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# Ethnobotany and phytopharmacology of *Leea indica*: An overview

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ABSTRACT

Herbal drug therapy is the most trusted system of medicine in countries like India, where people strongly believe in Ayurveda as herbs are the part of rural Indian lifestyle. Most of the diseases which have no medicine in allopathic system can be cured successfully by using traditional medicines. *Leea indica*, a traditional Chinese medicinal plant is the sole member of the family Leeaceae, which is closely related to the economically important grape family, Vitaceae. It is widely distributed from Southern Asia to Northern Oceania. The plant parts are enriched with various bioactive compounds such as gallic acid, quercitrin, β-amyrin, β-sitosterol and lupeol, *etc*. Traditionally, it is used to treat itchy skin, fever, diarrhea, and body aches. The current review attempts to encompass the available literature on *Leea indica* with respect to its phytochemistry, traditional uses and gist of its various pharmacological activities.

## 1. Introduction

The herbals have occupied a distinct place in the life right from the primitive period till date and in recent time there has been a marked shift towards herbal cures because of pronounced cumulative and irreversible reactions of modern drugs[1,2]. Today, the revival of interest in plant derived drugs is mainly due to the current widespread belief that green medicine is safe and more dependable than the costly synthetic drugs, many of which have adverse side effects[3]. A number of scientific investigations have highlighted the importance and the contribution of many plant families, *i.e.* Asteraceae, Liliaceae, Apocynaceae, Solanaceae, Caesalpinaceae, Rutaceae, Piperaceae and Sapotaceae which are used as medicinal plants[4]. Medicinal plants have a promising future because there are about half million plants around the world and most of them have not yet been investigated for their medicinal activities. These pharmacological activities could be decisive in the treatment of present or future studies[5].

*Leea indica* Merr. (*L. indica*) (Leeaceae), is a shrub widely distributed in forests of tropical and subtropical India, from Himalayas as far west as Kumaon and southwards to the Peninsula. Its leaves, roots and flowers are widely used as they are reported to have medicinal values. The roots have antidiarrheal and antidysenteric properties while leaves are digestive and useful in vertigo[6]. The pharmacological activities reported from various sources are cytotoxicity, anxiolytic potential, antioxidant, antiviral, antiprotozoal, thromobolytic, analgesic and phosphodiesterase inhibitory activities[7,8].

### 1.1. Plant description

*L. indica* (synonyms: *Leea sambucina*, *Leea staphylea*)[7], commonly known as Chhatri in Sanskrit[6], is a large evergreen perennial shrub growing up to 2–3 m in height with stout, soft woody stems with numerous stilt roots; flowers greenish-white in large trichotomous, divaricated cymes on short peduncles which flower during June to August[8].

### 1.2. Taxonomical classification

*L. indica* is under the scientific classification as follows:

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| | |
|---|---|
| Kingdom: | Plantae |
| Division: | Magnoliophyta |
| Class: | Eudicots |
| Order: | Vitales |
| Family: | Leeaceae |
| Genus: | *Leea* |
| Species: | *indica* |

### 1.3. Common vernacular names

*L. indica* has many common vernacular names such as chhatri (Sanskrit), bandicoot berry (English), hastipalash/kurkurjiwah (Hindi), karkani (Marathi), ottannalam (Tamil), manipiranta (Malayalam), huo tong shu (Chinese)[9,10].

### 1.4. Distribution

*L. indica* is a large evergreen shrub indigenous to tropical Asia, Australasia, Bangladesh, India, China, Bhutan, and Malaysia. In Bangladesh, it grows in hilly forests of Chittagong and Sylhet. This plant is also widely spread in disturbed areas of lowland and upland rain forest in Asia-Pacific islands[10,11].

### 1.5. Chemical constituents

The chemical constituents of *L. indica* are shown in Table 1[7,8,12,13].

**Table 1**
Chemical constituents of *L. indica*.

| Phytoconstituent | Molecular formula | Extract | Parts | Reference |
|---|---|---|---|---|
| β-Sitosterol | $C_{29}H_{50}O$ | Ethanol | Root, leaves | [7,8] |
| Lupeol | $C_{30}H_{50}O$ | Ethanol | Root, leaves | [7,8] |
| Di-*n*-octyl phthalate | $C_{24}H_{38}O_4$ | Ethanol | Root | [7] |
| β-Amyrin | $C_{30}H_{50}O$ | Ethanol | Root | [7] |
| Gallic acid | $C_7H_6O_5$ | Ethanol | Root, leaves | [7,8] |
| Quercitrin | $C_{21}H_{20}O_{11}$ | Ethanol | Root | [7] |
| Dibutyl phthalate | $C_{16}H_{22}O_4$ | Ethanol | Root | [7] |
| α-Tocopherol | $C_{29}H_{50}O_2$ | Ethanol | Root | [7] |
| Di-iso butyl phthalate | $C_{16}H_{22}O_4$ | Essential oil | Flowers | [8] |
| Di-*n*-butyl phthalate | $C_{16}H_{22}O_4$ | Essential oil | Flowers | [8] |
| *N*-butyl iso butyl phthalate | $C_{16}H_{22}O_4$ | Essential oil | Flowers | [8] |
| Mollic acid arabinoside | $C_{35}H_{56}O_8$ | Ethyl acetate | Whole plant | [12] |
| Mollic acid xyloside | $C_{35}H_{56}O_8$ | Ethyl acetate | Whole plant | [12] |
| Phthalic acid | $C_8H_6O_4$ | Petroleum ether | Leaves | [13] |
| Palmitic acid | $C_{16}H_{32}O_2$ | Petroleum ether | Leaves | [13] |
| Eicosanol | $C_{20}H_{42}O$ | Petroleum ether | Leaves | [13] |
| Solanesol | $C_{45}H_{74}O$ | Petroleum ether | Leaves | [13] |
| Farnesol | $C_{15}H_{26}O$ | Petroleum ether | Leaves | [13] |
| Ursolic acid | $C_{30}H_{48}O_3$ | Petroleum ether | Leaves | [13] |
| *N*-butyl gallate | $C_{11}H_{14}O_5$ | Butanol extract | Leaves | [13] |

### 1.6. Traditional uses

The whole plant is used traditionally for headache, body pains and skin complaints[10]. The root of *L. indica* has been traditionally used in relieving diarrhea, dysentery, spasm and as sudorific. The decoction of the root is given in colic, cooling and relieves thirst. The juice of young leaves is used as digestive whereas roasted leaves are applied to relieve vertigo[6,9]. The decoction of leaves is consumed by pregnant women for delivery of child and treating obstetric diseases[14,15]. The ingredients of this plant are applied in the treatment of leucorrhea and intestinal and uterus cancer[15].

### 1.7. Ayurvedic properties

The Ayurvedic properties of *L. indica* are as follows: Rasa: Kashaya, Tikta; Guna: Lakhu and Virya: Seeta.

## 2. Morphology

It is a perennial shrub or small tree, 2–16 m tall with stout, soft wooded, glabrous to pubescent stems; leaves pinnate bearing 7 leaflets with 7–20 cm long petioles; leaflets ovate-lanceolate slightly hairy with crenate to serrate margins. Flowers are greenish white, trichotomous, divaricated cyme; fruits are purplish black berries having 4–6 seeds[10].

## 3. Microscopy

Transverse section of stem shows the cortex region, collenchymatous tissue, closed vascular bundle surrounded by fiber layer, and secretory cells. Starch grains are absent.

Transverse section of midrib consists of open vascular bundle not surrounded by fiber layer, druses crystals and secretory cells. Trichomes are absent.

Transverse section of margin shows the presence of secretory cells. Trichomes are found to be absent.

Transverse section of lamina shows uniseriate and smooth epidermis with trichomes, palisade cells, raphid, druses crystals and secretory cells.

Transverse section of the petiole consists of collenchymatous cortex, closed vascular bundle, druses and raphid crystals and trichomes. Starch grains are absent[10,16].

## 4. Pharmacological review

Paul *et al*. investigated cytotoxic activity of ethanol extract of *L. indica* leaves[4]. The cytotoxic activity of *L. indica* ethanolic extract was assessed by brine shrimp lethality bioassay method. The results of the study demonstrated that ethanolic extract of *L. indica* leaf exhibited lethality (2.477 1 μg/mL with 95% *CI*) in a dose dependent manner. More specifically 0%, 10%, 10%, 30%, 30%, 40%, 50%, 60%, 70% and 100% mortality of brine shrimp was observed at 20, 40, 60, 80, 100, 200, 400, 600, 800 and 1 000 μg/mL concentrations, respectively, which supported that *L. indica* ethanolic extract

exhibited very potent cytotoxic effect in experimental models. Thus, these results can be used as strong scientific evidence to use this plant as an antioxidant. However, further studies are still required to elucidate a mechanistic way how the plant contributes in these pharmacologic properties[4].

Srinivasan *et al*. reported antimicrobial activity of essential oil obtained from flowers of *L. indica* by using diffusion disc technique[8]. Cephatoxime, bavistin and carbendazim were used as standard. The screening showed that essential oil has antibacterial activity against *Escherichia coli, Salmonella typhimurium, Bacillus subtilis, Bacillus cereus, Staphylococcus aureus* and antifungal activity against *Penicillium notatum, Aspergillus niger* and *Fusarium monelliformae*[8].

Rahman *et al*. investigated the phytochemical, antioxidant, antimicrobial and cytotoxic effects of *L. indica* leaf ethanolic extract[11]. Total phenolic and flavonoid contents, total antioxidant capacity, 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging effect, $FeCl_3$ reducing power, dimethylsulfoxide superoxide scavenging effect and iron chelating effects were studied by established methods. Antibacterial, antifungal and cytotoxic effects were screened by disc diffusion technique, food poison technique and brine shrimp bioassay, respectively. Preliminary investigation of ethanolic extract showed the presence of alkaloids, glycosides, cardiac glycosides, terpenoids, flavonoids, steroids and tannins. The results showed that ethanolic extract exhibited significant antioxidative, antimicrobial and cytotoxic activities[11].

Wong *et al*. evaluated two cytotoxic cycloartane triterpenoid glycosides, namely, mollic acid α-L-arabinoside (MAA) and mollic acid β-D-xyloside (MAX), isolated form *L. indica* for its cytotoxic effects by using MTT assay[12]. Preliminary studies showed that cytotoxicity of MAA was associated with the decrease in proliferating cell nuclear antigen expression, cell cycle S and G2/ phases arrest, and induction of hypodiploid cells. Both MAA and MAX inhibited the growth of Ca Ski cervical cancer cells with $IC_{50}$ value of 19.21 and 33.33 μmol/L, respectively. MRC5 normal cell line was used to calculate selectivity index. MAA and MAX were found to be about eight and four times more cytotoxic to Ca Ski cells compared to MRC5. The cytotoxicity of MAA was characterized by both cytostatic and cytocidal effects. This study provided the evidence for the ethnomedicinal use of *L. indica* and paved the way for future mechanism studies on the anticancer effects of MAA[12].

Sim *et al*. investigated antioxidant and cytotoxic activities of ethanolic and fractionated extracts (hexane, ethyl acetate and water) of leaves of *L. indica*. The antioxidant activity was measured by employing DPPH radical, reducing power assay and superoxide dismutase activity assay, and cytotoxic activity was evaluated against three colon cancer cell lines with varying molecular characteristics (HT-29, HCT-15 and HCT-116) by MTT assay. The results of antioxidant activity revealed that water extract showed significantly antioxidant potential among ethanol and its fractionated extracts, whereas all four extracts of *L. indica* leaf did not show cytotoxic effect against the three tested human colon cancer cell lines after incubation for 72 h[17].

Emran *et al*. studied centrally acting analgesic property of ethanol extract of whole plant of *L. indica* by using formalin induced licking response model and peripheral pharmacological actions using acetic acid-induced writhing test[18]. In acetic acid-induced writhing test, the ethanolic extract at dose level of 200 mg/kg orally exhibited a significant reduction of writhing response in a dose dependent manner; in formalin induced licking response model a significant result was comparable to the standard drug diclofenac sodium (40 mg/kg, *i.p.*). This data thus supported the claims that ethanol extract of *L. indica* used by traditional medicine practitioners could be a good source of analgesic drugs[18].

Rahman *et al.* evaluated *in vitro* thrombolytic activity to check the clot lysis effect of ethanolic extract of *L. indica* by using streptokinase as a positive control and water as a negative control[19]. Cytotoxicity was screened by brine shrimp lethality bioassay using vincristine sulfate as a positive control. The extract showed very significant ($P < 0.0001$) percentage of clot lysis compared to the reference drug streptokinase [(75.00 ± 3.04)%]. In brine shrimp cytotoxic assay, the ethanolic extract of *L. indica* showed $LC_{50}$ value (2.65 ± 0.16) μg/mL with reference to vincristine sulfate [$LC_{50}$ = (0.76 ± 0.04) μg/mL]. Thus *L. indica* could be used as a thrombolytic agent with *in vivo* effects to improve the atherothrombotic patients[19].

Raihan *et al*. examined *L. indica* for their anti-tumor, anti-oxidant and cytotoxic activities[20]. *In vivo* anti-tumor activity was studied against Ehrlich ascites carcinoma cells in Swiss albino mice by using parameters like tumor weight measurement, survival time and tumor cell growth inhibition. Bleomycin was used as a positive control (0.3 mg/kg). It was found that the extract at the dose of 40 mg/(kg·day) (*i.p.*) significantly reduced tumor weight, tumor cell growth rate and increased life span in comparison to those of Ehrlich ascites carcinoma bearing mice receiving no extract. *In vitro* antioxidant potentiality was tested by using DPPH radical scavenging assay, total phenol and flavonoid content and reducing power determination assays. The extracts showed moderate antioxidant activity in a dose dependent manner. The cytotoxic activity of the extract was assessed by brine shrimp lethality bioassay technique which showed a significant result ($LC_{50}$ less than 25 μg/mL). Anti-tumor properties of *L. indica* may be due to the presence of antioxidant and cytotoxic activity. The experimental findings indicated that *L. indica* may be used as anti-tumor agent[20].

Raihan *et al*. reported the crude methanolic extract of *L. indica* to possess central nervous system depressant effect (sedative and anxiolytic activity) by using rodent behavioral models such as hole cross, open field and thiopental sodium induced sleeping time tests for its sedative properties and an elevated plus-maze (EPM) test for its anxiolytic potential[21]. The methanol extracts at doses of 200 and 400 mg/kg, *o.p.* displayed a dose dependent suppression of motor activity, exploratory behavior (in hole cross and open field

tests) and prolongation of thiopental induced sleeping time in mice; the highest central nervous system depressant effect was shown at a dose of 400 mg/kg, *o.p.* In the EPM test, both doses of methanol extract significantly ($P < 0.01$) increased the exploration time spent by the treated mice in EPM open arms in a dose dependent manner. The results confirmed that the methanol extract from *L. indica* leaves possessed a strong sedative and anxiolytic potential. Conclusively, it was suggestive that this extract might fulfil the therapeutic need for the treatment of anxiety and related neuropsychiatric disorders[21].

Reddy *et al*. studied *L. indica* leaves crude ethanol and its fractionated extracts (hexane, ethyl acetate and water) for their phenolic content, antioxidant effect and cytotoxic activity[17]. Folin-ciocalteau method was used for the measurement of total phenolic content of the extracts. The antioxidant activity was measured by employing three different established testing systems, such as scavenging activity on DPPH radicals, reducing power assay and superoxide dismutase activity assays. The cytotoxic activity of extracts were evaluated against three colon cancer cell lines with varying molecular characteristics (HT-29, HCT-15 and HCT-116) by MTT assay. Amongst the crude ethanol and its fractionated extracts, fractionated water extract showed the highest total phenolic content and the strongest antioxidant effect in all the methods adopted. All the four extracts exerted no damage to the selected colon cancer cells[17].

From the thorough study and extensive literature survey of *L. indica*, it is clearly shown that the plant serves as an important source of many therapeutically efficient phytoconstituents such as β-sitosterol, lupeol, di-*n*-octyl phthalate, β-amyrin, gallic acid, quercitrin, dibutyl phthalate and α-tocopherol, *n*-tetratriacontane, *n*-tritetracontane and many others constituents which are responsible for various biological activities. The traditional and ethno medicinal literatures showed that the plant is very effective and safe for medicinal uses. However, investigation needs to be carried out on *L. indica* in order to explore the concealed areas and their practical clinical applications, which can be used for the welfare of the mankind.

## Conflict of interest statement

We declare that we have no conflict of interest.

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