Traditional uses, chemistry and pharmacological activities of *Leea indica* (Burm. f.) Merr. (Vitaceae): A comprehensive review

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Abstract

Plants have been used for various purposes of humans including medicinal purposes since time immemorial. Plants are an integral part of traditional medicine. *Leea indica* (Burm.f.) is a large shrub and belongs to the family Vitaceae. The plant *L. indica* is used traditionally in various countries of the world such as India, Malaysia, Thailand, Nepal, and Indonesia. The plant is used as a remedy for ailments such as diarrhea, dysentery, diabetes, bone fracture, body ache, fever, and wound treatment. Phytochemical groups such as alkaloids, flavonoids, terpenoids, glycosides, saponins, and steroids and compounds, namely, quercetin, gallic acid, lupeol, β-sitosterol, ursolic acid, mollic acid arabinoside, and mollic acid xyloside have been identified in various parts of the plant. Literature survey carried on biological activities of *L. indica* revealed that the plant showed bioactivities such as antimicrobial, antioxidant, cytotoxic, enzyme inhibitory, analgesic, hepatoprotective, hypoglycemic, hypolipidemic, and antidiarrheal activity. The observed bioactivities of the plant might be related to the presence of bioactive phytoconstituents as compounds such as gallic acid, quercetin, mollic acid arabinoside, and mollic acid xyloside are known to exhibit marked pharmacological activities.

Key words: Ethnomedicine, *Leea indica* (Burm.f.) Merr., Vitaceae, pharmacological activities, phytochemicals

INTRODUCTION

The term “ethnobotany” was proposed by Harshberger. Ethnobotany is a multidisciplinary science of interactions between people and plants. Plants are widely used to meet various needs of humans such as food, cloth, shelter, dyes, fuelwood, fodder, and medicine. Besides, plants have also found ritual uses. In recent years, the field of ethnobotany is on rise. Throughout the world, many plants with therapeutic values have been used to treat several human and veterinary diseases. Traditional medicinal practitioners, especially from rural areas, utilize plants singly or in certain formulations to treat various diseases. A majority of population in the world, especially those living in remote areas, rely on traditional medicine for meeting primary health care. Plants form an integral part of medicinal systems such as Unani, Sidda, Ayurveda, and traditional Chinese medicine. More emphasis is devoted on searching natural products with therapeutic values due to many adverse effects associated with the use of modern drugs.¹⁻¹⁰ Therapeutic values of plants lie in the presence of bioactive secondary metabolites such as alkaloids, terpenoids, and polyphenolic compounds including flavonoids distributed in various parts of plants. Compounds such as vincristine, vinblastine, taxol, quinine, digoxin, reserpine, nicotine, codeine, and morphine are from plant origin. Studies have shown that crude solvent extracts and purified components from plants exhibit a wide array of biological activities including anticancer activity.¹¹⁻¹⁹

*Leea indica* (Burm.f.) Merr., [Figure 1] belonging to the family Vitaceae, is commonly known as Bandicoot berry in English, Chhatri in Sanskrit, and Hastipalash in Hindi. The

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Received: 05-02-2018
Revised: 24-02-2018
Accepted: 05-03-2018
The plant *Leea indica* has ethnomedicinal importance worldwide. Various parts of the plants, namely, leaves, roots, stem bark, inflorescence, and flowers in certain formulations such as paste and decoction are being in use for treating several ailments. Roots and leaves are predominantly used. The plant is used medicinally in several formulations to treat ailments such as fever, bone fracture, diarrhea, dysentery, body ache, head ache, malaria, rheumatism, asthma, and gastric ulcer. A brief detail on some of the uses of *L. indica* to treat diseases and disorders in India and in other parts of the world (namely, Nepal, Bangladesh, Malaysia, Indonesia, and Thailand) is presented in Table 1.

### CHEMISTRY OF *L. INDICA*

Plants produce a number of primary and secondary metabolites. Metabolic pathways such as shikimic acid pathway and malonate/acetate pathways are involved in the synthesis of secondary metabolites, most of which are phenols or their oxygen-substituted derivatives. Most of the metabolites serve many functions such as defense against insects and herbivores and contribute color, flavor, and aroma to plants. Besides, many of the secondary metabolites produced by plants possess therapeutic values. Advancements made in chromatographic and spectral analyses such as column chromatography, high-performance thin-layer chromatographic (HPTLC), gas chromatography-mass spectrometry (GC-MS), high-performance column liquid chromatographic, infrared, and nuclear magnetic resonance led to the identification of several plant secondary metabolites. Studies have shown that the plant *L. indica* contains a wide variety of phytochemicals which have been identified by several methods such as standard phytochemical tests, GC-MS analysis, HPTLC, and spectral analyses. Table 2 shows the chemicals/phytochemical groups detected in different parts of *L. indica* by various detection procedures.

### BIOLOGICAL ACTIVITIES OF *L. INDICA*

The plant *L. indica* is shown to exhibit a range of biological activities such as antimicrobial, antioxidant, cytotoxic, larvicidal, hepatoprotective, antidiarrheal, thrombolytic, analgesic, sedative, and antimalarial activity. A brief detail on the biological activities exhibited by *L. indica* is presented.

#### Antibacterial Activity

The essential oil obtained from the flowers of *L. indica* was effective against Gram-positive and Gram-negative bacteria. The ethanolic extract obtained from leaves of *L. indica* was shown to inhibit Gram-positive and Gram-negative bacteria in disk diffusion assay. It was observed that the extract inhibited Gram-positive bacteria to higher extent when compared to Gram-negative bacteria as revealed by lower MIC values.

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**Figure 1:** *Leea indica* (Burm.f.) Merr. (Photograph by Vinayaka K.S)
Table 1: Reported ethnobotanical uses of different parts of *L. indica*

<table>
<thead>
<tr>
<th>Region</th>
<th>Part</th>
<th>Uses</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singhanakhon district, Songkhla Province, Thailand</td>
<td>Root</td>
<td>Fever</td>
<td>Neamsuvan <em>et al.</em>[27]</td>
</tr>
<tr>
<td>Kut Chum District, Yasothon Province, Thailand</td>
<td>Root</td>
<td>Diarrhea</td>
<td>Chuakul <em>et al.</em>[28]</td>
</tr>
<tr>
<td>Chittagong Hill Tracts, Bangladesh</td>
<td>Leaf</td>
<td>Joint pain</td>
<td>Khisha <em>et al.</em>[29]</td>
</tr>
<tr>
<td>Jalpaiguri district, West Bengal, India</td>
<td>Root</td>
<td>Bone fracture</td>
<td>Bose <em>et al.</em>[30]</td>
</tr>
<tr>
<td>Hassan district, Karnataka, India</td>
<td>Root</td>
<td>Sudorific, diarrhea, dysentery, colic</td>
<td>Kumar and Shiddmamallayya[31]</td>
</tr>
<tr>
<td>Thrissur district, Kerala, India</td>
<td>Root</td>
<td>Diarrhoea, dysentery, hyperdipsia, ulcer, skin diseases</td>
<td>Deepa <em>et al.</em>[32]</td>
</tr>
<tr>
<td>Rajasthan, India</td>
<td>-</td>
<td>Body ache</td>
<td>Choudhary <em>et al.</em>[33]</td>
</tr>
<tr>
<td>Dindigul district, Tamil Nadu, India</td>
<td>Root</td>
<td>Dysentery</td>
<td>Shanmugam <em>et al.</em>[34]</td>
</tr>
<tr>
<td>Andaman and Nicobar Islands, India</td>
<td>-</td>
<td>Malaria, contraception, dysentery, fever, bone fracture, headache, pruritus, skin injuries</td>
<td>Chander <em>et al.</em>[35]</td>
</tr>
<tr>
<td>Sumatra, Indonesia</td>
<td>-</td>
<td>Abscess</td>
<td>Hariyadi and Ticktin[36]</td>
</tr>
<tr>
<td>Golaghat district, Assam, India</td>
<td>Fruit</td>
<td>Extracts used for purple dye</td>
<td>Barukial and Sarmah[37]</td>
</tr>
<tr>
<td>Visakhapatnam district, Andhra Pradesh, India</td>
<td>Tuber</td>
<td>Liver enlargement</td>
<td>Rao <em>et al.</em>[38]</td>
</tr>
<tr>
<td>Thrissur district, Kerala, India</td>
<td>Stem bark</td>
<td>Treatment of wound</td>
<td>Udayan <em>et al.</em>[39]</td>
</tr>
<tr>
<td>Kannur district, Kerala, India</td>
<td>Root, leaf</td>
<td>Diarrhea, dysentery and ulcer</td>
<td>Ranjith and Ramachandran[40]</td>
</tr>
<tr>
<td>Lubuk Ulu Legong, Kedah, Malaysia</td>
<td>Leaf</td>
<td>Diabetes</td>
<td>Mohammad <em>et al.</em>[41]</td>
</tr>
<tr>
<td>Ulu Kuang village, Malaysia</td>
<td>Leaf and shoot</td>
<td>Wound treatment</td>
<td>Azliza <em>et al.</em>[42]</td>
</tr>
<tr>
<td>Rajasthan, India</td>
<td>Inflorescence, tuber</td>
<td>Chest pain treatment in children (inflorescence extract), allergy (tuber paste)</td>
<td>Swarnkar and Katewa[43]</td>
</tr>
<tr>
<td>Jessore District, Bangladesh</td>
<td>Leaf</td>
<td>Joint pain</td>
<td>Akter <em>et al.</em>[44]</td>
</tr>
<tr>
<td>Shimoga district, Karnataka, India</td>
<td>Leaf</td>
<td>Diarrhea and dysentery in cattle</td>
<td>Rajakumar and Shivanna[45]</td>
</tr>
<tr>
<td>Car Nicobar island, Nicobar, India</td>
<td>Leaf</td>
<td>Cuts and wounds</td>
<td>Verma <em>et al.</em>[46]</td>
</tr>
<tr>
<td>Kalakad Mundanthurai Tiger Reserve, Tamil Nadu, India</td>
<td>Leaf, flower</td>
<td>Rheumatism</td>
<td>Sutha <em>et al.</em>[47]</td>
</tr>
<tr>
<td>Kanyakumari district, Tamil Nadu, India</td>
<td>Root</td>
<td>Diarrhea</td>
<td>Sukumaran and Raj[48]</td>
</tr>
<tr>
<td>Banjar, South Kalimantan, Indonesia</td>
<td>Root</td>
<td>Asthma</td>
<td>Anshhari <em>et al.</em>[49]</td>
</tr>
<tr>
<td>West Nepal</td>
<td>Leaf</td>
<td>Young leaves digestive; leaf useful in spleen problems</td>
<td>Kunwar <em>et al.</em>[50]</td>
</tr>
<tr>
<td>Northern Thailand</td>
<td>Root, stem</td>
<td>Diarrhea, hemorrhoid, gastric ulcer</td>
<td>Tangijitman <em>et al.</em>[51]</td>
</tr>
<tr>
<td>Eastern Himalaya</td>
<td>-</td>
<td>Fuelwood</td>
<td>Bhatt <em>et al.</em>[52]</td>
</tr>
<tr>
<td>Chittagong hill tracts, Bangladesh</td>
<td>Leaf</td>
<td>Sore, leprosy, eczema, itching, bone fracture, and sprain</td>
<td>Yusuf <em>et al.</em>[53]</td>
</tr>
</tbody>
</table>

*L. indica*: Leea. indica
A herbal formulation, THR-SK009, containing *L. indica* (used for the treatment of wound or skin inflammation) was shown to exhibit inhibitory activity against drug-resistant bacteria.\(^{[70]}\) The study carried out by Harun *et al*.\(^{[63]}\) revealed the potential of dichloromethane extract of *L. indica* leaf, stem, and root to inhibit *Staphylococcus aureus* and *Staphylococcus epidermidis*. Tareq *et al*.\(^{[64]}\) showed the inhibitory potential of methanolic extract of *L. indica* leaves against Gram-positive and Gram-negative bacteria. The study carried out by Chander and Vijayachari\(^{[67]}\) and Chander and Vijayachari\(^{[67]}\) showed the ineffectiveness of methanol extract of leaves of *L. indica* to inhibit *C. albicans* and *A. niger*, respectively.

### Antifungal Activity

Essential oil, obtained from flowers of *L. indica*, was effective in inhibiting molds, namely, *Penicillium notatum*, *Fusarium moniliforme*, and *Aspergillus niger*.\(^{[60]}\) The study by Rahman *et al*.\(^{[61]}\) revealed the antifungal potential (as revealed by poisoned food technique) of ethanolic extract of *L. indica* leaves to inhibit the growth of *Aspergillus flavus*, *Candida albicans*, and *Fusarium equiseti* by 38.09 ± 0.59, 22.58 ± 2.22, and 22.58 ± 2.22%, respectively. Ramesh *et al*.\(^{[62]}\) evaluated the antifungal potential of leaf and bark extract of *L. indica* against molds, namely, *Colletotrichum capsici*, *Helmithosporium* sp., and *Curvularia* sp. Among extracts, marked inhibitory potential was shown by leaf extract. Among fungi, *Helmithosporium* sp. and *Curvularia* sp. were inhibited to the highest and least extent, respectively. Tareq *et al.*\(^{[64]}\) showed the inhibitory potential of methanolic extract of *L. indica* leaves against pathogenic yeasts and molds. The study carried out by Chander and Vijayachari\(^{[67]}\) and Chander and Vijayachari\(^{[71]}\) showed the ineffectiveness of methanol extract of leaves of *L. indica* to inhibit *C. albicans* and *A. niger*, respectively.

### Antiviral Activity

Ethanolic extract obtained from leaves of *L. indica* was shown to exhibit antiviral activity against herpes simplex virus type-1 with an MIC value of 0.05 mg/ml. The extract was ineffective against vesicular stomatitis virus.\(^{[73]}\)

### Antioxidant Activity

Studies have shown the potential of *L. indica* to exhibit free radical and antioxidant activity. Methanol extract of

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**Table 2: Chemicals/phytochemical groups detected in *L. indica***

<table>
<thead>
<tr>
<th>Plant part</th>
<th>Method</th>
<th>Compounds identified</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaf</td>
<td>GC-MS</td>
<td>Phthalic acid, palmitic acid, 1-eicosanol, solanesol, farnesol, three phthalic acid esters, gallic acid, lupeol, δ-sitosterol, ursolic acid</td>
<td>Srinivasan <em>et al</em>.(^{[69]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Standard tests</td>
<td>Alkaloid, terpenoids, flavonoids, sterol, tannin</td>
<td>Emran <em>et al</em>.(^{[60]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Standard tests</td>
<td>Alkaloid, glycoside, cardiac glycoside, terpenoids, flavonoids, steroid, tannin</td>
<td>Rahman <em>et al</em>.(^{[61]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Chromatographic and spectral analyses</td>
<td>Triterpenoid glycosides, namely, mollic acid arabinoside and mollic acid xyloside</td>
<td>Wong <em>et al</em>.(^{[21]})</td>
</tr>
<tr>
<td>Fresh plant material</td>
<td>HPTLC</td>
<td>Quercetin, gallic acid</td>
<td>Patel <em>et al</em>.(^{[62]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Standard tests</td>
<td>Alkaloids, saponins, steroids, saponins, terpenoids</td>
<td>Harun <em>et al</em>.(^{[63]})</td>
</tr>
<tr>
<td>Stem</td>
<td>Standard tests</td>
<td>Saponins, steroids, terpenoids, tannins, cardiac glycosides, flavonoids</td>
<td>Harun <em>et al</em>.(^{[63]})</td>
</tr>
<tr>
<td>Root</td>
<td>Standard tests</td>
<td>Saponins, steroids, terpenoids, tannins, cardiac glycosides, flavonoids</td>
<td>Harun <em>et al</em>.(^{[63]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Standard tests</td>
<td>Alkaloids, flavonoids, steroids, glycosides, tannins</td>
<td>Tareq <em>et al</em>.(^{[64]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Standard tests</td>
<td>Alkaloids, flavonoids, tannins, sterols, glycosides, phenols, saponins</td>
<td>Ghagane <em>et al</em>.(^{[65]})</td>
</tr>
<tr>
<td>Stem bark</td>
<td>Standard tests</td>
<td>Alkaloids, flavonoids, glycosides, phenolic compounds</td>
<td>Mishra <em>et al</em>.(^{[66]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Standard tests</td>
<td>Alkaloids, flavonoids, triterpenoids, sterols</td>
<td>Chander and Vijayachari(^{[67]})</td>
</tr>
<tr>
<td>Leaf</td>
<td>Standard tests</td>
<td>Saponins, tannins, alkaloids, steroids, flavonoids, cardiac glycosides, terpenoids</td>
<td>Dalu <em>et al</em>.(^{[68]})</td>
</tr>
</tbody>
</table>

*L. indica*: *Leea. indica*, HPTLC: High-performance thin-layer chromatographic, GC-MS: Gas chromatography-mass spectrometry
*L. indica* was shown to exhibit marked scavenging activity against DPPH radicals. The crude ethanol extract and hexane, ethyl acetate, and aqueous fractions of ethanol extract obtained from leaves of *L. indica* were evaluated for antioxidant activity by DPPH scavenging, superoxide radical scavenging, and reducing power assay. Aqueous fraction of ethanol extract was found to contain high phenolics and exhibited marked antioxidant activity when compared to other fractions. The study carried out by Ghagane et al. revealed the antioxidant activity of solvent extracts obtained from leaves of *L. indica* by DPPH, ferric reducing antioxidant power, and phosphomolybdenum assays. The antioxidant activity observed was in the order: Methanol extract > ethanol extract > aqueous extract. Table 3 presents the free radical scavenging and antioxidant potential of *L. indica* being revealed by other researchers.

### Cytotoxic/Anticancer/Antitumor Activity

Methods such as brine shrimp lethality assay and MTT assay are routinely used to evaluate cytotoxic potential of plants. It is evident from the studies that crude solvent extracts and isolated compounds from *L. indica* exhibit *in vitro* and *in vivo* cytotoxic/antitumor activity. Hsiung and Kadir investigated anticancer potential of ethanol extract and ethyl acetate, hexane, and water fraction *L. indica* leaves against various cell lines (Ca Ski, MCF 7, MDAMB-435, KB, HEP G2, WRL 68, and Vero) by MTT assay. It was shown that the ethyl acetate fractions showed greatest cytotoxic effect against Ca Ski cervical cancer cells. Treatment of cells with the fraction showed typical apoptotic morphological changes such as DNA fragmentation and chromatin condensation.

In another study, Wong isolated two cycloartane triterpenoid glycosides, namely, mollic acid arabinoside and mollic acid xyloside. These compounds were subjected to cytotoxicity against Ca Sk cervical cancer cells. Mollic acid arabinoside and mollic acid xyloside inhibited the growth of Ca Sk cervical cancer cells with IC₅₀ values of 19.21 μM and 33.33 μM, respectively. Rahman et al. determined *in vivo* antitumor activity of leaf extract of *L. indica* in Ehrlich ascites carcinoma (EAC) bearing mice. It was found that the extract at the dose of 40 mg/kg/day significantly decreases tumor weight, increases lifespan, and reduces tumor cell growth rate in comparison to those of EAC bearing mice receiving no extract. The study of Saha screened cytotoxicity of Ethanolic extract of *L. indica* by brine shrimp lethality assay. The leaf extract displayed cytotoxicity against brine shrimps with an LC₅₀ value of 2.47μg/ml. Reddy et al. screened crude ethanol extract and solvent fractions, namely, hexane, ethyl acetate, and water fractions of leaves of *L. indica* for cytotoxicity activity against colon cancer cell lines, namely, HT-29, HCT-15, and HCT-116 by MTT assay. It was observed that the crude extract and solvent fractions did not exert any cytotoxicity against cell lines. Rahman et al. screened cytotoxic potential of ethanol extract of *L. indica* by brine shrimp assay. The extract caused dose-dependent mortality of shrimps with an LC₅₀ value of 2.65 μg/ml. More recently, Ghagane et al. revealed cytotoxicity of *L. indica* leaves against two cancer cell lines, namely, DU-145 and PC-3 by MTT assay. Based on IC₅₀ values, the degree of cytotoxicity of solvent extracts observed was in the order: Methanol extract > ethanol extract > aqueous extract. Moreover, the extracts were not effective against normal mice embryo fibroblast cells. The study carried out by Ali et al. revealed ineffectiveness of ethanolic extract of leaves of *L. indica* to exhibit cytotoxicity against HeLa cells. The study by Avin et al. revealed the modulation of neovessel formation in non-tumorigenic and tumorigenic conditions by crude ethanol extract of *L. indica* by performing assays, namely, VEGF165-induced *in vivo* CAM assay, rat corneal micropocket assay, and tumor-induced peritoneal angiogenesis assay. It was found that the crude extract of *L. indica* inhibited the sprouting vessels.

### Thrombolytic Activity

Ethanol extract of *L. indica* leaves was screened for thrombolytic activity *in vitro* by clot lysis activity. The extract produced a significant clot lysis activity of 39.30 ± 0.96%. Ethanol extract of *L. indica* leaves was screened for antidiarrheal activity by castor oil-induced

### Table 3: Free radical scavenging and antioxidant activity of *L. indica*

<table>
<thead>
<tr>
<th>Part</th>
<th>Assay/technique</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaf</td>
<td>Total antioxidant capacity, ferric reducing power,</td>
<td>Rahman et al. [86]</td>
</tr>
<tr>
<td></td>
<td>superoxide scavenging, iron chelating activity</td>
<td></td>
</tr>
<tr>
<td>Leaf, bark</td>
<td>DPPH assay</td>
<td>Ramesh et al. [72]</td>
</tr>
<tr>
<td>Leaf</td>
<td>DPPH assay</td>
<td>Emran et al. [60]</td>
</tr>
<tr>
<td>Leaf</td>
<td>DPPH, superoxide, and hydroxyl radical scavenging</td>
<td>Sulistyaningsih et al. [76]</td>
</tr>
<tr>
<td></td>
<td>assay</td>
<td></td>
</tr>
<tr>
<td>Leaf</td>
<td>DPPH assay, reducing power assay</td>
<td>Raihan et al. [77]</td>
</tr>
<tr>
<td>Stem, leaf, root</td>
<td>DPPH assay</td>
<td>Harun et al. [63]</td>
</tr>
<tr>
<td>Leaf</td>
<td>DPPH assay</td>
<td>Chander and Vijayachari [67]</td>
</tr>
</tbody>
</table>

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diarrhea in mice. The extract at the doses of 500 mg/kg and 250 mg/kg significantly reduced the total number of stool as well as increased the latency period of defecation in comparison to the control groups.

**Hepatoprotective Activity**

Ethanolic extract obtained from the stem bark of *L. indica* was shown to exhibit hepatoprotective activity against liver injury induced by paracetamol in rats. The treatment of animals with the extract at two doses, namely, 200 and 400 mg/kg body weight resulted in significant decrease in elevated level of serum marker enzymes, bilirubin, and triglycerides when compared to positive control group of rats.[66]

**Enzyme Inhibitory Activity**

The plant *L. indica* is reported to possess inhibitory activity against enzymes such as phosphodiesterase, pancreatic lipase, and glucosidase. In a study, Ado *et al.*[82] investigated lipase inhibitory activity of methanolic extract of *L. indica* leaves against porcine pancreatic lipase. It was observed that the extract was effective in inhibiting the activity of lipase by 48.5%. The study carried out by Temkitthawon *et al.*[83] indicated the potential of ethanol extract of *L. indica* root to inhibit the activity of phosphodiesterase measured using the SPA radioassay (with an IC$_{50}$ value of 2.62 ± 0.25 µg/ml). Ridhwan[84] revealed the potential of *L. indica* root to strongly inhibit activity of α-glucosidase.

**Antihyperglycemic Activity**

Dalu *et al.*[68] evaluated hypoglycemic activity of alcoholic and hydroalcoholic extracts of *L. indica* leaves using glucose tolerance test and alloxan-induced diabetes model in rats. The extract administration significantly reduced blood glucose level indicating hypoglycemic activity of leaf extracts. The study of Patel *et al.*[85] also revealed the antidiabetic activity of methanol extract of *L. indica* leaves in alloxan-induced diabetic rats.

**Hypolipidemic Activity**

The administration of alcoholic and hydroalcoholic extracts of *L. indica* leaves in rats resulted in significant decrease in the level of triglycerides, total cholesterol, LDL, and VLDL and increased HDL indicating hypolipidemic activity of leaf extract.[68]

**Sedative Activity**

Raihan *et al.*[86] evaluated the sedative property of crude methanol extract of *L. indica* leaves by hole cross, open field, and thiopental sodium-induced sleeping time tests. It was shown that the leaf extract displayed a dose-dependent suppression of motor activity, exploratory behavior, and prolongation of thiopental induced sleeping time in mice in a dose-dependent manner.

**Anxiolytic Activity**

An elevated plus maze (EPM) test was performed to evaluate anxiolytic potential of crude methanol extract of *L. indica* leaves by Raihan *et al.*[86] The methanol extract at the dose of 400 mg/kg body weight, significantly increased the entries of mice into the open arms, and the time spent in the open arms of the EPM.

**Wound Healing Activity**

The study carried out by Azizi *et al.*[87] revealed the wound healing potential of ethanolic extract of *L. indica* in NIH 3T3 mouse fibroblast cells and RAW 264.7 mouse macrophage cells by scratch assay. It was found that the extract treatment triggered migration of cells at the site of the gap (the wound) being created by scratching the area of cells (0.5 mm width) indicating the potential of *L. indica* to heal the wound.

**Analgesic Activity**

Emran *et al.*[88] investigated the analgesic activity of leaf extract of *L. indica* by acetic acid writhing test and...
formalin-induced licking response test. Oral administration of the extract significantly inhibited writhing response induced by acetic acid. The administration of extract also suppressed formalin-induced pain response in mice.

**Larvicidal Activity**

The leaf extract of *L. indica* was investigated for insecticidal activity against larvae (I to IV instar) of *Culex quinquefasciatus*. The leaf extract exhibited larvicidal effect which was more effective against earlier stages of larval development.[89]

**Antimalarial Activity**

The study of Abd Razak et al.[90] revealed the ineffectiveness of solvent extracts of *L. indica* leaf to exhibit antiplasmodial activity against *Plasmodium falciparum* K1 by HRP2-based assay. In another study, Sulistyaningsih et al.[96] investigated antimalarial activity of leaf extract of *L. indica* in male Balb/c mice. The leaf extract was found to decrease the parasitemia level by 3.50 ± 1.26% on the 4th day and yielded 24.85 ± 1.28% of suppression.

**Biosynthesis and Biological Activity of Nanoparticles from *L. indica***

Few studies have been carried out on synthesis of nanoparticles from *L. indica*. The study of Rokhade and Taranath[91] revealed the synthesis of silver nanoparticles using aqueous extract of *L. indica* leaves. The nanoparticles exhibited synergistic antibacterial activity with antibiotic against Gram-positive and Gram-negative bacteria. In another study, Rokhade and Taranath[92] synthesized silver nanoparticles using fruit extract of *L. indica*. The nanoparticles showed synergistic antibacterial activity with antibiotic against Gram-positive and Gram-negative bacteria.

**CONCLUSION**

In the present review, an extensive literature review carried out to compile information related to ethnobotanical uses, chemistry and pharmacological activities of *L. indica* indicated that the plant is widely used in traditional medicine in India and other countries such as Thailand, Nepal, Indonesia, and Malaysia for the treatment of ailments or disorders such as diabetes, dysentery, wounds, body ache, bone fracture, and fever. Phytochemical groups such as alkaloids, terpenoids, flavonoids, terpenoids, tannins, steroids, and glycosides have been identified in the plant. Triterpenoid glycosides with cytotoxic activity have been isolated from the leaves of *L. indica*. The presence of these phytochemicals may be responsible for the observed biological activity such as antimicrobial, antioxidant, cytotoxic, enzyme inhibitory, analgesic, hepatoprotective, and antimalarial activity of the plant *L. indica*. The results of pharmacological activities being conducted support the traditional uses of the plant. A much detailed literature review carried out in this review indicated that the plant appears to be a suitable alternative for current chemotherapeutic agents which often possess many drawbacks such as high cost and side effects. However, more studies are required to identify therapeutic principles from the plant and their utilization for a remedy against several dreadful diseases due to agents such as pathogens and free radicals.

**ACKNOWLEDGMENTS**

Authors thank Dr. Vinayaka K.S, Principal, KFGC, Shikaripura, for providing plant picture and some useful information on the plant.

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Source of Support: Nil. Conflict of Interest: None declared.