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Leea indica (Burm.f.) Merr.: A Systematized Acquaint

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Abstract

Leea indica is extensively employed for the treatment of disorders like asthma, diabetes, pyrexia, rheumatism, wounds etc. An attempt has been made in the present review to frame an overall informative picturesque of the plant species to showcase its medicinal utilities and fetching out the significant futuristic applications and usages. The relevant information on all possible aspects of was extracted using different databases *viz*., Web of Science, Scopus, PubMed, Google scholar and Science direct etc. It was revealed that *L. indica* is primarily used for ethno-medicinal applications as different formulations in order to cure more than 20 to 25 dissimilar types of ailments. Another very interesting finding is role of *L. indica* in the treatment of neurological disorders as recently has been reported. Pharmacological exploration specified the potential anti-cancer, anti-gastro-intestinal, anti-microbial and sedative characteristics etc. Also, variety of secondary metabolites belonging to different classes of compounds are reportedly isolated from *L. indica*. In spite of having better efficiency of ethno-medicines and good pharmacological potential, *L. indica* till now only have been proved to be a potential herbal remedy for disorders including asthma, cancer, gastro-intestinal disorders', pyrexia, rheumatism and up to some extent neurological diseases. The in-attendance explorative review also accentuates the need to document the mechanism responsible for making the plant species stand against neurological disorders such as Alzheimer's' in a much more detailed manner. This could improve the traditional anti-sedative formulations'/forms' and might contribute to a better integration of *L. indica* in modern medicine which in-turn may prove beneficial for the health system in near future.

Keywords: Alzheimer's'; Bandicoot berry; Neurological; Sedative; Traditional medicine

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Introduction

Innumerable rudiments of human life are met with extensive utilization of plants. Besides, plants have also found ritual efficacies. Round the globe, many plants with therapeutic potency have been employed in treating copious human and veterinary ailments. Conventional usage of plants executes their consumption either individually or in definite formulations in order 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 needs.

Leea indica (Burm.f.) Merr. (Vitaceae), commonly known as Bandicoot berry (English), Chhatri (Sanskrit), Hastipalash (Hindi) [1], 'Huo Tong Shu' (Malay) have been traditionally employed as a natural remedy in folk medicine by the locals [2]. The plant is medicinally imperative and is widely used in indigenous systems of medicine [1] such as by the tribes of Bangladesh [2] *viz*., 'Marma' of Chittagong Hill Tracts, Bangladesh, prescribes combined root paste of the plant along with the roots of Oreocnide integrifolia and Cissus repens for treating bubo (an enlarged lymph node that is tender and painful) and boils. Leaves are employed as folk medicine in the treatment of insomnia, although it is not reported yet in the literature [4]. Roots are anti-diarrheal, anti-dysenteric, anti-spasmodic, cooling and sudorific [1]. Young leaves (juice) is digestive and an ointment, prepared from roasted leaves relieves vertigo [1]. Flowers are anti-inflammatory, anti-microbial, anti-oxidant, hypo-glycemic and phosphodiesterase inhibitory [5].

Several known phytoconstituents have been isolated from the leaves, including 1-eicosanol, farnesol, gallic acid, lupeol, palmitic acid, phthalic acid, β-sitosterol and ursolic acid. Among the isolated compounds, di-N-butyl phthalate exhibits antibacterial and antifungal characteristics wherein, butyl gallate is an antioxidant.

The in-attendance review discusses and hearsays information and evidences available on the traditional uses, chemical edifice and biological activities of *L. indica*. Literature was surveyed by

Figure 1: An illustrative figure of *L. indica* (Burm.f.) Merr. with synonyms.

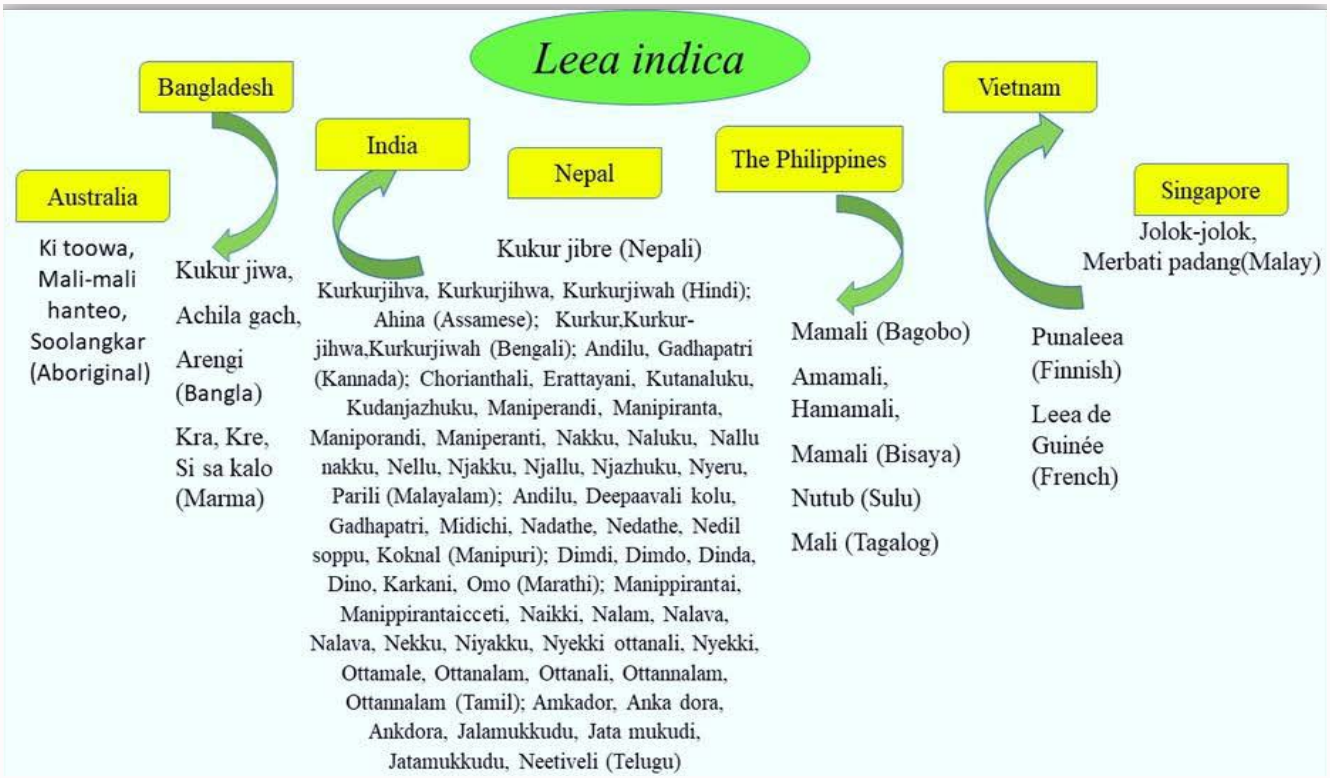


Figure 2: A descriptive graphical representation of *L. indica* vernacular names.

extracting information from different scientific search engines such as PubMed, Scopus, Web of Science, Science Direct and Google Scholar. Floras, journals, books, leaflets etc. were also referred [1]. In light of the conventional utilities, ethno-medicinal diversity, phytoconstituents organization, therapeutic customs & benefits, related biological significance of *L. indica* and, on account of a recent finding by Raihan et al. [6] which reported the significant sedative and anxiolytic potentiality of *L. indica* leaves, it is suggested that *L. indica* extracts may have the persuasive molecules that are active against BACE1 enzyme, and therefore have the therapeutic values against Alzheimer's' disease [7,8]. The study encouraged us to hypothesize that futuristic layout can be designed and experimented by evaluating

Table 1: Recounted ethnobotanical uses of different parts of *L. indica*.

S. No.	Plant Parts	Region	Ailments
1	Roots	Singha Nakhon District, Songkhla Province, Thailand	Fever
2		Kut Chum District, Yasothon Province, Thailand	Diarrhea
3		Jalpaiguri district, West Bengal, India	Bone fracture
4		Hassan district, Karnataka, India	Sudorific, Diarrhea, Dysentery, Colic
5		Thrissur district, Kerala, India	Diarrhea, Dysentery, Hyperdipsia, Ulcer, Skin diseases
6		Dindigul district, Tamil Nadu, India	Dysentery
7		Kanyakumari district, Tamil Nadu, India	Diarrhea
8		Banjar, South Kalimantan, Indonesia	Asthma
9	Tuber	Visakhapatnam district, Andhra Pradesh, India	Liver enlargement
10	Roots, stem	Northern Thailand	Diarrhea, Hemorrhoid, Gastric ulcer
11	Stem bark	Thrissur district, Kerala, India	Wounds
12	Leaves	Chittagong Hill Tracts, Bangladesh	Joint pain
13		Lubuk Ulu Legong, Kedah, Malaysia	Diabetes
14		Jessore District, Bangladesh	Joint pain
15		Shimoga district, Karnataka, India	Diarrhea and Dysentery in cattle
16		Car Nicobar island, Nicobar, India	Cuts and Wounds
17		West Nepal Leaf Young leaves digestive;	Spleen problems
18	Leaves, flowers	Kalakad Mundanthurai Tiger Reserve, Tamil Nadu, India	Rheumatism
19	Leaves and shoots	Ulu Kuang village, Malaysia	Wound treatment

the present accessibility and availability of database available on *L. indica* like, its status, vulnerabilities, readiness and experimental potentiality on account of which, studies could be premeditated and a probable cure for Alzheimer's' disease can be brought into existence.

Experimental

The study has been designed to accumulate the diversified information of several published research articles on medicinal uses, phytoconstituents as well as pharmacological profiling of *L. indica*. A total of 40 published papers (on account of different keywords such as, medicinal uses, chemical composition, diseases caused, ethno-medicinal uses, folk medicinal uses, pharmacological profile/ properties of *L. indica*) were consulted using different scholarly databases such as, Google scholar, PubMed, Science direct, Scopus and Web of Science etc. In present review, restriction of language was considered, only the published articles in English version were included for conducting search targets through different databases using a combination of key words including, *L. indica*, ethno-pharmacology, phytochemistry, pharmacological terminology such as anti-microbial, anti-oxidant anti-sedative, anxiolytic properties etc. [9].

In this review, the information has been accumulated from above mentioned scientific scholarly databases which are having only scientific publications. Although, some additional information has been attained from less available sources like unpublished thesis and reports. All the obtained data from previous published scientific articles is summarized in 2 tables and 6 figures for the better understanding of traditional uses, phytochemistry and pharmacological activities of *L. indica*. All the reported phytochemicals obtained from this species are presented with their IUPAC names, chemical and structural formulae, verified from PubChem [10].

Results and Discussion

Inclusive literature-based information on

Botanical description: *L. indica* is a large perennial shrub with stout, soft-wooded stems, alternate leaves (2-3 pinnate, sometimes 1-pinnate), leaflets ovate or oblong-lanceolate, 25 cm × 10 cm, apex acuminate, margin irregularly serrate, base truncate, pinnately veined. Flowers are pale-green/greenish-white, bisexual, in large terminal compound corymbose cymes, bracts minute, calyx 5-lobed, petals 5, and spreading. Stamens 5 in number, stamina tube white in color, anthers are united in buds. Fruit is a berry, 8 mm across, globose, often 2-6 lobed, to 0.5 cm in diameter, purplish–black when ripe. Flowering occurs more or less throughout the year [1]. An illustrative description of the plant along with its synonyms is being represented in Figure 1.

Distribution and Habitat: The plant is distributed in various parts of the world such as India, Malaysia, China, and Thailand [1]. It prefers to grow in disturbed areas of lowland and upland rain forest in Asia–Pacific islands [5]. The plant is distributed in forests of tropical and subtropical India, from Himalayas to southward to the Peninsula [1]. The species has extremely large ecological amplitude and is extremely widespread i.e., it is found in back mangroves, secondary forests, primary forests in the lowlands and wet ridges up to 1,700 m altitude. In Singapore, it is found in many habitats *viz*., in coastal vegetation, back mangroves, secondary forests, freshwater swamp forests near the edges or in gaps, and also in the undergrowth of primary forests [11]. In Bangladesh, it grows in hilly forests of Chittagong and Sylhet [5]. It is cultivated largely throughout India and also found wild from Punjab to West Bengal, Assam, Konkan, Dekkan, Rampa Hills [11]. It is also cultivated in China [11].

Vernacular names of *L. indica*: *L. indica* has altered synonyms and vernacular names which varies area, region as well as country-

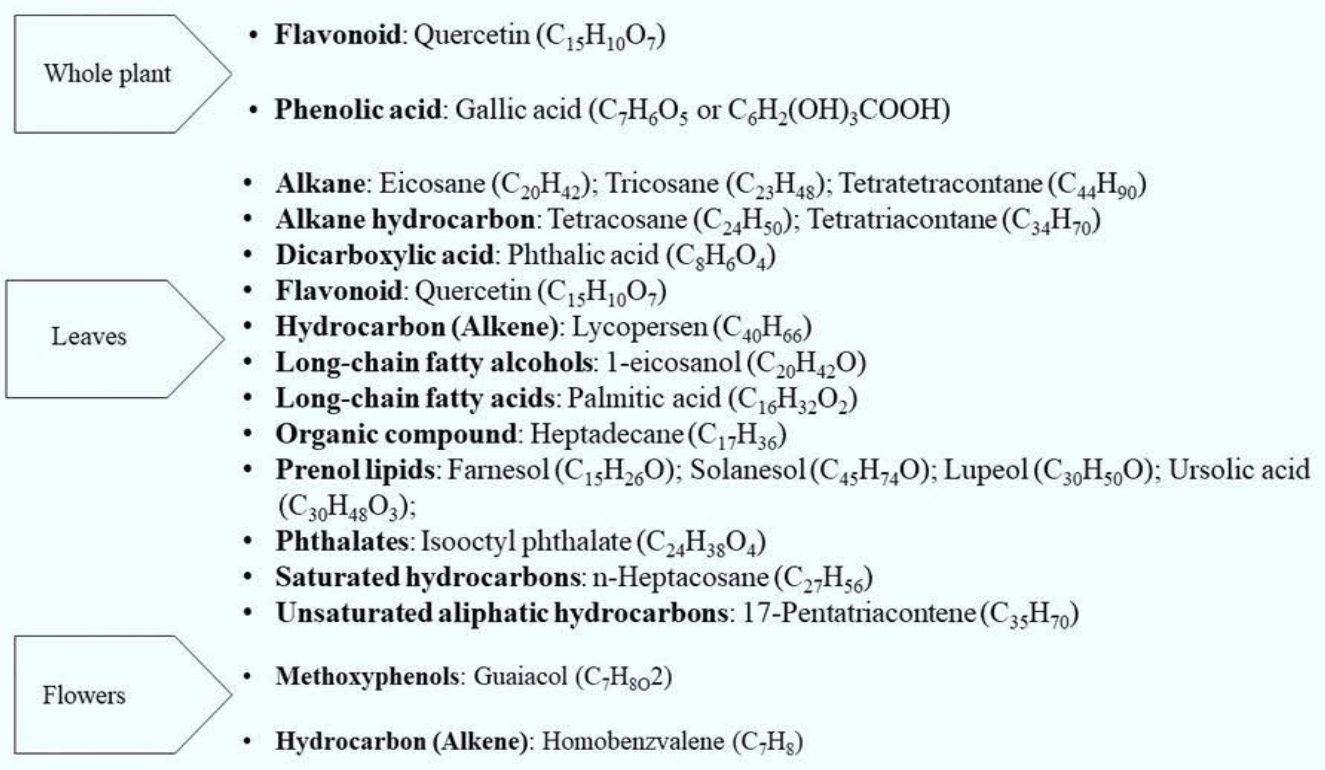


Figure 3: Phyto-constituents of *L. indica* with their major classes.

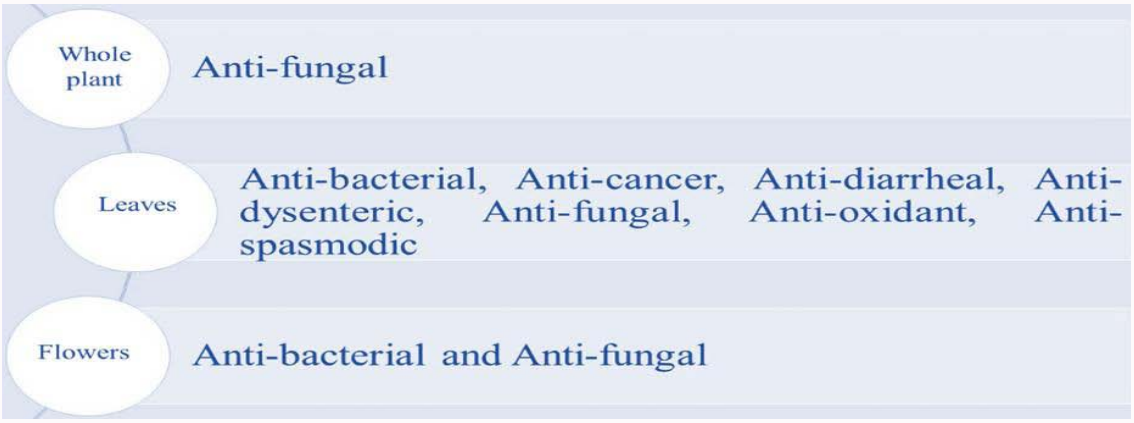


Figure 4: Part-wise therapeutic characteristics of *L. indica*.

wise. An emblematical presentation of the vernacular names with their specific languages and countries across the globe are displayed in Figure 2.

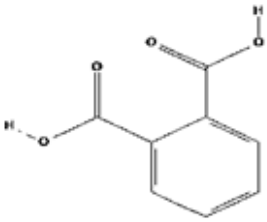
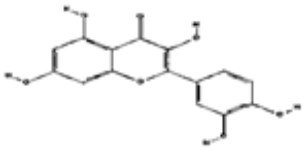
Ethno-Medicinal Conventions of *L. indica*

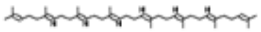
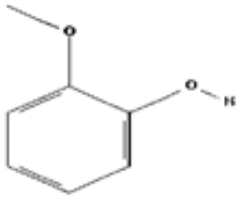
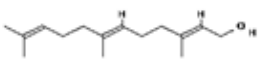
Ethnic communities in various parts of the world utilize several plants to treat a number of diseases/disorders. Traditional medicine based on plants is widely practiced in countries such as India, China, Sri Lanka, Pakistan, Thailand, and many African countries. Plant-based medicines are cheaper, often safer and are the only therapeutic agents for people from poor economic background and living in rural areas. *L. indica* has ethnomedicinal importance worldwide. Various parts of the plants, namely, roots, stem bark, leaves, inflorescence and flowers in certain formulations such as paste and decoction are being in use for treating several ailments in which roots and leaves are predominantly used. The plant is utilized medicinally in several formulations to treat ailments such as asthma, bone fractures, body ache, diarrhea, dysentery, fever, headache, malaria, rheumatism and gastric ulcer etc. A brief detail on some of the uses of *L. indica* to treat diseases in India and in other parts of the world (namely, Nepal, Bangladesh, Malaysia, Indonesia, and Thailand) is presented in Table 1 [1]. The leaves of *L. indica* are reported to have various therapeutic characteristics *viz*., anti-cancer, anti-diarrheal, anti-dysenteric and anti-spasmodic etc. [12].

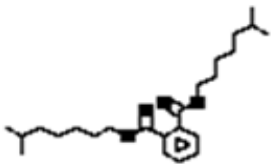
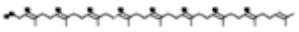
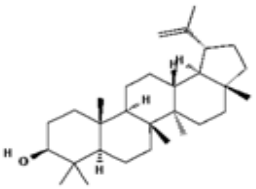
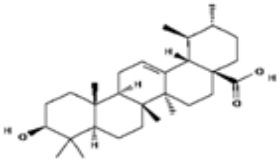
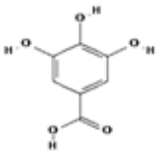
Phyto-Constituents Outlining of *L. indica*

L. indica contain chemical compounds belonging to different classes, including alkaloids, anthraquinone, benzoic acid derivatives,

Table 2: Major chemical compounds and groups of *L. indica*.

S. No	Phyto-constituents	IUPAC Names	Chemical Structures	Pharmacological activity	Reference
1.	Eicosane	Icosane		Antibacterial	[19]
2.	Tricosane	5-chloro-2-(2,4-dichlorophenoxy)phenol		Anti-oxidant	[19]
3.	Tetracosane	Tetracosane		Anti-oxidant	[19]
4.	Tetratetracontane	Tetratetracontane		Anti-oxidant	[19]
5.	Phthalic acid	Benzene-1,2-dicarboxylic acid		Anti-oxidant	[19]
6.	Quercetin	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one		Antifungal	[8]
7.	Homobenzvalene	Tricyclo[4.1.0.02,7]hept-3-ene		Antibacterial and Antifungal	[20]

8.	Lycopersen	(6E,10E,14E,18E,22E,26E)-2,6,10,14,19,23,27,31-octamethyldotriaconta-2,6,10,14,18,22,26,30-octaene		Anti-oxidant	[19]
9.	Tetratriacontane	Tetratriacontane		Anti-oxidant	[19]
10.	1-eicosanol	Icosan-1-ol		Antioxidant	[19]
11.	Palmitic acid	Hexadecanoic acid		Anti-oxidant	[19]
12.	Guaiacol	2-methoxyphenol		Antibacterial and Antifungal	[20]
13.	Heptadecane	Heptadecane		Anti-oxidant	[19]
14.	Farnesol	(2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-ol		Antibacterial	[19]

15.	Isooctyl phthalate	bis(6-methylheptyl) benzene-1,2-dicarboxylate		Anti-oxidant	[19]
16.	Solanesol	(2E,6E,10E,14E,18E,22E,26E,30E)-3,7,11,15,19,23,27,31,35-nonamethylhexatriaconta-2,6,10,14,18,22,26,30,34-nonaen-1-ol		Anti-oxidant	[19]
17.	Lupeol	(1*R*,3a*R*,5a*R*,5b*R*,7a*R*,9*S*,11a*R*,11b*R*,13a*R*,13b*R*)-3a,5a,5b,8,8,11a-hexamethyl-1-prop-1-en-2-yl-1,2,3,4,5,6,7,7a,9,10,11,11b,12,13,13a,13bhexadecahydrocyclopenta[a]chrysen-9-ol		Antidysenteric, Antispasmodic, Anticancer, Antidiarrheal	[7]
18.	Ursolic acid	(1*S*,2*R*,4a*S*,6a*R*,6a*S*,6b*R*,8a*R*,10*S*,12a*R*,14b*S*)-10-hydroxy-1,2,6a,6b,9,9,12a-heptamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydro-1*H*-picene-4a-carboxylic acid		Anti-oxidant	[19]
19.	Gallic acid	3,4,5-trihydroxybenzoic acid		Antifungal	[8]
20.	n-Heptacosane	Heptacosane		Anti-oxidant	[19]
21.	17-Pentatriacontene	(E)-pentatriacont-17-ene		Anti-oxidant	[19]

NOTE: Chemical structures are extracted from PUBCHEM

catechins, coumarins, flavonoids, glycosides, dihydrochalcones, lignin's, lupeol, megastigmanes, oxylipins, phenolics, reducing sugars, saponins, sterols, tannins and ursolic acid [7,13]. Several known chemical compounds have been isolated from the leaves of *L. indica*, which includes butyl-2-phthalate, butyl-2-ethylhexyl phthalate, di-N-butyl phthalate, butyl gallate, 1- eicosanol, farnesol, gallic acid, heptadecane, lupeol, lycopersen, iso-octyl phthalate, palmitic acid, phthalic acid, β-sitosterol, sterol, triterpenes and ursolic acid from the methanolic extract [14]. Among these isolated compounds, di-N-butyl phthalate exhibits anti-bacterial and anti-fungal properties, while butyl gallate is an anti-oxidant. Interestingly, gallic acid is the one that has been reported to have several biological activities, mainly anti-cancer, anti-inflammatory, anti-microbial, anti-oxidant, anti-tyrosinase and neuro-protective [3]. A demonstrative illustration of phytoconstituents and therapeutic characteristics of *L. indica* are showcased in Figure 3, 4 and Table 2, respectively.

Pharmacological Profile of *L. indica*

L. indica displays abundant pharmacological activities, *viz*., analgesic, anti-angiogenesis, anticancer, anti-inflammatory, anti-microbial, anti-oxidant, anti-proliferative, anxiolytic, hepatoprotective and sedative etc.

Anti-cancer

Chloroform, ethyl acetate, methanol, ethanol and aqueous extracts from *L. indica* leaves had anti-cancer effect against DU-145 and PC-3 human prostate cancer cell lines, among which only the methanol and ethanol extracts exerted potent effect with IC_{50} values of 529.44 ± 42.07 & 677.11 ± 37.01 µg/mL for DU-145 and 547.55 ± 33.52 & 631.99 ± 50.24 µg/mL for PC-3 respectively [13].

In another study, Yau Hsiung et. al., reported that crude ethanol extract and their fractions (ethyl acetate, hexane, and water) possess anticancer effects against various cancer cell lines Ca Ski (cervical epidermoid carcinoma cells), MCF 7 (breast carcinoma cells), MDA-MB-435 (melanoma cells), KB (nasopharyngeal epidermoid carcinoma cells, HeLa derivative) HEP G2 (hepatocellular carcinoma cells), WRL 68 (liver embryonic cells, HeLa derivative) and Vero (kidney epithelial cells) among which, *L. indica* Ethyl Acetate Fraction (LIEAF) was found displaying the highest cytotoxic effect against Ca Ski cervical cancer cells with IC_{50} value of 85.83 ± 6.01 µg/ml and induced apoptosis [15].

Mollic Acid Arabinose (MAA), for the first time from *L. indica* was evaluated for anti-cancer activity against human cervical epidermoid carcinoma (Ca Ski, ATCC number CRL-1550) cell line. MAA, exerted number of cells nuclear shrinkage and chromatin condensation at 60 µM and at 100 µM of MAA, nearly 50% of the cells underwent DNA fragmentation and was found to appear in all phases of the cell cycle. These findings suggested that MAA induced mitochondrial-mediated apoptosis in Ca Ski cells [16].

Anti-fungal

Md. Atiar Rahman et, al., reported that *L. indica* leaf ethanol extract displays inhibition of *Aspergillus flavus*, *Candida albicans* and *Fusarium equisetii* by 38.09 ± 0.59, 22.58 ± 2.22, and 22.58 ± 2.22%, respectively and when compared with reference antibiotic fluconazole, shows 67.01 ± 1.8, 40.00 ± 2.5, and 72.32 ± 2.3% of inhibition against the fungal strains [17]. *L. indica* essential oil obtained from the flowers had been reported to have good anti-fungal activity against *P. notatum* with 21 mm zone of inhibition whereas, moderate activity against *A. niger*, and *F. monelliformae* with 5 mm & 7 mm zone of inhibition when compared with Bavistin carbendazim (standard) [18,19].

Anti-microbial

Ethanol extract from *L. indica* leaf have anti-microbial activity with significant ($P<0.05$) zone of inhibition against gram +ve (*Bacillus subtilis*, *Bacillus cereus*, *Bacillus megaterium*, and *Staphylococcus aureus*) and gram -ve (*Salmonella typhi*, *Salmonella paratyphi*, *Pseudomonas aeroginosa*, *Shigella dysenteriae*, *Vibrio cholerae*, and *Escherichia coli*) bacteria when compared with standard drug with standard antibiotics *viz*., Ampicillin and Tetracycline with 16 and 20 mm zone of inhibition, respectively. *L. indica* essential oil obtained

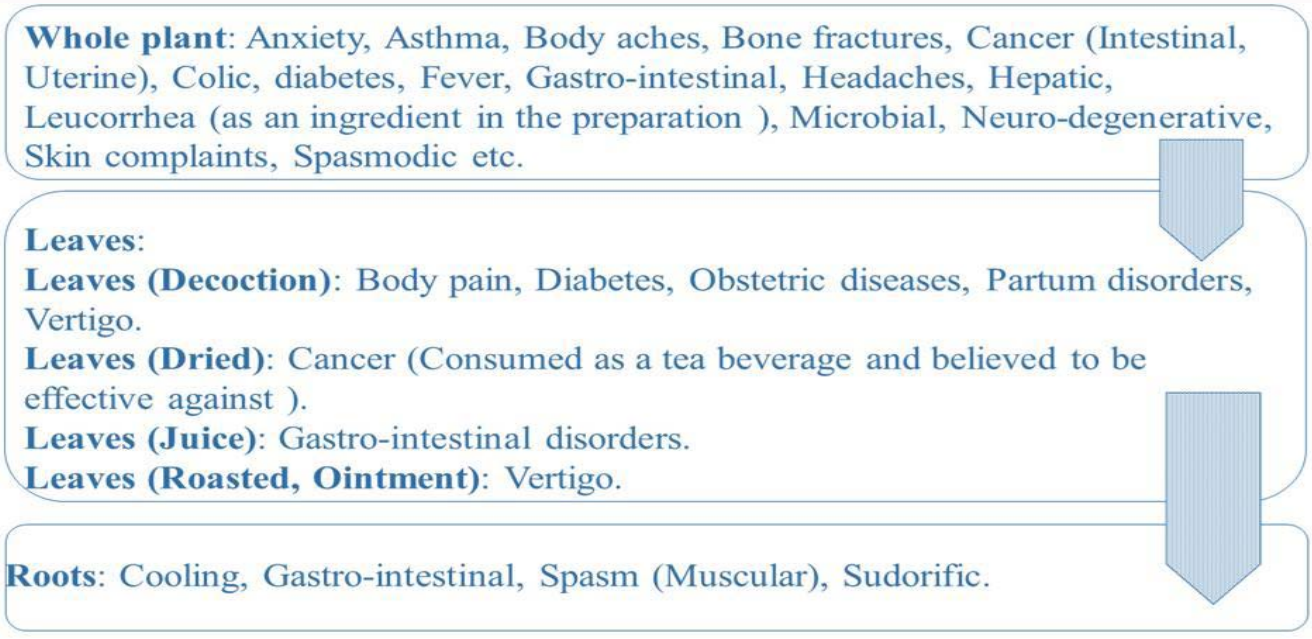


Figure 5: Part-wise medicinal efficacies of *L. indica*.

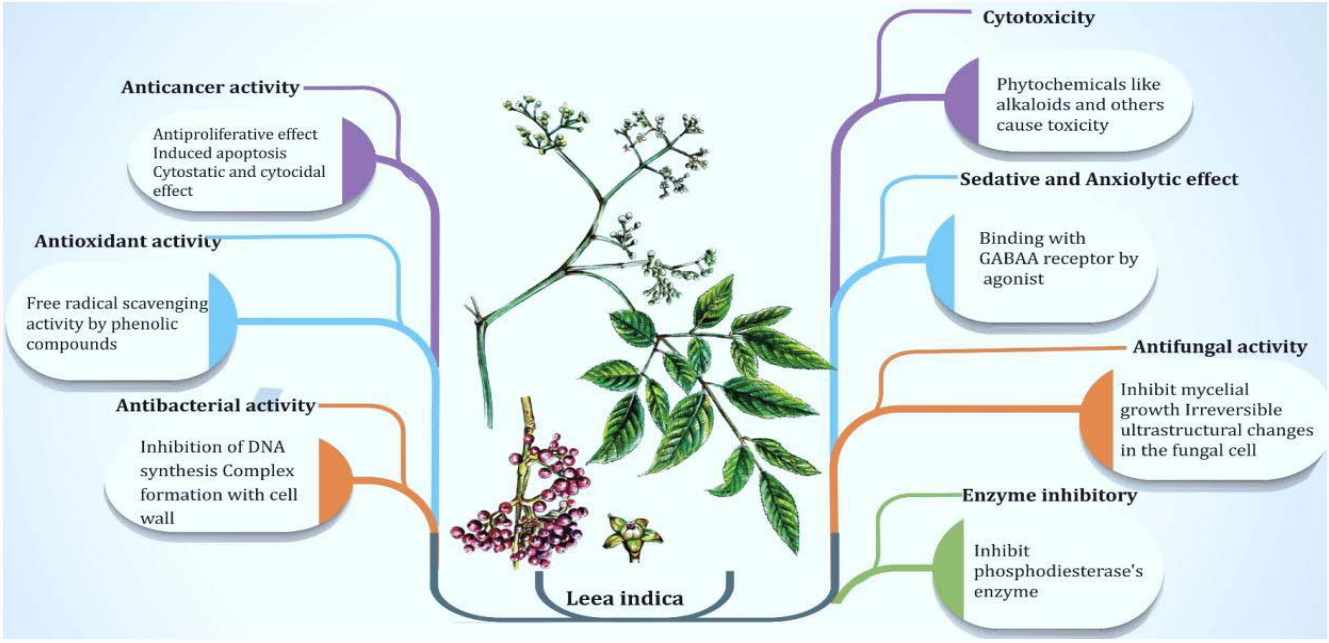


Figure 6: Diagrammatic representation of different pharmacological activities of *L. indica* and their probable mechanisms.

from flower has good anti-microbial effect against gram -ve bacteria *E. coli* and *S. typhimurium* with 8 mm & 10 mm zone of inhibition whereas, moderate activity against gram +ve bacteria *B. subtilis*, *B. cereus*, and *S. aureus* with 5, 6 & 7 mm zone of inhibition when compared with cefotaxime (standard drug) [17].

Anti-oxidant

Crude ethanol and its fractionated extracts (hexane, ethyl acetate and water) from *L. indica* leaves exhibits anti-oxidant activity at 0 mg/ml to 5 mg/ml, 0 mg/ml to 0.8 mg/ml & 0 mg/ml to 20 mg/ml by DPPH, SOD (Superoxide Dismutase) and reducing activity assays, respectively. Among the four extracts, the fractionated water extract shows strongest scavenging activity with EC_{50} value of 48 µg/ml followed by ethanol and ethyl acetate with EC_{50} value of 60 & 68 µg/ml. The hexane extract displays weakest scavenging activity on DPPH radicals with the EC_{50} value of 1285 µg/ml. Moreover, reducing power of the four extracts varies significantly ($p<0.05$) at different concentrations and demonstrates similar levels of SOD activity with 94.36% to 100.00% inhibition rate [2]. Md. Atiar Rahman et al., reported that *L. indica* leaf ethanol extract shows potential anti-oxidant capacity by DPPH radical scavenging effect, FeCl3 reducing power, DMSO superoxide scavenging effect and Iron chelating effects with IC_{50} values of 139.83 ± 1.40 µg/ml, 16.48 ± 0.64 µg/ml, 676.08 ± 5.80 µg/ml & 519.33 ± 16.96 µg/ml, respectively when compared with ascorbic acid (standard) [17].

Cytotoxic

Two cycloartane triterpenoid glycosides, Mollic Acid Arabinoside (MAA) and Mollic Acid Xyloside (MAX) have been reported to have cytotoxic activity against Ca Ski cervical carcinoma cells with IC_{50} value of 19.21 & 33.33 µM, respectively when compared with MRC5 normal cell line, used to calculate selectivity index about 8 and 4 times. MAA decreased the expression of proliferative cell nuclear antigen and increases sub-G1 cells, and arrested cell cycle in S and G2/M phases indicating to have cytotoxic effect [P4]. Leaf ethanol extract of *L. indica* displays cytotoxicity by Brine shrimp lethality bioassay with LC_{50} value of 2.65 ± 0.16 l g/ml, significantly ($p<0.05$) different from that of positive control (vincristine sulfate with IC_{50} value of 0.76 ± 0.04 g/ml) [17].

Enzyme inhibitory

Prapapan Temkitthawon et. al., reported that ethanol extract from *L. indica* roots exerts enzyme inhibitory activity against Phosphodiesterase (PDEs) enzymes using 3-Isobutyl-1-Methylxanthine (IBMX) as standard inhibitor of PDEs. *L. indica* was found to exhibit PDEs inhibitory activity with IC_{50} value of 2.62 ± 0.25 µg/ml when compared with standard IBMX with IC_{50} value of 0.68 ± 0.14 µg/ml. Thus, the extract could be used for enzyme inhibition [20].

Neuroprotective

Ursolic acid, lupeol compounds isolated from *L. indica* leaves and flowers have been identified as a potent BACE1 inhibitor by using virtual screening approaches. Lupeol shows better binding free energy in MM/GBSA, MM/PBSA and MM/GBVI approaches, furthermore classical and steered dynamics revealed the favorable hydrophobic interactions between lupeol and the residues of flap or catalytic dyad of BACE1, however, ursolic acid shows disfavorable interactions with the BACE1. This study, therefore, unveiled lupeol as a potent BACE1 inhibitor [12].

Anti-proliferative

Water, ethanol and methanol extracts from leaves of *L. indica*, evaluated for anti-proliferative activity against twelve human cancer cell lines derived from breast (MDA-MB-231, T47D), cervical (C33A), colon (HCT116), leukemia (U937), liver (HepG2, SNU-182, SNU-449), ovarian (OVCAR-5, PA-1, SK-OV-3) and uterine (MES-SA/DX5) revealed the activeness of the plant only, against cervical C33A, liver SNU-449, and ovarian PA-1 cancer cell lines with IC_{50} values of 31.5 ± 11.4, 37.5 ± 0.7 and 43.0 ± 6.2 µg/mL, respectively in comparison to other medicinal plants [21].

Sedative and anxiolytic

Md. Obayed Raihan reported the sedative and anxiolytic effects of *L. indica* crude methanol extract for its Central Nervous System (CNS) depressant effect using white female albino mice (Swiss-webstar strain models, by 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, respectively. The methanol extract at doses of 200 mg/kg, p.o. and 400 mg/kg, p.o., displays 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 CNS depressant effect was shown at a dose of 400 mg/kg, p.o. In the EPM test, both doses of methanol extract significantly ($p<0.01$) increased exploration to and time spent by the treated mice in EPM open arms in a dose dependent manner [16].

Widespread Medicinal Employment of *L. indica* Extracts in Various Disorders

Diabetes

Diabetes mellitus, usually referred to as diabetes, is a chronic metabolic disorder characterized by hyperglycemia, glycosuria, negative nitrogen balance, polydipsia and sometimes ketonemia [22,23]. In animal studies, it is reported that *L. indica* leaves, ethanol & hydroalcoholic administration reduces the serum glucose, triglycerides, cholesterol, low density lipoproteins and very low-density lipoproteins, alanine transaminase and aspartate aminotransferase and elevated HDL levels. The extract also decreases serum creatinine and urea levels and increase liver glycogen. *L. indica* has beneficial effects in reducing blood glucose and lipid levels. The anti-hyperglycemic and hypo-lipidemic properties of *L. indica* could be chiefly because of presence of major compounds like ursolic acid (an effective insulinomimetic) and gallic acid (insulin secretagogue) [24].

Gastrointestinal diseases: Diarrhea & Dysentery

Diarrhea can have many causes: types of food or allergy to food; contaminated or poisoned food; infectious diseases, such as dysentery is diarrhea with abdominal cramps, tenesmus and passage of mucus in the stools, and may be bacillary and amoebic; sometimes worry or other emotions [22,23]. Animal studies have shown that *L. indica* extract administration reduces diarrheal frequency & increases the latency period of defecation. The extracts display antimicrobial activity against *V. cholerae, S. dysenteriae, S. sonnei, S. aureus, B. subtilis, P. aeruginosa* and *B. megateriuum*. The plant extracts contain active phytoconstituents that can be used for the treatment of diarrheal and microbial diseases [25].

Pyrexia

Most fevers are caused by infections. Infections which result in fever include dengue, malaria etc. [22,23]. Animals *in-vivo* studies shows that *L. indica* methanolic leaves extract possess antimalarial effects which may be due to the presence of phenolic compounds [11]. The roots of *L. indica* are employed as sudorific agents which could be applied for the treatment of fever.

Rheumatism

Pain is defined as the feeling of severe discomfort which a person has when hurt. In rheumatism there is pain and stiffness in the joints and muscle [22,23]. In animal studies, *L. indica* ethanolic extract shows anti-nociceptive activity by central and peripheral mechanism(s). The analgesic effect of *L. indica* has been studied only in animal models and these findings will provide the step towards further studies [26].

Hepatic disorders

Liver disease has become one of the main causes of global morbidity and mortality. Among them, synthetic drug-induced liver injury is one of the most common pathogenic factors, posing a major challenge to clinical and regulatory ones. In animal studies, it was discovered that in comparison with the positive control group, treatment with ethanol bark extracts (200 mg/kg and 400 mg/kg b.w.) displays elevated levels of serum marker enzymes, bilirubin (direct total) and a significant reduction in. The results suggests that, ethanolic bark extract have hepatoprotective effect on PCM induced liver damage in rats [27].

Wounds

Defined as damage to external tissue which allows blood to escape. Uninfected wounds heal rapidly [22,23]. *L. indica* extracts have shown antimicrobial activities against *V. cholerae*, *S. dysenteriae*, *S. sonnei*, *S. aureus*, *B. subtilis*, *P. aeruginosa* and *B. megateriuum*. The plant extracts contain active phytoconstituents that can be used for the treatment of wound infections [25].

Other medicinal utilities of *L. indica*

L. indica is medicinally imperative and is widely used in indigenous arrangements of medicine [1]. The plant is believed to have therapeutic activities to expel wind and eliminate dampness in traditional Chinese medicine, as well as clearing internal heat and poison. Here "poison" is a term in traditional Chinese medicine that refers to the body´s infectious factor [2]. Flowers have previously been studied for anti-microbial, anti-oxidant, anti-inflammatory, hypoglycemic, and phosphodiesterase inhibitory activities [5]. Innumerable disorders are treated by using different parts of *L. indica*, parts, formulations and extracts. A detailed ethno-botanical description is being shown in Table 1 and other medicinal utilities are being displayed in Figure 5.

Conclusion

There are still, existing gaps in the scientific studies on *L. indica*, and some aspects are in need to be reconnoitered comprehensively. In-spite of a very important finding by Raihan et. al., (2011), there are not much comprehensive studies to clarify the neuro-pharmacological aspects actually involved in treating sedative and anxiolytic effects, which would be helpful to understand the medicinal aid, *L. indica* renders. We suggest strengthening the detailed bioactivities assessment of *L. indica* while studying its chemical components and related therapeutic relevance. In addition, there are some differences in the medicinal parts used, chemical composition distribution, and medicinal functions of the plant. This suggests that further studies on quality control of *L. indica*, should consider the part-wise utilization of the plant so that, sustainable methodologies can be performed thus, delivering fruitful outcomes in long run. Also, analysis on detailed chemical composition should be performed which can yield specific or targeted neuro-pharmacological conductions. Though, there are some applications in the clinical practice of *L. indica*, the existing studies on the plant are still limited. For more profound studies of *L. indica*, in-depth study of additional forms and varieties, which may possess bioactivities to treat diseases *in vitro*/*in vivo* and as well as in clinical, should be carried out. Studies on their useful substances, pharmacology mechanisms, quality control, clinical uses, and new drug research should be conducted.

In summary, based on the traditional medicinal value and modern scientific research into *L. indica*, we found that it is a valuable medicinal plant, rich in flavonoids, hydrocarbon (alkanes & alkenes), organic compounds, phenols etc., with various pharmacological and therapeutic characteristics. Further studies should not only increase the phytochemical and pharmacological evaluations of the less-explored species but also fill in the gaps in the chemical and pharmacology research of *L. indica*.

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