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Medicinal Plant Species: *Pistacia integerrima* galls – A Comprehensive Review

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Abstract

Karkatasringi, whose botanical name is *Pistacia integerrima* and belongs to the Anacardiaceae family, is a well-known medicinal plant. This plant is native to India and is distributed along the Northwest Himalayan region at about 500–2500 m above the sea level. Various parts of the plant including roots, bark galls, and leaves contain a number of secondary metabolites. Galls are most commonly used in unconventional medicines. There are various Ayurvedic formulations which include Chyavanaprasha, Shringyadi cuma, and Dasamularista and these formulations are used in the treatment of various diseases including ajeema (indigestion), jwara (fever), and yakrit roga (liver disorders) and also in the treatment of swasa (asthma), yakshma (tuberculosis), and hridyaroga (heart diseases). Furthermore, the galls contain secondary metabolites such as flavonoids, terpenoids, and alkaloids. The bark of this plant contains flavonoids and terpenoids. The roots and leaves contain terpenoids and tannins. The presence of tannins as major constituents is responsible for the astringent action. The plant species *P. integerrima* which belongs to the family Anacardiaceae is known for its many uses globally and thus represents the whole family for its high therapeutic value. It is used in the treatment of various diseases including some common conditions such as vomiting, fever, asthma, diarrhea, and cough and also used in modern medicine. Commonly known as crab's claw, *P. integerrima* is a tree anciently found in Asia and is a botanically important tree. The galls of this plant have been used in treating dysentery, asthma, liver disorders, and cough and also used to cure snakebites. Using the extracts of *P. integerrima*, various secondary metabolites including sterols, phenolic compounds, and terpenoids have been isolated. In this review, we highlight the description of plant in classical literature of Ayurveda, and also in this review, we try to discuss about the therapeutic properties and chemical constituents of this plant. An attempt is made to assess the therapeutic potential of this plant in both conventional and modern systems of medicine. This review includes the traditional medicinal uses along with the phytochemical and biological evaluation of this plant species. Furthermore, after considering this review, one can build a foundation for further exploration on this topic and utilization of these resources for further research as well.

Keywords: *Pistacia integerrima*, Phytochemistry, Galls, Constituents, Toxicity

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Introduction

Pistacia integerrima is a single stemmed, multibranched, and deciduous tree belonging to the family of Anacardiaceae.[1] This plant is found in native to Asia broadly circulated in West Himalaya to Kumaon, East Afghanistan, Northwest, and Pakistan.[2] Furthermore, in the Siwalik ranges/Rohilkhand,[3] zebrawood and crab's claw are the widespread names intended for this medicinally vital plant species though it has various vernacular names in the Pakistan (thoak, khanjar, and shnai) along with India (kakarsinghi, kakroi, kakra, kakar singhi kakring, and kakkar) in Tables 1 and 2[4] The plant is well-known as kakra in Hindi, chakra, shikari, and chandraspada in Sanskrit Table 3,[5,6] worms make typically horn-shaped galls on the leaves and branches. These galls consist of a pinkish, pale greenish, and brown horn shaped, curved or straight, twisted, elongated, and hollow, while young they are coriaceous, however, afterward become hard. This gall is caused through the insect Dasia aedifactor (Homoptera), (plant produce resin against insect). They create these galls beside sucking juice as of the leaves. Then, they are called karkatshringi.[7] The galls are well thought-out as store houses of secondary metabolites so have consequence in Indian established medicine system.[5] Leaves are ovate and board and are present in pairs. Flowers are red in color and small. Fruits are brown in color when mature and shiny. The rugose, horn-shaped, and hollow galls similar to excrescences are used intended for medicinal purposes and they have a bitter taste and very sharp. The galls are astringent aromatic and have elevated value in Ayurvedic medicines as a remedy intended for asthma, fever, psoriasis, pharyngitis, phthisis, dysentery, ulcers, general debility, dyspepsia, skin diseases, leprosy, anorexia, vitiated condition of tridosha, inflammation, leukorrhea, irritability of stomach, and other disorders for the respiratory tract, vomiting of children, in high cough, modern medicine for the treatment of diseases which are fever, scorpion sting, and snakebite. The bark and galls of the plant have a number of secondary metabolites containing anti-inflammatory, antimicrobial, antibacterial, and analgesic activities[8,9] and hyperuricemic effect.[10] Chemically, it has sterol,[11,12] flavonoids,[13,14] monoterpenes,[11,15-19] and dihydromalvalic acid and the leaf galls used for rejuvenator are well known along with endorsed to antioxidant pro to being there

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of flavonoids and phenolics.[20] Majorly, a gall includes tannins, resins, tetracyclic triterpenes, dihydromalvalic acids, camphene, amino acids, sterols, pistacienoic acid, pistancin, luteolin, and pistacinin.[21] At the time of teething in children, it is also very helpful. It has been informed to have hyperuricemic effect disorder, analgesic anti-inflammatory activities, and depressant.[22] *Pistacia integerrima* has altitude between 12,000 and 8000 feet and 10–12 m in height[23] and large pinnately compound leaves, with many branches, single stem. Twenty-five cm long leaves consisting of lanceolate leaflets 2–6 pairs. Flowers are arranged in panicles band reddish in color. Globular fruits consist purple to blue in color 4–6 mm diameter.[24,25]

Broad Features

P. integerrima consists height up to 18 m and the barks are blackish or dark gray. Distinctive galls are formed on the leafy branches. Flowers are dioecious, small, unisexual, and reddish. Female flowers have long lax panicles. While male panicles short, compact, Drupe globose, rugose, wrinkled and gray while ripe. The leaves vary, pinnate, 15–23 cm long, with or without terminal leaflet, leaflets 4–5 pairs, acuminate, lanceolate, coriaceous, sub-opposite, and 7–12 cm long.

Microscopic Characters

Transverse section of mature root illustrates exfoliating at places, a wide zone of stratified cork occurs thin-walled, rectangular, radically arranged cells, upper few layers filled with reddish-brown contents, tangentially elongated, left over cells cortex, colorless, a wide zone of rounded cells through fiber groups in the direction of the central and middle region, cells demolished at places, slightly thick walled, phloem not distinct, endodermis barrel-shaped, xylem forms bulk of root consisting of parenchyma fibers vessels, and pericycle, medullary rays not separate, and fibers thick-walled, pitted thickening, vessels illustrate with elongated or annular having a small number of simple pits. It shows fibers and xylem vessels with fragments of corks, powders are yellowish-brown, under microscope Table 4.[26]

Phytochemical Constituents

Karkatshringi contains many important phytoconstituents which have therapeutic and commercial importance. The main active constituents in Karkatshringi include tannins, tetracyclic triterpenes, beta-pinene, caprylic acid, alpha-terpineol, triterpenic acids-pistacienoic acids A and B, 1:8-cinol, hydrocarbons, tannins (leaves, bark), dihydromalyalic acid, triterpene alcohol-tirucallol, dllimonene, triterpenoids (seeds oil), protein (seeds), and sterols. Kaur devoid of some negative consequence on crop growth and whole yield under usual field condition, the growth of weeds is decreased through phytotoxicity of plants. At a strength of 500 ppm, various reagents showed different growth obstruction with a minimum of 60% growth inhibition through methanol, followed by 70% using chloroform while the maximum growth of inhibition was shown by ethyl acetate 90%. The phytotoxic effect is shown by the fractions of these active compounds.[29] On the phytochemical analysis of *P. integerrima*, we get that leaf contains flavonoids, triterpenoids, carotenoids, and catechins.[30] On the screening study, leaves galls oil were found as β-pinene, sabinene, α-pinene, and limonene while terpinen-4-ol, α-terpinol, and α-pinene in bark oil also the presence of terpenoids, alkaloids, flavonoids, and tannins in galls extract, terpenoids, and flavonoids in bark was exposed.[31] The lanostanes which were separated from galls showed highly strong anti-inflammatory activity even in small quantity.[32] The high- performance thin-layer chromatography and high performance liquid chromatography used for detection of Pistacienoic acids.[33] In the leaves of *P. integerrima*, the polyphenolic compounds were studied. Farman (2005), as a candidate for drug development, the importance of phytochemicals is understood.[34] In the synthesis of synthetic drugs, phytochemicals can also act as source of precursors.[35] On the galls extract of *P. integerrima*, different isolation studies were conducted, which led to the purification of hydroxydecanyl arachidate, pisticialanstenoic acid, β-sitosterol, octadecan-9, and 11-diol-7-one, an[9,36] Phenolic components were characterized as 3′-(1,3-dihydroxy-5-phenoxy-1′,5′-dimethoxbenzene (pisticiphloro-glucinyl ether), 2, 4′-phenoxy-n-butyl-1′-(3- oxy-5-hydroxy) benzoic acid (pistaciaphenyl ether). Ethyl gallate which was isolated from galls of P. integerrima shows good anti-inflammatory diseases in Table 5.[37] *P. integerrima* gained special attention of phytochemists due to their traditional is medicinal uses; however, stem, bark, and leaf were also investigated phytochemically. In general, *P. integerrima* contain different phytochemicals including alkaloids, flavonoids, tannins, saponins, sterols, and essential oils. From the ethyl acetate and chloroform extract, a new compound beta-sitosterol was isolated.[38] In *P. integerrima*, qualitative phytochemical evaluation was done between root extracts, leaf, and galls Figure 1. Pistagremic acid, which shows significant leishmanicidal activity, was isolated from the whole plant extract of *P. integerrima* as compared to standard sample of amphotericin.[39]

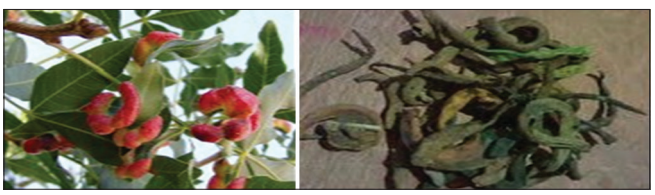


Figure 1: Leaves and galls of *Pistacia integerrima*

Pharmacological Activity

Antimicrobial Activity

Due to the fact that the synthetic drugs are more resistant to microbes and also these synthetic drugs are bio-friendly in nature, the demand for antimicrobial natural products is being enhanced nowadays. On the determination of antibacterial and antifungal activity, it was observed that *P. integerrima* showed significant antifungal activity, but low antibacterial activity. The medical importance of *P. integerrima* is well-known.[40] All fractions of this crude drug showed significant activity against *Salmonella setubal* and *Staphylococcus aureus* whereas aqueous fraction of *Bacillus subtilis* showed maximum inhibition.[41] On subjecting these methanolic bark extract and solvent-based fractions to antimicrobial activity, it was observed that ethyl acetate fraction showed excellent antibacterial activity whereas no antifungal activity was observed.[42]

Table 1: Classical categorization

Caraka Sushruta Vagbhata	Madhur skandha, Hikkanigrahana, and Kasahara Padmakadi and Kakolyadi These medicinal plants were described in Kesave Paddhati. Both caraka and Sushruta consider this plant as a poison for a vegetable origin. Acharya Sushruta kept this plant in Visa khand. Similar confusion is apparent in the context of Gunja which is categorized under Mula visa (root poison). Caraka interpreted it as amalaka and the toxic symptoms are mentioned by Acharya Sushruta. Likewise, Dalhana's comments add more confusion about its identification since Mesasringi, Ajasringi, and Uttamarni are equated to Karkatshringi because, the Asclepiadaceae family may have the same synonyms (Jivanti).[26]

Table 2: The other names of the plant are as follows

S. No.	*Language*	*Names*
1	English	Crab's claw
2	Hindi	Kakra, Kakarsingi, Kakkatasimgi, and Kakdashingi
3	Urdu	Kakra and Kakrasinghi,
4	Bengali	Kakrashingi, Kandashringi, and Kakra
5	Assam	Kakiasrngi
6	Bengali	Kakra, Kandashringi, and Kakrashingi
7	Gujarati	Kakadasingi, Kakarshingi, and Kakra
8	Punjabi	Tanbari, Kakar, Kangar Masna, Kakala, Karkarshingi, Shne, Gurgu, Kakkeran, Tungu, Kakkrangehe, Sumak, and Drek
9	Malayalam	Karkktakasingi and Karkatasringi,
10	Telugu	Kakarasimga, Kakarashingi, and Kakatakashrungi
11	Tamil	Kakkatashingi, Karkata, and Singi
12	Oriya	Kakadashringi, Kakadashrungi
13	Marathi	Kakarsingi, Kakadshingi, Karkadasringi, and Kakra[26]

Table 3: Ayurvedic properties

Parameter	*Properties*
Rasa	Tikta (Pungent)
Veerya	Ushna (Hot)
Vipaka	Katu (pungent)
Effect on tridosha	Pacifies Kapha and Pitta[26]

Antioxidant Activity

There is a significant role of plant-based antioxidant in the treatment of oxidative stress damage in human beings. Moreover, due to the presence of phenolic components, *P. integerrima* is considered a rich source of antioxidants, that is, possesses high antioxidant activity.[43] The leaf extract of *P. integerrima* also inhibits xanthine oxidase and also radical scavenging.[10]

Antibacterial Activity

Using the agar well diffusion method, the antibacterial activity of *P. integerrima* was studied using the ethanolic and aqueous fractions and on the completion of this experiment, it was observed that Gram-positive bacterium showed more antibacterial activity as compared to Gram-negative bacterium which shows less antibacterial activity. Furthermore, it was observed that ethanolic extract shows better activity than the aqueous extract.[15] When the galls are treated with aqueous extract for 10 days, it shows protection

Table 4: Macroscopic importance of *Pistacia integerrima* Bibi

Parts	*Administration mode/ form*	*Uses*	*Reference*
Stem/ branches	Topical	Stem resin as wound healer	[27]
Bark	Decoction	Hepatitis and jaundice	[27]
Galls	Roasted galls with honey taken orally	Cough, asthma, and diarrhea, Hepatitis, snakebite, and scorpion sting	[9,28]
Fruits	Raw form, fresh fruits crushed in water and taken orally	Edible, jaundice, and hepatitis	[27]

Table 5: Chemical compounds and their name[27]

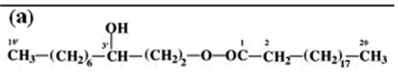
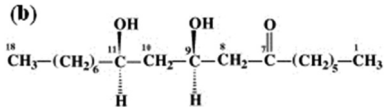
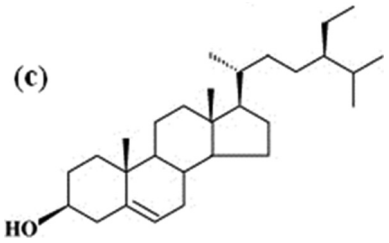
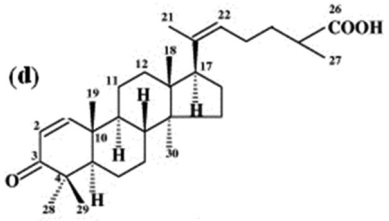
S. No.	*Name*	*Chemical structure*
1	Hydroxydecanyl arachidate	
2	Octadecan-9, 11-diol-7-one,	
3	β-Sitosterol	
4	Pisticialanstenoic acid	

Table 6: Identity, purity, and strength

S. No.	*Identity*	*Purity*	*Strength*
1	Foreign matter	Not more than	2%
2	Total ash	Not more than	11%
3	Acid-insoluble ash	Not more than	2%
4	Alcohol-soluble extractive	Not less than	9%
5	Water-soluble extractive	Not less than	16%[26]

against histamine-induced bronchospasm in guinea pig, and in the isolated guinea pig tracheal preparation, it shows the spasmolytic activity against histamine-induced contraction. In the galls extract, antiasthmatic activity arises due to the inhibition of antigen-induced histamine release, suppression of antibody production, and also due to membrane stabilizing potential Table 6.[44]

Toxicity and Other Activities

P. integerrima is placed in Ayurvedic anticancer plant medicines.[45] Fractionated stem extract of *P. integerrima* has proved cytotoxic against breast cancer cell line MCF-7,[41] bark extract of

P. integerrima, and its solvent-based fractions were also subjected to phytotoxic studies and ethyl acetate fraction inhibited Lemna minor significantly (90%) followed by chloroform and methanol fraction suggesting their phytotoxic composition.[42] Galls of *P. integerrima* were reported to have significant analgesic and anti-inflammatory activity.[46] Galls were found more potent than leaves as far as analgesic and anti-inflammatory activities were concerned; however, no acute toxicity was found in oral administration of extracts.[9] Galls of *P. integerrima* were also known to lower uric acid content in mice in a dose-dependent manner.[43] Aqueous extract of *P. integerrima* was found effective in the treatment of hepatic injury in CCl4-treated rats.[47] *P. integerrima* galls and leaves extracts have proved anti-nociceptive and analgesic on mice with no apparent acute toxicity on oral administration.[9] Bark extract of plant has also proved to have analgesic and anti-gastrointestinal motility effect.[48]

Traditional Uses

1) *P. integerrima* used as anti-inflammatory and antidiabetic agent and also a remedy for gastrointestinal disorder.[30]
2) It is also useful in pulmonary injection and vomiting, diarrhea by hackims, and local vaidhyas.[49]
3) Hepatitis and other liver disorders are treated by galls of *P. integerrima*.[28]
4) Common disease such as cough, cold, asthma, and fever also treated by herbal remedy.
5) Bleeding form nose and suppress hemorrhage and children's ear treated by *P. integerrima*
6) Pain, liver infection, diabetes, and common fever also treated by herbal drugs by its gall in North India
7) Snakebites, jaundice, and diarrhea treated by household medicine gall and leaves, barks of *P. integerrima*.[27]
8) The Ayurvedic formulation of gall like "Chvyanprash avaleha," "kumari kalp" which is generally preferred for weakness.[44]

Conclusions

In view of its wide range of phytochemical constituents along with bioactivities supported from its traditional uses; *P. integerrima* is a good for candidate of new drug synthesis. There is an urgent need to further standardize this medicinally important species and to explore more about its pharmacological actions. This plant is a unique source of various types of compounds having diverse chemical structures and is thus considered a multipurpose plant. The biological activity and possible medicinal applications of this compound are still unexplored. Thus, we require an large-scale examination/analysis to explore their therapeutic activities to eventually fight against diseases. The present review offers a scientific basis for the traditional uses of the various extracts of *P. integerrima*. Recent research on this species shows that the bark of the plant shows promising antibacterial as well as antiasthmatic activity.

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