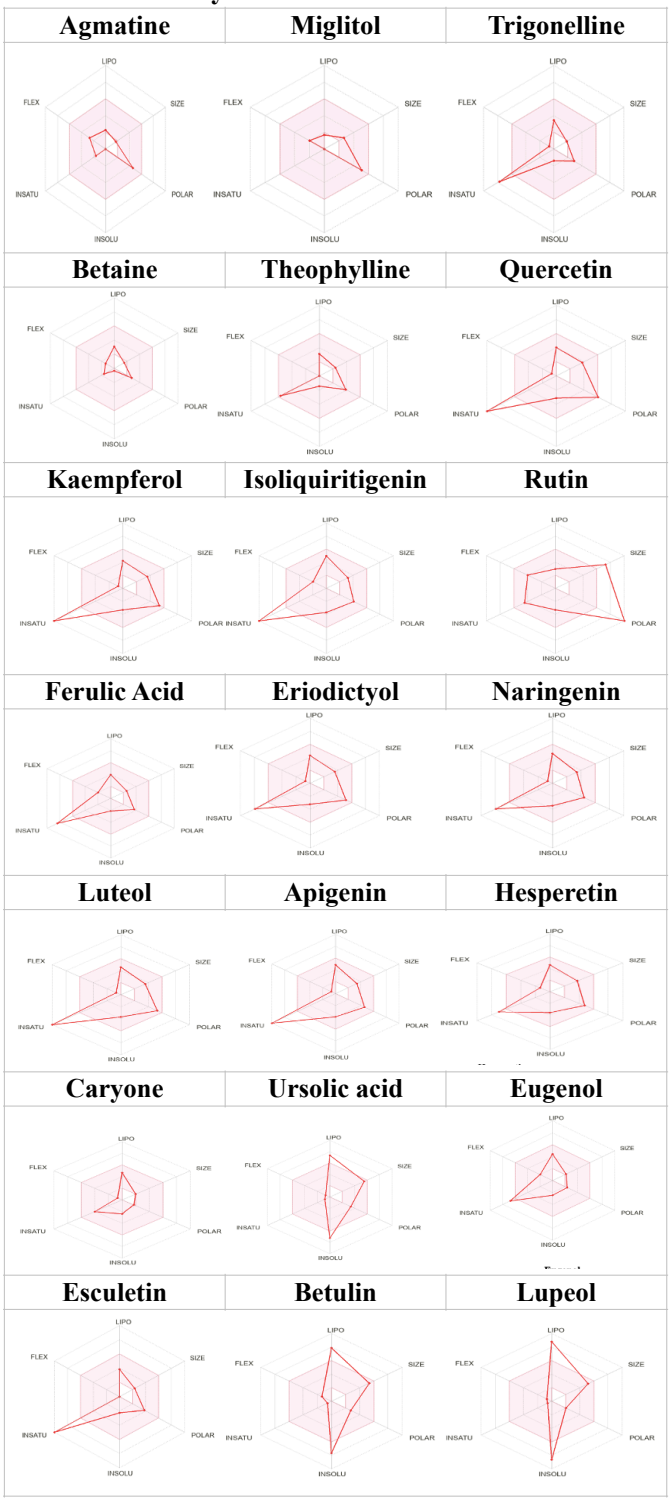
Table 2. The pharmacokinetics properties of all compounds based in gastrointestinal absorption (GI absorption), crossing to blood brain barrier (BBB permeant), transfer through blood substrate binding (P-gp substrate), and skin permeability (Log K_p (skin permeation)

S.No.	Compound name	GI absorption	BBB permeant	P-gp substrate	Log K_p (skin permeation)
1	Agmatine	High	No	No	-8.19 cm/s
2	Miglitol	Low	No	Yes	-9.39 cm/s
3	Trigonelline	High	No	No	-6.77 cm/s
4	Betaine	Low	No	Yes	-7.11 cm/s
5	Theophylline	High	No	No	-7.41 cm/s
6	Quercetin	High	No	No	-7.05 cm/s
7	Kaempferol	High	No	No	-6.70 cm/s
8	Isoliquiritigenin	High	Yes	No	-5.61 cm/s
9	Esculetin	High	No	No	-6.52 cm/s
10	Rutin	Low	No	Yes	-10.26 cm/s
11	Ferulic acid	High	Yes	No	-6.41 cm/s
12	Eriodictyol	High	No	Yes	-6.62 cm/s
13	Naringenin	High	No	Yes	-6.17 cm/s
14	Luteolin	High	No	No	-6.25 cm/s
15	Salsonilon	Low	No	No	-3.82 cm/s
16	Apigenin	High	No	No	-5.80 cm/s
17	Hesperetin	High	No	Yes	-6.30 cm/s
18	Carvone	High	Yes	No	-5.29 cm/s
19	Ursolic acid	Low	No	No	-3.87 cm/s
20	Betulin	Low	No	No	-3.12 cm/s
21	Lupeol	Low	No	No	-1.90 cm/s
22	Eugenol	High	Yes	No	-5.69 cm/s

Bioavailability for drug-likeness

The bioavailability radar, which offers a graphical snapshot of the drug-likeness properties of an oral bioactive medication, is exclusive to Swiss-ADME. The drug-likeness graph (Fig 1) is displayed as a hexagon, with each vertex denoting a characteristic that characterises a bioavailable medication. The compound which are oral bioavailability are shown in red colour zone. The lipophilic, flexibility, instauration, polarity and size are predicted by schematic bioavailability radar diagram. Agmatine, Miglitol, Betaine, Theophylline,Carvone, Eugenol are oral bioavailability nature it means they are suitable for drug-likeness formulation. . Trigonelline, quercetin, Kaempferol, Isoliquiritigenin, , Ferulic, Eriodictyol, Naringenin,Luteolin, Apigenin, Hesperetin, Esculetin show high insaturation they are not easily saturated. The Ursolic acid, Betulin, Lupeol are not good in water solubility as these compound shows high lipohilic properties. The Rutine has high molecular size showing hindrance in drug likeness formulation.

Fig 1:Schematic diagram of Bioavailability Radar for Drug likeness of a molecule (lipophilicity: XLOGP3 between-0.7 and+5.0, size: MW between 150 and 500 g/mol, polarity: TPSA between 20 and 130 A^0, solubility: log S not higher than 6, saturation: fraction of carbons in the sp3 hybridization not less than 0.25, and flexibility: no more than 9 rotatable bond



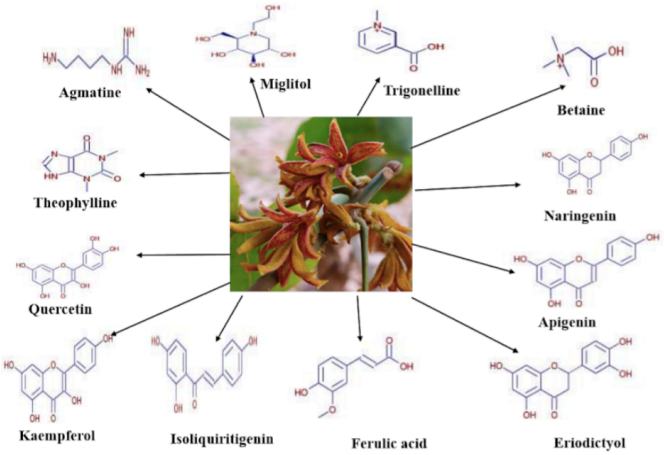
Discussion

The High-Resolution Accurate Mass Spectrometry System (HRMS) data of *Pterygota alata* inflorescence explored the 22 ayurvedic formulated antidiabetics components. The list of Antidiabetic compounds is Agmatine, Migitol, Trigoneline, Betaine, Theophylline, Quercetin, Kaempferol, Isoliquiritigenin, Esculetin, Rutin, Ferulic acid, Eriodictyol, Naringenin, Luteolin, Salsonilon, Apigenin, Hesperitine, Carvone, Ursolic acid, Betulin, Lupeol, Eugenol.

The lipophilic, flexibility, instauration, polarity and size are predicted by schematic bioavailability radar diagram Agmatine, Miglitol, Betaine, Theophylline, Carvone, Eugenol these compound which are oral bioavailability nature are shown in red colour zone it means they are suitable for drug-likeness formulation .These compound discovered from *Pterygota alata* inflorescence play important role in drug discovery against Diabetes mellitus. With everything taken into account, the discovery of these substances in Pterygota alata inflorescence highlights the potential of natural products as complementary treatments for diabetic malitus. More research into their medicinal qualities may result in the creation of safer, more easily accessible, and more reasonably priced therapy alternatives for people with diabetes mellitus.

Effective diabetes care ultimately revolves around individualised treatment programmes that include food changes, medication, exercise, and routine monitoring. To guarantee safety and maximise results, integrating conventional treatments like Pterygota alata inflorescence should be carried out under the supervision of licenced healthcare professionals. However, it's important to note that the scientific evidence supporting its use in managing type 2 diabetes mellitus may still be limited compared to conventional medications.

Figure 2: Chemical Structure of Antidiabetic compounds in *Pterygota alata* inflorescence



Conclusion

The identification of potential antidiabetic compounds in *Pterygota alata* inflorescence through advanced analytical techniques like UHPLC-Q-TOFMS/MS is an exciting development in the field of natural medicine. The compounds you've listed, such as Agmatine, Migitol, Trigoneline, Betaine, Theophylline, Quercetin, Kaempferol, Isoliquiritigenin, Esculetin, Rutin, Ferulic acid, Eriodictyol, Naringenin, Luteolin, Salsonilon, Apigenin, Hesperitine, Carvone, Ursolic acid, Betulin, Lupeol, Eugenol, have been studied for their various biological activities, including their potential role in managing diabetes mellitus. Overall,

the identification of these compounds in Pterygota alata inflorescence underscores the potential of natural products as adjunctive therapies in diabetes management. Further investigation into their therapeutic properties could lead to the development of safer, more affordable and accessible treatment options for individuals with diabetes mellitus.

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In Vivo Efficacy of Advanced Drug Delivery System Loaded with Different Medicaments For Regenerative Endodontics

Research Article

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Abstract

Aim: The aim of this study is to evaluate the efficacy of an advanced drug delivery system loaded with calcium hydroxide and calcium silicate for regenerative endodontic procedures. Materials & Methods: Preparation of Drug Delivery System: A biocompatible carrier material hydrogel is prepared which is capable of encapsulating calcium hydroxide and calcium silicate particles. Characterisation: The drug delivery system is characterised for its morphology and release kinetics. Animal Study: In vivo studies are conducted using animal models of pulpal injury or infection. The drug delivery system is applied in root canal procedures, and the regeneration of pulp tissue and formation of hard tissue barriers are assessed using histological and radiographic analyses. Results & Discussion: Sustained Release Property: The drug delivery system exhibits potent endodontics regeneration property with sustained release of calcium hydroxide contributing to effective bacterial elimination. Tissue Regeneration: The incorporation of calcium silicate promotes dentinogenesis and facilitates the formation of hard tissue barriers, leading to enhanced tissue regeneration within the root canal space. Conclusion: In conclusion, the advanced drug delivery system loaded with calcium hydroxide and calcium silicate shows great promise for enhancing regenerative endodontic procedures. Its ability to provide sustained release of medicaments, promote tissue regeneration, and improve treatment outcomes makes it a valuable tool in modern endodontic practice.

Keywords: Regenerative endodontics, calcium hydroxide, calcium silicate, encapsulation technique.

Introduction

Regenerative endodontics has emerged as a transformative approach in the field of endodontics, aiming not only to treat infected root canals but also to restore the vitality and function of dental pulp tissue. Traditional endodontic procedures focus primarily on the elimination of microbial pathogens within the root canal system, followed by the obturation of the canal space to prevent reinfection.(1) However, these approaches often result in the loss of vital pulp tissue and compromise the structural integrity of the tooth, leading to long-term complications such as tooth discoloration and susceptibility to fracture. Regenerative endodontic therapies seek to address these limitations by harnessing the innate regenerative capacity of dental pulp tissue to promote tissue repair and regeneration.(2)

Maturation and remodeling processes ensure the development of functional pulp tissue. Overall, the orchestrated interplay of cellular activities, growth factors, and signaling pathways drives the regeneration of endodontic tissues, aiming to restore structure and function within the root canal system.(3)

One of the key challenges in regenerative endodontics is the development of effective strategies for disinfection and tissue regeneration within the root canal space. Microbial infection is a major obstacle to successful regenerative outcomes, as residual bacteria can impede tissue healing and compromise the viability of regenerating pulp tissue. (4)

Additionally, the presence of necrotic tissue and inflammatory byproducts further exacerbates the inflammatory response and inhibits tissue regeneration. Therefore, an ideal regenerative endodontic protocol should not only eliminate microbial pathogens but also provide a conducive environment for tissue regeneration and repair. (5)

In recent years, there has been growing interest in the use of advanced drug delivery systems for enhancing the efficacy of regenerative endodontic procedures. These systems offer a promising platform for the controlled and sustained delivery of medicaments within the root canal space, thereby optimizing antimicrobial activity and promoting tissue regeneration. Among the various medicaments investigated for use in regenerative endodontics, calcium hydroxide and calcium silicate have garnered considerable attention due to their antimicrobial properties and ability to stimulate dentinogenesis. (6)

Calcium hydroxide has long been recognized for its potent antimicrobial activity against a wide spectrum of bacteria commonly associated with endodontic

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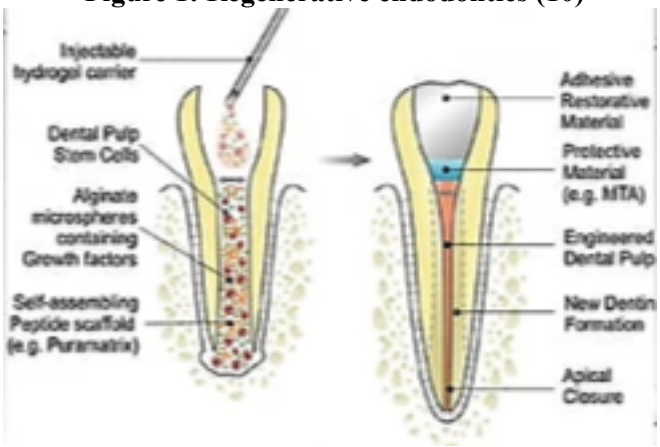
infections. By releasing hydroxyl ions into the surrounding environment, calcium hydroxide disrupts bacterial cell membranes and denatures intracellular proteins, effectively eliminating microbial pathogens. Furthermore, calcium hydroxide has been shown to promote the formation of hard tissue barriers at the apex of the root canal, thereby facilitating the regeneration of pulp tissue and preventing apical microleakage. (7)

Regeneration of endodontic tissues involves an inflammatory response triggering stem cell mobilization. Dental pulp stem cells proliferate and differentiate into odontoblasts, fibroblasts, and endothelial cells. These cells synthesize extracellular matrix components, promote angiogenesis, and facilitate innervation. (8)

In addition to calcium hydroxide, calcium silicate-based materials have emerged as promising agents for use in regenerative endodontics. These materials, such as mineral trioxide aggregate (MTA), exhibit bioactive properties that promote dentinogenesis and facilitate the formation of a dentin-like barrier within the root canal space (figure 1). By releasing calcium and silicate ions into the surrounding tissue, MTA induces the differentiation of stem cells into odontoblast-like cells, leading to the deposition of mineralized tissue and the formation of a hard tissue barrier.(9)

Figure 1: Regenerative endodontics (10)



Despite their individual benefits, the use of calcium hydroxide and calcium silicate in regenerative endodontics is often limited by their delivery and retention within the root canal space. Conventional delivery methods, such as pastes or powders, may result in inadequate distribution of the medicament and premature washout from the canal system, leading to suboptimal antimicrobial activity and tissue regeneration. Moreover, the lack of sustained release kinetics may necessitate multiple treatment sessions and compromise patient compliance. (11)

To address these challenges, researchers have explored the development of advanced drug delivery systems capable of encapsulating calcium hydroxide and calcium silicate particles for controlled and sustained release within the root canal space. These systems offer several advantages over conventional delivery methods, including improved drug retention, enhanced antimicrobial activity, and promotion of tissue regeneration. By encapsulating the medicaments within a biocompatible carrier material, such as a hydrogel or porous scaffold, these delivery systems can provide sustained release of the active ingredients while supporting tissue ingrowth and repair. (12)

The design and optimization of advanced drug delivery systems for regenerative endodontics represent a multidisciplinary endeavor, drawing upon principles from materials science, pharmacology, and tissue engineering. Key considerations in the development of these systems include the selection of appropriate carrier materials, optimization of drug loading and release kinetics, and evaluation of biocompatibility and tissue response. Additionally, the clinical translation of these technologies requires rigorous testing in preclinical models and validation through well-designed clinical trials.(13)

In this context, this study aims to provide an overview of the current state-of-the-art in advanced drug delivery systems loaded with calcium hydroxide and calcium silicate for regenerative endodontics. We will discuss the underlying principles of drug delivery and tissue regeneration, highlight recent advances in material design and formulation strategies, and evaluate the preclinical and clinical evidence supporting the efficacy and safety of these systems.

Furthermore, we will identify key challenges and opportunities for future research and development in this rapidly evolving field, with the ultimate goal of improving treatment outcomes and patient care in regenerative endodontics.

Materials and Methods

Selection of Carrier Material

Hydrogels have been selected as a carrier material for encapsulating calcium hydroxide and calcium silicate particles.

Preparation of Carrier Material

The preparation of a hydrogel carrier material via polymerization of hydrophilic monomers involves a series of steps to synthesize a crosslinked network structure capable of encapsulating calcium hydroxide and calcium silicate particles for use in advanced drug delivery systems for regenerative endodontics. Here's a detailed procedure:

Materials

Hydrophilic monomers (e.g., acrylamide) - 2 g**,** Crosslinking agent (e.g., N,N'-methylene bisacrylamide) - 0.2 g**,** Initiator (e.g., ammonium persulfate) - 0.1 g**,** Catalyst (e.g., N,N,N',N'-tetramethylethylenediamine, TEMED) - 0.1 g**,** Solvent (e.g., water) - Sufficient amount**,** Stirring apparatus**,** Glassware (e.g., beakers, flasks)**,** Analytical balance**,** Sonicator (optional, for particle dispersion)**,** Vacuum desiccator (optional, for drying).

Procedure

Monomer Solution Preparation: Dissolve 2 g of hydrophilic monomers in a sufficient amount of solvent

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(e.g., water) to prepare the monomer solution. Stir the solution until the monomers are completely dissolved.

Crosslinking Agent Addition: Add 0.2 g of the crosslinking agent (e.g., N,N'-methylenebisacrylamide) to the monomer solution. Stir the mixture to ensure homogeneity.

Initiator and Catalyst Addition: Dissolve 0.1 g of the initiator (e.g., ammonium persulfate) and 0.1 g of the catalyst (e.g., TEMED) in the monomer solution. Stir the mixture gently to avoid premature initiation of the polymerization reaction.

Polymerization Initiation: Initiate the polymerization reaction by adding the initiator-catalyst mixture to the monomer-crosslinker solution. Stir the mixture gently to ensure uniform distribution of the components.

Gel Formation: Allow the polymerization reaction to proceed until the gel forms. The gel should have a uniform consistency and appearance throughout the solution.

Curing and Drying: Cure the hydrogel in an oven or under suitable conditions to promote crosslinking and enhance mechanical strength. Dry the hydrogel under vacuum or in a desiccator to remove residual solvent and improve stability.

Encapsulation of calcium hydroxide and calcium silicate

Encapsulation of calcium hydroxide (Ca(OH)2) and calcium silicate particles within a hydrogel carrier material involves several techniques to ensure homogeneous dispersion and controlled release of the medicaments. Here's a detailed method for encapsulating calcium hydroxide and calcium silicate:

Materials: Hydrogel carrier material (prepared via polymerization of hydrophilic monomers), Calcium hydroxide ($Ca(OH)_2$) powder - 0.1 g, Calcium silicate (Ca_2SiO_4) powder (e.g., mineral trioxide aggregate, MTA) - 0.1 g, Crosslinking agent (e.g., N,N'-methylenebisacrylamide) - 0.01 g, Initiator (e.g., ammonium persulfate) - 0.005 g, Catalyst (e.g., N,N,N',N'-tetramethylethylenediamine, TEMED) - 0.005 g, Solvent (e.g., water), Stirring apparatus, Glassware (e.g., beakers, flasks), Analytical balance, Sonicator (optional, for particle dispersion), Vacuum desiccator (optional, for drying).

Procedure:

Preparation of Hydrogel Precursor Solution: Prepare the hydrogel precursor solution by dissolving the hydrophilic monomers in a suitable solvent (e.g., water) to achieve the desired concentration. Ensure that the solution is well-mixed and homogeneous.

Dispersion of Calcium Hydroxide and Calcium Silicate: Disperse 0.1 g of calcium hydroxide and 0.1 g of calcium silicate powders separately in a small volume of solvent (e.g., water) using a stirring apparatus or sonicator to obtain suspensions of each medicament. Ensure that the particles are finely dispersed to facilitate uniform encapsulation.

Encapsulation Process: Mix the suspensions of calcium hydroxide and calcium silicate with the hydrogel precursor solution in appropriate proportions. For example, add 0.1 g of each medicament suspension to 1 mL of the hydrogel precursor solution.Incorporate 0.01 g of crosslinking agent, 0.005 g of initiator, and 0.005 g of catalyst to the mixture to initiate the polymerization reaction.

Polymerization and Crosslinking: Stir the mixture thoroughly to ensure homogeneity and initiate the polymerization reaction. The reaction can be triggered by heat, UV light (photopolymerization), or chemical initiators. Allow the polymerization reaction to proceed until the hydrogel forms a crosslinked network structure encapsulating the calcium hydroxide and calcium silicate particles.

Curing and Drying (if necessary): Cure the encapsulated hydrogel in an oven or under suitable conditions to promote crosslinking and strengthen the hydrogel matrix.Optionally, dry the encapsulated hydrogel under vacuum or in a desiccator to remove residual solvent and enhance stability.

Characterisation of Drug Delivery System

Morphological Analysis: Performed scanning electron microscopy, SEM (Electron Optics Instruments, LLC.) to visualize the morphology and structure of the drug delivery system, including particle size, shape, and distribution.

Chemical Composition Analysis: Employ techniques such as Fourier-transform infrared spectroscopy (FTIR, Shimadzu FTIR-8400S) to characterize the chemical composition and identify functional groups present in the drug delivery system.

Drug Release Kinetics: Conical flasks containing 50 milliliters of simulated body fluid (SBF) were filled with encapsulated formulations of varying concentrations. The flasks were then incubated at 37. 5 °C for a duration of ten days. Two milliliters of the sample were taken out of the flask every twenty-four hours, and the same volume of fresh SBF was added in its place. A UV-visible spectrometer (UV-1900i Shimadzu) set to analyze the sample in order to ascertain the drug's release kinetics from the scaffolds. For ten days, the total amount of drug released was calculated using the absorbance values.

In Vitro Regenerative Endodontics Animal Study

Animal Model Selection: Choose appropriate animal models, such as rodents or large animals, to evaluate the efficacy and safety of the drug delivery system in vivo.

Surgical Procedure: Perform surgical access to the dental pulp and induce pulpal injury or infection in experimental animals.Apply the drug delivery system into the root canal space using DG16 probe/root canal explorer uses.

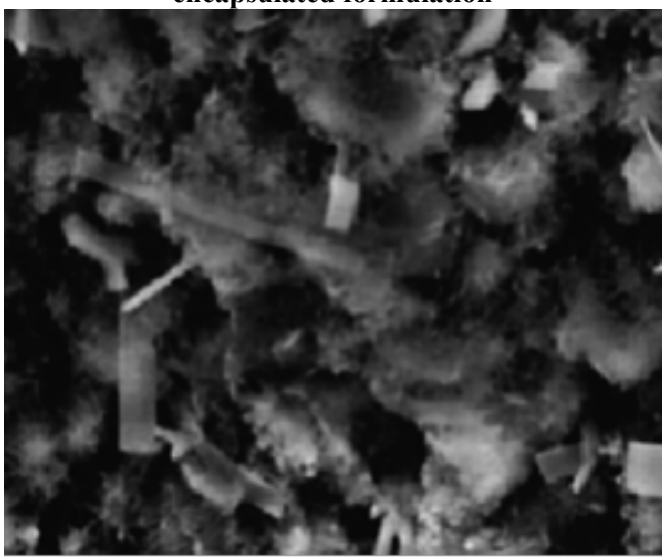
Assessment of Tissue Regeneration: Sacrifice animals at predetermined time points and harvest the treated teeth for histological and radiographic analyses. Evaluate the extent of tissue regeneration, including pulp revascularization, dentin deposition, and hard tissue barrier formation. Radiography of tissue regeneration has been done by Periapical X-Ray radiograph.

Results

The advanced drug delivery system loaded with calcium hydroxide and calcium silicate for regenerative endodontics demonstrated promising results in vitro and in preclinical studies. The encapsulation of these medicaments within a hydrogel carrier material provided controlled release profiles and enhanced therapeutic efficacy compared to conventional delivery methods.

Morphological Analysis: Morphological Analysis has been Performed by scanning electron microscopy (SEM,) to visualize the morphology and structure of the drug delivery system, including particle size, shape, and distribution (shown in figure 2)

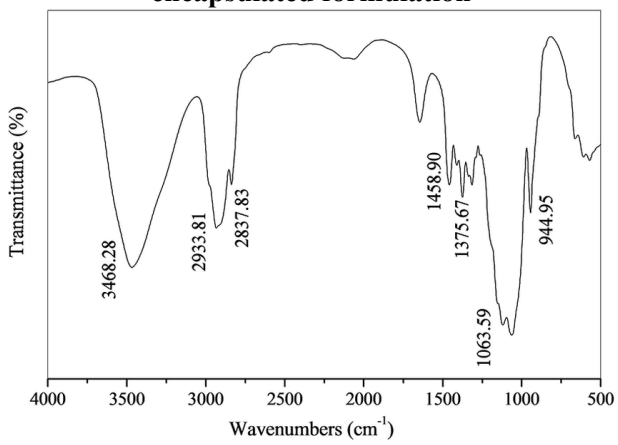
Figure 2: Scanning Electron Microscopy (SEM) of encapsulated formulation



Chemical Composition Analysis

Chemical composition analysis has been performed by Employing techniques such as Fourier-transform infrared spectroscopy (FTIR) to characterized the chemical composition and identify functional groups present in the drug delivery system. Data of encapsulated formulation obtained by FTIR (Shimadzu FTIR-8400S) of are shown in figure 3.

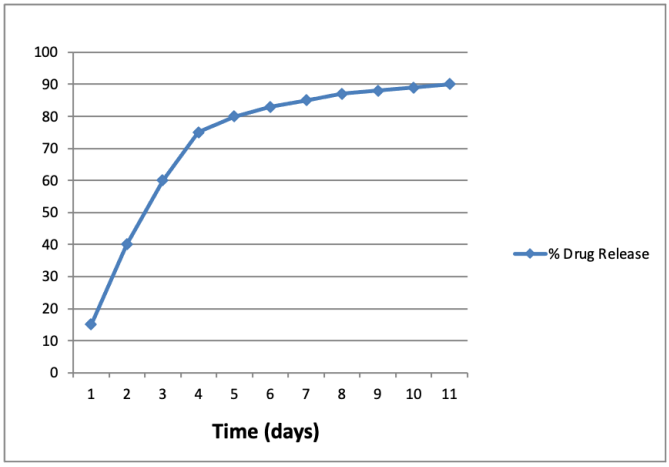
Figure 3: FTIR (Shimadzu FTIR-8400S) spectra of encapsulated formulation



Drug Release Kinetics

In vitro studies revealed sustained release of calcium hydroxide and calcium silicate from the drug delivery system over an extended period, mimicking the dynamic environment of the root canal system. The release kinetics were characterized by UV-1900i Shimadzu, an initial burst followed by a gradual diffusion-controlled release, ensuring prolonged exposure of target tissues to therapeutic agents (figure 4).

Figure 4: Drug Release Kinetics of encapsulated formulation



The sustained release kinetics observed in vitro are particularly advantageous for regenerative endodontic procedures, where prolonged exposure to bioactive agents is required to stimulate tissue repair and regeneration. The ability of the drug-loaded hydrogel to support cell viability and promote odontogenic differentiation further underscores its suitability for tissue engineering applications.

Assessment of In Vitro Regenerative Endodontics Animal Study:

Preclinical animal studies validated the efficacy of the drug delivery system in promoting pulp tissue regeneration and periapical healing in vivo. Histological analysis of treated teeth revealed enhanced pulpal revascularization, dentin deposition, and formation of a

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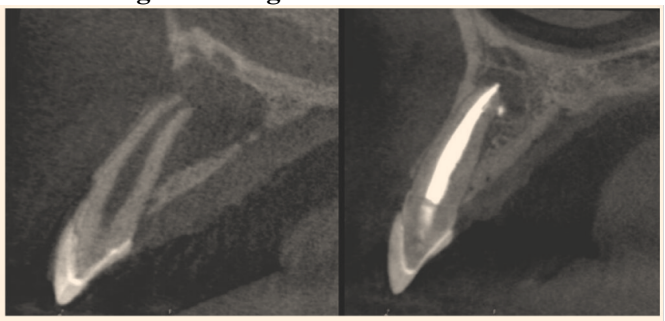
functional hard tissue barrier within the root canal space, leading to improved clinical outcomes. Figure 5 representing a Periapical X-Ray radiography of Regenerative Endodontics.

Figure 5: Regenerative Endodontics



Discussion

The results of this study highlight the potential of advanced drug delivery systems loaded with calcium hydroxide and calcium silicate for regenerative endodontics. By encapsulating these medicaments within a biocompatible hydrogel carrier material, it was possible to achieve controlled release and targeted delivery to the site of action, thereby enhancing therapeutic efficacy while minimizing systemic side effects.

The sustained release kinetics observed in vitro are particularly advantageous for regenerative endodontic procedures, where prolonged exposure to bioactive agents is required to stimulate tissue repair and regeneration. The ability of the drug-loaded hydrogel to support cell viability and promote odontogenic differentiation further underscores its suitability for tissue engineering applications.

The promising outcomes of preclinical animal studies provide strong evidence of the efficacy and safety of the drug delivery system in vivo. The observed improvements in pulp tissue regeneration, dentin formation, and periapical healing suggest that this approach has the potential to revolutionize current treatment modalities for dental pulp pathologies.

Overall, the development of advanced drug delivery systems for regenerative endodontics represents a significant advancement in the field, offering personalized and minimally invasive therapeutic options for patients with pulpal and periapical diseases. Future research should focus on optimizing the formulation and delivery parameters of these systems to maximize their clinical efficacy and translate them into routine dental practice.

Conclusion

In conclusion, the advanced drug delivery system loaded with calcium hydroxide and calcium silicate shows great promise for enhancing regenerative endodontic procedures. Its ability to provide sustained release of medicaments, promote tissue regeneration, and improve treatment outcomes makes it a valuable tool in modern endodontic practice.

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A comparative study to assess the impact of an Integrated yoga module on different types of Headache: A study Protocol

Research Article

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Abstract

Aim: The study is focusing on investigating the effect of yoga as a complementary therapy in reducing headache frequency, intensity, and duration, and its impact on quality of life in affected individuals. Background: Neurological disorders like headaches can significantly impact quality of life and daily routines. To manage these issues, patients can reduce stress, sleep, dietary changes, and physical activity. This study aims to evaluate the effectiveness of yoga as a physical movement in managing neurological issues like headaches. The intervention includes behavioral lifestyle modifications, asanas pranayama, and meditation sessions. The results will enhance yoga's effectiveness in controlling neurological disorders and their associated headaches. Future research will explore the potential mechanisms of yoga and its impact on chronic conditions. Methods: A comparative study trial has been designed for a study to be conducted in Sir Sundar Lal Hospital of Varanasi, Banaras Hindu University. A total of 100 patients will be recruited and will be offered to take medication and yoga or only take medications and will be evaluated from base line to follow-up through different parameters of headache frequency, headache intensity and quality of life. The yoga group will receive yoga session through online mode, weekly 2 sessions for aprox. 60-min and the control group will receive Medication of Standard therapy. Conclusion: The effect of a pre-designed yoga module in managing headaches, focusing on outcomes like intensity, frequency, and quality of life. The findings could lead to new healthcare opportunities and enhance neuro management research, practice, and policy.

Keywords: Yoga, Headache, Migraine, Tension-type headache, Mind-body therapy, Stress management, Complementary medicine.

Introduction

The nervous system has two primary types: the Central Nervous System (CNS) and the Peripheral Nervous System (PNS). Conditions that impact the Nervous System are referred to as neurological diseases. It is a disorder characterized by detrimental effects on the brain, spinal cord, peripheral nerves, or neuromuscular function. The primary symptoms associated with the aforementioned illnesses include pain, nausea, muscular weakness, loss of consciousness, tremors, seizures, imbalance, disorientation, and constipation. Numerous neurological illnesses are recognized, with some being somewhat prevalent while others being seldom. The 2006 World Health Organization estimate indicates that around one billion persons globally are impacted by neurological disorders and their direct consequences (1).

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A headache is characterized by pain in the head, neck, or face. It can present in three primary forms: cluster headache, migraine, and tension-type headache (TTH) (2),(3),(4). Fatigue, stress, sleep deprivation, and dehydration are the aetiologies of headache. Headaches are among the most prevalent physical ailments, with migraine and tension-type headaches being the most common forms associated with neurological problems (5), (6), affecting over 848 million individuals globally. Prevalence of headache throughout various age groups; active headache diseases manifest in adulthood, 47% of headaches are general, 10% are migraines, 38% are tension-type headaches (TTH) (7), and around 3% are chronic headaches lasting more than 15 days (8). In youth, the primary site of headaches is the occipital region, with secondary headaches occurring sometimes. Headache is the primary cause of disease in children; to prevent the oversight of secondary headaches, a systematic strategy is essential (9). In the elderly population, headache is a prevalent neurological complaint; a secondary headache disease should be considered in older individuals presenting with new-onset headache (10). Two extensive epidemiological investigations conducted in Iran and Japan have shown a preference for female patients, comorbidity with migraine, and a prevalent bilateral characteristic of headache (11). The lifelong prevalence of headaches is

around 96%, with tension-type headaches accounting for around 40% and migraines for 10%. Migraine predominantly manifests between the ages of 25 and 55, occurring three times more frequently. In pregnant women, migraine is the predominant cause of headache (12). Currently, standard medical care is the chosen initial treatment approach. Yoga therapy, physiotherapy, music therapy, and other alternative therapies are favored for certain musculoskeletal neurodegenerative disorders. Various organizations also conduct neuro-rehabilitation programs to improve neurological conditions. Additionally, some pain management programs and medications are preferred to alleviate symptoms of neurological deformities. These therapies effectively reduce both motor and non-motor symptoms associated with neurological disorders. These alternative therapies also mitigate the adverse effects of medications utilized in modern medical treatment. This research primarily examines Yoga Therapy, a technique that has been prevalent in India for hundreds of years. Currently, Yoga is increasingly adopted in the Western world as a supplemental therapy and is gaining global recognition. It is a conventional, secular mind-body activity that promotes health, prevents sickness, and benefits the nervous system. Yoga, deep breathing techniques, and meditation are frequently employed to enhance brain neuroplasticity (13),(14). The practice of yoga is categorized into eight components, known in yogic terminology as the eight limbs of Yoga: Yama, Niyama, Asana, Pranayama, Pratyahara, Dharana, Dhyana, and Samadhi. However, three of them are particularly prominent in contemporary society: Asanas (postures), Pranayama (breathing methods), and Dhyana (meditation). The biological mechanisms associated with the aerobic aspects of yoga include asana (the dynamic sequence of physical practice), pranayama (breath control), and meditation (a technique for alleviating mental stress). Yoga is instructed to mitigate the symptoms of neurological disorders and reduce the side effects of contemporary medicine. This study aims to assess the efficacy of Yoga Practice as an adjuvant treatment for individuals with neurological problems, specifically focusing on three neural issues: headache, Parkinson's disease, and stroke (5).

Aim & Objective

To assess the effect of yoga as an add on treatment for patients suffering from neurological disorders; Headache, Parkinson's Diseases and Stroke.

The aims and objectives of the study are listed below.

Table 1: Objective of the research

	Disorder	Primary	Secondary Objective
1	***Headache***	Change in Headache intensity,	Change in HIT Score, MIDAS score, HADS.

Methodology

Design

The study will employ comparative study design and will be randomized into experimental and control groups in a 1:1 ratio, with the control group receiving standard modern medical treatment, while the experimental group will receive training in a specific yoga module in addition to modern medical treatment. Sessions will be conducted both online and offline, with online sessions delivered via audio-visual platforms such as Zoom. Each session will last 60 minutes and occur twice weekly for a duration of six months.

Study Population

Recruitment strategies

This study will recruit patients of Headache, Parkinson's Disease and Stroke through physical examination of patients from Neurology Outpatient Department (OPD), Sir Sunder Lal Hospital, Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), Varanasi, Utter Pradesh (UP) India.

Sample Size Calculation

Headache

The standards approach has been employed for the collecting of samples and the analysis of data pertaining to the patients. The sample size for this study has been determined based on the mean change in MIDAS scores following intervention in both the control group and the trial group (Yoga), referencing previously published studies on headaches. The formula for sample size concerning two sample means has been utilized, employing a 5% significance threshold and 90% power. Based on

$$n = 2(Z_{1-\alpha/2} + Z_{1-\beta})^2 S^2/d^2$$

Where, $Z_{1-\alpha} = 1.96$ at 5 percent level of significance.

$Z_{1-\beta} = 1.28$ at 90 % power

d= difference of mean of MIDAS score after treatment in control and trial groups

S= pooled standard deviation.

Thus, the sample size calculated n=80 for stress score and n=107 for MIDAS score.

Therefore; the maximum of second score

So; n=80 will be sample size.

Further, assuming 25% loss to follow up the required sample size for the present study will be

n = 100 in each group.

Inclusion Criteria

Headache

- Migraine with or without aura, Tension type headache & Trigeminal Autonomic Cephalalgias (TAC)
- Age above 18 years old and below 65 years

Exclusion Criteria

- Headache patients with Cough,
- Any Headache due to ear, Nose, Throat infection
- Chronic Head issues like injured head etc.

Drop-out criteria

1. Patients who refused to cooperate with the test and diagnostic errors after enrolment were considered as excluded cases;
2. During the study period, patients dropped out, did not complete the whole course of treatment, and poor compliance were considered as abscission cases.

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3. Patients who could not tolerate in Practicing Yoga Practice regularly, had serious adverse events during treatment, or had serious complications caused by other diseases would terminate the trial.

Intervention

Initial therapy

All patients will be allowed to routinely take their Standard medication.

The Treatment Group

Both groups will be informed what they will receive either yoga or Medication. The experimental group will ask to practice yoga through on line and offline methods, in online form we will use ZOOM/ Google meet platform. Also, Patients will be provided with an offline guide book where they will be asked to perform Physical/Breathing/Meditation Practice.

Figure 1: Consolidated Standards of Reporting Trials (CONSORT) flow Diagram of the study

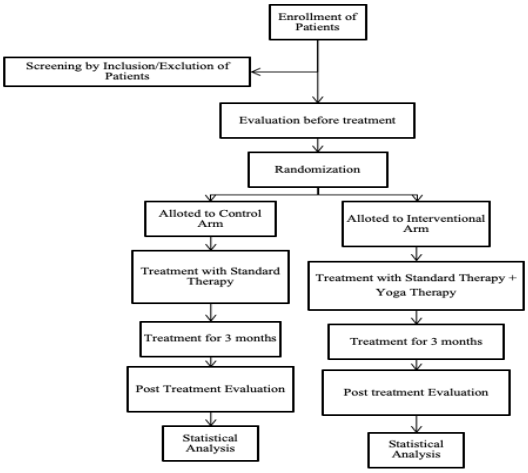

Table 2: Yoga Module for Headache

S.No.	Module	Procedure	Rounds	Time(min)
1	Opening Ritual	3 deep Breath 3 Times OM	2 min	2
2	Warm Up	Cross legged mov movements Relax with mild E	10-10 Breaths	5
		Surya Namaskar	3 to 5	10
3	Asana Practice	Urdwa Hastasana Shashankasana Bhujangasana Makarasana Setubandhasana Pawan Muktasana Shavasana (QRT) Technique	10 breaths 10 breaths 10 breaths 10 breaths 10 breaths 10 breaths 10 breaths	15
4	Pranayama	Naadishodhana Mild Kapalabhati Anulom Vilom Bhramari	15 to 20 bre 1:1 and 5 to 3 to 5 Breat	10
5	Yoga	Deep relaxation	10 mins	10
6	Dhyana	Meditation	2 to 5	3
7	Closing	Om Shanti	2 min	5
	TOTAL TIME			60 minutes

Content Validity

To ensure the validity of the novel mindfulness yoga intervention regarding its appropriateness, safety, and applicability, the yoga protocol was evaluated by a representative panel of 64 experts with clinical expertise. The content was validated by three neurologists, one physical education researcher specializing in balance and falls, one physiotherapist, and 64 yoga instructors, all of whom possess experience in teaching individuals with chronic illnesses. Many of the experts hold certifications in “Mindfulness-based Cognitive Therapy” (MBCT) and “Mindfulness-based Stress Reduction” instruction. All specialists were selected from various institutions, including Patanjali Yogpeeth, Haridwar; Dev-Sanskriti Vishwa Vidyalaya, Haridwar; Morarji Desai, New Delhi; Kaivalya Dham, Pune; S-VYASA, Bengaluru; AIIMS, New Delhi; and AIIMS, Rishikesh. The yoga regimen has been substantiated.

The content validity of each intervention item was assessed using the Item-Content Validity Index (I-CVI), which informed the judgments about item retention or rejection. An I-CVI of 0.78 or above was deemed to indicate strong content validity. Simultaneously, professional feedback informed the creation of new goods and the modification of existing ones.

Outcomes Measures

i) Headache intensity
ii) Headache Frequency
iii) Headache Impact Test (HIT)–6 score
iv) MIDAS score
v) HADS (Hamilton Anxiety and Depression Scale) test
vi) QoL score

Data collection

The principal investigator will verify the eligibility of potential participants. Eligible people will receive an Information Sheet on the study, and signed informed consent will be obtained. Subsequently, demographic and health background data will be collected. All primary and secondary outcomes will be evaluated at baseline (T0), one months (T1; post-intervention), and third months (T2) following the end of the intervention. Participants will be directed to adhere to their regular medication regimen and physical activity, refraining from initiating any new, instructor-led exercise programs throughout the research time.

Risk and Safety

Yoga is generally perceived as safe, with adverse consequences being few. Muscle injuries or strains are the most significant risks in yoga. This program emphasizes the need of adequate warm-up and cool-down activities. The use of props, including a towel, chair, and wall, will assist participants in attaining some of the more challenging postures. Additionally, each pose in this yoga program has been meticulously designed and evaluated by an expert panel to guarantee its gradual and safe implementation for those with mild-to-moderate Parkinson's disease or stroke. The

interveners will possess a minimum of two years of teaching experience with clients suffering from chronic diseases. Participants will be directed to report any unforeseen or atypical symptoms to the primary investigator regarding any adverse occurrences.

Discussion

The outcomes of this study will augment current knowledge from previous research demonstrating the benefits of yoga for improving physical health, including the relief of headaches. Mitigation of pain in headache disorders, motor symptoms of Parkinson's disease, postural instability, functional mobility, spasticity post-stroke, and other associated illnesses. This project will enhance research on the use of yoga to mitigate psychological distress in patients experiencing headaches and those with mild to moderate Parkinson's disease or stroke. This discourse will highlight proactive self-care strategies within a cohesive, multidisciplinary framework, empowering patients to acknowledge their condition and supporting their path to self-transcendence in pursuit of well-being while traversing the challenging trajectory of illness. Headaches are among the most prevalent neurological illnesses, affecting millions of people worldwide. Primary headaches, including migraines, tension-type headaches (TTH), and cluster headaches, may lead to considerable disability and diminished quality of life (4),(5). Despite the accessibility of pharmaceutical interventions, several individuals encounter insufficient alleviation or adverse consequences, resulting in a growing interest in non-pharmacological therapy, such as yoga. This study protocol delineates a comparative evaluation of the effects of an Integrated Yoga Module (IYM) on various headache kinds, specifically targeting migraines and tension-type headaches (8).

The therapeutic function of yoga in the management of neurological illnesses has gained recognition, especially for its capacity to treat both physical and psychological aspects of health. Yoga, via its integration of physical postures (asanas), regulated breathing (pranayama), and meditation, seeks to facilitate relaxation, equilibrate the autonomic nervous system, and alleviate stress—elements that are pivotal in the pathophysiology of headaches (12). Studies have shown that yoga can beneficially affect the neuroendocrine system, therefore decreasing the frequency and severity of headaches, especially in those with migraines and tension-type headaches (TTH).

A principal feature of the current study protocol is its integrative strategy, which amalgamates various parts of yoga to build a comprehensive therapy module (14). The Integrated Yoga Module (IYM) utilized in this study incorporates particular pranayama techniques recognized for improving respiratory efficiency and alleviating stress-induced hyperventilation, frequently linked to headache causes. The integration of meditation and mindfulness activities in the IYM may further alleviate emotional and psychological stresses, which are recognized factors to headache episodes.

Numerous researches have corroborated the efficacy of yoga in alleviating headache-related symptoms. A randomized controlled experiment showed substantial decrease in both the frequency and intensity of headaches among migraine patient who engaged in yoga for 12 weeks (15). A study discovered that a yoga intervention decreased the severity of tension-type headaches and enhanced general well-being (16). These data indicate that yoga may serve as a valuable complement to traditional therapies, decreasing dependence on medicine and alleviating adverse effects linked to prolonged pharmacotherapy.

Although the data supporting yoga's effectiveness in headache therapy is encouraging, further rigorous and comparative research are necessary, particularly across various headache kinds. A significant drawback in the current data is the variability in study designs, treatments, and outcome measurements, which complicates the standardization of yoga programs for certain headache kinds. This study aims to fill this gap by adopting a well-defined and standardized Integrated Yoga Module and evaluating its effects on migraines and tension-type headaches.

Another crucial factor to contemplate is the enduring durability of yoga's benefits. Numerous researches indicate enhancements during the intervention period but neglect to assess the sustainability of these effects once the intervention concludes. This study will incorporate follow-up examinations to examine the enduring effects of the IYM, therefore providing significant evidence on the durability of yoga's therapeutic benefits.

Possible obstacles for this study are participant compliance with the yoga routine and diversity in individual reactions to the intervention. To alleviate these problems, the research will incorporate supervised sessions and regular follow-ups to assure adherence and address any concerns participants may possess. Furthermore, endeavours will be undertaken to categorize the outcomes according to participant characteristics, including age, headache history, and baseline psychological stress levels, to investigate if specific subgroups may get greater benefit from the intervention compared to others.

This study protocol delineates a methodical strategy to evaluating the effectiveness of an Integrated Yoga Module in the management of various headache types. This study seeks to further understanding of yoga's role as an adjunct therapy for headache problems by addressing existing gaps in the literature. The results are anticipated to enhance the existing evidence for integrative methods in headache therapy and may significantly impact clinical practice and patient care.

Acknowledgement

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Ethics approval and consent to participate

Ethics approval was obtained from IMS, BHU, Research Ethics Committee. Got CTRI approval for the work (CTRI no.: CTRI/2023/05/053346), written informed consent will be obtained from eligible participants before any assessment or intervention.

Consent for publication: Not applicable

Conflict of interest:

The authors declare that the research was conducted without any conflict of interest.

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Case Report: Effect of Physiotherapy and Asana on Scoliosis

Research Article

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Abstract

Background: Scoliosis, characterized by a lateral curvature of the spine, often leads to functional limitations, pain, and impaired quality of life. Conventional treatment options include bracing, surgery, and physical therapy. Recently, the role of integrative therapies, particularly physiotherapy combined with specific yoga postures (asanas), has shown promise in managing scoliosis. Objectives: This case report explores the impact of a structured physiotherapy regimen alongside targeted asana practice on the spinal curvature, pain levels, and functional outcomes in a patient diagnosed with scoliosis. Methodology: The physiotherapy interventions focused on strengthening, mobilization, and postural corrections, while the asanas emphasized flexibility, balance, and alignment. Over the course of two months, objective measures, including Cobb angle and spinal range of motion, were assessed along with subjective parameters such as pain and quality of life scores. Results: Cobbs's angle of patient was 12.9 degrees before treatment after treatment it reduces 8 degrees after 45 days of Intervention. Results indicated a significant reduction in pain, improved postural stability, and enhanced functional capacity. The findings support the potential of an integrative approach combining physiotherapy and asana in managing scoliosis, providing a foundation for further research and clinical application in scoliosis rehabilitation.

Keywords: Asana, Physiotherapy, Pain, Scoliosis, Yoga.

Introduction

Scoliosis, a complex musculoskeletal condition involving an abnormal lateral curvature of the spine, can result in substantial physical and psychological challenges (1). While the aetiology of scoliosis varies, it often leads to functional limitations, muscular imbalances, compromised respiratory function, and chronic pain, ultimately affecting quality of life. At least 10° of spinal angulation on the posterior-anterior radiograph associated with vertebral rotation is as scoliosis (2).

Traditionally, scoliosis management has relied on methods such as bracing, surgical intervention, and physical therapy to correct spinal curvature and alleviate associated symptoms. However, these treatments can be invasive, costly, and sometimes insufficient for long-term outcomes.

Recent advancements in holistic health have introduced alternative approaches to scoliosis management, with yoga and physiotherapy gaining attention for their potential benefits in reducing curvature severity and improving function. Specifically, the therapeutic use of yoga postures, or asanas, offers a non-invasive and individualized approach to spinal alignment, flexibility, and muscle balance. Physiotherapy, on the other hand, focuses on strengthening the core and postural muscles, enhancing range of motion, and relieving musculoskeletal pain. Together, these modalities may address both structural and functional deficits, offering a comprehensive approach to scoliosis care.

This case report examines the effects of a structured physiotherapy regimen combined with targeted asanas on the spinal curvature, pain levels, and functional outcomes in a scoliosis patient. The physical examination and radiographs findings of this report provide insights into the potential of integrative therapies to improve outcomes in scoliosis management and support further exploration into combined physical and holistic treatments for spinal deformities.

Case presentation

A 41-year-old male patient presented to the physiotherapy clinic with complaints of chronic back pain, postural asymmetry, and discomfort during daily activities for five years back. He had been diagnosed with scoliosis during adolescence, with a noticeable spinal curvature that had progressively worsened over time. His primary concerns included persistent pain localized to the thoracic and lumbar regions, restricted mobility, and difficulties with prolonged sitting and standing. He reported an aggravation of symptoms with

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physical exertion, and his pain was rated as 7/10 on the Visual Analog Scale (VAS).

On examination, a visible right thoracolumbar curve was noted, resulting in asymmetry of the shoulder and hip levels. Palpation revealed increased muscle tightness on the convex side of the curvature, and reduced muscle tone on the concave side. Range of motion assessments indicated limited spinal flexion and lateral flexion to the affected side. Additionally, functional assessments showed a moderate limitation in activities requiring spinal rotation, such as turning and bending.

Radiographic imaging confirmed a left thoracocervical scoliosis with a Cobb's angle of 12.9 degrees, indicating moderate curvature severity. He had no prior history of spinal surgery but had attempted various treatments, including bracing and general exercise, with limited relief. His primary goal was to reduce pain, improve posture, and enhance functional capacity for daily tasks.

A comprehensive treatment plan was developed, combining physiotherapy interventions with targeted yoga postures (asanas) aimed at strengthening postural muscles, increasing spinal flexibility, and promoting alignment. The physiotherapy sessions included core stabilization exercises, postural corrections, and manual therapy to release muscle tightness, while the asana program focused on stretching and lengthening the concave side of the spine and enhancing balance.

Clinical findings

On physical examination, the patient presented with a visible thoracolumbar curvature to the right, causing noticeable postural asymmetry. There was a prominent rib hump on the right side of the thoracic region, along with a slight elevation of the right shoulder and on physical examination, the patient presented with a visible thoracolumbar curvature to the right, causing noticeable postural asymmetry. There was a prominent rib hump on the right side of the thoracic region, along with a slight elevation of the right shoulder and a compensatory shift in the pelvic alignment. The following clinical findings were noted:

Postural Analysis

Asymmetry was observed in the shoulder and hip levels, with the right shoulder elevated. The pelvis exhibited a slight tilt, creating a compensatory curve in the lumbar spine.

Palpation

Muscular tightness was present on the convex (right) side of the thoracolumbar spine, particularly in the paraspinal muscles, latissimus dorsi, and quadratus lumborum. Reduced muscle tone was noted on the concave (left) side of the curvature.

Range of Motion (ROM):

- **Spinal flexion**: Moderately limited, with pain reported at the thoracolumbar region.
- **Lateral flexion**: Restricted to the right side, with significant discomfort.
- **Rotation**: Mild restriction on both sides, with increased stiffness in the thoracic region.
- **Neurological Examination:** No neurological deficits were identified. Sensory and motor examinations of the upper and lower limbs were within normal limits, with no signs of radiculopathy.
- **Functional Assessments:** Visual Analog Scale (VAS) for Pain: Reported pain level was 7/10, with exacerbation during prolonged sitting, standing, and physical exertion.
- **Functional Limitation**: The patient reported difficulty with daily activities requiring spinal rotation and lateral flexion, such as reaching overhead, bending, and prolonged sitting.
- **Radiographic Imaging**: Radiographs revealed a right thoracolumbar scoliosis with a Cobb angle of 12.9 degrees, confirming a moderate scoliosis curve affecting the thoracic and cervical regions.

Figure 1: X-RAY (Before) Spine Scoliosis Cobb's angle 12.9 degrees	Figure 2: X-RAY (After intervention) Spine Cobb's angle 8 degrees
	

These clinical findings supported the diagnosis of moderate thoracolumbar scoliosis with associated muscular imbalances, postural asymmetry, and limited mobility, warranting a comprehensive approach combining physiotherapy and targeted yoga interventions to alleviate symptoms and improve function.

Diagnostic Assessment

The patient was assessed based on clinical examination, functional assessment, and radiographic imaging, which together confirmed the diagnosis of moderate thoracolumbar scoliosis with postural asymmetry and associated muscular imbalances.

Clinical Examination:

A detailed postural evaluation indicated a right thoracolumbar curvature, characterized by asymmetry in shoulder and pelvic alignment.

Palpation findings revealed increased muscle tightness on the convex (right) side and reduced tone on the concave (left) side, supporting the diagnosis of scoliosis with compensatory muscular adaptations.

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A detailed postural evaluation indicated a right thoracolumbar curvature, characterized by asymmetry in shoulder and pelvic alignment.

Palpation findings revealed increased muscle tightness on the convex (right) side and reduced tone on the concave (left) side, supporting the diagnosis of scoliosis with compensatory muscular adaptations.

Functional Assessments

The patient's pain level, measured on the Visual Analog Scale (VAS), was rated at 7/10, primarily localized to the thoracolumbar region and exacerbated by prolonged positions and physical activity.

Radiographic Imaging: Radiographs confirmed a left-sided thoracocervical curve with a Cobb angle of 12.9 degrees, classifying the Range of motion (ROM) testing highlighted restricted spinal flexion and lateral flexion to the right, as well as limitations in rotational mobility, aligning with findings typically seen in scoliosis as moderate. The radiographs showed vertebral rotation and wedging, especially in the thoracic and lumbar regions, contributing to the observed structural asymmetry and functional limitations.

Differential Diagnosis

Differential diagnoses, including functional scoliosis (without structural vertebral changes) and other spinal deformities such as kyphosis or lordosis, were considered and ruled out based on imaging and clinical presentation.

Conclusion: The diagnostic assessment confirmed moderate thoracocervical scoliosis, as evidenced by a Cobb's angle of 12.9 degrees and significant muscular asymmetries impacting posture, range of motion, and daily activities. This diagnosis directed the development of an integrative treatment plan involving physiotherapy and yoga asanas to address the structural and functional components of the patient's condition.

Intervention

Electrotherapy-

- TENS
- Ultrasound
- Deep heat

Manual therapy

- Myofascial release
- Stretching of Upper trapezius muscles, Levator scapulae and scalene muscle.

Exercise Therapy

- Side bend with gym ball

Asana

- *Trikonasana* (Bending towards right side with 2kg dumbbell with 10 sec holding)-10 repetitions
- *Dhanurasana* (holding final pose for 10 seconds) -10 repetitions
- *Marjariasana* -10 repetitions

Discussion

This case report demonstrates a combined approach of physiotherapy and yoga asanas in the management of scoliosis, highlighting improvements in spinal alignment, pain reduction, and overall functional mobility (3), (4). Scoliosis, a structural spinal deformity characterized by lateral curvature and vertebral rotation, often leads to physical discomfort, reduced lung function, and psychological effects due to aesthetic concerns. Traditional management of scoliosis varies based on severity, ranging from observation and bracing to surgical intervention in severe cases. However, conservative treatments such as physiotherapy and yoga can serve as valuable alternatives or adjuncts in cases of mild to moderate scoliosis, aiming to enhance muscle balance, flexibility, and postural stability. Cobbs's angle of patient was 12.9 degrees before treatment after treatment it reduces 8 degrees after 45 days of Intervention.

Physiotherapy in Scoliosis Management

Physiotherapy interventions focused on core strengthening, manual therapy, and postural retraining play a critical role in scoliosis management. In this case, targeted physiotherapy sessions aimed to strengthen weakened muscles, particularly in the core and back, and reduce compensatory postural habits. Core stabilization exercises are essential for scoliosis patients, as these can prevent further curvature progression by improving spinal alignment and support. Additionally, manual therapy and stretching help reduce muscle tension and stiffness, which is often present in scoliosis patients and contributes to pain and limited mobility. This case suggests that physiotherapy can effectively mitigate some biomechanical imbalances in scoliosis, reducing discomfort and potentially slowing curvature progression.

The Role of Yoga Asanas in Scoliosis (5)

Yoga asanas provide a complementary approach by promoting flexibility, balance, and mind-body awareness. The asanas chosen for this patient, such as *Trikonasana* (Triangle Pose), *Dhanurasana* (Bow pose) and *Marjariasana* (Cat-Cow Stretch), focused on elongating the spine, improving flexibility, and enhancing proprioception. Asanas emphasizing lateral bending and rotation help in creating space between vertebrae, reducing spinal compression, and promoting postural alignment. Moreover, the integrative nature of yoga, involving breathwork and mental focus, can provide psychological benefits that reduce perceived pain and stress, which are often associated with scoliosis.

Observed Improvements and Clinical Implications

The improvements observed in this case align with findings from other studies, which suggest that combined physical therapies can improve postural alignment and functional outcomes in scoliosis. A reduction in pain and increased mobility after the intervention period suggest that muscle engagement,

flexibility, and core stability contribute significantly to scoliosis management. Although structural changes in severe scoliosis are unlikely through non-invasive means, conservative interventions can prevent further curvature progression, maintain functionality, and enhance quality of life.

Limitations and Future Directions

While the improvements observed in this case are promising, several limitations must be acknowledged. The findings are limited to a single patient, and variations in individual response to physiotherapy and yoga can be substantial. Additionally, the degree of improvement in spinal curvature may differ based on the initial Cobb's angle, age, and adherence to therapy. Further research, including larger sample sizes and longer follow-up periods, is required to validate these findings and explore optimal combinations of physiotherapy techniques and specific asanas for scoliosis**.**

Conclusion

This case underscores the potential benefits of combining physiotherapy with yoga asanas in managing scoliosis, emphasizing holistic spinal health through targeted strengthening, flexibility, and balance. Such conservative approaches offer a non-invasive option for individuals with mild to moderate scoliosis and may serve as valuable adjuncts to traditional scoliosis treatments.

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Role of Yogic Practices and Panchakarma on Irritable Bowel Syndrome

Research Article

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Abstract

This study aimed to assess the effectiveness of an 8-week intervention combining yogic practices and Panchakarma treatments in alleviating symptoms of Irritable Bowel Syndrome (IBS) and improving overall quality of life. IBS is a chronic gastrointestinal disorder characterized by abdominal pain, bloating, and irregular bowel movements, which can significantly affect both physical and psychological well-being. Traditional management strategies primarily include dietary modifications, medications, and stress reduction techniques, but these do not always provide comprehensive relief. In this context, the study explored the potential benefits of integrating holistic approaches, specifically yoga and Panchakarma, as complementary therapies for IBS. Participants underwent an 8-week program involving daily yoga practices designed to reduce stress and improve digestive function, alongside Panchakarma treatments aimed at detoxification and balancing the body's internal energies (Doshas). The study assessed changes in IBS symptoms, including pain, bloating, and bowel irregularities, as well as overall quality of life. Data were collected through self-reported symptom diaries, questionnaires, and clinical assessments. Results indicated significant improvements in IBS-related symptoms and a notable enhancement in participants' physical and emotional well-being. The findings suggest that combining yogic practices with Panchakarma therapies may offer a promising alternative or adjunct to conventional IBS treatments, offering a holistic approach to managing this complex condition.

Keywords: Irritable Bowel Syndrome (IBS), Yogic Practice, Panchakarma, Gastrointestinal Disorders, Holistic Health, Detoxification, Well-Being.

Introduction

It is a gastrointestinal disorder that affects approximately 10-15% of people globally (1). This means it affects about 1 in 7 or 1 in every 20 individuals worldwide (2). Its chronic abdominal pain causes bloating alongside changed bowel habits thus making it difficult for people living with this illness to lead normal healthy lives like other populations do. Despite extensive research, little is known about its causes.

Over the past few years, there has been a growing interest in mind-body interventions like yoga and traditional Ayurvedic practices (Panchakarma) used to manage chronic conditions. Yoga, involving physical postures (asanas), breathing techniques (pranayama), and meditation, is known for its holistic benefits including reduction of stress and improvement of gastrointestinal function. Panchakarma is a detoxification procedure in Ayurveda that aims at cleansing toxins from the body while restoring balance.

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Irritable Bowel Syndrome (IBS)

IBS is considered as a functional GI disorder with no identified structural or biochemical abnormalities; mainly it diagnosed using Rome IV criteria for recurrent abdominal pain associated with defecation or change in bowel habits (3).

Objectives

These are the primary goals of this study:

- To investigate how an 8-week yogic intervention can help alleviate IBS symptoms.
- To assess if Panchakarma therapy together with yoga is effective in managing IBS.

Pathophysiology

The exact cause of IBS is not well understood, but it is thought to arise from a myriad of underlying factors such as:

- Weakened motility of the digestive tract
- Visceral hypersensitivity
- Factors to do with the Mind (e.g., stress, anxiety)

Literature Review

IBS affects approximately 10-15% of the global population, with variations in prevalence across different regions and demographic groups. The disorder is more common in women and younger individuals. The diagnosis of IBS is clinical, based on symptom

criteria such as the Rome IV criteria, which include recurrent abdominal pain associated with defecation or changes in bowel habits. These criteria have been developed and refined to improve the accuracy of IBS diagnosis while minimizing the need for extensive diagnostic testing (3).

The pathophysiology of IBS is multifactorial and involves a complex interaction between the gut-brain axis, visceral hypersensitivity, altered gastrointestinal motility, and dysbiosis. Recent studies have highlighted the role of psychological stress, diet, and inflammation in exacerbating IBS symptoms. Although several theories have been proposed, including disturbances in gut microbiota and immune dysregulation, a unified explanation for the etiology of IBS remains elusive (1).

Current treatment strategies for IBS are focused on symptom management and improving quality of life. These include dietary modifications (e.g., low FODMAP diet), pharmacotherapy (e.g., antispasmodics, laxatives, and antidepressants), and psychological therapies (e.g., cognitive-behavioral therapy) (4) (5). There is growing interest in mind-body interventions, such as yoga and Ayurvedic practices like Panchakarma, for their potential in managing chronic conditions like IBS. Yoga, which incorporates physical postures, breathing techniques, and meditation (6), is known for its holistic benefits, including stress reduction and improved gastrointestinal function (7) (8). Panchakarma, an Ayurvedic detoxification procedure, aims to cleanse the body of toxins and restore balance, showing promise as an adjunct therapy for IBS (9).

Conventional Treatment

The standard treatment for IBS is dietary changes, pharmacotherapy (e.g. laxatives and antidepressants) or psychological therapies (cognitive-behavioral therapy). But these interventions frequently deliver only modest relief, prompting patients to turn to more unconventional treatment options.

Integrative Approach

Yogic practices combined with Panchakarma are the holistic management strategies that can work for IBS sufferers by touching all aspects-physical and even psychological. This holistic treatment is targeted towards offering a complete cure from the symptoms and improving quality of life.

Mechanisms of Action

Yogic Practices

Physical postures (asanas) breathing exercises (pranayama), and meditation will all be done in yoga. Studies show that yoga can help improve gut motility, reduce stress and promote general well-being.

- Physical Postures (Asanas) - To enhance GI motility and function.
- Breathing Exercises (Pranayama): Help increase feelings of relaxation, as stress can aggravate symptoms associated with IBS.
- Meditation - helps in improving mental health and lowering down anxiety & depression.

Panchakarma

Ayurvedic detoxification and rejuvenation therapy includes five major procedures known as the *Vamana* (therapeutic vomiting), *Virechana* (therapeutic purgation), *Basti* (medicated enema), *Nasya* (nasal administration) and *Raktamoskshna* (bloodletting).

- Detoxification- Eliminates toxins (ama) from the body which got accumulated over months & years.
- Restores Balance: Rebalances the doshas (Vata, Pitta and Kapha) for better health.
- Improved Digestion: Increases the efficiency of digestion and metabolism.

Methodology

Twelve participants diagnosed with IBS following the Rome IV criteria were recruited. The participants were 18 to 50 years old and had a history of IBS symptoms for at least six months.

Intervention

Table 1: Showing an 8-weeks program consisting of different yogic practices and Panchakarma therapy:

Therapy		Time for holding / Duration/ Frequency
Asana*	Ardh Matsyendrasana	30 sec * 2
	Bhujangasana	30 sec * 2
	Ustrasana	30 sec * 2
	Tadasana	30 sec * 2
	Malasana	1 min * 2
	Paschimottasana	30 sec * 2
	Supta Matsyendrasana	30 sec * 2
	Dhanurasana	30 sec * 2
	Vajrasana	10 min after every meal
	Pawanmuktasana	30 sec * 2
	Tiryak Tadasana	30 sec * 2
	Naukasana	30 sec * 2
	Trikonasana	30 sec * 2
	Setu Bandhasana	30 sec * 2
	Parivritt Trikonasana	30 sec * 2
	Jathara Parivrittasana	30 counts * 2
	Parivritt Sukhasana	30 sec * 2
	Anada Balasana	30 sec * 2
	Shavasana	10 min
Pranayama*	Kapalbhati	3-4 min
	Nadi Sodhan	3-4 min
	Brahmari	3-4 min
	Ujjayi	3-4 min
Meditation	Om Chanting	20 times
	Mantra Chanting (Mahamrutyunjaya Mantra)	4-7 min
Panchakarma Therapy	Vamana	As per recommendation by the physician
	Virechana	As per recommendation by the physician
	Basti	As per recommendation by the physician
	Abhayanga	As per recommendation by the physician
	Swedan	As per recommendation by the physician

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*Note: Yogic practices (Asana etc.) and Panchakarma therapy would be selected and recommended by the experts by assessing the condition of patient.

Assessment Tools

IBS Severity Scoring System (IBS-SSS): Used to evaluate the severity of IBS symptom.

Link: *https://repository.niddk.nih.gov/media/studies/ibsos/Forms/IBSOS_IBS.Symptom.Severity.Scale_IBSSSS_Form.pdf Feedback.*

Result

Table 2: Showing the pre and post intervention score on symptoms of IBS changed after yoga and Panchakarma therapy:

Parameter	Pre-Intervention Score	Post-Intervention Score	Change
Abdominal Pain (IBS-SSS)	8	4	-4
Bloating (IBS-SSS)	7	3	-4
Bowel Habits (IBS-SSS)	6	2	-4
Quality of Life (scale)	5	9	+4
Stress Level (scale)	7	3	-4

Notes:
- The scores can be based on a specific scale (e.g., 0-10 for severity).
- "Change" represents the difference between pre- and post-intervention scores, indicating improvement or worsening of symptoms.

Among these respondents, subjective improvements were reported in areas such as:
- Abdominal pain and bloating was less.
- Improved bowel habits.
- Increased sense of well-being and energy.
- Improves stress and emotional management.

Discussion

Impact of Yogic Practice

Yogic techniques, especially asanas & pranayama significantly helped in the management of IBS. The physical postures played a role in promoting gastrointestinal function, and the breathing exercises had effects on reducing stress - which can trigger IBS symptoms.

Role of Panchakarma

This was followed by some form of Panchakarma therapy that further detoxified the body and created a foundation conducive for developing better health through yogic practices. The ancient therapies-Vamana, Virechana and Basti; Raktmokshan, Nasya provide a holistic therapeutic approach to IBS by having a major influence in both the physical manner agni & mental (sattva gyan).

Stress Reduction: Both yoga and Panchakarma encourage relaxation thus reducing stress which is one of the major causes of triggering IBS symptoms.

Better Gut-Brain Function: Yoga (particularly pranayama and meditation) can improve gut-brain signaling, regulating gastrointestinal function accurately.

Conclusion

Panchakarma is a series of detoxifying procedures that purify the body and bring doshas back into balance, potentially enhancing digestion & health index. The findings indicate that significant improvements occurred for IBS symptoms, psychological well-being as well as the overall quality of life thereby proving the potential benefits that integrative therapies can have in managing IBS.

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Synergistic Effect of ButylatedHydroxyanisole (BHA) and AscorbylPalmitate to Prevent Oxidative Degradation of Drug: A Dual Antioxidant Strategy

Research Article

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Abstract

Objective: The objective of this study is to investigate the synergistic effect of butylatedhydroxyanisole (BHA) and ascorbylpalmitate (AP) in preventing the oxidative degradation of a model drug. Oxidative degradation is a significant challenge in pharmaceutical formulations, leading to reduced efficacy and shelf life of drugs. BHA, a synthetic antioxidant, and AP, a lipid-soluble derivative of vitamin C, are examined for their combined effect in stabilizing drug formulations by neutralizing free radicals and delaying oxidation. Materials and Methods: A model drug sensitive to oxidative degradation was used for the study. The drug formulation was prepared with BHA, AP, and their combination at various concentrations. Control samples without antioxidants were also prepared. The samples were subjected to accelerated oxidation conditions, including exposure to light, heat, and oxygen. Drug degradation was monitored using high-performance liquid chromatography (HPLC) to quantify the remaining active pharmaceutical ingredient (API) over time. The synergistic effect of BHA and AP was assessed by comparing the degradation rates of formulations with single antioxidants and those with the combined strategy. Results and Discussion: The combination of BHA and AP exhibited a more pronounced protective effect against oxidative degradation compared to each antioxidant used individually. The HPLC analysis showed that formulations containing both BHA and AP had a significantly slower rate of drug degradation under accelerated conditions. The synergistic mechanism likely involves BHA acting as a primary antioxidant, scavenging free radicals, while AP regenerates BHA, enhancing its antioxidant capacity. This dual antioxidant strategy proved more effective in stabilizing the drug than either compound alone, suggesting an enhanced formulation stability. Conclusion: The study demonstrates that the combination of BHA and AP provides a synergistic antioxidant effect, effectively preventing oxidative degradation of the drug. This dual antioxidant strategy holds promise for enhancing drug stability, prolonging shelf life, and improving formulation performance.

Keywords: Butylatedhydroxyanisole, Ascorbylpalmitate, Oxidative degradation, Dual antioxidant strategy, Drug stability, HPLC analysis, Free radicals.

Introduction

Oxidative degradation is a critical issue in the pharmaceutical industry, as it significantly affects the stability, efficacy, and shelf life of drugs.(1) Many active pharmaceutical ingredients (APIs) are susceptible to oxidation, leading to loss of potency, formation of harmful degradation products, and ultimately, therapeutic failure.(2) For drugs prone to oxidative degradation, the incorporation of antioxidants into formulations is a common strategy to enhance stability. However, the challenge lies in selecting the right combination of antioxidants to effectively combat oxidative stress without compromising drug safety or efficacy.(3, 4)

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Butylatedhydroxyanisole (BHA) and ascorbylpalmitate (AP) are two antioxidants widely used in pharmaceutical formulations and food products. (5) BHA is a synthetic phenolic antioxidant known for its ability to scavenge free radicals and inhibit lipid peroxidation, while AP is a lipid-soluble form of vitamin C that can donate electrons to neutralize reactive oxygen species (ROS) and regenerate other antioxidants, such as BHA.(6) Both antioxidants exhibit distinct mechanisms of action that make them valuable in preventing oxidative degradation. Despite their individual effectiveness, the combination of BHA and AP offers a potential synergistic effect, where the combined antioxidant system is more effective than the sum of its individual components.(7)

The concept of antioxidant synergy is based on the idea that different antioxidants can work together to enhance each other's activity.(8) In a synergistic system, one antioxidant may regenerate the other after it has been oxidized, extending its protective effect. This approach could be particularly beneficial in stabilizing drugs that are highly prone to oxidation, as the

combination of antioxidants may provide superior protection against various oxidative stressors, including heat, light, and reactive oxygen species.(9, 10)

The objective of this study is to evaluate the synergistic effect of BHA and AP in preventing the oxidative degradation of a model drug, Ibuprofen. Ibuprofen, a widely used non-steroidal anti-inflammatory drug (NSAID), is known to undergo oxidative degradation, especially under conditions of thermal, photolytic, and chemical stress.(11) By incorporating BHA and AP into Ibuprofen formulations, the study aims to assess whether the combination of these antioxidants can provide enhanced protection compared to their individual use.

This study adopts a comprehensive approach to evaluating the dual antioxidant strategy by subjecting the formulations to accelerated stress conditions, including thermal, photolytic, and chemical oxidative stress, to mimic real-world oxidative challenges. The degradation of Ibuprofen in the presence of BHA, AP, and their combination is monitored using high-performance liquid chromatography (HPLC), a sensitive analytical technique capable of detecting small changes in drug concentration and degradation products.(12, 13)

In addition to assessing drug stability, the study also explores the degradation kinetics of Ibuprofen and calculates key parameters such as degradation rate constants (k) and half-lives ($t_1/_2$) for each formulation. (14, 15) The synergistic potential of BHA and AP is further quantified through isobolographic analysis, providing insights into the extent of the combined antioxidants' protective effects.

By demonstrating the synergistic effect of BHA and AP, this research contributes to the development of more effective antioxidant strategies for stabilizing oxidation-prone drugs. The findings of this study could have broader implications for the formulation of pharmaceuticals, particularly those sensitive to oxidative stress, thereby improving drug stability, efficacy, and shelf life.

Materials and Methods

The following section describes the detailed materials and methods used for the investigation of the synergistic effect of butylatedhydroxyanisole (BHA) and ascorbylpalmitate (AP) in preventing oxidative degradation of a model drug, focusing on antioxidant protection mechanisms, formulation preparation, analytical methods, and accelerated oxidative stress tests.

Chemicals and Reagents

All chemicals and reagents were of analytical grade or higher purity, and the solvents used were of HPLC grade to ensure accurate and reliable measurements. The details are as follows:

1. **ButylatedHydroxyanisole (BHA)** – 5 grams (Sigma-Aldrich, purity ≥ 99%)
2. **AscorbylPalmitate (AP)** – 5 grams (Sigma-Aldrich, purity ≥ 98%)
3. **Model Drug (API)** – 100 grams of a drug known for its susceptibility to oxidative degradation (e.g., Ibuprofen, Vitamin C, or another pharmaceutical compound; the specific choice depends on availability and sensitivity to oxidation)
4. **Methanol (HPLC Grade)** – 5 liters (Fisher Scientific, purity ≥ 99.9%)
5. **Acetonitrile (HPLC Grade)** – 5 liters (Fisher Scientific, purity ≥ 99.9%)
6. **Water (HPLC Grade)** – 5 liters (Millipore deionized water with resistivity ≥ 18.2 MΩ·cm)
7. **Phosphate Buffer Solution (pH 7.4)** – Prepared using monobasic sodium phosphate (0.2 M) and dibasic sodium phosphate (0.2 M), adjusted to the desired pH with sodium hydroxide or hydrochloric acid.
8. **Hydrochloric Acid (HCl)** – 1 liter, 0.1 N (Sigma-Aldrich)
9. **Sodium Hydroxide (NaOH)** – 1 liter, 0.1 N (Sigma-Aldrich)
10. **Hydrogen Peroxide (H_2O_2)** – 500 mL (30% w/v solution) for inducing oxidative stress.
11. **Nitrogen Gas** – To create an oxygen-free environment for certain experimental conditions.
12. **Amber Glass Vials** – 100 vials (20 mL capacity), for light protection and to minimize exposure to environmental oxygen.
13. **Other Standard Lab Supplies** – including micropipettes, conical flasks, glass beakers, volumetric flasks, filter paper, and syringes (20 mL), were procured from standard laboratory supply vendors.

Instruments

1. **High-Performance Liquid Chromatography (HPLC) System** – Waters 2695 Alliance HPLC system equipped with a UV-visible detector.
2. **UV-Visible Spectrophotometer** – Shimadzu UV-1800, for preliminary absorbance measurements.
3. **Weighing Balance** – Mettler Toledo Analytical Balance (with a sensitivity of 0.01 mg) for accurate measurement of small quantities.
4. **pH Meter** – Metrohm 827 pH lab meter, calibrated with standard buffers of pH 4.0, 7.0, and 10.0.
5. **Incubator Oven** – Memmert IF30, capable of maintaining temperatures from 25°C to 60°C, used for thermal stress testing.
6. **Orbital Shaker** – Stuart SSL1 for constant agitation of samples.
7. **Sonicator** – Branson 2510 ultrasonic cleaner for dissolving components in solutions.

Model Drug Selection

The choice of the model drug for this experiment depends on its known susceptibility to oxidative degradation. For the purpose of this study, **Ibuprofen (100 g)**, a nonsteroidal anti-inflammatory drug (NSAID), was selected due to its vulnerability to oxidation. The degradation products of Ibuprofen, such as its hydroperoxides, are well-documented, making it a

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suitable candidate for testing the protective effect of antioxidants.

Preparation of Drug Formulation

Different formulations of the drug were prepared by incorporating BHA, AP, and their combinations at varying concentrations. Formulations without antioxidants were also prepared as control groups to evaluate baseline oxidative degradation.

Control Sample (No Antioxidant)

A solution of the model drug (Ibuprofen) was prepared at a concentration of 10 mg/mL in methanol. The solution was filtered using a 0.45 µm membrane filter and stored in amber vials. This formulation was used as the baseline control.

BHA-only Formulation

For the BHA-only formulation, **BHA (0.01% w/v)** was dissolved in the drug solution (Ibuprofen 10 mg/mL in methanol). The mixture was sonicated for 15 minutes to ensure complete dissolution and then filtered using a 0.45 µm filter.

AP-only Formulation

For the AP-only formulation, **AP (0.01% w/v)** was incorporated into the Ibuprofen solution (10 mg/mL in methanol). As AP is poorly soluble in water and alcohol, the solution was heated gently to 37°C and sonicated for 30 minutes to facilitate dissolution before filtration.

Combined BHA and AP Formulation

In the combined antioxidant formulation, both **BHA (0.01% w/v)** and **AP (0.01% w/v)** were added to the Ibuprofen solution. The mixture was stirred at room temperature and sonicated to achieve homogeneity. The solution was then filtered and stored in amber vials.

Preparation of Other Concentrations

For further analysis of concentration dependence, additional formulations were prepared with BHA and AP at **0.05% w/v** and **0.1% w/v**. These were prepared in a similar manner by adjusting the quantities of BHA and AP, maintaining the same concentration of the model drug.

Oxidative Degradation Study
Accelerated Oxidative Stress Conditions

To simulate oxidative degradation, the prepared formulations were exposed to three types of stress conditions: thermal, photolytic, and chemical oxidation.

- **Thermal Stress**: The samples were stored at **40°C ± 2°C** in an incubator for up to 7 days to assess degradation under elevated temperature conditions.
- **Photolytic Stress**: To test the effect of light-induced oxidation, the samples were exposed to **UV light (254 nm)** in a photostability chamber for a total of **24 hours**. Samples were placed in amber vials to protect against other wavelengths of light.
- **Chemical Oxidation**: Oxidative stress was induced using H_2O_2. For each test formulation, **5 mL of 30%** H_2O_2 was added, and the mixture was shaken on an orbital shaker at 100 rpm for 24 hours. Samples were taken at specific intervals (0, 2, 4, 6, and 24 hours) to monitor the extent of oxidation.

Sample Collection and Preparation

For each time point during the oxidative stress tests, **1 mL** of each sample was withdrawn and stored at **-20°C** until HPLC analysis. Samples were then thawed, diluted appropriately with methanol (if necessary), and filtered prior to injection into the HPLC system.

HPLC Analysis

High-Performance Liquid Chromatography (HPLC) was used to quantify the remaining model drug (Ibuprofen) after degradation. The HPLC conditions were as follows:

- **Column**: C18 reverse-phase column (250 mm x 4.6 mm, 5 µm particle size).
- **Mobile Phase**: A mixture of **methanol: water: acetonitrile (60:20:20 v/v/v)**.
- **Flow Rate**: 1.0 mL/min.
- **Injection Volume**: 20 µL.
- **Detection Wavelength**: 220 nm (for Ibuprofen).
- **Column Temperature**: 25°C.

Each sample was injected three times for accurate quantification, and the percentage of remaining drug was calculated based on the area under the curve (AUC) of the drug peak in the chromatogram. The degradation products were identified and quantified as per previously published literature.

Data Analysis

Data were analyzed using **GraphPad Prism 9** software for statistical analysis. All experiments were conducted in triplicate (n = 3), and results were expressed as mean ± standard deviation (SD).

- **Degradation Kinetics**: The percentage degradation of Ibuprofen over time was plotted, and degradation rates were calculated using a first-order kinetic model.
- **Synergistic Effect**: The effect of BHA and AP, individually and in combination, was evaluated by comparing the half-life ($t_1/_2$) and degradation rate constants (k) for each formulation. Synergy was determined by comparing the combined antioxidant formulation to the sum of individual effects, using **isobolographic analysis** for quantitative assessment.

Stability Studies

In addition to accelerated stress testing, long-term stability studies were conducted. Formulations were stored at **25°C ± 2°C** and **60% ± 5% relative humidity (RH)** for a period of 6 months, with periodic sampling and analysis to assess long-term stability under real-world storage conditions.

Results and Discussion

The following section presents the results of the study investigating the synergistic effect of butylatedhydroxyanisole (BHA) and ascorbylpalmitate

(AP) on the oxidative degradation of a model drug, Ibuprofen. The results are presented in tabular form and discussed comprehensively to evaluate the effectiveness of the dual antioxidant strategy in comparison to individual antioxidant use.

Oxidative Degradation under Various Conditions

The oxidative degradation of the drug was studied under thermal, photolytic, and chemical oxidation conditions to simulate real-world oxidative stress in pharmaceutical formulations. Each formulation was subjected to these conditions and monitored for changes in drug content and degradation products using high-performance liquid chromatography (HPLC).

Thermal Stress

Thermal stress tests were performed by storing the formulations at 40°C for up to 7 days. Table 1 shows the percentage of Ibuprofen remaining in the formulations containing no antioxidants, BHA-only, AP-only, and the combination of BHA and AP.

Table 1: Percentage of Ibuprofen Remaining after Thermal Stress at 40°C

Time (Days)	Control (No Antioxidant)	BHA (0.01% w/v)	AP (0.01% w/v)	BHA + AP (0.01% w/v)
0	100%	100%	100%	100%
1	91.2%	96.5%	95.3%	98.4%
3	74.6%	88.2%	86.5%	93.8%
5	59.4%	81.3%	79.7%	90.4%
7	45.7%	72.5%	70.6%	85.1%

Discussion of Results (Thermal Stress)

- The control sample (without antioxidants) showed significant degradation, with only 45.7% of the drug remaining after 7 days. This rapid degradation highlights the susceptibility of Ibuprofen to oxidative processes under thermal stress.
- The formulations containing either BHA or AP exhibited moderate protection, with 72.5% and 70.6% of the drug remaining, respectively. BHA showed a slightly better performance than AP, which aligns with its known capacity to act as a primary antioxidant.
- The combination of BHA and AP demonstrated superior protection, with 85.1% of the drug remaining after 7 days. This result suggests a synergistic effect between the two antioxidants, as the combination is more effective than either compound alone in delaying the degradation process.

Photolytic Stress

To assess the effect of light on the stability of the formulations, photolytic stress testing was performed by exposing the samples to UV light (254 nm) for 24 hours. Table 2 shows the percentage of Ibuprofen remaining in each formulation after UV exposure.

Table 2: Percentage of Ibuprofen Remaining after Photolytic Stress (UV Light, 24 Hours)

Time (Hours)	Control (No Antioxidant)	BHA (0.01% w/v)	AP (0.01% w/v)	BHA + AP (0.01% w/v)
0	100%	100%	100%	100%
2	83.4%	89.5%	87.3%	92.7%
4	68.7%	80.1%	78.6%	86.4%
8	53.5%	70.2%	68.9%	80.1%
24	35.1%	58.3%	55.7%	72.6%

Discussion of Results (Photolytic Stress)

- Under UV exposure, the control formulation showed a rapid decline in the amount of Ibuprofen, with only 35.1% of the drug remaining after 24 hours. This demonstrates the significant impact of light-induced oxidative degradation.
- Formulations with BHA or AP alone showed improved stability compared to the control. The BHA-only formulation retained 58.3% of the drug, while the AP-only formulation retained 55.7%.
- The combined formulation with BHA and AP exhibited the greatest protection, with 72.6% of the drug remaining after 24 hours of UV exposure. This further suggests a synergistic antioxidant effect when BHA and AP are used together, as their combination effectively reduces light-induced degradation.

Chemical Oxidation

Chemical oxidation was induced using hydrogen peroxide (H_2O_2) to mimic oxidative stress caused by reactive oxygen species. Table 3 shows the percentage of Ibuprofen remaining in each formulation after exposure to H_2O_2 for 24 hours.

Table 3: Percentage of Ibuprofen Remaining after Chemical Oxidation (30% H_2O_2, 24 Hours)

Time (Hours)	Control (No Antioxidant)	BHA (0.01% w/v)	AP (0.01% w/v)	BHA + AP (0.01% w/v)
0	100%	100%	100%	100%
2	75.8%	82.1%	80.6%	89.3%
4	54.3%	71.5%	69.2%	82.4%
8	38.7%	60.8%	58.9%	76.5%
24	21.5%	44.7%	41.6%	67.2%

Discussion of Results (Chemical Oxidation)

- Under chemical oxidative stress, the control formulation exhibited the most rapid degradation, with only 21.5% of the drug remaining after 24 hours.
- Formulations containing BHA or AP showed improved protection against chemical oxidation, with 44.7% and 41.6% of the drug remaining, respectively.
- The combination of BHA and AP again demonstrated superior performance, with 67.2% of the drug remaining after 24 hours. This suggests that the combined antioxidant strategy is highly effective

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in neutralizing reactive oxygen species and preventing oxidative degradation of the drug.

Synergistic Effect of BHA and AP

The effectiveness of BHA and AP in preventing oxidative degradation was evaluated both individually and in combination. The synergistic effect was determined by comparing the degradation rates (k) and half-lives ($t_{1/2}$) of the formulations.

Degradation Kinetics

The degradation kinetics of Ibuprofen were calculated based on first-order rate equations. Table 4 presents the degradation rate constants (k) and half-lives ($t_{1/2}$) for each formulation under different stress conditions.

Table 4: Degradation Rate Constants (k) and Half-Lives ($t_{1/2}$) for Ibuprofen Formulations

Stress Condition	Formulation	Degradation Rate Constant (k) (hr^{-1})	Half-life ($t_{1/2}$) (hr)
Thermal Stress	Control	0.151	4.59
	BHA (0.01% w/v)	0.095	7.29
	AP (0.01% w/v)	0.101	6.86
	BHA + AP (0.01% w/v)	0.065	10.66
Photolytic Stress	Control	0.177	3.92
	BHA (0.01% w/v)	0.128	5.41
	AP (0.01% w/v)	0.135	5.13
	BHA + AP (0.01% w/v)	0.081	8.56
Chemical Oxidation	Control	0.223	3.11
	BHA (0.01% w/v)	0.142	4.88
	AP (0.01% w/v)	0.149	4.65
	BHA + AP (0.01% w/v)	0.097	7.14

Discussion of Results (Degradation Kinetics):

- The control formulation consistently showed the highest degradation rate and shortest half-life across all stress conditions, confirming its susceptibility to oxidative degradation.
- The formulations containing BHA or AP alone had significantly lower degradation rates and longer half-lives, indicating the effectiveness of each antioxidant in delaying drug degradation.
- The combination of BHA and AP yielded the lowest degradation rates and the longest half-lives, particularly under thermal and chemical oxidative stress. The longer half-life of the combined formulation suggests a synergistic effect, where the presence of both antioxidants enhances the overall protective mechanism.

Isobolographic Analysis of Synergism

To quantify the synergistic effect of BHA and AP, an isobolographic analysis was conducted. The observed effects of the combined antioxidants were compared to the predicted additive effects based on individual antioxidant performance.

Table 5: Synergistic Effect of BHA and AP (Isobolographic Analysis)

Stress Condition	Observed Effect (BHA + AP)	Predicted Additive Effect	Synergism (%)
Thermal Stress	0.065	0.098	33.67%
Photolytic Stress	0.081	0.131	38.17%
Chemical Oxidation	0.097	0.145	33.10%

Discussion of Results (Synergism)

- The isobolographic analysis confirms the presence of synergism in the combined formulation of BHA and AP. The observed degradation rate constants were significantly lower than the predicted additive values, indicating enhanced protection beyond what would be expected from the simple sum of their individual effects.
- The highest degree of synergism (38.17%) was observed under photolytic stress, followed by thermal and chemical stress. This suggests that the combined antioxidant system is particularly effective in mitigating the impact of light-induced oxidation.

Long-Term Stability Study

The long-term stability of the formulations was evaluated by storing the samples under real-world conditions (25°C ± 2°C and 60% RH) for six months. The remaining drug content was measured at regular intervals, and the results are presented in Table 6.

Table 6: Percentage of Ibuprofen Remaining after 6 Months of Storage

Time (Months)	Control (No Antioxidant)	BHA (0.01% w/v)	AP (0.01% w/v)	BHA + AP (0.01% w/v)
0	100%	100%	100%	100%
1	95.6%	98.7%	98.2%	99.3%
3	82.3%	92.6%	91.8%	96.5%
6	71.4%	85.1%	84.2%	92.8%

Discussion of Results (Long-Term Stability):

- The control formulation showed a gradual loss of drug content over six months, with only 71.4% of Ibuprofen remaining by the end of the study.
- Formulations containing BHA or AP alone provided moderate protection, with 85.1% and 84.2% of the drug remaining, respectively.
- The combined formulation with BHA and AP demonstrated the best long-term stability, with 92.8% of Ibuprofen remaining after six months. This result further supports the synergistic effect observed in the accelerated stress tests.

Mechanistic Insights into Synergism

The observed synergistic effect between BHA and AP can be attributed to their complementary mechanisms of action. BHA acts primarily as a chain-breaking antioxidant by scavenging free radicals and preventing the initiation and propagation of oxidative reactions. AP, on the other hand, plays a dual role as both a free radical scavenger and a regenerator of BHA, thereby enhancing its antioxidant capacity.

- **BHA**: As a phenolic antioxidant, BHA donates hydrogen atoms to neutralize reactive oxygen species (ROS), effectively terminating oxidative chain reactions. However, once oxidized, BHA loses its effectiveness unless regenerated by a co-antioxidant.
- **AP**: As a lipid-soluble derivative of ascorbic acid, AP can regenerate oxidized BHA by donating electrons, thus restoring BHA's antioxidant activity. Additionally, AP itself can scavenge ROS, providing independent antioxidant protection.

This dual antioxidant system creates a self-sustaining cycle where BHA and AP work together to neutralize oxidative stress more efficiently than either compound alone.

Conclusion

The results of this study clearly demonstrate the synergistic effect of BHA and AP in preventing the oxidative degradation of Ibuprofen under various stress conditions. The combination of these two antioxidants provided superior protection compared to their individual use, as evidenced by lower degradation rates, longer half-lives, and improved long-term stability. The dual antioxidant strategy, where BHA and AP complement each other's mechanisms, offers a promising approach for enhancing the stability of pharmaceutical formulations prone to oxidative degradation.

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Evaluating the Efficacy of Yoga & Ayurveda as a Complementary Treatment for Primary Dysmenorrhea: A Case Report

Research Article

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Abstract

Primary dysmenorrhea, characterized by painful menstrual cramps without underlying pathology, is a prevalent gynecological issue that significantly impacts the quality of life for many women. This case study explores the effectiveness of a holistic treatment approach combining Ayurvedic interventions and yoga to manage primary dysmenorrhea symptoms in a 19-year-old female patient. The Ayurvedic treatments included Rajparivartini Vati, Ajmodadi Churna, and Kumariasava, known for their analgesic, anti-inflammatory, and antispasmodic properties. Complementing these treatments, a yoga regimen comprising specific asanas and pranayama was implemented. Over three menstrual cycles, the patient experienced significant pain relief, reduced symptom severity, and an overall improvement in well-being. The case study highlights the potential benefits of integrating traditional Ayurvedic medicine and yoga as a non-invasive, multimodal approach to managing primary dysmenorrhea. These findings suggest a promising avenue for further research and the development of standardized protocols for the combined use of these therapies in treating dysmenorrhea. The study assessed pain intensity, frequency of analgesic use, and the patient's subjective experience of menstrual symptoms before and after the introduction of yoga. Results demonstrated a marked reduction in pain levels, decreased reliance on pain medication, and an enhanced sense of well-being. The findings suggest that yoga, as a non-invasive and holistic practice, can effectively complement traditional treatment methods for primary dysmenorrhea. This case highlights the potential for integrating yoga into routine care, offering a sustainable and empowering option for pain management.

Keywords: Primary Dysmenorrhea, *Ayurveda, Yoga*, Prostaglandin, *Kumariasava*, Pain.

Introduction

Menstrual cramps, also known as dysmenorrhea, are characterized as periodic pain that is directly associated with the menstrual cycle. Just before or at the start of menstrual flow, the pain starts, and it goes away during menstruation. The lower back, upper legs, pelvis, breast all may be affected by the pain(1). Once ovulatory cycles are established, primary dysmenorrhea typically manifests within the first six months following menarche. The frequency of dysmenorrhea ranged from 25% of women who are menstruating to 90% of teenage girls or 45% to 95% of women of any age (2). It appears that dysmenorrhea is the most frequent gynecological condition. It frequently starts at the same time as menstruation. Usually, the lower abdomen or pelvis is where the pain (3) which could spread to the upper thigh and low back Colicky pre- or mid menstrual pain in the pelvis, lower back, or upper thighs that lasts for 48–72 hours is commonly referred to as menstrual cramps (4). Lower back discomfort, stomach distension, indigestion, headaches, nausea, diarrhea, and stress are some more symptoms. Nausea, exhaustion, diarrhea, lethargy, sensitivity, breast tenderness, cyclical mastalgia (breast pain) (5) (6) fluid accumulation, autonomic nervous system symptoms, attention deficit, depression, and emotional distress and disturbance have all been recorded as manifestations (7). Period pain and discomfort can result in several health issues that might impact day-to-day tasks including housework, employment or work hours, and scholastic achievement (8). In contemporary medicine, medications such as OCPs, NSAIDs, antispasmodics, and analgesics are used to treat dysmenorrhea. When these chemical agents are used over an extended period of time, harmful side effects such as hepatotoxicity, nephrotoxicity, headaches, vertigo, dizziness, depression, and skin rashes can occur. Therefore, there is a lot of room for research to identify an Ayurvedic and Yoga treatment for kashtartava (dysmenorrhea) that is safe, effective, and affordable in order to close the aforementioned gap. Yoga and Ayurveda is cost effective and more safe treatment for Primary Dysmenorrhea (9).

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Case Report

Patient information and clinical finding

A 19-year-old unmarried female presented with complaints of pain in lower abdomen and back during the days of menstruation and before two days of periods for last 2-year Pain intensity was measured on Visual Analogue scale (VAS) Her menstrual period was of 6 days and on 1st day she was changing 1–2 pads per day partially soaked. From 2nd to 4th day, she was changing three pads per day partially soaked and from 4th–6th day, one pad per day partially soaked. There was no history of any surgical or medical illness. The patient was conscious and oriented. Blood pressure was 124/80 mmHg, heart rate was 78 beats/min, respiratory rate was 18/min, and oxygen saturation was 100% at room air she was a student. She was very fond of fast food and a sedentary lifestyle. On physical examination, there was no sign of anemia, malnutrition and other systemic diseases. Patient was advised to go for blood investigations (CBC, Thyroid Profile) and trans-abdominal pelvic scan. Laboratory findings were within normal range and USG showed no pelvic pathology. However, on local examination, no sign of complaint was noticed.

History of Present Illness

At the age of thirteen, she experienced menarche. She has been complaining for the past six months. Lower abdominal cramps begin with the onset of menstruation and last for two days. Radiating to both thighs, back discomfort begins one or two days before menstruation and lasts for two days. When menstruation began, the nausea got worse. Her periods were so painful that she was unable to attend college.

Past History: Nothing relevant

Family History: Nothing relevant

Personal History

Diet	Veg
Appetite	Reduce
Bowel	Regular
Urine	Normal
Sleep	Sound
Allergy	No
Addiction	No

Menstrual History

Menarche - 13 years
LMP – 25/02/2024
PMP- 23/01/2024
Interval – 28-30 days
Duration – 5 days Amount- 2-3 pads/day
Clots – 4-5 cm
Lower abdominal pain – Grade III (VAS - 10/10)
Low back ache - Grade II (VAS - 5/10)

Physical Examination

Built – Normal
Nutritional status – Moderate
Height – 160 cm
Weight – 51 kg
Pulse rate – 71 beats/min
Heart rate – 71 beats /min
BP – 124/76 mmHg
Temperature – 98.6°F

Laboratory and Ultrasonography Report

On laboratory investigations her hemoglobin was 12g/dL and her Ultrasonography abdomen report was normal.

Timeline: Patient timeline shown in Table 1.

Table 1: Timeline Table Patient visit
OPD = Out Patient Department

Time line	Clinical event and intervention
22-03-2024	Patient visited OPD Prescribed Ayurvedic medicines and practice Yogas Asana
24-04-2024	Symptomatically improved Continued Ayurvedic medicines and practice Yog asana
26-05-2024	Pain subsided significantly Continued Ayurvedic medicines and practice Yoga Asana
24-06-2024	Pain Reduced

Therapeutic Intervention

The treatment principles of the primary Dysmenorrhea to reduce the pain duration and pain intensity and menstruation related symptoms.

Ayurvedic Intervention

The patient was prescribed the following Ayurvedic medicines by the Ayurvedic Gynecologist .
1. Rajah pravartani vati, is given two pills, 2(BD) twice Daily after meal.(Choudhary & Sharma, n.d.)
2. Kumariasav 20ml with equal water, twice in a day after meal.
3. Ajmodadi churna 3gm BD twice in a day after meal.

Table 2: : List of prescribed Ayurvedic medicines with their possible effects

NAME OF MEDICINES	DOSAGE	POSSIBLE EFFECTS
Rajparivartini Vati	2 BD twice daily	Stimulate the ovulation and correct overian function.
Ajmodadi Churna	3 Grams BD twice daily	Managing pain in abdomen and back.
Kumariasava	20ML with equal quantity of water twice daily	Help to relax the muscles and gives relief from cramps.

BD=Bis in die , twice daily

Yogic intervention

The yogic intervention duration was 30 min/day, five times/week for three consecutive menstrual cycles. A combination of asana, pranayama and relaxation protocol was practiced by the patient. The protocol was as follows: Cat pose, Cobra pose, Fish Pose, *Setubanda, Paschimottanasana, and Nadishodhana Pranayama*.

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Dietary advice

To avoid oily, spicy, fried food, fermented, tart and fast food. She was advised to take high-fiber fruits, green vegetables, simple food and protein rich food and drink adequate water. According to Ayurveda, *Ruksha, Sushka Ahara, and Ratri Jagran* were avoided .

Follow up and outcome

The patient revisited outpatient department after 1st month of treatment abdominal pain was mildly reduced. The pain subsided, as reported after 2nd month of treatment. Moreover, after 3rd month completion of treatment, she reported no pain, and no other complain related to menstruation.

Table 3: Visual Analog Scale score

Visit Periods	Number of visits	VAS Score
1st day of OPD visit	1st visit	10(severe)
Visit after her cycle	2nd visit	8(severe)
2nd visit after cycle	3rd visit	5(moderate)
3rd visit after cycle	4th visit	3(mild)

VAS, Visual Analogue Scale; OPD, Outpatient department

Discussion

The present case is discussed here of a 19-year-old female patient with a primary dysmenorrhea and related symptoms treated with Ayurvedic medicines and yogic practices.

Treatments for primary dysmenorrhea, which is defined by painful menstruation without underlying pathology, include *Ajmodadi Churna, Kumariasav, and Rajparivartini Vati*. In addition to providing analgesic and anti-inflammatory properties and relieving uterine spasms, *Rajparivartini Vati* balances the *doshas of Vata and Kapha*. The main benefits of *Ajmodadi Churna* include vata balancing, improved digestive health, pain reduction, and uterine muscle relaxation. As a uterine tonic, *kumariasava* lowers inflammation, balances hormones, and enhances blood flow to the pelvic area. When used in tandem, these formulations treat the underlying causes and symptoms of primary dysmenorrhea by balancing doshas, easing cramps, promoting digestive health, and improving overall uterine function. Dysmenorrhea is characterized by excruciating cramps that interfere with regular activities and occur during menstruation. Dysmenorrhea is a significant health issue that negatively impacts everyday activities and quality of life for adolescents in school and for healthcare professionals. The most prevalent gynecological issue that affects women is dysmenorrhea, which is brought on by aberrant uterine anatomy and function, psychosomatic causes, prostaglandin release, pelvic congestion, and other factors. yoga in the form of asanas, pranayama and meditation on a regular basis so as to alleviate dysmenorrhea effectively. The therapeutic intervention in this case study incorporated three main Ayurvedic treatments: *Rajparivartini Vati, Ajmodadi Churna, and Kumariasava* (11). These herbal formulations are known for their analgesic, anti-inflammatory, and antispasmodic properties, which are crucial in managing dysmenorrhea symptoms. *Rajparivartini Vati*, in particular, is recognized for balancing the *Vata* and *Kapha doshas*, which are often associated with menstrual disorders. *Ajmodadi Churna's* role in enhancing digestive health and relaxing uterine muscles further supports its effectiveness in reducing pain and discomfort during menstruation. *Kumariasava* acts as a uterine tonic, promoting better blood flow and hormonal balance, which are essential in alleviating menstrual cramps. The incorporation of yoga, particularly the specific asanas (Cat, Cobra, Fish Pose, *Setubanda*) and pranayama (*Nadishodhana pranayama*), (7) (12) added a non-invasive, holistic dimension to the treatment. Yoga's effectiveness in managing dysmenorrhea is well-documented, with studies showing that regular practice can reduce the intensity and duration of menstrual pain by improving blood circulation, enhancing pelvic flexibility, and reducing stress and tension in the body. The patient in this case study experienced significant pain relief and a reduction in the frequency of analgesic use, which aligns with existing research on the benefits of yoga for menstrual health. The combination of Ayurvedic treatments and yoga practice over three menstrual cycles led to a marked improvement in the patient's symptoms. This approach not only reduced the intensity of pain but also enhanced the patient's overall well-being, indicating that a multimodal, holistic treatment strategy can be more effective than relying solely on pharmacological interventions (9). The findings from this case study underscore the potential of integrating traditional and complementary therapies, such as Ayurveda and yoga, into routine care for primary dysmenorrhea. This integrative approach offers a sustainable, non-invasive, and empowering option for pain management, allowing patients to take an active role in their health and well-being. However, while the results are promising, further research is necessary to establish standardized protocols for the combined use of Ayurvedic medicine and yoga in treating dysmenorrhea (9). Larger studies with control groups would help validate these findings and assess the long-term benefits of this integrative approach. Additionally, exploring the mechanisms through which these therapies alleviate dysmenorrhea could provide deeper insights into their effectiveness and guide future treatment recommendations.

Conclusion

This case study demonstrates the potential efficacy of combining Ayurvedic medicine and yoga as a complementary treatment for primary dysmenorrhea. The patient, a 19-year-old female with a history of severe menstrual cramps, experienced significant relief from pain, a reduction in symptom severity, and an overall improvement in well-being after undergoing a treatment regimen that included Ayurvedic formulations (*Rajparivartini Vati, Ajmodadi Churna, and Kumariasava*) and specific yoga practices. The findings suggest that this integrative, non-invasive approach can

be a viable alternative or complement to conventional pharmacological treatments for dysmenorrhea.

The holistic approach not only addressed the physical symptoms but also contributed to the patient's mental and emotional well-being, highlighting the benefits of a multimodal strategy. However, while the results are promising, further research with larger sample sizes and control groups is necessary to validate these findings and develop standardized treatment protocols. This case study opens the door for more extensive exploration into the integration of traditional Ayurvedic medicine and yoga in managing primary dysmenorrhea, offering a sustainable and empowering solution for those affected by this common condition.

Declaration of patient consent

Before start the treatment obtained her consent to be part of this study.

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Conflicts of interest: There is no conflict of interest.

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Pharmacognostical Evaluation of Jeevak/*Crepidium acuminatum* (D.Don) Szlach. Pseudo bulb

Research Article

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Abstract

Background: *Crepidium acuminatum* (D.Don) Szlach. Syn. *Malaxis acuminata* D.Don belonging to the family Orchidaceae is a rare medicinal plant found in Himalayan region in temperate zone that has high therapeutic value. It is known as Jeevak in Ayurveda and is one among the astavarga (group of eight highly important vitalizing plants). It has been praised to be immunomodulatory, vitalizer, adaptogenic, muscle bulk promoting drug in Ayurveda. Although a very important plant in Ayurveda proper pharmacognostical data is not available regarding this plant. Materials and Methods: The plant was collected from Chandravadani, Garhwal district, Uttarakhand and was authenticated from Botanical Survey of India, Kaulagadh road, Dehradun. The pharmacognostical, histochemical and micrometric evaluation was performed at the Department of Pharmacognosy, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurveda University, Jamnagar, Gujarat. Organoleptic features was observed with naked eyes. The transverse sections was stained with phloroglucinol along with hydrochloric acid. The photomicrographs were taken using Carl Zeiss trinocular microscope. Results: Jeevak was found in Himalayan region growing among stony soil in colonies together. The mucilaginous property in fresh sample was lost after getting dried. The pharmacognostical evaluation shows oval or irregularly shaped parenchymatous and mucilage cells with acicular raphides abundantly; acicular crystals of calcium oxalate scattered singly or in broken pieces or in bundles scattered in parenchymatous cells and simple starch grains with striations that help to distinguish it from other allied and non-allied drugs. Conclusions: The obtained results would be helpful for proper identification and standardization of Jeevak and hence provide the pharmacopeial standards and reference information for manufacturers and researchers.

Keywords: *Ashtavarga, Ayurveda, Crepidium acuminatum, Jeevak.*

Introduction

Crepidium acuminatum (D. Don) Szlach. is known as Jeevak and is used as an immunomodulatory, adaptogenic, aphrodisiac and vitaliser (1). It is mentioned in ancient Ayurvedic classics with its various uses and formulations (2). It is among the vital component of the formulations like *Chyavanprasha avaleha* (3), *Bala taila* (4), *Prasarini taila* (5), *Shatavari ghrita* (6), *Baladi Choorna* (7), *Phalaghrita* (8), *etc. It is also one of the component of popular astavarga* (9). The chemical constituents in Jeevak are Aluminium, Boron, Calcium, Chlorine, Iron, Copper, Barium, Potassium, Magnesium, Manganese, Molybdenum, Zinc, etc. like metals and minerals; fatty acids like Eicosadienoic, Eicosanoic, Alpha Linolenic, Terpenoids, Alpha-Tocopherol, Gamma- Tocopherol, Beta Sitosterol, ceryl alcohol, glucose, rhamnose, choline, limonene, eugenol, citronellal, 1,8-cineole, piperitone, p- cymene, Eugenol, Caryophyllene, Humulene, Phenol, 2, 4bis (1,1dimethylethyl), Caryophyllene oxide, 2,5 Octadecadiynoic acid, methyl ester (10,11,12,13). It possesses antioxidant (14,15), antimicrobial (16,17) and anti-inflammatory activity (18). It was a rare drug since sixteenth century (19). In this present era, it is substituted and adulterated. The review of literature also shows few pharmacognostical studies relating to it (20, 21,22). Considering it a preliminary pharmacognostical profile of Jeevak/ *Crepidium acuminatum* pseudo bulb was investigated which can be used for further research.

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Materials and Methods

The plant was collected from Chandravadani, Garhwal district, Uttarakhand on 12th to 15th August, 2018. It was then authenticated from Botanical Survey

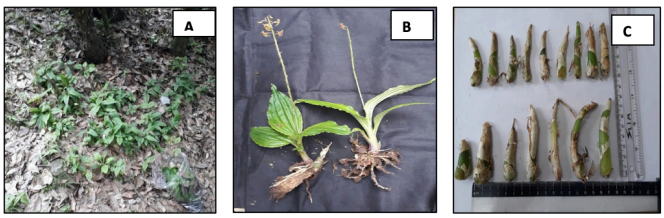
of India, Kaulagadh road, Dehradun on 2018-09-07 with voucher number Tech./Herb (Ident.)/2018-19, Account number 118498. The collected pseudo bulb was washed with plain water thoroughly for removing physical impurities and other plant parts. The organoleptic evaluation of the plant Jeevak was performed at the Department of pharmacognosy, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurveda University, Jamnagar. Fresh and dried pseudo bulb along with the powder were evaluated for their organoleptic features i.e. size, shape, colour, odour, taste and texture with naked eyes. Thin free hand transverse section of different parts of pseudo bulb were taken. The sections were first observed in distilled water then stained with phloroglucinol (20 mg/ml of alcohol) along with hydrochloric acid (6N). It was again examined to assess different cellular structures and lignified elements like fibers, sclerides, xylem vessels, etc. The powder microscopy of powder 60 mesh was carried along with their physico-chemical profiling. The photomicrographs were taken using Carl Zeiss trinocular microscope attached to camera.

Results

Morphology

Crepidium acuminatum (D. Don) Szlach. is a terrestrial, lithophytic orchid 14-30cm tall (Plate 1.A). Leaves 3 or 4, thinly membranous, ovate-lanceolate, acute to acuminate, narrowed to sheathing base, petiolate, margins undulate, 5.5-12 x 2.5-6 cm; petiole 3-4 cm long (Plate 1.B). It has racemose inflorescence, laxly many-flowered. The flowers are 5-8 mm long, uniformly yellowish-green, yellow tinged with red-purple or pink-purple. The roots are fasciculate, slender and about 1mm wide. It has a glabrous, cylindrical, fleshy stem sheathed at base (Plate 1.C). The fruit is a capsule obovoid-oblong with many seeds (23).

Plate 1: A. *Crepidium acuminatum* (D. Don) Szlach. in wild B. Morphology of leaf of *Crepidium acuminatum* (D. Don) Szlach. C. Measurement of pseudo bulb of *Crepidium acuminatum* (D. Don) Szlach.



Organoleptic characters

The organoleptic characters of fresh and dry sample of pseudo bulb of Jeevak/ *Crepidium acuminatum* (D. Don) Szlach. shows various features. There was marked change in colour of the pseudo bulb after drying which changed from dark green to brownish yellow. The smooth fracture of fresh sample was changed into hard, granulated and irregular fracture in dry sample. (Table no 1).

Table 1: Showing organoleptic characters of fresh and dry sample of Jeevak/ *Crepidium acuminatum* (D. Don) Szlach. pseudo bulb

Observations	Fresh sample (pseudo bulb)	Dry sample (pseudo bulb)
Colour	Dark green to light greenish yellow	Brownish yellow
Odor	Characteristic	Characteristic
Taste	Astringent, sweet; slightly mucilaginous	Astringent, sweet
Fracture	Smooth	Hard, irregular; cut surface brownish yellow; granulated

Macroscopic characters

The pseudo bulb were 3-8 cm in length and 1-1.5 cm in diameter in fresh state; when dried were 2-7cm in length and 0.5-0.7 cm in diameter. It was conical, smooth and shining, fleshy,

covered with translucent light green papery membranous cover in fresh state while conical, rough, covered with yellowish papery membrane with whitish yellow spots in dry state.

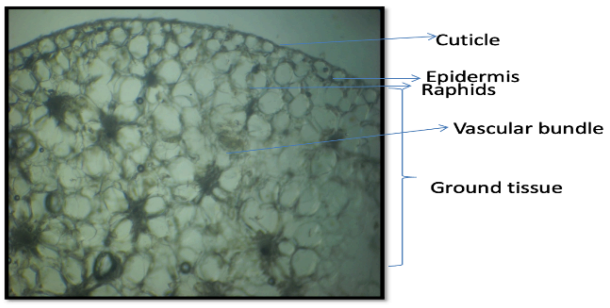
Dried pseudo bulb is conical in shape, straight or slightly curved, about 2 to 7 cm long and 0.5 to 1 cm thick, broader at the base with broken rootlets; surface dark brown to nearly black, wrinkled with 2 to 4 obliquely arranged rings of papery white remnants of dried leaf bases; taste mucilaginous; odourless.

Microscopic characters

Transverse section of pseudo bulb

Diagrammatic Transverse characters of cut surface of the pseudo bulb is circular to oval with irregularly crenate margins in out line and shows a layer of epidermis and wide parenchymatous ground tissue with scattered vascular bundles and mucilage cavities. (Plate 2.A) The detailed transverse section of pseudo bulb shows a layer of epidermis of tubular, tangentially running cells of irregular size with thin cuticle followed by ground tissue of parenchymatous cells traversed by wide air spaces, vascular bundles, numerous mucilage cells and cells containing bundles of acicular crystals of calcium oxalate; vascular bundles consisting of 3 to 5 xylem vessels and a narrow zone of phloem. (Plate 2.B)

Plate 2A: Diagrammatic photograph of transverse section of pseudo bulb



T.S. of Pseudo bulb

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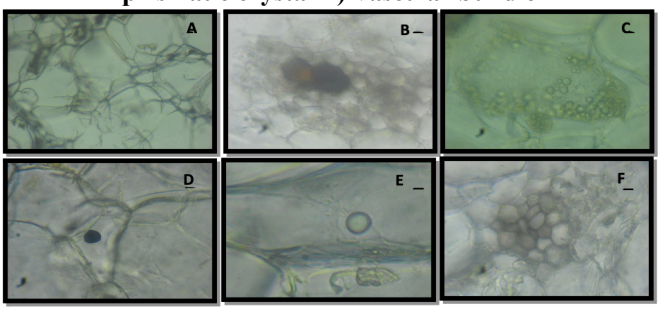
Plate 2B: Descriptive photographs of transverse section of pseudo bulb.; A) Acicular crystal with starch grain; B) Brown constant; C) Parenchyma cells with oil globules; D) Iodine stained starch grain ; E) Oil globule with prismatic crystal F) Vascular bundle

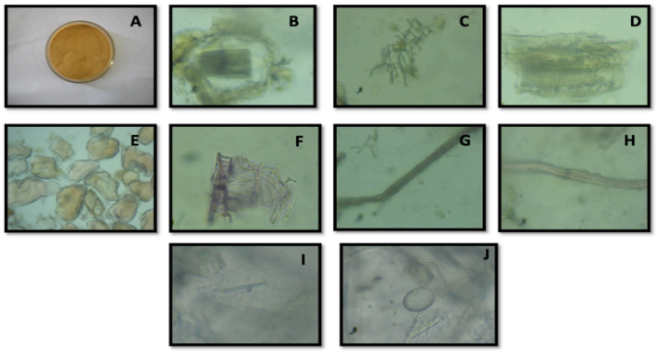


Powder microscopic characters of dry sample

Organoleptic and Microscopic characters

Diagnostic microscopic characters are abundant, oval or irregularly shaped parenchymatous and mucilage cells with acicular raphides (Plate 3 B); acicular crystals of calcium oxalate scattered singly or in broken pieces or in bundles scattered in parenchymatous cells and rarely reticulate vessels.

Plate 3: Powder microphotographs of *Jeevak/ Crepidium acuminatum* (D. Don) Szlach. *A) Pseudo bulb powder ; B) Raphids; C) Fragment of leaf part; D) Annular and spiral vessels; E) Fragments of Parenchyma cells; F) Lignified leaf components; G) Simple fiber; H) Lignified fiber ; I) Acicular crystal; J) Simple starch grains with striations*



Histochemical evaluation

The thick sections and powder was subjected to various reagents in chemical tests to detect the different chemical constituents.

Table 2: Histochemical evaluation of thick sections

S.N.	Reagent	Observation	Characteristic feature	Result
1	Phloroglucinol + Concentrated Hydrochloric acid	**Red**	Lignified cells	++
2	Iodine	**Blue**	Starch grains	++
3	Phloroglucinol + Concentrated Hydrochloric acid	**Dissolved**	Calcium Oxalate crystals	++
4	Ferric chloride/ $FeCl_3$ solution	**Dark blue**	Tannin cells	++
5	Ruthenium red	**Red**	Mucilage	++

Micrometric evaluation

Micrometric measurements of T.S. of pseudobulb shows 6.2 μm^2, other powder characters are given in table.

Table 3 : Micrometry value of pseudobulb powder

Sr. No.	Character	Measurement (400×)
1	Silica deposition	1.5 × 1.2 µm
2	Starch grain	0.4 × 0.6µm
3	Annular vessel	1.6 × 0.9 µm
4	Brown constant	1.3 × 1.2 µm
5	Acicular crystal	3.9 × 0.1 µm
6	Fragment of fibre	2.8 µm × 0.2 µm
7	Raphides	2.5 × 3.9 µm

(× Magnification)

Discussion

Jeevak /*Crepidium acuminatum* (D. Don) Szlach. is one of the prized drugs of choice in Ayurveda found in Himalayan region used in various formulation ranging from powder, pills to oil or ghee based formulation. It was rare and often substituted as mentioned in Bhavaprakash nighantu (an Ayurveda textbook of 16th century) (24). It was a necessity to identify, authenticate and standardize it pharmacognostically. This study revealed the diagnostic microscopic feature includes abundant, oval or irregularly shaped parenchymatous and mucilage cells with acicular raphides; acicular crystals of calcium oxalate scattered singly or in broken pieces or in bundles scattered in parenchymatous cells and simple starch grains with striations that help it distinguish from other allied and non-allied drugs.

Most of the preparation with Jeevak in Ayurveda are ghee or oil based. Starch and oils present in Jeevak being non polar can get properly incorporated with ghee and oil preparations. Starch is known to increase body weight and promote bulk in the body. The presence of starch can be attributed to one of the reasons for the strength promoting and bulk promoting activity of Jeevak.

Conclusion

The present study of provides the pharmacognostical information for identification, authentication and standardization of Jeevak/*Crepidium acuminatum* (D. Don) Szlach. The microscopic features that distinguishes Jeevak is the presence of abundant, oval or irregularly shaped parenchymatous and mucilage cells with acicular raphides. The acicular crystals of calcium oxalate was found to be scattered singly or in broken pieces or in bundles scattered in parenchymatous cells and simple starch grains with striations. Very few published reports are available on this plant which are either vaguely described or incompletely arranged. Hence the results obtained in this study may be referred to as a standard for upcoming future studies.

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Conflict of interest: None

Sources of funding: None

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The Importance of Guru - Shishya Parampara in Nath panth

Review Article

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Abstract

The worship of Lord Shiva and the application of sophisticated yogic techniques are the main focuses of the *Nath Sampradaya* (also known as the Nath tradition), a spiritual and religious movement within Hinduism. The custom, which dates back to the eighth century, is strongly linked to mythical saints like *Matsyendranath* and *Gorakhnath*. It places a strong emphasis on using Hatha Yoga, Kundalini Yoga, and other meditation techniques to achieve self-realization, spiritual awakening, and liberation (Moksha). The Guru-disciple relationship, in which the Guru imparts spiritual wisdom and esoteric knowledge, is what defines the Nath tradition. Additionally, the tradition encourages the development of mental and physical discipline, asceticism, and the use of mantras. The Nath Sampradaya has influenced the development of various schools of yoga, and its teachings continue to impact Hindu philosophy, meditation practices, and spiritual literature across India and beyond.

Keywords: *Nath Sampradaya, Siva-cult, Adiyogi, Gorakhnath Temple, Nath-Yogi, Siddha-Yogi.*

Introduction

A South Asian religious order consisting of various ascetic "sorts" is commonly referred to as the *or Nath Panth.* This order is typically linked with yoga. There is householder castes associated with the *Naths,* although renunciates make up the majority of its adherents. Although there are branches in other areas as well, they are primarily found in the northern part of the Indian peninsula. The *GorakhNath* Mandir in Uttar Pradesh, India, is currently the most well-known and significant temple. It serves as both the *Nath* headquarters and the residence of Yogi Adityanath, the Chief Minister of Uttar Pradesh and the mahant of the *GorakhNath* Mandir. The people who follow the panth are commonly referred to as *Nath Yogis,* but in the literature that still exists and in folklore, they are also occasionally called jogis, which is the vernacular for *yogi siddhas*, or *avadhutas* which is another term for someone who has rejected the constraints of secular life. Additionally, the somewhat ambiguous term "*NathSiddhas"* is mentioned in some academic and indigenous texts(1).

The application of these and other names varies amongst sources and historical periods. There also appears to be a wide range in their actual meanings and denotations. According to James Mallinson's estimation, *Nath* literature did not use the term *"Nath* Siddha" until the latter part of the 20th century (1). The two terms may have been combined due to a loose combination of Northern Yogis and Tamil Siddhas in some scholarship, or to the constant interaction of ascetics who used one name and then the other, without necessarily coming together into a single tradition, or sampradaya. Since the motif was a prominent element in some of the temples built by Man Singh of Mewar, we do know that by the nineteenth century, the authoritative status of a symbolic idea of a group of Nine *Naths* (not to mention that of the Eighty-Four *Siddhas*) was seemingly well established(2).

It is plausible that approximately during the 16th century, a cohort of *Saiva* ascetics started to gradually distinguish themselves from other related communities and employ the term *yogi* in a particular context, distinct from a general one.

The *Naths,* as they are popularly called, are deeply ingrained in a custom linked to the study and practice of yoga. *Haṭha yoga* is the specific style of yoga associated with the *Naths,* though this connection has been questioned in more recent research. In addition to being appropriate for a *Nath* province, *haṭha yoga* was also widely practiced by other ascetic communities. That being said, particularly in the last few years, the *Nath yoga* relationship has been crucial to the development of a *Nath* identity. Consequently, a significant portion of the literature associated with the *Nath Yogis* discusses *yoga,* and occasionally *haṭhayoga* in particular(1).

One intriguing aspect of the *Natha sampradaya* is that its imagery and ideology are drawn from three literary corpuses: folk tales, Sanskrit texts on yoga, and a variety of literature written in vernacular languages(2). In a way, the *Nath* tradition is predicated on how these three sources are interpreted. It is difficult

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to determine which *Nath* authors actually wrote the Sanskrit texts on *yoga,* but tradition has established a link between them, strengthening the yogic aspect symbolically. The primary genres of the vernacular literature are religious dialogues and poetry. The latter was produced mostly in the seventeenth century and is of a mystical and devotional nature. Its poetic style is similar to that of the bhakti verses written by the *Nirguni* poets of North India, who were particularly active in the second millennium. With the tales of archetypal personages like *Gorakh, Matsyendra, Gopicand, Caurangi* and others, the legends of *Nath* renowned figures have been a potent means of disseminating the influence, aura, and appeal of the *Naths*. Ideally, there exists a roster of nine enlightened *Nath* Yogis, a cohort that occasionally functions similarly to the Eight-Four Siddhas(3).

This poem might not belong to the Nath but rather to a different fore, most likely *Nirguni*. Recognising that the Nine *Naths* and the Eighty-Four Siddhas belong together is crucial for our current goal. The fact that they both practice *yogic* postures, or *asanas*, is particularly noteworthy.

But siddhas and yogis are all grouped together, but only as vague groups, not as distinct communities of relatively concrete figures. Even older poetry contains references to individual Yogis and Siddhas by name, but not enough to draw any firm conclusions. The and *Caryapadas* the *Sadhanamala* from the approximately twelfth century do not include or mention *Gorakṣa, Caurangi, Nagarjuna, Carpaṭa, Kanthali, Kapala, Nagabodhi* or Vyali. However, the *Goraksasiddhanatasamgraha* from the eighteenth century provides the following account: *Adinatha, Matsyendranatha, Udayanatha, Dandanatha, Satyanatha, Santosnatha, Kurmanatha, Bhavanarji, Gorkshanatha:* these individuals make up the divine succession *(isvarasantanah*)(4). Does this refer to a family history or a custom.

Hāth yoga and Nath yoga

There are two main ways that we understand yoga generally: the scholarly way and the practitioner way. Though there is a difference between South Asian "traditional" practitioners and modern non-renouncer (often urban) practitioners, they may occasionally coincide. The scholarly method is based on textual sources, mostly composed in Sanskrit, but it also includes documents written in other languages from the eighteenth century onwards. Based on these sources, it seems that hatha yoga is not quite the same as what modern practitioners do in yoga studios all over the world (5). Compared to "textual" haṭhayoga, contemporary *haṭhayoga* places a lot more emphasis on physical postures *(asana)*. Throughout ancient texts, the central idea of *haṭhayoga* appears to have been breath control *(praṭayama),* which can be practiced in different ways *(mudra, bandha)* to become perfect(1). A *Nath* attribution to various yoga texts, usually written in Sanskrit, is what links the *Nath* Yogis to *haṭhayoga.* It is not possible to determine with certainty that "*Nathas"* wrote these texts. Nonetheless, a lot of them have been consistently released by *Nath* monasteries and presses, and this editing work has contributed to strengthening the connection (2). A few of the pertinent titles have already been mentioned once. *Gorakṣasataka, Vivekamartaṇḍa, Amaraughaprabodha, Yogabija, Amanaskayoga, Gorakṣasiddhantasaṃgraha,* and *Siddhasiddhantapaddhati* are some of the most famous texts; most of these have been credited to Gorakh or other fabled *NathYogis.* While they are related, some texts on *haṭhayoga (Haṭhapradipika, Gheraṇḍasaṃhita, Sivasaṃhita)* have not been attributed to the *Naths;* other works, though attributed to Matsyendra, do not deal directly with *haṭhayoga* or the panth *(Kaulajnananirṇaya*, for instance) (3). The *Yoga Upaniṣads,* a collection of late Sanskrit texts on yoga, most likely have a significant influence from *haṭhayoga,* though the precise amount of a potential *Nath* influence is not yet known. Furthermore, it is problematic to consider that many texts commonly associated with early *haṭhayoga* fail to define their system as "*haṭha"* Regarding the method used by the ascetic practitioners, there is an intriguing discrepancy between their comprehension of the text and that of the yogis. According to a recent ethnographic study, the meaning of *haṭhayoga* varies among ascetics from different denominations, such as *Nagas, Ramanandis,* and *NathYogis. Haṭhayoga* is not always a distinct yoga system; for many ascetics, it is nearly equivalent to general austerities (tapas). Due to its rigorous practices, *haṭhayoga* is commonly understood by scholars as a "forceful yoga" (3). However, there is another widely accepted meaning that explains this yoga in a symbolic way. The combination of the syllables HA and ṰHA, which represent the sun and the moon, respectively, or the subtle channels within the yogic body, is *Haṭha.* Thus, *haṭhayoga* would mean the union of the two main breaths, which seems to be in accord with some pre-modern sources that lay stress on breath control (3). However, in a recent ethnographic study, just three out of eighty respondents referred to this symbolic, esoteric explanation of *haṭhayoga* Clearly, the idea that there is a harmonized continuity of *haṭhayoga* and its transmission is put into question

In general, *haṭhayoga* imagery depends on an intense work with and on an energetic, subtle physiology. The yogic body is

In general, *haṭhayoga* imagery depends on an intense work with and on an energetic, subtle physiology. The yogic body is commonly understood as a network of delicate cakras, granthis, and conduits *(naḍis)*. The primary drive is to channel vital energies, specifically the *kuṇḍalini,* a potent life force that, when properly "awaken," can enhance unimaginable capacities and immortality, and the *praṇa,* which is itself a rich network of breaths. In *haṭhayoga,* there are two primary trends that can be distinguished. Since semen is symbolic of the seed of eternal life, the first and ostensibly older one focusses on the retention of

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semen *(bindu, amṛta)*. The second focusses on increasing *kuṇḍalini,* a subtle psychophysical force The primary goal in both situations is to become successful, acquire extraordinary abilities (siddhi), and become free while remaining in the body. In this sense, liberation in this scheme is not otherworldly but asserted in the phenomenal realm. It should be noted that *haṭhayoga* seems to have first appeared in Buddhist tantric literature, and then later entered both *Saiva* and *Vaiṣṇava* texts that sometimes dealt with *rajayoga* (6).

It has been noted previously that the *Nath* attribution to the Sanskrit texts is uncertain, as is the actual relationship that the *Nath Yogis* had with *haṭhayoga* in pre-modern India. It has to be pointed out that some scholars (2). are working on visual evidence such as sculpture, miniature, and painting so as to ascertain that The *Naths* were the ascetics portrayed there in *asana* and *praṇayama* practices(7). Whether these yogis were, in fact, *Nath* Yogis and not followers of some other ascetic order or lineage remains to be established, particularly since we do not yet know when the *Naths* started using their unique insignia as exclusively as they do now. Still, *haṭha* has emerged as a central figure in *Nath* imagery and tradition. It is interesting to note that the *yoga sthala* at Gorakhnath Mandir is staffed by laypeople rather than renunciate yogis or *Nath* ascetic teachers. Other *Nath* sites do not necessarily have to be like this. An illustrative leaflet published by the Gita Press and the Gorakhnath Mandir presents what appears to be an institutional position on yoga(4). This text is An Introduction to *Natha-Yoga* (INY from now on). Although the author and publication date are unknown, it was most likely published in the final decades of the 20th century with the intention of advancing the official interpretation of the *Naths' yoga*(5). The INY covers a wide range of yogic themes in thirty-one chapters and slightly less than one hundred pages, including philosophical ideas, physical practices, institutional locations, and aspects of worship. Generally speaking, the INY provides an overview of prior, accepted knowledge about yoga. It echoes the scriptures of *haṭhayoga* more strongly than *Patanjali.* Though the *Haṭhapradipika* is obviously not a *Nath* text, the atmosphere of *Svatmarama's* work lurks behind the exposition; it does not include quotes, direct references, or a bibliography(8).

While not all *Nath* ascetics adhere to the INY, it does represent an intentional effort to promote an ideal *Nath*image connected to *haṭhayoga*. Regardless of the historical accuracy, this association holds significance. Regardless, the historical stories have already portrayed the *Naths* as dominant because they were skilled in *yoga.*

A.K. Banerjea, who wrote a biography of *Baba Gambhir Nath*, a former mahant of the Gorakhpur Temple, and wrote other books on the *Naths,* including The Philosophy of *Gorakhnath,* published in 1962 and reprinted from time to time, is also worth considering. This is by no means a treatise on *yoga,* but one can still learn something about the general understanding of *yoga* in relation to the Gorakhpur *Naths.*

Not surprisingly, Banerjea explains yoga as a system based on *Patanjali* philosophy. In this life story, *Gambhirnath* appears as a renunciant who had mastered all aspects from the reputed philosophical system. Yet, the young *Nathbaba* decided to undertake a long pilgrimage so as to further penetrate into the mysteries of yoga. In several pages, Banerjea speaks of "esoteric aspects of yoga", thus implying that some issues are not covered in the *sastras. Gambhirnath* was to spend a few years in Varanasi and Prayag intent on fully mastering *yoga,* although it rarely receives a qualifier—it usually just remains "*yoga*" in general. While *Gambhirnath's* biography touches on some forms of yoga, it does not advocate for anything known as "*Nath-Yoga,"* unlike the INY previously discussed. It takes its cues straight from *Patanjali,* as mentioned earlier. Literally speaking, it also alludes to *"Karma-yoga,"* which is described as "the well-regulated performance of various forms of work with one high ideal in view". This is appropriate because the biographer wants to portray his subject as a great devotee, or in this case, a "true *bhakta-sadhaka,"* who not only claimed to be an infinite and unwavering devotee but also a renouncer who had accepted all of the *Nath* insignia. reverence and esteem for *Gopalnath*, his guru. *Gambhir Nath* was frequently depicted as ardently practicing "*yoga and deep meditation,"* particularly "in certain solitary places."

While the term "sadhaka" is rarely used as a synonym for "*yogin"* in most h*aṭha yogic* texts it is frequently used in Banerjea's biography of *Gambhirnath,* who is also referred to as *Yogiraj,* the king or conqueror of yoga. As Bevilacqua's study demonstrates, there is, in fact, a confusion of ideas about deeds, devotion, meditation, and energy control, not unlike the common understandings shared by other sadhus and *saṃnyasis.* The concept of yoga here negotiates with the ethos and praxis of various religious groups, just as the lists demonstrate its interaction with various *Vaiṣṇava, Saiva,* and Buddhist realms. However, the *Naths* continue to emphasise how they are different from other religious groups.

By contrasting these sources, we can observe a synthesis of various types: a renouncer motivated by devotion and an ascetic connected to yoga. While the second figure seems to be more passive and is fully engrossed in religious meditation, the first can be perceived as highly energising and endowed with numerous supernatural abilities. There appears to be a negotiation going on between a later, pious halo of *sant*-like ethos and a former, powerful, tantric aura. The Vedic ṛṣis and other related figures are not considered the key figures for the *Nirguṇi* poets. Nor are they intended for *NathYogis*. The semi-legendary *NathSiddhas*, who have inhabited the public consciousness for several centuries, are considered to be the primary figures. The panth was founded by the divine expounder of yoga's secret lore, *Sdinatha/Siva,* who is the only exception. Every teacher since *Ṣiva* has been a human being with a purported historical

background. Their poses are flawless. However, in contrast to certain *Nirguni* Sants, the *Nath*ha Geographical narratives lack the biographical details necessary to accurately situate these characters in space and time. It is important for us to understand that *Nath* historiography rarely deals with certainty. If there is a difference between the *Naths* and the *Nirgunis* in this aspect, it is because the *Naths* are not exactly sants; rather, they are similar to most Sants but never the same. Rather, the *Nath* Yogis function as proto-*Nirgunis* in some sense (perhaps through oral or minstrel traditions), since they foresee the kind of popular poetry that would appeal to the masses and would exhibit a set of mystical meanings distinct from those of *Brahmanic* and Islamic orthodoxy(6).

It appeared that the *Naths* had created a tradition *(sampradaya)* and a sect (panth), but not a definitive spiritual lineage *(parampara)*. That helps partially account for the stark differences between the lists. It certainly also demonstrates the early order's lack of denominational identity and cohesiveness. The yogis in premodern India were not merely accepting their elder models without question; rather, they were challenging them in order to define and set themselves apart from other lineages(6). More significantly, the different lists attest to an amalgamation of varied regional traditions that occasionally clash but also occasionally blend into one another. Understanding *Nath* historiography requires an understanding of the *Naths* identity and kinship, even though these topics are still up for debate regarding names and numbers Specifically, the Gorakhpur-affiliated *Nath* lineage has been determined to establish the Gorakhnath Mandir as a prominent hub for yogis; they have attempted to transform it into the *Nath* capital, if you will. The Gorakhnath Mandir has attempted to strengthen their connection to an all-powerful yoga and to augment a spiritual legacy by promoting the sacred biographies of the legendary yogis. Additionally, by highlighting the lives and deeds of their former mahants, the temple has strengthened its spiritual lineage and its importance within the South Asian yogic community. We found the following in a Gorakhnath Temple publication:

The soil, water, and air of the area become saturated with their influence when those spiritual vibrations are produced by the *sadhana* and siddhi of a long line of spiritually great men from ancient times. They become eternal, inexhaustible, and indestructible. This is true for the majority of locations that are revered. In fact, the Temple's propagandistic efforts aim to elevate Gorakhpur's soil to the same sacred and meritorious status as any other well-known Hindu pilgrimage site. They benefit from their previous yogi leaders and gurus' success (siddhi).

Conclusion

A variety of vast literature that talks about these *'Nath-Yogis'* and the principles and practices of '*Yoga',* are available in Sanskrit. Guru Gorakhnath, himself is reputed to be author of great treatise like, *Gorasha-Sanhita Goraksha-Satak, Yoga-Siddhanata-Paddhati, Siddha-Siddhanta-paddhati, Hatha-Yoga, Jnanamrita* and many other Sanskrit texts. Some other important books on Yoga, whose author is believed to be the member of the sect includes *'Hatha-Yoga-Pradipika',* '*Siva-Samhita'* and '*Gheranda-Samhita'*. While *'Goraksha-Shinita', 'Goraksha- Kaumundi',* '*Goraksha- Saharsranama'*, '*Yoga-Sangraha'*, *Yoga-Manjari'* are some works based on the teachings of Gorakhnath.

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Yoga for PCOS: A Holistic Approach to Improving Symptoms, Quality of Life, and Mental Well-Being

Review Article

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Abstract

Introduction: Polycystic Ovarian Syndrome (PCOS) is a common endocrine disorder affecting 11–13% of women globally during reproductive age. It is characterized by a complex interaction of genetic and environmental factors, leading to a wide array of symptoms, including menstrual irregularities, insulin resistance, obesity, infertility, and mental health challenges. Obesity, often exacerbated by lifestyle factors such as poor diet and inactivity, worsens PCOS outcomes. While medications provide short-term relief, they often have side effects, highlighting the need for non-pharmacological approaches. Yoga therapy, which combines physical, mental, and dietary practices, has emerged as a potential adjuvant therapy for managing PCOS symptoms. Methods: This study evaluated the feasibility and effectiveness of yoga as an adjuvant therapy for PCOS. Data were collected from 150 women diagnosed with PCOS based on the Rotterdam criteria, with 34 participants completing the 12-week online and offline yoga program. A structured questionnaire assessed patient satisfaction with the yoga intervention, focusing on symptom management, mental well-being, sleep, and quality of life. The yoga program included postures, breathing exercises, meditation, relaxation techniques, and dietary guidance. Statistical analysis was conducted to examine the relationship between yoga practice duration and improvement in PCOS-related outcomes. Results: Out of 43 respondents, 55.8% found the yoga program "very easy" to attend, and 30.2% reported significant improvement in PCOS symptoms. 55.8% experienced moderate mental well-being improvements, and 72.1% rated their post-intervention quality of life as "good" or "excellent." Yoga was found to be "very helpful" for managing PCOS by 48.8% of participants, and 62.8% found it an "acceptable" complementary therapy. The data showed statistically significant improvements in PCOS symptoms and quality of life, correlating with the duration of yoga practice. Discussion: The study demonstrated that yoga is a feasible and effective adjuvant therapy for PCOS. Although participants initially faced challenges incorporating yoga into their routines, they gradually adapted and reported positive outcomes in terms of physical, mental, and emotional well-being. Yoga provided benefits beyond medication, offering a holistic approach without adverse effects. These findings align with previous research, suggesting that yoga can help regulate menstrual cycles, manage weight, and improve mental health in women with PCOS. Conclusion: Yoga is a viable non-pharmacological approach for managing PCOS, with potential long-term benefits for physical and mental health. The integration of yoga with dietary guidance shows promise in improving both quality of life and symptom management. Future studies should explore objective clinical measurements to validate these results further and investigate the physiological and biochemical mechanisms underlying the effectiveness of yoga in PCOS.

Keywords: Polycystic Ovarian Syndrome (PCOS), Yoga therapy, Yoga based life style modification (YBLI), Lifestyle intervention, Mental well-being, Complementary therapies for PCOS.

Introduction

Polycystic Ovarian Syndrome (PCOS) is a prevalent endocrine disorder that affects a large number of women in their reproductive age, ranging from 11% to 13% globally (1). This condition presents a complex interplay of genes and environment factors that causes a lot of reproductive health problems , leading to various health challenges and impacting a woman's quality of life (2). Women with PCOS experience various symptoms and commodities, such as missed menstrual periods, unwanted hair growth, not ovulating, infertility, acne, sleep disorders, psychosomatic disorders, insulin resistance, impaired glucose tolerance, and even issues like type 2 diabetes and obesity (3).

Specifically, obesity significantly contributes to the worsening of PCOS and can exacerbate irregular

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menstrual periods. These challenges intensify with the increasing age of women, complicating the process of implantation and making it harder to get pregnant (4). The issue is exacerbated, particularly for younger females, by lifestyle choices such as consuming unhealthy foods and being less physically active in their daily routines. Many choose fast food or snacks over healthier options. These habits can lead to hormonal imbalances that contribute to weight gain. This sedentary lifestyle and fast-food consumption contribute to hormonal imbalances and increase the risk of obesity (5).

Because of these concerns, doctors are looking into holistic approaches to PCOS management. While medications and surgeries provide immediate relief, they are not without limitations (6,7). This is where yoga becomes relevant. Recently, this ancient Indian practice has attracted interest and attention as a potential treatment for women with PCOS. Many studies showed that it can help with several symptoms associated related to these reproductive health issues (8-10).

While medication can relieve the PCOS symptoms quickly, it does not always provide long-term relief. Additionally, they can lead to undesirable side effects like lower abdominal pain, unexpected spotting, nausea, weight gain, back pain, and prolonged hypomenorrhea. Many women find that their menstrual cycles return to normal only while they'reon medication (11-12); this highlights the importance of long-term and comprehensive management measures.

Yoga therapy, rooted in ancient practices, offers a promising non-pharmacological alternative to PCOS management. It's a non-drug option for treating PCOS. In ancient times, women stayed active doing chores without machines. Imagine drawing water from wells, grinding flour by hand, and washing clothes by hand—those tasks kept them healthy (13,14). Today's lifestyle is significantly different, as most people do not engage in this type of physical activity. By tapping into these old traditions, yoga offers a balanced way to manage PCOS and its worries—without the cost or side effects of medication (15). Understanding the need for affordable options, this study explores how well a yoga program works as part of managing PCOS (16). The program includes yoga postures, breathing exercises (pranayama) , guided relaxation, meditation techniques, and dietary guidance . These practices aim to improve participant's physical, psychological, and emotional health with PCOS (17-20).

This study aims to determine the feasibility and comfort of incorporating yoga therapy into regular routines, as well as the effectiveness of a yoga intervention as an adjuvant therapy for polycystic ovarian syndrome (PCOS). This questionnaire analyzed the PCOS patient satisfaction with yoga intervention as an adjuvant treatment, covering aspects such as the feasibility of yoga practices, sleep patterns, mental health, and menstrual cycles.

Methodology

In this study, we evaluated the effectiveness and feasibility of a yoga intervention as a adjuvant therapy for managing polycystic ovarian syndrome.

Ethical Considerations

The study was conducted in compliance with ethical norms and approved by Ethical committee of Institute of Medical Sciences, Banaras Hindu University.

Participants and Recruitment

Data were collected from Department of Obstetrics & Gynaecology at the Institute of Medical Sciences , Banaras Hindu University. A total number 220 PCOS patients were diagnosed using Rotterdam criteria, out of which 150 patients enrolled in the study . Out of these , 43 patients regularly participated in the online and offline yoga program.

PCOS Diagnostic criteria

According to the 2003 Rotterdam meeting, the diagnosis of PCOS requires the presence of two of the following criteria:

a) Oligo-ovulation;
b) Clinical or biochemical hyperandrogenism;
c) Ultrasound shows polycystic ovaries.

Assessment

We used a structured questionnaire to assess patients' satisfaction with the yoga intervention, covering topics such as feasibility to yoga postures, early difficulties adhering to a workout regimen, and effectiveness of yoga program in managing PCOS symptoms, as well as general satisfaction such as quality of life , physical and mental well-being .

Intervention

The yoga intervention program employed a holistic approach that encompassed[21]:

Yoga Postures: Specifically chosen because of their potential benefits in addressing PCOS symptoms.

Breathing Exercises: Techniques to regulate breath and promote relaxation.

Guided Relaxation: Practice to alleviate stress level and improve sleep disorder.

Meditation: Mindfulness yoga therapy to enhance emotional well-being.

Dietary Guidance: Advice on making healthy dietary plans to manage PCOS symptoms. A yoga program aimed to assess its effects on the physical and mental health of women with PCOS. Participants engaged in a variety of yoga styles, including Surya namaskar, Hatha and Vinyasa, alongside guided meditation sessions[21,22]. The program had the following goals:

Enhancing Physical Fitness: Improving strength, flexibility, and overall well-being.

Promoting Physical Fitness: Improving stress levels and fostering emotional balance.

Encouraging Regular Practice: Developing a lifestyle habit to continue beyond the program's duration.

Inclusive criteria

Patients aged between 15 to 35 years with a confirmed diagnosis of PCOS, who satisfied the Rotterdam criteria and were willing to participate in the yoga program.

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Exclusion criteria

Women suffering from ovary tumours, ovarian cancer, or ovarian cyst excision surgery or any medical condition that could interfere with the yoga practices or the assessment of PCOS-related outcomes, such as a history of cancer or other serious medical disorders.

Statistical Data Analysis:

Table 1

1. Did you find the yoga intervention program easy to attend regularly?		
	Frequency	Percent
Very Easy	24	55.8
Somewhat Easy	12	27.9
Neutral	2	4.7
Somewhat Difficult	5	11.6
Total	43	100.0

Table 2

2. Did you experience any physical improvements in your PCOS symptoms after participating in the yoga sessions?		
	Frequency	Percent
Significant improvement	13	30.2
Moderate improvement	16	37.2
Slight improvement	12	27.9
No improvement	2	4.7
Total	43	100.0

Table 3

3. Did you notice any changes in your mental well-being (e.g., reduced stress or improved mood) as a result of practicing yoga?		
	Frequency	Percent
Significant improvement	13	30.2
Moderate improvement	24	55.8
Neutral	6	14.0
Total	43	100.0

Table 4

4. How would you rate your overall quality of life before participating in the yoga intervention?		
	Frequency	Percent
Good	1	2.3
Fair	6	14.0
Poor	34	79.1
Very Poor	2	4.7
Total	43	100.0

Table 5

5. How would you rate your overall quality of life after participating in the yoga intervention?		
	Frequency	Percent
Excellent	7	16.3
Good	31	72.1
Fair	5	11.6
Total	43	100.0

Table 6

6. To what extent did yoga interventions help you manage your PCOS symptoms and overall well-being?		
	Frequency	Percent
Extremely helpful	4	9.3
Very helpful	21	48.8
Somewhat helpful	15	34.9
Not very helpful	2	4.7
Not at all helpful	1	2.3
Total	43	100.0

Table 7

7. Did you find the yoga intervention program to be an acceptable complementary therapy for PCOS management?		
	Frequency	Percent
Highly acceptable	8	18.6
Acceptable	27	62.8
Neutral	5	11.6
Unacceptable	3	7.0
Total	43	100.0

Out of the 43 participants, In (Table 1) , 55.8% found the yoga intervention program “very easy” to attend, while 27.9% found it “somewhat easy”. Regrading the effectiveness of yoga on PCOS symptoms, 30.2% reported “significant improvement” and 37.2% noted “moderate improvement” (Table 2). Additionally, 55.8% experienced “moderate improvement” in mental well-being, and 30.2% saw “significant improvement”(Table 3).

Before the yoga intervention, 79.1% rated their quality of life as “poor”, with only 2.3% reporting it as “good” (Table 4). Post- intervention, 72.1% described their quality of life as “good”, and 16.3% as “excellent” (Table 5). In terms of managing PCOS symptoms, 48.8% found yoga “very helpful”, while 34.9% found it “somewhat helpful” (Table 6). Lastly, 62.8% found the yoga intervention “acceptable”, and 18.6% rated it as “highly acceptable” as a complementary therapy for managing PCOS (Table 7).

The correlation between the duration of yoga practice and improvement in PCOS symptoms, mental well-being, and quality of life was statistically significant, for all tables. This emphasises the positive impact of yoga over time.

Figure 1

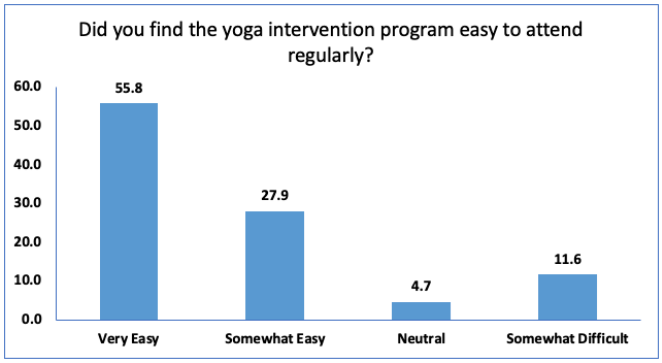


Figure 2

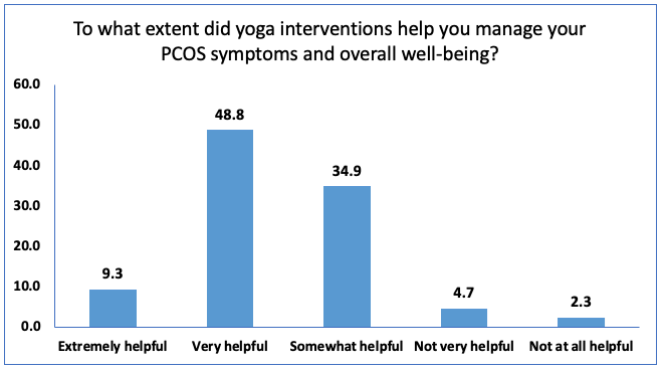


Figure 3

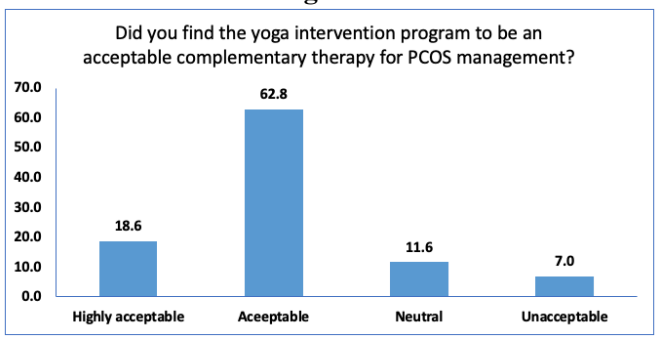
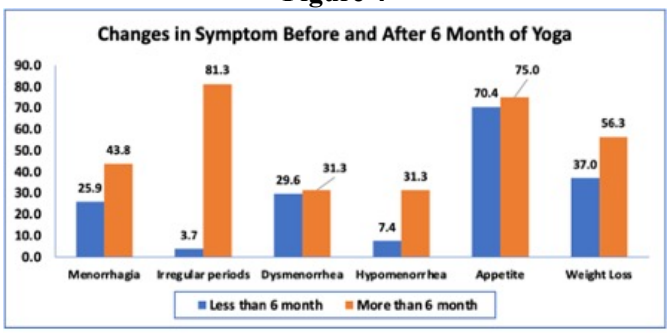


Figure 4



In Figure 1, illustrate that 55.8% of participants found the program "very easy" to attend, while 27.9% found it "somewhat easy." And in Figure 2 shows the impact of yoga on PCOS symptoms and well-being, with 48.8% rating it "very helpful" and 34.9% as "somewhat helpful". Figure 3 reveals that 62.8% considered yoga an "acceptable" complementary therapy for PCOS management, Figure 4 shows changes in symptoms over six months, showing significant improvements, with p-values <0.05, indicating statistical significance in symptoms reduction and quality of life enhancement.

Discussion

Feasibility and Comfort of Yoga as a Therapeutic Practice: Overcoming Initial Challenges for Long-Term Wellness

Patients who take part in the yoga program initially experience difficulties to incorporate yoga into their everyday routines. However, as they progressed, they reported feeling more comfortable and feasible with yoga postures. The yoga program to be accessible and adaptable, allowing patients to gradually ease into the practice without any physical demands.

Through consistent encouragement and support, participants mentioned that the yoga sessions were not tough but rather contributed to comfort over time. This determines yoga is a feasible and comfortable as an adjuvant treatment. Despite initial discomfort, patients adopted yoga easily, reporting that yoga session was not only feasible but also beneficial for long-term wellness. The only experience minor discomfort, but soon they develop soon comfort and confidence in their yoga practice.

The effectiveness of a yoga intervention in managing PCOS

The purpose of this study evaluates a feasibility and comfort to including yoga therapy into regular routines as well as assessment of the effectiveness of a yoga intervention as an adjuvant therapy for Polycystic Ovarian Syndrome (PCOS). Based on a patient's feedback, the results deliver valuable information about the feasibility and potential benefits of incorporating yoga into regular PCOS therapy. However, there are limited active treatment options for PCOS, leading many women seek complementary therapies to manage their symptoms. The purpose of this study was to investigate the effectiveness of yoga training online, covering aspects such as the feasibility of yoga practices, sleep patterns, mental health, and menstrual cycles, as an additional PCOS treatment over a 12-week period.

The study results showed that yoga intervention served as an effective adjuvant therapy for PCOS management over a duration of 12-weeks. Participants reported improved menstrual pain control and better weight management as a result of incorporating yoga into regular treatment for PCOS. In addition, the online yoga classes made the intervention easy and feasible to women who may have difficulty attending in-person sessions due to transportation or scheduling morning time.

According to the outcomes, yoga is effective for managing PCOS in a similar way to previous studies. PCOS women who practice yoga have shown improvements in their androgen levels, metabolic markers, and psychological distress. In addition, yoga is a cost-effective, self-directed therapy that can easily be integrated into everyday life, thereby serving as a valuable addition to standard medical care.

Yoga as an Adjuvant Therapy for Managing PCOS: Improving Quality of Life

Since PCOS and its related comorbidity are so common, there is a need for long-term, cost effective treatment options. Medical approaches are beneficial, but they don't provide long-term relief and may have adverse side effects like wright gain, back discomfort, leg pain, prolonged hypomenorrhea, and unusual spotting. These limitations show how significant it is to investigate complementary therapies like yoga.

In this study found that participants initially struggled to integrate yoga practice into their daily routines, but gradually became more feasible and comfortable with it. Despite early challenges, some

participants experience difficulty incorporating the yoga practices into their busy lives but gradually became more at ease and, with consistent encouragement and support, enabled women dealing with PCOS to incorporate yoga into their everyday routines.

In addition to be observed enhancement in both physical and mental well-being, this led to a significant improvement in their overall quality of life. This highlights the yoga therapy has the potential benefit of being an adjuvant approach for managing PCOS symptoms and promoting holistic well-being.

Conclusion

This study shows significant results for the potential benefits of adding a yoga program as a part of treatingPo lycystic Ovarian Syndrome (PCOS). Bringing about this lifestyle modification was initially a challenge. Despite initial challenges, participants successfully incorporated yoga into their daily lifestyle routines. It demonstrates that with adequate support from coaches or friends, women with PCOS can overcome barriers to consistent practice. The positive responses we received via our online questionnaire regarding the feasibility of online yoga delivery suggest that this approach can effectively engage participants and promote ongoing adherence.

The integration of dietary advice with yoga practices enhances a comprehensive management strategy that addresses both the psychological and physical aspects of PCOS (23-26). Participants reported significant improvements in their weight management alongside regularity in menstrual cycles, which suggests that yoga may help PCOS-affected women psychologically and physiologically (27-30).

However, the study's dependence on patient satisfaction underscores the necessity for additional research using objective clinical measurements to validate these preliminary results. Future research should investigate the physiological and biochemical impacts of yoga on PCOS to better understand its mechanisms and effectiveness. Overall, this study suggests that the feasibility of yoga intervention in a regular routine is comfortable, and particularly yoga combined with dietary changes has potential as a long-term, non-pharmacological approach for managing PCOS.

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Effect of Pranayama on Human Body and Mind

Review Article

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Abstract

A branch of yoga called *pranayama* is very helpful to people in maintaining good physical and mental health. As *prana* is the definition of life or energy, practicing *asana* entails controlling the flow of *prana* through the body. All aspects of breathing, including inspiration, expiration, and retention, are regulated in part by *pranayama*. One of the yogic practices for healthy people is *pranayama,* which can elicit a variety of physiological reactions for breathing exercises, stress reduction, relaxation, and control of psychophysiological conditions. *Pranayama* controls lung motion, which in turn controls the heart and vagus nerve. As a result, *pranayama* is closely related to the autonomic nervous system and uses breathing patterns and lung and diaphragm movements to bring its functions under conscious control. In disciplines like *yoga* and meditation, *pranayama* refers to the regulation and control of breath, also referred to as the life force. Numerous health advantages have been linked to it, such as enhancements in brain activity, heart function, blood oxygenation, and lung function. Different breathing techniques and habits can have a substantial impact on the autonomic nervous system, which can decrease negative reactions to stressors.

Keywords: *Yoga, Pranayama,* Mental health, Diseases, Breathing techniques.

Introduction

Yoga is a traditional practice that aims to improve an individual's physical, mental, emotional, and spiritual well-being. It is a long-standing custom in India that is spreading throughout Western culture. "Yoga" refers to the superconscious state known as Samadhi, which is the union of our individual consciousness with the Universal Divine Consciousness (1) The Rigveda, the oldest book of the human race, speaks of the wise practicing yogic meditation, and the Yajurveda encourages us to practise yoga to improve our physical and mental well-being as well as our prosperity. Yogic ideas are widely present in the Upanishads. In addition, the Bhagavad-Gita frequently uses terms associated with yoga, such as pranayama and samadhi. The ancient Indian rishis realised that in order to perform Raja-yoga, which is a concentration technique used to free the soul or *atma* from the bonds of maya and transform it into *paramatma,* one must always have a healthy body. This is why they said, "*Sharirmadyam, khalu dharma sadhanam*." Thus, they created "Hatha yoga," which consists of various asanas, mudras, and pranayama. According to "*Gharanda samhita*," out of 84 lakh asanas, 16,000 are considered the best, and only roughly 300 are widely practiced(2). Once more, "*Hathayoga-pradipika*" divides all asanas into four fundamental classes: padmasana, sinhasana, vadrasana, and sidhyasana(3). Additionally, there are two types of asanas: *shasthyasana* (to achieve a healthy body) and *dhyanasana* (a posture that shifts the centre of gravity to the ribs and maintains the spinal cord free)(1).

The Sanskrit word "pranayama" is created by combining the terms "prana," which means life breath or vital energy, and "*ayama*," which means expansion, regulation, or control(4) It is the yogic art of breathing, which consists of purposeful adjustments to the breathing mechanism, usually performed in a seated position. These adjustments include rapid diaphragmatic breathing, slow/deep breathing, alternate nostril breathing, and breath holding/retention(5) Pranayama incorporates four key breathing techniques: *Antaḥ kumbhaka* (retention of the internal breath), Bahir *kumbhaka* (retention of the external breath), and *Pūraka* (inhalation) and *Recaka* (exhalation). The most authoritative book on yoga in India, the Yoga-Sutra of Patanjali, states that pranayama is the fourth limb of the eight-fold holistic process that is defined as yoga(6).

Method & Methodology

Types of *Pranayama*

1. ***Nadi shodhanam***- Three equal-length cycles of breathing out through the left nostril and breathing in through the right, followed by three cycles of breathing out through the right nostril and breathing in through the left.

Benefits - gives the body an oxygen boost, removes and discards toxins, lowers anxiety and tension, revitalises and soothes the nervous system, aids in hormone

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balance, promotes balanced and unobstructed breathing channels, reduces the irritation of the respiratory system.

2. ***Kapalbhati*** - forceful and vigorous breathing out through the diaphragm and abdominal muscles. After that, the abdominal muscles relax, causing the breath to enter slowly and passively.
Benefits - It elevates heart rate and contributes to better oxygen and blood circulation. It improves lung capacity and strength while unclogging the nasal passages.

3. ***Bhastrika*** - It means bellows, as in the bellowing action of the abdominal muscles. Here, there is a strong and forceful inhalation and exhalation. Hyperventilation is a potential complication, and the effects are comparable to kapalbhati.
Benefits - It facilitates the brain's oxygenation, it is advantageous to the motor and neurological systems alike, it revitalises the mind and body in equal measure, Beneficial for people with anxiety and depression, it helps with fibrosis treatment.

4. ***Ujjayi*** - It denotes mastery over triumph, resulting from an expansion process that improves lung ventilation. The glottis partially closes during slow, deep inhalation and exhalation. It eliminates expectoration, relaxes the parasympathetic nervous system, and infuses wellness throughout the body.
Benefits - warms the body's centre from the inside out to control body temperature. Make your concentration better. Let go of all the tension in your body.

5. ***Bhramari*** - It denotes the presence of a large bee and the sound produced by a bee exhaling. Take a deep breath in through both nostrils and release the air with a humming sound.
Benefits- The best stress reliever is Bhramari Pranayama, which lowers blood pressure and relieves hypertension. It is suggested as a regular yoga practice at night to improve sleep because it eases cerebral strain, relaxes the nervous system, and stimulates the pineal and pituitary glands, supporting their healthy functioning. Finally, it helps you achieve inner calm, which facilitates self-healing.

6. ***Sitali*** - The tongue becomes like a tube when it is fully curled lengthwise. The tongue's tip stuck out from the lips. The act of inhaling produces a hissing sound. Fully exhale through both nostrils.
Benefits- Pitta excess is balanced. reduces heat build-up and helps the body cool. helps with digestion by igniting the digestive fire. lessens the digestive tract's acid production. Skin inflammation is alleviated. helps to lessen inflammation all over the body. helps to maintain mental peace by relaxing and easing the mind.

7. **Sitkari** - The lips split and clench as the tongue rolls back towards the soft palate. Now take a deep breath through your teeth, letting out a hissing sound. Completely exhale through both nostrils.
Benefits- helps bring chaos under control and calms the mind.

8. ***Suryabhedana*** - The right nostril is used to breathe in, hold the breath, and then release it.
Benefits - There is a decrease in anxiety, depression, and other mental illnesses. It is conventional wisdom that Surya Bhedi stimulates the brain. and increase core body temperature boosts the body's vitality, or prana, particularly during times of depression. purges blood impurities and restores skin health illnesses.

9. ***Murcchna***- Full inhalation through both nostrils is followed by a slow exhale that creates chin lock.
Benefits- provides comfort, stability, and mental serenity. The happy state that swooning produces is one in which the mind is calm and clear. By stimulating the nadis, this method raises the body's prana levels.

10. ***Plavini*** - Air first fills the stomach to capacity, and at the same time, air fills the lungs to capacity as well. After holding the breath, it is eventually released. It is a pranayama advanced mode.
Benefits - The Yogi can float in the water for hours by opening their chest and expanding their lungs. This technique is also believed to facilitate the removal of pollutants by enhancing blood circulation(7).

11. ***Purak*** - Breathe in slowly and rhythmically for a single, uninterrupted breath after a brief exhale. When you start breathing in, try to focus on your abdomen. Note the length of time you spend taking breaths(6).

12. ***Kumbhak*** - Sit in a comfortable position for meditation to start. One possible exercise would be Sukhasana. Start with some basic, natural breathing exercises. Antara *Kumbhaka* is the term for internal retention. Release your hand and raise your head, then take a proper breath out through both nostrils. For a further ten to fifteen minutes, repeat the exercise(6).

13. ***Rechak*** - Breathe in deeply and rhythmically for three seconds at a time, without stopping. Take six seconds to hold your breath. Breathe out slowly and gently for the next 12 seconds, taking care not to move quickly or forcefully. Exhaling for longer periods of time is the aim(6).

Results

Advantages of *Pranayama*

- **Increase quality of life** - One of the most common reasons people seek treatment with complementary therapies like yoga is for mental health issues like depression, anxiety, stress, and insomnia(8).
- **Enhances the quality lung capacity** - Lung function can be improved by pranayama practice. This includes strengthening your respiratory muscles and enabling you to hold your breath for longer. Pranayama can be beneficial for various lung conditions. It might strengthen asthmatic lungs and speed up the healing process from pneumonia(8).

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- **Calmness of mind** - Similar to yoga styles that are more widely accepted, pranayama helps improve mindfulness. Its breath-focused, mindfulness-based meditation technique can help you become more adept at living in the present(9).
- **Disorders pertaining to the mind and body**- Psychosomatic disorders are mental and physical illnesses. Psoriasis, ulcers, and migraine headaches are a few psychosomatic illnesses. Pranayama may assist in managing these by tying the mind and body together through the breath(9).
- **Enhances the quality of sleep** - Pranayama's calming properties may also aid in your ability to fall asleep.

Discussion

The purpose of pranayama is to raise and lower the respiratory organs in a focused, rhythmic, and deliberate manner. It consists of a long, delicate waft of breath holding (*kumbhaka)*, expiration (*rechaka*), and inhalation (*puraka*). The system is activated by Puraka, contaminated air and pollutants are expelled by *Rechaka*, and *kumbhaka* distributes energy at some point throughout the body. The movements stand for the circumferential extension (*visalata*), vertical ascent (*aroha*), and horizontal expansion (*dairghya*) of the lungs and rib cage. The concept can listen better and live a longer, healthier life thanks to this controlled breathing. It has been observed that pranayama reduces stress in young, healthy people. Experts claim that pranayama enhances your stress response by calming your nervous system. Pranayama's ability to reduce stress may also aid in sleep. Practitioners of pranayama showed greater states of mindfulness than non-practitioners. Additionally, the emotional control of the same students improved. This has been linked to the calming effects of pranayama, which help you become more aware. When your blood pressure reaches an unhealthful level, you have hypertension. It raises the possibility of developing certain potentially fatal illnesses like heart disease and stroke. Pranayama is considered the most efficient penance system. It is analogous to cooking. For instance, the body automatically consumes the right food, inspects it, and discards any components that are no longer needed. In a similar vein, pranayama purges impurities from the body while focusing the mind on a particular subject. Pranayama is the greatest penance there is. It tarnishes the ignorance and propels the numbers upward. Pranayama contributes to the reduction of amazing diseases. Furthermore, because breathing, or pranayama, is the most essential thing we can do for our body and because it supplies all of our organs with prana, or oxygen, it is vital to our enduring. The fact that breathing is one of the most effective ways for us to successfully eliminate waste products and toxins from our bodies is another important reason why pranayama is essential(10).

Contraindications

Additionally, those who have recently undergone abdominal surgery, high blood pressure, heart disease, hernia, gastric ulcer, epilepsy, vertigo, severe nosebleeds, detached retina, glaucoma, or are at risk of stroke should not use it.

Conclusion

This calming breathing exercise, also referred to as alternate nostril breathing, balances the left and right hemispheres of the brain. Additionally, it facilitates the body's blocked energy channels to release tension and exhaustion. It brings us to a state of deep balance and balances all internal opposing forces.

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Conflict of interest

The authors have declared that no competing interests exist.

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Ghrita and different herbal inclusions on neurological disorders - A perspective review

Review Article

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Abstract

Introduction: Ayurveda *ghrita* dosage forms are well appreciated in the Classical treatises for different diseases and may be useful in neurological conditions such as these formulations are recommended since birth for memory enhancement and improving intellect as the major development of brain completes within the initial 5 years. So, these PUFA embedded preparations with DHA, AA, BA, etc are extensively screened out for the cognition, memory, neuro-protective, genesis of plasticity, etc in terms of herbal constituents added with the dosage form. Material and Methods: The Classical Ayurveda treatises and the databases like Pubmed, Scopus, Web of Science, etc were searched with the words like nootropic, PUFA, DHA, etc. The articles related with synaptic transmission and the phytochemical domination in the neurotransmission were separated for further understanding of mechanism. Results: AChE inhibitory action can preserve the acetyl choline activity while the synaptic transmission exhibited by α-Asarone of AC, BM, etc. Similarly, the Glutamate transmission with the NMDA receptor protected the neuronal degeneration from β-Amyloid like protein accumulation in CP constituents. The Serotonergic and Dopaminergic neurotransmission pathway were also regulated by the herbal and the lipid factors. These different pathways were somehow involved in the memory enhancement. Conclusion: The *ghrita* and the herbals mentioned were maintaining the neuronal synaptic transmission. Further clarification is necessary regarding the intrinsic pathway related to the mechanism of *ghrita* dosage form.

Keywords: *Ayurveda, Medhya, Ghrita,* Nervous System, Neuroprotective, Psychiatric, and Memory enhancer, Glutamate activity, Acetylcholinesterase activity.

Introduction

The incidence of neurological diseases are at such an alarming rise that every third person has been reported as a vulnerable candidate. The cardinal factors that are contributing for such a situation includes stress circumstances, sedentary life style adoptions, changing environmental conditions and anthropological activities apart from the microbial contributions. In 2019, a research involving 204 countries, there were 805.17 million neurological disorder cases with an age-standardised incidence rate of 10 259.50 per 100 000 population and death around 10 million worldwide.(1) In India only, the prevalence rate in 2019 range from 3·0 to 11·9 per 1000 of the population and incidence from 0·2 to 0·6 per 1000 of the population per year. (2) These neurological diseases include Alzheimer's disease, Parkinson's disease, idiopathic epilepsy bipolar disorder, autism spectrum disorders, neurological cancers and different type of dementia. These diseases are not only concerned with individual disabilities but also drains out the economical and stability of livelihood of the individual, society and nation. Despite the tremendous achievement in medical and technological realms, there still exists the need of either a preventive strategy or a treatment aspect to be generated for combating these group of diseases.

Traditional medicine from Indian sub-continent practices the use of clarified butter or *ghrita* as daily regimen to be followed. The use of *ghrita* can be seen in the early hours of birth *Kashyapa Samhita* emphasizes the use of *ghrita* along with the practice of *Swarna Bhasma* in young children for intellect and immunological significance. The traditional form of this includes the custom of rubbing gold against the stone along with *ghrita* and given to the baby. The conventional medicine also has accepted the lipid collection in *ghrita* can surpass the Blood Brain Barrier (BBB). The endothelial cells of brain tissue can passively diffuse many lipid compounds when the same is impermissible to polar compounds that are more than 80 $Å^2$ in surface area.(3) Similarly, the *ghrita* can be seen extensively used in neurological conditions i.e.

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Unmada and *Apasmara* in the relevant classical treatises. *Ghrita* therapeutically purposes in every type of *Shodhana* protocol either as a pre-procedure or as a treatment regimen. In *Shamana* form *ghrita* pacifies the *Vata-pitta dosha* combination. Many studies have been conducted on different herbal plants which are mentioned in these formulations for both neurological and psychiatric manifestations such as *Vacha (Acorus calamus* Linn.*),Shankhpushi* **(***Convolvulus pluricaulis* Choisy*), Guduchi (Tinospora cordifolia* (Willd.) Hook. f. & Thomson*), Yashthimadhu (Glycyrrhiza glabra* (Licorice)*), Bramhi* **(***Bacopa monnierie*)*, Mandukaparni (Centella asiatica* (Linn.))*, Kushmanda (Benincasa hispida*(Thunb.) Cogn.*)) etc* and are incorporated in such *ghrita* formulations. Ayurveda explains this property of *ghrita* as *'Samskara Anuvartana'*, which specifies the imbibing nature of phytochemicals. This work extensively screens out the common ingredients in the mentioned *ghrita* formulas and revalidates among the available literature the contributory role in neurological manifestation.

Materials and Methods

Ghrita and the above mentioned herbal constituents were thoroughly checked for the protective action against the neuronal fraction in various in-vitro, in-vivo and clinical trials. The interrelated literatures were derived from Ayurvedic classical texts, research articles and journals. The search in digital databases were conducted using the following keywords: "Ayurveda", Nervous System, Neuroprotective, Psychiatric, and Memory enhancer, Glutamate activity, Acetylcholinesterase activity, etc. Among the search, 100 related articles were screened out and those related to the core synaptic activity were separated for further validation. The studies related to neurogenic transmission and the neurotransmitters interfered with the herbal constituents as a whole or the respective phytochemicals were validated for the neuroprotective activity.

Result

The interrupted neuronal transmission is one of the early disturbances that deteriorates the further cascade of functions. The impairment of memory or cognition and even the coordination of both the central or peripheral motor activity is disrupted due to deranged neuro transmitter metabolism and receptor bindings. The AChE inhibition promotes the Acetyl choline to bind to the related receptors. Similarly, the NMDA receptor activity binds with the glutamate fraction. The Serotonin and the Dopamine levels directly surmount in the quantification aspects to the related receptors. Table no:1 denotes the frequent herbal constituents denoted in the various *ghrita* formulations. Table 2 represents the various experimental models on neurological degradation and the pathways maintained by the herbal inclusions.

Table 1: Various *ghrita* preparations and the respective herbal constituents

S.No.	Name of the *ghrita*	Contents
1	*Brahmi ghrita*	*Brahmi, Vacha, Kushtha, Shankhapushpi* (4)
2	*Saraswata ghrita*	*Abhaya, Trikatu, Patha, Vacha, Shigru*(5)
3	*Ashtanga ghrita*	*Mandukaparni, Vacha, Shankhapushpi, Brahmi, Guduchi, Shweta Bakuchi, Shatavari, Brahmasoma*(6)
4	*Saptanga ghrita*	*Shankhapushpi, Guduchi, Vacha, Shatavari, Arkavallika, Malapu,*
5	*Ashtamangala ghrita*	*Vacha, Kushtha, Brahmi, Siddharthaka, Sariva, Pippali* (8)
6	*Shankhapushpadyam ghrita*	*Shankhapushpi, Vacha, Kushtha, Brahmi* (9)
7	*Vachadi ghrita*	*Vacha, Guduchi, Shathi, Haritaki, Shankhapushpi, Vidanga, Shunthi,*
8	*Mahapaishachik ghrita*	*Jatamansi, Haritaki, Shankhapushpi, Bharangi, Markati, Vacha, Trayamana, Jayanti, Veera, Chorak, Katurohini, Kutki, Brahmi, Varahi, Soya, Palankasha, Guggulu, Shatavari, Kayastha, Rasna, Prasarini, Vrishchikali,*
9	*Pathadya ghrita*	*Patha, Vacha, Shigru, Pathya, Trikatu,* (12)
10	*Phala ghrita*	*Manjishtha, Kushtha, Tagara, Triphala, Vacha, Haridra, Daruharidra, Madhuka, Meda, Dipyaka, Katurohini, Payasya, Hingu, Kakoli,*
11	*Abhaya ghrita*	*Brahmi, Siddharthaka, Kushta, Vacha, Sariva, Pippal, Saindhava lavanan* (14)

Table 2: Herbal constituents and the targeted activity in different experimental models

Herbs	Results	Functions/Outcome measure
Vacha *(Acorus calamus* Linn.)	1.Both α- and β-asarone exhibit multiple pharmacological properties including anti-apoptotic, and neuroprotective effects. Surpasses the blood-brain barrier. (15) 2. β-Asarone inhibited the ACh esterase activity. (16) 3. α-Asarone induced memory traits with d by its GABA antagonist and N-methyl-D-aspartate	Antioxidant, anti-inflammatory, anti-apoptotic, neuroprotective, inhibits AChE and suppresses TNF-α and IL-1β, GABA antagonist and NMDA receptor agonist learning and memory-enhancing activity

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Shankhpushpi *(Convolvulus pluricaulis* Choisy*)*	Reduced the oxidative stress in aluminium induced toxicity and scopolamine induced amnesia in brain of male albino Wistar rats. (18) 2. CP reduced the β-amyloid deposition in the brain to protect from memory dysfunction. (19) 3. It possess memory-enhancing, anxiolytic and CNS-depressant activity with CP showing the maximum activity.(20)	Reduce the production of Aβ, anxiolytic and CNS-depressant activity. Improves the cholinergic behaviour, reduction in oxidative stress, neuroprotective, and immunomodulatory
Brahmi (*Bacopa monnieri*)	Neuronal protection from beta-amyloid-induced cell death. This neuroprotection was possibly due to its ability to suppress cellular acetylcholinesterase activity. (21) 2.BM extract reduced the oxidative stress and prevent the loss of memory. (22) 3. BM reportedly downregulated the activity of MMP-3 and caspase 1 and 3 enzymes that modulate systemic inflammation in N9 microglial cell line. BM inhibits the release of inflammatory cytokines from microglial cells and inhibits enzymes associated with inflammation in the brain. (23)	Reduced the neuronal cell death and improved the memory cognititon, as well as the blocking in production of Aβ
Guduchi *(Tinospora cordifolia* (Willd.) Hook. f. & Thomson)	1.Butanol extract of TC pre-treatment given in Glutamate induced neurotoxicity resulted in downregulation in the expression of neuronal markers and anti-apoptotic marker Furthermore, Butanol extract of TC was observed to promote regeneration, migration and plasticity of cerebellar neurons. (24) 2. TC produced significant neuroprotection by increasing the dopamine level. Parkinson's disease in male Wistar rats. (25) 3. TC effectively mitigated ROS generation and prevented oxidative stress in mitochondrial dysfunction. (26)	Neuronal plasticity maintenance and protection against degeneration.
Shatavari *(Asparagus racemosus)*	1.*Shatavarin* improved Parkinson's disease symptoms by reducing accumulation of alpha-synuclein, lipid accumulation and increased the dopamine level. (27) 2. . AR enhanced the brain-derived neurotrophic factor (BDNF) and ERs up-regulation which may be	Enhanced BDNF and reduced the Oxidative stress.
Patha *(Cissampelos Pareira* Linn.)	1.*Patha* reduced the age related cognitive decline . (29) 2. Patha showed significant results in comparison with the Daizepam for the anxiety-like behaviour in adult albino rats. (30)	Protects from cognitive decline and exerts the anxiolytic behaviour.
Shigru *(Moringa oleifera Lam)*	Leaf extract showed potent nootropic activity.(31)	Nootropic and antidepressant activity.
Trikatu *(Zinziber officinale* Roscoe*, Piper nigrum*(L.), *Pippali, Piper longum* L. *)*	1.*Piperine* protected from mitochondrial integrity via reducing oxidative stress and improving mitochondrial membrane potential and neuronal survival in a cerebral ischemia rat model. (32) 2. Piperine exhibited the antioxidant and cognitive enhancement in streptozotocin (STZ)-induced dementia in Male Wistar rats. (33)	Improved mitochondrial membrane potential and neuronal survival.
Triphala *(Emblica officinalis Gaertn, Terminalia bellerica (Gaertn) and Terminalia chebula* Retz.*)*	1.*Triphala* polyphenols reduced the stress induced cognition deficit.(33) 3.*Triphala* enhanced the memory functions in the AD (34)	Improved the cognition deficiency and the memory functions

Discussion

Ghrita is included under *Chatushasneha*, along with *Taila,Vasa and Majja*. The quality to imbibe the features of the coalesced ingredients and the unique ability to reach within the deepest tissue in a *ghrita* dosage form makes this oily preparation significant from the rest of the lipid fractions. It is used as food as well as for therapeutic purposes. *Acharya Kashyapa* has

mentioned, various herbs that are utilized in conjunction with *ghrita* to strengthen *Medha* given in the concept of *Jatakarma Samskara*. *Kashyapa* also mentioned various formulations i.e. *Abhaya Ghrita* which contain herbs which have nootropic effect. *Acharya Charaka* has also mentioned various *ghrita* such as *Brahmi ghrita, Kalyanka ghrita, Mahakalyanaka ghrita* etc. which is recommended in *Unmada* and *Apasmara*. It can be utilized not only for the growth and development of young children but also for older adults due to its abilities to support memory, cognition, and bodily functions that are necessary for the body to function properly.

In conventional science *ghrita* can be regarded as a lipophilic dairy product containing lipid, water and less than of non-fat substances. It is rich in Polyunsaturated fatty acid (PUFA) of omega-6 and omega-3 series, especially Docosahexaenoic acid (DHA) and Arachidonic acid (AA) which is responsible for the development and maintaining the function of the brain since childhood and throughout life. Another constituent Butyric acid (BA) was found to combat the *Porphyromonas gingivalis* and *Fusobacterium nucleatum* that leads to periodontitis. This was by preventing the apoptosis rate, accelerating the SOD, CAT enzymes and preserving the mitochondrial status. (35) The neurons utilize the oxygen to generate Reactive Oxygen Species (ROS) that directly depletes the anti-oxidant enzymes which are also seen in age old conditions or when disease pathogenesis encroaches the body. The above mentioned herbals constituents exhibit the anti-oxidant and anti-inflammatory activity besides the antiepileptic, antidepressant, nootropic activity, etc. The active component of these herbs could be the main reason for the pharmacological activity in the brain through different pathways. *Ghrita* as main ingredient not only act on the brain and perform different functions i.e. neural development, nerve cell differentiation and migration, myelinations and synaptogenesis, but also act as target-delivery agent for the active chemical constituent of these herbs through synergistic effect.

Memory loss is an initial symptom of neuronal degeneration other than confusion, irritation, behavioural changes and other cognitive deficits. In the most common Scopolamine related models the Akt, MAPK and ERK pathways are found to be affected. This muscarinic receptor antagonist models targeted the acetylcholinesterase inhibitor research. The methanolic extract of AC rhizome are found in many such induced model for such inhibitory activity. The aqueous and dichloromethane extracts were showing the dose related deviations and (36) α-Asarone is the major compound isolated acting upon the cortex, hippocampus and the striatum regions. The acetylcholine preservation at the synaptic sites are found to be the reason inferred from these models. CP exerted the activity in the cortex and the hippocampus regions of male Wistar rats. (37) BM carries the phytochemicals like quercetin, apigenin, wogonin, and bacopaside X, which were showing the affinity towards the Acetylcholinesterase (AChE) with weak hydrogen bonds and vander walls force of attraction for the inhibition via anionic sub-active site of AChE which is same as the mechanism shown by Donepezil. (38) AR exerted the evidence of AchE inhibition on the hippocampal and the prefrontal cortex of the charles foster male albino rats by the steroidal saponin content. (39) Tinosporide and 8-hydroxytinosporide isolated from TC were the other phytomolecules with this synaptic inhibition of the AChE. (40) The combined effects of Triphala or Trikatu are not much explored in this aspect even though individual drugs like Emblica officinalis is reported with this activity. (41)

The L –glutamate and the ROS induced neuronal cell death are the other target specified pharmacological models with confined effects on the NMDA receptors. These are the glutamate receptors that influence the synaptic plasticity along with the memory and learning. α-Asarone of AC was exerting the protection on the hippocampal cells against Endoplasmic Reticulum stress with the phosphorylation of the protein kinase RNA-like ER kinase (PERK). (42) An in-vitro model on mice hippocampal cell line (HT22 cell line) exhibited the protective model activity with the hexane extract from BM. (43)

In similar fashion the serotonin transmission and synthesis is also necessary for the proper psyche. The Selective Serotonin reuptake inhibitors are regarded as one of the effective anti-depressant medicines. BM has been found to increase the tryptophan hydrolase activity which is the enzyme needed for Serotonin synthesis. This increases the levels of serotonin synaptic activity by the drug. (44)The same upregulation can be seen in the SERT (Serotonin Transport Proteins), which are the transport proteins for the further metabolism which creates the contrast activity but indicates the adaptability of neuronal fraction to the available phytochemicals. (45) . But AC has seen only to increase the serotonin levels. (46). Whereas the CP and TC can regulate the dopaminergic and the serotonergic pathways.

The lipid fractions of *ghrita* like DHA along with these herbal contents can improve the synaptic transmission. The passive diffusion of DHA might be facilitated due to the concentration of the neuronal grey matter, synopsis, mitochondria and microsomal factors embedded with such lipid fractions. (47) Many in-vivo models also report the high DHA diet and synaptic improvement of the DHA levels. There are evidences for less neuronal cognitive decline in regions consuming the heavy DHA embedded diets. (48)

Conclusion

We can conclude that *ghrita* base formulation is a special product in terms of both as a food and medication which is beneficial to all age groups particularly from the time of birth for the development of brain. *Ghrita* carries the better bio-availability, when processed with nootropic herbs increasing the potency and have better absorption and transportation of phyto-constituents. More researches have to be conducted to determine the pharmacodynamic and pharmacokinetics characteristics of these formulations.

Abbreviations:
AA : Arachidonic acid
Aβ : Amyloid beta peptide
ACh : Acetylcholine
AChE : Acetylcholinesterase
AD : Alzheimer's disease
AR : *Asparagus racemosus*
BA : Butyric acid
BM : Bacopa monnierie
BDNF: Brain-derived neurotrophic factor
CAT :Chloramphenicol acetyltransferase
CNS : Central Nervous System
CP : Conculvulus pluricauli
DHA : Docosahexaenoic acid
GABA : Gamma-aminobutyric acid
IL-1β : Interleukin-1β
NMDA receptor : N-methyl-D-aspartate receptor
TC : *Tinospora cordifolia*
TNF-α :Tumor necrosis factor alpha
STZ : streptozotocin
PUFA : Polyunsaturated fatty acid
SOD : Superoxide dismutase
ROS : Reactive oxygen species

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Yoga - A Paramount Approach to Human Health

Review Article

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Abstract

Within the realm of yoga, the Eight Limbs Path facilitates various aspects such as mental and physical coordination, cultivates positivity in the mind, and keeps the body healthy and fit, all of which enhance bodily functioning. Modern living is characterised by a variety of diseases and deformities, the majority of which are brought on by imbalanced diet and other factors. The mind is never present in the moment; it is constantly inquiring and rebelling. The mind's task is to think; it interprets everything without stopping. This pattern of habit changes behaviour and attitude and is observed, perceived, and experienced. Yoga is practiced by many people who want to maintain their health and well-being, get fitter, reduce stress, and live better lives. It can also treat certain health conditions such as back pain, neck pain, cancer and anxiety. In fact, yoga performed better than the control and waitlist methods, but not better than the treatment comparison groups, such as other types of exercise. Several other trials compared groups of yoga and vigorous exercise. Once the physical and mental health benefits of yoga were determined, participants were assigned to an inactive control group. Short breaks should be investigated to determine effectiveness and daily performance.

Keywords: *Yoga,* Illness, Eight Limbs Path, Vigorous exercise, Rebelliousness.

Introduction

Yoga is a philosophic form of physical exercise and meditation that dates back 2000–4000 years to what is now India. Yoga comes in a variety of forms, all with different practices but the same goal of aligning the mind and body(1). Asanas (postures) that are held for a predetermined amount of time, pranayama (controlled breathing exercises), and meditation are common components of many forms. The general goal of yoga practice is to support the integration and development of the body, mind, and breath in order to produce effects that are structural, physiological, and psychological (2). In particular, the growth of a pain-free, flexible, and strong body; a balanced autonomic nervous system that permits all physiological systems to operate at peak efficiency; and a peaceful, clear-headed mind (1).

Yoga science is essentially a philosophical psychology. The very first instruction in Patanjali's Yoga system is to control your mind. This is known as Yoga's chitta-vritti-nirodhah. The philosophical underpinnings of the need to control the mind, which are found in Samkhya and Vedanta, are not covered in detail by Patanjali(3). He states quite succinctly that yoga is mental control and mental restraint.

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Yoga is a science of experience. The primary advantage of yoga is its ability to harmonise our mental and physical states. Yoga can help to slow down the ageing process, which is primarily an artificial condition brought on by autointoxication or self-poisoning (Alleger, I. 2007). We can considerably lessen the catabolic process of cell deterioration by maintaining the body hydrated, pliable, and clean. We must combine the practices of yoga asanas, pranayama, and meditation in order to reap the full benefits of yoga.

In Western societies, hatha yoga is the most widely practiced style of yoga. It uses asana to improve balance, strength, flexibility, and mental-physical coordination. breath to quiet the mind and cultivate self-awareness, along with pranayama and meditation exercises(4). The rate at which asanas are executed, the physical intensity and degree of difficulty, the relative emphasis on body alignment and relaxation, and the surrounding temperature are the characteristics that distinguish the various hatha yoga styles that have emerged. Living yoga is more in line with its traditional principles. It consists of controlled breathing (pranayama), asana, and awareness of the mental-controlling yoga sutms (principles).

Regular yoga practice improves body-mind awareness, which is important for diabetic self-management of diet and exercise regimen. Eight steps, or limbs, make up Patanjali's theory of yoga. Each step is equally significant and interconnected as a component of the whole. Self-realisation or discriminative enlightenment is the goal of these eight limbs(5). However, the focus here will be on the

advantages to health. The following are the eight steps, or limbs, of yoga:

- *Yama*: Self-regulation, abstinence, and codes of restraint;
- *Niyama*: self-training, practices, and observances;
- *Asana*: Pose for meditation
- *Pranayama*: Breath and prana expansion, control, and regulation;
- *Pratyahara*: turning inward and withdrawing the senses;
- *Dharana*: mindfulness;
- *Dhyana*: Calm Possession
- *Samadhi*: The ultimate state of concentration, deep absorption, and elevated meditation.

The two pillars of the yoga lifestyle are "spreading the Light" and "cleaning the mirror." The body and mind are the mirror. They must be tidied upand pure to initially capture the light. So, living a yoga lifestyle is about maintaining physical health and mental purity. The yoga lifestyle is based on a set of ideals and principles, some of which are related to the *YAMAS*, or the five rules of social conduct:

1. *AHIMSA* = non-aggression
2. *SATYA* = veracity
3. *ASTEYA* = not pilfering 4.
4. *BRAHMACHARYA* = signifies loyalty
5. *APARIGRAHA* = Anticipate no greed

Yoga way of life (healthy routines): Swami Satchidananda gives whatever you do your all and everything inside of you. Don't just try it once. Give everything you do your whole attention.

The healthy habits of yoga, as advocated by Swami Satchidananda. Give whatever you do your all and everything inside of you. Don't just try it once. Whatever you do, put your all into it. focus. That's what yoga is. Yoga is more than just putting yourself in a corner, sitting up straight, and then practising breathing exercises or japa. Everything revolves around my yoga. You only practise yoga. When you begin working on something, give it your whole attention. The Bhagavad Gita states, "Yogaha karmasu kaushalam." This implies that yoga is perfectionism in all of your actions.

The first and (generally acknowledged to be) most significant yoga principle is ahimsa. Ahimsa is applicable to everything, including how we treat every other creature as well as our own bodies and minds.
Our thoughts and the topics they explore; our speech and topics discussed; and our eating habits and the foods they choose.

Yoga combines physical exercise with an inwardly focused, mindful focus on awareness of the breath, energy, and self. It is a type of mind-body fitness. The therapeutic methods and teachings of yoga are based on four fundamental ideas(6). The first is that the human body is a holistic entity made up of different interconnected dimensions that are inextricably linked to one another, and that any illness or health state that affects one dimension also affects the other dimensions. The second tenet is that every person has different needs, and that each person must be treated as an individual with a practice that is customised to meet those needs. The third tenet of yoga is that each practitioner is an empowered self-healer. Yoga involves the student in the healing process; by actively participating in their path to wellness, the student gains a greater sense of autonomy and the healing occurs internally rather than externally. The fourth principle holds that mental health and well-being are essential to recovery. Healing occurs more quickly when the person is in a positive mental state; on the other hand, healing may take longer when the person is in a negative mental state(6).

Aim of this study

Yoga is now widely practiced in health clubs, community centres, yoga studios, and schools for fitness and well-being.

Because of its popularity, carefully monitored research is now required and clinical trials to assess its effectiveness in promoting overall health, averting disease, and assessing its potential as a supplemental or adjuvant treatment for the treatment of chronic illnesses or pain. Although studies involving children and young adults have also been conducted, the majority of yoga studies that are currently available in the published literature have been done with adults. The purpose of the review study was to conduct a systematic search of the scientific literature, focusing on finding narrative, critical, and systematic reviews that included studies on the health benefits of yoga in individuals in good health.

Methodology

Search engines used to locate published articles included MEDLINE, EMBASE, Scopus, Science Direct Databases Directory of Open Access Journals (DOAJ), PubMed, and Google Scholar. The conjunctions OR/ AND were used as well as the terms yoga, illness, treatment, and mechanism.

Searches could only be conducted in English studies detailing the use of yoga in the treatment of life disorders. Research published in languages other than English, research published in letters to the editor, conference proceedings, grey literature, previously unpublished data, news items, abstracts and full texts that couldn't be retrieved, and studies that weren't relevant to the current review weren't included.

Discussion

Health Benefits of Exercise

There is historical evidence that exercise can be used to maintain optimal health and aid in rehabilitation civilisations. The Greek philosopher Hippocrates, known as "the father of medicine," recognised the benefits of exercise for both physical and mental health in the fourth century B.C., and the ancient Indian medical system (Ayurveda) recommended exercise and massage for the treatment of rheumatism as early as the ninth century B.C. (7). More recently, a number of epidemiologic studies have shown inverse relationships of differing degrees between the risk of multiple chronic conditions, such as osteoporosis, depression, anxiety, thromboembolic stroke, hypertension, Type 2 diabetes

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mellitus, coronary heart disease, and obesity(8). Furthermore, an expanding corpus of studies over the previous 20 years has offered "persuasive" proof of an opposite physical activity and colon cancer risk correlation . Additionally, there is proof of a "probable" inverse relationship between physical activity and the chance of developing additional cancers, such as breast cancer after menopause, endometrial cancer, and restricted suggestive" proof of a comparable correlation between physical lung, pancreatic, and breast activity prior to menopause cancer (1). In addition to its significant contribution to the main prevention of several chronic illnesses, regular physical activity lifestyle can offer numerous health advantages to people who are bearing the weight of long-term illness. There is proof that many chronic diseases have benefits to both physical and psychosocial health when people exercise regularly conditions and as a result, government health departments now advocate maintaining good physical health as a crucial component of self-care to enhance overall wellbeing, increase mobility, and lessen symptoms. In addition to extending survival and improving overall health-related quality of life, an active lifestyle can play a significant role in managing or lessening the effects of a chronic illness (secondary and tertiary prevention)(1).

Health Benefits of Yoga

Yoga has fewer health benefits than other exercise regimens when it comes to disease risk and its ability to manage chronic conditions distinctly established. Research has examined the differences in the physiological reactions elicited by yoga practice versus traditional exercise regimens. Some studies have demonstrated that the heart rate response to regular yoga sessions in healthy adults at normal room temperature is comparable to low-intensity walking exercise (9). This level of exercise is not sufficient to support cardiovascular fitness and overall health at the current recommended level. Studies on healthy adults, however, have shown mixed results; higher levels of cardiopulmonary stress were noted during yoga sessions (10).

Furthermore, certain studies (though not all of them) have shown improvements in cardiometabolic health indices in healthy adults who practise yoga.

Maximum oxygen capacity , muscular flexibility and blood cholesterol profile(11)have all been shown to improve in a number of single group (uncontrolled) studies. Additionally, there has been a decrease in physiological effort at submaximal exercise intensities and a lower level of perceived exertion at maximal exercise capacity . These changes in cardio metabolism imply that yoga can induce a high enough degree of cardiopulmonary stress to have health benefits. There have been reports of additional advantages for healthy individuals practicing yoga, including enhanced respiratory expiratory and inspiratory pressures, as well as improved visual and reduced weight gain in those who were already overweight and slower auditory reaction times. While some studies (e.g. Blumenthal and others, 22) have found no improvement in cardiopulmonary variables after programmes of yoga practice, the type of yoga practiced, the practitioner's experience level, and the session's ambient temperature are likely to have a significant impact on the actual level of physical exertion experienced during a session, and thus the stimulus for cardio metabolic adaptations. In addition to the physical exercises, yoga incorporates a spiritual component and breathing techniques that are uncommon in other types of exercise and may have additional health advantages(1).

The Canadian Agency for Drugs and Technologies in Health (CADTH) recently conducted a thorough evaluation of the available data and guidelines, analysing the standard of the evidence supporting the use of yoga as a treatment for a few particular mental health conditions, along with links to research and best practices for each of these mental health conditions. The evidence-review report found evidence in favour of yoga as a treatment or adjunctive treatment for depression, to summarise its conclusions. However, yoga may be suggested as a second- or third-line treatment after medication and psychotherapeutics, depending on the kind and severity of depression. In cases of severe depression where there is a significant risk of suicide, yoga is best viewed as a treatment adjunct.

Stress-relieving effects of Yoga

Stress is necessary to maintain homeostasis, but it can be harmful when it overtakes a person or interferes with homeostasis(12). Stress stimulates the nervous system, which also lowers immunity and overworks the adrenal glands(13). Stress throws off the balance between the parasympathetic and sympathetic nervous systems, affecting the body's equilibrium and, ultimately, quality of life(12). Since more young people are experiencing mental health problems and leading challenging lives, there is a pressing need to develop solutions that can reduce stress levels in this demographic (13).

Role of Yoga in preserving physical health

Yoga is more effective in managing both mental and physical health (Chen, K.-M. et al., 2010). The Yogic Intervention has been demonstrated to have a major impact on overall wellbeing; (Kumar K 2012). Yoga could be used as a preventative measure. A different study conducted in Toronto, Canada, unequivocally shows that people who engage in physical activity have a lower risk of developing hypertension than people who lead sedentary lives (Shephard RJ. 2001). According to a 2013 study by Pokhariyal K P and Kumar K, there is a substantial impact of Hatha Yogic Practices on Body weight of the Human subjects. After 4-14 weeks of yoga practice, a study on patients with coronary risk factors and angina revealed a positive response in their lipid profile.

Numerous studies have supported the notion that exercise raises HDL cholesterol, which is supported by an Ontario, Canada study that also supports our findings (Katzmarzyk PT 2001). In his research, Kumar K. (2013) found that yogic cleansing, or shatkarma,

decreased the subjects' blood glucose and cholesterol levels(10),(14). Another study found that the subjects' overall body weight was affected by the yogic intervention (Kumar Kamakhya 2015).

Yoga practice has a positive effect on physical health on a number of general health factors(1).

Impact of Yoga on obesity

Obesity is one of the most common metabolic disorders in the modern world. Due to the continuous changes in lifestyle, environment, and dietary habits in the modern era, man has become susceptible to a wide range of illnesses like obesity. Given the importance of health in today's quickly globalising society, obesity is essentially a lifestyle disorder. As BMI increases, lifespan and life expectancy decrease. It's one of the most common nutritional problems. Obesity is a contributing factor to many diseases, such as diabetes mellitus and hypertension(15). Whether an asana is done alone or in a continuous sequence, such as the sun salutation, it can have varying effects on the body. However, there is no doubt that yoga encourages better calorie burning (15).

Impact of Yoga on Diabetes

It is claimed that practicing yoga reduces stress in life and can even lower blood glucose levels after eating (16). Research has shown that yoga improves the chest wall's dynamic flexibility (17). The flexibility of the hip flexors, anterior trunk, hamstrings, and upper back are targeted in the second and third poses, which involve bending forward and backward; the gastrocnemius is the focus of the fourth and sixth poses. The last elements include the cobra stance, which is perfect for this use(16),(18).

In cases of low back pain, yoga, a self-controlled spinal adjustment, can produce better spinal adjustments(19).

Cardio-respiratory efficiency is enhanced by yoga

According to Madanmohan et al. (2008), six weeks of yoga instruction reduces the sweating reaction to steps test and causes both male and female subjects' respiratory pressures and endurance in the 40 mm Hg test to significantly increase. In a different study, the researchers found that practicing yoga for 12 weeks significantly increases hand grip strength, maximum expiratory pressure, maximum inspiratory pressure, and breath holding time after expiration and inspiration (Madanmohan, 1992)(20). The significance of Nadi Sodhan and Kapalbhati on forced ventilation capacity (FVC), maximum voluntary ventilation (MVV), and picks expiratory flow rate (PEFR) is demonstrated by Kumar K. (2013) in his study(14). Additionally, Joshi et al. (1992) showed that a six-week pranayam breathing course improved ventilation as evidenced by a decrease in respiratory rate and increases in the maximum voluntary ventilation, peak expiratory flow rate, forced expiratory volume at the end of the first second, forced vital capacity, and extended breath holding time(1).
After practicing yoga for ten weeks, Makwana et al. (1988) saw similar positive results. An increase in both expiratory and inspiratory pressures indicates that practicing yoga strengthens both the expiratory and inspiratory muscles.

Skeletal muscles and respiratory muscles are similar. Isometric contraction, a component of yoga techniques, is known to boost skeletal muscle strength. The initial lung volume determines the breath holding duration. Gains control over breathing by overriding the stimuli to the respiratory centres. This and enhanced cardiorespiratory function could account for the subjects who trained in yoga's extended breath holding periods(21).

Impact of Yoga on the reproductive system

Women are more likely than men to experience health issues like irregular menstruation. They also have a duty to have a healthier population if they want to be a wealthy nation. In case of premenstrual syndrome has an effect on the everyday lives of women, especially college-age women. Premenstrual syndrome may be exacerbated by the sedentary lifestyles of college females, which also affect their BMI ratio. The body and the mind need to be active for one to be in good health. Everyone's general health will improve with physical and breathing exercises(22). According to studies, performing the yoga on a regular basis may help women with irregular menstrual cycles and guarantee simple labour. It helps to bring back the lustre. It helps to prolong the appearance of wrinkles, restore the sheen throughout, and improve its durability and brilliance (23),(24). Numerous menopause symptoms can be lessened by regular yoga practise (25). Every age range can gain from it is used because it can improve physical performance prior to adolescence(26). Based on the research, abnormal BMI has an impact on premenstrual syndrome. Combining Surya Namaskar with walking can help relieve menstrual pain and help shed pounds gained from a sedentary lifestyle. The results of the study show that teenage girls who exercise regularly can permanently prevent the symptoms of premenstrual syndrome(22). Every female experiences menarche, which comes after puberty and is a critical stage in preparing her body for reproduction. Due to dietary habits and environmental factors, menarche and puberty occur earlier than they should when the body is not ready for those changes procedures. This lowers life expectancy, raises the risk of cardiovascular disease, and causes dysmenorrhea, infertility, and a host of other menstrual cycle-related problems(27). For girls, yoga is crucial for delaying puberty and readying the body for the necessary changes. As a result, it's imperative to begin teaching yoga to children as early as age 7. Twelve weeks of yoga classes lasting an hour, covering asanas, pranayama, meditation, and yoga. Results of the yoga for teenage girls suffering from PCOS (polycystic ovarian syndrome) demonstrated(27) alterations in cholesterol, insulin, and blood sugar levels that were significant(27). Additionally, in a study involving 42 men, practicing yoga decreased seminal oxidative stress and enhanced sperm motility and oxidative DNA

damage, which together have a positive effect on the sperm's dynamics(27). Research highlights the importance of prenatal yoga in mitigating pregnancy-related stress, hormone fluctuations, and labour pain Nonetheless, caution is advised when recommending asanas and consideration of contraindications during pregnancy. Prenatal yoga is claimed to have positive effects on musculoskeletal activities and to help hospitalised high-risk pregnant patients relieve stress.

Yoga helps with common disorder management

These days, depression, hypertension, and joint-related issues are all very common. Yogic intervention has a significant impact on serum glucose levels, according to Kumar K (2012). on People with depression People with rheumatoid arthritis who took part in a yoga programme for three months showed stronger handgrips than those who did not practice yoga, according to Haslock, et al. (1994). In their study, Negi A and Kumar K noted that Yogic Intervention had a significant impact on the R A Factor in gout patients. People with hypertension have shown to have significantly lower blood pressure when they practise yoga (Blumenthal JA 1989). Yogic intervention has been shown to have a significant impact on blood uric acid levels in another study(1).

Conclusion

The findings indicate that yoga enhances physical strength of respiratory muscles, treats premenstrual symptoms, and lowers blood pressure, stress, flatulence, body weight constipation, and blood sugar levels. It also lessens the chance of high-risk pregnancy, enhances male sperm motility, and reduces oxidative stress and damage to seminal DNA. As a result, we conclude that in order to benefit from yoga, everyone should do it every day. There is still more to discover about the health benefits of yoga, as its full benefits are still unknown.

Limitations

More research is needed to fully understand yoga's molecular influence before recommending it in future disease management strategies. Subsequent investigations featuring a sound methodology, a substantial sample size, and advanced techniques should, however, corroborate the results of the present investigation.

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Conflict of interest

Authors declare no conflicts of interest.

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Concept of *Kala*: Ayurvedic & Modern Perspective

Review Article

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Abstract

Ayurveda, much like an ocean, offers an endless horizon of topics that remain unresearched and full of potential. *Rachana Sharir* is one of the fundamental part of *Ayurveda* that deals with the different structures of human body like *Asthi, Sandhi*, *Twacha*, different Indriya and *Kala* etc. '*Kala Sharir'* is one such important concept that requires a comprehensive understanding, despite the limited descriptions provided in our classical texts. *Kala* is a limiting membrane act as boundaries between the tissues (*Dhatus*)and their respective organs or cavities (*Ashayas*). *Kala* was first time described by *Acharya Sushruta* in the "*Sushrut Samhita Sharir Sthana"*. Comprehensive study of *Kala Sharir* will definitely aid important information in better understanding of human body anatomy as well as physiology. Through this Article, we are trying to explore, that how the concept of *kala* can be integrated with modern medical practices for a more holistic approach to diagnostic or treatment modalities. This will help to shed light on the topic and make it easier to understand its usefulness in Medical Science.

Keywords: *Kala, Kala Sharir, Dhatu, Aashaya*.

Introduction

Ayurveda is an extensive body of literature whose purpose is the attainment of *Dhatu Samya,* which translates to the balance of bodily tissues. This can be achieved through a fundamental understanding of the body's basic principles. *Rachana Sharir* is one of the fundamental part of Ayurveda that deals with the different structures of human body like *Asthi, Sandhi*, *Twacha*, different Indriya and *Kala* etc. As diagnosis of disease is crucial before proceeding to treatment, similarly relevant knowledge of the systems of *Rachana Sharir* are very crucial for better understanding of the root cause of diseases and their cure, by applying medicinal management and surgical procedures**.**

'Dosha dhatu mala moolam hi shareeram' ||

The root causes of a living body are *Dosha, Dhatu and Mala*. These three entities are compared to the roots of a plant or tree by *Dalhana,* the Commentator of *Sushruta Samhita*. Ayurveda characterizes health as a complete four-dimensional status of bio-equilibrium (*Tridosha, Agni, Saptadhatu, Trimala*) and psycho-spiritual wellbeing of delightful state (*Atma, Indriya, Mana*). *Kala* is defined by *Acharya Sushruta* as " *Dhatu Ashaya antar maryada*" we can also corelate it as *dhatu- "dharnath dhatava*" i.e content which is holding and *Ashaya as "aadhar/ adhishthan* or as container". The concept of *Kala* also revolves around the concept of *Dosh Dhatu and Mala*. As out of seven 4 *kala (Rakta, Mamsa,Meda,Shukra*) are inculcated in *dhatu*. 2 (*Shleshma,Pitta*) are inculcate in *dosha,1(Purish*) is inculcate in *mala*.

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Kala Sharir

Definition

"*Kala khalvapi saptbhavanti DhatuAsayantare maryadah*" (1).

Kala is unique *Ayurvedic* concept explained by *Acharaya Sushrut* in *Sushrut Samhita*. *Acharya Sushruta* while explaining the detailed development of body parts in *Garbhavyakaran Sharir.* In the fifth Chapter of *Sharir Sthan* mentioned the concepts of *Kala*. He has explained *Kala* as a barrier between dhatu and its ashaya. There is total Seven *kala* in body. They form a protective coating for the *Ashayas* as well as boundary between the Ashayas and dhatus. Kala is limiting membrane or layer in our body situated between *Dhatu* and *Aashaya*. These are Extremely minute structures and invisible to naked eye, similar to cell. Their existence can be understood by their functions in the body. The word *kala* stands for the property or a quality so these are pecial membranes in the body which are having important role in performing body physiology. There are many layers or membranes in the body which form an envelope over the organs. The cell membranes separating each cell from each other can be considered as *Kala*.

General understanding of *Kala*

In *Vedic* and other ancient literature, the word "*kala"* has been used in various contexts and

meanings.one of the meaning of *Kala* is *"Guna"* .In ordinary language it means quality.

Acharya Sushruta stated the *"Kala"* or membranes as those limiting layers of the body organ and tissue which keep them in their normal position. Here the word "*Ashaya"* has been used for organ also with an example- "when wood is cut, a liquid flows out, representing the essence of the tree. Similarly, when a muscle is cut, tissues ooze out as plasma (*Rasa)* and blood (*Rakta*). Parts of the body covered by ligaments and tendons (*Snayus*), enveloped by membranes (*Jarayu*), and smeared with mucus (*Kapha*) are referred to as Kalas.

Acharya Vagbhata describes that the moisture *(kleda*) between a tissue (*Dhatu*) and its cavity (*Aashaya*) converts into *Kala* due to the body's heat. This *Kala* contains a small quantity of the essence of the tissue (*Dhatu rasa*), similar to the liquid that oozes from freshly cut wood. It is surrounded by muscle fibers, ligaments, tendons *(Snaayu*), and membranes (*Jarayu*).

Acharya Sharandhar adds that the moisture (*kleda*) between a tissue (*dhatu*) and its cavity (*ashaya*) undergoes transformation by body heat, resulting in the formation of Kala.

Table 1: Types of kala

S. no.	***Sushruta***	***Vagbhata***	***Sharangadhara***
1	*Mamsadhara kala*	*Mamsadharakala*	*Mamsadharakala*
2	*Raktadharakala*	*Raktadharakala*	*Asrugdharakala*
3	*Medodharakala*	*Medodharakala*	*Medodharakala*
4	*Shleshmadharakala*	*Shleshmadharakala*	*YakritaPittadharakala*
5	*Purishadharakala*	*Purishadharakala*	*Antradharakala*
6	*Pittadharakala*	*Pittadharakala*	*Agnidharakala*
7	*Shukradharakala*	*Shukradharakala*	*Retadharakala*

Table 2: Location & Functions of kala

S.No.	Kala	Site & Functions
1	*Mamsadhara kala*	Present at Mamsa (muscles), Sira (veins), Snayu (tendons), Dhamni (arteries) and Srotas (capillaries) & holds them
2	*Raktadhara Kala*	Present at inside Mamsa (muscles) and specially in Sira(veins), Yakrat (liver) and Pleeha (spleen),helps in maintaining blood integrity.supporting haemopoiesis, preventing pathology
3	*Medodhara Kala*	Present at Udar (abdomen) of all Prani(animals) and Anuasthi(small bone), holds fat tissue or form fatty layer
4	*Shleshmadhara kala*	Present at all Sandhies (joints) of all animals & helps in restriction free movement of joints.
5	*Pureeshadhara kala*	Present at Koshtha and divide Mala in Pakvashaya, helps to separate water and nutrient from stool.
6	*Pittadhara kala*	Present at between amashaya & Pakvashaya and recive all four types of foods,holds pitta and facilitate complete digestion of semi-digested food
7	*Shukradhara kala*	*"Sarvasharir Vyapini"* of all living beings & associated with the reproductive system, holds reproductive fluid

Table 3: Modern correlation of *kala*

S.No.	***Kala***	Modern Corelation
1	*Mamsadhara kala*	Deep fascia, Intermuscular septa
2	*Raktadhara Kala*	Endothelial lining of the blood vessels and sinuses in the liver and spleen
3	*Medodhara Kala*	Omentum, deep fascia
4	*Shleshmadhara kala*	Synovial membrane
5	*Pureeshadhara kala*	Mucous membrane of the colon and rectum
6	*Pittadhara kala*	Mucous membrane of the small intestine
7	*Shukradharakala*	Mucous membrane of the vasiculae seminalis,vas deferens

Kala and its Pathological Co-relation

Talking about the sequence of *kala*, a question often came to mind why this sequence of kala has decribed by our acharyas, why after *Medodhara Kala*, *Shlesmdhara kala* is included, *Acharayas* has mentioned a word 'खलु' which means definite i.e. number of *kala* is seven only neither less nor more perhaps the reason behind this will be its corelation with the pathology, that how a pathogen will enter in our body. For example-

According to [*Su. Ka*.4/39], snake venom attacks the seven layers (*kalas)* in sequence, leading to seven stages of poisoning. The prognosis for a snakebite victim depends on how deeply the toxin has penetrated these layers.In the first stage, the venom contaminates the blood, causing it to turn black, which results in the skin darkening and a sensation that " ants are crawling on the body".In the second stage, the poison affects the muscles, leading to severe blackening, inflammation, and the formation of cysts.During the third stage, it affects the fat, causing the bite site to become moist, with heaviness in the head and stiffness in the eyes.In the fourth stage, the poison reaches the thoraco-abdominal cavity, disturbing the *dosha*, mainly *kapha,* causing drowsiness, salivation, and joint weakness.The fifth stage involves penetration into the bones, where it disrupts *prana* and *agni*, leading to joint pain, hiccups, and a burning sensation.In the sixth stage, the venom reaches the bone marrow, severely affecting the small intestine (*grahani)* and causing body heaviness, diarrhea, cardiac pain, and fainting.Finally, in the seventh stage, the venom enters the semen (*shukra*) and

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severely disrupts *vyanavayu,* resulting in discharge of kapha from minute channels, intense pain in the waist and back, loss of movement, excessive salivation and sweating, and ultimately death due to respiratory failure.As the venom penetrates deeper into the tissues (*dhatus*) through the kalas, the patient's condition becomes increasingly critical.

Discussion

The layer that forms a boundary around the plasma and blood, separating them from their surrounding walls *(ashayas*), is known as *kala.* They can be compared to mucous membranes, epithelium, and the synovial membrane, which cover joint spaces *(ashayas*) and separate them from surrounding tisse. When comparing the structure of Kala with the skin based on its location, it is described that the seven layers of the Twacha (skin) cover the body from the outside inwards. These layers are arranged sequentially, but unlike the Shukradhara Kala, which pervades the entire body, the other types of Kala are located in specific regions and perform specialized functions.

Exploring how the concept of kala can be integrated with modern medical practices for a more holistic approach to treatment.Investigating the role of *kala* in tissue repair and regeneration, which could inform regenerative medicine and therapies.Understanding how *kala* influences metabolism and energy storage, potentially offering insights into metabolic disorders such as obesity and diabetes. Examining the role of *Pittadhara* and *Purishadhara Kala* in maintaining digestive health and preventing disorders like IBS and inflammatory bowel diseases.Studying *Shleshmadhara Kala's* involvement in mucosal immunity, which could lead to novel approaches to enhancing immune function. Utilizing the concept of kala to develop personalized treatment plans based on individual body constitution and health needs.Applying Ayurvedic principles of *kala* to preventive healthcare strategies, promoting longevity and overall well-being.Investigating the potential connections between kala and neurological health, possibly offering new perspectives on mental health and cognitive function.Conducting rigorous clinical trials to scientifically validate the therapeutic effects of treatments based on *kala* concepts.

Conclusion

In conclusion, the concept of *kala* in Ayurveda is one of the most unique and underrated concept that is described in various classical text.*Kala* can be understood as a *Aavran*/layer/membranes/fascia of our body which form an envelope over the organs & help them to function easily. According to ayurveda, a pathology is created in the body only when *tridoshas* are not in their *samawastha* and the foremost treatment for that is *'Nidan Parivarjanam'* hence a precise knowledge of kala is important for the physicians to make a diagnosis at the right time so that it allows them to reverse the progression of pathology and prevent its further advancement from the stage of *Sadhakriyakala* & also to know if the disease at which level of *Kala*. Understanding the anatomical relevance of *Kala* can help in the better understanding of the functioning of the human body and the development of new therapies. Research in these areas can bridge traditional Ayurvedic knowledge with contemporary scientific understanding, potentially leading to new therapeutic approaches and a broader acceptance of Ayurveda in global health systems.

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Finger Millet: A Comprehensive Review

Review Article

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Abstract

This review aims to evaluate the nutritional and health benefits of Finger millet, as well as its production and utilization. Finger millet (*Eleusine coracana L.*), also known as *ragi* or *mandua*, is one of the key millets cultivated widely across various regions of India and Africa. It is a highly nutritious grain, rich in calcium, dietary fibre, iron, protein, antioxidants, and vitamins. Thanks to its nutrient density, it aids in managing diabetes, preventing osteoporosis, improving digestion, and supporting weight loss. Agriculturally, finger millet is a resilient crop, thriving in drought conditions with minimal input, contributing to sustainable farming practices. Its adaptability and low resource needs make it valuable for climate-resilient agriculture. Known for its antioxidative and anti-inflammatory properties, finger millet may also help in preventing cardiovascular diseases and cancer. The production of rice influences the consumption of millet in India. Millets offer exceptional nutraceutical properties and exhibit resilience to adverse climatic conditions, which can contribute to food and nutritional security in the modern era. This review synthesizes current research on the health-promoting properties of finger millet, including its potential to combat lifestyle diseases. Overall, this review highlights the multifaceted importance of finger millet as a nutritionally dense, environmentally sustainable, and health-promoting crop, advocating for its wider inclusion in both rural and urban diets as a response to contemporary food security and health challenges.

Keywords: Nutrient Density, Antioxidant, Food Security, Diabetes, Dietary Fibre.

Introduction

Finger millet (*Eleusine coracana*) is a cereal cultivated for food in Africa and Southern Asia, particularly in India (notably in the states of Uttar Pradesh, Bihar, Tamil Nadu, Karnataka, and Andhra Pradesh) and Nepal (1). In Africa, it is primarily grown in the eastern regions, especially in Uganda, Kenya, and Tanzania, with smaller-scale cultivation in Ethiopia, Rwanda, Malawi, Sudan, Zambia, and Zimbabwe (2). A large portion of the global population relies on cereals such as wheat, rice, and maize as their primary food sources, while millets have been largely overlooked, especially following the Green Revolution (1). Millets are a varied group of small-seeded grasses cultivated for food, animal feed, or forage. These plants and their grains are resilient to drought, pests, and diseases, and are rich in polyphenols, particularly calcium (3).

Brief History of the Crop

Finger millet originated and was domesticated in Africa. Archaeological and linguistic evidences show that around 5,000 years ago, farming communities in eastern Africa were already cultivating this millet (4). The exact area of domestication is unknown, and it has been suggested that it may have occurred anywhere between western Uganda and the Ethiopian highlands of Eastern Africa (2). From Africa, the crop was transported to India about 3,000 years ago, whereupon the subcontinent became its secondary center of diversity. The maritime connections between East Africa and the Arabian Peninsula played a role in its transfer to the Indian subcontinent (5). Finger millet, commonly called *Ragi*, is an exceptional cereal known for its extensive nutritional benefits that can help prevent a variety of diseases. In India, it is also referred to by names such as *mandua* and *nachani*. It is also known to possess immunomodulatory properties(6).

Methodology

A comprehensive literature search was conducted using PubMed, JSTOR, Google Scholar along with specific search terms and keywords included “Finger millet”, “Health Benefit”, “Production Pattern”, and the search was limited to studies published in English between 2010 and 2024. Studies were selected based on relevance to the topic focusing on Finger millet. Articles were excluded if they addressed other cereals and grains.

Taxonomy and Botanical Description

Finger millet (*E. coracana*) and its related species are part of the subfamily *Chloridoideae* within the

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Poaceae family. This crop falls under the genus *Eleusine* and is commonly known as ragi and *mandua* in India, *kaddo* in Nepal, and *fingerhirse* in Germany. It serves as a vital staple food in regions of eastern and central Africa, as well as in India.

Ecological requirements

Millets require warm temperatures for germination and development and are sensitive to frost. For these reasons, they are normally planted from mid-June to mid-July period. Finger millet Best Grows with Medium Rainfall and Annual Temperature Range of 11 to 27 degrees Celsius Low Relative Humidity. It can be grown on a variety of soil ranging from rich loam to poor shallow upland soil with good organic matter (7). Black soil with good drainage can also be considered for cultivation as this crop is sustainable for waterlogging to some extent. Finger millet grows best in soil having pH 4.5-8. Soil having water logging problem should not be used for cultivation of finger millet (8).

Millet Consumption and Nutritional Significance

Reports of the National Nutrition Monitoring Bureau indicated that consumption of millets in general was higher in the states of Gujarat (maize, pearl millet), Maharashtra (sorghum), and Karnataka (finger millet) but almost nil in the states of Kerala, West Bengal, Orissa, and Tamil Nadu where rice forms the major staple (9). The consumption of millets in Gujarat and Maharashtra was 200 g/CU/day and 132 g/CU/day, respectively, which was higher compared to Karnataka (75 g/CU/day), Madhya Pradesh (32 g/CU/day), and Andhra Pradesh (16 g/CU/day). In contrast, Tamil Nadu (3 g/CU/day) and Orissa (1 g/CU/day) showed minimal consumption. millet consumption is relatively low while cereals remain the main staple in Indian diets, contributing 70–80% of total energy intake for the majority of the population (10). Millet consumption is significantly lower compared to rice, as highlighted by a recent study on the dietary profile of urban Indians from the Chennai Urban Rural Epidemiology Study (CURES). The study found that millets contributed to only about 2% of total daily calories (6.7 g/day), whereas nearly half of the daily caloric intake came from refined grains like polished white rice (253.4 g/day) (11).

Nutrient Composition of Finger Millet

Finger millet is a rich source of carbohydrates, containing free sugars (1.04%), starch (65.5%), and non-starchy polysaccharides or dietary fibre (11.5%). Its dietary fibre content (11.5%) is notably higher than that of brown rice, polished rice, and other millets like foxtail, little, kodo, and barnyard millet (12).

Most finger millet varieties have a crude protein content ranging from 5.6% to 12.7%. The protein levels specifically range from 6.7% to 12.3%, with an average of 9.7%. Finger millet is rich in essential amino acids, such as lysine and methionine, which are typically deficient in other plant-based diets. There is variation in protein content across different varieties of finger millet, and prolamins make up the majority of its protein fractions (13).

Finger millet has superior keeping qualities than other minor cereals like pearl millet, barnyard millet, and foxtail millet since it has a lower fat content. Its claimed fat content is between 1.3 and 1.8%. Finger millet has a higher ash content compared to other major cereal grains, with its ash concentration ranging from 1.7% to 4.13% (14). The mineral content of finger millet per 100 grams includes phosphorus (130–283 mg), potassium (430–490 mg), magnesium (78–201 mg), calcium (162–398 mg), sodium (49 mg), zinc (2.3 mg), iron (3.3–14.39 mg), manganese (17.61–48.43 mg), and copper (0.47 mg) (15). When compared to rice and wheat, finger millet has a greater nutritional density. Finger millet is a source of carbohydrates like any other cereal. However, the proportion of dietary fibre in finger millet is higher than in many other kinds of cereal. The dietary and crude fibre of finger millets are 18.6% and 4.3%, respectively (16) . Despite having a minor amount of vitamins A and B, finger millet grains are not a particularly abundant source of vitamins. The grains are lacking in vitamin C but have higher levels of riboflavin, niacin, thiamine, and folic acid (17).

Health Benefits of Finger Millets

The World Health Organization (WHO) has identified 4 major forms of malnutrition crippling globally. This includes vitamin A deficiency, iron deficiency, iodine deficiency and protein energy malnutrition. Millets are a storehouse of nutrients and are a remedy for the malnutrition that affects a vast majority of our population (18). Millet Network of India (Deccan Development Society, FIAN, India) confirmed in their study that, as compared to the other crops (rice and wheat), it is an exceptionally rich source of calcium chromium, zinc, copper and magnesium, essential for good health (17). It is a rich source of non-available carbohydrates with a low glycaemic index, which is beneficial for the prevention of diabetes and cardio-vascular diseases. It also helps in delaying aging by reducing glycosylation of body proteins (19).

Nutrient-rich

Ragi is packed with calcium, iron, dietary fibre, antioxidants, and essential amino acids, making it a highly nutritious grain. It is especially beneficial for individuals with iron deficiency and those needing increased calcium intake.

Gluten-Free and Easily Digestible

Naturally gluten-free, ragi is an excellent choice for people with gluten sensitivities or celiac disease. It is also easily digestible and gentle on the stomach.

Promotes Bone Health

With its high calcium content, ragi supports bone development and helps maintain bone density, making it beneficial for children and older adults in preventing conditions like osteoporosis.

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Manages Diabetes

Ragi's low glycaemic index helps manage blood sugar levels. Its high fibre content slows sugar absorption, making it ideal for those with diabetes or at risk of developing it.

Aids in Weight Loss

The high fibre content in ragi promotes satiety, curbing hunger and supporting weight management. Its low-fat content also makes it a healthy choice for weight loss diets.

Rich in Antioxidants

Ragi is a good source of antioxidants like polyphenols and flavonoids, which combat oxidative stress and lower the risk of chronic diseases.

Improves Digestive Health

Ragi's dietary fibre supports healthy digestion, helps prevent constipation, and promotes overall gut health.

Boosts Immunity

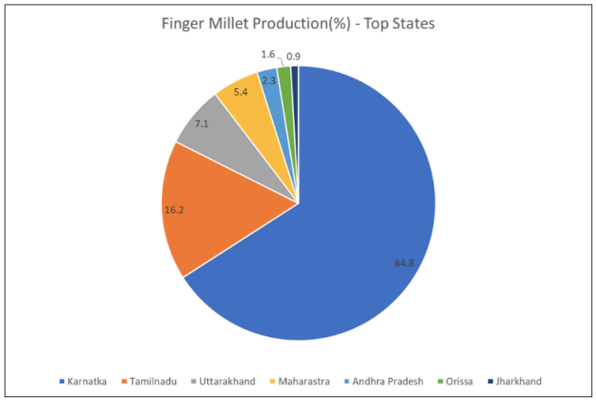
The vitamins and minerals in ragi contribute to a stronger immune system, enhancing overall health and well-being.

Finger Millets Consumption and Distribution in India

Finger millet, or *Eleusine coracana*, is primarily grown in Africa and Asia. In Africa, it is mainly grown in highland areas and marginal land where other cereals could not grow (20). The major countries are Ethiopia, Uganda, Tanzania, Kenya, and Rwanda While in Asia it is prevalent in India, Nepal, and Sri Lanka (21). Ragi, is an important staple crop in India, particularly in the southern and eastern regions. The nutritional value of Finger millet is higher than other grains. It is rich in calcium, protein, and fibre, finger millet is often considered a superfood (22). It is especially beneficial for people with lactose intolerance and is used in various health foods. Various Culinary uses of Ragi are Flour, Beverages, and Snacks (23).

The resilient nature of finger millet makes it particularly well-suited for cultivation in harsh agro-climatic conditions. Its adaptability to low-input cereal-based farming systems in Africa highlights its role in supporting traditional agricultural practices (7). With an estimated global annual planting area of 4-4.5 million hectares and a total production of 5 million tons of grains, finger millet plays a pivotal role in ensuring food security and sustenance for millions of people (13). India plays a major role in finger millet production, contributing around 2.2 million tons, with Africa following closely at approximately 2 million tons. Other South Asian countries also add to the remaining global production, underscoring the importance of this staple crop worldwide. Figure. 1 reveals that in the year 2017-18, Karnataka leads with 64.8% of the country's Ragi production, followed by Tamil Nadu at 16.2% and Maharashtra at 7.1%. Other key producers include Andhra Pradesh, Jharkhand, Odisha, Chhattisgarh, and Gujarat.

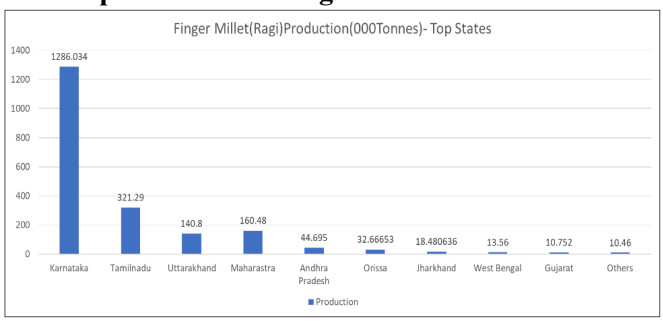
Figure 1: Shows pie chart represents top producer of finger millet



Ragi is a drought-resistant crop, well-suited for semi-arid regions, requiring minimal inputs and often cultivated as a mixed crop. Figure 2 shows that in 2018 Karnataka produces 1286.034 tonnes of Ragi while Tamil Nadu and Uttarakhand closely followed it with figure 321.29 and 140.8 Tonnes. Furthermore, it is clear that southern states namely, Karnataka and Tamil Nadu are the leading producer of Finger millet in India While Uttarakhand leads in northern states with 140.8 tonnes of Ragi with other millets (22). In India, it is cultivated over an area of 11.38 lakh hectares with total production of about 18.21 lakh tonnes and with productivity of 1601kg/hectare during the year 2015-16.

Of the total area under Finger millet Karnataka alone occupies 60% followed by Uttarakhand and Maharashtra with 10% each. Tamil Nadu has the highest productivity(2580kg/ha) followed by Karnataka(1801kg/ha) and Uttarakhand(1372kg/ha) (24).

Figure 2: Depicts graphs showing state wise production of Finger millet in Tonnes



Revival in the 21st Century

In recent years, finger millet has been rediscovered as a superfood, especially among health-conscious consumers. Its rich nutrient profile, particularly its high calcium, dietary fibre, and essential amino acids, has brought it back into focus for addressing malnutrition and lifestyle diseases like diabetes (25). With growing concerns about climate change, finger millet is increasingly valued for its ability to grow in harsh, dry conditions. Efforts are being made to promote its cultivation as a climate-resilient crop, suitable for sustainable agricultural systems. In 2023, as part of the International Year of Millets, finger millet has been spotlighted globally,

highlighting its importance for food security, particularly in regions vulnerable to climate change (26).

Discussion

Finger millet serves as a great source of carbohydrates, comprising free sugars, starch, and non-starchy polysaccharides, or dietary fibre. Its fibre content is notably higher than that of brown rice, polished rice, and other types of millet like foxtail, little, kodo, and barnyard millet. It is an abundant source of calcium, chromium, zinc, copper, and magnesium, all essential for promoting good health. Furthermore, it offers a substantial amount of non-digestible carbohydrates with a low glycaemic index, helping to prevent diabetes and cardiovascular disease. It also contributes to slowing the aging process by reducing glycosylation of proteins in the body. Ragi is an important staple crop in India, especially in the southern and eastern regions. Karnataka produces the most ragi in India, followed by Tamil Nadu and Maharashtra. Gujarat, Jharkhand, Odisha, Chhattisgarh, and Andhra Pradesh are some of the other major producers. Moreover, Millets are integral to the diets and cultures of many communities, especially in rural areas. They are often used in traditional dishes and festivals, preserving cultural heritage. Cultivating millets often involves traditional agricultural practices and knowledge, promoting biodiversity and sustainable farming methods.

Result

The nutritional profile of finger millets shows that it is rich in dietary fibre, essential amino acids, vitamins and minerals. Finger millets have low fat content and high fibre content which helps in improving digestive health. Finger millet is particularly well suited for cultivation in arid and semi-arid region due to its ability to thrive in low fertility soils and it is water efficient. overall, finger millet presents a promising solution for improving nutritional outcomes and sustainability in agriculture, particularly in regions vulnerable to climate change.

Conclusion

Finger Millets are a type of grain that provides various health benefits to the body by containing vitamins and minerals. Also, it is rich in dietary fibre, which helps to keep the digestive system healthy. It can also serve as a great alternative to rice and wheat, which is why it is regarded as one of the best grains for weight loss in India. finger millet is not only a coarse cereal but also referred as a Nutri-cereal or as a nutraceutical crop and is regarded as a potential remedy for food and nutritional security under the changing climatic conditions globally. In the past, millets were considered inferior to other cereals like wheat or rice due to their lower gluten content and ease of digestion. However, some studies suggest that millets are beneficial since they provide essential nutrients such as proteins, amino acids, insoluble fibre, and more, contributing to improved health and weight loss.

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Cadaveric Study on *Kurcha Sharir* along with its modern perspectives

Review Article

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Abstract

In *Ayurveda*, *Rachana Sharir* examines the embryological and structural organization of the human body. One of the branches of *Rachana Sharir* that describes a certain body structure is *Paribhasha Sharir.* Literally, *Paribhasha* signifies terminology. The first step in understanding any given subject is to grasp its basic terminology and main concepts. *Kurcha* is among such unexplored topics that come from the *sannipat* of *dhamani* and *snayu. Kurcha* is examined in this study from the perspective of modern anatomy, contrasting its location and related elements with knowledge from both Ayurvedic and Modern medical literature. The purpose of the cadaveric dissection method is to investigate the anatomical structures related to the *kurcha* and to evaluate the applicability of traditional *Ayurvedic* concepts, such as those described by *Sushruta*, in the context of modern medical understanding.

Keywords: *Paribhasa Sharir, Kurcha,* Palmar aponeurosis, Plantar aponeurosis, Ligamentum nuchae, Suspensory ligament of penis.

Introduction

Ayurveda, a well-known Indian system of medicine, is more than just a life science; it is a rich source of knowledge. Despite being ancient, its principles are still relevant today. The branch of *Ayurveda* called *Sharir* also reflects this enduring relevance. *Sushruta*, known as the father of surgery, made significant contributions in his famous work, the *Sushruta Samhita*. The *Sharirsthana* section of this text is particularly important for its detailed explanation of human anatomy. Understanding anatomy is crucial for maintaining the body's health, as this knowledge provides the foundation for effective treatment. A knowledgeable physician seeks a deep understanding of anatomy, which involves studying the different parts of the body.

Haranchandra in his commentary states that *Kurchas* are derived from the *Sannipat* of *Snayu* and *Dhamani* . *Sannipat* here means intersection. Their total number is 6. These are fibrous or membranous brush like structures.

षट् कूर्चाः, ते हस्तपादग्रीवामेढ्रेषु; हस्तयोर्द्वौ, पादयोर्द्वौ, ग्रीवामेढ्रयोरेकैकः ॥१३॥ (4)
षट् कूर्चा इत्यादि|
कूर्चा इव कूर्चाः, नाम्नैवाकृतिरुन्नेया; ते पुनर्मांसास्थिसिरास्नायूनां जालकप्रभवाणां ।१।
सन्ततिविरचिताः (*Dalhana)*

In the context of "*Kurcha,*" the important terminologies are explored with regard to their *Vyutpatti* (word formation), *Nirukti* (etymology), and their equivalents in modern scientific terminology. There are three main references about *Kurchasharir* in ancient texts: *Sushruta Samhita (Shareersthana*) (1), *Ashtang Samgrah* (2), and *Bhavaprakasha Prathamkhanda* (3). These texts suggest that there are six *Kurchas* in the human body, located in the hands (*Hasta*), feet (*Pada*), neck (*Greeva*), and genitals (*Medhra*). Specifically, there are two *Kurchas* in each hand and foot, and one each in the neck and genitals (4).

In the *Sushruta Samhita*, it is referred to as "*Kunchika*," meaning a brush-like structure or "*Kunchala*." (5) In the *Ashtang Hridaya, "Kurcha*" is used to mean "*suchi*" (needle), indicating a sharp-ended needle (6). In various dictionaries, the term "*Kurcha*" has multiple meanings, such as a bunch or bundle of anything, a handful of *Kusa* grass, or a peacock's feather (7). According to *Acharya Charaka*, in *Chikitsasthana*, uses the term "*Shastra*" for "*Kurcha*.". An important reference in the *Sushruta Samhita* notes that there are six *Kurchas* in the human body, all with brush-like structures.

Materials and Methods

This article will gather information from primary *Ayurvedic* texts knows as *Samhitas* , as well as modern anatomy books, national and international journals, various databases.

Cadaveric study

Methodology

1. The anatomical analysis of *Kurcha is done* through studying relevant *Ayurvedic* and modern textbooks.
2. Dissection of a selected male cadaver was conducted using a dissection kit over the region considered specific to the *Kurchas* at the dissection hall of the

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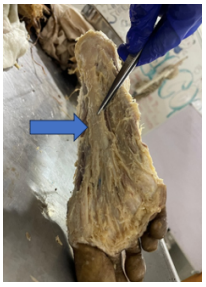
3. The identification of the *Kurchas* on the cadaver was based on findings from the literary study.
4. The area around the *Kurchas* was marked according to proportions specified in the *Samhitas*.
5. Detailed dissection focused on specific anatomical landmarks.
6. Through precise dissection, structures related to the *Kurchas*, including Palmar Aponeurosis, Plantar Aponeurosis, Ligamentum Nuchae & Suspensory ligament of the Penis are identified.

Fig 1: Plantar Aponeurosis	Fig 2: Ligamentum Nuchae	Fig: 3 : Suspensory Ligament of Penis
		

Structure associated with "*Kurcha*" in the hand refers to specific anatomical formations or features present within the hand

The palmar aponeurosis

This well-defined, strong triangular section of the deep fascia in the hand, known as the palmar aponeurosis, covers the soft tissues and lies over the long flexor tendons of the palm. The proximal end of the aponeurosis is continuous with the flexor retinaculum and the tendon of the palmaris longus muscle. At the base of the fingers, the distal end of the aponeurosis splits into four longitudinal bands. Each band attaches to the base of the proximal phalanx and merges with the fibrous digital sheath (8).

Applied Anatomical Aspects

Dupuytren's contracture is a progressive disorder of unclear origin that involves the fibrous thickening and contraction of the palmar aponeurosis, predominantly affecting the little and ring fingers.

Structure associated with "*Kurcha*" in the foot refers to specific anatomical formations or features found within the foot

The plantar aponeurosis

The central portion of the plantar fascia thickens significantly to form the plantar aponeurosis. This structure has a strong, thick central section, along with thinner, weaker medial and lateral portions. Covering the entire sole of the foot, the plantar aponeurosis is composed of dense fibrous connective tissue arranged in longitudinal bands. It originates at the tuber calcanei (heel bone) and spreads out over the sole, becoming broader and slightly thinner. The aponeurosis then divides into five bands that split to surround the digital tendons and attach to the edges of the fibrous digital sheaths and the sesamoid bones of the big toe. From the edges of the central part of the plantar aponeurosis, vertical septa extend deeply into the sole to create three compartments: the medial, lateral, and central compartments of the foot (9)

Applied Anatomical Aspects

Palpating the dorsalis pedis pulse is crucial, especially when diagnosing intermittent claudication, which is characterized by calf cramps induced by exercise and relieved by rest. This pulse is typically felt on the top of the foot, where the artery runs over the navicular and cuneiform bones, just beside the extensor hallucis longus tendon. It can also be detected near the base of the first interosseous space. A weak or absent dorsalis pedis pulse may indicate arterial insufficiency. However, in about 14% of individuals, the dorsalis pedis artery may be absent, too small to palpate, or located differently than usual. Therefore, not finding this pulse does not always confirm the presence of arteriosclerotic disease.

Structure Associated with *Kurcha* in the Neck

Ligamentum nuchae

The ligamentum nuchae is a bilaminar fibroelastic intermuscular septum that, while similar to the supraspinous and interspinous ligaments in the neck, has distinct structural features. Its dense fibroelastic layers merge along the posterior free border, which is superficial and extends from the external occipital protuberance to the spine of C7. These fibroelastic layers attach to the external occipital crest, the posterior tubercle of C1, and the medial aspects of the bifid spines of cervical vertebrae, serving as a septum for the attachment of cervical muscles and their sheaths. Additionally, it has a midline connection to the posterior spinal dura at the atlanto-occipital and atlanto-axial levels. In bipeds, the ligamentum nuchae is a reduced version of a more complex, thicker elastic ligament found in quadrupeds, where it helps support the head and manage its flexion (10).

Applied Anatomical Aspects

The ligamentum nuchae is a well-developed part of the supraspinous ligament located in the cervical region. It extends from the external occipital protuberance along the tips of the cervical vertebrae's spinous processes, ending at the spinous process of the vertebra prominens, usually at C7. The supraspinous ligament can be seen as a superficial extension of the interspinous ligament, which runs between adjacent vertebrae from the base to the tip of each spinous process. The ligamentum nuchae is mainly formed from the aponeurotic connections of the surrounding and underlying muscles. From superficial to deep, the muscles associated with the ligamentum nuchae are the trapezius, rhomboideus minor, splenius capitis, and serratus posterior superior. There are fibrous connections between the ligamentum nuchae and the spinal dura mater between the occiput and C1, as well as between C1 and C2. Additional attachments were

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found between the ligamentum flavum and the spinal dura between C2 and C3, although these connections were less pronounced than those at higher levels. Contrary to previous reports, no direct attachments were found between the spinal dura and the rectus capitis posterior minor (RCPM). This thin membrane extends from the posterior edge of the foramen magnum to the upper border of the posterior arch of C1. Interestingly, while most of the cranial dura is innervated by the trigeminal nerve (CN V), the infratentorial portion—below the cerebellar tentorium—is innervated by upper cervical nerves. The cranial dura mater consists of two layers: the outer, or endosteal layer, and the inner, or meningeal layer. These layers remain in contact throughout most of the cranial cavity, except where they separate to form the dural sinuses. The outer layer ends at its attachment around the foramen magnum, while the inner layer continues through the foramen magnum to become the spinal dura mater. The periosteum of the vertebral canal is equivalent to the outer layer of the cranial dura mater. In summary, several cervical structures are connected to the cranial dura through their attachments to the spinal dura. The ligamentum nuchae has a direct attachment to the spinal dura, and the ligamentum flavum also attaches, but to a lesser extent. The sensory innervation of both the cervical spinal dura and the cranial dura in the posterior cranial fossa is provided by the upper cervical nerves. These nerves also supply sensation to the deep muscles of the back and the skin overlying the back. While the trapezius muscle is innervated by the accessory nerve, its sensory innervation comes from the upper cervical nerves. Therefore, a therapist working on a client's neck could find the effort worthwhile, given the interconnectedness of these structures.

Structure associated with *Kurcha* in the pubic region

Suspensory ligaments of penis

The body of the penis is supported by two ligaments, the fundiform ligament and the triangular suspensory ligament, both of which are continuous with its fascia and primarily composed of elastin fibers. The fundiform ligament originates from the lower part of the linea alba, splits into two layers that encircle the penis, and then merge below with the scrotal septum. The triangular suspensory ligament, located deeper than the fundiform ligament, attaches to the front of the pubic symphysis and blends with the fascia of the penis on each side. Unlike structures in the hand and foot regions, these ligaments do not resemble a brush-like form. However, Sushruta, using his ancient dissection techniques, might have observed these structures appearing like "*Kunchi*" and referred to them as "*Kurchas*." The ancient methods of dissection were distinct, and the instruments used were different from those used today. Additionally, in the penile region (*Medhra Pradesha*), the presence of "*Dhamani Sannipata*" is mentioned, which could correspond to the arterial structures in the penile region that resemble a brush-like pattern (11).

Applied Anatomy Aspects

In males, the suspensory ligament of the penis is attached to the pubic symphysis, which holds the penis close to the pubic bone and supports it when erect. Surgically cutting this ligament allows more of the penis to hang outside the body, thereby increasing its length. The ligament is then encouraged to heal in an extended state, promoting a longer penis overall. Until this ligament is properly healed, the penis cannot achieve a high angle of erection when engorged. At the base of the body of the penis, identify the fundiform ligament of the penis. This ligament is derived from the membranous Scarpa's fascia of the anterior abdominal wall. The fundiform ligament of the penis extends from the linea Alba to the penis and surrounds it laterally and it ends in the scrotal septum. The fundiform ligament supports the penis in a sling-like fashion. Deep to the fundiform ligament - identify the suspensory ligament of the penis. This short, strong ligament that arises from the anterior surface of the pubic symphysis attaches to the deep fascia (Buck's fascia) of the penis.

Discussion

According to Ayurvedic literature, the study of the human cadaver serves two primary purposes:

1. **Sharir Vichaya** – Dissection of the body.
2. **Sharir Shodhana** – Exploration or examination of the body.

These practices are to be carried out with the intent of "*Sharir Upakarartha*," meaning for the benefit of the body. The term "*Kurcha,*" mentioned in *Sushruta's Sharir Sthana*, has been examined and elaborated upon. This concept falls under the category of *Sandigdha* (ambiguous) and *Upaman Sharir* (comparative anatomy).

In relation to *Kurcha Sharira*, there are three key commentaries, with notable contributions from *Dalhana, Haranachandra*, and *Indu*. Focusing on *Dalhana's* commentary, he describes six *Kurchas*, which have a brush-like appearance, as the term "*Kurcha"* itself suggests. According to *Dalhana,* these structures are formed by the union of muscles (*Mamsa*), bones (*Asthi*), blood vessels (*Sira*), and ligaments (*Snayu*). They resemble a reticular network (*Jalaka*) and extend from the forearm and leg into the hand and foot. This interconnected network creates a brush-like appearance in the hand and foot, leading *Dalhana* to refer to it as *Kurcha*.

In modern anatomy, it is noted that the *Palmaris longus* muscle evolves phylogenetically into the palmar aponeurosis. The concept of *Kurcha*, as explained by *Sushruta*, has been discussed in the earlier review of literature.

Haranachandra describes *Kurchas* as brush-like structures formed by the union of ligaments, specifically referring to fibrous or aponeurotic tissues. He identifies five such fibrous or aponeurotic structures: one in the neck (*Greeva*), two in the armpits (*Kaksha*), and two in the groin (*Vankshana*). Here, *Kaksha* and *Vankshana* can be interpreted as referring to the hand and foot. All three commentaries relate *Kurcha Sharira*

to the palmar and plantar aponeurotic (or fibrotic) structures in the hands and feet.

Conclusion

Kurchas resemble "*Kunchi*," or brush-like structures, and are six in number. They are located as follows: two in the hands, two in the feet, one in the neck (*Greeva*), and one in the genital region (*Medhra*). The *Kurchas* in the hands and feet are fibrous or aponeurotic structures found on the palmar and plantar surfaces.

In Hasta (hands) and Pada (Feet)– 2 each and in Griva (neck) and Medhra (penis) there is 1 Kurcha each. Following brush like structures in body can be compared with Kurchas.

1. In Hasta (hands)– Palmar aponeurosis
2. In Pada (feet)– Plantar aponeurosis
3. In Griva (neck)– Nuchal ligament
4. In Medhra (penis)– Suspensory ligament of penis

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Pharmacological and Traditional Applications of Medicinal Plant *Clerodenderum phlomidis (Agnimantha)*: A Comprehensive Review

Review Article

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Abstract

The World Health Organization (WHO) reports that approximately 80% of the population in developing countries depends on traditional herbal remedies for their primary healthcare. *Clerodendrum phlomidis* or Agnimantha in Ayurveda belonging to the Lamiaceae family, is a crucial ingredient in the Ayurvedic formulation Dashamoola, a blend of ten roots that enhances vitality and promotes overall health. Traditionally, various parts of this plant—roots, stems, leaves, and flowers—are used in Indian and Chinese medicine to treat ailments such as inflammation (Shotha), diabetes (Prameha), fevers (Jwara), gonorrhoea (Upadamsha), and obesity (Sthaulya). Research has focused on isolating its chemical constituents, leading to the identification of 283 compounds, including monoterpenes, sesquiterpenes, diterpenoids, flavonoids, and glycosides, which exhibit a wide range of pharmacological activities, including anti-inflammatory, antimicrobial, antioxidant, anticancer, hepatoprotective, hypoglycemic, and neuroprotective effects.The roots and leaves are traditionally used as astringents, stimulants, and antibacterial agents, treating conditions such as fever, cold, headaches, asthma, and allergies. Agnimantha includes two main types: Laghu Agnimantha (*Premna integrifolia*) and Brihat Agnimantha (*Clerodendrum phlomidis*), both of which hold significance in modern and traditional medicine.Overall, this review underscores the plant's substantial medicinal value, consolidating its importance in health and wellness based on traditional knowledge and contemporary research findings.

Keywords: *Agnimantha,* Medicinal value**,** Phytochemical constituents, Pharmacological activity, Ayurveda, Traditional medicine.

Introduction

Throughout history, medicinal plants have been central to healthcare practices, particularly in developing regions where modern medicine may not always be accessible. The World Health Organization (WHO) reports that about 80% of people in these areas still rely on traditional plant-based medicines for their primary healthcare needs (1). Among these medicinal plants, *Clerodendrum phlomidis* from the family Lamiaceae holds a special place in Ayurvedic medicine**.***Clerodendrum phlomidis* is a key ingredient in "Dashamoola," a revered Ayurvedic formulation that has been used for centuries to promote vitality and well-being (2,3). Traditionally, various parts of the plant—such as the roots, leaves, stems, and flowers—have been employed to treat a broad range of ailments, including inflammation, arthritis, diabetes, digestive issues, and respiratory disorders. Its therapeutic potential has long been acknowledged in both Indian and Chinese systems of medicine (2).Recent scientific studies have begun to validate many of these traditional uses. Phytochemical investigations have uncovered over 283 bioactive compounds in *Clerodendrum* species, including monoterpenes, flavonoids, diterpenoids, and glycosides (4). These compounds have demonstrated powerful pharmacological properties, such as anti-inflammatory, antioxidant, antimicrobial, and antidiabetic activities, making the plant a valuable subject for modern research (5).

In Ayurveda, *Clerodendrum phlomidis* is revered as "Agnimantha," known for its ability to balance the Kapha and Vata doshas, which are thought to be responsible for a variety of physical and mental health conditions. Despite the presence of substitutes like *Premna integrifolia* and *Premna mucronata*, *Clerodendrum phlomidis* remains the preferred species in many traditional formulations due to its wide range of therapeutic actions (6).

As scientific interest in ethnopharmacology grows, the potential for *Clerodendrum phlomidis* to be incorporated into modern medicine is becoming increasingly clear. This review explores the botanical characteristics, chemical composition, and medicinal properties of this important plant, compiling both

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traditional knowledge and modern research findings to offer a comprehensive look at its role in human health.

Regional names of *Clerodendrum phlomidis*

The plant *Clerodendrum phlomidis* is known by various names across different Indian languages. In Sanskrit, it is referred to as *Agnimantha, Gandhapushpa, Nadeyi, Jayanti, and Tarkari*. In Marathi, it is called *Arani, Arni, Airanamula, Takalimula, and Tekar*, while in Hindi, it is known as *Arni, Piran, Pirun, and Urni*. The Tamil language uses names like *Takkari, Thalangi, Thalludhalai, Sayandi, Taludalai, Tirugdalai, and Vadamadakki* for the plant. In Telugu, it is called *Nelli, Taluki, Takko-lamu*, and *Tekkali*. Malayalam names for the plant include *Munja, Peruvelum, and Tirutalai*, whereas in Bengali, it is known as *Arni, Ganiyari, and Goniari*. In Kannada, the plant is called *Taggi and Taggi-Beru*, while in Gujarati, it is referred to as *Aranimula, Arni, and Irun*. In Oriya, the plant is called *Hontari and Ganiary,* while in Santali, it is known as *Panjot*. In Sindhi, it is called *Gharyat*, and in Las Bela (Balochistan), it is referred to as *Tankar*. (7–11)

Botanical description of *Clerodendrum phlomidis*

The anatomy of *Clerodendrum phlomidis* reveals significant features across its various parts.

Root

It showcases an exfoliating cork with 10-15 layers of tangentially elongated, thin-walled cells. The secondary cortex is composed of round to oval parenchymatous cells, some containing rhomboidal crystals of calcium oxalate. The secondary phloem consists of isodiametric, thin-walled parenchyma, with distinct phloem rays made of radially elongated cells. The secondary xylem is broad, featuring lignified elements, and vessels that occur both singly and in groups, alongside xylem parenchyma with simple pits and abundant starch grains measuring 6-17 µm in diameter (12).

Leaf

The leaf structure is dorsiventral, with one to three layers of palisade cells and both glandular and non-glandular hairs. Stomata are of the cruciferous type (13).

Flower

The flower is moderately sized, fragrant, and arranged in small dichotomous axillary cymes that form a rounded terminal panicle. The bracts are either obovate or lanceolate and acute. The calyx measures over 1 cm in length and is divided halfway down into ovate segments that are acutely acuminate and veined. The corolla is either white or pinkish, with a tube length of 2-2.5 cm, slightly pubescent on the outside and glabrous inside. The lobes are nearly equal and exceed 6 mm in length. The filament is slightly pubescent below, and both the ovary and style are glabrous (11).

Stem

The stem is characterised as straight, unbranched, cylindrical, measuring 9 cm in length and 2.5 cm in diameter, with an uneven surface marked by irregularly interconnected, axially elongated ridges (14).

Distribution

Clerodendrum phlomidis is a common shrub of arid plains, low hills and tropical deserts. They are distributed throughout the drier parts of India (Andhra Pradesh, Uttar Pradesh, Diu Island, Delhi, Gujarat, Haryana, Karnataka, Madhya Pradesh, Maharashtra, Bihar, Orissa, Punjab, Rajasthan, Tamil Nadu, Uttar Pradesh and West Bengal) , Pakistan (Sindh, Baluchistan and north-western provinces), Sri Lanka, Myanmar (7,11,15,16).

Propagation and cultivation

It can be propagated through seeds and root suckers and thrives in various soil types. In its natural habitat, it typically grows in wastelands, along riverbanks, and beside railway tracks (13).

Substitutes

In the Ayurvedic pharmacopeia of India, *Clerodendrum phlomidis* Linn. is recognized as Agnimantha, while *Premna integrifolia* Linn. and *Premna mucronata* Roxb. are regarded as substitutes (17).

Chemical constituents

- **Root :** β-sitosterol, γ-sitosterol, ceryl alcohol, clerodin (C24H34O7), clerosterol (C29H48O) and clerodendrinA (C27H26O17)7 . α-L-rhamnopyranosyl- (1→2)-α-D-glucopyranosyl-7-O-naringin-4′-O-α-D-glucopyranoside-5- methyl ether (C34 H44 O19) (18).
- **Stem :** D-mannitol, β-D-glucoside of β-sitosterol, β-sitosterol and ceryl alcohol (19).
- **Aerial parts:** Lup-20 (29)-en-3-triacontanoate ($C_{60}H_{108}O_2$), tetratriacontanol and 24β-ethylcholesta-5, 22E,25-triene3β-ol were reported isolated from aerial parts (9).
- **Leaves:** A crystalline non-glucoside bitter principle ($C_{17}H_{16}O_6$), ceryl alcohol, β-sitosterol, γ-sitosterol, palmitic acid, cerotic acid and an unidentified sterol ($C_{28}H_{48}O$)11. Scutellarein (5,6,7,4′-tetrahydroxy flavones), pectolinaringenin (6,4′-dimethoxy scutellarein) and a flavanone. A chemotaxonomic marker of the genus, (24S)- ethylcholesta-5,22,25-triene-3β-ol ($C_{29}H_{46}O$) was isolated from the leaf (13). Chalcone glycoside (4,2′,4′-trihydroxy-6′-methoxychalcone-4,4′α-D-diglucoside m.p.186— 188 °C, $C_{28}H_{34}O_{15}$), pectolinarigenin, 7-hydroxy flavone and 7- hydroxy flavanone 7-O-glucoside (18).
- **Flowers:** 6,4′-dimethyl-7-acetoxyscutellarein, pectolinarigenin, hispidulin, apigenin and luteolin15 . Chalcone glycoside (4,2′,4′-trihydroxy-6′-methoxychalcone-4,4′α-D-diglucoside, $C_{28}H_{34}O_{15}$), pectolinarigenin, 7-hydroxy flavone and 7-hydroxy flavanone 7-O-glucoside (18).
- The stem, leaf and flower parts were reported positive for alkaloids, saponins and tannins (20).

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- **Leaf oil** : terpinen-4-ol (25.92%); caryophyllene (26.71%) and beta-bisabolene (18.10%) as the major and phytol (5.08%) as the minor constituent (21).

Ethnomedicinal uses of parts of *Clerodendrum phlomidis*

Clerodendrum phlomidis, commonly known as Arni, holds significant ethnomedicinal value, particularly in Ayurvedic and traditional medicinal systems. Indigenous communities have long used various parts of this plant to treat a range of ailments. The roots, stems, and leaves are known for their therapeutic properties, being used in remedies for ailments such as fever, inflammation, digestive disorders, and respiratory issues.Some of them are given in Table 1.

Table 1: Ethnomedicinal uses of different parts of *Clerodendrum phlomidis*

PARTS	ETHNOMEDICINAL USES	Ref.
Root (22)	• 12 to 24 gas decoction is used in Sotha (inflammation, swelling), Pandu (jaundice), Arsa (haemorrhoids, piles), Vibandha (constipation), Agnimandya (slowness of digestion, dyspepsia), Adhmana (swelling of the body), Gulma (a chronic enlargement of the spleen or any glandular enlargement in the abdomen), Mutrakrcchra (painful discharge of urine, a class of urinary affections) and Mutraghata (urinary disease). • Used as bitter tonic, antidote, analgesic, anti-asthmatic; for inflammatory diseases and in rheumatism. • Used as bitter tonic, for nervous disorder and in debility	11, 23, 24
Root Bark	• Used in cough, asthma, cold, anaemia, oedema and nervous disorders	22, 25
Root and Root Bark	• Used as alterative, bitter tonic, and is given in the convalescence of measles by natives of Western India	10, 16
Root decoction	• Used as aromatic, astringent and as demulcent in gonorrhea	10, 24
Root juice	• Used to reduce over-corpulence.	26
Whole plant	• Used as hypoglycemic	27, 28
Whole plant	• Used for ailments involving swellings, joint pains and inflammation • The properties are quoted same as those of Premna integrifolia but *Clerodendrum phlomidis* is considered better in inflammation. • The tribes "Santals" rub the plant over their bodies in dropsy. • The tribals "Sahariya" use the plant in fever, postnatal complaints, dyspepsia, colic and anthrax. • Used in colic, body-ache, diarrhoea, cholera, dysentery, dyspepsia, fever, headache, post natal fever, stomach ache, during convalescence from measles and specially used for mental diseases	29 - 31
Whole plant decoction	• Used to treat diabetes	32
Whole plant and root	• Used as bitter tonic and for neglected syphilitic complaints	8
Leaf	• Used as a remedy to treat diabetes in southern parts of India especially tribals of Nilgiris • Used in fever due to sunstroke and malaria • Grinded leaves are given in stomach pain, digestive disorders, eye complaints, lung diseases, rheumatism, asthma, inflammatory diseases • Locally tied for the treatment of Guinea worms	24, 33-35
Leaf juice	• Used to treat mental tension in Tamil Nadu	36
Leaf and Leaf juice	• Used as bitter tonic, alternative and prescribed in neglected syplitic complaints in dose of half an ounce or twice daily in southern India	10, 22, 37
Leaf decoction	• Used for inflammation, and is effective in treating bronchitis, headache, weakness, drowsiness and digestive problems.	10
Leaf and Root	• Used for body-ache, headache and unconsciousness.	38
Aerial parts	• The tribals "Sahariya" apply the paste on body joints for about a month to reduce pain or stiffness of joints.	39

Pharmacological actions of *Clerodendrum phlomidis* according to Ayurvedic Science

Dosha Karma: *Clerodendrum phlomidis* possesses *Ushna Virya* (hot potency), making it effective in pacifying Kapha and Vata doshas. Consequently, it is recommended for treating conditions arising from these doshas.

Systemic Actions (Sansthanika Karma):

- **External Application (Bahya)**: Due to its hot potency, it alleviates edema (*Shotha*) and pain (*Vedana*), making it suitable for managing external swelling and discomfort (40)
- **Digestive System (Pachana Sansthana)**: Its *Ushna Virya* properties enhance digestion (*Dipana*), promote digestion of toxins (*Pachana*), and aid in regulating bowel movements (*Anulomana*). It is thus indicated for conditions like loss of appetite (*Agnimandya*), toxin buildup (*Amadosha*), and constipation (*Vibandha*) (40)
- **Circulatory System (Raktavaha Sansthana)**: *Agnimantha* acts as a blood purifier (*Raktashodhaka*), cardiac stimulant (*Hridayottejaka*), and anti-inflammatory (*Shothahara*), making it beneficial for treating blood disorders (*Raktavikara*), cardiac weakness (*Hridaya Daurbalya*), and edema (40).
- **Respiratory System (Shwasana Sansthana)**: Its Kapha-pacifying properties make it useful in treating Kapha-related respiratory conditions (40).
- **Urinary System (Mutravaha Sansthana)**: It acts as a remedy for urinary disorders, including diabetes (*Pramehaghna*), and is used in the treatment of urinary diseases such as *Prameha* (diabetes) (40).
- **Antipyretic Action (Tapakrama)**: Known for its antipyretic properties (*Jwaraghna*), *Agnimantha* is used to manage fevers (*Jwara*) (40).
- **Rejuvenative and Restorative (Satmikarana)**: Due to its *Katu Pausthika* (pungent and nourishing) properties, it is recommended for post-fever recovery, general weakness, and anemia (*Pandu*) (40).

Parts Used: The juice from leaves (*Patra Swarasa*), bark (*Twak*), root (*Moola*), and root bark (*Moola Twak*) are utilized for medicinal purposes.

Dosage:

- Leaf juice: 10-20 ml
- Powder (*Churna*): 1-3 grams
- Decoction (*Kwatha*): 50-100 ml

Types (Bheda): There are two types of *Agnimantha*: *Kshudra Agnimantha* and *Brihat Agnimantha (40).*

Pharmacological actions of *Clerodendrum phlomidis* according to Modern science

Antiinflammatory activity

Aerial Parts

In the carrageenin-induced paw edema model, the aerial parts of *Clerodendrum phlomidis* at doses of 200 and 400 mg/kg significantly reduced paw edema by 34.02% and 26.80%, respectively, 4 hours after carrageenin administration. The study demonstrates that the chloroform extract of *Clerodendrum phlomidis* exhibits a notable anti-inflammatory effect in albino rats, with results comparable to the standard drug phenylbutazone (41,42).

Leaves

In a cotton pellet-induced granuloma model, the ethanol extract of *Clerodendrum phlomidis* at 100, 200, and 400 mg/kg inhibited granuloma formation by 22.29% , 33.03%, and 48.07% respectively. Hexane and chloroform extracts did not show significant inhibition (43)

In adjuvant-induced arthritis, *Clerodendrum phlomidis* ethanol extract reduced foot swelling and redness in a dose-dependent manner, inhibiting arthritic swelling by 51.71%, 57.58%, and 62.48% at 100, 200, and 400 mg/kg, respectively ($p < 0.005$). Indomethacin showed 68.75% inhibition. Treated animals also showed a dose-dependent increase in body weight over 28 days. The extract reduced lysosomal enzymes (acid phosphatase and cathepsin D) and plasma protein-bound carbohydrates while lowering proinflammatory cytokine levels and serum marker enzymes significantly, compared to adjuvant control animals. (43)

In a carrageenan-induced inflammation model, hexane and chloroform extracts of *Clerodendrum phlomidis* showed moderate inhibition of edema at 400 mg/kg by 30.66% and 36.23% at the third hour, increasing at the fifth hour Ethanol extracts at 100, 200, and 400 mg/kg demonstrated stronger inhibition, with up to 53.31% at the third hour and 65.15% at the fifth hour. The reference drug inhibited edema by 60.27% and 71.42% at the third and fifth hours, respectively) (43)

The study aimed to assess the anti-inflammatory and anti-arthritic activities of *Clerodendrum phlomidis* leaves, traditionally used for treating these conditions. Bioactivity-guided fractionation led to the isolation of a novel compound, 3-hydroxy, 2-methoxy-sodium butanoate. This compound significantly reduced paw edema in carrageenan and FCA-induced arthritis models. It also lowered lysosomal enzymes, protein-bound carbohydrates, and plasma acute phase proteins, while decreasing pro-inflammatory cytokines (TNF, IL-1, IL-6) in the joints in a dose-dependent manner. Histopathological data supported its anti-arthritic potential. This is the first report of this bioactive compound (44)

Carrageenan-induced paw edema is a widely used model for screening anti-inflammatory activity, involving the release of proinflammatory mediators like histamine, serotonin, kinins, and prostaglandins in a biphasic response. The first phase (60 min) releases histamine and serotonin, while the second phase is mediated by prostaglandins and kinins. Oral administration of petroleum ether (200 and 400 mg/kg), ethyl acetate, and alcoholic extracts (400 mg/kg) significantly reduced paw edema in rats at 1, 2, 3, 4, and

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6 hours compared to controls in carrageenan, serotonin, and histamine-induced edema models (45)

Root Bark

Clerodendrum phlomidis (CP) exhibited moderate anti-inflammatory activity, with the intermediate dose (21.6 ml/kg) showing the most significant effects. In the pedal inflammation model, this dose reduced oedema by 132.48 ± 4.99, significantly lower than the vehicle control (157.43 ± 13.59, $p < 0.05$), and was comparable to standard drugs like aspirin and DA. While no dose-dependent trend was observed, the intermediate dose consistently performed better than the low and high doses. Additionally, CP significantly reduced granuloma formation at the intermediate (50.38%) and high doses (46.83%, $p < 0.01$), with a greater reduction than aspirin (40.78%) and DA (41.73%), though not statistically significant (46)

Antiarthritic activity

Leaves

The anti-arthritic effects of orally administered ethanolic extract of *Clerodendrum phlomidis* were evaluated in Wistar albino rats with Freund's adjuvant-induced arthritis. Treatment with the extract at doses of 250 and 500 mg/kg corrected the weight loss associated with arthritis. Paw swelling during the secondary lesion phase was significantly reduced by the extract, a finding supported by radiographic analysis. Additionally, changes in Hind Limb Bone Mass (HLBM) were measured using a photo densitometer and aluminium step wedge, revealing a significant reduction in HLBM with both doses of the extract, comparable to the effect of the standard drug Indomethacin (10 mg/kg) (47)

The study evaluated the antiarthritic activity of *Clerodendrum phlomidis* leaf extracts on FCA-induced arthritis in rats. Petroleum ether (PECP), ethyl acetate (EACP), and alcoholic extracts (ACP) were administered orally at doses of 100, 200, and 400 mg/kg from day 13 to 21. Key parameters such as body weight, arthritic score, paw volume, and ankle diameter were assessed. Significant improvements, including increased body weight and reductions in arthritic score, paw volume, and ankle diameter, were observed in the PECP (200 and 400 mg/kg), EACP, and ACP (400 mg/kg) groups.Hematological results further confirmed the antiarthritic activity, showing improved Hb and RBC counts, and reduced WBC, ESR, CRP, and TNF alpha levels. The findings suggest that *Clerodendrum phlomidis* leaves have significant antiarthritic effects in rats (48)

Antioxidative activity

Leaves

The antioxidant activity of the methanol leaf extract was evaluated using the DPPH free radical scavenging assay at doses of 31.25, 125, 500, and 1000 µg/mL. The extract exhibited significant antioxidant activity, with an IC50 value of 71.64 µg/mL. GC-MS analysis revealed several compounds in the extract, many of which are known for their medicinal properties, including antioxidant activity (49)

The study aimed to isolate antioxidant compounds from the methanol extract of *Clerodendrum phlomidis* leaves. Nine compounds were isolated and characterized using various techniques. Among them, compound 6 (3,6,7-trihydroxy-2-(3-methoxyphenyl)-4H-chromen-4-one) and compound 9 (isopropyl linoleate) exhibited strong antioxidant activity, with IC50 values of 63.16 µg/mL and 61.13 µg/mL, respectively, as determined by the DPPH free radical scavenging assay. These results suggest significant antioxidant potential in these isolated compounds (50)

Root

The study aimed to estimate the total phenolic and flavonoid content and evaluate the in-vitro antioxidant activity of various extracts from the root of *Clerodendrum phlomidis*. The ethanolic extract demonstrated the most significant free radical scavenging activity compared to other extracts, with higher amounts of phenols and flavonoids. The antioxidant activity was concentration-dependent. Ongoing research is focused on isolating constituents from the extract and exploring their biological activities (51)

Acetylcholinesterase inhibitory activity

Leaves

Clerodendrum phlomidis (CP) leaf extracts were studied for their phytochemical composition, antioxidant properties, and acetylcholinesterase (AchE) inhibition. Leaf powder was prepared, and alcoholic and hydroalcoholic extracts were analysed using gas chromatography. In vitro assays showed that the extracts scavenge free radicals, with FRAP assay results of 215.20 µg/ml (alcoholic) and 288.70 µg/ml (hydroalcoholic), and DPPH results of 167.70 µg/ml (alcoholic) and 347.19 µg/ml (hydroalcoholic). AchE inhibition was dose-dependent, with inhibition observed at 250 µg/ml. These findings suggest CP extracts may help reverse cholinergic deficits in neurological diseases (52)

Hepatoprotective activity

Leaves

The study found that SGOT, SGPT, ALP, and Serum Bilirubin levels significantly decreased in animals treated with *Clerodendrum phlomidis* (CP) extracts (Leaves>Root >Stem) and CCl_4 compared to those given CCl_4 alone, indicating reduced liver damage. Histopathological studies confirmed hepatic damage in CCl_4-treated animals, showing centrizonal necrosis, focal necrosis, and ballooning. In contrast, animals treated with CP extracts exhibited only mild ballooning and binucleate cells, indicating liver regeneration. The leaves of CP were the most effective in providing hepatoprotection. These findings suggest that CP has antioxidant and hepatoprotective properties against CCl_4-induced liver damage in rats (53)

Crude extract

The antihepatotoxic activity of chloroform, petroleum ether, and methanol fractions of *Clerodendrum phlomidis* whole plant was evaluated through biochemical parameters and histopathological studies against carbon tetrachloride-induced toxicity. Histopathological analysis of the liver in CCl_4-treated rats revealed swelling and necrosis of hepatocytes. Treatment with the various plant fractions significantly reduced hepatocyte necrosis and swelling. The biochemical parameters further confirmed the significant antihepatotoxic effects of these fractions (54).

Hypoglycemic activity

Root Bark

The study examined the effect of hydroalcoholic bark extract of *Clerodendrum phlomidis* (CPE) on blood glucose levels (BGL) in diabetic rats. The diabetic control group (DCG) showed a significant increase in BGL compared to the normal control group (NCG). Treatment with 200 mg/kg of CPE significantly reduced BGL at various time intervals with the maximum effect observed at 4 hours post-dosing, indicating prolonged glycemic control. However, 100 mg/kg of CPE did not significantly reduce BGL, and the hypoglycemic effect was not dose-dependent. The results suggest that 200 mg/kg of CPE effectively controls blood sugar in diabetic rats (55).

Stems

The methanolic and ethyl acetate extracts of *Clerodendrum multiflorum* stems were evaluated for their in-vitro alpha-amylase inhibitory activity and hypoglycemic effects through oral administration at varying doses in rats. Both extracts demonstrated strong alpha-amylase inhibitory activity compared to the standard drug acarbose. Additionally, oral administration of the extracts at a dose of 200 mg/kg body weight showed significant hypoglycemic effects in normal rats and antihyperglycemic activity in alloxan-induced diabetic rats (56).

Antifeedant, larvicidal and growth inhibitory activities

The study demonstrated that chloroform extract fractions from *Clerodendrum phlomidis* exhibited significant antifeedant and larvicidal activities, effectively reducing the adult emergence of *Earias vittella*. These findings suggest that the active fraction from the chloroform extract has potential for developing a novel pesticidal formulation for insect pest management programs. (57)

Anti-obesity activity

Roots

The roots of *Clerodendrum phlomidis* are traditionally used in Dibrugarh, Assam, to treat obesity. This study evaluated the anti-obesity effects of methanolic extract of *Clerodendrum phlomidis* (MECP) in models of cafeteria diet (CD) and progesterone-induced obesity. In the CD model, MECP (400 mg/kg) suppressed weight gain, reduced fat storage, and lowered triglyceride and cholesterol levels while increasing HDL cholesterol. MECP also improved hyperglycemia, hyperinsulinemia, dyslipidemia, and fat cell hypertrophy. In the progesterone model, MECP reduced hyperphagia in a dose-dependent manner. The anti-obesity effects are likely due to β-sitosterol, saponins, and flavonoids in MECP, which suppress appetite and inhibit fat absorption. This is the first report showing *Clerodendrum phlomidis* can ameliorate insulin resistance and visceral obesity (58)

Anti-amnesic activity

Root Bark

Clerodendrum phlomidis root bark was studied for its nootropic potential in mice. Aqueous extracts (100 and 200 mg/kg) were administered for 6 days, and memory was assessed using behavioral models. The extract significantly improved short- and long-term memory, reversing amnesia induced by scopolamine, diazepam, and aging. It also reduced brain acetylcholinesterase levels, suggesting enhanced cholinergic function. These findings indicate that *C. phlomidis* bark may be useful in treating cognitive disorders like amnesia and Alzheimer's disease (59)

Antimicrobial activity

Leaves

The n-hexane and dichloromethane extracts of *Clerodendrum phlomidis* were found to reduce the mean fluorescence intensity in Bacillus licheniformis, indicating a disruption of membrane potential. This suggests that the antibacterial mechanism involves damaging the membrane integrity. Among the two extracts, the dichloromethane extract was more potent in disrupting the membrane potential, providing significant evidence of its stronger antibacterial activity (60)

Among the 15 fungal strains which were Fluconazole and Clotrimazole resistant, seven were susceptible to the petroleum ether and ethyl acetate extracts. Petroleum ether extract showed the highest zone of 13±0.00 mm against Trichophyton rubrum, followed by ethyl acetate which showed a zone of inhibition of 11±0.00 mm and 10±0.25 mm against A. niger and Scedosporium sp. respectively. The study concludes that petroleum ether and ethyl acetate extracts of *Clerodendrum phlomidis* leaves are potent sources of antimicrobial compounds effective against multidrug-resistant organisms (61).

Root

Clerodendrum phlomidis has demonstrated significant antibacterial activity, particularly in its ethyl acetate and ethanol root extracts, which are effective against *Staphylococcus aureus* and *Bacillus subtilis*. The ethanolic extract showed the highest activity against all tested bacteria, including *Klebsiella pneumoniae*, though petroleum ether and aqueous root extracts lacked antibacterial properties (62)

The ethanol extract at 106.66 µg/ml demonstrated significant antimicrobial activity against *Escherichia*

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coli, showing the highest sensitivity with a 15.33 mm zone of inhibition. The chloroform extract also exhibited strong activity against *Staphylococcus aureus* with a 14.67 mm inhibition zone. Among the isolated compounds, Ethyl-2-hydroxy-4-methyl benzoate showed superior antimicrobial activity compared to 3,6,7-trihydroxy-2- (3-methoxyphenyl)-4H-chromen-4-one and phenyl acetic acid, particularly against *Staphylococcus pyogenes* and *Candida albicans*, with a 9 mm zone of inhibition at 60 µg/ml (63)

Stem and Leaves

Methanolic and acetone extracts from combined stems and leaves were tested against five Gram-positive bacteria, seven Gram-negative bacteria, and three fungi using the agar diffusion method. While the acetone extract showed no activity, the methanolic extract inhibited the growth of *Citrobacter freundii* and *Staphylococcus epidermidis*. Additionally, ethyl acetate and hexane extracts of leaves and stems, at a concentration of 1 mg/ml, were evaluated against human and plant pathogens using the poison plate technique. The hexane leaf extract exhibited greater activity than the stem extract against both types of pathogens (64)

Aerial Parts

The aerial parts of the plant were successively extracted using petroleum ether, chloroform, ethyl acetate, and methanol, in order of increasing polarity. The dried extracts were tested for anthelmintic activity against *Pheretima posthuma* (earthworms), with their paralysis and death times compared to the standard drug albendazole. Both the ethyl acetate and methanol extracts demonstrated anthelmintic activity comparable to albendazole (65)

Anti-asthmatic activity
Leaves

The ethanol extract of *Clerodendrum phlomidis* leaves significantly reduced contractions at 100 mg/ml in isolated guinea pig ileum, inhibiting histamine-induced bronchoconstriction. At a dose of 400 mg/kg (orally), it notably extended the latent period of convulsions after exposure to histamine aerosol, offering 59.04% protection at the 4th hour, compared to 65.04% protection provided by the standard drug chlorpheniramine maleate at 1 mg/kg orally (66)

Immunomodulatory activity
Roots

Oral administration of methanol extracts from *Clerodendrum phlomidis* and *Premna integrifolia* roots (300 mg/kg for 7 days) in mice prior to immunization with Sheep Red Blood Cells (SRBC) resulted in a significant increase in haemagglutinating antibody titre, plaque-forming cell assay, and delayed-type hypersensitivity to SRBC. *C. phlomidis* exhibited stronger specific immune activity compared to *P. integrifolia*. Both plants also enhanced non-specific immune responses in the carbon clearance test and demonstrated significant immunoprophylactic effects against *E. coli*-induced abdominal sepsis. While *C. phlomidis* showed a higher response in specific immune activity, both roots exhibited nearly equal responses in non-specific immune activity (67)

Anti-diarrhoeal activity
Leaves

(1)The methanolic extract, at doses of 200, 400, 600, and 800 mg/kg, was tested in albino rats (Wistar strain, 180-200 g, both sexes) for its effects on castor oil-induced diarrhoea, gastrointestinal motility, and prostaglandin E2-induced enteropooling. At doses of 600 and 800 mg/kg, the extract significantly reduced defecation frequency and slowed the propulsion of the charcoal meal through the gastrointestinal tract. Additionally, it showed significant inhibition of prostaglandin E2-induced enteropooling at nearly all dose levels (68)

Conclusion

Clerodendrum phlomidis, an integral plant in traditional medicine, particularly in Ayurveda, has demonstrated significant therapeutic potential. Revered as Agnimantha, it is a key ingredient in the renowned Ayurvedic formulation Dashamoola and has been used for centuries to treat a wide range of ailments, including inflammation, diabetes, fevers, and digestive disorders. Modern pharmacological studies have validated many of these traditional uses, revealing its anti-inflammatory, antimicrobial, antioxidant, hepatoprotective, and antidiabetic properties.The plant's diverse chemical profile, consisting of flavonoids, terpenoids, glycosides, and other bioactive compounds, underpins its broad-spectrum pharmacological actions. Its ability to alleviate conditions associated with Kapha and Vata doshas, as well as its systemic benefits for the digestive, circulatory, and respiratory systems, further highlight its medicinal significance. Additionally, *Clerodendrum phlomidis* shows promise in contemporary healthcare for treating lifestyle disorders such as diabetes and cardiovascular conditions.

Given the extensive use of *Clerodendrum phlomidis* in folk medicine and its growing relevance in modern pharmacological research, this plant holds vast potential for the development of novel therapeutics. Further studies focusing on its phytoconstituents, clinical efficacy, and potential adverse effects will be instrumental in harnessing its full medicinal potential. *Clerodendrum phlomidis* stands as a bridge between traditional knowledge and modern science, offering immense value in the quest for effective, plant-based remedies for today's health challenges.

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Exploring therapeutic potential of fasting (Upvasa)– A comprehensive review

Review Article

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Abstract

Background: Fasting, an ancient practice observed in many cultures, holds potential therapeutic value beyond its traditional spiritual significance. It may be defined as complete voluntary self-restraint from taking any kind of food for specific time, in order to give rest to digestive system". In Ayurvedic classics it may correlated with *Upvasa* which is one among the ten types of *Langhana* (lightness promoting therapy) and also included in *Daivavyapashraya chikitsa* (Therapeutic Rituals). Research suggests that Fasting (*Upvasa*) can positively affect various aspects of health, including weight management, metabolic health, cellular repair mechanisms, cognitive function, mood regulation, inflammation reduction, and immune system modulation. Objective: This review examines current research to elucidate the therapeutic potential of Fasting (*Upvasa*) for promoting health and facilitating healing processes. Material and Method: This review paper has been taken from different Ayurvedic manuscripts, Modern literatures and Various searching engines like PubMed, Web of Science Scopus, Google Scholar, SCI, Research gate and government portal like Ayush Portal, Namaste Portal etc. Discussion: Research suggests that fasting regimens, such as intermittent fasting or prolonged fasting, can lead to reductions in body weight, body fat percentage, and improvements in metabolic markers such as insulin sensitivity and cholesterol levels. It also enhances cognitive performance, memory, and focus, possibly through the upregulation of brain-derived neurotrophic factor (BDNF) and other neuroprotective pathways. By reducing inflammatory markers and promoting immune cell regeneration. Fasting stimulates autophagy, which promotes cell renewal and slows down the aging process. Conclusion: This paper discusses the physiology, historical views, and benefits of fasting on many health parameters. Integrating fasting into healthcare practices requires comprehensive understanding and guidance to ensure safe and effective implementation.

Keywords: Autophagy, Intermittent fasting, Insulin sensitivity, *Langhana, Obesity, Upvasa*.

Introduction

Fasting, or "Upavasa," is an ancient practice that has been deeply embedded within various cultural and religious traditions across the globe. In the context of Ayurveda, fasting holds a special place as a method to promote physical and mental well-being, believed to balance the three doshas and cleanse the body of toxins (Ama). While fasting has long been practiced for spiritual purification and self-discipline, modern science is now beginning to unveil its wide-ranging therapeutic benefits, particularly in the prevention and treatment of chronic diseases. In recent years, there has been a surge of interest in intermittent fasting, caloric restriction, and prolonged fasting regimens for their potential health benefits. Studies have shown that these fasting protocols may improve metabolic health, enhance cellular repair mechanisms like autophagy, reduce inflammation, and even extend lifespan. Beyond weight loss and metabolic improvements, fasting has been investigated for its role in improving cognitive function, promoting longevity, and reducing the risk of diseases such as diabetes, cardiovascular disorders, and certain types of cancer. In 2016, Yoshinori Ohsumi was awarded the Nobel Prize in medicine for his studies on autophagy, a mechanism that allows cells to recycle and regenerate their material. Through the evolutionarily conserved lysosomal catabolic process of autophagy, cells break down and recycle intracellular external (bacteria and viruses) and endogenous (damaged organelles, misfolded or mutant proteins and macromolecules) components. Although Yoshinori Ohsumi's work has little to do with this review, it does contribute to our understanding of how cells survive and maintain their health during fasting, as they break down into proteins and unnecessary components that they can repurpose for energy. His research focuses on a process that is essential to the survival and well-being of cells. Higher creatures, including humans, use the autophagy genes and metabolic pathways he found in yeast. Aim of the research paper is to evaluate the therapeutic potential of fasting, drawing on a variety of scientific studies, traditional Ayurvedic texts, and clinical trials, to offer a holistic understanding of its effects on human health.

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Materials and Methods

Comprehensive information about the topic has been examined and gathered by a systematic screening of many Ayurvedic classical books, such as the Charaka Samhita, Sushruta Samhita, Astanga Hridaya, Chakradutta, Yogaratnakar, Ayurvedic vocabularies, etc. With the use of the Boolean operators "AND," "OR," and "NOT," various literature databases, including PubMed, Google Scholar, Web of Science, Scopus, MEDLINE, DHARA, AYUSH Portal, and Namaste Portal, were searching for terms like "Upvasa," "Fasting," "Intermittent Fasting," "Intermittent fasting -Autophagy," " Intermittent fasting -Insulin Sensitivity," "Upvasa-Langhan," "Upvasa- Agni," "Intermittent - Fasting," and "Fasting- Gut microbiota," Filters including free full papers, within ten years, review articles, clinical trials, and others were employed in this paper.

Results

Etymology and Definition

According to contemporary science, fasting is" Complete voluntary abstinence from taking any kind of food for a specific period of time, in order to give the digestive system a rest." The term “Upvasa” in Sanskrit refers to fasting and Upa means "near" and Vasa means "to stay". The phrase "to sit or stay near (the Lord)" implies that fasting is a way to keep the Lord at the forefront of your heart and mind. Vachaspatyama defines Upvasa as abstaining from food during the day and night. There are two sorts of Upvasa: “avaidh,” or unlawful fasting, and “vaidha,” or lawful fasting (Vachaspatyama, 1322). Classical Ayurvedic texts define fasting as Upvasa. It is described as refraining from eating, drinking, licking, or chewing any of the four types of food(1). Upvasa refers to a particular kind of Daivavyapasraya chikista, which is the practice of fasting to treat illness. (Namaste Portal)(2).

Ayurvedic perspectives of Upvasa

The two therapeutic modalities /techniques described by Ayurvedic texts, brihmana or nourishing therapy and langhana or depletion therapy, aim to alleviate pain and diseases. Langhana therapy is characterized as a method that results in a decrease or depletion of the bodily virtues, leading to a lighter body. Fasting, exercise and sun exposure and elimination therapies are some examples of depletion therapies that are described(3). Therefore, it is imperative to thoroughly understand and apply the crucial function that fasting plays as one of the therapeutic modalities during the treatment of various diseases and during different stages of the diseases, as detailed in the renowned Ayurvedic classics.

Principal of fasting

The ash particles that stay on it lessen the intensity of the fire, which hinders the burning process. Similar circumstances apply to the vitiated dosha of the human body, particularly to the digestive viscera, or Aamashaya in Ayurveda. In addition to producing ama (metabolic toxins), which are said to be the fundamental cause of all ailments, this weakens and disables the digestive fire and debilitates the stomach. which ultimately cause blockages in the body's pathways, resulting in various illnesses. When combined with low nourishment in the viscera, fasting not only clears the channels and ignites the digestive fire, but it also significantly destroys a number of metabolic toxins. Fighting sickness is aided by this procedure. All the same, it is not advised at all to feast before or after keeping a fast(4). Ayurveda suggests that following a fast, one should eat something that is simple to digest, such as freshly made rice gruel. This food should be hot, light enough to be assimilated, and liquid in consistency. The cold and moist season from the end of February onwards is unusually ideal for fasting, according to Ayurveda, which maintains that spring (Shishira Rutu) is the finest time for fasting. The body's self-cleaning mechanisms are activated when the force of the sun begins to boost. Ayurveda does not advocate giving up all food; rather, it advises taking light meals during fasting, the number of which can be adjusted based on body type and dosha. According to Ayurveda, the type and timing of fasting for detoxification varies depending on the body type of the individual. Fasting according to one's bodily type resembles to fasting according to doshas. This is due to the fact that every Ayurvedic treatment should be tailored to the unique constitution of each individual. Different toxicities arise from the vitiation of the mental doshas Tamas and Rajas in addition to the physical doshas Vata, Pitta, and Kapha(5). The body should eliminate waste products, body fats, and metabolic deposits while fasting. As a result, losing body weight is a continual component of this process.

Table 1: Therapeutic effect of Fasting (Upvasa) in Ayurvedic Classics

S.No.	Vyadhi (disease)	Stage/Duration
1	Jwara (Fever)	According to Acharya Vagbhata fasting indicated in Purva Roopa Avastha (prodromal stage).(6) On the basis of patient's Bala (strength) and also the bala of the disease, fasting should be recommended.(7)
2	Raktajaroga (blood borne diseases)	Ama dosha generally aggravates pitta (the biological element responsible for digestion & metabolism, color complexion, vision, etc. and rakta). Thus, the patient has to be kept on a fast at first in raktajaroga(8).
3	Santarpanajanyavikara (diseases due to over nutrition)	Over nutrition-related diseases include Diabetes Mellitus, small abscess including diabetic boils, itching, urticarial patches, leprosy, anemia, fever, dysuria, anorexia, drowsiness, frigidity, excessive obesity, heaviness of body, obstruction of sense organs and channels, confusion/ delusion of intellect, always closing eyes, edema/ inflammation and with additional conditions. To

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4	Chardi-roga (vomiting)	In Ayurveda, chardi is caused by the disease connected to Amashaya (stomach), which is the sthana or seat of Kapha dosha. Therefore, the treatment for the disease is considered to be langhana (depletion therapy) in terms of Upvasa.(10)
5	Atisara (diarrhoeal diseases)	In the early stages of Atisara (diarrhea), body is associated with ama (metabolic toxins), fasting is recommended. Fasting eases the removal of toxins and makes the body for added therapy. If there is a lot of watery diarrhea, emesis (vamana) should be performed under medical supervision, and fasting must come after.
6	Visoochika (gastroenteritis)	Fasting is recommended.(12)
7	Shotha-Roga (Oedema)	The patient has to undergo langhana based on their strength if ama is the reason for the shotha (oedema).(13)
8	Vataja abhishyanda	Patient should fast for 3 days or only at night food can be given.(14)
9	Pratishyaya (rhinorrhoea)	When taking carminative drugs for Jeerna pratishyaya (chronic rhinorrhea), which is marked by fever, vomiting, body aches, heaviness, tastelessness,

Naturopathy perspectives of Fasting

One of the pancha-mahabhootas, Akasha, is represented by fasting. The easiest way to rid the body of sickness and cleanse it is by fasting. Fast therapy expert Dr. Carington states that a fast begins with skipping the first meal and concludes when a true hunger sensation arises. Fasting is a great way to improve your physical, mental, and spiritual well-being, but its benefits may only be seen if you follow a methodical approach(15). Fasting is recognized as a therapy in naturopathy for the majority of diseases. The body significantly regains the Aakash tatva (space element) while fasting(16). Dr. Herbert M. Shelton successfully treated hundreds of patients with a variety of chronic illnesses throughout his extended study on fasting(17),(18). Fasting, according to naturopathy, is a way to give the digestive system a break. The important energy required for food digestion is entirely focused on curing the body of illnesses throughout this procedure(19). In his book Key to Health, Mahatma Gandhi outlined his beliefs regarding fasting, writing, "We must not fill the digestive tract with unnecessary food stuffs." Eat little more than what our bodies require. It happens frequently that people overeat or consume indigestible foods without realizing it. One can maintain equilibrium by fasting once a week or once every two weeks, for example. One should skip one or more meals during the day if they are unable to fast for the entire duration(20).

Modern perspectives of fasting

Concept of Intermittent Fasting

Many protocols and strategies for intermittent fasting have been proposed and are currently being used. Some of the common fasting approaches are shown in **Table: 2** (21), (22).

Table 2: Some of the common fasting approaches

S. No.	Practice	Frequency	Duration	Other Considerations
1	Alternate day	Every alternate day	24 hours	-
2	5:2	Two days weekly	24 hours each day	2 other days involve a very low-calorie diet
3	Time-restricted feeding	Daily	14 hours	Food is eaten over 6 hours period
4	B2 regimen	Daily		Breakfast 6a.m-10a.m, lunch 12-2p.m, no dinner
5	Weekly 1 day Fasting	Once a week	24 h	One-day-a-week diet consisting mainly of water and six days of usual meals
6	Intermittent very low-calorie diet (VLCD) therapy	Variable	24 h	1-d VLCD refers to VLCD for one day per week, and 5-d VLCD is VLCD for five days in a consecutive, repeated every five weeks.

Discussion

Intermittent fasting in Obesity

It has been demonstrated that intermittent fasting reduces adiposity, especially from visceral and truncal fat due to comparatively small calorie deficits. Patients may have changes in their leptin/adiponectin levels and sensitivity as a result of this decrease in adiposity, which would lead to better appetite control(23).

Intermittent Fasting in Cardiovascular Disorders

Lower adiponectin, higher C-reactive protein, smaller LDL particles, and other metabolic variables that are linked to the development of atherosclerosis and coronary artery disease are all indicators of increased inflammation that are brought on by insulin resistance(24). Moreover, insulin raises the risk of fluid retention and congestive heart failure in addition to being linked to atherogenic dyslipidaemia(25). Therefore, it would be expected that cutting insulin levels with intermittent fasting will lower serious adverse cardiovascular events.

Intermittent Fasting in Hypertension

The parasympathetic nervous system's activation, resulting from an increase in the activity of the brainstem's cholinergic neurons, may be the mechanism underlying the lowered blood pressure during intermittent fasting(26). Although glutamatergic receptor activation is the primary stimulus that causes brain-derived neurotrophic factor (BDNF) to be created, studies have shown that intermittent fasting is an important environmental trigger as well(27).

Intermittent Fasting in Prediabetes, Diabetes and Insulin Resistance

Regarding the emergence of insulin resistance, various mechanisms have been hypothesized. Increasing adiposity and chronic inflammation that follows, which causes tissues to become insulin resistant, are linked, according to a well-known notion. By reducing calorie intake and altering the metabolism, intermittent fasting can lower obesity and the associated insulin resistance. Another theory is that lower energy intake, like that obtained by intermittent fasting, will result in higher levels of AMPK and a sustained drop in insulin secretion, which probably contributes to the improvements in glucose homeostasis and insulin sensitivity(28).

Intermittent Fasting in Neurodegeneration

Fasting therapy has not been investigated as a potential treatment for individuals with Alzheimer's disease (AD), Parkinson's disease (PD), or Huntington's disease (HD)(29). However, research on ketogenic diets in a variety of diseases has only shown indirect evidence. Ketogenic diets, also known as high-fat, adequate-protein, low-carb diets, drive the body to use fat for energy rather than carbohydrates, creating ketones and triggering a number of fasting-related metabolic processes to mimic a fasted metabolic state. A small case series of PD patients exhibited better motor symptoms after four weeks on a ketogenic diet(30). After eight weeks on a ketogenic diet, several of the most crippling non-motor symptoms that are least sensitive to levodopa improved in a later randomized controlled research with forty-seven patients with mild-to-severe Parkinson's disease (PD)(31). Regarding the effect of a ketogenic diet on AD, one case series consisting of fifteen people with mild-to-moderate AD showed some improvement in cognitive function after a 12-week program(32). The fact that AD does not significantly influence ketone utilization despite a major decrease in brain glucose absorption may help to explain these results(33).

Intermittent Fasting in Cancer

The feasibility and beneficial weight loss effects of various forms of Intermittent Fasting (IF) in overweight and obese men and women have led to clinical trials testing its effects on metabolic and hormonal end points associated with cancer development or prognosis, mostly in patients without cancer. Although studies of IF in nonhuman primates have not been reported, those trials have been carried out(34),(35). A 5:2 diet or alternate day fasting has been shown to improve some cancer risk factors in a number of short-term (2–6 months) randomized clinical trials. These include increased adiponectin and decreased levels of leptin, insulin, and glucose during fasting, (36) all of which have been linked to the pathogenesis of cancer(37). Autophagy, a process that enables cells to remove damaged components and recycle them for energy, is another mechanism activated during fasting. IF has been shown to enhance autophagic activity, which can promote the elimination of precancerous and cancerous cells(38).

Conclusion

In conclusion fasting represents a profound intersection between ancient wisdom and modern science, offering a holistic approach to health and well-being. From its roots in Ayurvedic tradition, where it is revered as a means of balancing the body's internal energies and detoxifying the system, to its growing recognition in contemporary scientific research, fasting emerges as a powerful therapeutic tool. Fasting has shown potential in regulating metabolism, promoting cellular repair through autophagy, reducing inflammation, and enhancing cognitive function, among other benefits. It helps in managing chronic conditions such as obesity, type 2 diabetes, cardiovascular diseases, and neurodegenerative disorders.

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Pharmacodynamic Evaluation of Polyherbs and its Formulation for Antitussive Activity Using Citric Acid Induced in Guinea Pig

Research Article

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Abstract

This review article focuses on the pharmacodynamic evaluation of polyherbal formulations for antitussive activity, utilising a citric acid-induced cough model in guinea pigs. The study explores various polyherbs traditionally used in cough treatment, aiming to validate their efficacy through scientific methods. By inducing coughing in guinea pigs with citric acid, the antitussive effects of different herbal combinations are assessed in comparison to standard cough suppressants. The review emphasizes the potential advantages of polyherbs, such as synergistic effects, reduced side effects, and natural origin, making them promising candidates for cough management. Furthermore, the article highlights the importance of evaluating dosage, formulation, and bioactive components to optimize therapeutic outcomes. This comprehensive review contributes to the growing body of evidence supporting the use of polyherbal remedies in the treatment of cough-related disorders.

Keywords: Polyherbal formulation, Antitussive activity, Citric acid-induced cough, Guinea pig model, Pharmacodynamics.

Introduction

Polyherbal formulations are combinations of two or more medicinal herbs designed to enhance therapeutic efficacy and reduce adverse effects. These formulations have been a fundamental part of traditional medicine systems, such as Ayurveda, Traditional Chinese Medicine (TCM), and Unani, for thousands of years. In these systems, multiple herbs are often combined to treat complex health conditions, utilising the synergistic effects of various plant compounds to target multiple biological pathways simultaneously (1).

This holistic approach is particularly beneficial in managing respiratory conditions like coughs and bronchitis, where different herbs can work together to relieve symptoms and address underlying causes.

The study of pharmacodynamics is crucial for understanding how polyherbal formulations work, especially for their antitussive (cough-suppressing) activity. By investigating the pharmacodynamic properties, researchers can determine how these formulations influence physiological processes, their mechanisms of action, and how they interact with the body to suppress cough.

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Overview of polyherbal formulations in traditional medicine

Polyherbal formulations have been an integral part of traditional medicine systems like Ayurveda, Traditional Chinese Medicine (TCM), Unani, and many indigenous healing practices worldwide. These formulations involve combining two or more herbs to achieve a desired therapeutic effect, based on the principle that the synergistic interaction between different plant compounds can enhance efficacy and reduce toxicity compared to single-herb remedies (2).

In traditional medicine, polyherbal formulations are meticulously crafted, often following ancient texts or local knowledge passed down through generations. The combinations are designed to address complex health conditions holistically, targeting multiple biological pathways simultaneously. For instance, a formulation aimed at respiratory health may include herbs that not only suppress cough but also reduce inflammation, fight infection, and strengthen the immune system (3).

Importance of studying their pharmacodynamics for antitussive activity

Studying the pharmacodynamics of polyherbal formulations for antitussive activity is vital to understanding how these complex mixtures work to alleviate cough. Pharmacodynamics involves analyzing how the active compounds within these herbs interact with the body to produce therapeutic effects. For antitussive activity, it's important to know which components are responsible for suppressing the cough reflex and how they modulate various physiological pathways, such as those involving the central nervous system, immune response, and inflammatory processes.

Understanding the pharmacodynamics allows researchers to optimize the herbal combinations and dosages to maximize efficacy and minimize side effects. Since polyherbal formulations are often composed of multiple active compounds, studying their interactions is crucial to ensuring that they work synergistically rather than antagonistically. This knowledge helps in refining traditional herbal practices and provides a scientific basis for their use in modern medicine (4).

Moreover, such studies can lead to the discovery of novel bioactive compounds with potent antitussive properties, potentially contributing to the development of new medications. By validating the effectiveness of these herbal formulations through pharmacodynamic research, healthcare providers can have greater confidence in prescribing these treatments, ultimately benefiting patients with safer and more effective options for managing cough and related respiratory conditions (5).

Rationale for herb selection

Criteria for Selecting Specific Herbs in the Formulation

The selection of specific herbs for a polyherbal formulation is guided by several key criteria. Firstly, the herbs are chosen based on their known pharmacological activities that align with the therapeutic goals of the formulation, such as antitussive, anti-inflammatory, or antimicrobial effects. Secondly, the safety profile of each herb is crucial, ensuring minimal side effects and toxicity when used individually and in combination. Thirdly, the potential for synergistic effects is considered, where the combined use of herbs enhances efficacy more than any single herb alone. Additionally, traditional use and historical efficacy in treating similar conditions play a significant role in herb selection, providing a foundation of empirical knowledge that supports their inclusion in the formulation. Finally, availability and sustainability of the herbs are considered to ensure that the formulation is accessible and environmentally responsible (6).

Ethnopharmacological Background of Each Herb Used:(7)

1. ***Curcuma zedoaria*** **(Dried Rhizomes):** Traditionally used in Ayurvedic and traditional Chinese medicine for its anti-inflammatory, antimicrobial, and digestive properties. It is believed to support respiratory health by reducing mucus production and inflammation.
2. ***Salvadora persica*** **(Dried Leaves):** Commonly known as the toothbrush tree or miswak, its leaves have been used in various cultures for oral hygiene and respiratory ailments, attributed to their antimicrobial and anti-inflammatory properties.
3. ***Glycyrrhiza glabra*** **(Dried Roots):** Widely used in traditional medicine for its demulcent, expectorant, and anti-inflammatory effects, particularly beneficial for soothing irritated mucous membranes in the respiratory tract.
4. ***Andrographis paniculata*** **(Dried Leaves):** Known for its bitter taste and potent immunomodulatory, anti-inflammatory, and antiviral properties, this herb is used extensively in Ayurvedic and traditional Chinese medicine to treat respiratory infections and boost immune responses.
5. ***Ocimum tenuiflorum*** **(Dried Leaves):** Also known as Holy Basil or Tulsi, it is revered in Ayurveda for its adaptogenic, antimicrobial, and anti-inflammatory properties, making it a common remedy for respiratory conditions and overall health enhancement.

Pharmacological profile of each herb

Curcuma zedoaria **Rosc. (Dried Rhizomes)**

Curcuma zedoaria, also known as white turmeric, has been traditionally used in Ayurvedic and traditional Chinese medicine to treat a variety of ailments, including respiratory disorders, digestive issues, and inflammatory conditions (8). The rhizomes of *Curcuma zedoaria* are known for their anti-inflammatory, antimicrobial, and antioxidant properties (9). These pharmacological actions are attributed to the presence of curcuminoids and essential oils, which help reduce inflammation, inhibit microbial growth, and neutralize free radicals (10).

Salvadora persica **(Dried Leaves)**

Salvadora persica, commonly known as the toothbrush tree or miswak, has a long history of use in traditional medicine for oral hygiene and respiratory health (11, 12). The dried leaves of *Salvadora persica* contain a variety of active compounds, including alkaloids, flavonoids, and saponins, which possess antibacterial, anti-inflammatory, and antioxidant properties (13). These compounds help protect the respiratory tract from infections, reduce inflammation, and support overall respiratory health (14).

Glycyrrhiza glabra **(Dried Roots)**

Glycyrrhiza glabra, commonly known as licorice root, contains several bioactive constituents, including glycyrrhizin, flavonoids, and saponins (15). Glycyrrhizin, the primary active compound, is known for its anti-inflammatory, expectorant, and demulcent properties, making it effective in soothing irritated mucous membranes and reducing cough reflexes. Flavonoids and saponins further enhance its expectorant effects, helping to clear mucus from the airways, thereby providing relief from cough and respiratory discomfort (16).

Andrographis paniculata **(Dried Leaves)**

Andrographis paniculata, often referred to as the "King of Bitters," is renowned for its potent immunomodulatory, anti-inflammatory, and antiviral properties. The dried leaves contain active compounds like andrographolides, which inhibit pro-inflammatory cytokines and enhance immune responses, making the herb effective in managing respiratory infections and reducing cough. Andrographolides also exhibit bronchodilatory effects, helping to open up airways and improve breathing, which contributes to its antitussive activity (17).

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***Ocimum tenuiflorum* (Dried Leaves)**

Ocimum tenuiflorum, commonly known as Holy Basil or Tulsi, is highly regarded in Ayurveda for its adaptogenic, antimicrobial, and anti-inflammatory properties. Several studies have demonstrated its effectiveness in treating respiratory disorders, including asthma, bronchitis, and coughs(18). The dried leaves of Tulsi contain essential oils, such as eugenol and camphor, which help reduce inflammation, enhance immune function, and clear respiratory passages. Additionally, its antioxidant properties protect the respiratory tract from damage caused by oxidative stress, further supporting its use in respiratory health (19).

Pharmacognostical profile of each herb

***Curcuma zedoaria* Rosc. (Dried Rhizomes) (20, 21, 22).**

- **Biological Source:** Curcuma zedoaria, commonly known as "Zedoary," is derived from the dried rhizomes of *Curcuma zedoaria* (figure 1).
- **Family:** Zingiberaceae

Figure 1: Dried Rhizomes of *Curcuma zedoaria* (23)

- **Morphological Characteristics**: The rhizomes are large, cylindrical, and branched, with a diameter ranging from 2-4 cm. They are covered in a light brown skin, which becomes darker when dried. The inner part of the rhizome is yellowish-brown, with a distinctive aromatic odour. The taste is slightly bitter and pungent.
- **Microscopy**: The microscopic examination reveals parenchymatous cells filled with starch grains, fibrovascular bundles, and scattered oil cells. The rhizomes show well-defined cork layers, prominent vascular bundles, and the presence of yellowish-brown oil globules.
- **Phytochemical Constituents**: Major constituents include curcuminoids (curcumin, demethoxy curcumin), essential oils (zingiberene, curzerenone), and sesquiterpenoids.
- **Pharmacological Properties**: Known for anti-inflammatory, antioxidant, and antimicrobial activities. Traditionally used for digestive and respiratory ailments.

***Salvadora persica* (Dried Leaves) (24, 25)**

- **Biological Source**: Derived from the dried leaves of *Salvadora persica* (figure 2), commonly known as the "Toothbrush Tree" or "Miswak."
- **Family**: Salvadoraceae
- **Morphological Characteristics**: The leaves are simple, alternate, and small, measuring about 4-6 cm in length. They are greenish when fresh and turn greenish-brown when dried. The shape is elliptical or lanceolate with entire margins, and the surface is smooth with a slightly bitter taste.

Figure 2: Leaves *Salvadora persica* (26).

- **Microscopy**: Microscopic examination reveals an epidermis covered with a cuticle, parenchymatous cells containing calcium oxalate crystals, and scattered oil cells. The vascular bundles are small, with a few fibers surrounding them.
- **Phytochemical Constituents**: The primary constituents are alkaloids (salvadorine), flavonoids, tannins, saponins, and essential oils (including sulfur-containing compounds).
- **Pharmacological Properties**: Exhibits antimicrobial, anti-inflammatory, and analgesic properties. Traditionally used in oral hygiene and respiratory health.

***Glycyrrhiza glabra* (Dried Roots) (27, 28).**

- **Biological Source**: The dried roots of Glycyrrhizaglabra (figure 3), commonly known as “Licorice.”
- **Family**: Fabaceae

Figure 3: Dried Roots Glycyrrhizaglabra (29)

- **Morphological Characteristics**: The roots are cylindrical, slightly twisted, and measure about 1-2 cm in diameter. The outer surface is yellowish-brown, and the inner part is pale yellow. The taste is sweet due to the high content of glycyrrhizin, a compound that is 50 times sweeter than sugar.
- **Microscopy**: The root shows medullary rays, parenchyma with starch grains, and prominent laticifers (latex cells). The vascular bundles are arranged radially, and the presence of tracheids and fibers is common.
- **Phytochemical Constituents**: The roots contain glycyrrhizin, glycyrrhizic acid, flavonoids (liquiritin), saponins, and coumarins.
- **Pharmacological Properties**:Possesses expectorant, anti-inflammatory, and antitussive properties. Widely used for cough suppression.

***Andrographis paniculata* (Dried Leaves)[30].**

- **Biological Source**: The dried leaves of *Andrographis paniculata* (figure 4), commonly known as "*Kalmegh*."
- **Family**: Acanthaceae

Figure 4: Dried Leaves of *Andrographis paniculata* (31)

- **Morphological Characteristics**: The leaves are simple, opposite, and lanceolate, with a dark green color when fresh and pale green when dried. They have a characteristic bitter taste.
- **Microscopy**: Microscopic analysis shows the presence of glandular and non-glandular trichomes, abundant stomata, and elongated vascular bundles. The epidermis is covered with a thick cuticle.
- **Phytochemical Constituents**: The major constituents include andrographolides (a diterpenoid lactone), flavonoids, and diterpenes.
- **Pharmacological Properties**:Known for its anti-inflammatory, antiviral, and immune-boosting effects. Used in respiratory infections and fever management.

***Ocimum tenuiflorum* (Dried Leaves) (32, 33)**

- **Biological Source**: Derived from the dried leaves of *Ocimum tenuiflorum* (figure 5), commonly known as "Holy Basil" or "*Tulsi*."
- **Family**: Lamiaceae

Figure 5: Derived leaves of *Ocimum tenuiflorum* (34)

- **Morphological Characteristics**: The leaves are small, ovate, and slightly toothed. They are greenish when fresh and dark brown when dried. The surface of the leaves is covered with fine hairs, and they have a strong, aromatic scent.
- **Microscopy**: The leaf microscopy shows glandular trichomes, stomata, and well-developed vascular bundles. The epidermal cells contain calcium oxalate crystals, and the mesophyll consists of loosely arranged cells.
- **Phytochemical Constituents**: The main constituents include essential oils (eugenol, ursolic acid), flavonoids, and tannins.
- **Pharmacological Properties**:Demonstrates anti-inflammatory, antitussive, and expectorant properties. Traditionally used for respiratory and cold-related ailments.

Phytochemical screening of each herb for antitussive activity

Phytochemical screening is crucial for identifying the bioactive compounds present in medicinal plants. The following is a review of the major phytochemicals found in *Curcuma zedoaria*, *Salvadorapersica*, *Glycyrrhizaglabra*, *Andrographispaniculata*, and *Ocimumtenuiflorum*, and their potential roles in antitussive activity.

Curcuma zedoaria (Dried Rhizomes) (35)

Phytochemical Constituents

- **Curcuminoids**: These are the primary active constituents, including curcumin, demethoxycurcumin, and bisdemethoxycurcumin. These compounds are known for their anti-inflammatory, antioxidant, and antimicrobial properties.
- **Essential Oils**: These include camphor, curzerenone, and zedoarol, which have antitussive and anti-inflammatory properties.
- **Terpenes**: These contribute to the plant's anti-inflammatory and bronchodilatory effects.

Role in Antitussive Activity: The anti-inflammatory effects of curcuminoids help reduce airway irritation, while essential oils provide a soothing effect on the respiratory system, which can suppress cough reflexes.

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***Salvadora persica* (Dried Leaves) (36, 37)**

Phytochemical Constituents:

- **Flavonoids**: Compounds such as quercetin and rutin, which exhibit anti-inflammatory and antioxidant properties.
- **Alkaloids**: Salvadorine, which is reported to have analgesic and anti-inflammatory effects.
- **Saponins**: Known for their anti-inflammatory and expectorant properties, aiding in mucus clearance.
- **Tannins**: These astringent compounds have antimicrobial and anti-inflammatory activities.

Role in Antitussive Activity: The anti-inflammatory flavonoids and saponins in *Salvadora persica* help reduce the irritation that triggers coughing. The presence of alkaloids may contribute to its analgesic effects, further aiding in cough suppression.

***Glycyrrhiza glabra* (Dried Roots) (37, 38).**

Phytochemical Constituents

- **Glycyrrhizin**: A triterpenoid saponin that has expectorant, anti-inflammatory, and antiviral properties. It is a key compound for soothing the throat and clearing mucus from the airways.
- **Flavonoids**: Liquiritin, isoliquiritigenin, and glabridin, which possess anti-inflammatory, antioxidant, and antimicrobial properties.
- **Coumarins**: Umbelliferone and herniarin, which have antitussive and bronchodilatory effects.
- **Polysaccharides**: These exhibit immunomodulatory and mucolytic properties, helping to break down mucus.

Role in Antitussive Activity: Glycyrrhizin and flavonoids work synergistically to reduce inflammation and soothe irritated airways. The expectorant properties help clear mucus, which can suppress the cough reflex.

***Andrographis paniculata* (Dried Leaves) (39, 40)**

Phytochemical Constituents

- **Andrographolide**: A diterpene lactone that is the major bioactive compound responsible for anti-inflammatory, antiviral, and immunomodulatory activities. It has also been shown to reduce airway inflammation and irritation.
- **Flavonoids**: Such as andrographin, which have antioxidant and anti-inflammatory effects.
- **Diterpenes**: These contribute to its bronchodilatory effects, helping to reduce airway resistance and cough reflex sensitivity.

Role in Antitussive Activity: The anti-inflammatory effects of andrographolide help suppress cough by reducing inflammation in the respiratory tract. Its antiviral properties also support its use in treating coughs caused by respiratory infections.

***Ocimum tenuiflorum* (Dried Leaves) (41)**

Phytochemical Constituents:

- **Eugenol**: A phenolic compound that exhibits strong antitussive, anti-inflammatory, and antioxidant effects. It helps in soothing the throat and suppressing cough reflexes.
- **Urosolic Acid**: A triterpenoid known for its anti-inflammatory and bronchodilatory properties.
- **Flavonoids**: Apigenin and luteolin, which possess anti-inflammatory and antioxidant activities.
- **Tannins**: Provide antimicrobial and anti-inflammatory effects, supporting the overall health of the respiratory system.

Role in Antitussive Activity: Eugenol is the primary compound responsible for the antitussive activity of *Ocimum tenuiflorum*, helping to suppress the cough reflex. The additional anti-inflammatory and bronchodilatory effects of other compounds, such as ursolic acid, further enhance its efficacy.

Table 1: Summary of Phytochemical Roles in Antitussive Activity (42)

Herb	Phytochemical Constituents	Role in Antitussive Activity
Curcuma zedoaria (Dried Rhizomes)	Curcuminoids, Essential oils (camphor, α-turmerone), Sesquiterpenes	Anti-inflammatory effects reduce airway irritation and inflammation, leading to cough suppression.
Salvadorapersica (Dried Leaves)	Flavonoids, Alkaloids, Saponins, Salvadorine, Tannins	Flavonoids and alkaloids modulate the cough reflex and reduce airway inflammation, alleviating cough symptoms.
Glycyrrhiza glabra (Dried Roots)	Glycyrrhizin, Flavonoids, Saponins, Isoflavones, Coumarins	Glycyrrhizin soothes mucous membranes, reducing cough reflex sensitivity. Flavonoids exert anti-inflammatory and expectorant effects.
Andrographispaniculata (Dried Leaves)	Andrographolide, Flavonoids, Diterpenes, Tannins	Andrographolide provides anti-inflammatory and immunomodulatory effects, reducing airway resistance and coughing.
Ocimumtenuiflorum (Dried Leaves)	Eugenol, Flavonoids, Triterpenoids, Saponins, Alkaloids	Eugenol acts as an antitussive by suppressing cough reflexes and reducing airway inflammation.

Table 1 summarises the key phytochemicals in each herb and their respective roles in reducing cough through mechanisms such as anti-inflammatory action, soothing irritated airways, and modulating the cough reflex. These bioactive compounds work together to provide a synergistic effect in polyherbal formulations for antitussive therapy.

Literature review

In the study of respiratory disorders, the evaluation of polyherbal formulations for their antitussive effects has been a subject of increasing research. The citric acid-induced cough model in guinea pigs is a widely accepted experimental model to assess the effectiveness of such formulations. The following review focuses on the individual herbs used in polyherbal formulations, specifically *Curcuma zedoaria, Salvadora persica, Glycyrrhiza glabra, Andrographis paniculata,* and *Ocimum tenuiflorum*, with reference to their antitussive activity.

***Curcuma zedoaria* (Dried Rhizomes)**

Phytochemical Constituents and Traditional Uses: *Curcuma zedoaria* (Zedoary) is a well-known herb in traditional medicine, valued for its anti-inflammatory, antioxidant, and antimicrobial properties. The active compounds, such as curcuminoids and essential oils, contribute to its pharmacological effects (43).

Antitussive Activity: In a study by Rao et al. (2015), the ethanol extract of *Curcuma zedoaria* was tested on guinea pigs using the citric acid-induced cough model. The results demonstrated a significant reduction in cough frequency compared to the control group, indicating its potential antitussive properties i-inflammatory effect of curcuminoids may contribute to the suppression of cough reflex by reducing airway irritation (44).

***Salvadora persica* (Dried Leaves)**

Phytochemical Constituents and Traditional Uses: *Salvadora persica* (*Miswak*), commonly used as a traditional oral hygiene tool, contains bioactive compounds such as salvadorine, flavonoids, and alkaloids, which are known for their anti-inflammatory and antimicrobial properties (45).

Antitussive Activity: A study conducted by Almas et al. (2017) tested the aqueous extract of *Salvadora persica* in the citric acid-induced cough model in guinea pigs. The results showed a significant reduction in cough episodes, likely due to its anti-inflammatory action, which reduces irritation in the airways. The fruit of *Salvadora persica* are believed to play a role in modulating the cough reflex (46).

***Glycyrrhiza glabra* (Dried Roots)**

Phytochemical Constituents and Traditional Uses: *Glycyrrhiza glabra* (Licorice) is a widely researched herb, known for its sweet taste due to glycyrrhizin. It has been used in traditional medicine for respiratory conditions like asthma, bronchitis, and cough (47).

Antitussive Activity: Studies have highlighted the cough-suppressing potential of *Glycyrrhiza glabra* in preclinical models. A study by Wang et al. (2019) demonstrated that the extract of *Glycyrrhiza glabra* significantly reduced cough frequency in guinea pigs in a dose-dependent manner using the citric acid-induced cough model. The glycyrrhizionoid content were believed to contribute to its antitussive and expectorant properties by soothing the airways and reducing mucus secretion (48).

***Andrographis paniculata* (Dried Leaves)**

Phytochemical Constituents and Traditional Uses: *Andrographis paniculata* (*Kalmegh*) is known for its strong bitter taste and is widely used for its immunomodulatory, antiviral, and anti-inflammatory effects. The main bioactive compound is andrographolide (49).

Antitussive Activity: A study by Liu et al. (2018) investigated the antitussive effects of Andrographis paniculata in guinea pigs using the citric acid-induced cough model. The study reported a significant decrease in cough reflex and airway resistance, which was attributed to the anti-inflammatory and immunomodulatory effects of andrographolide. The study also highlights role in managing respiratory infections that contribute to cough (50).

***Ocimum tenuiflorum* (Dried Leaves)**

Phytochemical Constituents and Traditional Uses: *Ocimum tenuiflorum* (*Tulsi* or Holy Basil) is a sacred plant in Ayurvedic medicine, known for its broad spectrum of medicinal properties, including antitussive, antimicrobial, and anti-inflammatory effects. Its essential oils, such as eugenol, play a crucial role in its pharmacological activities (51).

Antitussive Activity: The antitussive activity of *Ocimum tenuiflorum* was demonstrated in a study by Khan et al. (2018), where the extract was evaluated using the citric acid-induced cough model in guinea pigs. The study showed a significant reduction in cough episodes, with eugenol being identified as a key compound responsible for the cough-suppressing effects. Additionally, the herb's expectorties helped clear mucus, further enhancing its antitussive potential (52).

Conclusion

The review on the pharmacodynamic evaluation of the polyherbal formulation comprising *Curcuma zedoaria* Rosc. (dried rhizomes), *Salvadora persica* (dried leaves), *Glycyrrhiza glabra* (dried roots), *Andrographis paniculata* (dried leaves), *and Ocimum tenuiflorum* (dried leaves) highlights the potential of this formulation in managing cough. The formulation's efficacy was tested using a citric acid-induced cough model in guinea pigs, demonstrating significant antitussive activity. Each herb contributes unique pharmacological properties: anti-inflammatory effects from *Curcuma zedoaria* and *Andrographis paniculata*, antimicrobial properties from *Salvadora persica,* expectorant and soothing effects from *Glycyrrhiza glabra,* and bronchodilatory actions from O*cimum tenuiflorum.* These properties collectively address various aspects of cough pathophysiology, including inflammation, mucus production, and airway irritation. This review underscores the importance of integrating traditional knowledge with modern pharmacological evaluation to develop effective and holistic therapeutic solutions.

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An Overview of Nirgundi (*Vitex negundo*): A Traditional Ayurvedic Herb for Pain Relief and Healing

Review Article

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Abstract

Vitex negundo is commonly referred to as Nirgundi, which is a small aromatic medicinal plant widely used by traditional as well as modern systems of medicine. In Ayurvedic medicine, Nirgundi is used because it has the ability to control the balance between *vata and kapha doshas*, as it possesses bitter, pungent, and astringent rasa (taste). Classical texts describe it as possessing *sheeta* (cooling) or *ushna* (warming) properties according to preparation, making it versatile in treating a wide range of diseases. *Nirgundi* has also been traditionally used for anxiety, pain, inflammation, and other disorders like respiration, or liver dysfunction etc. Its time-honoured uses have been validated by extensive pharmacological studies, confirming a broad range of bioactive effects. *Vitex negundo* shows strong analgesic, anti-inflammatory, anticancer, cardiotonic, antihistaminic, anti-asthmatic, anxiolytic, and hepatoprotective activities. Its bioactivities prove to be helpful for the treatment of arthritis, asthma, allergic conditions, cardiovascular disorders, and mental illness. The possibility of its hepatoprotective role underscores the protection of the liver from toxic and potential damage effects. Its anticancer potential is considerably of interest in research on oncology. Strong efficacy in both experimental and clinical studies by various applications, this herb finds legitimacy in the disciplines of integrative medicine. Its multifarious pharmacological profile and a very benign safety profile open opportunities for the creation of drugs and alternative health practices. This review focuses on the holistic health benefits of the *Vitex negundo*, highlighting its relevance in both traditional and modern healthcare systems. It has an elaborate pharmacological activity profile and is a highly important botanical resource for the betterment of health and well-being of humans, including animals.

Keywords: Anti-inflammatory, Analgesic, Ayurveda, Complementary and Alternative Medicine, Herbal Drugs, Traditional Herb.

Introduction

Nirgundi (*Vitex negundo*) is a large aromatic the five-leafed shrub tree. This plant is of the Verbenaceae family. Nearly each component of this plant has therapeutic significance, and it is used to treat a wide range of illnesses in traditional alternative medicine systems including Ayurveda, alternative, Siddha, and Unani.(1) The Vitex plant describes its medicinal importance in Sanskrit. **"Nirgudati Shareeram Rakshati Rogebhyah.**" Nirgundi is the term for the person who defends the body from illness.(2) This plant is a fiery scented plant. It is a deciduous shrub of Its plant is bushy 6-12 feet high, covered with microscopic hairs and aromatic.This species is also seen throughout the greater part of India and often gown for reclamation of forest land.(3) This study presents not only the importance of Nirgundi but also traditional and modern medical uses of Nirgundi based on pain relief.

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Geographical distribution of Nirgundi (*Vitex negundo*) –

Over the world, Nirgundi is grown in China and the West Indies, America, Europe, Afghanistan, Pakistan, India, Sri Lanka, Thailand, Malaysia, and Eastern Africa and Madagascar. It also grows well in wastelands and mixed open forests near water channels or in humid conditions. Plants that are fruit bearing and in flower from March to August.(5)

Properties of Nirgundi (*Vitex negundo*):

There are some following properties of Nirgundi on the basis of Ayurvedic texts-

निर्गुन्डी कटुतिक्तोष्णा कृमिकुष्टरुजापहा।
वात्श्लेष्मप्रशमनी प्लीहगुल्मारुचीरजयेत्॥ (ध. नि.)(6)
निर्गुण्डी तुवरा तिक्ता मेध्या शीतोषणा लघुः॥
चतुष्या दीपनी केश्या कफानिल विषापहा।
हन्त्यरोचक शूलाम गुल्म मेदोव्रणकृमीन्॥
शोफकुष्टप्रतिश्याय श्वासकासांश्च सा द्विधा॥

शेफालिका तयोः पथ्या विषपित्तविनाशिनी॥
श्लेष्मानिलघ्नं लघुदीपनीयं, निर्गुण्डिकाया कृमिघातिपत्रम्।
कषायं कटुकं तिक्तं दुष्टव्रणविशोधनम्।
बलासानिल वातास कुष्ठकण्डू विषप्रणुत्॥ (कै.नि ११४ / ३४२)(7)
सिन्दुकः स्मृतिदस्तिक्तः कषायः कटुको लघुः।
केश्यो नेत्रहितो हन्ति शूल शोथाम मारुतान्।
कृमिकोष्ठारुचि श्लेष्मज्वरान्नीलापि तद्विधा॥ (भा.प्र.)

Nirgundi enhances concentration. It aids in hair growth and is good for the eyes. Nirgundi reduces pain, inflammation and works in worm infections, skin disorders and loss of appetite. Along with this, it is useful in rheumatoid arthritis and fever caused due to Kapha imbalance.(8)

Figure 1: *Nirgundi* (4)

Taxonomical Classification of Nirgundi (*Vitex negundo*) – There is botanical classification of Nirgundi (Vitex negundo) (9) –

Kingdom	**Plantae**
Subkingdom	Tracheobionta
Division	Tracheobionta
Class	Magnoliopsida
Subclass	Asteridae
Order	Lamiales
Family	Verbenaceae
Genus	*Vitex*
Species	*Negundo*

Vernacular Names of Nirgundi:(10) -

Table 1: Vernacular names

Language	Name
Botanical Name	Vitex Negundo
Sanskrit	Sindhuvara, Nirgundi, Bhoothakeshi, Indrasurasa, Neelamanjari, Neelika.
Hindi	Nirgundi, Samhalu, Newri, shiwali, shivari, sinuar, sinduari, siwain, bannah, nirgud, veeru, tarvan, shimalu, kali-nirgundi, shinduca, sinduari, khanni etc.
English	Indian privet, Five-leaved chaste tree.
Bengali	Nishinda, Nirgundi.
Gujarati	Nagod
Kannada	Bile-nekki
Malayalam	Indrani
Tamil	Nirkunnchi, Nallanochi
Telugu	Nallavalli, Vavilli, Tellavavilli, chirvaavili, mella-vavili, vavalipadu.

Traditional properties of Nirgundi (*Vitex negundo*) –

Traditional property of Nirgundi (*Vitex negundo*) is used worldwide.(11) These are following–

Table 2: Traditional properties of Nirgundi

1	Rasa	Kashaya, Katu
2	Guna	Laghu
3	Veerya	Usna
4	Vipaka	Katu
5	Karma	Krimighna

Effects on Doshas of Nirgundi (Vitex Negundo) –

Dosha-karma - Due to being Ushna virya, it is Vata, Kapha shamak.(12)

Which part used: Root, leaves, flowers, fruits, bark. (13)

Classical Uses of Nirgundi (Vitex Negundo): These are following classical Uses of Vitex Negundo(14) –
Charaka Samhita: Visaghna –Anti-poisonous shrub. Krimighna – Anti-helminthic shrub (15)
Susrutha Samhita: Surasadi (16)

Morphological Characteristics of Nirgundi (Vitex negundo): A shrub or small tree about 3 metre or 6-12 feet in height. There are following morphological character.
Leaves: The leaves are broken or unbroken like arhar. On a tree, three to five leaflets, 2-6-inch-long leaves, give a distinctive smell and middle one will be longer.
Flowers: Flowers are lavender blue. There is a variety "incisa" in this species, which is with deeply toothed leaves.Small, bluish purple up to 30 cm long and in lateral cymes.
Fruits: Fruit - spherical, 12-inch diameter when ripe there are black colours. Globose and black when ripe.
Seeds: Obovate or oblong. (17)

Figure 2: Nirgundi (Vitex negundo) – Leaf-stem(18), flower(19), root(20) and seeds(21)

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Table 3: Pharmacodynamic Properties of Nirgundi (Vitex negundo) according to texts of Ayurveda

Name of text	Properties				
Nighantu	Rasa	Guna	Virya	Vipaka	Prabhava
Bhavaprakash Nighantu(22), (23), (24)	Katu, Kashaya	Laghu	Ushna	Katu	Vata, Kapha Nashak
Shankar Nighantu(25)	Katu, Kasaya	Charpy, bitter, dry, hot, astringent, reminiscent, beneficial to the eyes, beautifying the hair, lightening the fire, irritating, pigmentary and anti-inflammatory, cough, removes breathlessness and bile.	Ushna	Katu	Vata, Kapha Nashak
Dhanvantari nighantu(26)	Katu, Tikta	It destroys worms, leprosy, vata, phlegm, spleen disease, gum and anorexia.	Ushna	Katu	Vata, Kapha rog Nashak
Kaidev niaghantu(27)	Katu, Tikta, Kashya, Medhya	Laghu	Sheet-Ushna	Katu	Vata, kapha Nashak, Krimighna, vish-pitta Vinashini
Mahaushadh Nighantu(28)	Katu, Tikta, Kashya, Medhya	Laghu	Ushna	Katu	Kaphghna, Vataghna, Vishaghna, Krimighna, Vedanasthapaka.

Chemical constituents of Nirgundi (*Vitex negundo*) and their Clinical Uses(29) –

These are following chemical constituents are found in Nirgundi (Vitex negundo)**.**

Table 4: Chemical constituents of Nirgundi (*Vitex negundo*) and their Clinical Uses (29)

Serial Number	Parts of Nirgundi (Vitex-negundo)	Chemical Constituents	Clinical Uses
1	Leaves	α -pinene, camphene, caryophyllene, citrol, zalaloids nishidine and hydrocotylene, amorphous glucoside, iridoid glucoside, phenolic acids, flavonoids casticin and luteolin. Leaves(30)	1.Hot infusion of the leaves very much useful in arthritis, myalgia and colics. 2. Bathing with infusion relieves body pains. 3. Leaf powder increases the sperm count in a period of 12-16 wks. Dosage: Infusion 50-100 ml., Leaf powder: 0.5-1g.(31) The leaf guards the pulses from insects and is utilized as a grain preservation material. Leaves possess antibacterial, antifungal, and pesticidal qualities.(32)
2	Seeds	Seeds of Nirgundi have these chemical constituents- hydrocarbons, β-sitosterol and benzoic acid and phthalic acid, (33) Anti-inflammatory diterpene, flavonoids, artemetin and triterpenoids,(34)	Seeds oil of Nirgundi is used for the most popular analgesic anti-inflammatory and natural anti-biotic, Nirgundi oil helps in reducing congestion, inflammation, the most popular, natural anti-biotic, anti-inflammatory analgesic, helps in reducing pain and inflammation, congestion and effective remedy used to treat anal fistula because it improves blood circulation, tones the surrounding area by treating lymph node hypertrophy, and is the most well-liked natural antibiotic, analgesic, and anti-inflammatory that also treats osteoarthritis, rheumatoid arthritis, and orchitis. (35) B-sitosterol, Seeds contain hydrocarbons, and benzoic acid and phthalic acid,(36) anti-inflammatory flavonoids, diterpene, artemetin and triterpenoids.(37)

3	Stem and Bark	Stem bark yields leucoanthocyanidins. Fatty acids, β-sitosterol, vanillic acid, p-hydroxybenzoic acid and luteolin have been isolated from bark.(38)	Nirgundi root and bark preparations contain large levels of the alkaloid nishindine, which has analgesic and anti-inflammatory qualities.(39)
4	Flowers	N-heptane, formic acid, p-cymene, β-caryophyllene, valencene, α-selinene, β-selinene, germacren-4-ol, P-(1,1-dimethylethyle) toluene, caryophyllene epoxide, and valencene are among the volatile oils isolated from V. Negundo flowers. (E)- nerolidol.(40)	Its astringent flowers are used in fever, diarrhoea, cholera, bleeding and heart disorders and liver diseases. (41)
5	Roots	Roots are tonic, anodyne, bechic, febrifuge, expectorant and diuretic.(42)	Roots are used to treat leprosy, inflammations, respiratory issues, flatulence, and joint pain.(43)

Pharmacological activities of Nirgundi (*Vitex-negundo*)

From the notable traditional use of Nirgundi (*Vitex-negundo*), the biological activities of various research papers have been studied to show that it possesses various therapeutic powers due to its chemical composition such as anti-oxidant, Analgesic activity, antiviral antidiabetic, anticancer and immunomodulatory activities. In this paper of ours, literary survey of Nirgundi (*Vitex-negundo*), biological activity research has been spotlighted. The whole plant of Nirgundi (*Vitex-negundo*) can be used for medicinal purposes in the medical system. Some main uses are following

Anti-oxidant Activity of Nirgundi (*Vitex-negundo*) – Vitex Negundo plant

Naturally source of many antioxidants which play a role protect your cells against free radicals.(44) Vitedoin,(45) a phytochemical derived from the Nirgundi plant, is a more effective antioxidant than L-cystine and Vit E. This research discovered that in Freund's adjuvant-induced arthritic rats, the antioxidant capacity of Vitex negundo leaf extract decreased the levels of superoxide dismutase, catalase, and glutathione peroxidise.(46)

Hepatoprotective activity of Nirgundi (*Vitex-negundo*)

Current researches about Nirgundi shows the various utility of this drug. Ethanolic extract of Nirgundi leaf showed a hepatoprotective activity against hepatotoxicity. The Nirgundi (vitex negundo) had highest estrogenic activity assessed on cell-based.(47)

Analgesic and Anti-inflammatory activity of Nirgundi (*Vitex-negundo*)

The compounds 5-hydroxy-3, 6, 7-trimethoxy-2 -4H-chromen-4-on and 5, 7-dihydroxy-2,4H-chromen-4-one are found in an ethanolic extract of Vitex negundo leaves. Additionally, negundoside, agnuside, and vitegnoside are present in the methanolic extract. P-hydroxybenzoic acid and β-sitosterol have been extracted from the bark of Vitex negundo Linn and identified by methanol and hexane extracts. Two phenylnaphtha-lene-type lignans, 6-hydroxy-4,3-hydroxy-methyl-7-methoxy-3, 4-dihydro-2-naphthaldehyde and vitedoamine A, have been isolated from the acetoacetate fraction of the seeds. Vitex negundo L. leaves significantly reduced experimentally produced colitis; as a result, niggundi has analgesic and anti-inflammatory properties.(48)

Anti-cancer Activity of Nirgundi (*Vitex-negundo*)

In the present study, some cancer cell lines were subjected to strong anticancer effects from chloroform, ethanol, and aqueous extracts derived from Vitex negundo. The current work aims to extract negundoside from dried Vitex negundo leaves and demonstrate its anticancer efficacy using in vitro MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium) test and in silico activity.(49) To assess cell viability, the microculture tetrazolium (MTT) experiment was performed as previously reported.(50)

Clinical Studies –

Kulkarni, *et al*.: Antioxidant and anti-inflammatory activity of (*Vitex-negundo*)

The ethno medical use of *V. negundo* has excellent anti-inflammatory and antioxidant potential. The results of this study have shown a significant relationship between V. negundo's antioxidant and anti-inflammatory properties. Study of this article we find probability p value is $p< 0.05$. So, the prevention of oxidative damage to tissue could therefore be one of the mechanisms responsible for the analgesic and anti-inflammatory.(51)

Tandon et. al.

Studies on the histomorphological effects of Vitex negundo extracts in rats revealed that even at hazardous levels, stomach tissue is undamaged. Both lower and larger dosages were shown to have a toxic impact on the heart. The cardiac specimens displayed vascular dilatation and bleeding considerably ($P<0.05$) in the 2.5 and 5 g/kg weight doses and ($P<0.01$) in the 7.5 and 10 g/kg weight doses of Vitex negundo extract under a microscope. The specimens also seemed thickened and hyperaemic. The liver showed ecomorphological alterations at moderate and higher dosages.(52)

Smit et. al.

This study shows the tissues of the heart, liver, and lungs showed dose-dependent alterations. Using COLO-320 tumor cells, the cytotoxic impact of Vitex

negundo leaf extracts was investigated and confirmed. The dried material of 14 species was extracted with 70% v/v ethanol, and the extracts' cytotoxicity was assessed using the microculture tetrazolium (MTT) assay on COLO 320 tumor cells. A measure of cytotoxicity was the IC50-value, or the concentration at which 50% of the tumor cells' ability to grow was inhibited. The maximum concentration examined, 100 micrograms/ml, was the limit at which the extracts of numerous other plants failed to exhibit cytotoxic effects. (53)

Conclusion

Ayurvedic and traditional medicine both use Nirgundi as a main herbal remedy. To make herbal medicines, almost every component of the plant is used. Many different ailments have been successfully treated using natural compounds derived from medicinal plants. Chloroform, ethanol, aqueous extract of V. negundo, and other chemical components have the potential to have antifeedant, anticancer, antimicrobial, anti-hyperpigmentation, hepatoprotective, antihistaminic, and analgesic properties, according to the current research. We're now doing further research to define the active ingredients and clarify the extract's mode of action. So, in the majority of life-threatening illnesses, these plant extracts may have therapeutic and clinical potential. Therefore, Nirgundi believes that plants may provide bioactive molecules that might be used to create new "leads" that could be used to fight a variety of ailments.

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The Role of Botanical Names in the Sourcing and Distribution of Ayurveda Raw Drugs for Better Efficacy of Treatment

Review Article

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Abstract

Ayurveda, a traditional system of medicine, relies heavily on medicinal plants for therapeutic efficacy. However, linguistic and regional diversity can lead to confusion in sourcing the right plant materials, compromising treatment effectiveness. This article emphasizes the crucial role of botanical names in accurate identification, quality control, and distribution of Ayurveda raw drugs. A qualitative review of classical texts, herbal pharmacopeias, and expert interviews reveals the challenges associated with traditional names, including ambiguity, regional variations, and adulteration. Standardized botanical nomenclature mitigates these risks, ensuring consistent identification across regions and supply chains. Case studies illustrate the consequences of misidentification, highlighting the importance of accurate botanical identification. Regulatory guidelines from WHO and Ayurvedic Pharmacopoeia of India reinforce the necessity of botanical names for quality control. This study underscores the imperative of adopting botanical names in Ayurveda practice, education, and trade. By prioritizing accurate identification and standardized nomenclature, the Ayurveda industry can enhance treatment efficacy, safety, and quality. Integration of traditional knowledge with modern scientific methods and collaboration among stakeholders are essential for promoting confidence in this ancient system of medicine. This research contributes to the ongoing efforts to standardize and legitimize Ayurveda, ensuring its continued relevance in modern healthcare.

Keywords: Raw drugs, Botanical names, Adulteration, Quality control, Efficacy, Supply chain.

Introduction

Ayurveda, one of the world's oldest systems of medicine, relies heavily on medicinal plants for treatment. Over centuries, knowledge of these medicinal plants has been passed down through oral traditions, classical texts, and vernacular references (1). The identification and use of correct plant species are crucial for the effectiveness and safety of Ayurveda therapies. However, in the modern context, linguistic and regional diversity can lead to confusion in sourcing the right plant materials, leading to substitutions or adulterations that may compromise the efficacy of treatments. However, traditional names for herbs can vary significantly across regions and languages, leading to potential errors, confusion, and even adulteration of raw drugs (2). In this context, botanical names provide a standardized method of identifying medicinal plants, ensuring that the right plant is used in Ayurveda formulations. This article focuses on the importance of botanical names for sourcing, quality control, and distribution of Ayurveda raw materials and discusses the challenges associated with relying solely on traditional names.

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Methodology

This study examines the role of botanical names in the sourcing and distribution of Ayurveda raw drugs, focusing on their contribution to treatment efficacy. The research is primarily based on a qualitative approach, involving the review of classical Ayurveda texts (such as Charaka Samhita, Various Nighantu etc.) and modern herbal pharmacopeias (Ayurvedic pharmacopeia of India). A comparative analysis was performed between vernacular and botanical nomenclature, to assess the accuracy and consistency of raw drug identification. Data was also collected from Ayurveda practitioners, suppliers, and pharmacists through semi-structured interviews to understand the challenges they face in sourcing raw drugs based on local names versus botanical names.

Result

Importance of Botanical Names in Ayurveda

Importance of botanical name can be explained by following points -

Accurate Identification

Botanical names follow a globally accepted system of nomenclature known as binomial nomenclature, developed by Carl Linnaeus. This system

assigns each plant a unique scientific name that helps in the precise identification of plant species. This is particularly important in Ayurveda, where different species can have varying therapeutic properties (3). For instance, the herb "Shankhapushpi" in Ayurveda refers to Convolvulus pluricaulis other species like Evolvulus alsinoides may be confused for the same herb when relying on vernacular names (4). Botanical names eliminate this confusion, ensuring that the correct species with the intended medicinal properties is sourced and used.

Standardization Across Regions

Ayurveda herbs often have multiple names in different regions or languages, which can create discrepancies during sourcing and distribution (5). For instance, the herb "Ashwagandha" is widely used in Ayurveda and is known scientifically as Withania somnifera. In different parts of India, it might also be called "Asgandha" or "Indian Ginseng," but the botanical name remains the same, offering clarity across regions (6). Botanical nomenclature enables uniformity in the trade and distribution of Ayurveda herbs. It helps manufacturers, suppliers, and regulatory authorities ensure that the same plant species is being sourced and distributed, regardless of the local vernacular names used.

Enhancing the Safety and Efficacy of Treatments

In Ayurvedic treatments, the therapeutic effectiveness of an herb is closely tied to the specific species used and the plant part utilized (e.g., root, leaf, bark). The correct botanical identification of plants is vital to ensure that the active compounds responsible for the therapeutic effects are present (7). For example, the herb "Vacha" is used for cognitive enhancement in Ayurveda and traditionally refers to Acorus calamus. However, it is essential to distinguish between Acorus calamus and other species like Acorus gramineus, which do not have the same pharmacological activity (8). Using botanical names minimizes the risk of such misidentifications and ensures better clinical outcomes.

Reducing Adulteration in the Supply Chain

One of the major issues faced by the Ayurvedic industry is the adulteration and substitution of herbs. This can happen either intentionally or due to misidentification when relying on traditional names. Botanical names help prevent such adulteration by providing a scientific and verifiable identity for each plant (9). For instance, Embelia ribes (Vidanga) is a highly valued medicinal plant in Ayurveda, but other species in the same genus, such as Embelia tsjeriam-cottam, are often used as substitutes (10).

Botanical names help avoid these confusions, thereby reducing the risk of adulteration and ensuring that the correct raw material is used.

Challenges of Using Traditional Names in Ayurvedic Herbs

There are multiple challenges being faced of using traditional name of herbs, ambiguity of synonyms by various Nighantus create complexity, can be understand by following points -

Ambiguity and Misidentification

Traditional names for herbs often vary widely between different regions, even within the same country. This creates ambiguity, as the same name may refer to different species of plants in different areas (11). For example, the herb "Rasna" refers to Pluchea Lanceolata, but in some parts of India, it is used to describe plants from different species like Alpinia galanga (South India) and Vanda roxburghii (Bengal region) (12). This ambiguity increases the risk of sourcing incorrect herbs, which may not only reduce the efficacy of the treatment but also lead to adverse effects. Botanical names provide clarity and help in the accurate identification of herbs.

Regional Variations in Vernacular Names

India is a diverse country with numerous languages and dialects, each of which may have a different name for the same medicinal plant (13). For example, "Bala" (Country Mallow) is a common herb in Ayurveda and is known as Sida cordifolia. However, in different parts of India, it is also called "Bariyara" or "Kharainti" (14). When Ayurveda raw drugs are sourced from multiple regions, this variation in vernacular names can lead to confusion and result in the wrong species being supplied. Botanical names eliminate this confusion by providing a universally accepted identity for the herb.

Adulteration Due to Confusion with Traditional Names

The reliance on traditional names, without proper botanical identification, can lead to both intentional and unintentional adulteration. Suppliers may substitute cheaper, readily available herbs for those that are more expensive or difficult to source, often due to confusion arising from similar traditional names. This practice compromises the quality and efficacy of Ayurvedic medicines (15). For example, "Aralu" is an important Ayurvedic herb used for Anti inflammatory and anti-arthritic activity. Traditionally, it refers to Oraxylum indicum, but due to similarities in vernacular names, it is often adulterated with other species like Ailanthus excelsa, which do not have the same pharmacological effects (16).

Lack of Standardization in Trade and Regulation

Traditional names, while culturally significant, do not meet the requirements of international trade and regulatory standards. Different countries and regulatory bodies have their own standards for the quality and safety of medicinal plants, which may conflict with traditional classifications (17). Botanical names, on the other hand, are recognized by pharmacopoeias and regulatory bodies worldwide, making them essential for ensuring that Ayurvedic raw materials meet global standards of quality and safety. They are also crucial for navigating the increasingly globalized trade in medicinal plants.

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Case Studies of Misidentification and Adulteration

Substitution of "Giloy" - Tinospora cordifolia (Giloy) is a highly valued herb in Ayurveda for its immunomodulatory and anti-inflammatory properties. However, it is often adulterated with species like Tinospora crispa and Tinospora sinensis, which do not have the same therapeutic effects (18). This adulteration occurs because local suppliers may not distinguish between these species due to similar traditional names.

Confusion Over "Sarpagandha"

Rauvolfia serpentina (Sarpagandha) is used in Ayurveda to treat hypertension and mental disorders. Due to its high demand, it is often substituted with other species like Rauvolfia tetraphylla, which do not have the same therapeutic properties (19). Botanical names help in preventing such substitutions and ensuring the correct species is used.

The Role of Regulatory Bodies and Guidelines

Role of key regulatory authority and their guidelines related botanical name explained briefly.

WHO Guidelines on Good Agricultural and Collection Practices (GACP)

The WHO's GACP guidelines emphasize the need for proper identification of medicinal plants using botanical names to ensure the quality, safety, and efficacy of herbal medicines (20). These guidelines recommend that medicinal plants be scientifically identified before they are processed or traded.

Ayurvedic Pharmacopoeia of India (API)

The API, published by the Ministry of AYUSH, is the official document for the standardization of Ayurvedic herbs in India. It includes detailed descriptions of medicinal plants, their botanical names, and the plant parts used in Ayurvedic formulations (21). The API helps prevent adulteration and misidentification of herbs in the industry.

Discussion

The use of botanical names plays a pivotal role in the accurate sourcing and distribution of Ayurveda raw drugs, directly influencing treatment efficacy. Ayurveda formulations depend on the precise identification of medicinal plants, as even minor variations in plant species can significantly alter the pharmacological profile and therapeutic outcomes. Standardized botanical nomenclature helps mitigate these risks by ensuring consistent identification across regions and supply chains, reducing the chance of adulteration or substitution, which are common when relying on local or vernacular names (22). For instance, research indicates that the substitution of plants with similar vernacular names but different species often results in reduced potency and therapeutic failure (23).

Conclusion

In conclusion, botanical names play an essential role in the sourcing and distribution of Ayurveda raw drugs. They provide a standardized system for the accurate identification of medicinal plants, ensuring that the right species are used in formulations. This is crucial for maintaining the efficacy, safety, and quality of Ayurveda treatments. The challenges of using traditional names, such as ambiguity, regional variations, and the risk of adulteration, further underscore the need for adopting botanical nomenclature in the Ayurveda industry. To safeguard the integrity of Ayurveda medicines, regulatory bodies, suppliers, and practitioners must prioritize the use of botanical names in sourcing and distribution practice.

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The Heart-Mind Connection: Exploring Ashru Vega Vidharna and Its Impact on Emotional Well-Being

Review Article

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Abstract

This study explores the concept of *Ashru Vega Vidharna*, which refers to the suppression of tears and emotions, and its effects on emotional well-being. By examining the heart-mind connection, we investigate how emotional repression can impact mental health and overall emotional resilience.. Findings suggest that allowing emotional expression through tears can enhance emotional regulation, reduce stress, and improve psychological health. This research underscores the importance of emotional expression for well-being and offers insights for therapeutic practices. In Ayurveda, there are natural urges, known as *Adharniya vega*, that can cause health problems if not expressed. One such urge is the tear reflex, or ashru vega. Prolonged suppression of tears may contribute to heart issues. However, traditional Ayurvedic texts provide limited insight into tear formation but the concept of *vegaavrodh*, or the suppression of these natural urges explained in detail. When health issues arise from Ashru *Vegaavrodh*, certain activities can be beneficial. These include sleeping, intake alcohol in medical dose (such as *Asava, Arista, Sidhu,* or brandy), sharing uplifting stories, and engaging in calming conversations with close friends and family members.

Keywords: *Adharniya Vega, Vyana Vayu,* Stress, Heart Disease, *Ashru, Vegaavrodha*.

Introduction

The idea of separating body and mind, often referred to as "the head and the heart," has a long history. However, science increasingly shows that physical and mental health are closely linked. Recent research highlights a reciprocal relationship:

1. Mental health issues can increase the risk of heart disease.
2. Conversely, heart disease can elevate the risk of mental health problems.

This emphasizes the importance of addressing both physical and mental well-being together.

In Ayurveda, The term “Vega” means natural urge, and “Dharana” means suppression, so collectively, the word Vega Dharana means forceful suppression of natural urge. Vegas are naturally created in the body in order to maintain bodily equilibrium. Initiation of urges is a normal body activity through which unwanted and waste body products are expelled from the body (1). In order to facilitate the elimination of these substances, the body is equipped with Adharniya Vegas, which appears naturally.

Humans naturally express their feelings through bodily reflexes. In Ayurveda, these reflexes are called Vegas. There are two types of Vegas (2):

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1. Dharniya Vegas: Urges that can be controlled.
2. Aadharniya Vegas: Urges that should not be suppresse

Ashru vega dharana refers to the practice of consciously controlling tears. While this might seem harmless, over time, it can lead to various health issues such as colds, eye problems, heart conditions, loss of appetite, and dizziness (3).

Fortunately, individuals affected by this practice can find relief through simple methods. Engaging in storytelling, particularly tales that involve rest and spending quality time with loved ones, can be beneficial. These activities promote emotional well-being and help restore balance

Vega dharana, or the suppression of urges, can put a significant amount of stress on the brain. This stress can lead to worsening mental health conditions. Over time, it can also impact the heart, resulting in noticeable changes in cardiovascular function.

Method

This study drew from traditional Ayurvedic texts, including Brihat Trayi and Laghu Trayi, as well as modern scientific literature. Additional sources included peer-reviewed research journals and published studies.

Results

Ashru vega" refers to the reflex that causes tears in response to strong emotions like sadness, happiness, or even yawning. Tears are produced by the lacrimal glands and are controlled by nerves in the brain.

Origin of Ashru

In Ayurveda, the concept of Ashru is linked to several physiological components and processes, though specific structures for their release are not explicitly defined in ancient texts. Here are the key points that clarify the origin and function of Ashru:

Role of Dosha

KaphaDosha: Ashru originates from the *Kaphadosha*, which contributes to its lubricating and immune-boosting properties, providing "Bala" (strength).

***Vyana Vayu*:** According to *Acharya Bhavamishra*, *Vyana Vayu* helps transport the "*Akshivita*" (waste from the *Majja* or bone marrow) to the eyes via blood vessels (4). This suggests a role in the distribution of tear components.

Blinking Mechanism: The act of blinking, which is also controlled by *Vyana Vayu*, helps spread *Ashru* over the surface of the eye, ensuring even distribution (5).

Role of Dhatus

Rasa Dhatu: The watery nature of Ashru suggests it may derive from Rasa dhatu (plasma) (6), which nourishes and lubricates the eye. Conditions like *Vataja Jwara*, (fever) (7) and *Vataja Pandu* (anemia) (8) that cause dryness can indicate a deficiency in Rasa dhatu.

MedaDhatu: *Medadhatu* (fat) may contribute to the nourishment of the eyeball (9), as indicated by changes in eye appearance when Meda is depleted.

MajjaDhatu: The presence of "*Tarun-asthis*" (young bones) in the eyelids may serve as a source for *Majjamala*, further indicating a connection between the *Majjadhatu* and tear production (10).

These *dhatus—Rasa, Meda, and Majja*—play critical roles in the formation and function of *Ashru*, which is layered in composition:

Lipid Layer: Corresponds to the lipoidal secretions of *Medadhatu*.

Aqueous Layer: Represents the water secretions of *Rasadhatu*.

Mucous Layer: Composed of secretions from the *Majjadhatu*, known as *Akshivita*.

Role of *Panchmahabhoota*

Tears also play a crucial role in maintaining the health of the cornea and conjunctiva, forming a high-quality refractive surface. Ashru is believed to be influenced by *JalaMahabhuta* (water element) (11), aligning with its watery composition.

Anatomical Structures Related to Ashru

AshruVahini *Dhamanis*: These channels carry Ashru, although their exact function in secretion versus excretion remains unclear (12).

***Ashrumargas*:** Associated with the drainage of tears, these passages are linked to the space element (Akasha *mahabhoota*) (13) and are anatomically positioned in the eye's structures.

According to Acharya Charak, holding back tears over a long time can lead to various health issues, including heart disease (*Hridyarog*), eye problems (*Akshirog*), and digestive issues (*Aruchi*),Dizziness (*Bhram*) and Cold (*Pratishyaya*) (14).

Treatment Approaches

The Ayurvedic treatment for *Ashru Vegavrodh* includes (15):

Swapan: Sleep-inducing agents that help improve rest and recovery.

Madya: Mind-calming agents to alleviate stress and anxiety.

Priya Katha: Behavioural therapies aimed at promoting emotional expression and coping.

Emotions and Body Reflexes

Emotional suppression, particularly of sadness and grief, can lead to (16):

1. **Cardiovascular Stress:** Chronic suppression of emotions increases stress hormones, blood pressure, and heart rate, contributing to cardiovascular disease.
2. **Mental Health Implications:** Bottling up emotions can lead to anxiety, depression, and emotional numbness.
3. **Physiological Response:** Suppressed emotions trigger the release of cortisol and adrenaline, affecting the body's "fight or flight" response and potentially harming the heart.

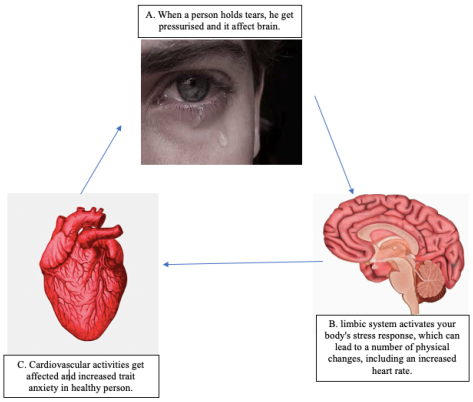
Key Findings

- Emotional suppression increases the risk of cardiovascular disease by 30-40%[17].
- Chronic tear suppression is linked to decreased parasympathetic activity, affecting heart rate variability.
- Ayurveda interventions, such as emotional expression and mindfulness, can mitigate these effects.

Discussion

The given schematic representation shows the side-effects of holding back tears on various organ.

Fig. 1 (A, B & C): Pictures showing how tear holding affect brain and heart



Vyaana Vayu plays a crucial role in regulating dynamic bodily functions. Originating from the heart (Hridye) (18), it facilitates expansion and contraction, which are essential for the movement of metabolites, controlled by Vata. When tears (ashru) are suppressed, it

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can disrupt Vyaana Vayu's functions, leading to serious heart conditions like stress-induced cardiovascular diseases (CVDs).

This can be understood in two ways:

1. Tears and Nutrition:

Tears have properties similar to Kapha, helping to lubricate the eyes. They are likely derived from the Rasa dhatu (nutritional fluid) and serve a similar role in the eyes as Rasa does in the body, providing nourishment and restoring tissue. The Rasa samvahan (circulation) process transports these nutrients through the body, starting from the heart and the brain (Dhimaya) (19). Habitually suppressing tears can disrupt this process, negatively affecting heart health and leading to heart diseases.

2. The Heart's Connection:

The heart (Hridye) is linked to various elements, including Vyana Vata, Sadak Pitta, and Kapha (20,21). Disruption in any of these can harm heart health. The mind (Mana) plays a role in regulating the senses, particularly vision. Tears keep the eyes moist and protect against infections. Continually resisting the urge to cry due to stress and emotions can strain the eyes and contribute to stress-related heart diseases.

Tears are also important for emotional release, as they trigger the release of hormones like oxytocin, which can alleviate both emotional and physical pain. The act of crying is facilitated by Udaana Vayu, with support from Vyaana Vayu (21). Suppressing tears due to anxiety and sorrow can disrupt nutrient balance and Vyaana Vayu in the heart, leading to heart diseases over time.

Conclusion

The factors discussed highlight the serious impact of mental health stress on overall well-being. Suppressing natural urges, such as the need to cry, can lead to significant health issues, including stress-related heart diseases. It's crucial to avoid vega dharana, or the suppression of bodily urges, as it disrupts essential functions in the body and contributes to mental and emotional strain. Promoting healthy emotional expression and managing stress are vital for maintaining good mental health. Encouraging individuals to acknowledge and release their emotions can lead to a more balanced and peaceful life (22). By fostering an environment where emotional well-being is prioritized, we can improve overall health and enhance the quality of life for everyone.

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Role of Ayurveda and Yoga in Treating Mental disorders - A Review

Review Article

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Abstract

A person's mental health is a personal and unique issue. We need to maintain good mental health because we are human. On the other hand, we form habits and behaviour's that can contribute to poor mental health. These behaviour's might be anything from minor annoyance to serious anxiety and sadness. The phrase "mental illness" is broad and encompasses nearly all mood-behaviour problems brought on by flawed perception, emotion, thought, and attitude. These people also struggle to fit in with other members of society. Mental illnesses impact individuals in every community worldwide and contribute significantly to the global burden of disease. Mental illnesses can begin early in life. If we take a look in Ayurveda so in Ayurveda also mental health has a great importance for all over healthy personality. Ayurveda consider prassana atma,indriya and mana beside the equilibrium of dosha, dhatu and mala as swastha.ayurvedadeals with four aspects of lifestyle which can ensure good health in us. These include right food (Ahara), right recreation (vihara), right routine (achara), and right thinking (Vichara) life. Observing certain practice ensure a healthy and happy life. There are lots of discussion regarding Aachar Rasayana, sadvrutta, pranayama, Aasans etc. in Ayurveda. All these are helpful to maintain proper mental health as well as to tackle mental illness. Role of these in altered mood behavior will be discussed in detailed in full paper.

Keywords: *Ayurveda,* Mental health*, Pranayama, Aasna*.

Introduction

A person's physical, mental, social, and spiritual well-being are all considered aspects of their health. As a result, one element of the larger idea of health is mental health. It focuses on the individual's ideal degree of emotional and behavioral adjustment. The devil of mental illnesses is getting worse, according to a number of statistics gathered. The World Health Organization (WHO) published it.An estimated 350 million people suffer from depression today (1). The globe. According to a global mental health survey, 1 in 20 adults on average reported experiencing an episode of depression. Globally, there is a growing need to address mental health issues including depression (2).

Mental disorder or Mental illness

A mental disorder or mental illness is a pattern of behavior or psychology that is not typical of a person's growth or culture and is typically linked to subjective distress or incapacity. Mental well-being characterizes the absence of a mental illness or a state of cognitive or emotional well-being. Subjective well-being, perceived self-efficacy, autonomy, competence, intergenerational reliance, and the awareness of one's capacity to reach one's full emotional and intellectual potential are all considered aspects of mental health. A person's mental health is a personal and unique issue. We need to maintain good mental health because we are human.On the other hand, we form habits and behaviors that can contribute to poor mental health. Such actions range from little annoyance to intense.

Three basic forms of mood disorders: 1. Major depressive disorder 2. Dysthymic disorder (a chronic, mild depression) 3. Bipolar disorder (also called manic Depression) Depression: Depression is one of the most global public health issue and common disease on human race. Its burden on society is really impressive. It is chronic illness that affects mood thoughts, physical health and behavior of any individual and has been estimated to affect up to 21% of the world's population. Depression is defined as a change in mood characterized by feeling of "tone of sadness" which may vary from mild despondency to the most abject despair .This change in mood is relatively fixed and can persist over a period of days, weeks, months or years. The symptoms of depression can be complex and vary widely between people. But as a general rule, if we are depressed, we feel sad, hopeless and lose interest in things we used to enjoy. The symptoms persist for weeks or months and are bad enough to interfere with our work, social life and family life.

1. Psychological symptoms include: Continuous low mood or sadness
2. Feeling hopeless and helpless

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3. Having low self-esteem
4. Feeling tearful
5. Feeling guilt-ridden
6. Feeling irritable and intolerant of others
7. Having no motivation or interest in things
8. Finding it difficult to make decisions
9. Not getting any enjoyment out of life
10. Feeling anxious or worried: Having suicidal thoughts or thoughts of harming yourself.

Psychotic disorders are severe mental disorders that cause abnormal thinking and perceptions. Delusions and hallucinations are the two main symptoms of psychosis. People with psychosis may also lose touch with reality . The collective incidence of all psychotic disorders in 2002–2017 was 26.6 per 100 000 people . According to a systematic review published in 2018, lifetime prevalence of psychosis was 7.49 per 1000. Schizophrenia is the most prevalent functional psychotic disorder among various psychotic spectrum disorders and ranks among the top 10 global burdens of disease identified by the WHO . In addition to the direct burden, there is substantial burden on the families who care for the sufferers. The management of schizophrenia is currently aimed at early diagnosis & treatment initiation, prevent relapses, provide rehabilitation services, and reintegrate the ill persons into the community so that they can lead as normal a life as possible .Ayurveda is a traditional system of medicine originating from India. It focuses on balancing the lifestyle and biorhythms through the application of herbal formulations and detoxification procedures. It has enormous potential to treat many disorders of the body and mind. Ayurveda understands schizophrenia spectrum and other psychotic disorders as *Unmada*. *Unmada* is described in the Ayurveda texts as a disorder that manifests when the physical and psychological stressors vitiate the humors- *Vata, Pitta*, and *Kapha*, displace them from their original site and expulse upward to the *manas* (mind) resulting in a wide range of physical and psychological symptoms .

According to ancient Ayurveda text *Charaka Samhita*, *unmada* can be classified into five subtypes:

1) *Vataja unmada* (*unmada* due to vitiation of vata humor),
2) *Pittaja unmada* (*unmada* due to vitiation of pitta humor),
3) *Kaphaja unmada* (*unmada* due to vitiation of kapha humor),
4) *Sannipataja unmada* (*unmada* due to vitiation of all three humors),
5) *Agantuja unmada* (*unmada* due to exogenous causes like non-observance of spiritual disciplines or supernatural things).

Although symptomatic manifestations vary according to the *dosha* (humor) involved, the following aspects of an individual personality are commonly affected in all three types of *Unmada*: *Mana*-thoughts/ mental faculties, *Buddhi*-intellect, *Samjna*-awareness, *Jnana*- orientation, *Smriti*-memory, *Bhakti*-desire, liking or attitude towards the society, *Sheela*-habits and temperament, *Cheshta*-psychomotor activities and *Achara*-routine activities of daily living . These changes may manifest acutely or take a chronic progressive course, resulting in the affected person losing touch with reality and his ability to sustain himself in society (3), (4), (5).

Discussion

Ayurveda also explains a systematic treatment protocol for *Unmada* which is based on three principles:

1) *Daivavyapashraya* (spiritual/divine therapy)
2) *Yukti vyapashraya* (therapy based on clinical reasoning)
3) *Satwavajaya* (psychotherapy).

The major focus in acute symptomatic phase is on the *Yuktivyapasraya chikitsa*, which involves treatment in the following phases:

1) *Deepana* and *Pachana* (correction of digestive fire)
2) *Snehapana* (Oral administration of medicated clarified butter or ghee)
3) *Mridu sodhana* (mild purification by induced emesis or purgation)
4) *Samsarjana krama* (Dietetic regimen). The aim of this treatment is to balance vitiated humors and facilitate the normal psychological functions.

Further treatment is planned to modulate the residual morbid humors and for maintenance purpose, which involves

1) "*Basti*" (medicated enema),
2) "*Shirovirechana*" (medicated nasal errhines) and
3) "*Samjna prabodhana*" (medications to improve awareness and orientation).

Along with these, several poly herbal formulations having disease modifying effects are also administered for a prolonged duration.

Ayurveda has numerous therapeutic formulations and treatment protocols described for psychotic disorders/schizophrenia. Although these therapies and methods have been in practice for several years, systematic evidence has not been generated for the same. Thus, in the current review an attempt has been made with an objective of summarizing currently available clinical trials exploring Ayurveda treatment protocols in psychotic disorders and evaluating them with conventional treatment procedures.

Yoga Vs Brain

Yoga is a movement-based embodied contemplative activity that can lead to a variety of neurobiological alterations in different brain regions. Yoga exerts a regulatory effect on brain synaptic plasticity and promotes cognitive tasks, particularly working memory. Furthermore, yoga increases inter-hemispheric coherence and symmetry and improves neurocognitive functions. Yoga may also exert pronounced anatomical changes in different brain regions, especially in the limbic system.

Effect of yoga on brain neurotransmitters γ-aminobutyric acid (GABA) is considered the main inhibitory neurotransmitter responsible for the regulation of cortical excitability and neural plasticity. Multiple lines of evidence suggest that yoga promotes cortical GABAergic inhibitory tone and modulates

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downstream brain regions. A 12 wk yoga practice markedly enhanced the thalamic GABA values, accompanied by improved mood and reduced anxiety. Higher thalamic GABA levels could be the result of enhanced (regional) cerebral blood flow in the prefrontal cortex of yoga practitioners, which can lead to the activation of the reticular nucleus of the thalamus and higher GABA production. A magnetic resonance spectroscopy study has shown that yoga practitioners exhibited greater brain GABA values after a 60 min session of yoga training compared to controls. In addition to GABA, an enhancement of dopamine has been observed in the ventral striatum of subjects who practice yoga. It has been suggested that yoga could cause a rise in serotonin. Several investigations performed on participants after their meditation sessions have shown an elevation of the serotonin metabolite levels in urine. Moreover, a regular yoga practice may cause a reduction in norepinephrine values. Patients with heart failure who practiced weekly yoga displayed lower levels of norepinephrine in blood samples (6) (7).

Benefits of Savasana

The physiological benefits of deep relaxation Are numerous likes-

- Savasana has a regenerative effect on the mind and the body.
- Savasana provides relief from any kind of stress and strain in few minutes.
- Savasana helps to strike a balance between work and rest.
- Savasana tackles restlessness, insecurity, frustration, anxiety, and fear.
- The ageing process is controlled.

Conclusion

Examining the literature reveals that Acharya Sushruta's concept of health, "Prassana Atma, Indira and Mana beside the equilibrium of Dosha, Dhatu and Mala as Swastha10," encompasses all facets of a healthy person and amply demonstrates the significance of mental health. The fast-paced, unpredictable lifestyle of today has brought wealth, but it has also had a significant negative impact on people's physical and mental well-being. In particular, when young, the person becomes mentally weary and looks for rescue. Numerous mental illnesses had emerged, burdening people's lives on a social and financial level. A detailed or brief description of a regimen for almost anything can be found in Ayurvedic texts. One of the fundamental ideas of Ayurveda is the mental element.

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Impact of Yoga Therapy for the Management of Type-2 Diabetes: A Systematic Review

Review Article

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Abstract

Background: The most prevalent type of diabetes, type 2 diabetes mellitus (T2DM), accounts for more than 90% of cases of diabetes globally. As of right now, 425 million adults worldwide are believed to have type-2 diabetes; by 2045, that number is expected to increase to 629 million. The main cause of T2DM is the deterioration of the regular functioning of pancreatic (β-cells) and insulin resistance. Yogic therapy is a proven method of stabilizing an individual from a metabolic disorder, and lifestyle disorder. Through asanas and pranayama, we can control the blood sugar level. Objective: To assess Yoga Therapy's effectiveness for managing Madhumeha (Diabetes mellitus-II) in the review article. Design: The PubMed, Google Scholar, Embase, and Cochrane databases were searched from January 2022 to February 2023 for eligible RCTs using the keywords 'Yoga Therapy' and 'Type-II Diabetes Mellitus'. Intervention: Treatment with any regimen of Yoga Therapy or Yogic Intervention (Asana, Pranayama). Outcome Measures: The number and results of the studies were identified and presented as a systematic review. Result: This systematic review resulted in understanding the different mechanisms by which Yoga Therapy works in type-2 Diabetes Mellitus. Which include Asanas and Pranayama, were effective in regulating fasting blood sugar ($p < 0.05$), Postprandial Fasting blood Sugar level ($p < 0.0001$), HbA1c ($p < 0.001$), Triglyceride (($p<0.05$), Low-Density Lipoprotein ($p>0.05$) and High-Density Lipoprotein ($p<0.05$), BMI Body Mass Index ($p < 0.001$), BP Blood Pressure ($P= 0.072$), Serum (p-value <0.0001) relative to the control group.

Keywords: Diabetes Mellitus, *Yoga, Asana, Pranayama*.

Introduction

Worldwide, diabetes mellitus has grown to be a serious health concern. One of the diseases with the fastest rate of worldwide disease growth is diabetes, according to recent data from the International Diabetes Federation (IDF) (1). The WHO estimates that 463 million people worldwide had Type-2 diabetes in 2019, and that number is expected to rise to 578 million by 2030 and 700 million by 2045. It is a complex metabolic disorder characterized by hyperglycemia and glucose intolerance resulting from defects in insulin secretion; the action of the produced insulin is ineffective, or both (2). Yoga was developed as a traditional mind-body practice about 5000 years ago in India. In the modern scenario, Yoga is becoming more popular daily due to its possible benefits in preventing the onset of various diseases and their related complications. The effectiveness of Yoga therapy has been studied in several chronic diseases, such as hypertension, asthma, chronic obstructive pulmonary disease, and diabetes (3). Previous studies have reported that Yoga Therapy might reduce Insulin Resistance Syndrome, an exclusive collection of risk factors for the development of T2DM, and has shown promising results in improving signs, improving prognosis, and reducing complications (4). The science of Yoga has proven its usefulness in treating certain diseases and preserving health in normal individuals. Studies have shown the useful role of Yoga Therapy in the management of type-2 diabetes mellitus by reducing fasting and postprandial blood sugar levels significantly. The benefits of Yoga Therapy include long-term control of blood sugar levels, reduced requirement of medicines, and reduction in acute complications (5). Yoga Therapy is a lifestyle intervention practice that has been identified and proven to benefit T2DM through several studies. Yoga is one of the cost-effective and non-pharmacological ways of adopting a healthy lifestyle. Multiple studies recommended the role of Yoga in the amelioration of type-2 diabetes mellitus in an effective way. Yoga Therapy is believed to exert long-term glycemic control. However, reduction in weight optimal glucose levels, and wellness can be achieved by regular Yogic practices. Yoga comprises various physical and respiratory exercises therefore it can be a suitable integral therapy for diabetic patients

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mediated by improvement of muscular-skeletal and cardiopulmonary function and also by improving mental health. However, the condition can be regulated with increased community awareness and care at the type-2 diabetes mellitus level. Yogic practices can be effectively used as a preventive care treatment in diabetic mellitus individuals.

Methods of the Systematic Review

Each trial's titles and abstracts were first reviewed to identify suitable studies for inclusion. The reviewing process considered the presence of adult patients with Madhumeha (Diabetes Mellitus-II). Papers that might be qualified were retrieved for a closer examination. Furthermore, we manually searched our records, the reference portions of current reviews on yoga and diabetes, and the citation sections of all identified articles.

Objective

To assess Yoga Therapy's effectiveness for managing Madhumeha (Diabetes mellitus-II) in the systematic review article.

Inclusion Criteria

- Age group >25 years and <74years
- Participants in the study must have type-2 diabetes mellitus.
- The study compared a control group to an experimental group that practices Yoga, pranayama, and meditation to improve the treatment of type-2 diabetes mellitus.
- Study exploring the circumstances in the intervention and control groups for glycemic control and other type-2 diabetes Mellitus management metrics such as HbA1c, FPS, PPBS, body mass index, Lipid Profile, BP, systolic and diastolic blood pressure.

Exclusion Criteria

- Participants of a specific age group aged <25 and > 74 years.
- Participants in the research had comorbid conditions such as diabetic retinopathy and nephropathy.
- Excluded are studies from conference proceedings, book reviews, commentary books, and book chapters.
- Study exploring the circumstances in the intervention and control groups for glycemic control type-2 diabetes management metrics such as HbA1c, fasting blood sugar, PP, systolic and diastolic blood pressure.

Type of interventions

Interventions were included in the study, which mentioned yoga interventions in the respective publications.

Other Search Strategies

The list of references for each of the relevant studies was searched. Experts and authors in diabetes care or Yoga were contacted for any studies that were not included at this point. The PubMed, Google Scholar, Embase, and Cochrane databases were searched from January 2022 to February 2023 for eligible RCTs using the keywords 'Yogic Practice' and 'Type-II Diabetes Mellitus'. Eligible trials were limited to adult human subjects, and only trials published with the full text and written in English were included in this work. The bibliographies of all potentially eligible studies, including reference lists, citation searches, and relevant systematic reviews, were searched by hand to ensure literature saturation.

Data Extraction

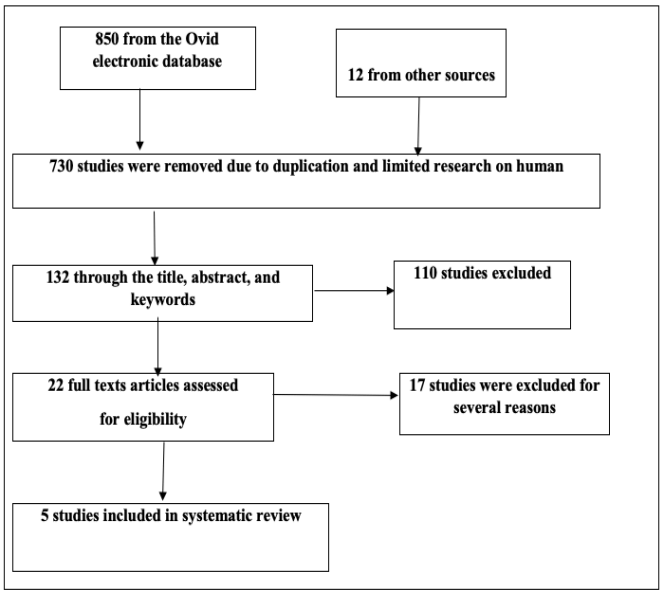
- The extracted details regarding the relevant studies were done using a data extraction form.
- The data extraction form collected information on the following items: methodological characteristics, study general information, demographic variables, Yogic intervention, duration, control groups, outcomes assessment, follow-up; and others. Finally, all differences will be resolved by consensus.

Results

A total of 862 studies were identified of these 850 studies were identified through the electronic search and 12 from other sources. From the initial searches of electronic databases, 850 citations (100 from Google Scholar, 350 from Cochrane Library, 300 from EMBASE, 50 from CINAHL, and 50 from PubMed). The titles and abstracts of these citations were reviewed. This resulted in 22 relevant citations of which the full text was received. After the final review of these texts, only five studies were included in this review. Reviewing the titles and abstracts of these studies resulted in seven studies in which their full text was retrieved and gave a final relevancy of 5 studies.

PRISMA: (Preferred Reporting Items for Systematic Reviews) diagram of search results from a systematic review (6).

Figure 1: Flow Chart of Searching Strategy of the Systematic Review



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Excluded Studies

A total of 17 studies were excluded in this systematic review article. Six studies were pre-post type of studies in which the participants acted as their control but without a separate control group. Five studies were reviews or discussions of the role of Yoga practice on diabetes but they were not trials. In three of the excluded studies, the intervention was not Yoga practice or it was not clear that Yoga practice was included and finally, three of the studies were not exclusive type II diabetic patients. These were the main reasons but some of these studies were excluded for more than one reason. No other outcomes were reported from any of the trials if they were not proposed originally in this review.

Table 1: Reasons for Excluded Studies

Excluded Study	Reason for Excluded
Amanda R. Bonikowske et al (7).	Trial Design: Pre-post-trial with no control group.
Bhavani Ahilan et al (8).	Trial Design: A review of Yoga effect on Type-2 diabetes but it was not a trial.
Manoj Sharma, et al (9).	Trial Design: A mini-review of relaxation techniques that was not a trial.
Vijaya Duraiswamy et al (10).	Trial Design: Pre-post-trial with no control group.
Maricarmen vizcaino et al (11).	Trial Design: A Review of Yoga Effect on Pilot Study in Diabetes.
Vanelli et al. et al (12).	Population: Type-2 Diabetic patients younger than 18 years.
Kerr et al (13).	Population: both type I and type II diabetes patients.
Ramya Ramamoorthi et al (14).	Population: The participants are out of range in inclusion criteria.
Khemayanto hidayat et al (15).	Intervention: Diet with a comprehensive lifestyle modification therapy involving diet.
Yadav Sunil Kumar et al (16).	Trial Design: Pre-post-trial with no control group.
Senthil Raj Thangasam et al (17).	Intervention: Biofeedback-assisted relaxation with mention of the usage of Yoga practices.
Khalsa et al (18).	Trial Design: A review not a trial on Yoga effect on several diseases including diabetes and other diseases.
Singh et al (19).	Trial Design: Pre-post-trial with no control group.
Tsujiuchi et al (20).	Intervention: Used alternative medicine interventions that did not include Yoga Therapy.
Shashikant Prajapati et al (21).	Trial Design: A review of Yoga effect on diabetes but it was not a trial.
P Kumaravelu et al (22).	Trial Design: Pre-post-trial with no control group.
Sudhan P, et al (23).	Trial Design: Pre-post-trial with no control group.

Studies and Participants

A total of five studies were included in this systematic review with 10 arms, comparing the intervention of Yoga practice alone or combined with other modes of interventions. Five arms participants 3 months at the latest 3 days/per week and another 5 weeks / 20 minutes a day (32-33). One arm and 44 patients regular Yoga practices for 3 months and 1 hour per day, and one arm and 60 participants 1 hour daily for more than 5 years (33). and the last arm with 64 participants 75min per week.

Exclusion Criteria of the Studies

In the included studies, the following were used as exclusion criteria for participants: Type-1 diabetes Mellitus will be excluded, severely ill patients, post-operative cases, drug abusers (under treatment & any other diseases), Persons suffering from any other systemic disorders (High B.P., Peptic ulcer, Heart patients, Kidney & G.B. disorders, Hernia) were excluded, Patients having fasting blood sugar more than 180mg/dl and Postprandial Blood Sugar more than 250mg/dl.

Interventions

Yoga intervention alone was used in three studies (24-25-26). It was combined with Yogic lifestyle modification only in one study. Yogic practices (Asan and Pranayama) were used in one study (27). All participants received Yoga practice training (Asana, Pranayama, meditation). The frequency range of the Yoga therapy sessions differed for example one study had 20-minute sessions per day for one of the trials (28). One study had 1 hour per day sessions in five years (28). and three studies had different sessions for one.

Table 2: Characteristics of Studies Included in the Systematic Review

Sr. No	Author and Year	Intervention	Age	No of patients	Follow Up Period
1	Shree Laxmi V. Hegde, et al. 2011 (29)	Yoga Intervention	40 -75 years	123 Patients	3 Months at least 3 days/ week
2	Duraiswamy et al. 2011 (30)	Yogic Intervention	40- 64 years	20 Patients	5 weeks/ 20 minutes a day.
3	Chattopadhyay K , et al. 2020 (31)	Yoga Intervention	18–74 years	64 Participants	75min per week.
4	Phatak MS et al. 2017 (32)	Yoga Meditation	40-60 years	60 Patients	1 hour daily for more than 5 years
5	P.A Balaji, Smitha R. Varne et al. 2011 (33)	Yoga and pranayama	40-55 years	44 Patients	3 months, 1 hour every day

Selection bias: Randomization and allocation concealment.

Performance bias: Any differences in care provided apart from the intervention

Attrition bias: Any systematic differences in the withdrawals or loss to follow-up. The studies should follow the concept of intention to treat analysis (ITT) with a full explanation of the withdrawal process.

Measurement (detection) bias: Any kind of bias related to the process of reporting the outcome of the studies.

Outcomes

After assessing the characteristics and quality of each trial included in this review, a pooled estimate using meta-analysis was not calculated. This was mainly attributable to the high level of heterogeneity between the characteristics of studies including the specific interventions particularly the method and frequencies in conducting the intervention.

Primary Outcomes

The primary outcome was the measurement of glycemic control (HbA1c), fasting blood glucose (FBG), and postprandial glucose (PPBG).

Fasting Plasma Glucose

Four studies provided results on fasting plasma glucose (FPG) and provided favorable results for the Yoga intervention. There was a statistically significant reduction in FBG concentration in the Yoga group in comparison to the control group. The decline in plasma glucose was more important (FPG $p < 0.05$) (32).

The pooled mean difference of FBG between the Yoga group and control groups from random effects analysis was- p=0.03). Only three studies show the result of PPBS postprandial Blood Sugar levels (33). The mean values of Fasting Blood Sugar and PPBS were significantly higher in diabetics as compared to controls ($p<0.05$), but these values in Yoga practitioners were significantly lower than in non-practitioners ($p<0.05$) (29).

Postprandial Blood Glucose

Three studies provided results on PPBS. These three studies provided favourable results for the intervention in lowering PPBS. There was a statistically significant reduction in PPBS concentration in the Yoga group in comparison to the control group. The pooled mean difference for PPBG between the Yoga group and control groups from random effects analysis was – Postprandial plasma glucose ($p < 0.0001$), 198.47±40.11 ($p<0.05$), Postprandial Plasma Glucose with ($p< 0.001$), [T1- 270.64 + 76.6 to 196.90 + 64.67, T 2 – 230.62 + 71.32 to 183.46 + 52.20] (31-32-33).

Glycolated Hemoglobin

Two studies provided results on HbA1c. These three studies provided valuable results for the intervention in lowering HbA1c. There was a statistically significant reduction in HbA1c concentration in the Yoga intervention group in comparison to the control group. The pooled mean difference for HbA1c between the Yoga intervention group and control groups from random effects analysis was – 6.25% (0.5 6 0.3%), $p < 0.001$ (32-33).

Secondary Outcomes

The secondary outcomes were other markers of type-2 diabetes management including triglycerides, High-density lipoprotein, low-density lipoprotein, blood pressure, BMI, and Serum SOD.

Lipid Profile

Triglycerides

Two of the included trials reported an effect on lowering cholesterol levels. On comparing the mean values of lipid profile in diabetic Yoga practitioners and diabetic non-practitioners it was found that only TC and TG were significantly lower in Yoga practitioners ($p<0.05$). There was a significant decrease with $p < 0.001$ in triglycerides $p<0.001$ (32-33).

Low-Density Lipoprotein

There were two studies in which the effect of Yoga on LDL was studied. The forest plot for LDL shows that there is a significant reduction in LDL in the Yoga group. The mean values of LDL were significantly higher in diabetic non-practitioners as compared to controls ($p>0.05$), $p < 0.001$ (32-33).

High-Density Lipoprotein

Two studies evaluated the effectiveness of Yoga on HDL in comparison to the control group. The mean HDL was significantly lower than controls in all diabetics ($p<0.05$) (32). only one study found no significant change in HDL levels in test groups (33).

Body Mass Index

Three studies evaluated the effectiveness of Yoga practices on BMI. The male and female ratio was 1.5; the average weight and height of individuals in the study group were 65 kgs (65.1±10.5) and 157 cm (157.2±6.5), ($p>0.05$) respectively (32-33). There was a significant decrease in the weight, BMI and waist-hip ratio in both T1 and T2 with $p < 0.001$ Such a substantial change in the control group was not found (30).

Blood Pressure

Only one study evaluated the effectiveness of Yoga intervention on blood Pressure. The results show a significant reduction of systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the Yoga practices group in comparison to the control group ($P = 0.116$) and ($P= 0.072$) with WMD = −1.66 and −0.26, respectively. However, the heterogeneity was mild (32).

Serum

Only one study shows that the test results decreased after practicing Yoga, the serum SOD (superoxide dismutase) enzyme activity levels increased

after the intervention and this was a significant increase (p-value <0.0001) (33).

Discussion

The impact of Yoga therapy on individuals with type-2 diabetes was examined in this review. Only five studies compared Yoga Therapy alone and in combination with additional co-interventions to a control group. We eliminated a lot of pre-post trials to identify high-quality studies. Regrettably, the data quality of the included studies was low. The findings point to the positive effects of Yoga therapy on type-2 diabetes-related short-term parameters, but not always for long-term consequences. The result of the trials' brief duration precluded the detection of long-term effects and the poor power of each trial brought on by its small participant base. Because of the clinical variability among the studies and the possibility of bias resulting from the low quality of the investigations, combining the data from the various studies would not be of scientific use in this systematic review. The included study's low quality may result from improper reporting, methodological flaws, or both. Across the included trials, different levels of methodological flaws including selection bias, randomization, and the use of multiple interventions for confounders were observed. In summary, Yoga therapy is effective for individuals with type-2 diabetes mellitus. The majority of these improvements had an immediate or short-term impact on Type-2 diabetes outcomes and not all of them were statistically significant. The Yoga therapy positively affected short-term glycemic control variables evaluated in this study, including fasting blood glucose and postprandial glucose. The systematic review shows that Yoga therapy had a beneficial effect on type-2 diabetes mellitus glycemic management.

Conclusions

Yoga therapy was beneficial and effective at controlling glycemic parameters in Type-2 diabetes when the correlation coefficient for different anthropometry measures was adjusted. Results from the systematic review show that Yogic therapy (Asana, Pranayama) both are helpful in glycemic control. Finally, we can show that Yoga therapy is very beneficial for type-2 diabetes patients and its efficacy depends on many health variables like human body weight, age, and environment. Patients with type-2 diabetes may benefit in the short term from Yogic practice (Asana, Pranayama). It is necessary to analyze practice specifics (Asana, Pranayama, Meditation) and frequency in the Yoga intervention. This comprehensive systematic review key finding is that large, carefully planned randomized clinical trials are required to determine whether Yoga therapy benefits people with type II diabetes mellitus. These experiments should focus on the methodological soundness and the characterization of Yogic Practice attributes.

The systematic review shows that Yoga therapy had a beneficial effect on type-2 diabetes mellitus glycemic management. In conclusion, there remains a need for systematic evaluation of the health outcomes of Type-2 diabetes and the benefits if any of its early treatment. Yoga therapy (Asana, Pranayama) remains essential to managing Type-2 diabetes.

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Seasonal regimen (*Ritucharya)* with special reference to Agni and Gut Microbiota

Review Article

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Abstract

Background: Ayurvedic Classics have stated six *Ritus* (seasons), three each under the broad classifications *Aadana kala* (Northern Solstice) and *Visarga kala* (Southern Solstice), with distinct dietary and lifestyle regimens prescribed for each. Human gut microbiome diverges seasonally and diet according to *Ritucharya* is the most effective method to manipulate and regulate the inherent host microbiota relationship. Aim: The present review work has been done to see the implementation of *Ritucharya* (Seasonal regimen) for a healthy life with special reference to gut flora. Material methods: Information regarding "*Ritucharya*" has been analyzed from classical textbooks like Charak Samhita, Sushruta Samhita, etc. Detailed evidence and information have been collected by searching MEDLINE, PubMed, Scopus, AYUSH Portal, and Namaste Portal. Research and review articles were selected by using the search terms: "*Ritucharya*", "human gut biome", "host-microbiome interaction", "gut microbiota", "seasonal microbiota", "season-agni", "*ritucharya-agni*", "*agni*-gut microbiota" and "diet-microbiota", "environment-gut bacteria. Discussion: The impaired *Agni* (digestive fire) is the basic cause of all illnesses. The entire Ayurvedic preventive and treatment system is based on the modulation and management of "*Agni*" (digestive fire). When *Agni*'s activity is disrupted, it affects *Mahasrotas (*gastrointestinal*)* and affects the gut microbiota of an individual. Dysbiosis of the gut microbial makeup has been linked to a variety of diseases including gastritis, obesity, colitis, and eczema. Providing the correct gut environment through the right seasonal diet helps nurture the right microbiome, which can result in good metabolic effects and help prevent seasonal and opportunistic infections. Conclusion: This review examines the seasonal regimens based on the current evidence on the interdependency of gut microbial ecology with changing seasons and consequent health effects.

Keywords: *Agni,* Diet microbiota, Gut Flora, Gut microbiota, *Ritucharya*, Seasonal Diet.

Introduction

According to *Ayurveda*, the year is divided into two parts. *Ayana* (solstice) is named after the direction of the sun's travel, which is *Uttarayana* (northern solstice) or *Dakshinayana* (southern solstice). Each consists of three *Ritus* (seasons). *Ritu* is a Sanskrit word that means "to go." It is the way nature presents itself in a certain and precise sequence in present forms, in short, the seasons (1). *Shishira* (winter), *Vasanta* (spring), and *Grishma* (summer) are the seasons in *Uttarayan*, and *Varsha* (monsoon), *Sharata* (autumn), and *Hemanta* (late autumn) are the seasons in Dakshinayana. Because Ayurveda originated in India, the above seasonal shifts are primarily observed in the Indian subcontinent. The states of *Agni, Dosha*, and *Bala* vary according to the seasons due to environmental variations. The *Agni* is a key factor for the health and *Bala* of an individual which is correlated with the gut microbiota as per some research, as the gut microbiota determine digestion and assimilation of ingested food.

A colony of microorganisms inhabits the human body and has a symbiotic relationship with its host. The term "microbiota" refers to a group of microorganisms, including bacteria, archaea, and some unicellular eukaryotes, that live in a specific environment, such as the stomach, mouth, skin, etc (2). Humans are now thought to have two genomes: one inherited from one's biological parents and one acquired after birth (the microbiome) (3). The inherited genome remains relatively stable throughout a person's lifetime, whereas the acquired microbiome is dynamic and strongly influenced by factors such as age (4), diet (5), lifestyle (6), seasons (7), geography (8), and therapies (9). However, diet according to particular seasons is recognized to be the utmost significant determinant of human gut microbiota configuration. The food ingested, immune system, homeostasis, and physiological function of the body are regulated by the gut microbiome of an individual. Healthy Gut microflora maintains the host homeostasis, and alternation in gut microflora leads to "Dysbiosis". This Dysbiosis leads to various chronic diseases like diabetes mellitus, metabolic syndrome, inflammatory bowel disease,

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atherosclerosis, non-alcoholic fatty liver disease, alcoholic liver disease, and cirrhosis (10), (11). Bacteroidetes, Actinobacteria, Proteobacteria, Firmicutes, and Verrucomicrobia occupy the majority of the human gut. Cyanobacteria, Fusobacteria, Saccharibacteria, and Spirochaetes are also present in small numbers (12).

Agni is believed to be a key factor for maintaining health and longevity. It is the factor responsible for digestion, metabolism, and assimilation of food substances (13). The quantum of food ingested should be based on an individual's *Agni* (14). *Agni* dysfunction, also known as *Vishama* (hypofunction or hyperfunction), disrupts homeostasis and can lead to ailment. If Agni ceases to function, the individual will die (15). In contemporary science disturbance in Agni is responsible for dysbiosis. The status of *Agni* alters in different seasons. Few modern Gut microbiome research also supports the relationship between the human gut microbiome and the changing seasons, as well as the relevance of seasonal regimens suggested in *Ayurveda* known as *Ritucharya*, is required.

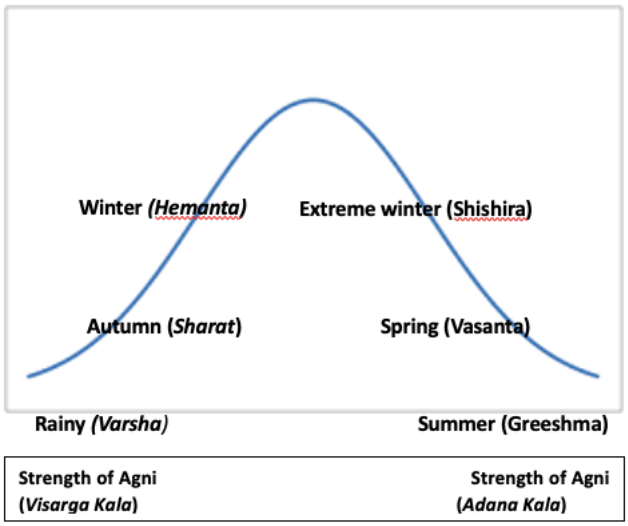
Material methods

Detailed Information on the topic has been reviewed and collected by systematic screening of different Classical texts of Ayurveda i.e. *Charaka Samhita, Sushruta Samhita, Astanga Hridaya, Bhavprakash, Yogaratnakar, Ayurveda* dictionaries, etc. Different literature Databases such as PubMed, Web of Science, Scopus, MEDLINE, DHARA, AYUSH Portal, and Namaste Portal were using keywords "gut microbiota", "human gut biome", "seasonal microbiota", "host-microbiome interaction", "season-*agni*", "*ritucharya-agni*", "*agni* - gut microbiota" "environment-gut bacteria", "diet-microbiota" and "microbiota modulators" with the help of Boolean operators "AND", "OR", and "NOT". Filters like clinical trials, review articles, within 5 years and free full articles were applied. Among those research papers containing data regarding the role of effects of diet on Gut microbiota, the role of seasons on the gut microbiome, diet and seasonal variations, environment and gut bacteria, and probiotics, were reviewed in detail.

Ritu (Season) and *Agni* (Digestive Fire)

At the beginning of the period of *Adana Kala* (Period of emission) and the end of *Visarga Kala* (Period of dehydration), weakness prevails in human beings. In the middle of the both strength becomes moderate. However, at the end of the period of emission and the beginning of the period of dehydration, human beings get a considerable amount of strength (16). Similarly, the strength of *agni* varies in different seasons as shown below (Figure 1)

Figure 1: State of strength & *Agni* during strength depleting (*Adana Kala*) seasons and strength promoting (*Visarga Kala*) seasons



Ritus (Seasons) and Gut Microbiota

Seasonal fluctuations in the microbial population were shown by the gut microbiome profile obtained from 16s ribosomal RNA sequencing in the Hadza (hunter-gatherers) and Hutterites (agriculturists) populations (17). During the rainy season in Hadza, when they ate more berries, honey, and other foraged foods, Bacteroidetes—primarily the Prevotellaceae spp.—reduced significantly. Prevotella species were found to be prevalent during the dry season, while the wet microbiota showed a sharp decline. The phylum Bacteroidetes was found to be more prevalent in the summer than in the winter in Hutterites individuals. The majority of food consumed by them in the winter is made up of fruits and vegetables that were frozen, canned, or preserved in the summer (18). According to Chevalier et al., the gut microbiota's ability to provide digestive services is also temperature-dependent. In mammals, exposure to cold causes a distinctive shift in the gut microbial community, which has an impact on overall energy homeostasis (19). The knowledge that food and seasonal fluctuations have an inevitable impact on the human gut microbiota places Ritucharya in the forefront as the most efficient way to control and modify the inherent host-microbiota interaction.

Hemanta and *Shisira Ritucharya* (Early and Late winter regimen)

The *Hemanta* (Early Winter Season) and *Shisira* Ritu (Late Winter Season) prevail from mid-November to mid-January (*Margasira-Pausa*) and mid-January to mid-March (*Magha-Phalguna*). The *Hemant and Shisira* seasons are almost similar in nature with the only difference being that in the latter, dryness caused by Adana (absorption) and cold caused by cloud, wind, and rain prevail. So, the entire prescription for Hemanta is to be followed in the *Shisira* seasons as well. *Hemanta* (Early Winter Season) and *Shisira Ritu* (Late Winter Season) are characterized by snowstorms and fog in various places. During this cold winter, the *Agni* (digestive power) of human beings possessing good health (strength) is enhanced due to restraint caused upon it by the cold wind, so that it can digest any foodstuffs irrespective of its heaviness and quantity. In

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case this enhanced *Agni* does not get the heavy edibles for consumption it acts upon the *Rasa Dhatu* and consumes it with the result of deficiency of *Rasa Dhatu* (tissues) which consequently causes provocation of *Vata* during *Hemanta* and *Shishira*. Therefore, it is recommended to consume *madhur* (sweet), *tikta* (bitter), *katu* (pungent), *amla* (sour), *lavan* (salt) (20), *snigdha ahara* (fatty foods), *til taila* (Sesame oil), *vasa* (muscle fat), and *sura* (fermented products) from jaggery, as well as foods made from *nava anna* (freshly harvested grains), *ikshu* (sugarcane), *sali* (rice), *masha* (black gram), Godhuma (wheat) and fresh meat of few animals like *prasaha, anupa*, etc. during *Hemanta and Shisira* (early and late winter) (21). This diet is high in fat and high in sugar. It is also advised to consume *Dadhi* (curd), *goghrita* (cow's ghee), and other *ksheera vikruti* (dairy products). This recommendation may be supported by the observation that consuming dairy products fermented with Lactobacillus may improve the butyrate-producing microbiota and may also prevent pathogen colonization in the gut, thereby preventing a variety of infections (22). Furthermore, *Lactobacillus* and *Bifidobacterium* spp. Present in dietary food products support the preservation of gut microbiota and normal intestinal permeability, as well as the improvement of the intestine's immunological barrier and intestinal inflammatory response (23).

Conversely, an overgrowth of the common gram-positive bacteria, Firmicutes, is directly linked to obesity. Practices such as *vyayama* (exercise), *abhyanga* (oil massage), *udvartana* (powder massage), *swedana* (sudation), and *aatapa-sevana* (basking in the sun) are recommended during these seasons. These can appropriately be complementary to the changes in gut flora and the resulting health effects. It has been established that regular exercise can prevent obesity despite of a high-fat diet by changing the population ratio of major bacterial phyla that protect the intestinal morphology and integrity, thereby reducing inflammatory infiltrate (24), (25).

The relative abundance of the phylum Verrucomicrobia decreases and that of Firmicutes tends to grow during the cold seasons (*hemanta, shisira*). Verrucomicrobia has a negative correlation with the ability of food to provide energy in cold climates. Therefore, the lack of Verrucomicrobia permits higher calorie absorption, while the cold microbiota Firmicutes boosts both calorie absorption and improves intestine absorptive ability. Therefore, a diet that supports the rise in Firmicutes and the fall in Verrucomicrobia must be adopted. As a co-evolutionary mechanism, a high-fat diet decreases the abundance of Akkermansia (Verrucomicrobia) in the gut, allowing for the consumption of increasingly accessible dietary energy. The bacteria Firmicutes, Mollicutes, and Eubacterium that create short-chain fatty acids (SCFAs) are also enhanced by a diet high in fat and sugar (26). According to reports, SCFAs can reduce colonic inflammation, activate regulatory T cells, inhibit the production of pro-inflammatory cytokines, and increase the expression of IL-10 (interleukin 10). Wong et al. 2006 in his studies found that short-chain fatty acids (SCFAs) promote have a favourable impact on colon biochemical and physiological processes (27). Intestinal epithelial cell proliferation, differentiation, metabolism, and colon defense barrier reinforcement are all significantly impacted by SCFAs, primarily butyrates (28). It has been demonstrated that there is a positive correlation between the quantity of fat ingested and the population of Actinobacteria, which is also observed to increase during the winter (18). These Actinobacteria have been proposed as modulators of the immune system, metabolism, gut-brain axis, and gut permeability (29).

Through mediating the remodelling of the adipose and intestinal tissues, these cold microbiotas assist the host in adjusting to cold seasons of high energy requirement. Therefore, eating the aforementioned items is wisely advised in *Hemanta and Shisira* (early and late winter) (30).

Vasanta Ritucharya (Spring regimen)

The *Vasanta Ritu* (Spring season) prevails from mid-March to mid-May (*Chaitra - Vaishaka*). This is the time of year when fresh leaves begin to emerge. The environment is fragrant with flowers, and the land is artfully blanketed with a variety of vibrant blooms (31). The intense light of the Sun heats the atmosphere. This heat is the reason for the melting of the *Kapha dosha*, elevated in the body as a result of cold during the *Hemanta Ritu*. *Kapha Prakopa* is therefore dominant in *Vasanta Ritu* and causes a variety of *Kaphaja* illnesses. In *Vasanta Ritu*, the strength of digestive power i.e. *Agni* is reduced. Food items that are *laghu* (light) and readily digested, such as *yava* (barley), *mudga* (green gram), *godhuma* (wheat), meat from *Sarabha, Sasa* (rabbit), *Ena* (antelope), *Lava* (quails), k*apinjala, Vishkira*, *Jangala Mamsa* (kind of meat), etc., and beverages like *madhvika and sidhuh* (kind of liquor) are advised during this season (32). It has been established that consuming barley enhances host blood glucose metabolism and encourages a high Prevotella/ Bacteroides ratio (33). Consuming barley lowers postprandial hyperglycemia and raises blood concentrations of butyric acid, which is produced by gut bacteria (34). These findings imply that barley may positively alter the gut flora's composition and enhance the metabolic health of the host.

During *Vasanta Ritu* it is advised to take therapies like *Vamana Karma* (Medicated Emesis) and exercise, *udvartana* (dry massage), *dhumpana* (medicated smoking), *kavala* (gargling), and *anjana* (collyrium) (35). The ratio of Firmicutes to Bacteroidetes is larger in obese persons than in lean ones, and those who reduce their body weight by calorie restriction show a shift in this ratio due to an increase in Bacteroidetes (36). The population of firmicutes increases during the spring season according to few studies. Research revealed that exercise, which began during the juvenile stage, changed several phyla, causing a drop in Firmicutes and an increase in Bacteroidetes (37).

Grishma Ritucharya (Summer regimen)

The Greeshma Ritu starts in mid-May and extends to mid-July (*Jyaistha-Asadha*). The season is

marked by the Sun's extreme heat and depletion of strength and *Agni*. Both the exterior and interior of the human body are dominated by *ushna guna* (heat) and *rookshatha*(dryness). Thus, it is recommended to have foods high in *swadu rasa* (sweet) and *sheeta guna* (cold in potency) during *Grishma* (summer), such as rice, milk, ghee, grapes, coconut water, fruit juices, and sugar. Coconut water is high in naturally occurring carbohydrates, proteins, and antioxidants but low in calories and fat (38). Products made with roasted barley flour, called *Saktu*, *Raga shadava*, a fruit drink made with sweetened mango, blackberries, and pomegranate juices, and well-churned curd with sugar and pepper i.e., *Rasala* are recommended (39).

Using the above food items may benefit the group Bacteroides (Bacteriodetes phylum), which includes the colon's polysaccharide-using bacteria and saccharolytic species of the genus Bifidobacterium and Ruminococcus that feed on carbohydrates. During *Grishma Ritu* (summer season), a high-fat, high-sugar diet must be avoided as it has been related to a decrease in Bacteroidetes (40). Whole grains are effective sources of resistant starch, oligosaccharides, and non-digestible carbohydrates that favor Prevotella, Treponema, and Xylanibacter which are favorable for fermenting carboxymethylcellulose, xylene and xylose to produce high levels of SCFAs (41). Throughout the summer, researchers saw the Bacteroidetes clade, which has genomes full of CAZymes, or carbohydrate-active enzymes, are mavens at breaking down complex carbohydrates and plant cell walls. That's why it is advised to take much fruits and vegetables in the summer season as compared to winter (42).

***Varsha Ritucharya* (Monsoon regimen)**

The Varsha Ritu starts in mid-July and extends to mid-September (Shravana and Bhadrapada). This season is characterized by cloudy skies, cold and humid climates, rains occurring without thunderstorms, ponds, and rivers overflowing with water, and occasional sunshine (43). In *Varsha Ritu*, the body is already weak due to the impact of Adana Kala, and weak Digestive power (*Agnimandya*) accompanied by stormy wind leads to vitiation of Vata (44). Further, an increase in the *Amlata* (acidity) of the earth, and water, due to perspiration caused by the rains over the hot earth leads to pitta accumulation. The strength and immunity of the person again becomes less. Weakness in the power of digestion also causes vitiation of all three dosa; *kapha* and pitta are vitiated due to the non-digestion or half-digestion of food. To maintain the normal power of digestion it is advised to take foods having *Amla* (tarty), *Lavana* (salty) taste, and *Sneha* (unctuous) qualities should be eaten. Old barley, wheat, *Sali* rice (Oryza sativum), the meat of arid animals, and *Yusha* (soup) are to be incorporated into the regular diet. Also, it is recommended to include ginger in the diet during monsoon season, along with whey or buttermilk, meals and drinks processed with honey, and ginger with rock salt before a meal (45). Honey composed mainly of fructose, fructo-oligosaccharides, and glucose has been considered a favorable bifidobacterial substratum (46). Using honey flourishes the lactic acid bacteria in the intestines of honey-fed rats, ultimately altering the intestinal microbiota (47).

***Sharad Ritucharya* (Autumn Season)**

Sharad Ritu prevails from mid-September to mid-November (*Ashwina-Kartika*). The autumn is preceded by the rainy season. Thus, a human body accustomed to the cooling effects of the rainy season here-to-fore gets all of a sudden exposed to the scorching rays of the sun during this season. Generally, this causes vitiation of *pitta*. This can be prevented if proper steps are taken to avoid the accumulation of *pitta* during the rainy season. In this season pacification of *vata dosha* also occurs. The strength of person's *bala* and *agni* remains medium. During Sharad *Ritucharya* (Autumn Season) it is recommended to take foods having *kashaya rasa* (Astringent), *swadu* (sweet), *tikta* (Bitter), *sheeta guna* (cold in potency) such as milk, goods of sugarcane juices (molasses, treacle, sugar, etc), honey, *mudga* (green gram), *sali rice*, and *jangala mamsa* (meats of arid land animals) (48). It is also advised to consume *amalaki* (Indian gooseberry), *draksha* (grapes) and *patola (Trichosanthes diocia)*.

Raisins (dry grapes/ *Vitis vinifera*) are rich in fermentable fibers such inulin-type fructans and phytochemicals like tartaric acid and phenolic acids that influence the composition of the gut flora (49). Using an in vitro model of gastrointestinal digestion, polyphenolic extracts from white and red grape pomace were studied. In comparison to baseline measurements, white grape pomace extract increased the total number of bacteria and the abundance of Bifidobacterium spp., while red grape pomace extract increased all the bacterial groups investigated (Actinobacteria, Proteobacteria, Bacteroidetes, Firmicutes, Bifidobacterium, and Lactobacillus) except for Bacteroides (50).

Discussion

Several studies data have revealed a strong relationship of the gut microbiota or gut microbiome with environmental factors like changing seasons and temperature as well as with food (51). The research conducted by Davenport (2014) on native communities such as Hutterites and Hadza hunter-gatherers demonstrates that the variety of the human gut microbiome varies throughout the year. Therefore, Food and lifestyle also varies according to season. Food can affect the composition of the gut microbiota in two ways: (1) by supplying non-digestible substrates that support the growth and activity of beneficial microbes (prebiotics), and (2) by incorporating live microorganisms known as probiotics that colonize the gut, resist digestion, and positively alter the microbial composition. The predominant energy sources for intestinal epithelial cells are acetate, butyrate, and propionates (SCFAs). They are produced by the fermentation of carbohydrates in the intestinal lumen. This process promotes the growth of beneficial bacteria, primarily Bifidobacterium and Lactobacillus species. Probiotics can alter the gut microbiota's diversity,

composition, and activity. Probiotics may strengthen the intestinal barrier against enteric pathogens by promoting the formation of mucin and maintaining tight junctions in the gut epithelium. By stimulating the production of IgA and β-defensin by the host, they also regulate the microbial flora population and intestinal immunity.

By providing the ideal gut environment through a seasonal diet, one can foster a microbiome that has the potential to improve metabolism and protect against opportunistic and seasonal illnesses.

Conclusion

This review article is on the interrelationship of gut microbial ecology with varying seasons and the resulting health effects are used to assess the relevance of *Ritucharya* (seasonal regimen). Diet and Lifestyle without seasonal regimens can have a significant impact on commensal microbial communities, resulting in dysbiosis, which can increase pathogen susceptibility, inflammatory disorders, and the current epidemic of metabolic disorders. In Ayurvedic advocacy, the status of the *Agni* depends on the *Ritu* (Seasons) and it helps to maintain the homeostasis microbiome of the gut. Adopting *Ritucharya* (seasonal regimen) helps to maintain the harmony of Dosha, Dhatu, Agni, Mala and also in contemporary science provide an adequate opportunity to fine-tune the dynamics of human gut flora and save the host from pathogenic symptoms of seasonal changes and other diverse causes. Reverting to seasonal foods can change the gut flora to promotes health.

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Acute Appendicitis - A Review

Review Article

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Abstract

The term appendicitis was first used by an epic publication by FITZ (Harvard Medical School) in 1886. FITZ outlined the clinical diagnosis and suggested early removal of the Appendix. Acute appendicitis is one of the most common abdominal emergencies worldwide. The cause remains poorly understood, with few advances in the past few decades. To obtain a confident preoperative diagnosis is still a challenge, since the possibility of appendicitis must be entertained in any patient presenting with an acute abdomen. Although biomarkers and imaging are valuable adjuncts to history and examination, their limitations mean that clinical assessment is still the mainstay of diagnosis. A clinical classification is used to stratify management based on simple (non-perforated) and complex (gangrenous or perforated) inflammation, although many patients remain with an equivocal diagnosis, which is one of the most challenging dilemmas. An observed divide in disease course suggests that some cases of simple appendicitis might be self-limiting or respond to antibiotics alone, whereas another type often seems to perforate before the patient reaches hospital. Although the mortality rate is low, postoperative complications are common in complex disease. We discuss existing knowledge in pathogenesis, modern diagnosis, and evolving strategies in management that are leading to stratified care for patients.

Keywords: Appendix, Appendicitis, FITZ.

Introduction

Acute appendicitis is one of the most common abdominal emergency managed by a general surgeon. The worldwide incidence of appendicitis is estimated to be 86 cases per 100,000 population annually(1, 2). The life time risk of developing acute appendicitis is 8.6% in males and 6.7% in females. Acute appendicitis also happens to be one of the common non-obstetric emergency during pregnancy, The incidence during pregnancy is variable. It is 6.3 per 10,000 pregnancies during the antepartum period and 9.9 per 10,000 during the postpartum period.(1,2) The overall morbidity rate during the postoperative period ranges from 9-18% (1). The mortality rate in non-perforated appendicitis is less than 1% while the mortality rate in perforated appendicitis climbs up to 5%(2).

Etiopathogenesis

The disease is less common in the Asian and African subcontinent due to dietary habits. Consumption of high dietary fibre leads to decrease in the viscosity of faeces,decreased bowel transit time and reduces the formation of faccoliths, which lead to obstruction and initiation of the inflammatory cascade(2-4). The disease is more common in males with a male to female ration of 3:2 in teenagers and young adults and 1.4 times more common in males than in females in rest of the adult population. Family history seems to play role in retrocaecal type of appendicitis. Positive family history increases the chance of having appendicitis 3.18 times. Old age, three or more co morbidities and male sex is associated with a high risk of perforation(3).

Majority of acute appendicitis are obstructive in nature. Faecoliths, lymphoid hyperplasia, foreign bodies, malignancy and parasites are the causes of obstruction. Uncommon causes of appendicitis may be foreign bodies in the lumen such as mutton bone fragments, fish bones, fruit seeds and nuts. However the incidence of this type is 0.0005%. Diverticulitis of the appendix can also give rise to acute inflammation. In rare circumstances appendicitis may develop while the appendix is a content of a hernia sac in less than 1% of cases. If present in an inguinal hernia it is designated as Amyand's while if encountered in a femoral hernia sac then it is designated as De Garengeot's hernia (5,6). Left sided appendicitis is seen in cases of situs inversus wherein a chest ray which reveals dextrocardia is diagnostic.

The pathological process passes through various stages in a sequential manner. Obstruction leads to blockage of the lumen. The secretions are unable to drain and accumulate. The appendix distends with a concomitant increase in the intraluminal pressure. There is vascular congestion due venous and lymphatic compression thereby leading to compromise in the blood supply of the appendix. Tissue ischaemia ensures

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with formation of multiple abscesses in the wall. This is typically called the catarrhal stage of acute appendicitis (all three layers of the wall of the appendix discernible). There is involvement of the serosal surface as well in the inflammatory process. Bacterial invasion of the luminal wall continues. The omentum gets adherent to the inflamed appendix. This is called the phlegmonous stage (layers of the appendix wall unclear). The local circulatory compromise continues leading to infarction usually at the junction of the appendix with mesoappendix as the blood supply is inadequate. The infarcted area undergoes gangrenous changes and eventually perforates (layer stratification of the wall completely lost). Perforation usually occurs at the tip. Subsequently peritonitis develops which may either be localized to the region by way of omental and intestinal adhesions or may generalized if the omentum is deficient as seen in children. If untreated bacterial peritonitis will lead to septicaemia, septic shock and multiorgan failure.

Clinical Features

Symptoms in acute appendicitis may not vary from case to case. However signs vary significantly due to the variable location of the appendix.mPain is the commonest symptom. Pain is usually periumbilical or epigastric in location to start with. However with time it localizes to the right iliac fossa (Volkvich-Kocher sign). The initial location of pain represents a referred pain resulting from visceral innervation of the mid gut and subsequent localized pain is caused by involvement of the parietal peritoneum as the inflammatory pathology progresses(2), anorexia is very common. Patient is unwilling to have food. If the patient wants to consume a favourite food item the clinician needs to consider other differential diagnosis instead of appendicitis (Hamburger sign). Anorexia is a very common symptom in appendicitis.Vomiting is a common accompaniment of gastrointestinal infection. It is due to reflex pylorospasm. Fever develops as the inflammatory process progresses with development of bacteraemia. Fever with chills is seen in patients who present late with complications such as abscess formation. Fever is suggestive of advancing septic process.In a few cases of retrocaecal appendicitis, pain may be referred to the right testis or to the right hemiscrotum.A multitude of signs have been described for diagnosing acute appendicitis(2).

Tenderness at the Mac Burney's point is pathognomonic in majority of cases. The only exception could be retrocaccal appendicitis. In addition to this there may be tenderness at the Lanz's and Munro's point. In pregnant women the signs may be seen higher up in the abdomen.Tenderness in the right iliac region which is aggravated by postural change of the patient from supine to recumbent is designated as Rosenstein sign. Blumberg's sign is pain elicited by steadily increasing pressure at the site of tenderness increases on abrupt release of the pressure (rebound tenderness) Rovsing's sign is palpation of the left lower abdomen causing pain and discomfort in the right iliac region. Psoas sign (Obreztsova's sign, Cope's psoas test) with the patient lying in left lateral position, extension of the right thigh will elicit pain due to the irritation caused to the right psoas muscle by the tip of an inflamed appendix. Obturator sign is flexion and internal rotation of the right hip eliciting severe pain due to irritation of the obturator internus muscle caused by an inflamed appendix. Markle test (heel drop jarring) elicits pain on walking or with jolts and is suggestive of peritoneal irritation.Discomfort or cutaneous hyperesthesia in the Sherren's triangle (triangle formed between the umbilicus, pubic tubercle and anterior superior iliac spine). Massouh sign is swishing two finger tips starting on the xiphoid down towards the left and right iliac fossa will cause hyperaesthesia on the right side due to peritoneal irritation. K sign is named after the region of origin that is Kashmir (2). It is seen in retrocaecal or paracolic postions of appendicitis. Percussion or palpation of the posterior abdominal wall co exists with psons sign. Symptoms and more so physical signs are difficult to interpret during pregnancy. Hence clinical examination just by itself does not suffice to even arrive at a provisional diagnosis and therefore needs imaging to confirm the diagnosis. A retrocecal position of an acutely inflamed appendix may at times pose a clinical and diagnostic dilemma. Varied clinical presentations need to be kept in mind while evaluating such patients, There may be an abscess in the retrocecal and subhepatic region, retroperitoneal necrotising fasciitis, acute right sided scrotal pain and inflammation (Fournier's gangrene) and retroperitoneal abscess tricking to the right thigh. Due to a vast variability in symptoms and signs in acute appendicitis one needs to be aware of all possibilities including anecdotal variations in presentation in order to avoid delay in the diagnosis. Delay in the diagnosis may be detrimental as the morbidity as well as mortality may rise.

Diagnosis

Meticulous evaluation of symptoms and signs can immensely help in arriving at a diagnosis of acute appendicitis especially in the adult population of patients. Various scoring systems have been developed which enable a systematic evaluation of relevant clinical features. Addition of laboratory values add to the accuracy of diagnosis. Two such scoring systems have been developed for evaluation of adults with suspected acute appendicitis.The Alvarado score was the initial system (Table la). It is a very lucid way of quantification of scores and has very good diagnostic accuracy. Based on the score the surgeon can arrive at a tentative diagnosis of acute appendicitis and thereafter proceed to imaging for confirming the diagnosis (14,15).

Investigations

Laboratory tests which are relevant and help in the diagnosis of acute appendicitis include complete blood count, CRP levels, urine examination and a urinary pregnancy test in female patients. Raised total leucocyte count with predominant polymorphonuclear neutrophils is highly suggestive of acute bacterial inflammation and correlates with the severity of the

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inflammatory reaction. However in pregnant women this finding has to be interpreted cautiously as there is a physiologically raised WBC count. CRP levels confirm the presence of inflammation. Levels 1 mg/dl are present in acute appendicitis. Very high levels are seen in gangrenous appendicitis. Raised CRP with neutrophilic leucocytosis is highly suggestive of complicated acute appendicitis. A normal value of CRP has a negative predictive value of 97-100% for appendicitis (16). Urine examination may not always be diagnostic. However it rules out urinary tract infection especially in females. Presence of RBC's in the urine may be suggestive of irritation of the ureter or bladder by a severely inflamed appendix. A urinary pregnancy test is mandatory in female patients to rule out pregnant state as a ruptured ectopic pregnancy can closely mimic appendicitis. In advanced presentations such as perforated appendix, the total bilirubin will also be raised.

Once a tentative diagnosis of acute appendicitis is made the surgeon needs to confirm the diagnosis by imaging modalities before formulating a treatment strategy. Radiological investigations undoubtedly hold a promising position and have a definitive role to play (18).

A plain X-ray of the abdomen is commonly done in all patients presenting with abdominal pain (19). Presence of a faecolith in the form of a radiopaque density and localized ileus in the region of the right lower abdomen are suggestive of the diagnosis. Faecal loading may be seen in patients presenting as right iliac fossa pain who are suffering from acute appendicitis. A perforated appendix will hardly give rise to gas under the diaphragm.

Ultrasonography (USG) of the abdomen is first line investigation for diagnosis of acute appendicitis (20). It has high sensitivity of 85%. A normal appendix is usually not picked up by USG. However when inflamed it enlarges in size rendering it visible on USG. A non-compressible tubular structure with diameter greater than 6 mm is diagnostic. Presence of periappendiceal or pericaecal fluid may be a usual accompaniment. However the findings may not always be so distinct. The challenge is in diagnosing cases where symptoms don't match with abdominal signs. If studied in detail the findings on USG are: hypertrophy of the appendicular wall, disturbance of the normal layered structure, destruction of the wall, purulent fluid or faecoliths within the appendicular lumen, high periappendicular echoes suggest the aggregation of omentum and other soft tissues like the small intestine what is classically described as an appendicular lump and periappendicular accumulation of fluid suggests an abscess formation secondary to a perforation in most cases.

Computed tomography (CT) is the investigation of choice wherein USG is inconclusive. Findings on CT are: hypertrophy of the appendiceal wall, enlargement of the appendix (diameter 6 mm), appendix mass, periappendiceal abscess formation, presence of faccolith, increased density of the periappendiceal adipose tissue and fluid filled pouch of Douglas.

CT can reveal an enlarged appendix but cannot reveal the structure of the appendiceal wall unlike USG. Hence USG is superior to CT for assessing the severity of appendicitis depending upon mural changes in the inflamed appendix (21,22).

MRI is the first line imaging modality for pregnant patients of any gestational age with suspected appendicitis (23, 24). It has sensitivity of 100% and specificity of 98%. There is no increased risk to the foctus. However gadolinium enhanced MRI in pregnancy is associated with increased risk of rheumatological, inflammatory and infiltrative skin conditions since birth. Still births and neonatal deaths have also been reported.

Discussion

Early diagnosis is pivotal for good outcomes. Delay in diagnosis can lead to increased morbidity and even mortality. Hence treatment should commence immediately after a confirmation of diagnosis. The initial treatment is supportive. It comprises of rehydrating the patient, administration of antibiotics and analgesia. Once the patient is hemodynamically stabilised by way of reduced tachycardia, stable blood pressure and improved urine output can one contemplate surgical intervention. Associated co-morbidities if present should be optimized as far as possible.

After the initial resuscitative measures are completed a clinical reassessment is essential. Depending on the duration of symptoms and the interval between onset of symptoms and presentation to hospital, the surgeon needs to ascertain whether surgery is feasible or not. This is dictated by the absence or presence of a lump or features of peritonitis.If patient presents early that is before the formation of a lump then surgery is the mainstay of treatment. Open appendectomy (OA) or laparoscopic appendectomy (LA) is the treatment of choice, (25-34) It is a matter of experience or availability of expertise which dictates the approach. It is important that irrespective of the approach, the pathology has to be removed without any residual disease thereby having extremely low morbidity and no mortality at all.

Mac Burney's grid iron incision continues to be the standard open approach for appendectomy for established cases. However if one anticipates operative difficulties or in female patients then a right lower para median or lower midline approach is justified. Inversion of the stump which once upon a time was a standard practice is no longer done.

The inverted stump may serve as an apex for intussusception. Covering the stump with omentum prior to closure of the incision is a safe practice at it reduces significantly the chances of postoperative adhesions. LA has certain distinct benefits over the open procedure, (2) In female patients a variety of adnexal pathologies can closely mimic acute appendicitis and pose both a clinical as well as imaging dilemma. Laparoscopic approach allows confirmation of diagnosis. The standard three port technique enables

successful appendectomy in majority of patients. Extensive adhesions obscuring anatomical identification as seen in complicated appendicitis and adhesions due to previous lower abdominal surgery are indications for conversion. The other advantages of LA are decreased incidence of surgical site infections, pain, incisional hernias and short hospital stay, other forms of minimal access surgery are single incision laparoscopic surgery (SILS) and natural orifice transluminal endoscopic surgery. However lack of expertise and evidence to support these methods have led to decreased utilisation of these methods.

In patients who present late with the formation of a lump or phlegmon, conservative approach is advisable. This comprises of intravenous antibiotics and fluids till the inflammatory process settles followed by an interval appendectomy. This reduces the chances of damaging the adherent bowel and a faecal fistula.15-25% of patients undergo appendectomy for a non- inflamed appendix during the course of surgery for suspected appendicitis. This is described as negative or white appendectomy. The logic underlying this concept is that leaving behind a normal appendix will have a chance of developing appendicitis at a later date or an appendicular malignancy could be missed. However with the advent of excellent imaging modalities and laparoscopic technology the incidence of negative appendectomy should be as low as possible.

Perforated appendix may present with localized peritonitis or generalized peritonitis. Localized peritonitis is in the form of an abscess. An appendicular abscess needs individualized treatment. Besides supportive therapy, invasive intervention does become necessary. USG guided aspiration of the abscess cavity is the mainstay of treatment. However, if the cavity is large with significant features of sepsis then an extra peritoneal drainage is necessary. Generalized peritonitis will require a formal laparotomy. The inflamed and perforated appendix can be dealt with meticulously. More surgical options can be exercised in case of friability of the caecum such as Z stitch. This has the added advantage of clearing the peritoneal cavity of pus and administering a rigorous saline lavage. Adequate drainage of the peritoneal cavity is mandatory to prevent the formation of residual abscesses. This can be done even by laparoscopic approach. But drainage may at times be inadequate leading to residual abscess formation.

Appendicular involvement in ulcerative colitis (UC) may clinically closely simulate routine appendicitis. However the histologic appearance is similar to involved colon during a UC flare with chronic inflammatory changes and characteristic crypt abscesses. Therefore patients of UC who present with right lower quadrant pain and have features suggestive of appendicitis on CT should not be subjected to appendectomy. Instead they should be started on antibiotics as a part of conservative approach followed by colonoscopy after attaining a quiescent state or remission.

The inverted stump may serve as an apex for intussusception. Covering the stump with omentum prior to closure of the incision is a safe practice at it reduces significantly the chances of postoperative adhesions.LA has certain distinct benefits over the open procedure(26) In female patients a variety of adnexal pathologies can closely mimic acute appendicitis and pose both a clinical as well as imaging dilemma. Laparoscopic approach allows confirmation of diagnosis. The standard three port technique enables successful appendectomy in majority of patients. Extensive adhesions obscuring anatomical identification as seen in complicated appendicitis and adhesions due to previous lower abdominal surgery are indications for conversion. The other advantages of LA are decreased incidence of surgical site infections, pain, incisional hernias and short hospital stay (27-29).

Other forms of minimal access surgery are single incision laparoscopic surgery (SILS) and natural orifice transluminal endoscopic surgery (30-31). However lack of expertise and evidence to support these methods have led to decreased utilisation of these methods.In patients who present late with the formation of a lump or phlegmon, conservative approach is advisable. This comprises of intravenous antibiotics and fluids till the inflammatory process settles followed by an interval appendectomy. This reduces the chances of damaging the adherent bowel and a faecal fistula.

Similarly, patients of abdominal tuberculosis with lump in the right iliac fossa presenting with features suggestive of acute appendicitis should be managed conservatively. Appendiectomy performed in these patients can lead to the formation of an intractable faecal fistula(35). Surgical management of appendicitis during pregnancy is a great challenge. If surgery is contemplated the surgeon needs to evaluate the duration of pregnancy or the size of the gravid uterus and identify the location of the caecum and appendix ether by USG or by MRI. This will. enable precise choice of the incision. If expertise is available then a laparoscopic approach may be contemplated. However a calculated risk to the pregnancy always remains which has to be explained to the patient.

An inflamed appendix in an inguinal or femoral hernia sac is the biggest challenge to the surgeon. Appendectomy can safely be performed through the groin incision. However prosthetic repair of the hernia needs to be avoided as the chances of the prosthesis getting infected is extremely high despite all aseptic precautions being taken.

It is good surgical practice to open a specimen of appendix at the time of surgery. This has twofold purpose viz. confirmation of the inflammatory pathology and ruling out the presence of a tumour. The commonest tumour of the appendix is a carcinoid. Adenocarcinoma of the appendix is rare. As majority of appendectomies are done as emergency procedures at odd hours, it is advisable to complete the surgery. In the event of a tumour being found intraoperatively the surgeon should await the histological diagnosis. This should be followed by staging of the tumour. A definitive surgery should be performed at a later date.With more appendectomies being done laparoscopically the incidence of stump appendicitis is

increasing proportionately. Stump appendicitis is defined as the development of obstruction and inflammation of the residual appendix after appendectomy. As this is a poorly defined condition it has always been under reported. The presentation is indistinguishable from acute appendicitis. The patient may present with this condition as early as from 2 months to 20 years after appendectomy. The length of the residual stump is responsible for developing this condition. Traditional recommendation of the stump length was 5 mm to prevent stump appendicitis. However most recent recommendation is that it should be less than 3 mm long. This is specifically pertinent to laparoscopic approach. A single endoloop is sufficient. There is no need to apply two endoloops as the residual stump length increases significantly (36). A CT will reveal the following findings in stump appendicitis: remnant of appendicular lumen, luminal dilatation, pericaecal inflammatory reaction and abscess formation.

Stump appendicitis also has a high propensity to perforate to extent of 60% (37). Duplication of the appendix is a rare condition which could closely mimic stump appendicitis. Treatment is completion appendectomy either open or laparoscopically.

Conclusion

An elaborate history and meticulous physical examination is pivotal for early diagnosis of acute appendicitis in adults. Scoring systems are a useful adjunct to diagnosis. Imaging modalities and laboratory investigations help in ascertaining the clinical diagnosis. Surgery is the mainstay of treatment. However, the therapeutic approach will vary depending upon the stage at which the patient presents. Awareness of therapeutic strategies in situations with concomitant conditions is necessary to prevent untoward complications.

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Management of skin disorders through ayurvedic dermatology and internal Ayurvedic medicines

Review Article

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Abstract

Background: Skin (*Twak* in Sanskrit) is the largest organ and covers the entire body surface. It acts as a chemical barrier and protects the body from various external hazards. Ayurveda emphasizes that prolonged ingestion of food during indigestion, use of *Viruddha Ahara* (food–food interactions, food processing interactions) and restricted dietary habits i.e. intake of sour, salty, curd, fish etc. excessively are the main causative factors of skin disorders. These causative factors vitiate the Tridosha (*Vata, Pitta & Kapha*) and affect tissues of Twak (skin), Rakta (blood), Mamsa (muscles), and Ambu (lymphatic tissue) of the body. These seven factors are pathogenic materials of skin disorders. Objectives: The present review is assessed Skin disorders can be managed using Ayurvedic dermatology and internal Ayurvedic medicines. Methodology: Literature available in authoritative Ayurvedic texts, and the research articles published in the journals indexed in Google Scholars, PubMed etc. are the main sources of information for the present review. Result: In Ayurveda, the concept of dermatology is very well addressed. Skin diseases are described under the chapter of *Kushtha Roga* (minor and major). The drugs used in the management of skin disorders possess the properties of *Raktashodana, Raktaprasadhak, Rakta Shamana, Vishagna, Krimighna, Kandughna* and *Rasayana*. Pharmacologically, these drugs are identified as antifungal, antiviral, antibacterial as well as cosmetic agents which not only use in the treatment of skin infections but also for beautification of skin. Conclusion: It is concluded that a good number of herbal and compound medicines are mentioned in Ayurvedic texts for skin care, and management of skin diseases. Most of the dosage forms, including *Churna, Kwatha, Vati, Rasashaushadhies, Ghrita, Rasayana, Bhasma,* and others, are being administered internally as an ailments of skin disorders.

Keywords: *Ayurveda, Dadru,* Dermatology, *Kushtha, Skin, Twag roga*.

Introduction

Ayurveda, the ancient Indian system of medicine, offers a unique approach to dermatology, emphasizing the interconnectedness of skin health with overall well-being. The anatomy and physiology of the skin have been extensively studied in Ayurveda. The imbalance of doshas in the body is often reflected in skin diseases because the skin is the substrate that determines the quality of food. The ICD-10 classification of human disease lists more than 1,000 skin disorders a pattern dominated by a few conditions accounting for most of the skin disease burden (1). Despite this profound impact, skin disease continues to receive relatively little attention in the national or global health debate. Collectively, skin conditions were the 4th leading cause of nonfatal burden expressed as years lost due to disability in 2010. It is estimated that around 5 to 10% of consultations in general practice involve a skin problem (2).

Here's an overview of the Ayurvedic concept of dermatology and the screening of internal Ayurvedic medicines in managing skin diseases is being discussed. Literature available in authoritative Ayurvedic texts including the Ayurvedic Formulary of India (Part -I & II), and the research articles published in the journals indexed in Google Scholars, PubMed, SCOPUS, Web of Science etc. are the main sources of information for the present review. Additionally, the topic has been looked up online.

Ayurvedic concept of dermatology

In Ayurveda, skin diseases are described by the name of *Kushtha* (3) and has pointed at its multifactorial aetiology. Ayurveda emphasizes that prolonged ingestion of food during indigestion, use of *Viruddha Ahara* (food–food interactions, food processing interactions) and restricted dietary habits i.e. intake of sour, salty, curd, fish etc. excessively are the main causative factors of skin disorders. These causative factors vitiate *Tridosha* (Vata, Pitta, Kapha) and affect Twak (skin), Rakta (blood), Mamsa (muscles), Ambu (lymphatic tissues) of body. These

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seven are pathogenic materials for skin disorders (*Figure 01)* [4]. These skin disorders manifest in a variety of forms and innumerable types of presentations are observed. A total of 166 skin diseases are described in Brihatryi (text triodes of Ayurveda). They can be identified and be named according to involvement of Dosha (*Figure 02)*.

According to Ayurveda, Kushtha is one of the most chronic conditions. The Kushtha Roga is classified into two groups in the majority of Ayurvedic texts (5): Mahakushtha (major group of skin diseases) and Kshudrakushtha (minor group of skin diseases), which are further subdivided into seven and eleven varieties, respectively. In Ayurveda, a vast array of dermatological illnesses (6, 7) is caused by etio-pathogenesis, which includes the Sapta Dravya (seven factors): Vata, Pitta, Kapha, Tvacha, Rakta Mansa, and Ambu/Lasika (3, 4). The psychosomatic approach to treating dermatological illnesses, which includes both pharmaceutical and non-pharmacological treatments, was defined by the Ayurvedic medical system.

1. Kapala– The skin resembling a brown colored piece of a pot shard; rough, course and thin; painful and intractable.
2. Audumbara– Pain, burning sensation, redness, and itching hair and nodules developing resembling the fruit of udumbara (Ficus infectoria).
3. Mandala – Skin is white or red in color, tight, thickened, and smooth with round elevated patches joined to one another.
4. Rushyajivha – Skin is very rough, red in color outside and black inside, painful and resembling the tongue of black deer.
5. Pundarika– Skin white in the center and red at the edges similar to the petals of the lotus flower with reddish elevated patches.
6. Sidhma– Skin white or coppery red in color, thin, scales coming on scratching, more common on the chest, resembling the flower of pitcher gourd.
7. Kakanaka – Color of Gunja (Abrus precatorius), undergoing pus formation, very painful and caused by all three Doshas and which does not respond to treatment.
8. Ekakushtha– Absence of perspiration, large skin area resembling as scales of fish.
9. Charmakhya (Xeroderma)– The skin becoming thick like an elephant skin.
10. Kitibha (psoriasis)– Spots that are dark (black), hard and rough in touch.
11. Vipadika (skin cracks)– Hands and feet cracking and forming painful fissures.
12. Alasaka (cracks)– Developing red colour nodules with itching.
13. Dadru (ring worm)– Raised patches studded with small, itching, reddish papules.
14. Charmadala (impetigo)– Skin studded with red, intolerable pain, itching nodules.
15. Pama (scabies)– Small, plenteous, exudating pustules with itching and burning sensation. The same symptoms of Pama if appears on the hands and the buttocks with severe pain and itching is called Kacchu.
16. Visphotaka– Thin skin with boils, black or blackish red in color.
17. Shataru (erythema)– Innumerable small ulcers, red or blue in color with severe burning sensation and pain.
18. Vicharchika (eczema)– Nodules which have itching, black color and copious exudation.

Although most of skin diseases are described under the *Kushtha* (skin diseases) and *Kshudraroga* (minor group of diseases) but description of some other skin diseases is also described under headings of *Bahaya Visarpa, Vidradhi, Shotha, Nanatmaja Vyadhi, Shukaroga, Granthi, Arbuda, Upadansh* and *Shilipada*. Allergic conditions which are not included in any of these are described as *Udarda- Kotha-Uattkotha* (8, 9, 10). Dermatological complications of diabetes mellitus are described as *Prameha Pidika* (11).

Figure 1: Common pathogenesis of skin diseases

Pathogenesis of skin diseases in general

Vitiation of Tridosha (Vata, Pitta and Kapha) due to causative factors

↓

Movement of above abnormal Tridosha in whole body

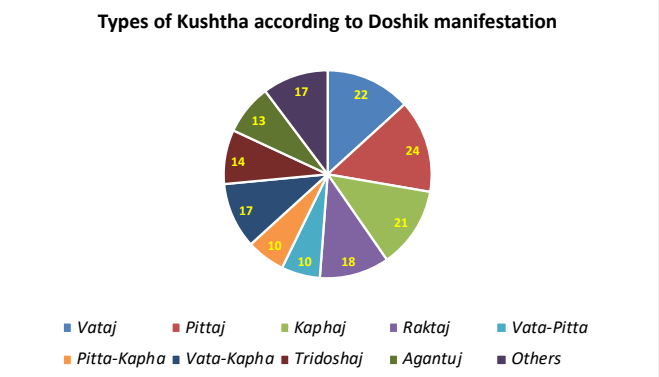
↓

Vitiation of tissues *viz.* Twak (skin), Rakta (blood), Mamsa (muscles), Ambu (lymphatic tissues) of the body

↓

Anatomical and physiological dysfunction of skin

Figure 2: Types of Kushtha according to Doshik manifestation



Management of skin diseases through internal Ayurvedic medicines:

In Ayurveda, skin diseases are very well managed by using of internal medicines as well as external application. A good number of single drugs and a variety of compound formulations are extensively used for the management of skin diseases *(Table 01)*.

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Table 01: Showing variety of internal medicines used in Kushtha and associated skin diseases

Sr. No.	Name of formulations	Dose	Indication (s)	References
1	Ayaskriiti (12)	12-24 ml	Kushtha (skin diseases)	A.H.Chi. 12/28-31
2	Babbularishta (13)	12-24 ml	Kushtha	Sh.S.M.Kh. 10/66-68
3	Ushirasava (12)	12-24 ml	Kushtha	B.R.Raktapittaadhikar, 137-141
4	Khadirarishta (12)	12-24 ml	Mahakushtha (group of major skin diseases)	Sh.S.M.Kh.10/60-65
5	Dantyadyarishta (12)	12-24 ml	Kushtha	A.H.Chi. 8/69
6	Dasamularishta (12)	12-24 ml	Kushtha	Sh.S.M.Kha.10/78-92
7	Madhukasava (12)	12-24 ml	Kushtha, Kilasa (vitiligo), Raktavikara (disorders of blood)	A.H.Chi. 10/47-50
8	Mrdvikasava (12)	12-24 ml	Kushtha	Sh.S.M.Kh. 10/39-43
9	Punarnavayarishtha (13)	12-24 ml	Kushtha, Kandu	B.R. Sotha -rogaadhikar, 192-196
10	Rodhrasava (Lodhrasava) (12)	12-24 ml	Kushtha	A.H.Chi. 12/24-27
11	Rohitakarishta (12)	12-24 ml	Kushtha	B.R.Plihayakritarogaadhikar, 84-87
12	Lohasava (12)	12-24 ml	Kushtha, Kandu (itching)	Sh.S.M.Kh. 10/34-36
13	Agastya Haritaki Rasayana (12)	6-12 g	Vali Palita wrinkles in skin and graying of hair)	A.H.Chi. 3/125-130
14	Kalyanaka Guda (12)	6-12 g	Kushtha	A.H.Kalpa 2/17-18
15	Danti Haritaki (12)	12-24 g of leha	Kushtha	A.H.Chi. 14/92-96
16	Madhusnuhi Rasyana (12)	12 g	Kushtha, Kilasa	Sahasrayoga, Lehaprakarana, 41
17	Bramha Rasayana (12)	12 g	Vali Palita	A.H.U. 39/15-23
18	Manibhadra Yoga (Guda) (12)	6 g	Kushtha, Svitra (leukoderma/ vitiligo)	A.H.Chi. 19/32
19	Shiva Gutika (12)	12 g	Kushtha	A.S.U. 49/193
20	Aragvadhadi Kwatha (12)	48 g	Kushtha, Kandu	A.H.Su.15/17
21	Trayantyadi Kwatha (12)	48 g	Kushtha	A.H.Chi. 13/11-12
22	Patoladi Kwatha (12)	48 g	Kaphapitta Kushtha (skin diseases caused by Kapha and Pitta)	A.H.Su. 15/15
23	Patolamuladi Kwatha (12)	48 g	Kushtha, Kilasa	A.H.Chi. 19/28
24	Brhan Manjishthadi Kwatha (12)	48 g	Kushtha, Upadamsha (Syphilis/Soft chancre)	Sh.S.M.Kh. 2/137-142
25	Kanchanaar Guggulu (12)	3 g	Kushtha	Sh.S.M.Kh. 7/95-100
26	Kaishor Guggulu (12)	3 g	Kushtha, Prameha Pidika (diabetic carbuncle)	B.R. Vataraktaadhikar, 97-105
27	Mahayogaraj Guggulu (12)	½ to 1 g	Kushtha	Sh.S.M.Kh.7/56-69
28	Saptavimashatika Guggulu (12)	6 g	Kushtha	B.R. Bhagandhararoga 16-21
29	Simhanad Guggulu (12)	3 g	Kushtha	B.R.Amavata, 130-135
30	AmritaBhallataka Ghrita (12)	12 g	Purana Twag Roga (chronic skin diseases), Vali, Palita	A.H.U 39/75-77
31	Brihta Ashwagandha Ghrita (13)	12 g	Vali-Palita	B.R.Vajikaradhikar, 52-62
32	Tiktaka Ghrita (12)	12 g	Pittaja Kushtha (skin diseases due to Pitta Dosha), Kandu, Ganda (maxillar prominence), Visphota (blister), Vyanga (pigmentation disorder)	A.H.Chi. 19/2-7
33	Dhanvantara Ghrita (12)	48 g	Kushtha	A.H.Chi. 12/19-23
34	Pancatikt Ghrita (12)	6 g	Kushtha	B.R. Kushthaadhikar, 114-117
35	Panchatikta Guggulu Ghrita (Nimbadi Ghrita) (12)	12 g	Kushtha	A.H.Chi. 21/57-60
36	Patoladi Ghrita (12)	12 g	Kushtha, Visarpa (erysipelas)	A.H.Chi. 13/6-9
37	Bramhi Ghrita (12)	12 g	Kushtha	A.H.U. 6/23-25

38	*Mahatiktaka Ghrita* (12)	*6-12 g*	*Kushtha, Visarpa*	*B.R. Kushthaadhikar, 118-124*
39	*Vajraka Ghrita* (12)	*6 g*	*Kushtha, Visarpa*	*A.H.Chi. 19/18*
40	*Gandhaka Rasayana* (13)	*1-3 g*	*Kushtha, Kandu*	*Y.R. Rasanadhikara, 1-4*
41	*Trikatu Churna* (12)	*1-3 g*	*Kushtha*	*B.R.Paribhasha, 16*
42	*Tripahala Churna* (12)	*3-6 g*	*Kushtha*	*Bhavaprakash, Haritkyadi Varga, 41-42*
43	*Navayasa Churna* (12)	*1 g*	*Kushtha, Prameha Pidika*	*B.R. Pandurogadhikar, 22*
44	*Narsimha Churna* (12)	*1.5 g*	*Kushtha, Vali-Palita*	*B.R. Vajikaranaadhikar, 30-40*
45	*Nimbadi Churna* (12)	*1-3 g*	*Kushtha, Svitra, Vicharchika, Kandu, Dadru, Kitibha Kushtha (depigmentation)*	*B.R.Vataraktaadhikar, 31-38*
46	*Panchanimba Churna* (13)	*1-5 g*	*Kshudra Kushtha (group of minor skin diseases), Mahakushtha (group og major skin diseases)*	*B.R.Kushthadhikar 86-91*
47	*Bhaskara Lavana Churna* (12)	*3 g*	*Kushtha*	*Sh.S.M.Kha. 6/138-144*
48	*Shiva Gutika (laghu)* (12)	*6 g (empty stomach)*	*Kushtha*	*Y.R. Rajyakshmaadhikar, 322*
49	*Kantavallabha Rasa* (12)	*125 mg*	*Kushtha*	*Vaidyayogaratnavali, 209*
50	*Makardhwaj*	*125 mg*	*Vali-Palita*	*B.R. Vajikaranaadhikar, 237-246*
51	*Rasa Karpura* (12)	*62.5 mg- 125 mg*	*Twag Rakta Roga (skin and blood diseases), Kandu, Mandala Kushtha (lepromatous lesion), Phiranga (Chancroid), Sphota (Boil)*	*R.T. Taranga 6/65-75*
52	*Panchamrita Parpati* (12)	*125-250 mg*	*Vali-Palita*	*B.R.Grahani-rogaadhikar, 461-466*
53	*Rasa Parpati* (12)	*250 mg*	*Kushtha*	*B.R.Grahani-rogaadhikar, 414-416*
54	*Tamra Parpati* (13)	*125 -250 mg*	*Kushtha, Dadru, Svitra*	*Siddhayogasangraha*
55	*Lauha Parpati* (12)	*250 mg*	*Kushtha, Vali-Palita*	*Siddhayogasangraha*
56	*Abhraka Bhasma* (12)	*125-375 mg*	*Kushtha, Twagroga*	*A.P. 2/132*
57	*Tamra Bhasma* (12)	*31.5 mg – 62.5 mg*	*Kushtha*	*R.T. Taranga 17/40-41*
58	*Lauha Bhasma* (12)	*120-250 mg*	*Kushtha*	*A.P. 3/280-281*
59	*Swarna Bhamsa* (12)	*15.5 mg-62.5 mg*	*Kushtha*	*Rasamrita, 3/16-18*
60	*Swarnamakshika Bhasma* (12)	*125-250 mg*	*Kushtha*	*R.S.S. 1/211-212*
61	*Shuddha Hartala (Hartala Bhasma)* (12)	*31.5 mg – 125 mg*	*Kushtha, Visarpa, Visphota, Svitra, Dadru (Taeniasis), Pama (eczema), Vicharchika (eczema)*	*A.P. 2/184-187*
62	*Shuddha Mandura* (12)	*500 mg- 1 g*	*Kushtha*	*R.T. Taranga 20/127*
63	*Mandura Vataka* (12)	*1 g*	*Kushtha*	*A.H.Chi. 16/16-19*
64	*Arogyavardhini Vati* (12)	*250mg – 500mg*	*Kushtha, Visarpa*	*R.R.S. Visarpadichikitsa, 20/106-112*
65	*Arkeshwar Rasa* (14)	*250 mg*	*Raktamandal Kushtha*	*R.S.S.*
66	*Bhutabhairav Rasa* (15)	*1 g*	*Nil, bahuruja, Dhatugat Arun shweta Analpa bhrush Kushtha , Ashadasha Kushtha*	*RA.Chi*
67	*Chaturbhuja rasa* (12)	*125 mg*	*Vali-Palita, Charmaroga (skin diseases)*	*R.S.S. Unmadachikitsa 20-26*
68	*Chaturmukha Rasa* (12)	*125 mg*	*Vali-Palita, Charmaroga*	*B.R.Vatavyadhiadhikar, 464-468*
69	*Chandraprabha Vati*	*125-250 mg*	*Shwitra*	*R.R.S.*
70	*Chintamani Chaturmukha Rasa* (12)	*125 mg*	*Vali-Palita*	*B.R.Vatavyadhiadhikar, 477-480*
71	*Kushtharakshas*	*12 g*	*Kushtha*	*R.R.S.*
72	*Kushathakuthar Rasa-1*	*250 mg*	*All Kushtha*	*R.R.S.*
73	*Kushthakalanalo Rasa* (14)	*750 mg*	*All Kushtha*	*R.S.S.*

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74	*Lakshmi Vilasa Rasa (Naradiya)* (12)	*250 mg*	*Kushtha*	*B.R.Rajyakshmadhiadhikar, 55-68*
75	*Mahalakshmi Vilasa Rasa* (12)	*250 mg*	*Kushtha*	*R.S.S. Kapharogachikitsa, 17-29*
76	*Manikya Rasa* (13)	*125 – 250 mg*	*Kushtha, Kandu*	*B.R. Kushtharogadhikar, 300-308*
77	*Navayasa Lauha* (13)	*250 mg*	*Kushtha*	*C.S.Chi. 16/70-71*
78	*Panchanana Rasa* (13)	*250 mg*	*Kushtha*	*Rasayogasagra, 35*
79	*Paribhadra Rasa* (14)	*3 g*	*Dadru Kushtha*	*R.S.S.*
80	*Rasaraj Rasa* (15)	*125 mg*	*Shwitra, Ashtadasha Kushtha*	*RA.Chi*
81	*Rasamanikya* (14)	*125 mg*	*Sputith,Galit Kushtha,vicharchi ka,Charmadal,vis phot,Mandal*	*R.S.S.*
82	*Shrinrapativallabha Rasa* (12)	*250 mg*	*Kushtha, Dadru, Upadamsha, Visarpa, Vaivarnya (discolouration)*	*B.R. Grahanirogadhikar, 523-532*
83	*Svarnabhupati Rasa* (12)	*250 mg*	*Kushtha*	*Y.R. Rajyakshmachikitsa, 332*
84	*Sarveshwar Rasa- 1* (16)	*125 mg*	*Prasupti Kushtha*	*R.R.S.*
85	*Sarveshwar Rasa-2* (16)	*250 mg*	*Supti, Mandal Kushtha*	*R.R.S.*
86	*Shwitrari Yoga* (15)	*375 mg*	*Shwitra*	*RA.Chi*
87	*Shwitrari Rasa* (16)	*125-375 mg*	*Shwitra*	*R.R.S.*
88	*Taleshwar Rasa* (15)	*6 gm*	*Kushtha, Kandu, sravyukta pidika, Galit Kushtha*	*RA.Chi*
89	*Talkeshwar Rasa (Siddha)* (15)	*125 mg*	*Ashtadash Kushtha*	*RA.Chi*
90	*Tripurantak Rasa* (16)	*375 mg*	*Sarvadoshaj Kushthanashak*	*R.R.S.*
91	*Udaybhaskar Rasa* (14)	*125 mg*	*Galit sputhit kushtha, vipul mandal kushtha, vicharchika, dadru,pama*	*R.S.S.*
92	*Vasanta Kusumakara Rasa* (12)	*125-250 mg*	*Vali-Palita*	*R.S.S.,Rasayanavajikaranaadhikar, 80-85*
93	*Vadvanal Rasa* (15)	*375 mg*	*Ashtadash Kushtha*	*RA.Chi*
94	*Varishoshana Rasa* (12)	*62.5 mg – 125 mg*	*Kushtha*	*B.R. Udarargaadhikar, 129-144*
95	*Varishoshan Rasa* (15)	*250 mg*	*Asadhya Kushtha*	*RA.chi*
96	*Vajra Vati* (14)	*500 mg*	*Pama*	*R.S.S.*
97	*Vijay Vati* (16)	*375 mg*	*Seven Kushtha*	*R.R.S.*
98	*Vijaybhairav Rasa* (14)	*125 mg with daily increase of 125mg for 7 days*	*All Kushtha, visphot*	*R.S.S.*
99	*Vishweshwar Rasa* (15)	*250 mg*	*Sravi kharsparsh asaukhyada sputhit asputhit visham asthisansthit shushka rakta krushna sadhya asadhya kushtha, Prasupta mandal Kushtha, Kakanak, Pundarik, Gajcharma, Dadru, Pama*	*RA.Chi*
100	*Vyoshadi Gutika* (16)	*1 g*	*Kushtha*	*R.R.S.*
101	*Yogaraja* (13)	*250 – 500 mg*	*Kushtha*	*Ch.S.Chi. 16/80-86*

The drugs used in the management of skin disorders possess the properties of *Raktashodana, Raktaprasadhak, Rakta Shamana, Vishagna, Krimighna, Kandughna* and *Rasayana*. *Haridra, Raktachandana, Nimba, Manjishtha, Aragvadh, Daruharidra, Guduchi* etc. are some frequently used herbal drugs which are the composition of many compound formulations (17, 18, 19). These drugs are identified as antifungal, antiviral, antibacterial as well as cosmetic agents pharmacologically which not only use in the treatment of skin infections but also for beautification of skin (20). For external application, *Taila* and *Lepa Kalpana* are used in regular practices. A variety of internal medicines are used in the management of skin diseases. The medicines like *Rasakarpura* (21), *Talakeshwar Rasa* (22), *Gandhak Rasayana* (23) etc. are some examples of *Rasaushadhies* (herbo-mineral medicines) which have also been proven as anti- microbial, anti-fungal medicines in the treatment of skin diseases.

Conclusion

It is concluded that a good number of herbal and compound medicines are mentioned in Ayurvedic texts

for skin care, and management of skin diseases. Most of the dosage forms, including *Churna, Kwatha, Vati, Rasashaushadhies, Ghrita, Rasayana, Bhasma,* and others, are being administered internally as an ailments of skin disorders.

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An Ayurvedic Approach to Benign Prostatic Hypertrophy: A single patient study

Review Article

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Abstract

Benign prostatic hypertrophy is benign enlargement of adenomatous part of prostate gland. It is present in patient in the 5th or 6th decade of the lives due to changes in the hormonal patterns in adult males chronic cripples the day to day activities. This is a case report of a 55 year male patient who presented with increased frequency of urination since past 5 months. Considering the symptom complex the case was diagnosed as a case of *Vata astheela*. The a course of ayurvedic medication such as *Chandraprabha vati, Mustadi kalpa* as internal medicine and lifestyle changes were advised for 4 months followed by a review after 7 months. The patient was also scored on measuring guidelines of which were seen to be promising.

Keywords: Adenomatous, *Chandraprabha Vati, Mustadi Kalpa, Vata Astheela*.

Introduction

Benign prostatic hypertrophy(BPH) is benign enlargement of adenomatous part of prostate gland. Symptoms of which include urinary frequency urgency hesitancy nocturia and incomplete emptying terminal dribbling and overflow or urge incontinence and complete urinary retention (1).

A remarkable new phenomenon is occurring through the world: old agers are becoming far more common. In most countries, the fastest growing age group is the oldest. Over the years, the occurrence of BPH and number of men seeking treatment for the condition are increasing. (2) BPH can be considered as a progressive disease. The treatment of BPH has begun to deviate from surgical to medical management for patients with mild to moderate symptoms, because of much advancement in the pharmacological management of the disease. (3)

According to Ayurveda *Basti* (urinary bladder) is the region where all the mootra roga occur: eg- *Mootraghata, Prameha, Shukradosha, Mootradosha* and other diseases (4). Among the 12 mootraghata where retention of urine is the cardinal feature, *vatashtila/mootrashtila* is considered in the context of BPH, as the nature of the pathology in both the conditions is similar: obstruction to the outflow of urine in *Vaatashtila* is due to an *ashtilavat granthi*(stony nodule), and in BPH, due to an enlarged, firm prostate. Ayurvedic pathophysiology describes that vitiated a type of vata (*Apaana Vata)*, which localises in between basti and *shakrut marga* (guda – the ano-rectum), produces a firm, stone-likegrowth. The growth in turn produces obstruction to passage of *vit, mootra and anila*, causing *adhmana of basti* and pain in the region of basti. (5)

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Table 1: Dosha dushya in Vata astheela

Dosha	*Vata(apana) predominant tridoshas.*
Dushya	*Rasa, Rakta. Kleda, Sveda, Mutra*
Agni (digestive power)	*Jatharagni mandhya*
Udbhava sthana	*Kostha*
Adhisthana	*Basti*
Srotas	*Mutravaha*
Srotodusti prakara	*Sanga, Vimarga-gamana. Sira, granthi*
Roga Marga	*Madhyma*
Vyaktha	During the act of micturition.

Patient information

A 57 year old male patient presented to OPD of Ayurved hospital with complaints in weak stream and dribbling of urine with nocturia on 10/12/2021 . The patient already had undergone modern medical management and found only minimal relief. A detailed history taking was taken followed by clinical examination. A per rectal examination also confirmed the diagnosis of Benign prostatic hypertrophy. The patient was asked as per IPSS (International Prostatic Scoring scale) (6) to asses his symptoms. The patient was advised dietary and lifestyle changes along with medication for a span of 90 days. The clinical examination details are as follows.

Clinical findings

Inspection

External urethral meatus appears normal in the case on inspection. No other gross deformity of the urethral opening was found (hypospadias). Foreskin was found to be normal and was fully retractable. As per patient information there was dribbling and weak stream of urine.

Palpation: No strictures were felt in the penile urethra

Per rectal examination

Per rectal examination and bimanual palpation confirmed medial lobe enlargement with a uniform soft swelling abutting the finger. Median ridge was not felt on per rectal examination.

Diagnostic Assessment

The patient was asked to fill the IPSS (International Prostatic Scoring scale) (6) to asses his symptoms.

Results

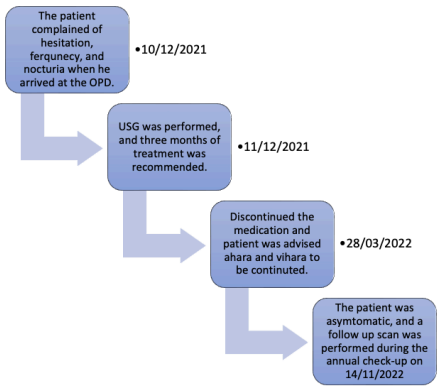
Table 2: International Prostatic Scoring Scale

Incomplete emptying	Before treatment (12.11.2021)	After treatment (14.11.2022)
Frequency	4	2
Urgency	4	2
Hesitancy	3	2
Weak stream	3	1
Straining	2	1
Nocturia	4	1
	20	10

It is evident that due to the a management of 3 months and with Lifestyle modification the patient showed a considerable production in the symptoms. The patient was asked to continue the non pharmacological management for another long time. The complaints of noturia during the course of medical management only. The symptoms above is again divided in two as obstructive and Irritative. The obstructive group comprise weak stream, dribbling and hesitancy while irritative symptoms are frequency, urgency and nocturia. There has been a significant reduction in the scoring of irritating signs in as per scoring.

Timeline of Intervention

Figure 1: Timeline



Intervention

The intervention in case of a BPH may be divided into two points

- *Dravya chikitsa* (medicinal regimes) (7)
- *Viharaja chikitsa* (non medicinal regimes)

Dravya chikitsa (Medicinal regimes)

Table 3: Drug and dosage

Drug	Dosage
Tab. Chandraprabha vati	250 mg tablet thrice daily after food for 3 months
Mustadi kalpa	1 tsp twice daily after food for a span of 3 month

***Chandraprabha vati* (8)**

Chandraprabha vati, Shilajathu well known for its *Rasayana* and *Vayasthapana* action is better in the disease related to old age. The properties like *Medhohara, Krimigna, Kaphahara* and *Lekhana* will help in minimizing the symptoms caused due to obstruction by a mass.

Amayika prayoga: *Mutraghata, Mutrasthila, Ashmari, Mutrakrucchra* etc.
Dosage: 1 karsha
Anupana: Jala (warm)

***Mustadi Kalpa* (9)**

In *Mustadi kalpa* most of the drugs have *Kashaya* and *Tikta rasa*, *Ushna Veerya, Madhura Vipaka* and *Kapha Vata Shamaka*. *Mustadi kalpa* is told in the context of Mootraghata chikitsa and it acts by the property of *Vyadhi hara.*

Amayika prayoga : *Mutraghata, Mutrasthila, Ashmari, Mutrakrucchra* etc.
Dosa : *1 karsha*
Anupana : Jala (warm).

In combination *Chandraprabha vati* and *Mustadi kalpa* acts by *Rasayana*, *Shothagna, Lekhana*, *Tridoshaghna* and *Vyadhihara* property.

Viharaja chikitsa (Non medicinal regimes)

The patient was also advised to follow the following viharas (habits and exercises) on a daily basis.

- Patient was encouraged to have double voiding before sleeping
- Was advised not to take alcohol or caffeine containing foods and dark chocolate specially in the 3 hours before sleep
- Also asked to minimise fluid intake after 7pm in the evening
- Was also advised undergo mooladhara bandha techniques to increase pelvic floor tone.

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Figure 1

S. No: 4067 Ref. By:
Dr. RUBINA

USG OF ABDOMEN / PELVIS

OBSERVATIONS:

Date: 11.12.2021

Hepatobiliary System:
The liver is normal in size and shows mild increased parenchymal echogenicity. No obvious focal parenchymal lesion or intra hepatic biliary duct dilatation. Portal vein and CBD shows normal course and calibre.
Gall bladder is well distended. No obvious wall thickening /intraluminal calculus / growth seen.

Spleen and Pancreas:
Spleen is normal in size and echogenicity. No focal lesion noted. Pancreas shows normal size and echogenicity. There is no evidence of focal mass, calcification, calculus or duct dilatation.

Kidneys:
Right kidney is normal in size measures ~116x46mm (parenchymal thickness ~20mm), shape and orientation. Normal echogenicity with normal corticomedullary differentiation noted.
No renal calculus /hydronephrosis.

Left kidney is normal in size measures ~114x48mm (parenchymal thickness ~ 20mm), shape and orientation. Normal echogenicity with normal corticomedullary differentiation noted.
No renal calculus /hydronephrosis.

Pelvic Structures: Urinary bladder is well distended, No wall thickening/intraluminal echoes.
Pre void volume - 520cc.
1st Post void volume – 375cc.
2nd Post void volume – 230cc.

Prostate: Is enlarged in size (volume – 38cc) with median lobe hypertrophy indenting bladder base.

Others: No ascites seen. No obvious bowel wall thickening noted.

No evidence of obvious defect in bilateral inguinal region.

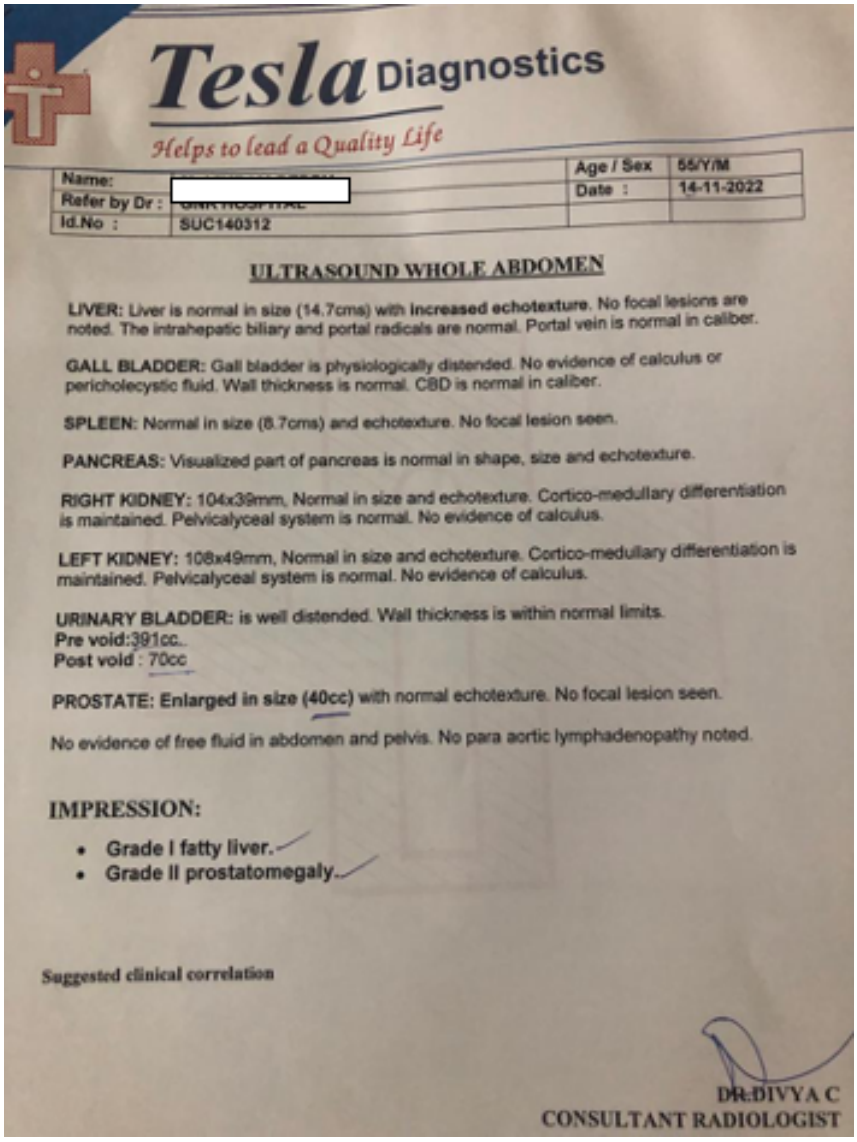
IMPRESSION:

- **Prostatomegaly with median lobe hypertrophy and significant post void residue.**
- **Grade I fatty liver.**

*** Advised clinical correlation.**

DR.
ASHITHA S. MBBS, DNB
RADIOLOGIST

Figure 2



Discussion

There are so many medicaments explained in our classics as; *Kashaya, Kalka, Sarpi, Lehya, Peya, Kshara, Madhya, Aasava, Swedana, Basti, Uttara basti* and *Ashmari hara chikitsa,* and also *Mutra udavarthahara chikitsa*. Thus, it is the medical management with various forms of formulations and in this study the drugs *chandraprabha vati* and *Mustadi kalpa* are in the form of *vati* and *churna* respectively taken.

In Chandraprabha vati, *Guggulu* that is known for S*hothagna Lekhana* and *Krimigna* helps to relieve obstructive symptoms and reduction in mass, which is already a proven anti inflammatory drug. *Swarnamakshika* known for *Mootrakricha* improves the bladder tone. Ksharas does act as alkalisers helps in reducing urine pH and controls the UTI. *Lavana* has *Shothagna* and *Lekhana* property, reduces the prostate size. Complimented action of herbal drugs will contribute further for the action of *Chandraprabhavati* is having *Vaatashaamaka* and *Rasayana* properties. These properties may help in enhancing the evacuation ability of bladder.

In Mustadi kalpa most of the drugs have *Kashaya* and *Tikta rasa*, *Ushna Veerya, Madhura Vipaka* and *Kapha Vata Shamaka.*

The *vihraja* management like avoiding caffeinated drink 3 hrs before sleep reduces the diuretic drive. Also alcohol as a known diuretic needs to be avoided.

With double voiding where the patient should voluntarily try to screenshot access amount of urine from his bladder. This significantly reduces the chances of post voidal urine to become stale and cause secondary infection inside the patient which further aggravates complain increase frequency of maturation.

The reduction of post voidal urine gave significant relief to the patient from the

Patient was advise to have no Fluids orally so that there is no diuretic potential in the Kidney during the sleeping hours.

Exercise like Mooladhara bandha (10) was advise to the patient to increase the tone of the muscles in the

perium by which features of hesitancy and urgency can be controlled.

The patient under went medical management for a span of 3 months following which the patient only practised mooladhara bandha as per protocols taught in during OPD visitation.

Technique 1

Stage 1:

- Sit in a comfortable meditative asana, preferably siddha/siddha yoni asana, so that pressure is applied to the perineal vaginal region.
- Close the eyes and relax the whole body.
- Be aware of the natural breath.
- Focus the awareness on the perineal vaginal region. Contract this region by pulling up on the muscles of the pelvic floor and then relaxing them.
- Continue to briefly contract and relax the perineal vaginal region as rhythmically and evenly as possible.
- Breathe normally throughout the practice.

Stage 2:

- Continue to breathe normally; do not hold the breath. Slowly contract the perineal vaginal region and hold the contraction.
- Be totally aware of the physical sensation.
- Contract a little tighter, but keep the rest of the body relaxed.
- Contract only those muscles related to the mooladhara region.
- In the beginning the anal and urinary sphincters will also contract, but as greater awareness and control is develop ed, this will minimise and eventually cease. Ultimately, only one point of contraction will be felt.
- Relax the muscles slowly and evenly.
- Adjust the tension in the spine to help focus on the point of contraction.
- Repeat 10 times with maximum contraction and total relaxation.

Technique 2 (with internal breath retention and *jalandhara bandha*)

- Close the eyes and relax the whole body for a few minutes.
- Inhale deeply, retain the breath inside and perform *jalandhara bandha*.
- Perform moola bandha and hold the contraction as tightly as possible. Do not strain.
- This is the final lock.
- Hold the contraction for as long as the breath can comfortably be retained.
- Slowly release moola bandha, then *jalandhara*, raising the head to the upright position, and exhale.
- Practise up to 10 times.

Breathing pattern while doing Moola Bandha – Perineum contraction

- The above practice may also be performed with external breath retention.

Awareness

- **Physical** – at the point of perineal contraction.
- **Spiritual** – on mooladhara chakra.

Sequence

- Moola bandha is ideally performed in conjunction with *mudras, bandhas and pranayamas*. If practised on its own, it should be performed after asanas and *pranayamas* and before meditation.

Precautions of doing Moola Bandha – Perineum contraction

- This practice should only be performed under the guidance of a competent teacher.
- Moola bandha raises the energy, and may precipitate hyperactivity.
- Do not practice during menstruation.

Moola Bandha (Perineum contraction) Benefits

- Moola bandha bestows many physical, mental and spiritual benefits.
- It stimulates the pelvic nerves and tones the uro-genital and excretory systems.
- It is helpful in psychosomatic and degenerative illnesses.
- It relieves depression and promotes good health.
- It helps to realign the physical, mental and psychic bodies in preparation for spiritual awakening.
- Moola bandha is a means to attain sexual control. It may be used to sublimate sexual energy for spiritual develop meant (brahmacharya), or for enhancement of marital relations.

Practice note

- Moola bandha is the contraction of specific muscles in the pelvic floor, not the whole perineum. In the male body, the area of contraction is between the anus and the testes.
- In the female body, the point of contraction is behind the cervix, where the uterus projects into the vagina.
- On the subtle level, it is the energising of mooladhara chakra. The perineal body, which is the convergence of many muscles in the groin, acts as a trigger point for the location of mooladhara chakra. Initially, this area is difficult to isolate, so it is recommended that *Ashwini* and *vajroli mudras* be performed in preparation for *moola bandha*.
- The Sanskrit word moola means ‘root’, ‘finally fixed’, ‘source ‘ or ’cause’. In this context it refers to the root of the spine or the perineum where mooladhara chakra, the seat of kundalini, the primal energy, is located. Moola bandha is effective for locating and awakening mooladhara chakra.(11)

Outcome and Conclusion

Significant reduction in post voided urination made the patient feel batter form his complaint of nocturia. The patient was advised medication for 3 month and has no remission for now, hence this modality can be considered as a treatment cases of benign prostrate hypertrophy. This case study proves that medication and dietary management can be helpful to reduce symptoms of BPH. The patient in this case has taken medication for 3 months after which patient was unable to continue medication despite having relief.

The patient was hence advised non medical management of fluid restriction and double voiding.

The patient by himself continued regimes of mooladhara bandha for a year. During the entire course the patient never had an episode of Lower Urinary tract infection. The patient also didn't have any active complaints of BPH. The effect of the reduction of size of prostrate cannot be completely transposed on medical management. During the initial days medical management may have reduced the symptoms but it seems that the yogic practice and non medical management made the disease well under control for a span of 9 months without medication. This case demonstrates the significance of yogic practices in management of a disease that is known to cause misery in elderly male population.

Patient consent

Informed consent was obtained from the patient for publication of this case report and any accompanying images are made available for verification by the editor of the journal.

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Declaration of conflict of interest: None

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The Role of Yogic Practices in Psychological Alteration: A Comprehensive Review

Review Article

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Abstract

This review explores the role of yogic practices in the physiological mechanisms and psychological alterations, focusing on the mental health benefits of yoga, particularly in managing stress, anxiety, depression, and emotional regulation. Yogic practices such as asanas (physical postures), pranayama (breathing techniques), and meditation are gaining recognition as complementary therapies for psychological well-being. Asanas help in reducing physical tension, promoting relaxation, and improving overall emotional regulation by fostering a mind-body connection. Pranayama techniques, through controlled breathing, activate the parasympathetic nervous system, lowering cortisol levels and inducing a state of calm, which helps alleviate anxiety and stress. Meditation, which encourages mindfulness, enhances emotional resilience by increasing self-awareness and promoting a non-judgmental attitude toward one's thoughts and feelings. These practices collectively contribute to a reduction in symptoms of anxiety and depression, while also improving cognitive function and emotional stability. While the existing literature strongly supports yoga's role in mental health, future research is needed to assess the long-term effects of yoga on psychological well-being. Additionally, studies should focus on integrating yoga into traditional mental health care approaches, providing an accessible, holistic strategy for improving emotional regulation and overall mental health outcomes. In this review we majorly describe that Yoga, through asanas, pranayama, and meditation, enhances emotional regulation, reduces stress, anxiety, and depression, and improves cognitive function. The findings suggest that yoga contributes to improvements in emotional balance, mental clarity, and stress reduction. Future research should explore its long-term effects and integration into mental health care.

Keywords: Anxiety, Depression, Emotional regulation, Mental health, Psychological alteration, Stress reduction, Yogic practices.

Introduction

The practice of yoga, originating from ancient Indian traditions over 5,000 years ago, has evolved from its spiritual and philosophical roots to become a widely accepted form of holistic exercise. Yogic practices, which encompass physical postures (asanas), controlled breathing exercises (pranayama), and meditation techniques, have been integrated into daily routines across the globe. While historically linked to spiritual growth and self-awareness, modern interpretations of yoga emphasize its physical, emotional, and psychological benefits, especially within the context of mental health (1).

In contemporary society, mental health disorders such as anxiety, depression, and stress have reached epidemic proportions. According to the World Health Organization, depression is one of the leading causes of disability worldwide, while anxiety disorders affect millions of individuals globally. Stress, a precursor to many psychological and physical conditions, has become an inescapable aspect of modern life, driven by factors like societal pressures, workplace demands, and the constant influx of information in the digital age (2). Conventional treatments for mental health disorders, such as pharmacological interventions and cognitive-behavioural therapies, though effective, often come with limitations such as side effects, accessibility challenges, or high costs. This scenario has led researchers and clinicians to explore complementary and alternative therapies, among which yoga has gained increasing attention.

The holistic nature of yoga is seen as particularly appealing in mental health care because it targets both mind and body, addressing emotional, cognitive, and physical components of well-being. Preliminary research has shown promising results, suggesting that yogic practices can reduce symptoms of anxiety, depression, and stress while enhancing mindfulness, emotional regulation, and overall psychological resilience (3). Furthermore, yoga's ability to modulate physiological processes such as the autonomic nervous

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system and the endocrine system underpins its efficacy in fostering psychological changes.

Despite growing interest in yoga's therapeutic potential, there remains a need for comprehensive reviews that consolidate current findings on its role in psychological alteration. This review will examine the existing literature on the mental health benefits of yoga, focusing on its impact on stress, anxiety, depression, emotional regulation, and mindfulness. The article will also explore potential mechanisms behind these psychological alterations, such as neuroplasticity, autonomic nervous system regulation, and the mind-body connection. Understanding these mechanisms will provide deeper insights into the efficacy of yoga as a tool for psychological well-being and inform its potential applications in clinical settings.

Thus, this review seeks to answer the following key questions:

(1) What are the psychological benefits of yogic practices, and how do they contribute to mental well-being?

(2) Through which mechanisms do yogic practices induce psychological alterations?

(3) What are the implications of incorporating yoga into conventional mental health care practices?

By addressing these questions, we aim to provide a comprehensive understanding of yoga's role in psychological alteration and its potential as a complementary therapeutic tool for mental health.

Stress Reduction through Yogic Practices

Stress, a significant contributor to mental health issues, impacts both psychological and physiological functioning. Studies suggest that yoga may help in modulating stress responses, leading to a reduction in cortisol levels and enhancing the parasympathetic nervous system, which promotes relaxation (4). Pranayama, or controlled breathing, has been particularly effective in reducing physiological markers of stress by regulating autonomic nervous system activity (5).

In a clinical study, yoga was found to significantly reduce stress in participants by balancing the sympathetic and parasympathetic nervous systems (6). This body of evidence supports the growing use of yoga as stress-reduction tool, making it an essential component of mental health care.

Alleviation of Anxiety and Depression

Anxiety and depression are among the most common psychological disorders affecting global populations. Numerous studies suggest that yoga may be effective in alleviating symptoms of both conditions. A meta-analysis conducted by showed that mindfulness-based interventions, which often include yoga, significantly reduced symptoms of anxiety and depression (7).

Yogic meditation techniques such as mindfulness meditation have demonstrated positive outcomes by promoting emotional regulation, increasing self-awareness, and reducing rumination (8). These findings indicate that yoga has therapeutic potential as a complementary treatment for anxiety and depression, fostering emotional balance and resilience.

Emotional Regulation and Cognitive Flexibility

Yoga's impact on emotional regulation is supported by evidence showing that yogic practices can help individuals process emotions more effectively. By encouraging mindfulness and present-moment awareness, yoga practices promote emotional clarity and reduce impulsive reactions to stressors (9).

Recent neuroimaging studies have linked yoga to increased gray matter volume in brain areas associated with emotional regulation, such as the hippocampus and prefrontal cortex (10). These changes may account for improvements in emotional resilience, reduced emotional volatility, and enhanced cognitive flexibility in individuals practicing yoga regularly.

Promotion of Mindfulness and Present-Moment Awareness

Mindfulness is a key component of many yogic practices, particularly meditation. Mindfulness involves cultivating present-moment awareness and nonjudgmental observation of thoughts and feelings. The mindfulness aspect of yoga has been associated with reductions in psychological distress, as well as improvements in cognitive function (11).

Regular yoga practice enhances mindfulness and self-awareness, which contributes to lower levels of stress, anxiety, and depression (12). By fostering a mindful approach to life, yoga promotes mental clarity and emotional well-being, improving overall psychological health.

Mechanisms Underlying Psychological Alteration

Several mechanisms have been proposed to explain the psychological alterations observed with yogic practices:

- **Neuroplasticity:** Research shows that meditation and yoga practices can enhance neuroplasticity, leading to structural changes in the brain that support emotional regulation and stress resilience (13). These structural changes may underlie improvements in mood and cognitive functioning.
- **Autonomic Nervous System Modulation:** Yogic practices, especially pranayama, modulate the autonomic nervous system, promoting relaxation by increasing parasympathetic nervous system activity (14). This mechanism is central to yoga's ability to reduce stress and anxiety.
- **Endocrine System Regulation:** Studies show that yoga influences hormone levels, including reducing cortisol (stress hormone) and increasing oxytocin (bonding hormone), which supports emotional connection and psychological well-being (15).
- **Mind-Body Connection:** By integrating physical postures with breath control and mental focus, yoga promotes harmony between the body and mind, which helps in managing stress and emotional regulation (16).

Conclusion

Yogic practices offer a powerful tool for psychological alteration, contributing to improved mental health and emotional balance. The evidence reviewed suggests that yoga is effective in reducing stress, anxiety, and depression, while also enhancing emotional regulation and mindfulness. The underlying mechanisms, including neuroplasticity and autonomic nervous system modulation, provide insight into how yoga influences psychological states. As yoga continues to gain popularity in mental health care, further research is needed to explore its long-term benefits and integration into therapeutic settings.

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Comparative analysis of Marma Vastu and Sira Marma Vidha Laxanas in The Context of Stroke Syndrome

Review Article

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Abstract

Marma shareera concepts were comprehensively discussed in Sharera Sthana of SushrutaSamhita, Marma locations; their types as well as the categorization of their fatalities are very much relevant till today. Here an effort is made to establish a relative hypothesis in vascularpathologies. A detail description is made on anatomical tissues or marma vastu especially on siraand dhamani which are involved in the marma injuries and also can be assessed by either in Sadhopranahara and vaikalykar marma viddha laxanas with the contemporary details of Brain stroke syndrome. The Brain stroke or Stroke syndrome is when blood flow to the brain isblocked or there is sudden bleeding in the brain. There are two types of strokes. A stroke that occurs because of blood flow to the brain is blocked called an ischemic stroke. Hemorrhagicstroke is due to bleeding into the brain by the rupture of a blood vessel. Hemorrhagic stroke maybe further subdivided into intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH).ICH is bleeding into the brain parenchyma, and SAH is bleeding into the subarachnoid spacemore specifically, nontraumatic (spontaneous) ICH.The brain cannot get oxygen and nutrients from the blood. Without oxygen and nutrients, brain cells begin to die within minutes. Theleaked blood results in pressure on brain cells, damaging them. The burden of stroke isincreasing in India; stroke is now the fourth leading cause of death and the fifth leading cause ofdisability. Research suggests that the incidence of stroke in India ranges between 105 and152/100,000 people per year. So, there is a need of understanding such disabilities by the meansof our concepts and try to avoid these by following certain regimes and activities which areexplained in our classics.

Keywords: *Marma shareera, Sira marma,* Brain stroke syndrome, *Madhyama Roga marga*.

Introduction

It is clear from Sushruta's explanation of the concept of marma viddha or marma injuries that the modern STROKE syndrome can be comprehended. Sushruta emphasized the fundamental bodily tissues and their physiological roles within the framework of Marma Shareera. The type of marma vastu and the type of fatality were used to determine the anatomical prevalence of these disabilities caused by marmaaghata and their prognosis. The tissue-level understanding of sira marma, or marma vastu, is discussed in this article along with some details on the characteristics of doshabhighata that have a lethal effect on marma locations.

Stroke is the leading cause of disability worldwide and the second leading cause of death. The Global Stroke Factsheet released in 2022 reveals that lifetime risk of developing a stroke has increased by 50% over the last 17 years and now 1 in 4 people is estimated to have a stroke in their lifetime. Stroke is a clinically defined syndrome of acute, focal neurological deficit attributed to vascular injury (infarction, hemorrhage) of the central nervous system. Stroke is the second leading cause of death and disability worldwide. Stroke is not a single disease but can be caused by a wide range of risk factors, disease processes and mechanisms.

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Definition of Sira:

ध्मानाद्धमन्यः स्रवणात् स्रोतांसि सरणात्सिराः | (1)

The term "saran function" also refers to nerve impulses or action potentials. It is important to understand that siras are not limited to the venous structures or veins that are most frequently compared.

Functions of Sira -

क्रियाणामप्रतीघातममोहं बुद्धिकर्मणाम् |
करोत्यन्यान् गुणांश्चापि स्वाः सिराः पवनश्चरन् | |
यदा तु कुपितो वायुः स्वाः सिराः प्रतिपद्यते |
तदाऽस्य विविधा रोगा जायन्ते वातसम्भवाः | | (2)

Vata, when flowing in its own siras, performs its duties without hindrance, enabling the mind to function correctly and preventing mental deviance.

चतुर्विधा यास्तु सिराः शरीरे प्रायेण ता मर्मसु सन्निविष्टाः | स्नाय्वस्थिमांसानि तथैव सन्धीन् सन्तर्प्य देहं प्रतियापयन्ति | (3)

The four types of siras found in the body are plac ed in the marmasthaan or near to the marma point, and they nourish the the structures like snaayu, mamsa, asthi and sandhi

Important Sira Marma located at the region of shiras

नीलधमनीमातृकाशृङ्गाटकापाङ्गस्थपनीफण...सिरामर्माणि || (4)

Neela,manya,matruka etc are grouped under sira marma.

References for Shiras:

प्राणाः प्राणभृतां यत्र श्रिताः सर्वेन्द्रियाणि च|

यदुत्तमाङ्गमाङ्गानां शिरस्तदभिधीयते (5)

Since the head is the part of the body that houses a living being's vital centers and all of its senses (indriya), it is the most important organ. Among all the other organs of the body, it is essential (uttama).

शिरसि इन्द्रियाणि इन्द्रियप्राणवहानि च स्रोतांसि सूर्यमिव गभस्तयः संश्रितानि (6)

According to Charaka, the prānavāhi srotāmsi of indriya are located in the head and are linked to the body in the same way that the sun is linked to its rays. Based on these observations, it can be inferred that the indriya-buddhi are also located in the head, as the head has been mentioned as the physical location of all indriya. The essential component of a sense that determines the ultimate understanding of the perceived object is called indriya [buddhi]. Therefore, the indriya buddhi is represented by logical centers located in the brain's cortex region.

The sypmtamatologies of Shiras related injuries:

शिरस्यभिहते

मन्यास्तम्भार्दितचक्षुर्विभ्रममोहोद्वेष्टनचेष्टानाशकासश्वासहनुग्रहमूकगद्गद त्वाक्षिनिमीलन (7)-

Injury to the shiras leads to manyastambha, ardita, chakshuvibhrama, udveshtana, cheshtanasha, kasa, shwasa, hanugraha, muka, gadgada, akshinimilana, gandaspandana, jrambhana, lalasrava, svarahani, vadana jihmatva etc

Pathophysiology of Brain Stroke

The brain, which is the main organ affected by stroke, is metabolically active and needs about 50ml/ 100g/min blood flow with an oxygen metabolic rate of 3.5cc/100g/min. If the blood flow drops below 10ml/ 100g/min, brain cell functions are severely affected, while neurons are unable to survive long at levels below 5ml/100g/min. In ischaemic stroke, disruption of blood flows to the brain for a few minutes' causes hypoxia and hypoglycemia, which leads to infarction of brain tissues. In hemorrhagic stroke, the haematoma causes compression of tissue resulting in tissue injury. The brain's regulatory mechanism attempts to maintain equilibrium by increasing blood pressure but the increased intracranial pressure forces out cerebrospinal fluid causing damage to circulation.

Vasculature of Brain

The paired internal carotid and vertebral arteries supply blood to the brain. Each internal carotid artery bifurcates into the anterior and middle cerebral arteries which supply the anterior cerebrum ('anterior circulation'). The vertebral arteries join to form the basilar artery (supplying the brainstem, cerebellum and pons) which bifurcates into the posterior cerebral arteries which supply the posterior cerebrum

Cerebral infarction

Cerebral infarction is usually due to atherothromboembolism. The source of embolism can be the heart, particularly when there is AF, or the rupture of large artery, atherosclerosis and subsequent thromboembolism from carotid arteries, vertebral arteries and aortic arch. Intracranial atheroma can lead to in situ thrombosis. Occlusion of the small perforating Occlusion of the small perforating lenticulostriate arteries in patients with sporadic or genetic small vessels diseases leads to 'lacunar' infarctions.

Cerebral small vessel disease (8)

Also known as cerebral microangiopathy, is an umbrella term for lesions in the brain attributed to pathology of small arteries, arterioles, capillaries, venules, or small veins. It is the most common cause of vascular dementia/cognitive impairment and is a major cause of ischemic and hemorrhagic strokes.

Non-traumatic Brain Injury

Refers to damage to the brain at the cellular level in the brain which is not hereditary, congenital, degenerative, or induced by birth trauma. Non-traumatic brain injury (also commonly referred to as an acquired brain injury or ABI) causes damage to the brain by internal factors, such as a lack of oxygen, exposure to toxins, or pressure from a tumor. Non-traumatic brain injuries can still result in psychological trauma.

Stroke

A stroke occurs when clots, plaque, or other particles block the blood supply to part of the brain, or when a blood vessel in the brain bursts. In either case, parts of the brain become damaged or die.

Lack of oxygen to the brain

Any event that causes oxygen to be cut off from the brain can cause a non-traumatic brain injury. When the brain is cut off from oxygen, it will result in a hypoxic or anoxic brain injury. This type of brain injury has its own set of symptoms and effects.

Brain aneurysm

A brain aneurysm occurs when a weakened blood vessel in the brain expands to the point that it can burst. Aneurysms can cause a brain injury whether the expanded blood vessel bursts or not. When the vessel

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expands, it can put pressure on areas of the brain that can cause an injury.

Infectious disease that affects the brain

Certain diseases like meningitis can attack the brain and cause health complications, including acquired brain injury

Symptoms of Brain Damage (9)

There are numerous symptoms of brain damage, whether traumatic or acquired. They fall into four major categories: Cognitive, Perceptual, Physical, Behavioral/ emotional

Cognitive symptoms of brain damage	**Shirogat / Sira marma Vidha lakshanas**
Difficulty processing information Difficulty in expressing thoughts Difficulty understanding others Shortened attention span Inability to understand abstract concepts Impaired decision-making ability Memory loss	मोह , उद्वेष्टन चेष्टानाष गद्गदता अक्षिन्मिलन लासस्राव स्वरहानि,

Interpretation

These vessels cause tissue damage, which leads to a variety of disorders affecting both the brain's structure and functions. In a similar fashion the vessels the siras—and particularly the siramarma structures also lead to the same clinical entities. Another point about the Doshabhighata concept that our Acharyas clarify is about the damage to these vessels, which are not only results in traumatic injuries but also manifests as obstructions in the vessel wall that are comparable to atherothromboembolism or thromboembolism.

Conclusion

1] शरीरं मन्दरुक्शोफं शुष्यति स्पन्दते तथा|सुप्तास्तन्व्यो महत्यो वा सिरा वाते सिरागते| (10) - Here a clear explanation is provided: when vitiated Vayu in sira gives rise to symptoms like *sirashoonyata, siratanutva, or siramahatva*, and it is evident that Vata is the primary cause for these symptoms, which are indicative of a kind of tissue and vascular injury called Doshabhighata.

2] मर्माभिघातस्तु न कश्चिदस्ति योऽल्पात्ययो वाऽपि निरत्ययो वा | प्रायेण मर्मस्वभिताडितास्तु वैकल्यमृच्छन्त्यथवा म्रियन्ते (11) – Injuries resulting from these marma locations undoubtedly cause tissue death or death of an individual even if they might not show any mild to severe symptoms.

3] मर्माण्यधिष्ठाय हि ये विकारा मूर्च्छन्ति काये विविधा नराणाम् | प्रायेण ते कृच्छ्रतमा भवन्ति नरस्य यत्नैरपि साध्यमानाः (12)- Treatment modalities may not yield adequate results for disorders or lesions affecting the marma site.

4] Concept of Doshabhighat in the Madhyama Roga marga and Marma patho physiology

त्रयो रोगमार्गा इति- शाखा, मर्मास्थिसन्धयः, कोष्ठश्च| मर्माणि पुनर्बस्तिहृदयमूर्धादीनि, अस्थिसन्धयोऽस्थिसंयोगास्तत्रोपनिबद्धाश्च स्नायुकण्डराः स मध्यमो रोगमार्गः;
पक्षवधग्रहापतानकार्दितशोषराजयक्ष्मास्थिसन्धिशूलगुदभ्रंशादयः शिरोहृद्बस्तिरोगादयश्च (13)

The basis of Roga Marga is Gati of Doshas. The specific and beneficial bond that the Doshas have with the Dhatus and organs is known as doshagati. The specific association in the pathological course is referred to as "rogamagga". Rogamarga is therefore the result and Doshagati is the cause in this stage of the sickness. Beyond prognosis, rogamagarga is important in the therapeutic domain. Furthermore, these three margas rely on one another for sustenance and the nourishment of these three margas is mutually dependent. So the Diseases of Madhyama rogamarga will have grave complications, and exhibit a large quantity of resistance. If the derailment of metabolic process, the complications surpass the resistance, and the grave and permanent structural or functional abnormality of the structures will occur. The reason Acharyas mentioned the kruchrasadhyata of Madhyama rogamarga is because its organs are always enclosed by various types of anatomical and physiological entities which makes it difficult to portray and not easy to access.

So, stroke entities can be compared to the concept of sira marma viddha laxanas, particularly vascular pathologies, and all nontraumatic brain pathologies can be considered as dosha abhighataja variety diseases and these are categorized under of madhyama rogamarga.

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Ayurvedic and Modern Nutritional Approaches for the Impact of Probiotics on Human Health: A Review

Review Article

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Abstract

Background: Human are unique reservoir of diverse and highly living community of microorganisms which collectively forms the human microbiome. The human gut is home to more than 100–1000 different types of microbes, all of which have a profound impact on host health by modulating the internal environment of the host. These organisms are essential for good digestion, anabolism and catabolism. Lactobacillus and Bifidobacteria are commonly used probiotic cultures. They play important role in maintenance of good health, immune system. In Ayurvedic classical text, Dadhi (Curd) and Takra (Buttermilk) are considered as the source of Probiotic, which is beneficial for the gut health. It is beneficil for the diarrhoel disease, constipation, gastroenteritis, inflammatory bowel disease, irritable bowel syndrome. Aims and Objectives: The purpose of the study is to highlight the various impact of probiotics on human health through Ayurvedic and Modern nutritional aspects. Method and Materials: This paper has been taken from various research paper from PubMed, Google scholar etc. Discussion & Conclusion: The microbiome diversity is likely important in health maintenance, and it is likely that broad-spectrum probiotics may increase the effectiveness of treatment. They have an important role in the maintenance of immunologic equilibrium in the GI tract through direct interaction with immune cells. Probiotics are useful and friendly microbes. There is a relationship between disease, health, the immune system, and changes in the microbiota. They are able to compete with the bad microbes and colonize our digestive system. They are also able to ferment our food to simpler by products and could promote our health by many different mechanisms. In Ayurveda, there are many Ahara Kalpana are mentioned, which are prepared by using Dadhi and Takra and those Kalpana are ensured as healthy microbiome.

Keywords: *Ayurveda,* Gut-microbiota, Microbiome, Probiotics.

Introduction

The concept of functional foods has gradually evolved in recent years to include dietary supplements that may have an impact on the composition and activity of gut microbes. For thousands of years, milk and dairy products have been a staple of human diets, contributing significantly to global human population growth and nutrition. (1) Probiotic bacteria, prebiotic fibres and synbiotic are the most widely used basic concepts in the creation of functional dairy products which are beneficial for the gut health.(2)

Probiotics (i.e. bacteria and yeast) are live microorganisms are beneficial for the health and studies has been found its role in the treatment of various diseases. (3,2) They have the potential to improve or prevent intestinal or systemic disease traits such as gut inflammation by restoring the composition of the gut microbiome and introducing advantageous functionalities to gut microbial communities. (3) Probiotics have been the subject of extensive study in the last few years, and numerous studies have demonstrated their critical function in preserving human health.

In Ayurveda, concept of microbiome and its importance in gut health is mentioned. Many Ahara Kalpana and Dravya described in Ayurvedic classical texts related to dadhi (Curd) or fermented product may provide maintain good health due to good bacteria. According to Acharya Charak, takra (buttermilk) is beneficial for the IBD (Inflammatory Bowel Disease). (4,5).

Probiotics in Modern Nutrition

The term of Probiotic is derived from Greek, which means “for life.” A probiotic is a live microbial feed supplement that exerts beneficial effects for the host via improvement of the microbiological balance in the intestine (Fuller, 1992,1997). (6,7) The most often used probiotics are lactic acid excretors, such as bifidobacteria and lactobacilli, which are added to fermented milk products or administered in lyophilized forms. Although, the traditional definition of probiotics states unequivocally that they are supplements containing living microorganisms. But there is conflict about whether dead microorganisms or even fragments of bacteria should be included. A non-viable dietary ingredient with selective fermentation that moves to the colon is called a prebiotic. The targeted stimulation of

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one or a small number of colonic bacteria's growth and/ or activity provides the benefit to the host. Prebiotic food ingredients have to be able to withstand hydrolysis or absorption in the upper gastrointestinal tract, act as a selective substrate for one or a small number of colonic bacteria, change the composition of the colon's microbiota to a healthier state, and have luminal or systemic effects that improve host health.(7,8) Good target species are lactobacilli and/or bifidobacteria. subsequently, probiotic and prebiotic combinations are known as synbiotics.(8) The combination would help the host by enhancing the microbial supplements implantation and survival. Foods serve as the primary delivery system for probiotic, prebiotic and synbiotics due to the nutritional advantages of microbiota management strategies. There might, however, also be some medicinal uses, albeit the majority of the study supporting this is speculative at this time.

Probiotics in Ayurveda

The production of medications using herbal, mineral, metallic, marine, and other substances is the focus of Ayurvedic pharmaceutics.(9) Dietetic preparations are another area of focus. Pathya plays a crucial role in preserving health. Ayurvedic pharmaceutics include a lot of dietary preparations, but not many fermentation products. Sandhana kalpanas are a type of preparation that has a hydroalcoholic quality. (10) These preparations provides both nutritional benefits and medicinal effects. These dietary supplements and formulations function as prebiotics and probiotics.(7)

Therapeutic preparations known as Asava-Arishtas (fermentation preparations) and a few pathya kalpanas (dietary preparations) are fermented products used in Ayurvedic pharmaceuticals. These preparations most likely have prebiotic and probiotic effects. (11) It mentions about sandhana kalpana, fermentation preparation made by using dravya (liquid ingredients) and other therapeutic medications placed in a closed, inert vessel and allowed to carry out fermentation for a predetermined amount of time (11).

Fermented beverages made with Curd (Dadhi) and butter milk (Takra) consist various probiotic properties and in Ayurvedic classical text books, it is mentioned that they are beneficial for the treatment of various diseases such as constipation (vishtambha) or malabsorption problems (Grahini), haemorrhoids (Arsha) etc. as well as in Ayurveda the properties of the curd are described as it is appetiser (deepan), ruchikarak (tatse enhancer). Studies reveals that Dadhi have probiotic effect due to presence of lactic acid bacteria which is beneficial for gut health and helpful in the treatment of diarrhoea(11,12).

Classification of Dadhi according to Ayurveda

1	Pranija Dravya (animal source) (13)
2	Gorasa varga or Ksheera vikruti (milk products) (14)
3	Sneha varga (fats)
4	Dadhi varga (fermented milk)

Types of Dadhi according to Taste by Acharya Susruta (15)

1. Madhura (Sweet)
2. Amla (Sour)
3. Atyamla (Excessive Sour)

Properties of Dadhi

Dadhi cures chronic coryza, Visham Jwara (irregular fever), diarrhoea, Aruchi (anorexia), Mutrakrichha (dysuria), and Krishta (emaciation). It is snigdha (unctuous), ushna (hot) & taste is kasaya (astringent). It is a revitalizer, aphrodisiac, and beneficial. According to Acharya Susruta, curd prepared from boiling milk is of high quality, alleviates Pitta and Vata, and enhances Dhatu, Agni, and strength. It is also appetising. (16)

Dadhimastu is a liquid part of a dadhi (curd) is amla (sour), kasaya (astringent), madhura (sweet) in properties. It diminishes Kapha and Vata, Laghu (easy to digest) and having Prinan (nourishment), Sadhya Balavardhan (instant strength booster), Pralhadankarmas (exhilirating). It removes trishna (thirst), Klama (exhaution) and works as a Strotovishodhana (purification of all the channels) and Ruchikarak (taste enhancer)(17). Curd's residual fatty layer is thick, aphrodistiac, vatapacifying, helps to increase semen and Kapha while decreasing Agni. (18)

Curd without the supernatant layer is Ruksha (rough), Grahi (absorbant), gas-forming, aggravates Vata, and easy to digest. On the other hand, Laghu (easy to digest) increases digestive power and is relishing. Jaggery and curd together are unctuous, wholesome, hridya (good for heart) and Vata pacifying.

Properties and Mode of Action of various types of Dadhi (19)

S. No.	Types of Dadhi	Properties	Mode of Action
1	Gavya dadhi (cow curd)	Sneegdha (unctuous), Madhur vipaki (sweet in final transformation),	Deepan (stimulates digestive power), promotes strength, alleviate Vata, relishing
2	Mahish dadhi (Buffalo Milk)	Madhur vipaki (sweet in final transformation), aphrodisiac	Pacifies Vata and Pitta, increases Kapha
3	Aajya dadhi (Goat curd)	Laghu (easy to digest), pacifies Kapha and Pitta, alleviates Vata, useful in Kshaya	Swasa (dyspnoea), Arsha (piles), Kasa (cough)

Effects of Dadhi (20)

Types of Dadhi	Effect on Dosha
Madhura	Vatashamana, Pittashaman, Kaphakar
Amla	Vatashamana, Pittakarak, Kaphakar
Atyamla	Vatashamana, Pittakarak, Raktadushtikar

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Effect of Dadhi on Dhatu, Mala, Strotas, Agni

Effects on Dhatus	Dhatuvardhan
Effects on Mala	Mutravardhan
Effect on Strotas	Abhishyandi
Effect on Agni	Deepan

Various types of Curd and its mode of Action (21)

S.No.	Type of Dadhi	Properties and Mode of Actions of Dadhi
1	Gavya dadhi (cow curd)	Sneegdha (unctuous), Madhur vipak (sweet in final transformation), Deepan (stimulates digestive power), promotes strength, alleviate Vata, relishing
2	Mahish dadhi	Madhur vipak (sweet in final transformation), aphrodisiac, pacifies Vata and Pitta, increases Kapha
3	Aajya dadhi (goat curd)	Laghu (easy to digest), pacifies Kapha and Pitta, alleviates Vata, useful in Kshaya, Swasa, Arsha, Kasa

Impact of Probiotics on Human Health

Probiotics have been defined by The Food Agricultural Organization/World Health Organization (FAO/WHO) as "live microorganisms which when administered in adequate amounts confer a health benefit to the host." They have been used for centuries in the form of dairy-based fermented products, but the potential use of probiotics as a form of medical nutrition therapy has not received formal recognition.

Additionally, there continues to be more to learn about the relationship between colonic bacteria populations and health. So as much as possible, pre- and probiotic applications require an understanding of the impact of colonic bacteria on host health. Particularly when it comes to the microbiota, the colon can be an organ of both health and sickness.

It has been suggested that disrupting the delicate balance in the gastrointestinal tract can contribute to diarrhoea (antibiotic-associated diarrhoea, traveler's diarrhoea, intestinal infections), gastroenteritis, constipation, irritable bowel syndrome, inflammatory bowel disease (Crohn's disease and ulcerative colitis), food allergies, and certain cancers. On the contrary, a balanced or "normal" enteric flora may competitively exclude possible pathogenic organisms, stimulate the intestinal immune system, and produce nutrients and other substances such as short-chain fatty acids, vitamins, amino acids (arginine, cysteine, and glutamine), polyamines, growth factors, and antioxidants.

There are some studies which claims the impact of probiotic in immune enhancement, intestinal health, lowering of cholesterol, prevention of cancer, diabetes control, diarrhoeal disease but the dosages requirement and its evidence related to probiotic treatment is still about to further study.[22,23]

Discussion & Conclusion

According to the study by Martin R et.,al. (2003)[24] and Marin ML et.,al.(2016)[25] LAB (Lactic Acid Bacteria) are naturally present in cow milk as well as human milk. They used for the fermentation of milk since a hundred of years and they increase the durability of the milk (25). Study by Elie Metchnikoff has shown the benefit of fermented dairy products to balance the microbes in gut (26).

Probiotics are a beneficial microorganism, which maintain flora intestine and thus enhances immunity. By protecting the intestinal surface against pathogen adhesion, preserving the epithelial barrier, and regulating and maturing the immune system appropriately, probiotics can enhance host protection. Additionally, by altering intestinal flora, probiotics can heal specific illnesses by enhancing host immunity. Probiotics, intestinal flora, and immunity have all been shown to be closely related in recent times (27).

Scientific research demonstrates that adding probiotics to diet can have positive effects on health. For the treatment and prevention of some disorders, this article appears sufficient, but for others, it is only encouraging or even debatable. Bowel diseases such as diarrhoea caused by antibiotics, lactose intolerance, allergies, and viral diarrhoea, among others, have the best documented side effects. These products are growing in popularity and are starting to represent one of the biggest functional food sectors at the same time that consumer awareness is rising. The non-dairy market is constantly changing due to advancements in food technology and rising consumer demand, but dairy products especially curd or yoghurt remain the most significant means of delivering probiotic bacteria to consumers. However, probiotic product development is still in its early stages.

Many Ayurvedic medications are said to have excellent Aupanam and Pathya in fermented milk. Takra and dadhi are considered natural probiotic diets since they are rich in beneficial bacteria that are good for the body overall, including the intestines. Other examples of fermented milk dosage forms are Takrarhista etc., Human gut microbiota is crucial to health, and a variety of disorders can be treated and prevented by modifying the gut microbiota. Recent cutting-edge studies demonstrate that the bacteria present in fermented milk can treat a wide range of digestive illnesses. While probiotics are an emerging area in the treatment of obesity and cancer, Takra was also utilised in ancient medicine to cure Gulma, Madoroga, Mandagani, and other conditions. It can also be said that traditional Indian medical science has contributed to the field of medicine by developing the idea of symbiotic relationships and using them to cure chronic illnesses. It is also urgently necessary in the present to ensure that the health claims and guidelines around the use of fermented milk are solidly established through carefully planned large-scale clinical investigations.

Probiotics hold tremendous potential for treating or preventing a variety of intestinal diseases. Probiotics help restock our digestive tract with beneficial microbes

to counterbalance the harmful ones. Moreover, the efficacy demonstrated for a particular strain of bacteria may not necessarily transfer to other probiotic species. Furthermore, there is still much to learn about the fundamental mechanisms behind the activity of probiotics. The research on explain how human health and well-being are impacted by native microbiomes and develop accurate models to anticipate how probiotic strains and native gut microbiota still needs to thoroughly explore.

Thus, a search of both modern and ancient literature and research articles about the probiotic qualities of curds has been carried out in relation to their usage in treating digestive diseases.

To ascertain which probiotics and dosages are most effective for certain patients, as well as to show their safety and limitations, but more research in the form of controlled human studies is required. Probiotics have a lot of potential as therapeutic or preventive treatments for diferent intestinal illness

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The Impact of Yoga Practice on Pulmonary Function: A Comprehensive Review

Review Article

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Abstract

Background: Pulmonary function is crucial for overall health, as it involves the efficient exchange of gases, ventilation, and maintenance of homeostasis. Yoga, particularly pranayama (breathing exercises), has been increasingly recognized for its potential benefits on respiratory health. However, the integration of yoga into clinical practice for managing respiratory conditions requires further exploration. Objectives: This review aims to evaluate the impact of yoga practices, with a focus on pranayama, on pulmonary function across various populations. The objectives include identifying patterns in existing research, understanding the physiological mechanisms involved, and providing recommendations for future research and clinical applications. Methods: A systematic literature review was conducted using databases such as PubMed, Scopus, and Web of Science. Studies published over the past 20 years that assessed the effects of yoga on pulmonary function in both healthy individuals and those with respiratory conditions were included. Data extraction focused on study design, population characteristics, type of yoga practice, duration, frequency, and measures of pulmonary function. Results: The review found consistent evidence that yoga, particularly pranayama, significantly improves pulmonary function, including increases in Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), and Peak Expiratory Flow Rate (PEFR). These benefits were observed in both healthy individuals and those with chronic respiratory conditions such as asthma and COPD. The underlying mechanisms include enhanced respiratory muscle strength, reduced inflammation, and better autonomic regulation. Conclusion: Yoga, especially pranayama, shows significant potential as a complementary intervention for improving pulmonary function. The findings support the integration of yoga into clinical practice for respiratory care, though further research is needed to optimize its use, particularly in terms of long-term effects and specific mechanisms. Personalized yoga interventions could be beneficial in enhancing respiratory health and overall well-being.

Keywords: *Yoga,* Pulmonary Function, Respiratory Health, Pranayama, Breathing Techniques, Respiratory Conditions, Integrative Medicine, Healthcare, Holistic Wellness.

Introduction

Pulmonary function research yields a plethora of supplementary data on health outcomes in general, since it includes respiratory measures such as ventilation and lung capacity (1). Listed homeostasis maintenance as one of the many important physiological roles played by the respiratory system. The generation of energy, the exchange of oxygen, and general health are all dependent on lungs that are in good condition. If you want to know how your respiratory system is doing and how it could affect your heart and muscles, you need to get a pulmonary function test.. Numerous clinical problems, including respiratory disorders and systemic diseases, are strongly correlated with impaired pulmonary function (1, 2).

Research into possible treatments that can enhance respiratory characteristics is extremely important because of the vital role that the lungs play in general health. The ancient practice of yoga, which incorporates physical postures, breathing exercises, and meditation, has lately gained significant appeal due to its potential health advantages. Yoga, according to a plethora of research, aids in maintaining healthy lung function. Much recent study has focused on how yoga affects lung function. What follows is a synopsis of the vast majority of these studies. The goal of this study is to find patterns and similarities in the various studies that have looked at how yoga affects breathing. In addition, the review will help find current gaps in knowledge, which will pave the way for future research efforts. Reviewing the literature on yoga's possible effects on improving pulmonary function and, by

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extension, general health, this work adds to the expanding body of information in this area.

Methodology

Literature Search Strategy

To ensure a comprehensive review of the impact of yoga practice on pulmonary function, a systematic literature search was conducted across multiple databases, including PubMed, Scopus, Web of Science, and Google Scholar. The search included articles published from inception to the present, with an emphasis on studies published in the last 20 years to capture the most recent findings. The search terms used were: "yoga," "pranayama," "pulmonary function," "respiratory health," "lung capacity," "COPD," "asthma," and "breathing techniques." Boolean operators (AND, OR) were used to refine the search results, and reference lists of relevant articles were also scanned for additional studies that may have been missed in the initial search.

Inclusion and Exclusion Criteria

The inclusion criteria for the review were as follows:

- Studies that evaluated the effects of yoga, specifically pranayama, on pulmonary function.
- Articles published in peer-reviewed journals.
- Research conducted on human subjects, including both healthy individuals and those with respiratory conditions (e.g., asthma, COPD).
- Studies that used objective measures of pulmonary function, such as Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), Peak Expiratory Flow Rate (PEFR), and other relevant respiratory parameters.
- Both randomized controlled trials (RCTs) and observational studies were included to provide a broad perspective.

The exclusion criteria were

- Studies that focused solely on the psychological aspects of yoga without addressing pulmonary function.
- Research conducted on animals or in vitro studies.
- Articles not available in English.
- Review articles, commentaries, and editorials were excluded unless they provided significant data that was not covered in primary studies.

Data Extraction and Synthesis

Two independent reviewers screened the titles and abstracts of all retrieved articles. Full-text articles were then reviewed to determine their eligibility based on the inclusion and exclusion criteria. Discrepancies between the reviewers were resolved through discussion or by consulting a third reviewer.

For each study included in the review, the following data were extracted:

- Study design (e.g., RCT, cohort study, case-control study)
- Population characteristics (e.g., age, gender, health status)
- Type of yoga practice or pranayama technique used
- Duration and frequency of the yoga intervention
- Measures of pulmonary function assessed
- Main findings related to the impact of yoga on pulmonary function

The extracted data were then synthesized to identify common patterns, trends, and gaps in the literature. Studies were categorized based on the population (healthy vs. those with respiratory conditions), type of yoga intervention, and the pulmonary outcomes measured.

Quality Assessment

The quality of the included studies was assessed using the Cochrane Risk of Bias tool for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies. Studies were evaluated based on criteria such as randomization, blinding, sample size, the validity of outcome measures, and the appropriateness of statistical analyses. Studies with high risk of bias were noted, and their findings were interpreted with caution in the synthesis.

Analysis and Interpretation

A narrative synthesis approach was employed to analyze the data due to the heterogeneity in study designs, populations, and outcome measures. Key findings from individual studies were summarized and discussed in relation to the broader literature. Where possible, results from meta-analyses were included to provide a quantitative summary of the effects of yoga on pulmonary function.

The analysis focused on:

- The overall effectiveness of yoga in improving pulmonary function.
- Specific benefits of different pranayama techniques.
- The impact of yoga on specific populations, including those with chronic respiratory conditions.
- Identification of physiological mechanisms by which yoga may influence pulmonary health.

Reporting and Conclusion

The results of the review were organized thematically, with separate sections addressing the impact of yoga on healthy individuals, those with respiratory conditions, and the underlying mechanisms of action. The review concludes with a discussion of the implications for clinical practice, the potential for integrating yoga into respiratory rehabilitation programs, and suggestions for future research.

The methodology was designed to provide a rigorous and comprehensive analysis of the available literature, ensuring that the conclusions drawn are based on a thorough evaluation of the evidence.

Results

Yoga and Pulmonary Function

· Yoga and Healthy Individuals:

The benefits seen in a study with healthy subjects and lung function may also be experienced by frequent yoga practitioners. The major finding that (1) reached after

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their comprehensive analysis was that yoga improved the lung function of healthy adults. Research has demonstrated that yoga can improve respiratory health in a number of ways, including increasing lung capacity and decreasing lung efficiency.

Also, in a study of teenagers who were generally healthy, (3) investigated if yoga may enhance pulmonary biomarkers. This study adds to the growing body of data that yoga treatment may have an effect on lung function.

In their assessment of a group of middle-aged, healthy, non-exercising persons, (4) looked at the possible therapeutic effects of yoga on the respiratory and muscular systems. Even people who don't often engage in vigorous physical activity found that breathing became easier for everyone once they began practicing yoga. A study conducted (5) found that pranayama, which are breathing techniques used in yoga, enhanced lung function.

· Yoga Intervention and Specific Populations

Research published by (6) found that aerobic exercise and yoga improved the health and lung function of young women with athletic gifts. Longitudinal comparisons of aerobic exercise and yoga's impact on respiratory parameters enriched the existing literature on the subject. A group of healthy women were studied to determine if yoga affected their body composition and cardiovascular health (7). There is some preliminary evidence that yoga may have a positive effect on respiratory health.

Multiple researches involving a diverse range of individuals and healthcare settings have found that yoga improves lung function. By pooling their results with those of other studies, researchers can learn more about the possible advantages of yoga treatment for respiratory health. More and more evidence is pointing to the beneficial effects of yoga on respiratory disorders.

Yoga Breathing Techniques and Pulmonary Function

Finding out how Bhastrika Pranayama, or bellows breath, affects important lung function metrics was the goal of the (8) study. Analysing each data separately can help you understand how this pranayama strategy could impact lung measures. What follows is new data regarding the interdependent relationships between pranayama teachers and their pupils' breathing exercises. Some of the symptoms of chronic respiratory disorders include difficulty sleeping, excessive weariness, and shortness of breath. To what extent may yoga breathing practices alleviate these symptoms. That was the question (9) set out to answer. The major objective of this research was to examine the impact of the intervention on the participants' self-assessments of respiratory health and lung function. Additionally, the study investigated the connection between the two. This study adds to the growing amount of evidence suggesting that pranayama can help those who have breathing difficulties. Aiming to examine the effects of pranayama breathing techniques on pulmonary function, general health, and asthma management, (10) planned to collect. In this study, we lay out a randomised controlled experiment to see whether certain breathing techniques improve respiratory health and reduce asthma symptoms. As an added bonus, this supports the idea that these methods could help asthma sufferers from both an objective and subjective perspective.

Meta-Analysis and Systematic Reviews

A large body of information regarding yoga's effect on lung function was gathered in the study by (2). Three independent investigations yielded these results. The meta-analysis deepens our understanding of how yoga intervention affects the outcomes of lung diseases by providing a comprehensive review. By simplifying the procedure for detecting trends and patterns across many research topics, this study contributes to the academic community. The beneficial impacts of yoga treatment on respiratory muscle strength and pulmonary function were investigated in a comprehensive literature review and meta-analysis by (11). A lot of their focus was on breathing exercises. This research contributes to the limited body of knowledge regarding the effects of yoga on lung health by combining the results of this investigation with other investigations. It is the goal of systematic assessments to collect and analyse all pertinent data in order to draw findings that are useful for both professional researchers and practitioners. After reviewing the studies in detail, it is evident that the yoga-related improvements in lung function are mostly attributable to the pranayama activities. In order to create more effective and tailored respiratory health regimens, it is essential to customise yoga treatments to each person's particular breathing patterns, according to the research. We will try to understand the physiological mechanisms at work in the following session as we examine how pranayama practices may affect lung function.

Mechanisms and Pathways

To study how yoga affects lung function, one must be well-versed in the physiological mechanisms at work. Our primary focus in this study was on studies that looked at how yoga's breathing methods could affect respiratory parameters. Practicing pranayama, like other yoga practices, can help to control breathing by drawing attention to breath and tensing muscles. (12) Emphasise the need of actively exercising the muscles that facilitate breathing in their complete yoga breathing training.

Asthmatics and others with other respiratory disorders have shown promise in using yoga to decrease systemic inflammation. The anti-inflammatory benefits of yoga may be useful for respiratory infections, according to a meta-analysis by (13). Due to its anti-inflammatory properties, yoga may help improve airway function and reduce the frequency of respiratory symptoms (4) and (14). It states that yoga places a premium on being cognizant of and managing the connection between the physical and mentally aspects

of one's existence. Just by paying closer attention to our breathing and consciously adjusting our respiratory parameters, we can increase our respiratory efficiency. Breathing will become less of a challenge eventually. Some research suggests that yoga, an exercise regimen that emphasises better breathing patterns, may improve lung function (15). Raghavendra P et al demonstrated, via their research on the effects of yoga on body composition and cardiovascular health, the comprehensive character of yoga regimens. Yoga can promote lung health because it is a full-body activity that includes the airways. Improved lung function could be a side effect of this all-encompassing approach to health. Yoga greatly enhances lung function, according to a research study. Reducing inflammation, strengthening respiratory muscles, and regulating autonomic function are just a few of the numerous mental and physical health benefits of yoga. Incorporating yoga into holistic respiratory health programmes and developing individualised yoga treatments for respiratory diseases requires an in-depth understanding of these systems. The following paragraphs elaborate on the possible therapeutic applications of these results and our suggestions for further study.

Discussion

Summary of Key Findings

The results of this review suggest that yoga, particularly pranayama techniques, can significantly improve pulmonary function in both healthy individuals and those with respiratory conditions. The consistent improvements in FVC, FEV1, and PEFR across diverse studies indicate that yoga has a measurable impact on respiratory health. The findings also highlight that yoga's benefits are not limited to those with chronic conditions but extend to healthy individuals, suggesting its utility as both a preventive and therapeutic tool.

Physiological Mechanisms

The improvements in pulmonary function associated with yoga can be attributed to several physiological mechanisms. Yoga practices, especially pranayama, emphasize controlled breathing and muscle engagement, which likely enhance respiratory muscle strength and lung capacity. Additionally, the anti-inflammatory effect of yoga is noted by (13) Agnihotri et al. It may contribute to improved airway function and reduced respiratory symptoms in individuals with chronic conditions. The reduction in systemic inflammation, coupled with the strengthening of respiratory muscles, creates a holistic improvement in lung function that is supported by the findings of this review.

Implications for Clinical Practice

The positive impact of yoga on pulmonary function has significant implications for clinical practice, particularly in the context of respiratory rehabilitation. Integrating yoga, especially pranayama, into standard care protocols for conditions like asthma, COPD, and other respiratory disorders could enhance patient outcomes. The review suggests that healthcare providers should consider incorporating personalized yoga interventions into treatment plans, particularly for patients who might benefit from a holistic approach to respiratory health. The evidence also supports the use of yoga as a preventive measure in healthy populations, potentially reducing the incidence of respiratory decline with age or inactivity.

Limitations and Future Research Directions

While the evidence supporting the benefits of yoga for pulmonary function is strong, there are several limitations that warrant consideration. The heterogeneity in study designs, populations, and yoga practices makes it challenging to generalize the findings across all contexts. Additionally, the long-term effects of yoga on pulmonary function remain underexplored, with most studies focusing on short to medium-term outcomes. Future research should aim to conduct long-term, randomized controlled trials that compare the effects of yoga with other forms of respiratory therapy. Additionally, studies should explore the molecular and cellular mechanisms underlying yoga's impact on pulmonary function to provide a more comprehensive understanding of how these practices influence respiratory health.

Conclusion

In conclusion, a review of the effects of yoga on pulmonary function in a variety of populations has revealed an overall positive trend. The incorporation of pranayama and yoga into one's routine can improve breathing for anyone, COPD or not, among other health advantages. According to the results, yoga could potentially serve as a comprehensive strategy for enhancing respiratory health. In addition to its physiological and psychological advantages for pulmonary function, yoga promotes mental health and a harmonious mind-body connection. This comprehensive approach aligns with the current trend in healthcare, which prioritizes patient-centered care and integrative medicine. Despite the encouraging data, there is still much to learn about the relationship between yoga and respiratory health. Although the reviewed studies provide a strong basis, further investigation is necessary to enhance methodologies, comprehend the enduring consequences, and formulate therapies tailored to specific populations. Novel and thrilling is the incorporation of yoga into clinical practice within the domain of respiratory medicine. The collaboration between healthcare providers and yoga practitioners will be critical for the continued development of the field of respiratory health to ensure a comprehensive and evidence-based approach.

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Internet addiction and Integrated-Yoga therapies: A review

Research Article

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Abstract

In the past few decades internet has drastically influenced human behaviour with its mixed positive and negative effects. It is emerging as a fast-paced medium to communicate and connect to people. It has a worldwide reach in urban as well as in remote areas. Consequently, its excessive use is leading to serious health hazards and leads to internet addiction too. Noticeably, Cognitive-behavioural therapy has been considered as an effective treatment for internet addiction. A few scientific researches in the past few years have proven that yoga intervention can be used as an effective tool to successfully combat the mental health disorders which arise due to Internet addiction. Aim: This report summarizes the current evidences of the varied integrated therapies and interventions which help fight Internet addiction and the serious health issues which are the outcomes of internet addiction. We focussed on the evidences described in review articles. Results: Collectively, these reviews suggest several areas where cognitive behavioural therapy and integrated yoga therapy are beneficial. Conclusion: Especially I-Yoga therapies require more intensive researches, so that its benefits can be firmly established. And how much useful it is in long terms and its impact on treating the health hazards caused due to internet addiction is still unclear. Yoga may be suggested as a supportive and effective aide to combat health issues arising due to internet addiction, yet it has not been proven as a stand-alone tool to fight the ill-effects of internet addiction.

Keywords: Internet, Addiction, Yoga, Therapy.

Introduction

Technology is evolving at a rapid rate, becoming more autonomous and simplifying life. The rising reliance and frequent use of smartphones has led to modifications in psychosocial behavioural elements. Internet addiction has a negative impact on one's physical and mental well-being and is emerging as a major contributing factor to psychosocial disorders.

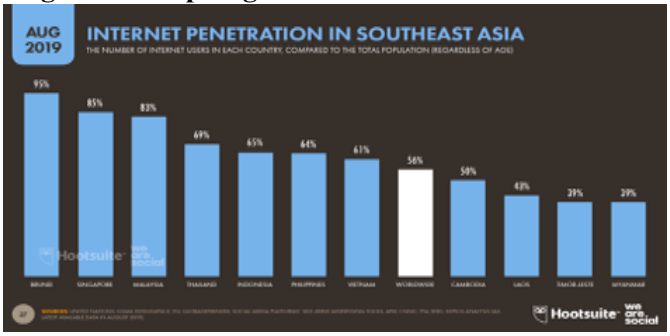
With millions of Internet users worldwide, India comes stands at second place when it comes to internet usage. Recent technological advancements have made it possible for people of all ages to access the internet, which has increased access to the internet and posed a threat to a number of people, but the majority of those affected are adolescents (1).

They use internet for academic references, social media, and online classrooms.

In the year 1996, Dr. Kimberley Young first time proposed the concept of Internet addiction in her seminal paper. In her opinion internet addiction is as much harmful as drug addiction and shows that digital devices deteriorate the brain in a very similar way as the harmful drugs do (2).

Internet is becoming an integral part of our daily lives- be it work, leisure or school activities. It has taken a significant place in everyone's life especially post- pandemic. A study done in South-East Asia showed the Internet Penetration Rate (IPR) which is defined as the percentage of total population who use internet. The Internet Penetration was the highest in Brunei-95% in the year 2019 (3). Many countries like South Korea and China have accepted Internet addiction as a serious health hazard and have started taking strict actions when it comes to its education, research and treatment (4,5).

Figure 1: Source: https://datareportal.com/reports/digital-2019-spotlight-ecommerce-in-southeast-asia



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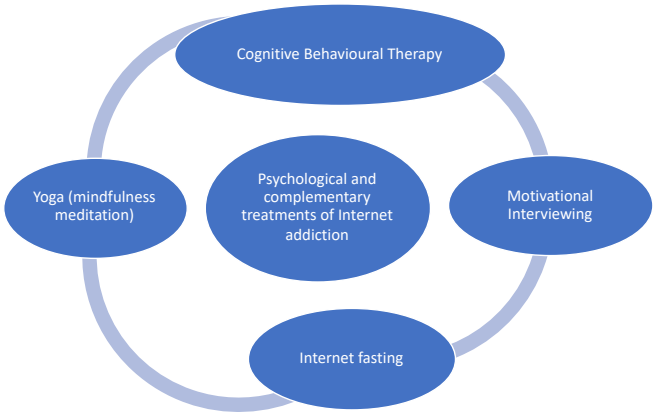
Integrated Therapies

Many kinds of Integrated therapies have recently been studied which deal with the health hazards which arise due to internet addiction.

Integrated yoga therapies have been found useful in the treatment of health hazards which are aggravated due to internet addiction. The review tries to highlight those integrated yoga therapies. The objective of this review is to compile a collection of the scientific studies done for dealing with the internet addiction and related health issues through integrated therapies in a systematic way.

Internet Addiction Disorder is associated with greater risks for hostility, depression, anxiety, interpersonal sensitivity, and psychoticism (6).

Fig 2: Suggestive integrated therapies for treatment of internet addiction



Social networking sites create negative health impact as well as the academic performances of students were also affected. So, the students get addicted to the networking sites and the young users socialize on the sites and are unfortunately unaware of the risks involved in it and indirectly they are hurting their privacy. A study held amongst the Asia Pacific University Scholars revealed the negative impact of social networking sites such as Facebook (7).

A study was done on Iranian University students which revealed that excess usage of internet lead to anxiety, depression, and mental health issues and ultimately affected their academic performance (8).

Internet addiction is also associated with poor dietary habits, sleep problems, and fatigue issues. A study done on Turkish students revealed these issues (9).

In terms of the IPR as of January 2020, the Southeast Asia region was ranked 9th (66.0%), with the first being Northern Europe (95.0%), followed by Western Europe (92.0%), and Northern America (88.0%) (10).

Methodology

Google scholar database was used to search the relevant studies done in the past. A set of criteria were pre-decided for this review. Studies done in languages other than English were excluded from this study. We as researchers have avoided taking reviews, opinion articles, and meta-analysis in this study. Many books have been written on Integrated therapies on Internet addiction, we have not included them in this review.

Table 1: Studies on the integrated yoga therapies given for internet addicts

Table: Summary of Results								
S. No.	**Reference**	**Year**	**Type of study**	**No. of subjects**	**Duration**	**Intervention**	**Parameters**	**Findings**
1	Tadpatrikar A & Manoj K Sharma et al (11)	Jun-23	Pre-post changes	4 cases	12 weeks	Physical postures (Asana), breathing practices (Pranayama), and meditation (Nadanusandhana), Integrated Y-CBT intervention	Internet addiction test (s-IAT), Smartphone Addiction Scale-Short Version, Kessler's Psychological distress scale for baseline, and follow-up assessment after completion of the program	Reduced internet and mobile phone use, psychological stress, Sleep quality improved
2	Rudra B. Bhandari et al. (12)	May-18	Pre-post changes	154 UG-PG students of Patanjali University, Haridwar	3-month yoga program	Yoga lifestyle prescription(YLP) for preventing and mitigating IA + Ayurvedic Swasthavritta(Ushapan+ Medicated oil application (Shadvindu Taila) into nostrils by fingers+ Medicated oil (Ksheera Bala tail) massage over the body	IAT is the 5-point Likert scale with 20 items to be rated as 0, 1, 2, 3, 4, and 5 if the given behaviour is applicable, rarely applicable, occasionally applicable, frequently applicable, often applicable, and always applicable in the user's life.	YLP is an effective therapy for treatment of addictive behaviours and they have significant impact on the psychological, behavioural and physical components. Significantly improved their body pain, sleep, appetite, communication, and outside recreational activities

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3	Sharma, M. K., & Bhargav, H. et al. (13)	2016	Pre-post changes	45 Internet addicts	3 months	The integrated yoga program involved: Joint loosening practices with breath synchronization for 10 min (moving head forward and backward as well as clockwise and anticlockwise ten times each), blinking of eyes (twenty times), stretching of hand/legs and moving the wrist/legs clockwise and anticlockwise (ten times each) followed by Kapalabhati Kriya (skull shining breath) at 100 strokes/min for 2 min, Nadi-shuddhi pranayama (alternate nostril breathing) for 5 min, and Bhramari (humming breath) pranayama for 5 min. Subjects were also offered yogic counseling based on the principles of mind management from Bhagavad Gita. These practices were demonstrated to them and supervised during sessions		Yoga practices brought positive lifestyle changes in the form of regulated sleep, improved appetite, enhanced communication with others, and increased recreational activities outside the home. Due to these positive lifestyle changes and reduced physical symptoms such as neck strain and body pain, they reported 30–40% reduction in their technology use at the end of 3rd month
4	Dadhore, Sadhna et al. (14)	2019	Randomized Control Trial	600 school students in a Bhopal school (15-18 years)		Yoga package schedule for Internet gaming Disorder	Internet Gaming Disorder(IGD), General Health Questionnaire- 12 item scale(GHQ) for screening of students	Yoga is found to be an effective tool and also reasonably good health improvement. The outcome of the studies suggests that there is a decrease of 35.77% with IGD cases with 8 set of yoga practices while GHQ study suggests that there is a 46.99% general health improvement
5	Eun-Hi Choi et al. (15)	2020	Pretest-posttest design	49 high school sophomores	Session was given twice a week, for 20 minutes\session- total of 12 weeks.	Mind-subtraction meditation+ lectures	Korean Smartphone Addiction Proneness scale, Self-control scale, Stress scale to assess emotional stress levels.	Experimental group saw a decrease in stress levels, changes in self-control and stress coping strategies.
6	Anurag Tripathi (16)	2017	Pretest-posttest design	24 adults + 8 adolescents with ADHD	Participants started meditating for 5 min at a time, which was gradually increased to 30 min. Each session comprised 2.5 h and was supplemented with daily home practice	Mindfulness training\ MT\ Mindful meditation	Brain activation checks using fMRI.	30% reduction in Attention Deficit Hyperactivity disorder (ADHD).

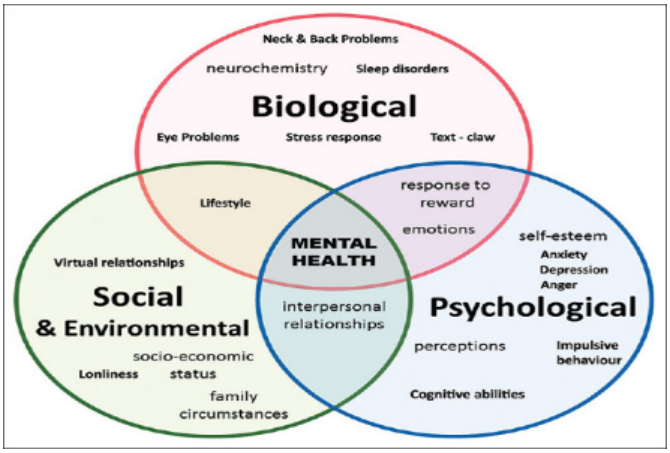
Internet addiction can have severe effects on mental, physical and emotional health of an individual. Cognitive skills are hampered; social involvements are put on stake when a person gets indulged in this kind of addiction.

Internet addiction- affecting various aspects of personality

Internet addiction can be cured through psychological and complementary treatments. Cognitive Behavioural Therapy- CBT is one of the most effective treatments used in modern world for Internet addiction (17). In fact, since the 1970s the Cognitive Behavioural Therapy has been used to deal with addiction, anxiety, depression and eating disorders (18).

Many alternative and integrated therapies are being scientifically studied these days. They are an effective treatment for the health hazards which are an outcome of Internet addiction.

Figure 3: Mental, physical, psychosocial health: inter-relations



Bio psychosocial perspective of smartphone addiction
(Putchavayala et al., 2022)

Discussion

Surprisingly, the rate of smartphone use in most Asian countries is almost 41-84 % which is more when compared to the United States. Countries like South Korea, Japan and China have significantly high ownership of smartphones, probably because they have strong infrastructures in the field of telecommunication (20).

Yoga and meditation has been a part of ancient India and scientific researchers have proven that people practicing meditation have better mental health (21).

Extensive scientific researches are being done which give evidences that yoga and meditation can be an effective to fight mental health issues, anxiety, depression as well it helps in improving metabolic and vascular functions of the human body (22).

Internet addiction effects school going children, aged people. Adolescents are specifically affected by this problem, which can further lead to many mental health issues like anxiety, anger, depression. Internet addicts also face physical health issues like backpain, frozen shoulders, cervical spondylitis. Emotional health hazards like eating disorders, Post-traumatic disorders, depression, schizophrenia can also be faced by the Internet addicts.

Nowadays, many corporate offices are also introducing yogic practices as a part of their routines. These programs are helping the employees to cope up with the stress, anxiety, depression, sleep disorders and many more such health issues which can be an outcome of internet addiction and increased screen time.

Conclusion

So, the conclusion can be drawn that mindful-meditation programmes could be an innovative way for adolescents to meet their challenging academic, psychosocial, behavioural, and mental health demands. These kind of treatments can be explored scientifically, as they don't have side-effects and have a reflective impact on holistic well-being of a person in this fast-paced era of technology. As these kind of therapies inculcate good practices in all age-groups, so they can be introduced widely as a part of the school curriculum and office routines. It can make a significant and positive impact on the mental health of people. Apart from adolescents, the children under the age of 15 are also having high exposure to mobile phones and internet, the Covid-19 pandemic forced the children to have unexpectedly heavy exposure to the social media and online gaming. Also the over-aged people also have good amount of internet exposure. To maintain healthy well-being of adolescents, children, old-aged, middle-aged- they should be made aware of the various mindfulness mediation techniques, internet fasting and a yogic lifestyle.

The Preksha Meditation technique of mediation, which was formulated by Acharya MahaPragya in the 20th century, based on the philosophy and teachings of Lord Mahaveera. It is said that Lord Mahaveera attained enlightenment through Preksha Dhyan. This simple spiritual practice of meditation is based on ancient Jain scriptures and is directed toward purification of the Self, transformation of consciousness and behaviour modification (Acharya Tulsi, 1994; Sadhvi Vishrut Vibha, 2009). So, it is suggestive to incorporate this meditation technique which has a comparatively young history, to combat the addiction issues in all age groups.

"The Internet has been a boon and a curse for teenagers" - JK Rowling

"According to experts the perception of psychic centers can modify the synthesis of endocrine output and weaken the intensity of impulses and urges (23), thus making them controllable by human mind. The perception of psychic centers is the most important stage of Preksha Dhyana with respect to emotional well-being. Because the perception of psychic centers is believed to have the capacity of regulating the urges and distortions, the libido can be put to creative activity."

Apart from mindfulness yogic practices today's youth should be exposed to moral values, should have connected family atmosphere, they should be given plenty of time to listen to their adolescent queries. In the tender adolescent age, their body and mind undergo many hormonal changes; they have lots of unanswered queries in their mind. And in that scenario if they do not get good company of healthy informative talks, guidance of their parents and good, healthy lifestyle tips there are very much chances that they go in wrong direction. So, proper taking care of physical, mental, and emotional health is a big priority. And yoga and

meditation can be an effective tool to combat the hormonal changes in body and take care of one's health.

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A Comparative Study of Yogic Practices and Diet Therapy in the Management of Pre-Diabetes wsr to Glycemic Control: A Case Report

Review Article

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Abstract

Pre-Diabetes is growing with an alarming rate all over the world. It is a clinical entity between the normoglycemia and stage of Type II Diabetes mellitus. Faulty dietary habits and lifestyle errors play a key role in the pathophysilogy of Pre-diabetes. Pre-diabetics have higher risk for cardiovascular diseases, fatty liver, kidney failure and other associated complications of diabetes. The reason for the rising incidence of Pre-diabetes is due to the lack of public awareness, observation, follow-up programs and self-awareness about the conditions of disease. This report is about a case of successful reversal of Pre-diabetes to normal stage through Yogic practices and diet therapy. The selected patient was prescribed Yogic practices and diet therapy throughout the intervention. The trial patient reported glycosylated (HbA1c) as high as 5.9 % and after the intervention of Yogic practice and diet therapy, it was reduced to 5.2%. After three months intervention, fasting blood sugar dropped from 110 mg/dl to 90 mg/dl and postprandial blood sugar dropped from 165 mg/dl to 132 mg/dl and Weight reduced from 93 kgs to 90 kgs. He was responded well in terms of clinical symptoms of Pre-diabetes after the completion of trial intervention. Besides, no other lifestyle modification interventions were enforced during the whole trial period. The results concluded that consistent diet therapy and regular Yogic practice can not only maintain the blood sugar levels in patient of Pre-diabetic but also improve the patient general health and wellbeing.

Keywords: *Asana,* Diet, Glucose, *Pranayama,* Pre-Diabetes, *Yoga*.

Introduction

Pre-diabetes is a type of metabolic disorders that is considered as early stage of Type-2 diabetes mellitus. From last few decades the cases of Pre-diabetes are increasing rapidly all over the world. The cases of Pre-diabetes have been continuously rising globally and become an epidemic. The global prevalence of Pre-diabetes was estimated at 7.3% of the adult population in 2017, equivalent to 352 million individuals. By 2045 the prevalence is anticipated to increase to 8.3% of the global adult population, equivalent to an estimated 587 million individuals (1). It is multifactor disorders and is associated with variety of causative factors such as genetic, environmental, mental stress or etc. that may lead to develop Pre-diabetes and its related consequences. Holistic health is the basic need of all human life. If health is good, anybody can get the success in his life. But health depends on many things such as thinking, Yogic practices, life style modification, diet and other aspects of life (2). Diet plays a very important role in care of health, care and cure of Pre-diseases. However, reduction in weight, optimal glucose levels and wellness can be achieved follow the dietary guideline. Yogic practices and diet therapy can easily care and cure the cases of Pre-diabetes for prolong period without any unwanted effect on the body systems (3). Regular Yogic practices calm the mind and improve overall health. Hence, it is useful in Pre-diabetes patients. It also stimulates the sympathetic nervous system and active pingala nadi, which increase metabolism (4). Yoga causes Parasympathetic activation which in turn helps to achieve overall metabolic and psychological improvement through stress reduction, increased insulin sensitivity and lipid metabolism (5).

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Patients Information

On 12/08/2023, a 40-year-old, married, non-smoking, non-alcoholic male patient reported to the out-patient Department of Kayachikitsa, Sir Sunderlal Hospital, Varanasi, India. He was complained of severe laziness, polydipisa, polyphagia and joint pain since the last 6-7 months.

The patient is a resident of the Chapra (Bihar State). He was screened for fasting blood sugar during the Sir Sunderlal Hospital, BHU, Varanasi to the treatment risk of polydipisa, weakness and joint pain based on symptoms. After his screening based on

symptoms, it was diagnosed that he was at high risk for Pre-diabetes with a risk score of 110 mg/dl fasting, as shown in Table-2. After taking the written informed consent, the measurement for FBG and PPBG, HbA1c were taken at baseline and after three months. The result of the HbA1c test at baseline is 5.9%, which falls into the category Pre-diabetes according to American Diabetes Association guidelines. After three months of Yogic intervention and diet therapy, Pre-diabetes was seen in normal range.

Timeline

In the present case, Yogic intervention and Diet therapy was continued for 3 months starting from 12/08/2023 to 13/11/2023. Table1 shows the timeline of follow-up, history and clinical outcomes.

Table 1: Timeline of disease activity and Intervention

Timeline	Clinical Intervention
August 2023	After history taking and blood investigation, the patient was advised Yogic Practices and Diet Therapy interventions for 3 months. [Table 4-5]
September 2023	The patient advised continued intervention. An improvement in symptoms of Pre diabetes was observed.
October 2023	After two months of follow-up, the patient was advised to continue the intervention.
November 2023	All reports were found to be in normal range. It was decided to continue the same intervention if Pre-Diabetic symptoms persisted again.

Clinical Findings

The patient was subjected to fasting blood sugar (FBS) 110 mg/dl and postprandial blood sugar (PPBS) 165 mg/dl on 12/08/2023. Glycosylated percentage (HbA1C) tested on 12/08/2023 showed 5.9 %. The subjective symptoms showed increased in **Table-3.** Thus the patient was diagnosed with Pre-Diabetes by the Ayurvedic physician at Kayachikitsa OPD, Sir Sunderlal Hospital, Banaras Hindu University, Varanasi, India.

Table 2: Biochemical characteristics of participant after three months of Yogic intervention and Diet Therapy

Variable	Before	After
FBG	110 mg/dl	90 mg/dl
PPBG	165 mg/dl	132 mg/dl
HbA1c	5.9%	5.2%

Table 3: Result Patients symptoms episodes before-after Intervention record

Sr. No	Variables	Before Intervention	1st Fellow-up	2nd Fellow-up	3rd Fellow-up
1	Polydipisa	+	-	-	-
2	Polyurea	-	-	-	-
3	Polyphagia	++	+	+	-
4	Burning sensation	+	+	+	-
5	Laziness	++	+	-	-
6	Joint Pain	+	-	-	-

(Nil -, Mild +, Moderate ++, Severe +++)

Therapeutic Interventions:

Under previous consultation patient was advised intervention treatment as mentioned (Table 4 and 5). The Pre-diabetic Yogic intervention session was conducted for a total period of 3 months with one session per day in morning for 6 days a week and each session was conducted for 30 minutes and dietary chart was hand over to the patients.

Table 4: Pre-Diabetes Yogic Intervention: (August 2023 to November 2023):

Sr. no	Yoga Practices		Duration
1	**Suksham –Vyayama**	· Griva-Shakti Vikasaka, Skandh-Shakti Vikasaka · Kati-Shakti Vikasaka, Gulphha-Pada- Shakti	6 minutes
2	**Asana**	· Trikonasana , Padahastasana , Mandukasana, Naukasana, Savasana, Bhujangasana	16 minutes
3	**Pranayama**	· Bhramari-Pranayama	6 minutes
4		· Om Chanting	2 minutes
	Total-time		**30 minutes**

Table 5: The Pre-Diabetic patients was advised follow this Diet Therapy plan

Time	Diet Regimen	Calories
Upon arising	1 Cup milk tea (No sugar)	62
Breakfast	Poha Cooked / Upmaa Cooked / Multigrain Dalia Cooked/ 1 Multigrain Paratha/1 Cup Milk (No sugar)	917
Mid Morning	Fruits (Apple/ Jamun/ Guava/ Amala some dry fruits like Almond)	52
Lunch	Salad (As desired)/ Mixed Vegetables/ Dal (1 Medium Katori dal)/ 4 Chapatti Multigrain/ Dahi (1 Medium Katori)/ 1 Medium Katori Cooked Rice	358
Evening	Roosted Channa with 1 cup milk tea	202
Diner before	Green Vegetables (1 Medium Katori)/ 3 Chapatti multigrain/1 Medium Katori dal	408
Bed time	1 Cup milk (No sugar)	62
Total		**2061**

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Follow-up and outcomes

The first follow up of FBS, PPBS, Blood Pressure and BMI were done after one month and HbA1c, Renal function test (RFT), Liver function test (LFT), General health variables follow before and after intervention. The patient was stable, without any new complaints. His complaints like polydipisa, polyphagia, burning sensation in hand and feet, laziness, flabbiness of the body and joint pain were reduced. After one month his FBS and PPBS were 106 mg/dl and 156 mg/dl respectively, showing a satisfactory reduction of blood sugar levels. He was advised to take a complete blood count (CBC), liver function test (LFT), renal function test (RFT), serum electrolytes and lipid profile tests (LPT) for a basic medical assessment and report back for follow up after a month. He was also advised to continue the Yogic practices and prescribed diet plan for another two months.

Table 6: The Significant improvements were observed in the subjective as well as objective parameters of the patient

Sr. No	Variables	Before Intervention 12/08/2024	After Intervention 1st 14/09/2024	After Intervention 2nd 10/10/2024	After Intervention 3rd 13/11/2024
1	FBG	110 mg/dl	106 mg/dl	98 mg/dl	90 mg/dl
2	PPBS	165 mg/dl	156 mg/dl	140 mg/dl	132 mg/dl
3	BMI	31.1 kg/m^2	30.7 kg/m^2	30.6 kg/m^2	30.1 kg/m^2
4	BP	138/98 mmhg	130/90 mmhg	128/84 mmhg	124/82 mmhg
5	HbA1c	5.9%	-	-	5.2%
6	General Health	14	-	-	10
7	Cholesterol	193 mg/dl	-	-	160 mg/dl
8	Triglycerides	253 mg/dl	-	-	200 mg/dl
9	Total-Bilirubin	0.80 mg/dl	-	-	0.68 mg/dl
10	SGOT	62 u/l	-	-	52 u/l
11	SGPT	127 u/l	-	-	108 u/l

Discussion

The traditional text descriptions of Yogic practices and dietary guidelines have a big impact on managing Pre-diabetes overall and they have emerged as adjuvant therapy for Pre-diabetes. Rajesh R et al. (2021) were found that Yoga therapy has a positive effect on FPG, PPG and HbA1c along with many anthropometry measures studied in this study. Yoga was found to be effective for controlling glycemic parameters in Pre-diabetes (6). Multiple studies suggest the role of Yogic practices in the amelioration of Pre-diabetes in an effective way. Yogic practices and Diet therapy are believed to exert long-term glycemic control (7). From this angle, Pre-diabetes can be prevented and managed with the use of Yogic practices and dietary therapy (8). The Pre-dietetic regimen that includes the exclusions of foods items those are high in sugar along with inclusion of pathyahara, eating in smaller portions thought the day and also adding a variety of fruits and vegetables every day helps to maintain the blood sugar levels (9). Yogic practices provide energy and endurance for daily activities (10).

Patient's Perspective on Yogic practices and Diet therapy Intervention treatment received

When I decided to take the Yogic practices and Diet therapy intervention, I was worried about getting relief from my problems. I found Yogic therapy to be very helpful. Both Yogic therapy and Diet therapy had positive effects on my health. All of my blood sugar reports (FBS, PPBS and HbA1c) are now in normal range. Thanks to Yoga Therapy and Diet Therapy for helping the patient to become healthy.

Limitation of case report

While this outcome was observed in a single patient, further research on a larger sample size would be necessary to establish evidence for the significant effectiveness of such dietary products and Yogic therapy in relieving symptoms of Pre-diabetes.

Conclusion

In this particular case study cited, it can be concluded that the Yogic practices and diet therapy not only control FBS (90mg/dl), PPBS (132mg/dl) and HbA1c levels (5.2%) but also improve the general health of patients with Pre-diabetes. Yogic practices and diet therapy prove to be promising in reversing the Pre-diabetic glucose threshold into normal glucose threshold. Although, the other factors like age, chief of complaints, sleep and bowel habit by the participant also play a prominent role in the overall positive effect on the Pre-diabetic condition.

Informed consent

Informed consent was obtained from the patient before the start of the intervention. Written consent for the publication of patient's clinical details was obtained before initiation of the therapy.

Conflict of Interest

No conflict of interest in any manner is there to be declared by the author.

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An Integrated Approach of Yoga Therapy and Naturopathic Diet for obesity management: A comprehensive case study

Review Article

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Abstract

Background and Objectives: Obesity is a complex condition often accompanied by stress, dyspnea, and hyperhidrosis. This case study aims to evaluate the therapeutic impact of a 30-day integrated intervention involving yoga therapy and a naturopathic diet on managing obesity and associated symptoms in a 21-year-old female. Methods: The subject, diagnosed with obesity and associated conditions, underwent a structured therapeutic program that combined Integrated Approach to Yoga Therapy (IAYT) and a detox-focused naturopathic diet. Physiological parameters including body mass index (BMI), weight, waist and hip circumference, blood pressure (BP), pulse rate, respiratory rate, and breath-holding time were measured pre- and post-intervention. A follow-up assessment was conducted 30 days post-intervention to monitor sustained effects. Results: Significant improvements were observed in key parameters post-intervention. BMI, weight, waist and hip circumference, BP, pulse rate, and respiratory rate all decreased, while breath-holding time showed improvement. These positive changes persisted at the 30-day follow-up, suggesting sustained benefits from the integrative approach. Conclusion: This case study indicates that combining IAYT with a naturopathic diet may effectively aid in managing obesity and associated conditions. Further research with larger sample sizes is recommended to explore the mechanisms and broader applicability of these integrative strategies for obesity management.

Keywords: Obesity, Yoga therapy, Naturopathic Diet, Integrated intervention, Physiological outcomes, Holistic health.

Introduction

Obesity, characterized by excessive fat accumulation, is a major health concern globally, posing significant risks to physical and mental well-being. Defined primarily by the Body Mass Index (BMI), a value greater than 30 kg/m² is considered obese (1). According to the World Health Organization (WHO, 2023), over 1.9 billion adults worldwide are overweight, with more than 650 million classified as obese. The prevalence of obesity has increased alarmingly, particularly in urban populations, contributing to a rise in chronic diseases such as cardiovascular disease, type 2 diabetes, hypertension, and certain cancers.

A growing body of literature has highlighted the limitations of conventional treatments for obesity, such as pharmacological interventions and bariatric surgery, which often focus on symptom management rather than addressing the underlying causes. This underscores the need for alternative, holistic approaches to obesity management. The WHO's *Global Strategy on Diet, Physical Activity, and Health* emphasizes the importance of healthy eating and physical activity as primary strategies to combat obesity (World Health Organization, 2023). Integrative therapies, particularly Yoga Therapy combined with dietary modifications, have gained attention as effective alternatives for managing both the physical and psychological aspects of obesity (2).

In line with this integrative approach, a 30-day combined yoga therapy and naturopathic diet intervention has shown significant improvements in BMI, body weight, blood pressure, and respiratory function, with sustained effects at a 30-day follow-up. These findings underscore the viability of integrative, non-invasive methods as long-term solutions for obesity management, highlighting the need for further research in broader populations.(3)Similarly, other studies have found that an integrated approach using naturopathy and yoga can improve glycemic control, lower blood glucose levels, and reduce the need for medications among patients with type 2 diabetes. These outcomes further support the potential of integrative lifestyle interventions in addressing complex health conditions, promoting long-term benefits across metabolic markers. (4)

Recent studies have shown promising results for integrative approaches such as the Integrated Naturopathy and Yoga Management (INYM) protocol. The INYM protocol, a 10-week intervention that

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combines yoga therapy with naturopathic principles, demonstrated significant improvements in weight, BMI, cholesterol, and blood glucose levels, alongside enhanced HDL and overall wellness, sustained through lifestyle adjustments. These findings suggest that INYM could be an effective, holistic strategy for obesity management (5). Furthermore, an integrated approach combining Ayurveda Panchakarma and yoga has demonstrated substantial improvements in managing obesity-related conditions, enhancing functional capacity, quality of life, and reducing musculoskeletal pain. This case study highlights the potential efficacy of combining Ayurvedic and yogic therapies as a holistic strategy for obesity management, warranting further research to confirm its applicability in larger, diverse populations(6).

Complementing these findings, a recent study demonstrated that a structured lifestyle intervention integrating yoga and naturopathy significantly reduces BMI, WHR, body fat percentage, and BMR in obese individuals, performing notably better than diet counseling alone. Such evidence underscores the effectiveness of non-pharmacological, integrative approaches in addressing obesity-related risk factors, suggesting their utility as valuable additions to holistic obesity management frameworks (7). Additionally, a short-term intensive yoga and high-fiber vegetarian diet program was shown to reduce BMI, waist and hip circumferences, serum leptin, and cholesterol levels, with noted improvements in postural stability and hand grip strength. However, observed decreases in lean mass, body water, and HDL underscore the need for cautious application and further research to evaluate the long-term safety and efficacy of such intensive interventions (8).

Several studies have demonstrated the therapeutic potential of yoga in promoting metabolic health, reducing stress, and improving overall well-being (Cramer et al., 2016). Yoga, a practice rooted in ancient Indian traditions, includes asanas (postures), pranayama (breathing techniques), and meditation, all of which contribute to enhancing physical and psychological health Stress, a key contributor to obesity, activates the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system, exacerbating unhealthy behaviors and poor lifestyle choices (Cramer et al., 2016). Yoga's efficacy in stress reduction has been well-documented, which in turn helps in breaking the cycle of stress-induced obesity (2).

Building on this evidence, the present case study demonstrates that an integrated approach combining yoga therapy and a naturopathic diet can effectively aid in managing obesity and improving associated physiological markers. Our findings show significant reductions in BMI, weight, body measurements, and respiratory parameters, with sustained benefits observed after a 30-day follow-up. This suggests that such integrative, non-invasive interventions could provide a valuable complementary method for long-term obesity management.(10)

Despite the growing evidence supporting the effectiveness of integrative approaches to obesity management, there is limited research on the combined impact of yoga therapy and dietary modifications on key physiological parameters. This study aims to fill this gap by investigating the effects of lifestyle changes, specifically yoga practices (Yogabhyas) and dietary modifications (Ahaara), on obesity-related physiological indicators such as waist circumference, Hip circumference, BMI, weight, blood pressure, pulse rate, respiration rate, and breath-holding time. Our study aims to provide a comprehensive understanding of how these integrative approaches can contribute to weight management, improve metabolic functions, and promote long-term health outcomes.

The objectives of this research are twofold:

(1) To evaluate the combined impact of yoga therapy and diet on various physiological markers in individuals with obesity.

(2) To explore the potential for these therapies to offer a sustainable, non-invasive, and holistic solution for obesity management, thereby complementing existing treatment strategies.

This study is significant as it aligns with the WHO's focus on lifestyle-based interventions for obesity and chronic diseases, offering valuable insights into how integrative methods, such as yoga and dietary modifications, can enhance obesity management. By investigating the combined effects of these therapies, this research may inform clinical practice and public health policies, contributing to the growing body of evidence supporting integrative approaches to obesity.

Case Presentation

➢ Patient Profile

- **Age:** 21 years
- **Gender:** Female
- **Diagnosis:** Obesity Grade 3, Stress, Dyspnea, Hyperhidrosis

A 21 year old female participant from New Delhi, enrolled himself at Prashanthi Kutiram on the 10th of september 2021 and was put in section 'H', which deals with Obesity. He resided in campus from 10.09.2021 to 10.10.2021 (30 days). He underwent Yoga therapy with some detoxification treatments like sauna bath, steam bath, hip bath and underwater massage as well as for more relaxation and aids more benefits Mud pack to abdomen and eyes for a week in between.

➢ Clinical Background

The patient presented with a two-year history of significant weight gain, approximately 20 kg, resulting in a pre-intervention weight of 91 kg and a Body Mass Index (BMI) of 40.5, categorizing her as Obese (Grade 3). Associated clinical manifestations included:

- **Irregular Menstrual Cycles:** Documented irregularities leading to previous medication for six months.
- **Hyperhidrosis:** Excessive sweating localized primarily to the hands.
- **Musculoskeletal Symptoms:** Occasional middle back pain.

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- **Dyspnea:** Notable shortness of breath during physical exertion, particularly when climbing stairs.

The patient had not undergone any prior treatments for obesity or associated symptoms and reported emotional distress, primarily due to family dynamics and future career uncertainties. She frequently expressed a desire to avoid stressful situations, indicating a psychological component to her condition.

➢ **Inteventions**

A 30-day integrated therapeutic intervention was designed, combining **Integrated Approach to Yoga Therapy (IAYT)** with a specialized **Naturopathic Diet**. The intervention protocol included:

❖ **Yoga Therapy:**

○ **Frequency:** 2 times a day for 1 hour each time (Daily practice for 2 times each for 1 hour).

◦ **Components:**

- Dynamic sequences (Suryanamaskar)
- Breathing practices
- Loosening practices
- Asanas (postures)
- Pranayama (breathing exercises)
- Shatkarm
- Relaxation
- Meditation
- Yogic counseling
- Bhagavad Gita chanting/Bhajan sessions

Yogic Intervention applied

Breathing Practices

- Hand in and out breathing
- Hand stretch breathing
- Tiger breathing
- Straight leg raising breathing
- Side leg breathing
- Bhujangasana breathing
- Dhanurasana breathing
- Vakrasana breathing
- Navasana breathinng
- Shashankasana breathing

Loosening Practices

- Jogging
- Back swing
- Jumping all the variations (Diagonal jumping, clap jump)
- Step climbing
- Hip stretch
- Back stretch
- Standing and supine situps
- Bhunamanasana twisting
- Paschimottanasana – halsana
- Alternate toe- touching
- Boating (Naukasanchalana)
- Chakki and chapatti making
- Janu sirshasana stretch
- Pawanmuktasana kriya
- Dhanurasana swing
- Parvatasana
- Swimming
- Cycling
- Rocking and rolling
- Leg rotation
- Jathar parivartansana
- Camel, crow, baby and drill walk
- Surya namskara 10 and 12 steps

Asanas

- Parivritta trikonasana
- Ardha katichakrasana
- Paschimottanasana
- Vakrasana
- Ardha matsyendrasana
- Bhunamnasana
- Bhujangasana
- Naukasana (Prone)
- Shashankasana
- Dhanurasana
- Chaturanga dandasana
- Navasana (supine)
- Setu bandhasana
- Vipreetkarni

Pranayama

- Right nostril breathing
- Nadishuddhi pranayama
- Brahmari Pranayam

Specific Practices-

1. Chappati And Chakki Chalana
2. Straight Leg Rising
3. Cycling
4. Dhanurasana Swing
5. Naukasana And Navasana
6. Paschimottanasana

Shatkarmas

- Kaplbhati

Relaxation

- Nadanusandhana
- IRT
- QRT
- DRT

Meditation

- Om meditation
- Cyclic meditation
- MSRT

These all practices are given alternatively.

❖ **Naturopathic Diet:**

◦ Emphasized whole foods, including:

- Fruits
- Vegetables
- Raw diet (raw vegetable Salad)
- Soups
- Kashayam
- Juices (vegetable juices, fruit juices, Bitterguard juice, Methi water, Papaya juice, Musk melon Juice, Carrot juice, coconut water, Buttermilk).

- Boiled diet (boiled vegetables)
- Lemon honey juice fasting (at every 2 days interveal)
- Occasional chapatti, tailored to the patient's needs

Mind Sound Resonance Technique (MSRT)

MSRT is one of the advanced yoga-based mindful relaxation techniques developed by SVYASA to specifically strengthen the immune defence, to develop will power and promote Health and happiness, that involves experiencing with closed eyes the internal vibrations and resonance developed while chanting the syllables A, U, M, Om and Mahamrityunjaya mantra sounds.(11). The details of MSRT practice including the steps involved are described elsewhere (12).

OM Meditation

OM meditation, as studied at SVYASA University, has shown various physiological and psychological benefits through scientific investigation. One notable study led by Dr. Shirley Telles and colleagues examined OM meditation's impact on the autonomic nervous system, revealing reductions in heart rate, increased parasympathetic (relaxation) activity, and lowered stress markers. This aligns with findings on the meditation's effect on both autonomic stability and improved mental clarity.(13)

Cyclic Meditation

Cyclic meditation is the meditation technique named as moving meditation taken from Mandukiya Upanishad which is a combination of the yoga postures. This that mindfulness-based intervention for incarcerated youth may mitigate the numerous psychological stressors associated with incarcerated living. Clinical implications and directions for future research are discussed.(14)

Diagnosis

The progression of obesity was assessed through anthropometric measurements provided by the patient.

Table 1: Vital Data and Anthropometric measurements:

Parameters	Pre-data	Post-data
Height in mt.	150cm	***
Weight in (kg)	91kg	84kg
BMI [Kg/mt2]	40.5(Grade-3 obesity)	37.33(Grade-2 obesity)
BP in mmHg	130/90	118/78
Pulse Beats/min	85	75
Respiratory Cycles/min	18	14
Bhramari Time (Sec)	26	35
Mid arm circumference	42cm	37cm
Waist circumference	110cm	105cm
Hip circumference	130cm	126cm

This case study highlights the positive effects of a 30-day intervention involving yoga therapy and a naturopathic diet on obesity and associated physiological parameters. The subject, an individual with Grade 3 obesity, exhibited notable improvements across multiple metrics following the intervention. Weight decreased from 91 kg to 84 kg, contributing to a reduction in BMI from 40.5 (Grade 3 obesity) to 37.33 (Grade 2 obesity). This reduction indicates movement toward lower obesity classifications, emphasizing the intervention's impact on weight management.

Further physiological improvements were observed in cardiovascular markers, with a reduction in blood pressure from 130/90 mmHg to 118/78 mmHg and a decrease in pulse rate from 85 to 75 bpm. Respiratory metrics also showed positive changes, with respiratory cycles per minute decreasing from 18 to 14 and an increase in breath-holding time from 26 seconds to 35 seconds, reflecting enhanced respiratory efficiency and potential improvements in stress tolerance. Anthropometric measurements also indicated favorable shifts, with waist circumference decreasing from 110 cm to 105 cm, hip circumference from 130 cm to 126 cm, and mid-arm circumference from 42 cm to 37 cm, suggesting a targeted reduction in central and peripheral adiposity.

Psychological assessments revealed a marked reduction in stress levels and an enhancement in the patient's overall quality of life (As just observed by patient). A follow-up evaluation conducted one month later confirmed that these positive changes were sustained, indicating the efficacy of the combined therapeutic approach.

These findings underscore the potential of combining yoga therapy with a naturopathic diet as an effective approach to managing obesity and related health risks. Further research involving larger cohorts could confirm these outcomes and clarify the specific mechanisms through which integrated lifestyle interventions benefit metabolic health and psychological well-being in obese individuals.

Discussion

This case study underscores the effectiveness of an integrative approach that combines yoga therapy with a naturopathic diet in managing severe obesity. Within a 30-day intervention period, the patient's vital health parameters showed significant improvement. Notably, the patient's BMI reduced from 40.5 (indicative of Grade 3 obesity) to 37.33, marking a meaningful reclassification in obesity grade and a decreased risk of associated comorbidities. Such BMI reductions in a short time frame indicate the potential of integrative approaches to drive clinically relevant weight changes, aligning with prior studies that emphasize the role of lifestyle interventions in managing obesity-related health risks.

Beyond BMI, other key health markers, including weight, waist circumference, and cardiovascular indicators like blood pressure and pulse rate, also exhibited notable improvements. These changes reflect a positive impact on both metabolic and cardiovascular health, essential components in comprehensive obesity management. Furthermore, a decreased respiratory rate and increased breath-holding time suggest enhanced respiratory efficiency, aligning with existing evidence on

the benefits of yoga in respiratory health. Psychological assessments during the study revealed reduced stress levels and an improved quality of life, highlighting the mental health advantages of this integrative intervention. Prior research has documented the positive effects of yoga and mindfulness practices in stress reduction, supporting the holistic nature of such interventions.

These findings collectively underscore the promising role of integrative therapies that target both physiological and psychological dimensions of health. As demonstrated in previous studies, combining yoga therapy with a naturopathic diet can improve multiple health parameters and address underlying stress, which is often a driver of unhealthy eating patterns and obesity. This case study contributes to the growing body of literature on non-pharmacological, holistic obesity management and provides a foundation for future research. Larger sample sizes are recommended to explore the generalizability of these results and further investigate the mechanisms behind these improvements. Such studies could offer insights into optimizing integrative therapies, particularly for individuals seeking sustainable, non-invasive alternatives to traditional weight loss interventions.

Conclusion

This case study indicates the efficacy of combining yoga therapies with a naturopathic diet for obesity management, resulting in significant decreases in BMI, weight, and other physiological parameters while also improving overall health. Notably, the patient's transition from Grade 3 to Grade 2 obesity demonstrates the effectiveness of this combined therapy. These findings illustrate the promise of yoga and dietary changes as holistic approaches to obesity management. Future research is suggested to investigate and clarify their broader applications and mechanisms with biochemical profiling like IL-6, vitamin D and diabetes risk factor assesments with greater sample size.

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