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Comparative anti-inflammatory potential of ingredients of *Purandara Vati* and *Shwasakuthar Rasa*: A preclinical evidence based portrayal

Review Article

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Abstract

Asthma is a multifaceted, long-term inflammatory disease linked to tissue remodelling of the airway structure and hyper-responsiveness of the airways. The goal is to get the best asthma control possible while using the least amount of medication. It has been reported that oral consumption of corticosteroids increases the chances of osteoporosis, bone fractures, cataracts, pneumonia, opportunistic lung infections, diabetes, and obesity in those with asthma. Inhaled corticosteroids have also been linked to an increased risk of cataract development, respiratory infections, and BMD loss in asthmatic patients. Aspirin and NSAIDs have enormous side effects, such as hyperacidity and gastrointestinal disturbances, so long-term use of these medications is not recommended. Therefore, medications with few adverse effects and strong anti-inflammatory and asthmatic effects are needed to treat inflammatory disease. *Shwasakuthara rasa* and *Purandara Vati* are two well-known formulations for management of asthma with quite similar ingredients and can be therapeutically implemented as anti-inflammatory formulation. This article delineates preclinical evidences for anti-inflammatory potential *Shwasakuthara rasa* and *Purandara Vati*.

Keywords: *Asthma,* Inflammation*, Purandara Vati, Shwaskuthar rasa*.

Introduction

Asthma represents an intense worldwide public health issue. Surveys among adults reveal a significant frequency of lung function impairment and asthma symptoms, especially among those from lower socioeconomic backgrounds. Asthma symptoms comprise dyspnoea (with exertion/ non-exertion), frequent coughing, tightness in chest region, and wheezing. Many nations have created guidelines for the treatment of asthma. The goal is to get the best asthma control possible while using the least amount of medication. The guidelines acknowledge that even in mild persistent asthma there is inflammation in the airways, and they provide a thorough evaluation of the evidence supporting corticosteroids' ability to decrease inflammation in asthma. As a result, managing asthma heavily relies on inflammatory control (1).

It has been reported that taking oral corticosteroids by asthmatic patient increases the chance of developing osteoporosis, bone fractures, cataracts, pneumonia, opportunistic lung infections, diabetes, and obesity (2). If inhaled, also impose risk of cataracts, respiratory infections, and decreased bone mineral density (3). Long terms administration aspirin or NSAIDs is not suitable due to its well-known side effects like hyperacidity GI disturbances. If patient is allergic to aspirin or NSAIDs, he tends to develop severe respiratory reactions such as bronchospasm or exacerbation of asthma, respiratory diseases and may cause serious illness up to the level of organ damages (4). Hence, to control inflammatory pathology, medicine having minimal side effect and potent action on inflammation and asthma are useful. The currently used anti-inflammatory agents like aspirin and NSAIDs, have well-known adverse effects, such as hyperacidity and gastrointestinal issues, and hence their long-term use is not advised. An individual with aspirin-induced asthma or NSAID-exacerbated respiratory disease is said to have either allergy to aspirin or NSAIDs and respiratory symptoms such as bronchospasm or asthma exacerbation. So, medications with few side effects and strong anti-inflammatory and asthmatic effects are helpful in managing inflammatory pathology.

In Ayurveda classics, the formulations which are commonly used to treat the Bronchial asthma (*Tamaka-shwasa*) are *Shwaskuthara rasa*, *Shwaskasa-chintamani rasa* and *Sameerpanaga rasa, Purandara Vati* (5). However, the ingredients of *Shwasakuthara rasa* and *Purandara Vati* are quite similar and effective in management of asthma. *Shwasakuthar ras* is commonly

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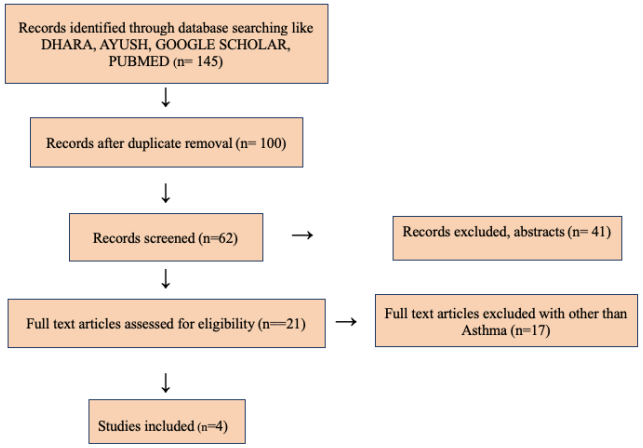
prescribed in Ayurveda for respiratory conditions, but it has *Vatsanabh* (*Aconitum ferox*) as one of the ingredients. But this plant is highly poisonous and can cause serious adverse effects if its shodhana (Purification) is not done properly. Purandar vati is also used for respiratory conditions and does not contain poisonous drug like aconite. Hence this drug is compared with *Shwasakuthar rasa* for their anti-inflammatory potential.

Methodology

Image 1: Search methodology (PRISMA flow chart)



The review was done by following inclusion criteria of articles reporting anti-inflammatory actions of *Parada* (Mercury), *Gandhaka* (Sulphur) , *Pippali* (*Piper longum* L), *Maricha* (*Piper nigrum*), *Shunthi* (*Zinziber officinale* L), *Vatsanabha* (*Aconitum ferox* L) , Tankana (Borax), *Manashila (*Arsenic disulphide), *P. longum* extracts, *Amalaki* (*Emblica officinalis*), *Haritaki* (*Terminalia chebula* L) , *Bibhitaki* (*Terminalia bellerica* L), *Ajaksheera* (goats milk) were reviewed from *PubMed, Scopus, Web of science indexed journals* with search engine of individual ingredients and 'asthma' 'anti-inflammatory action', 'inflammation management' etc. The articles reporting anti-inflammatory action or specific metabolite responsible for anti-inflammatory effect were compiled. Articles not satisfying search strategies and not satisfying the inclusion criteria were excluded from this review. The data was presented in systematic manner and included test drug information viz. part used or extract information, dose, duration, route of administration, experimental model, evaluating parameter and salient findings.

Literature review illustrates utility of *Shwasakuthara rasa* in conditions namely asthma and allergy, laryngitis, cough, respiratory infections, tuberculosis, mental disorders, coma conditions, hyperacidity, and heart diseases.

The ingredients of Shwaskuthara Rasa and Purandara Vati are explained in table 1. Both formulation contains five ingredients in common i.e. Shudhha Parada (purified mercury), *Shudhha Gandhaka (purified sulphur), Pippali (Piper longum* L. i.e. long pepper), *Maricha* (*Piper nigrum* L. i.e. black pepper), and *Shunthi* (*Zingiber officinale* L. i.e. dry ginger). *Shwaskuthara Rasa* differentiately contains *Shuddha Vatsanabha* (purified *Aconitum ferox* i.e. *Aconite*), *Shuddha Tankana* (purified borax), *Shuddha Manashila* (Purified arsenic). *Purandara Vati* additionally contains *Amalaki* (*Emblica officinalis* Gartn), *Haritaki* (*Termnalia chebula* L), *Bibhitaki* (*Terminalia bellerica* L). and *Ajaksheera* (Goat's milk).

Table 1: Comparative assessment of ingredients

SN	Ingredients	*Shwaskuthara Rasa*	*Purandara Vati*
1	*Shudhha Parada*	+	+
2	*Shudhha Gandhaka*	+	+
3	*Pippali*	+	+
4	*Maricha*	+	+
5	*Shunthi*	+	+
6	*Shuddha Vatsanabha*	+	-
7	*Shuddha Tankana*	+	-
8	*Shuddha Manashila*	+	-
9	*Amalaki*	-	+
10	*Haritaki*	-	+
11	*Vibhitaki*	-	+
12	*Ajaksira*	-	+

The anti-inflammatory potential of above-said ingredients is mentioned in table 2.

Table 2: Anti-inflammatory potential of *Shwasakuthar rasa* and *Purandara vati*

Ingredient	Details of In-vivo study	Extract used	Useful part	Model	Parameter	Results	Ref
Shudhha Gandhaka	Dose 37.5,75,150 and 300 mg/kg body weight of *Gandhak churna*	NA	NA	Carrageenan induced Paw edema	Reduction in paw edema	Significantly inhibits values of edema at 3hrs post carrageenan were 125.9%, 113.4% and 111.0% for 45, 90 and 180 mg/kg of *Gandhka churna* respectively which inhibited paw oedema by 78.71% at the 2nd hour after carrageenan administration	(6)

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Pippali	Wistar rats, 200 mg/kg, orally	Methanol	Fruit	Carrageenan induced Paw edema and Formaldehyde induced paw edema	Paw edema reduction	Inhibition in swelling of paw induced by 28% carrageenan, inhibition in formaldehyde induced paw edema. By 46% against standard drug diclofenac and Phenyl butazone	(7)
Maricha	Swiss albino mice of wither sex, Piperine doses of 10 and 15 mg/kg bw	Ethanol and hexane extracts	Fruit	Carrageenan induced Paw edema	Reduction in paw edema	Ethanl extract of Piperine at all doses of 5, 10 and 15 mg/kg was reported for significant inhibition of edema when compared to control, but less significant activity when compared to standard. Maximum activity reported at a dose of 15 mg/kg after 120 min Hexane extract at a dose of 10 mg/ kg after 60 min, ethanol extract at dose of 10 mg/kg possess significant activity compared to control but non-significant when compared to standard.	(8)
Sunthi	C57BL/6 female gender (6–8 weeks) and Thy1.1+ mice, intraperitoneally every second day for 45 days	*NA*	[6]-Gingerol	Mouse model of TB infection (Mtb strain H37Rv)	*Almar blue assay*	6-Gingerol inhibited Growth of mycobacterial tuberculi in the lung, liver, and spleen. Modulation of pro- and anti-inflammatory innate cytokines was found after 6-gingerol treatment. Cytokine measurements from peritoneal macrophages suggested increase in number of CD4± and CD8+ T cells or Cd11b± and CD11c± cells with 6-gingerol treatment and enhanced p38 MAPK phosphorylation. Improvement in host-protective Th1 (type 1 T helper) and Th17 (T-helper 17) immune responses was found against infection by tubercular organisms.	(9)
Triphala	Wistar albino rats of either sex, 125–150 g	Aqueous extract of T. *chebula*, E. *officinalis*, & T. *bellerica* fruits in equal (1:1:1) proportion	Fruit	Carrageenan induced Paw edema	Reduction in paw edema	Suppression in inflammatory mediator levels was found in serum (IL-1b: 99%, TNF-a: 75.5%, MCP-1: 76.4%, VEGF: 75.2%, and PGE2: 69.9%) and in paw tissues suppression was found as follows: (IL-1b: 75.5%, TNF-a: 71.6%, MCP-1: 69.1%, VEGF: 55.1%, and PGE2: 66.8%)	(10)
Ajaksira	Rats, kept on similar diet with different sources of fiber (5% of the diet): cellulose or a mixture of cellulose and goat's milk oligosaccharides.	Goat's milk oligosaccharides	NA	DSS treatment induced colonic inflammation	intestinal micorbiota and gene expression by DNA microarray technology	Reduction in gut inflammation which helped in the healing of damaged digestive epithelium.	(11)

Vatsanabha		ethanol extract	Root	Carrageenan induced Paw edema	Reduction in paw edema	Ethanol extract at dose of 50and 500 mg/kg significantly (p<0.05) inhibited carrageenan-induced rat paw edema in dose-dependent manner i.e. by 65.31 % and 77.85 %, respectively in comparison with control group after 1 hour	(12)
Tankana						Tankana showed minimum inhibitory concentrations 1.9 ± 0.5 mg mL^{-1} against P. acne. It inhibited TNFα by 59.09% and IL-8 production by 47. 92% in *P. acne*-stimulated THP-1 cells.	(13)
Manashila	Manahshila (95% w/v purity) at doses of 0.35, 0.7, and 1.4 mg/kg, orally in rats	Shodhita & Ashodhita	NA	egg albumin-induced hind paw edema	Reduction in Hind paw edema volume	Crude realgar i.e. The *Ashodhita* (impured) *Manahshila* is fatal as shown mortality, while purified i.e. *Shodhita Manahshila* in different four media didn't possess mortality up to a dose of 2,000 mg/kg. Significant inhibition ($p < 0.05$) of egg in albumin-induced hind paw edema was seen at dose level of 1.4 mg/kg by both *Ashodhita* and *Shodhita Manahshila* Anti-inflammatory activity of *Shodhita Manahshila* was more potent at all three dose levels in a dose-dependent manner. *Aadrak bhavita* (Ginger juice treated) *Manahshila* was best in alleviating rat's response to egg albumin-induced inflammation	(14)
Shudhha Parada						No data available on direct use of only mercury in rats	

Discussion

Purandara Vati and *Shwasakuthar rasa* are two herbo-mineral compositions that are useful in treating asthma symptoms.

The primary chemical form found in conventional oral mercury medications is mercury sulphide which is an insoluble inorganic mercury molecule. For thousands of years, traditional Chinese medicine has employed cinnabar, which contains mercury sulfide, as a component in a variety of treatments. Mercury sulphide contains nano-particle of mercury and sulphur which offer a unique set of properties for drug delivery in controlled and sustainable manner and provides extended stability and longevity, with targeted distribution of drug molecules. This strengthens the anti-inflammatory effects of HgS. The non-toxic form of sulphur prevents the binding of NF-κB protein and IL-1β (high glucose expression induced), IL-6, and TNF- α and binding of NF-κB protein to the DNA of pro-inflammatory cytokines. Due to its potent anti-inflammatory effects many countries, including the USA are using non-toxic form of natural sulphur or dietary sulphur for treating inflammatory conditions (15).

P. longum has long been associated with Ayurvedic claims of anti-allergic and anti-asthmatic properties (16). In mice, *P. nigrum* inhibited and decreased eosinophil infiltration, hyper-responsiveness, and inflammation (17). *Z. officinale* is helpful in treating and preventing allergic illnesses because of its ability to decrease allergic responses (18) .

Chronic disorders like inflammatory problems can be effectively treated with *piperine* alone or in combination with other treatments. Through the regulation of ICAM-1 expression, *Piperine* inhibits the inflammatory process. Furthermore, the activity of macrophages in eliminating necrotic and apoptotic cells that accumulate after inflammatory injury is enhanced by the repression of their ICAM-1 protein expression (19). Moreover, *piperine's* anti-inflammatory properties stem from its capacity to inhibit TNFα-induced production of cell bond molecules, including E-selectin and vascular cell adhesion molecule-1 (VCAM-1) (20). When taken in combination with traditional medical treatments, piperine's anti-inflammatory effects can be enhanced.

It is reported that, bioavailability of the antibiotics increases when piperine is added to the oral treatment given to rabbits that included ampicillin and norfloxacin (21). It has been demonstrated that administering *piperine* with a range of spices results in an additively beneficial biological and pharmacological effect. In *Shwasakuthara rasa and Purandara Vati* both *Zinziber officinale* and *Piper nigrum* have been included. Furthermore, piperine functions as an immunomodulator, which is beneficial for asthma patients (22).

Triphala has the anti-inflammatory and anti-nociceptive actions. Anti-inflammatory potential is due to steroidal-like action and by inhibition of cyclooxygenase pathway (23). The anti-nociceptive action of *Triphala* is regulated via both peripheral and partly central nervous system. *Triphala* efficiently inhibits production/gene expression of inflammatory and pro-inflammatory cytokines and other inflammatory mediators. This is due to up-regulation of HO-1 and by suppressing transcription factor NF-κB nuclear translocation. In-vivo studies confirms anti-inflammatory effects of Triphala is by reducing expression of inflammatory mediators and via inhibition of NF-κB activation (24).

A. ferox possess anti-inflammatory action by inhibiting biosynthesis of leukotriene B4 in bovine polymorphonuclear leukocytes supports (25.) The analgesic and anti-inflammatory effect of aconite species is due to its content Lappaconitine and Yunaconitine.

Research depicts anti-inflammatory action of *Tankana* is due to membrane stabilisation effect by stabilising lysosomal membrane. It inhibits the anti-inflammatory response by preventing lysosomal constituents of activated neutrophils like bacterial enzymes and protease which reduces inflammation and further damage (26).

The purified arsenic inhibits inflammation by stabilising the RBC membrane and by inhibiting release of various lytic enzymes and active mediators of inflammation. Zingiberine acts as chelating agent which acts on nuclear factor kappa. It also enhances the anti-inflammatory action of *Shodhita Manashila* (27).

Purandara Vati has additionally *Triphala*, a potent anti-inflammatory combination and *ajaksheera* which also impart anti-inflammatory effect. Additionally goat milk contains olgosaccharides which has healing effect on epithelial cells. In asthma pathology is reduction in inflammation and healing is expected.

Importance of *Yogavahi* ingredient in managing episodes of asthma

The ingredients *Parada*, *Gadhaka* and its combination *Kajjali*, *Pippali* etc are *Yogavahi* (bio-enhancer) in nature. The various mechanisms are reported for proving bio-enhancer action comprises of modulation of cell signal, inhibition of enzymes participating in biotransformation of drugs and DNA receptor binding, transduction and inhibition of drug efflux pump etc. Use of bio-enhancer helps to reduce drug cost, toxicities, and other side effects, and enhancing favourable therapeutic impact (28). *P. longum* is reported for its bio-enhancer action by inhibition of principal metabolizing enzyme CYP3A4 and P-gp efflux transporter present in gastrointestinal wall (29).

Conclusion

Shwasakuthara rasa and *Purandara Vati* contains ingredients which possess anti-inflammatory action. The additional ingredient in *Purandara Vati* probably will have more potent action than *Shwaskuthara rasa* as evident from preclinical analysis. Both the formulation contains bio-enhancers which will exert a positive effect on the inflammatory pathology of asthma.

Conflict of interest: Nil

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