

Leea macrophylla Roxb. ex Hornem.: An ethnomedicinal, ethnic food, economical, and pharmacological update

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Abstract

Recent ethnobotanical survey studies highlight about various economic and pharmacological uses of plant *Leea macrophylla* (LM) Roxb. Ex Hornem. (family: *Vitaceae*). The aim of the article is bird's eye view of the plant regarding all reported ethnomedicinal information and research works on LM. Information of ethnomedicinal uses of the plant, until December 2018, from available 13 books on ethnobotany, 8 books related to medicinal plants, and 85 research articles on ethnomedicinal claims and pharmacological studies, uses as an ethnic food and economical uses. Information about its use by different tribes across India, parts used, therapeutic indications comprising external (E) and internal (I) usage of drug, recent pharmacological studies, and uses as ethnic food and economical uses are presented in a systematic manner. Root, leaves, and fruits of LM are used in the treatment of various ailments through 26 E applications and 27 I administrations. Root has maximum applications in 31, leaves in 14, seeds in 3, and stem in 1 disease conditions. 12 pre-clinical studies have been conducted on plant to elucidate its pharmacological response in a given disease condition, which includes antiurolithiatic (whole plant), antimicrobial (leaf, seed, and root tuber), anti-inflammatory (leaf), membrane stabilizing (leaf), antithrombotic (leaf and whole plant), hepatoprotective (leaf), antioxidant (leaf), antinociceptive (root), cytotoxic (root), neuroprotective (root), antidiabetic (leaf), wound healing (root tuber), and cardiogenic (whole plant) activity. LM is used as medicine and ethnic food and also for economical usage implying its therapeutic importance. Reported claims can be further revalidated extensive pharmacological and clinical studies, namely bone fractures, healing cut injury, typhoid, sexual weakness, impotency, and cancer.

Key words: Ethnobotany, ethnomedicine, folklore, hastikarna palasha, *Leea macrophylla*

INTRODUCTION

Plants have been an indispensable use to the food and health of human mankind since time immemorial. Ethnobotany is the study of a region/s plants and their practical uses through the traditional knowledge of a local culture and people.^[1] Results of these ethnobotany surveys are mainly used for generating hypothesis for the future researches on medicinal plants to combat various disease conditions. *Leea* genus contains 70 species and is placed under *Vitaceae* family, distributed throughout Northern and Eastern Australia, New Guinea, South and Southeast Asia, and parts of Africa.^[2] Of these, 11 species are mentioned in the database of the Botanical Survey of India.^[3]

One species of the genus *Leea* of family *Vitaceae*, namely *Leea macrophylla* (LM) Roxb. Ex Hornem., has been ascribed with abundant

therapeutic claims for its ethnomedicinal and economical uses.

In India, LM is distributed in sub-Himalayan tract and Western Ghats, mounting up to 2250 m in the Himalaya. Uttar Pradesh, Bihar, West Bengal, Sikkim, Assam, Meghalaya, Odisha, Madhya Pradesh, Maharashtra, Andhra Pradesh, Karnataka, Tamil Nadu, Kerala, and Andaman. It has its distribution in other countries such as Nepal, Bhutan, Bangladesh, Myanmar, Laos, Cambodia, and Thailand

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also.^[4] Due to its therapeutical potential, it has been used since pre-historic period for the various ailments by the traditional healers. Many ethnobotanical claims have been conveyed during different survey studies in the tribal regions of various states of India and other parts of the world. Single hand information about the ethnobotanical, its uses as ethnic food, ethnopharmacological uses, pharmacological studies, and economical uses of LM is still lacking. Hence, in the present article, data from available books, research journals, and survey study reports are reviewed and analyzed in a systemic manner.

Information of all the ethnobotanical claims of the LM from available 13 books on ethnobotany, 8 books related to medicinal plants, and 85 research articles published during 1997–2018 in peer reviewed journals about its ethnomedicinal claims, pharmacological studies, uses as an ethnic food, and economical uses has been compiled from library source as well as from Google Scholar, Dhara, PubMed, Ayusoft, and AYu, Web-based search engines during July 2017–December 2018.

The obtained data are organized in a systemic manner in a separate column with individual references with regard to area of reporting, name of the tribes those use the plant for medicinal purpose, local names, as known by different tribes across India, part used, therapeutic indications, external (E) usage and internal (I) usage of the drug.. Recent researches carried out were also compiled and presented till date.

LOCAL NAMES

LM is identified by various vernacular names by the traditional healers in their local languages. A total of 34 local names of plant have been reported in ethnomedicinal literature of plant. Of which in Bangladesh, plant has been identified by 13 local names. In Nepal, it is known by 1 name and in India by 20 local names [Tables 1-4].

AREA OF REPORTING

It is seen that LM is being reported from mainly two countries, i.e., India and Bangladesh where it is used as medicine and ethnic food and for economic purpose. It is used in nine states of India, namely Jharkhand, Maharashtra, Sikkim, West Bengal, Kerala, Rajasthan, Madhya Pradesh, Uttar Pradesh, and Odisha [Tables 1-4]. This shows the wide availability and use of this plant throughout India. In Bangladesh, this plant is also reported for its multifaceted uses [Tables 1-4].

TRIBES

India has >300 tribal communities.^[5] In the present review, it is noticed that about 36 tribes/communities use LM. In the eastern territory of India, it is accustomed by four tribes of

three states, namely Santhal Pargana community of Jharkhand, Lepchas and other communities of West Bengal, and tribes of Odisha. In the western part of India, it is accustomed by nine tribes of two states, i.e., Agari, Bhil, Raikare, Korku, Bhilla, Pawra, and other tribes of Maharashtra and tribals of Sitamata Wildlife Sanctuary, Rajasthan. In South India, it is accustomed by two tribes of one state, i.e., Malampadaram and other tribals of Kerala. In North India, it is accustomed by one tribe of one state, i.e., Tharu tribes of Dudhwa National Park, Uttar Pradesh. In Northeast India, it is accustomed by two tribes of one state, i.e., tribes of Eastern Sikkim Himalaya and Lepcha tribe of Dzongu Valley in North Sikkim. In Central India, it is accustomed by three tribes of one state, i.e., tribals of Harda district, Chhindwara district, and Betul district of Madhya Pradesh.

In Bangladesh, it is used by 15 tribes, i.e., communities and Kavirajes of Rajshahi District, folk medicinal practitioners of Pabna District and Dinajpur district, communities living in villages adjoining the Ghaghot, Bangali, and Padma Rivers; communities of Chakma, Sherpur District; Chakma tribe in hill tract districts, Chonia and Jolchotra, Tangail, Mandi ethnic communities, communities of Tonchongya - Baggach, Naramuk, Rajsthali and tribal peoples in the Chittagong hill tracts to combat various disease conditions [Tables 1-4].

THERAPEUTIC USES

It is seen that various parts of LM are used in 33 different disease conditions. It is exclusively used in bone fracture, followed by body pain, vermicide, sexual debility, rheumatism, and impotency, to stop bleeding and heal cut injury, indicating its vast range of therapeutic claims [Tables 1-4].

PART USES

Various parts of LM are used in the treatment of several diseases. Among them, 26 through E applications and 27 I administrations in addition to medicinal uses. Root, leaves, and fruit of the plant are used as an ethnic food, and leaves and root are used for economical purpose. Root, as a part used, has maximum applications in 31 disease conditions, leaves in 14, seeds in 3 disease conditions, and stem in only 1 disease condition, and 12 pre-clinical studies have been conducted up to the date on the plant to elucidate its pharmacological response in a given disease condition [Tables 1-4].

DOSAGE FORM

Root, stem, and leaf are internally taken in extract or juice form and also used in the form of powder or decoction and locally applied in the form of paste as a single or mixed with oil. Seeds are mainly crushed in the form of powder or are

Table 1: Ethnomedicinal uses of root of LM

Local name	Tribes/Areas	Dosage form, E application (E); I application (I)	Therapeutic claims
Hathkan ^[13]	Santhal Pargana, Jharkhand	The root paste is applied (E)	Body pain
Dinda ^[14]	Agari, Bhil, Raikare, and other tribes of Maharashtra.	Extract of root is taken (I)	Vermicide
Bulyetra ^[15]	Eastern Sikkim Himalaya	Tuber (I)	Ringworm and guinea worm
Hatikanpolash ^[16]	Rajshahi District, Bangladesh	Roots are made into small balls and orally taken for 7 days (I)	Piles
Horsthi-tolshi ^[17]	Bangladesh	The leaves and roots are crushed, mixed with oil, and applied to affected areas (E)	Body pain, paralysis, throbbing pain
Hostikornopolash ^[18]	Bangladesh	Stems and roots of LM are made into a paste with leaves of <i>Kalanchoe pinnata</i> . ¼ teaspoonful of the paste is taken with 1 teaspoon honey thrice daily for 7 days, and if not cured within 7 days, for another 7 days (I)	Typhoid
Harmadare ^[19]	Santal community of Bangladesh	Root (E)	Healing cut injury
Hastikarnapolash, Hatikan, Dholsamudra, Hatkan (Santali) ^[20]	West Bengal	Tuberous root (I)/(E)	Guinea worm, Ringworm. To allay pain
Chrianathali ^[21]	Tribals of Kerala	Root: Oral administration of infusion (I)	To expel worms from the intestine.
Lalpatta ^[22]	Sitamata wildlife sanctuary, Rajasthan	Powder of tuber is given (I)	To treat sexual debility in males
Dalavad ^[23]	Sitamata, Rajasthan	Tribals take root powder once a day for 7 days (I)	To treat sexual debility in males
Ash gaas ^[24]	Chakma tribe, Bangladesh.	Root extract is taken (I)	Tetanus
Njellu ^[25]	Malampadaram tribals of Kerala	Root extract is applied over the fractured area and tighten with cloth (E)	Fracture
Baggach ^[26]	Chakma community of Bangladesh	Root (E)	Fracture, rheumatism
Mothi-deni ^[27]	Tribes of Maharashtra	Root powder (E)	Bone fracture
Hatikan ^[28]	Tribals of Madhya Pradesh	Root paste is applied (E)	Skin diseases
Hatkan ^[29]	Tribal of Madhya Pradesh	Root (paste) (E)	Cut, swelling, pain
Hathpan ^[29]	Tribal of Madhya Pradesh	Root (Paste) (I)	Dysentery
Him-polash ^[30]	Kavirajes of Bangladesh	Root (I)	Impotency, headache, cough, cold
Hostikornopolash ^[31]	Folk medicinal practitioners Bangladesh	Root (I)	Sexual weakness, tumor
Udum-sam, A-thi-nache ^[32]	Chonia and Jolchotra, Tangail; Mandi ethnic community in Bangladesh	Small pieces of root are done and soaked in water for 4–5 h. Internally, the mucilaginous extract is used (I)	For increasing sperm count
Lepcha: Punthum/Phunthom ^[33] Nepali: Bungbungey ^[33]	Lepchas of West Bengal	Root mixed with Globba and Fraxinus and crushed. Decoction is used as medicine (I)	Arthritis
Hatikarn ^[34]	Korku tribes of Maharashtra	Root paste or powder is given (I)	Jaundice
Hatikana ^[35]	Folk medicinal practitioners of Bangladesh	Crushed roots are applied to affected areas (E)	Rheumatic pain
Hishirkorno ^[36]	Folk medicinal practitioners of Bangladesh	Paste of root is taken with milk (I)	Kidney problems

(Contd...)

Table 1: Continued

Local name	Tribes/Areas	Dosage form, E application (E); I application (I)	Therapeutic claims
Hathikan, Badiassidh ^[37]	Tharu tribes of Uttar Pradesh	Root paste mixed with goat milk applied as E bandage (E)	Bone fracture
Hathikan ^[38]	Madhya Pradesh	Root paste applied externally on the body (E)	Chest pain
----- ^[5]	Bhilla tribe of Maharashtra	Are Roasted pieces of rhizome and tuberous roots are eaten to expel foetus (I)	To Expel foetus
Hathikana, Hathkan ^[39]	Ramatirtha tribe of Odisha	Paste prepared from fresh roots with water applied externally on waist (E)	Lumbago

LM: *Leea macrophylla*, E: External, I: Internal

Table 2: Ethnomedicinal uses of stem of LM

Local name	Tribes/areas	Dosage form, E application (E); I application (I)	Therapeutic claims
Hostikornopolash ^[18]	Chakma tribe of Bangladesh	Stems and roots of LM are made into a paste with leaves of <i>Kalanchoe pinnata</i> . ¼ teaspoonful of the paste is taken with 1 teaspoon honey thrice daily for 7 days, and if not cured by the, for another 7 days (I)	Typhoid

LM: *Leea macrophylla*, E: External, I: Internal

chewed.

AS AN ETHNIC FOOD

LM (Dholsamudra) is a non-wood forest product used as ethnic food in India.^[6] Its leaves are eaten as vegetable^[7,8] and roots of the plant are cooked as vegetable.^[9] Its fruits are also edible^[8,10] and the fruit juice is taken orally as nutritive.^[11]

ECONOMICAL USES

LM leaves are used in making small flute.^[12] They are also used as platters.^[7] The root is said to yield a dye.^[11]

RECENT RESEARCHES

Antiuro lithiatic

I administration of whole plant ethanolic extract (500 mg/kg body weight [BW]/day) to rats for 14 days significantly reduced as well as prevented the growth of kidney stones and improved the renal impairment in the ethylene glycol-induced urolithiatic model of rats.^[45]

Antimicrobial

Crude extract of leaf displayed mild-to-moderate antimicrobial activity against the test organisms, i.e., *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella paratyphi*, *Shigella dysenteriae*, and *Shigella*

sonnei and the test sample demonstrated strong antifungal activity against *Pityrosporum ovale* (31 ± 1), *Trichophyton* Sp. (28 ± 1), *Candida albicans* (26 ± 1), *Cryptococcus neoformans* (26 ± 1), and *Microsporum* Sp. (26 ± 1).^[46]

Ethyl acetate extract of seed was more effective against *Staphylococcus aureus* compared to n-hexane, chloroform, and methanol extracts.^[47] Joshi *et al.* recently reported that root tuber ethanolic extract is highly effective against *S. aureus*, *Staphylococcus flexneri*, and *Staphylococcus boydii*, whereas less effective against *Staphylococcus typhi* and *Klebsiella pneumoniae*. MIC depicted values ranging from 0.195 mg/mL to 3.125 mg/mL.^[48]

Anti-inflammatory

In *in vitro* anti-inflammatory screening, the ethanolic leaf extract (500 µg/ml) showed mean protein denaturation inhibition 47.4 ± 0.001 as compared to that of 52.35 ± 0.0007 produced by standard acetylsalicylic acid.^[46] Oral administration of methanol extract of leaves (100 and 200 mg/kg) exhibited dose-dependent inhibition of carrageenan-induced inflammation ($P < 0.05$) and the granuloma tissue formation reduction ($P < 0.05-0.01$). The extract in the dose of 100 and 200 mg/kg orally exhibited significant central and peripheral analgesic activity in hotplate test ($P < 0.01$) and acetic acid-induced writhing test ($P < 0.05-0.01$), respectively, in experimental mice.^[49] Treatment with extract in the dose of 100 and 200 mg/kg orally significantly reduced the yeast-provoked elevated body temperature in experimental rats ($P < 0.05-0.01$).^[49]

Ethanolic leaf extract (500 µg/ml) inhibited the heat-induced total hemolysis of human red blood cells by 57.63

Table 3: Ethnomedicinal uses of leaf of LM

Local name	Tribes/areas	Dosage form, E application (E); I application (I)	Therapeutic claims
Bulyettra ^[15]	Eastern Sikkim Himalaya	Leaves paste (E)	To stop bleeding.
Horsthi-tolshi ^[17]	Bangladesh	The leaves and roots are crushed, mixed with oil, and applied to affected areas (E)	Body pain, paralysis, throbbing pain
--- ^[40]	Tonchongya-Baggach, Naramuk, Rajsthali; Bangladesh	Leaf juice is rubbed on affected area and heated with warm cloth (E) Leaf paste is applied on boil to burst (E)	Boil, arthritis
Ash gach ^[41]	Chakma community of Bangladesh	Leaf extract (I)	Tonsillitis
Lalpatta ^[22]	Sitamata Wildlife Sanctuary, Rajasthan	Powder of leaves mixed with honey is given (I)	Cancer
Ash gaas ^[24]	Chakma tribe of Bangladesh	Leaf paste is applied to the whole body (E)	Tetanus
Ash gaas ^[24]	Chakma tribe of Bangladesh	Leaf extract mixed with warm water is used for gargling and drinking (E/I)	Tonsillitis
Hottigach ^[42]	Tribals OF Bangladesh	Leaf juice (I/E)	Worm, bleeding
Baggach ^[26]	Chakma community of Bangladesh	Leaf (E)	Fracture, rheumatism
Him-polash ^[30]	Kavirajes of Bangladesh	Leaf (I)	Impotency, headache, cough, cold
Hostikornopolash ^[31]	Folk medicinal practitioners of Bangladesh	Leaf (I)	Sexual weakness, tumor
Udum-sam, A-thi-nache ^[32]	Chonia and Jolchotra, Tangail; Mandi ethnic community in Bangladesh	Small pieces of leaf are done by cutting and soaked in water for 4–5 h. For increasing sperm count, mucilaginous extract is used (I). Leaf paste is applied externally for treating fractured bones (E)	For increasing sperm count, fractured bones
Hatikana ^[35]	Folk medicinal practitioners of Bangladesh	Crushed leaves are applied to affected areas (E)	Rheumatic pain
Hishirkorno ^[36]	Folk medicinal practitioners of Bangladesh	Paste of leaf is applied to penis (E)	Impotency

LM: *Leea macrophylla*, E: External, I: Internal**Table 4: Ethnomedicinal uses of seeds of LM**

Local name	Tribes/areas	Dosage form, E application (E); I application (I)	Therapeutic claims
---- ^[43]	Lepcha tribe of North Sikkim	Seeds are wrapped, as small pack, in a cloth and tied around the neck of the children, which is believed to cure stomach pain (E) To treat viral fever, the seeds are chewed (I)	Stomach pain, viral fever
Hishirkorno ^[36]	Folk medicinal practitioners of Bangladesh	Paste of seed is applied to fractures for healing (E)	Bone fractures
Mothadini ^[44]	Pawra tribe of Maharashtra	Seeds are crushed in water and given orally until the patient causes vomiting (I)	Snake bite (Viper snake)

LM: *Leea macrophylla*, E: External, I: Internal

± 0.002 , whereas the standard aspirin showed 89.83 ± 0.002 . The result provides evidence for moderate membrane stabilization, a mechanism to support its anti-inflammatory effect.^[46]

Antithrombotic

Addition of 100 μ l streptokinase, a positive control (30,000 IU), to the clot along with 90 min of incubation at 37°C

showed 81.53% clot lysis. On the other hand, after treatment of clots with 100 μ l of test sample, 20.61% clot lysis was obtained.^[46] Whole plant extract showed the highest significant (47.47 \pm 6.65%) clot lysis activity among all the extracts studied, i.e., *Ocimum tenuiflorum*, *Andrographis paniculata*, *Adhatoda vasica*, and *Litsea glutinosa* ($P < 0.001$).^[50]

Hepatoprotective

Among the treatment groups, chloroform 100 mg/kg BW and methanol extract 200 mg/kg BW significantly restored the increased amount of serum total protein. In normal group, serum total protein (4.63 \pm 0.51) was reduced to 3.97 \pm 0.15 by chloroform (100 mg/kg BW) and 2.50 \pm 0.20 by methanol extract (200 mg/kg BW). Most of the treatment groups except methanol extract (200 mg/kg BW) helped in normalizing the serum creatine kinase MB (CK-MB) level in hepatic damage. Ethyl acetate 200 mg/kg BW and chloroform 100 mg/kg BW restored the serum CK-MB level.^[51]

Antioxidant

Different fractions of leaf showed very potent 2,2-diphenyl-1-picrylhydrazyl radical scavenging effect, FeCl₃ reducing effect, superoxide scavenging effect, and iron chelating effect.^[51]

Antinociceptive activity

In acetic acid-induced writhing test, the ethanolic root extract at the dose of 200 mg/kg BW reduced the number of writhes significantly ($P < 0.001$) with 62.37% of inhibition when compared to the control group which was comparable to that of the standard drug diclofenac sodium (61.85% inhibition, $P < 0.001$). At the same dose, petroleum ether, carbon tetrachloride, and ethyl acetate soluble fractions of the ethanolic root extract exhibited moderate antinociceptive activities with 36.59%, 30.92%, and 27.83 % inhibition of writhing as compared to control, respectively.^[52]

Cytotoxic

In Brine shrimp lethality bioassay, the lethal concentration 50 (LC₅₀) values of the ethanolic extract, carbon tetrachloride, chloroform, and ethyl acetate soluble fractions of roots were found to be 2.39, 0.049, 4.53, and 0.09 μ g/ml, respectively, which were comparable to the standard vincristine sulfate whose LC₅₀ was 0.34 μ g/ml.^[52]

Neuroprotective

Methanol extract of root studied at the dose of 100 mg/kg BW and 200 mg/kg BW significantly ($P < 0.05$) reduced locomotor activity and increased duration of sleeping of animals. Morris

water maze test showed that treatment of animals with LM decreased the mean escape latency significantly ($P < 0.05$) compared to animals in diazepam group. LM also reduced the content of malondialdehyde, nitric oxide, and advanced oxidation protein product and, in hippocampus, increased the activities of superoxide dismutase, catalase, and glutathione peroxidase.^[53]

Antidiabetic

Leaf extract studied at doses of 100 mg/kg BW, 200 mg/kg BW, and 300 mg/kg BW with a 4-week duration of intervention showed that it can exert a potential effort to restore pancreatic β -cell damaged by streptozotocin induction.^[54]

Wound healing

In incision model, bioadhesive gel (5% w/v) showed a higher increase in wound breaking strength (44.68%) as compared to oral treatment (23.41%) at the dose of 500 mg/kg. Complete wound contraction occurred in 20 days with topical application, whereas 22 days taken by oral treatment. Topical treatment also produced a significant ($P < 0.05$) increase in antioxidants glutathione, superoxide dismutase, and catalase, whereas the level of enzymes lipid peroxidation and nitric oxide and inflammatory marker myeloperoxidase was reduced.^[55]

Cardiotonic

With the increasing dose of LM aqueous and alcoholic extracts from 0.1 ml to 0.4 ml, a significant effect was observed on the height of force of contraction (positive inotropic effect) or the heart rate (positive chronotropic effect).^[56]

CONCLUSION

The present ethnobotanical and pharmacological review on LM shows multifaceted uses including its use as an ethnic food and economical usage, thus implying its significance. Its traditional uses have been reported from two countries and nine states of India by 36 tribes/communities. It is utilized in 33 diseased conditions, of which in 27 as I administration and in 26 as E applications. Among the parts used, root has maximum applications (31), followed by leaves (14), seeds (3), and stem (1) disease condition. Maximum ethnomedicinal claims are in the management of bone fracture, followed by body pain, worms, sexual debility, rheumatism, and impotency. Among the traditional claims, very few are proved through experimental and clinical researches, and up to date, only 12 pharmacological actions have been reported. This review further reports its use as an ethnic food, which can also be further strengthened through pharmacoclinical studies.

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