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Systematic review of *Priyangu* (*Callicarpa macrophylla*)

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ABSTRACT

In this modern era of scientific research, traditionally used medicines are being researched and used. *Priyangu* or *Callicarpa macrophylla* is a medicinal plant which has references in *Charak Samhita* and *Nighantus*. It is widely used in Ayurveda. We searched for all the references in *Charak Samhita* and other *Nighantus*. We searched PubMed, Google Scholar, Researchgate, Sciencegate and other internet resources for all the published papers. Its phytochemistry, active ingredients, mechanism of action and clinical uses are being studied. It is *Pittashamak* and effective in *Raktapradoshaja Vikaras* as per Ayurveda. Its anti-bacterial, analgesic, anti-inflammatory, anti-arthritis, antifungal and anti-diabetic actions are being studied. Here we have carried out a systematic review of *Callicarpa macrophylla* documenting all its references in ancient texts and modern scientific studies.

Key words: *Priyangu*, *Callicarpa macrophylla*, *Charak Samhita*, *Bhavprakash Nighantu*, *Dhanvantari Nighantu*.

INTRODUCTION

In this era of modern medicine and scientific research, traditionally used medicines in various indigenous systems of medicine are increasingly being researched. They are rightfully gaining their deserved place in the armamentarium of the modern physician. One such medicinal plant which has plenty of prescribed uses in the classical Ayurvedic texts, and has been studied scientifically, is *Priyangu*. Here we make a systematic effort to study and compile all the references to it in various *Samhitas* and *Nighantus*. We have studied its descriptions, prescribed uses and

effects on various ailments. *Priyangu* means 'one who is dear' or 'liked by all'. Three different herbs have been used as *Priyangu*, but *Callicarpa macrophylla* is the most accepted and widely used, others being *Prunus mahaleb* and *Aglaia roxburghiana*. Further, we have reviewed the literature for all the studies that have been carried out on it in the modern context. We have compiled its phytochemistry, mechanism of action and explained all its uses and effects in a modern scientific context.

AIMS AND OBJECTIVES

1. A complete literary review of all the references to *Priyangu* in classic Ayurvedic texts like *Charak Samhita* and *Nighantus*.
2. Review of literature analyzing all the studies carried out on *Callicarpa macrophylla*, studying its phytochemistry, mechanism of action, identification of active metabolites and clinical research trials.

METHODOLOGY

1. A complete search of *Charak Samhita* was done and analysed for all the references to *Priyangu*.

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2. *Bhavprakash* and *Dhanvantari Nighantus* were studied for all references to *Priyangu*. *Gunakarmatmak Adhyayan* (mechanism of action) of *Priyangu* was done based on it.
3. We searched PubMed, Google scholar, Research gate, Science gate and other internet resources for all the published papers about *Callicarpa macrophylla*. A systematic review of literature of all the published data was carried out.

<i>Charak Samhita</i>	<i>Bhavprakash Nighantu</i>	<i>Dhanvantari Nighantu</i>
<i>Raktapitta</i>	<i>Raktatisaar</i>	<i>Chardi</i>
<i>Pittaj Kushtha</i>	<i>Daha</i>	<i>Daha</i>
<i>Arsha</i>	<i>Sweda</i>	<i>Jwara</i>
<i>Raktatisaar</i>	<i>Jwara</i>	<i>Moha</i>
<i>Visha</i>	<i>Durgandha</i>	<i>Raktapitta</i>
<i>Dantamukha Roga</i>	-	-

Description of *Priyangu* in ancient texts

Priyangu has been extensively studied and finds references in various ancient texts. According to the descriptions found in *Nighantus* and *Samhitas*, *Priyangu* is a climber or a shrub. Its flowers have sweet aroma and the plant looks very beautiful in the flowering season. It is appropriately called 'Mahilapriya', as it attracts females.^[1]

In *Charak Samhita*, it is included in *Sandhaniya Mahakashaya*, *Purishasangrahaniya Mahakashaya*, *Mutravirajaniya Mahakashaya*, *Prajasthpana Mahakashaya* and *Shonitasthapana Mahakashaya*.^[2] *Priyangu* is mentioned in *Pittashamak* (pacifies vitiated *Pitta*) *Dravyas*. We have come across a total of fifty-eight references of *Priyangu* in *Charak Samhita*, of which thirty-one pertain to blood disorders (*Raktapradoshaja Vikara*).

In *Bhavprakash Nighantu*, two varieties of *Priyangu* are described: 1. *Priyangu*. 2. *Gandha Priyangu*. it is included in *Karpooradi Varga*. In *Dhanwantari Nighantu*, it is mentioned in *Chandanadi Varga*.

In *Charak Samhita*, it is mainly recommended in bleeding disorders (*Raktapitta*). It is also recommended in disorders related to vitiated *pitta* and in patients with *Pitta Prakriti*.^[3] In antenatal care, use of *Priyangu* is recommended mainly for its antiseptic activity.

In *Ashtanga Hrudaya*, it is recommended for stopping excessive bleeding. It can also be used in chronic diarrhoea and *Pittaja* disorders. It helps in healing fractures and wounds.^[4]

As per *Bhavprakash Nighantu*, it is recommended for treatment of dysentery (*Raktatisara*), fever (*Jwara*), excessive sweating, burning sensation of the body (*Daha*), body odour (*Durgandha*) and tumors (*Gulma*).^[5]

In *Dhanvantari Nighantu*, it is recommended to be used in delirium (*Moha*), burning sensation of the body (*Daha*), fever (*Jwara*), vomiting (*Chardi*) and bleeding disorders (*Raktapitta*).^[6]

As per various *Nighantus*, its *Rasa Panchak* is as follows:

- *Rasa* - *Kashaya, Tikta*
- *Virya* - *Sheeta*
- *Vipaka* - *Katu*
- *Guna* - *Guru, Ruksha*
- *Doshaghanata* - *Pittashamak*

As per *Bhavprakash Nighantu*, its fruits and flowers are used for preparing various treatment formulations. It can be used either in a powdered form or as a decoction. Oil prepared from it, called *Priyanguvadi Taila*, is recommended to be applied externally on the wounds. *Priyangu* flowers are recommended to be used for syrup (*Asava*) preparations as per *Charak Samhita*.

Taxonomy

Three different plants have been used as *Priyangu* in different parts of India:

- *Callicarpa macrophylla* Vahl.
- *Prunus mahaleb* Linn.

▪ *Aglaiia roxburghiana* Miq.

After taking into consideration the descriptions found in *Samhitas* and *Nighantus*, it is seen that the most popular and likely herb that has been used as *Priyangu* is *Callicarpa macrophylla*. As per descriptions in *Bhavprakash Nighantu*, *Prunus mahaleb* qualifies as *Gandha Priyangu*.^[7] *Aglaiia roxburghiana* is a tree and does not ideally qualify as *Priyangu*.

Scientific classification of *Callicarpa macrophylla*

Kingdom	Plantae
Division	Angiospermae
Order	Lamiales
Family	Verbanaceae
Class	Dicotyledons
Genus	Callicarpa
Species	<i>Macrophylla</i>

Description

Callicarpa macrophylla is an erect shrub about 3-5 m high. Its stem and branches are densely covered with a greyish tomentum of stellate hairs.

Leaves are elliptic-oblong to lanceolate, 10-35 cm long, 2-18 cm broad, mature glabrescent and rugose above or with numerous stubble-like small hairs, densely greyish-white stellate-tomentose beneath; petiole 4-12 mm long, densely floccose-tomentose.

The inflorescence is densely stellate-hairy; primary peduncles equal to or a little longer than the petioles, 1-2.5 cm long. Flowers are on short, slender pedicels; pedicel gland-dotted, tomentose.

Fruit is globular, ± 2 mm in diameter, glabrous, glandular, smooth, white. It flowers from May to August and fruits from September to February.^[8]

Distribution

Globally, *Callicarpa macrophylla* is widely distributed across India, China, Bhutan, Myanmar, South East Asia

and Nepal. In India, it is found up to an altitude of 1800 meters, in Jammu & Kashmir, Himachal Pradesh, Uttar Pradesh, Bihar, Sikkim, West Bengal, Arunachal Pradesh, Assam, Meghalaya, Nagaland, Manipur, Mizoram, Tripura and Andhra Pradesh.

Phytochemistry

Mahesh Chandra et al. studied essential oils from three different aerial parts and analysed them by GC-MS. Over 51, 53, and 40 compounds were identified in *C. macrophylla* leaves essential oil (CMLEO), *C. macrophylla* pre mature seeds and fruits essential oil (CMEO-I) and *C. macrophylla* mature seeds and fruits essential oil (CMEO-II), respectively. These oils differ in relative contents of major compounds viz; β-selinene (37.51% in CMLEO, 44.66% in CMEO-I and 57.01% in CMEO-II), phyllocladene (9.76% in CMLEO, 5.80% in CMEO-I and 12.38% in CMEO-II), caryophelline oxide (7.34% in CMLEO, 8.74% in CMEO-I and 5.0% in CMEO-II), 9E-epi-caryophelline (6.23% in CMLEO, 1.27% in CMEO-I and 3.43% in CMEO-II), longipinocarvone (4.96% in CMLEO, 1.17% in CMEO-I and 2.0% in CMEO-II), and 1,8-cineole (2.23% in CMLEO, 3.10% in CMEO-I and 1.62% in CMEO-II).^[9]

According to Chatterjee et al, 1972, two tetracyclic diterpenes, calliterpenone and calliterpenone monoacetate have been isolated from the petrol extract of the aerial parts.^[10]

Ursolic acid, β-sitosterol and 5,4'-dihydroxy 3'-7-3'-trimethoxy flavone have been isolated from the petroleum ether extract of leaves.^[11] Methanol extract of the deposit of the water extract obtained after distillation of the essential oil of the leaves yielded 16α,17-isopropylideno-3-oxo-phyllocladane (isopropylidenocalliterpenone) along with calliterpenone and its monoacetate.^[12]

C. macrophylla leaves contain α-amyrenol, α-amyrin, ursolic acid, 2α, 3α, 19α-trihydroxy-12-dien-28-ursolic acid, betulinic acid, β-sitosterol, daucosterol;^[13] flavanoids such as luteolin, apigenin, luteolin-7-O-glucuronide, apigenin-7-O-glucuronide, β-sitosterol-β-D-glucoside, 2α-hydroxy ursolic acid, crategolic acid, docosanoic acid, tricosanoic acid, tetracosanoic acid,

ethyl tricosanoate, 3,7,3'-trimethoxy- 4', 5-dihydroxyflavone.^[14,15]

The bark contains betulinic acid. The roots and aerial part contain essential oil, (diterpene) calliterpenone, calliterpenone monoacetate. Seeds contains calliterpenone, calliterpenone-17-acetate, oleanolic acid.^[16]

Pharmacological activities

Priyangu is *Kashaya*, *Tikta Rasatamaka*, *Sheeta Viryatamaka*, *Vatapittashamaka* and *Sandhaniya* so it is used in bleeding disorders (*Raktapitta*). Being *tikta Rasatmaka* and *Sheeta Viryatmaka* it is useful in burning sensation in body (*Daha*), fever (*Jwara*), excessive thirst (*Trushna*). Being *purish Sangrahaniya* (absorbent) it is useful in dysentery (*Raktatisara*) and bleeding disorders (*Raktapitta*). Being *Pittashamaka*, *Priyangu* is recommended in excessive sweating and body odour (*dourgandhya*). Being *sandhaniya* it helps in healing wounds (*Vrana Ropana*).

1. Anti-bacterial activity

Many studies have been done to study the antibacterial activity of extracts and preparations of *Callicarpa macrophylla*. Yadav et al studied ex vivo antibacterial activity of ethanolic (SEE) and aqueous (SAE) stem bark extracts of *Callicarpa macrophylla* against gram positive and gram negative strains using Kirby bauer agar disc diffusion assay techniques. SEE, showed moderate growth inhibitory activity against all the bacterial strains, but SAE was exceptionally inactive against all strains except *Salmonella typhimurium*.^[17]

Rubaiyat Islam Mona studied cytotoxic and antibacterial activity of methanol extract of *Callicarpa macrophylla* leaves. The highest (92%) cells growth inhibition occurred at the 2.5 mg/mL concentration and maximum zone of inhibition (22 mm) was found against *Bacillus cereus* bacterial strain at the highest concentration of 350 µg/disc. It demonstrated that the methanolic extract of *Callicarpa macrophylla* leaves have potent cytotoxic but moderate antibacterial activity.^[18]

2. Analgesic activity

The effects and actions of *Callicarpa macrophylla* have shown promising results in studies carried out in animals. Aqueous as well as ethanolic extracts of its roots (at two concentrations 200 & 400 mg/kg) were evaluated for its analgesic and anti-inflammatory potentials using tail immersion test and carrageenan paw edema method in albino rats respectively by Yadav et al, 2012. A significant reduction of the painful sensation due to tail immersion in warm water was observed followed oral administration of the ethanolic and aqueous extract at dose of 200, 400mg/kg of leaves and roots of *Callicarpa macrophylla* Vahl. The effect was found to be dose dependent. In this model, higher dose of the aqueous extract (400mg/kg) at an interval of 60 min has exhibited better analgesic activity than the standard drug.^[19]

Several flavonoids isolated from medicinal plant have been discovered to possess significant analgesic effects.^[20] The analgesic activity of ethanolic, aqueous extract of roots of *Callicarpa macrophylla* Vahl. may be due to the presence of flavonoids compound.

3. Anti-Inflammatory Activity

The ethanolic and aqueous extracts (200 mg/kg, 400 mg /kg) of leaves of *Callicarpa macrophylla* showed significant ($p < 0.05$) anti-inflammatory effect in the acute phase of the inflammation process as compared with standard drug, Diclofenac sodium (20 mg/kg body wt). Further, the ethanolic and aqueous extracts were found to contain carbohydrates, steroids, flavonoids and tannins, through preliminary photochemical screening. The anti-inflammatory activity may be due to one/more group of above Phytoconstituents which may cause inhibition of histamine, serotonin or prostaglandin synthesis.^[21]

4. Anti-Arthritic Activity

Anti-arthritic effect of *Callicarpa macrophylla* was studied by testing various in-vitro parameters like protein denaturation and membrane stabilization by Gupta et al. at different dose levels (50, 100, 200, 400 and 800 µg/ml). They concluded that it provided

significant protection against denaturation of proteins and hypotonic saline induced RBC membrane damage.^[22]

Denaturation of tissue proteins is one of the well documented causes of inflammatory and arthritic diseases. Production of auto-antigens in certain arthritic diseases may be due to denaturation of proteins in vivo.^[23, 24]

5. Antifungal Activity

YC Tripathi et al., 2017 studied aqueous extracts of leaves of *Callicarpa macrophylla* Vahl. for antifungal efficacy against six pathogenic fungi namely viz, *Alternaria alternata*, *Aspergillus flavus*, *Aspergillus niger*, *Cladosporium cladosporidies*, *Drechslera halodes* and *Fusarium moniliforme* by agar-well diffusion method. Aqueous extract of *Callicarpa macrophylla* leaves exhibited varying degrees of antifungal activity against all the six test fungi. Radial growth inhibition of fungi at concentration of 5, 10, 20 and 30 mg/ml was much less than that of positive control. However, 40 and 50 mg/ml test concentration of extract was considerably effective on growth inhibition of all the test fungi. Test concentration of 50mg/ml showed growth inhibition almost at par with synthetic fungicide Carbendazim taken as positive control.^[25]

Another study was carried out by Yadav et al., 2012 for antifungal activity of ethanolic and aqueous extracts of the stems of *C. macrophylla* Vahl. Agar disc diffusion method was adopted for the antifungal screening against seven fungal strains. The ethanolic extract of stem exhibited antifungal activity against six strains in both 200 µg/disc and 400 µg/disc concentration. The largest zone of inhibition (17 mm in diameter) was recorded against *G. fujikoro* but aqueous extract did not exhibit any antifungal activity.^[26]

6. Antidiabetic Activity

The study of the antidiabetic activity of the flower extract of *Callicarpa macrophylla* was investigated in dexamethasone-induced diabetic rats. Rats were treated with dexamethasone at a dose of 5 mg/kg s.c.

for 10 days to develop insulin resistance. The blood glucose level, body weight and lipid profile were estimated. The blood glucose level decreases gradually in the animals treated with *Callicarpa macrophylla* flower extract (100 mg/kg b.w. and 200 mg/kg b.w., orally) and the antidiabetic effect was compared with that of Glibenclamide 1 mg/kg p.o., to conclude with the results that *Callicarpa macrophylla* shows antidiabetic activity in dexamethasone model.^[27]

7. Hepatoprotective Activity

Hepatoprotective activity of extract was studied in Albino rats against Paracetamol (3 g/kg b.w./p.o. 3 days) and carbon tetrachloride (2 ml/kg, b.w. /s.c. 4 days) induced hepatotoxicity. Standard drug was used for hepatoprotection (Silymarin 25 mg/kg, b.w./p.o.). Treatment of animal with hydro-alcoholic extract of aerial parts of *Callicarpa macrophylla* significantly ($p < 0.05$) decreased the levels of SGOT in serum which is an indicative of hepatoprotective activity. Also brought down was the level of serum glutamic pyruvic transaminase (SGPT) significantly ($p < 0.05$ in 200 mg/kg b.w. and $p < 0.01$ in 100 mg/kg b.w. doses). Other than these parameters level of Bilirubin (Total and Direct) and histopathological studies also was indicative of hepatoprotective property of the plant extract. In conclusion, it is observed that hydro-alcoholic extract of aerial parts of *Callicarpa macrophylla* possess hepatoprotective property which was evident by biochemical parameters and histopathological reports.^[28]

Presence of flavonoids in hydro-alcoholic extract of aerial parts of *Callicarpa macrophylla* may be a factor to contribute antihepatotoxicity ability through inhibition of cytochrome P-450 aromatase.^[29]

8. Cytotoxic, acute toxicity and phytotoxic activity

The study describes the cytotoxic, acute toxicity and phytotoxic activities of *Callicarpa macrophylla*. Brine shrimps cytotoxic bioassay of crude extract of bark of *Callicarpa macrophylla* (CBE) showed 975.22 LD50 value and crude extract of leaves of *Callicarpa macrophylla* (CLE) showed no significant results. However, all the test animals were found absolutely

safe in acute toxicity test. In phytotoxic assay against *Lemna minor*, CLE showed FI50 value of 464.55 and CBE showed no significant results. In conclusion, the CLE showed significant phytotoxic activity and therefore, could be a useful natural herbicidal.

When the crude extract of barks and laves of the plant was tested in brine shrimp cytotoxic assay, no such anticancer potential was observed and thus ruled out the presence of anticancer constituents in the extracts of both leaves and barks of the plant. Additionally, the extracts of both leaves and barks of the plant neither impart any change in animal behavior in acute toxicity test nor caused any mortality and thus was found absolutely safe during 24h assessment times.

The crude methanolic extract of both leaves and bark of *Callicarpa macrophylla* exhibited absolute safety in both in-vitro and in-vivo models with significant phytotoxicity in concentration dependent manner.^[30]

CONCLUSION

Priyangu or *Callicarpa macrophylla* has many references both in *Charak Samhita* and various *Nighantus*. It is widely distributed in India and is readily available. As per Ayurveda, it is *Shrestha Hitakara Dravya* for *Raktapitta*. It is *Kashaya*, *Tikta Rasatamaka*, *Sheeta Viryatamaka*, *Vatapittashamaka*, *Sandhaniya* and *Purishasangrahaniya* and so it is used in *Raktaja* and *Pittaja Vikara*. It can be used in the form of *Bahya* and *Abhyantar Kalpanas*. Scientific research is being done extensively on *Callicarpa macrophylla*. As seen in our review of literature, studies have been done to isolate its active ingredients. Number of studies have documented the action of extracts of its flowers, stem, leaves and other aerial parts. It is seen to have anti-inflammatory, analgesic, antibacterial, antifungal, hepato-protective as well as antidiabetic properties. These effects seem to collaborate in some ways with the way the drug has been prescribed to be used in Ayurveda. Most of the studies that have been done are on animal subjects. Human trials need to be conducted for validating its use in modern medicine. The studies are promising and *Callicarpa macrophylla* holds a lot of potential for research and clinical use.

This study will prove beneficial for further clinical research.

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