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A Review on pharmacological properties of *Rubus fructicosus*

Review Article

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Abstract

Medicinal plants are an excellent source of physiologically active phytochemicals with long-recognized medicinal properties. *Rubus fruticosus* also known as blackberry plant. The parts are employed for their therapeutic benefits. The purpose of this study was to review the pharmacological characteristics of *R.fruticosus* and its associated phytochemicals. Its extractions have a significant impact on the phytochemical and pharmacological activities. In this review, the most useful phytochemicals include flavonoids, anthocyanins, tannins and phenolic compounds, which are acquired from the plant's components. The various pharmacological actions of plants are mostly caused by phytoconstituents produced in plant tissues. It has demonstrated antibacterial, antioxidant, anti-inflammatory, antiwrinkle, anxiolytic, SPF and other actions that may be helpful in the creation of future pharmaceutical products.

Key Words: *R.fructicosus,* Blackberry, Anti-inflammatory, Anticancer, Antioxidant, Antimicrobial.

Introduction

Rubus fructicosus commonly known as blackberry belonging to family *Rosaceae.* It contains roughly 700 species. It's widely known for its fruit which has medicinal, nutritional and beauty purpose. In English is generally called, covert or European blackberry or scald head or shrubby blackberry or Wild blackberry. In India, particularly in Hindi, it's known as Vilaayati Anchhu or kaalaa jaamun. It's known as Tût shawkî or' Ullayq in Arabic(1). Blackberry leaves have been traditionally used as an antimicrobial agent and for their healthy antioxidant effect. In Europe it used for treating diabetes. An extract of the leaves showed a hypoglycemic effect on diabetic rats, Juice, fruits is effective in condition of anemia. Leaves and roots of the plant are long- standing home remedy for anaemia, regulates menstruation, diarrhoea, and dysentery(5).The blackberry gave triterpene erosive and rubitic erosive described as 7 alpha - hydroxyursolic erosive. Blackberries are outstanding for their high nutritional substance of salutary fibre, nutrient C, nutrient K, and mineral manganese. The root contains saponins and tannins. Fruits are assembled for jam, bathos, wine, and alcohol (7). *Rubus fruticosus*; fruits, leaves, stems, and roots shows essential medical applications. *Rubus fruticosus* are well known for its antidiarrheal, antioxidant, anti-inflammatory, anticancer and other properties. Phenolic compounds are the major active component present in large number. The aroma compounds were identified as 2-heptanol, p-cymen-8-ol, 2-heptanone, 1-hexanol, α-terpineol, pulegone,1-octanol, isoborneol, myrtenol, 4-terpineol, carvone, elemicine, and nonanal in thornless evergreen blackberry(6). Cyanidin-3-glucoside, a natural product present in blackberries, possesses chemo-preventative and chemotherapeutic conditioning in experimental models(8). Ripened fruit when taken in combination with leaves of Achyranthes aspera is used in treating eye diseases(9). The ideal of this review is to explore the recent activities on anticancer, antidiarrheal, antioxidant, anti-inflammatory eventuality of *R.fruticosus* and identify its active fragments from which implicit the activity.

Aim

Encourage research on *Rubus fructicosus* for its potential to treat a range of illnesses.

Objective

To enable research on *Rubus fructicosus* for its potential medical benefits.

Table no.1 Classification for Kingdom *Plantae* Down to Species *Rubus fruticosus* L. (10)

Rank	Scientific name and common
Kingdom	Plantae – Plants
Sub-kingdom	Tracheobionta – Vascular plants
Super division	Spermatophyta - Seed plants
Division	Magnoliophyta - Flowering plants
Class	Magnoliopsida - Dicotyledons
Subclass	Rosidae
Order	Rosales

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Family	Rosaceae Juss. - Rose family
Genus	*Rubus* L. – blackberry
Species	*Rubus fruticosus* L. - shrubby

Phytochemistry

Blackberry fruit itself, and its products as well as by- products are a rich source of phytochemicals and natural antioxidants which are being explored for their health promoting conditioning. Different cultivars of *Rubus fruticosus* present different chemical composition with regard to different areas of globe. still, the *Rubus fructicosus* generally contain following phytochemical ingredients alkaloids, flavonoids, polyphenols, tannins, anthocyanins, saponins, glycosides, terpenoids, sterols, and carbohydrate(1). Blackberries, among fruits, rank veritably largely for their anti-oxidant exertion which is substantially because of high phenolic contents and major phenolic contents are flavanols, ellagic acid, cyanidins, ellagitannins, anthocyanins, quercetin, tannins, gallic acid. Essential phytoconstituents are Anthocyanins, Quercetin and ellagic acid. The compounds reported particularly, in seed oils of Korean thorn less blackberries were, γ-tocotrienol, α-tocopherol, δ-tocopherol and γ-tocopherol. Four variation in blackberries of fatty acid composition in the seed oil is given in table no.1 (2). Blackberries contain the utmost position of the anthocyanins the main anti-oxidants which is superior to strawberry(3). These flavonoids or hydrophilic colour shades give a variety of tones of blue, orange and red because of reversible variation in the structure of flavylium cation which is sensitive to natural pH revision in factory; and are present in flowers, leaves, roots, and fruits. Blackberry seed oil painting contains high numbers of tocopherols(the vitamin E) and intriguing make up of adipose acids. GCMS analysis is used for in order to find out the chemical profile of oil painting.

Blackberry Description (11)

Seeds

Seeds are light to dark brown in colour, round, 2 – 3 mm long with irregular and deep recesses.

Leaves

The upper side of leaves is dark green while underpart is lighter green. Short pinpoints cover the stalks and modes of leaves. Leaves are ternate over, tending to 5 or 7 palmate circulars towards the base. Axial sides of these circulars are folded into pleats and glabrate which are dark red- purple in fall, green in summer and deciduous in downtime. Biennial stems or semi woody called nightsticks. They vary from sprawling to nearly erect, spreading shrubs with nuisance and leaves.

Stem

The stem grow up to 7 m in length that is greenish, purplish or red in colour.

Flower

They are formed in clusters at the end of floricanes. Diameter of a flower is about 2 – 3 cm having 5 pale pink or white petals. Flowers have multiple stamens .

Fruit

A thick cluster of separate units or drupelets forms the fruit which on growing turn black or dark purple from red.

Root

50 – 80 mm per day. They are distributed into two groups in terms of branch structure generative club(floricane

Table 2: Fatty acid composition in the seed oil of Four blackberry variation (2)

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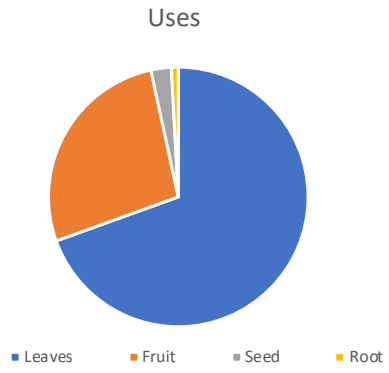
Fatty acid (%)	Young	Boysen	Hull	Kiowa
16:0 (Palmitic)	2.59	3.19	3.58	4.28
16:1 (Palmitoleic)	0.10	0.10	0.08	0.10
18:0 (Stearic)	1.16	1.75	2.25	1.63
18:1 (Oleic)	11.99	20.45	9.41	19.19
18:2(n6) (Linoleic)	51.67	57.92	69.28	62.81
18:3(n3) (Linolenic)	31.55	15.14	13.99	10.60
20:0 (Arachidic)	0.37	0.68	0.85	0.70

Fig no.1 Blackberry mostly parts used from 2017-2022 (4).



Pharmacological and some other actions

Antimicrobial

Utmost anthocyanins are released in acid phase and pepsin phase during in vitro release. The stylish carrier agent for the protection of anthocyanins is Whey Protein Insulated(WPI). In vitro release studies showed that encapsulation stabilizes anthocyanins and functions as a delivery method. The anthocyanins have been studied recent in the last times due to adding reports of health benefits. also, anthocyanins have been reprised using a variety of methods. Microencapsulated anthocyanin by spray drying of berries and roselle were estimated to determine the effect of different carrier agents. WPI which is known as Whey Protein Isolated and agave fructans) on " In vitro " release of anthocyanins, which has functional and antimicrobial properties. The attention of all carrier agents, was 0.5

percent (in base, the total soluble solids % of berries and roselle extract part)(12).

Plant derivations from *R. fruticosus* leaves considered in this study were suitable to decelerate down the growth kinetics of L. monocytogenes(covered by plate counting), indeed if added at concentrations corresponding to half of MIC. In general, both Phenolic extract[PEs]and Essential Oil[EO] significantly reduced the maximum cell culturability of approx. 1 log unit. PEs were less effective than EOs in limiting the growth performance of L. monocytogenes. Indeed, no loss of culturability was observed for the PE of *R. fruticosus* leaves. The antilisterial exertion was more applicable using EOs, particularly the one deduced from *R. fruticosus* leaves. This ultimate caused the most severe effects, since it was suitable, in a many hours of incubation, to nearly fully inhibit the cell culturability. According to the fow cytometry analysis, the presence of this EO was suitable to induce the death of the major part of cells(> 99). Concerning the other factory derivations, the distinction observed in some cases between viability and culturability could indicate the presence of cells not suitable to grow in culture media(at least in the espoused conditions). Blackberry leaves and juniper needles, that can be exploited in food product and other artificial sectors (13).

Nanoscience has developed different greener approaches as an alternate system for the development of nanoparticles .The extract of *R.fructicosus* was used rather of poisonous reducing and stabilizing chemicals. The average particle size of fabricated 'ZnO nanocomposites 'was calculated as 102.47,102.97, and 151.99 nm by using Debye-Scherrer'sequation.. Characterization of synthesized nanocomposite were done by SEM, UV/ VIS spectrophotometry, Fourier transform infrared (FTIR) spectroscopy, and XRD ways. Crystalline nature of the synthesized nanoparticles was checked by XRD pattern in the range of 10- 80 nm. The UV immersion peak of Elaeagnus umbellate (ZnO- EU) nanocomposite at 340 nm, *Rubus idaeus* (ZnO- Ri) nanocomposite at 360 nm, and *Rubus fruticosus* (ZnO- Rf) nanocomposite at 360 nm was observed. The nanocomposites were checked for their antimicrobial and set up to be effective against three phytopathogens. The antimicrobial exertion of ZnO nanocomposites showed good results against Escherichia coli(341), Staphylococcus aureus(345B), and Pseudomonas aeruginosa(5994 NLF)(14).

Chemotherapy is an invasive medicine treatment that uses chemical medicines dangerous for fast-growing cells. Cyclophosphamide(CP) is one of the medicines belonging to the group of cytotoxic medicines, which is used in chemotherapy. Medicinal plants with their defensive goods are suitable to help cell destruction conditioning as well as the dangerous effect of some chemicals and drugs. Vitamins similar as A, C, E and folic acid in the berry fruit powder have been mentioned in anti-cancer studies. It was demonstrated that CP had the effect of destroying hematopoietic tissues. The number of red blood cells, white blood cells, and platelets was significantly reduced in the rats who were receiving CP. Contemporaneous treatment of rats with fruit extract improved their blood parameters. These results indicate that different useful composites in the fruit can cover the bone marrow tissues against the destructive of CP in the tested rats(15).

Antioxidant, Anti-inflammatory, Gastroprotective

The Juice of *R. fruticosus*(RFJ) fruits grown in Sicily was analysed for polyphenol composites and tested to estimate in vitro antioxidant and in vivo anti-inflammatory and gastroprotective activity. RFJ, containing substantially anthocyanins, similar as cyanidin derivations, significant quantities of phenolic acids, and lower quantities of flavonoids, showed significant antioxidant exertion in DPPH. In vivo studies showed that RFJ inhibit significantly the carrageenan - induced paw oedema(63 – 71%) in rats and have anti-inflammatory activity particularly significant in association with phenylbutazone(94 – 96%). In addition, RFJ pre-treatment was suitable to help the ethanol-induced ulcerogenic effect in rats. The veritably high content of polyphenol composites with cyanidin-3-O-glucoside as the most abundant , the suitable antioxidant and free radical scavenging properties juice of *R. fruticosus*(RFJ)(16).

The phytochemical analysis of RFE (*R.fruticosus* extract)possesses higher polyphenolic and flavonoid content ,highest antioxidant activity. The studied extracts showed a concentration-dependent protective effect on DNA cleavage induced by H2O2, UV photolysis. The daily oral administration of 200 mg/kg of RFE during three weeks showed an improvement of the blood total antioxidant capacity: The topical application of 2 mg/ear of RFE inhibited the croton-induced ear oedema by 75.72%. These inhibitions were higher than that of indomethacin, used as a reference. Moreover, the oral administration of 400 mg/kg of RFE inhibited significantly (11.57%) acetic acid induced vascular permeability in mice. However, this effect was lower than that of indomethacin(21).

The ellagitannins of *fruticosus* has shown in the drop of Ulcer Index by 88% and were defensive against the oxidative stress of the rats induced by ethanol. likewise, the findings showed that the ellagitannins had inhibitory action on the secretion of IL- 8 induced by low-concentrated IL- 1β and TNF- α. It may be concluded that *R.fructicosus* hydroalcoholic extract (RFHE) may be suitable to maintain the inflammatory marker TNF- α and IL- 6 through its antioxidant effect and elimination of free radicals, thereby affecting the complication of Diabetes Milletus. *R.fruticosus L.* have anti-inflammatory impacts on the gastric lesions of the rat model induced by ethanol. Diabetes causes oxidative damage and accordingly the serum position of inflammatory rises. RFHE was shown to be significantly identified with lowering the position of malondialdehyde(MDA) tumour necrosis factor (TNF)-α, interleukin (IL)-6, and C-reactive protein(CRP)of diabetic rats (22).

The optimal blending ratio of extracts of Hippophae rhamnoides (H. rhamnoides) fruit, *Rubus*

fruticosus (R. fruticosus) leaf, and Perillae folium (P. folium) leaf as a potential functional material for antiwrinkle, antioxidant, anti-inflammatory, and whitening properties. The most efficacious ratio of H. rhamnoides fruit: *R. fruticosus* leaf: P. folium leaf was 0.25:0.7:0.05. At this ratio, the elastase inhibitory effect, an indicator of wrinkle improvement, was 28% compared to the control. The antioxidant activity was 71.8% higher than the control. Additionally, NO formation was significantly suppressed by the extract complex. Tyrosinase inhibitory activity, a whitening index, showed 24.4% improvement over the control. Finally, hydrogen peroxide-induced cytotoxicity was significantly inhibited (23).

The non-polar seed extracts obtained using the Blig Dryer method for *Rubus fruticosus* and grape has shown high level of total phenolic compounds and antioxidant activity but the extracts obtained through Sox showed inhibitory effect against E. coli (IAL 2064) and Staphylococcus aureus (ATCC 13565). As for cell viability, the non-polar extracts did not show cytotoxicity or antiproliferative effect in the different cell lines, which shows their relative toxicological safety. It is concluded that grape and blackberry seeds can be used as sources of derived lipid antioxidants in different technological applications (24).

Sun Protection Factor [SPF]

Sunscreen medications are ornamental medications that are used as protection to reduce the impact of sun exposure, where the formula contain active constituents to absorb or reduce sun, especially in areas exposed to ultraviolet shafts and infrared. One of the implicit natural constituents for sunscreen is blackberry fruit (*Rubus sp.*). Contains flavonoid composites that can help the dangerous side-effects of UV light. The study aims to determine the stability of the *R.fructicosus* extract sunscreen gel formula stored for 90 days to determine the SPF value test results of blackberry fruit extract using UV- Visible. After doing exploration, physical stability test for 90 days of store in a hot oven at a temperature of 40 °C and moisture< 75 % sunscreen gel of extract (*Rubus fruticosus L.)* was stable during 's necessary to carry out chemical stability tests and long-term stability tests at storage of 2 years 30 ± 2 °C with a moisture of 75 ± 5. % (17).

Antidiabetic

R.fructicosus leaves extract was prepared by maceration system and gavaged for 28 successive days to the rats. Rats whose level of glucose in blood lesser than 200 mg/ dl, after injection of 70 mg/ kg STZ (Streptozocin), were enrolled in the study. In rats the blood glucose position at 0-time, 1 hour and 3 hours after gavages, and each week was measured. In the 14th and 28th days, serum factors, and on the last day, the weight of liver, kidney and heart were measured. Within four weeks, level of glucose in blood in the group entering the *R. fruticosus* extract had a significant lowering trend. Groups who were entering Blackberry extract, the serum lipid parameters and liver function tests, dropped from alternate to fourth week, compared with positive control group, was significant. The study showed that aqueous oral administration of extract of Blackberry leaves can have the antidiabetic effect(18).

Intestinal α-glucosidase and α-amylase break down nutritive poly-and oligosaccharides to monosaccharides and their activity significantly contributes to postprandial hyperglycemia. Inhibitor such as Competitive inhibitor of these enzymes, similar as acarbose, are effective antidiabetic medicines, but have unwelcome side effects. The setup of wild strawberry (Fragaria vesca), blackberry *(Rubus fruticosus),* and European blueberry (Vaccinium myrtillus) extract of leaf inhibit α- glucosidase and α-amylase enzyme exertion in vitro and are effective in precluding postprandial hyperglycemia in vivo. Toxicology tests on H9c2 rat embryonic cardiac muscle cells extant of berry alone or as an admixture to normal(control), fat, prediabetic, and streptozotocin-convinced diabetic mice downgraded the rise of blood glucose. The effectiveness was equal to that of acarbose on blood glucose. These results show extract of berry leaf for testing in clinical trials in order to assess the clinical significance of their goods on glycemic control(20).

DNA Damage Protective

Blackberry root system methanolic extract exhibited the highest levels of TPC, TFC, DPPH, and ferric reducing capacity activity. Blackberry root extracts were tested for antibacterial activity against clinical isolates of Escherichia coli, Klebsiella spp. , Proteus spp. ,Staphylococcus aureus and Pseudomonas spp.) using the Kirby Bauer technique. Despite a dosage of 100 mg/mL, methanolic extract exhibited strong antibacterial activity. These outcomes showed that the antioxidant compounds found in blackberry root system extract (*Rubus fruticosus L*) is able to counteract the negative effects of free radical (27).

Natural Food Colorant

Four distinct cyanidin derivations were linked, such as cyanidin- O- hexoside, cyanidin-3-O-glucoside, cyanidin- O- pentoside, and cyanidin-3-O-dioxaloilglucoside. It has richness in anthocyanin composites, *R.fructicosus* juice were also used to prepare solid colourings for operation in industries such as food industry. Through the spray- drying method for each fruit three formulation were obtained, and stability was assessed over 12 weeks which was stored at room and refrigerated temperatures. In general, the colourings revealed a great and stable colouring capacity over time, without toxin for non-tumour cells and microbial loads within the values limit for food. Therefore, these fruits can be considered as good natural sources of anthocyanins to be used as natural colourings, not only in industries such as food, but also in medicinal, cosmetics, or fabrics, among others (19).

Anxiolytic-like effect

The rats were treated with blackberry juice for 21 days and also tested in the elevated plus maze, locomotor exertion test and forced swim test. The

Table no. 3 Pharmacological properties of various part of Rubus fructicosus

Species	Sr.no	Part	Chemical constituent	Activity	References	Year
Rubus fructicosus	1	Berries	Anthocyanins with agave fructans.	-anti-microbial -inhibition of E.coli 67% Microencapsulation by spray drying.	12	2018
	2	Leaves	Phenolic	-Anti-microbial against L.monocytogenes Scott.A -Prevent food borne pathogen	13	2022
	3	Fruit	Extract	Anti-microbial against E.coli, S,aureus, P.aeruginosa -Synthesis of ZnO nanocomposites -green approach	14	2022
	4	Fruit	Extract	Anti-oxidant, anti-inflammatory -To protect bone marrow tissue against cyclophosphamide	15	2021
	5	Fruit juice	Polyphenols Cyanidin-3-O-glucoside Flavonoids	-Anti-inflammatory, gastroprotective, anti-oxidant	16	2018
	6	Fruit	Flavonoids	Stability during storage -sunscreen gel	17	2020
	7	Leaf	Extract	Anti-diabetic	18	2017
	8	Fruit	Anthocyanins	Food colorant -by spray drying technique as natural additive food colorant	19	2021
	9	Leaf	Flavonoids	Alleviate starch induce hyperglycemia	20	2020
	10	Leaves	Phenolics Flavonoids	Anti-oxidant, Anti-inflammatory	21	2017
	11	Plant	Ellagitanin	Ani-diabetic, Anti-inflammatory, Anti-oxidant	22	2020
	12	Leaves	Extract	Anti-wrinkle	23	2019
	13	Seeds	Extract	Cytotoxicity, anti-microbial, anti-oxidant	24	2021
	14	Fruit juice	Anthocyanins Flavonoids	Anxiolytic	25	2019
	15	Fruit Juice	Anthocyanins Polyphenols	Cisplatin induce toxicity	26	2020
	16	Root	Phenolic Flavonoids	DNA protective damage	27	2022

results were compared with a reference anxiolytic medicine diazepam (2.0 mg/ kg) and vehicle (8.7 ml/ kg). The blackberry juice intermediate dose shown an anxiolytic-like effect that was same to diazepam, without affecting locomotive activity. Blackberry juice intermediate dose of (5.83 mg/ kg anthocyanins,27.10 mg/ kg polyphenols) shown an anxiolytic-like effect. The implicit remedial use of this natural substance to help reduce anxiety that's associated with acute stressful event (25).

Cisplatin-Induced Testicular Toxicity

Common problem associated with chemotherapy are testicular toxicity and infertility. Cisplatin (CP) considered as most reported chemotherapeutic agent. It was found that Cisplatin was reported to damage synthesis of spermatogenesis and testerone the well-established mechanisms explaining cisplatin induced testicular toxicity is its ability to induce oxidative damage .CP caused an elevation in lipid peroxidation level (MDA) paralleled with significant decline in GSH content, SOD and CAT activities in testes as well as decrease of serum testosterone levels compared to control group. Co-administration of blackberry juice with cisplatin ameliorates all the biochemical deteriorations with preserve the normal histological architecture of testes (26).

Conclusion

The medicinal plant *Rubus fruticosus,* also known as blackberry, has been used for its several therapeutic benefits. *R.fruticosus* has an intriguing chemical makeup because a number of its constituents have pharmacological and therapeutic effects. The purpose of this study was to review the pharmacological characteristics of *R.fruticosus* and its associated phytochemicals. Its extractions have a significant impact on the phytochemical and pharmacological activities .

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Conflict of interest

There are no conflicts of interest with this data.

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