Description

L. camara is a low erect or subscandent vigorous shrub with triangular stem. It grows up to 1–3 m and in width, it can spread to 2.5 m. Leaves are ovate, acute or subacute, crenate serrate, rugose above, and scabrid on both sides. They are green in color, 3–8 cm long, and 3–6 cm wide. Leaves and stems are covered with rough hair. Small flower held in clusters. Color usually orange, white to red in various shades and usually change colors as they ages. Flowers have a yellow throat, in axillary head almost throughout the year. The calyx is small, corolla tube slender, the limb spreading 6–7 mm wide and divided into unequal lobes. Inflorescences are in pairs in the axils of opposite leaves. They are compact, dome-shaped 2–3 cm across and contained 20–40 sessile flowers. The root system is very strong and it gives out new fresh shoots even after repeated cuttings [13].

Traditional uses

Conventionally, the plant is used as diaphoretic, carminative, antispasmodic, tonic, antiemetic, to treat respiratory infections, and disorders (cough, cold, asthma, and bronchitis), in the treatment of tetanus, epilepsy, dysentery, and gastropathy. Powdered leaves are used for cuts, wounds, ulcers, and swellings. An infusion of the leaves is used for bilious fever, eczema, and eruptions. The fruits are used in fistula, pustules, tumors, and rheumatism. The root is used in malarial, rheumatism, skin rashes, dermatitis, eczema, mycotic infections, and respiratory tract infections, including influenza and tuberculosis. A decoction of fresh roots is used as a gargle for odontalgia [14-16].

Parts used

The whole plant, leaves, roots, and bark are used medicinally [14-16].

Physicochemical characteristics

Physicochemical characteristics of the leaves of *L. camara* were: Total ash 8.06, water-soluble ash 0.95, acid insoluble 1.96, water-soluble extractive value 27.5, and alcohol soluble extractive value 25.1% [17].

Physiochemical characteristics of the fruits were: Total ash 1.59, water-soluble ash 0.48, acid insoluble ash 2.1, sulfated ash 10.3, water-soluble extractive value 6.0, alcohol soluble extractive value 2.1, and loss on drying 11.3% [18].

CHEMICAL CONSTITUENTS

Phytochemical analysis of the leaves of *L. camara* showed that the plant contained alkaloids, glycosides, steroids, saponins, flavonoids, coumarins, tannins, carbohydrates, hydroxy anthraquinones, anthraquinone glycosides, proteins, phytosteroids, fixed oils, fats, and triterpinoids [9,17-20].

Chemical analysis of the leaves and flower extract gave an idea of similar carbohydrates and lipid compositions. The flowers contained carbohydrate more than the leaves, while the lipids were greater in the leaves extracts [21].

Quantitative phytochemical screening of *L. camara* showed that the leaves contain flavonoids (11.08±0.05 mg/g), tannins (9.0±0.03 mg/g), alkaloids (9.76±0.02 mg/g), saponin (6.07±0.06 mg/g), reducing sugar (4.86±0.05 mg/g), carbohydrate (5.08±0.03 mg/g), Vitamin A (0.50 mg/100 g), Vitamins C (6.5 mg/100 g), Vitamin E (1.6 mg/100 g), and total phenolic compounds (2.36 gallic acid equivalent [GAE]) [22]. Lantanoside, lantanone, linaroside, and camarinic acid were isolated from the aerial parts of *L. camara* [23].

Analysis of *L. camara* essential oil from Algeria showed large amounts of sesquiterpene hydrocarbons, mainly β-caryophyllene [24]. The results of gas chromatography–mass spectrometry analysis of hexane: chloroform (50:50) fraction of the hexane extract of *L. camara* leaves from Thanjavur district, showed that the leaves contained eight compounds, these included isoterpinolene, santolina triene, isoterpinolene, elemene, germacrene, cadinene, bicycle, and katonic acid [25].

L. camara leaves yielded 0.8% of essential oil. α-guaiene, α-humulene, α-copaene, α-cubebene, α-selinene, β-elemene, β-selinene, delta-cadinene, germacrene D, B, aromadendrene, caryophyllene oxide, nerolidol, and spathulenol represented the major components of the essential oil of *L. camara* [26].

However, 36 compounds were characterized from essential oil of *L. camara* from Tamil Nadu regions, these included: Bicycloelemene, α-cubebene, α-copaene, β-elemene, bicyclo, germacrene, α-guaiene, α-humulene, aromadendrene, naphthalene, germacrene D, β-selinene, epi-bicyclosesquiphellandren, α-selinene, 1-hydroxy-1, 7-dimethyl-4-iso, β-cadinene, caryophyllene oxide, nerolidol, salvia-4 (14)-en-1-one, veridifloral, 12-oxabicyclo[9.1.0] dodeca-3, naphthalenamine, 4-bromo, (-)-spathulenol, isospathulenol, tetracyclo, delta-cadinene, 1-napthalenol, 1, 2, 3, 4, 4a, 7, 1R-2, 2, 4, 8-tetrame, alloaromadendrene oxide-(2), aromadendrene oxide-(2), 6-isopropenyl-4,8a-dimethyl-, 4,4-dimethyl-3-(3-methyl but, 1H-cycloprop [e] azulen-7-ol, 6-isopropenyl-4,8a-dimethyl-, phthalic acid, butyl hexyl, and 2-hexadecen-1-ol [26,27].

Volatile contents of the essential oil of *L. camara* included: α-pinene 1.04, sabinene 2.12, α-terpineol 1.83, geranyl acetate1.03, β-elemene 1.03, cis-caryophyllene 16.24, α-humelene 23.26, bicyclogermacrene 12.54, Aromadendrene 1477 7.00, zingeberene 1.11, germacrene-D 13.16, ß-curcumine 4.02, caryophyllene oxide 1.78, humulene oxide 2.54, and others compounds 11.28% [28].

Kurade *et al*. identified five constituents in the volatile oil of *L. camara* oil, included: 3,7,11-trimethyl-1,6,10-dodecatriene (28.86%), β-caryophyllene (12.28%), zingiberene (7.63%), γ-curcumene (7.50%), and α-humulene (3.99%) represented the major ones [29].

Pentacyclic triterpenoids (camaryolic acid, methylcamaralate, and camangeloyl acid), β-sitosterol 3-O-beta-D-glucopyranoside, octadecanoic acid, docosanoic acid, palmitic acid, oleanolic acid, lantanolic acid, camaric acid, lantadene A, lantadene B, icterogenin, and lantadene C were isolated from the aerial parts of *L. camara* [30-33].

Triterpenoids (28-norolean-12,17-diene triterpene lantigdienone oxidized at C-11 and C-22 and camarinin) were isolated from the aerial parts of *L. camara* [34].

The polyphenol content of *L. camara* was 917.60 mg/100 g in the leaves and 328.56 mg/100 g in the stem, while flavonoids content was 3.29 mg/100 g in the leaves and 8.03 mg/100 g in the stem [35].

PHARMACOLOGICAL EFFECTS

Antimicrobial effects

The antimicrobial activity of the petroleum ether, methanolic, and water extracts of *L. camara* was investigated against *Bacillus subtilis*, *Escherichia coli,* and *Candida albicans*. At concentration of 250 mg and more, petroleum ether and methanolic extracts of the leaves showed potent antibacterial and antifungal activity [17].

Antibacterial activity of *L. camara* crude hexane extract, ethanolic fraction, aqueous fraction, and essential oil was evaluated *in vitro*. Only leaf ethanolic fraction and essential oil, among four extracts of *L. camara* leaves, showed antibacterial activity against *B. subtilis, S. aureus*, *E. coli,* and *S. gallinarum*. The minimum inhibitory concentration (MIC) of essential oil ranged from 312.5 to 10,000 µg/ml, it was better than leaf ethanolic fraction (1250–5000 µg/ml). The lowest MIC of essential oil was recorded against *B. subtilis* at 312.5 µg/ml and 2500 µg/ml against *E. coli* [20].

The antimicrobial activity of *L. camara* extracts and its isolated constituent and was studied *in vitro*. Alcoholic and aqueous extracts of *L. camara* possessed significant antibacterial activity against *E. coli* and moderate antibacterial activity against other microbes. However, alcoholic extract showed more antibacterial activity than water

extract against *E. coli*, *Bacillus cereus*, *Pseudomonas aeruginosa,* and *Staphylococcus aureus* [36].

The antibacterial activity of the ethanolic extracts of *L. camara* leaves and roots was studied against *S. aureus* (ATCC 12692), *Proteus vulgaris* (ATCC 13135), *Pseudomonas aeruginosa* (ATCC15442), *Víbrio cholerae* (ATCC 15748), and *E. coli* (ATCC 2992) and two multi-resistant strains obtained from clinical material: *E. coli* (Ec 27, from sputum) and *S. aureus* (Sa 358, from surgical wound). The extracts exerted antibacterial activity against all tested bacteria. MICs of the of *L. camara* leaves ethanolic extracts and roots against *E. coli* (ATCC 25922) were 256 and 512, *P. vulgaris* (ATCC 13315) 128 and 64, *P. aeruginosa* (ATCC 15442) 256 and 128, *V. cholerae* (ATCC 15748) 128 and ≤1024, *S. aureus* (ATCC 12692) ≤1024 and ≤1024, *E. coli* (Ec 27) 256 and ≤1024, and *S. aureus* (Sa 358) 512 and ≤1024 mg/ml, respectively [16].

The antimicrobial activities of the methanolic leaf extracts of *L. camara* were investigated against 16 bacterial isolates (*Bacillus polymyxa*, *Micrococcus luteus*, *E. coli*, *Streptococcus faecalis*, *Bacillus cereus*, *Clostridium sporogenes*, *Klebsiella pneumoniae*, *P. aeruginosa*, *Corynebacterium pyogenes*, *S. aureus*, *Pseudomonas fluorescence*, *P. vulgaris*, *Bacillus anthracis*, *S. faecalis, Bacillus stearothermophilus,* and *Bacillus subtilis*). Eight out of the 16 isolated were sensitive to 25 mg/ml of the methanolic extract of *L. camara* leaf, showing zones of inhibition ranging from 16 mm to 26 mm. The MIC showed by the crude extract against the tested bacteria ranges from 0.195 mg/ml to 3.125 mg/ml, while the minimum bactericidal concentration ranges from 0.390 mg/ml to 6.25 mg/ml [37].

The antimicrobial activity of crude methanolic and acetone extracts of *L. camara* was studied against (*E. coli* [MTCC-443], *B. subtilis* [MTCC1789], *S. aureus*, *Streptococcus* sp., *P. aeruginosa*, *Vibrio cholerae*, *Alcaligenes faecalis*, *B. cereus*, *Klebsiella pneumoniae* [MTCC 2405], *Vibrio haemolyticus*, *C. albicans*, *Candida tropicalis*, *Saccharomyces cerevisiae*, *Aspergillus niger*, *Aspergillus flavus*, *Penicillium* spp., *Fusarium oxysporum*, *Alternaria alternata*, *Sclerotium rolfsii*, and *Curvularia lunata*). The results showed that both extracts were active against various Gram-positive and Gram-negative bacteria. Among the tested bacterial strains alcoholic extract of the test plant inhibited the growth of *S. aureus* to the maximum followed by *B. subtilis* and *B. cereus*. Intermediate zone of inhibition was observed against *Streptococcus* sp. and *E. coli,* while minimum antibacterial activity was reported against *V. haemolyticus* and *V. cholerae*. No inhibition zone was observed for any species of *Candida* sp. Acetone extract of lantana leaves showed comparatively less antibacterial activity than the alcoholic extract. A maximum effect was observed on *B. cereus* followed by *S. aureus* and *B. subtilis*. Mild antibacterial activity was observed with *Streptococcus* sp. and the minimum activity was observed against *K. pneumoniae* and *V. cholerae*. The fungi toxic spectrum of leaf and stem extracts indicated maximum percentage growth inhibition at 1000 µg/ml concentration against *Alternaria alternate* [38].

Methanol, ethanol, and water *L. camara* leave extracts were evaluated against four Gram-positive and Gram-negative bacterial isolates (*S. aureus, P. aeruginosa*, *Klebsiella pneumonia,* and *B. subtilis*) and two fungal strains (*Aspergillus fumigatus* and *A. flavus*). Methanol leaf extract of *L. camara* showed maximum antibacterial activity against *S. aureus* and *P. aeruginosa* and was also effective against other bacterial strains as compared to ethanol and aqueous extracts of leaves. The methanol leaf extract of *L. camara* exhibited significant inhibition (71%) and (66%) against *A. fumigatus* and *A. flavus,* respectively [39].

The essential oil of *L. camara* showed antibacterial activity against *A. protophormiae*, *M. luteus, R. rhodochrous,* and *S. aureus* with MBC of 50, 25, 12.5, and 200 µg/ml, respectively, but not against *E. coli* [29].

The antimicrobial activity of the bioactive compound obtained by crude extract and the column extract from *L. camara* was studied *in vitro*. Crude extract showed antimicrobial activity against *E. coli*, *P. aeruginosa*, *B. subtilis,* and *E. faecalis* (zone of inhibition: 6.8–8.1 mm) and column extract (zone of inhibition: 4.0–6.2 mm) [40].

The antimicrobial properties of the aqueous and ethanol extracts of *L. camara* flowers, leaves, stems, and roots in comparison with selected commercial mouthwashes (Crest, ACT, Ultra Care, Cari-Med, and Listerine) against *Streptococcus mutans*, *E. coli*, *Streptococcus pneumoniae,* and *P. aeruginosa* from oral cavity. The results showed that *L. camara* extracts possessed higher zone of inhibition against the oral microorganisms compared to the commercial mouthwashes. *S. pneumoniae* being the most susceptible organism to *L. camara* ethanolic extracts (red flower) in all concentrations (10–50 mg). The growth of *S. mutans* bacteria was inhibited by *L. camara* extracts; it was the most sensitive organism to the ethanolic extracts of pink flower *L. camara*. *E. coli* was susceptible to *L. camara* aqueous extracts at high concentrations and resistant at low concentrations. The growth of *P. aeruginosa* was strongly inhibited by *L. camara* ethanolic extracts (pink flower) [41].

Terpenes rich extract of *L. camara* leaves was prepared for the synthesis of silver nanoparticles (AgNPs). AgNPs were found to exhibit good to moderate antibacterial activity against *S. aureus, E. coli* and *P. aeruginosa* [42].

The antimicrobial efficacy of flavonoids (free and bound) and crude alkaloids of *L. camara* was studied against *E. coli, Proteus mirabilis, S. aureus, C. albicans,* and *Trichophyton mentagrophytes*. *C. albicans* was the most susceptible microorganism followed by *P. mirabilis, S. aureus, E. coli,* and *T. mentagrophytes* [43].

The antibacterial activity of the ethanolic extracts of *L. camara* leaves and roots was investigated against Gram-positive and Gram-negative strains standard and multi-resistant bacteria isolated clinically. The extracts demonstrated antibacterial activity against all the tested bacteria [16].

Different polar (aqueous and methanolic) and non-polar (hexane) solvent extracts of leaves of *L. camara* at 250 µg/ml were investigated for antimicrobial potential against *S. aureus, B. subtilis,* and *Bacillus licheniformis*. Methanolic and aqueous extracts possessed strongest antimicrobial activity in comparison to that of hexane extracts. Among all extracts, methanolic extract had significant antibacterial activity against *B. subtilis* (45 mm) and *B. licheniformis* (50 mm) while aqueous extract was found to have antibacterial activity against *S. aureus* (43 mm), while, hexane extract exerted antibacterial activity against all the tested microbes [44].

Methanol and chloroform extracts of *L. camara* were screened against three strains of *Mycobacterium tuberculosis* (rifampicin-resistant TMC-331, H37Rv, and a non-resistant wild strain) using agar well diffusion method. The methanol extract showed the highest activity against all three strains, with zones of inhibition of 18.0–22.5 mm and MIC values of 20 µg/ml for H37Rv and 15 µg/ml for wild stain and TMC-331. The values for rifampicin were 1.0 µg/ml for both H37Rv and wild strain, but rifampicin did not show activity on TMC-331. The MBC value for the methanol extract of *L. camara* was 30 µg/ml for the H37Rv and 20 µg/ml for both the TMC-331 and wild strains of *M. tuberculosis*. The MBC for rifampicin was 2.0 µg/ml for both H37Rv and the wild strain [45].

Different antibacterial effects were recorded for different *L. camara* leaves extracts (ethyl acetate, methanol, acetone, and chloroform), Gram-negative bacterial pathogens (*K. pneumoniae* and *E. coli*) were more susceptible to the extracts compared to Gram-positive bacteria (*S. aureus, M. luteus* and *B. subtilis*). Methanol extract had the highest inhibition activity against all the tested microbes [46].

The antifungal activities of the leaf extract of *L. camara* in different solvents (acetone, chloroform, ethanol, and methanol) were studied against *A. flavus* and *A. niger*. Methanol leaf extract of *L. camara* showed antifungal activity against both fungal strains [47].

Antidermatophytic potential of *L. camara* was studied in experimentally induced dermatophytic lesion in mice. Mice were experimentally inoculated with *T. mentagrophytes* and infected animals were

topically treated with 5 mg/g terbinafine and two concentrations, 5 and 10 mg/g of test extract ointment. Complete recovery from the infection was observed on 12th day of treatment for terbinafine and 10 mg/g concentration of the test extract ointment, whereas 5 mg/g concentration of test extract ointment showed complete cure on the 16th day of treatment [48].

Antiparasitic effects

Lantanilic acid, camaric acid, and oleanolic acid isolated from the methanolic extract of the aerial parts of *L. camara* possessing nematicidal activity. These compounds exhibited 98%, 95%, and 70% mortality, respectively, against root-knot nematode *Meloidogyne incognita* at 0.5% concentration [33]. However, lantanoside, linaroside, and camarinic acid showed 90, 85, and 100% mortality, respectively, at 1.0% concentration against root-knot nematode *M. incognita* [23].

The anti-filarial activities of two *L. camara* extracts were tested *in vitro* on the bovine model parasite, *Onchocerca ochengi* as well as *Loa loa* microfilariae. Extracts showed 100% activity at 500 µg/ml against *O. ochengi* adult worms and microfilariae. The highest activity against *O. ochengi* was observed with the hexane extract of *L. camara* leaves, with IC_{50} of 35.1 µg/ml for adult females and 3.8 µg/ml for the microfilariae. This extract was more active against *O. ochengi* microfilariae than *L. loa* microfilariae. Lantadene an extracted from the methylene chloride extract of *L. camara* leaves, showed IC_{50s} of 7.85 µg ml for adult males, 10.38 µg/ml for adult females, 10.84 µg/ml for *O. ochengi* microfilariae, and 20.13 µg/ml for *L. loa* microfilariae [49].

The extract of stem portion of *L. camara* possessed antifilarial activity. The crude extract (1 g/kg, for 5 days) orally killed 43.05% of the adult *Brugia malayi* and sterilized 76% of surviving female worms in a model of *Mastomys coucha* in the rodent. A 34.5% adulticidal activity along with sterilization of 66% of female worms was exerted by the chloroform fraction. Remarkable antifilarial activity was observed in the adult *B. malayi* transplanted gerbil model where up to 80% of the adult worms killed at the same dose and all the surviving female parasites were found sterilized. The extract was also effective against a subcutaneous rodent filariid *Acanthocheilonema viteae* maintained in *M. coucha*, where it exerted strong microfilaricidal (95.04%) and sterilization (60.66%) efficacy with mild macrofilaricidal action. Two compounds, oleanonic acid and oleanolic acid, isolated from hexane and chloroform fractions showed LC_{100} at 31.25 and 62.5 mug/ml, respectively, on *B. malayi in vitro* [50].

The aqueous extract from the leaves of *L. camara* was evaluated against filarial vector mosquito *Culex quinquefasciatus* and dengue vector *Aedes aegypti*. The aqueous extract (1000, 500, 250, 125, and 62.5 ppm) was tested against I, II, III, and IV instar larvae of *C. quinquefasciatus* and *A. aegypti*. The LC_{50} values of *L. camara* against I, II, III, and IV instar larvae of *C. quinquefasciatus* were 35.48, 46.74, 67.64, and 95.51 ppm and against *A. aegypti* 35.19, 38.26, 65.98, and 91.90 ppm [51].

The decoctions of *L. camara* inhibited the process of *Haemonchus contortus* larval exsheathment, which may be related to tannin action because the addition of PVPP reversed the inhibitory effect [52].

The larvicidal activity of the aqueous extract of dried leaf powder of *L. camara* was studied against the larvae of mosquito. *L. camara* was an ideal candidate as a larvicide, 80 mg/100 ml concentration of the aqueous extract was required for 100% mortality in 6 h [53].

The extracts (10, 50, and 100 mg/ml) of the leaves of *L. camara* were investigated for their anthelmintic activity against *Pheretima posthuma.* The ethanolic extract exhibited significant anthelmintic activity at highest concentration (100 mg/ml) [54].

L. camara methanolic leaves extract at a concentration of 0.04 g/ml exerted the highest larvicidal activity toward the *Musca domestica* (housefly) larvae [55].

The larvicidal activity of *L. camara* was investigated against the larvae of common species of mosquitoes in the Philippines. After the 24 h of observation, researchers found that all the methanolic extracts of *L. camara* leaves were not significantly effective against the larvae, causing only 0–20% mortality [56].

The insecticidal effect of essential oil of *L. camara* was studied against the 3rd instar larval stage of *A. aegypti*. The essential oil (2500 10000 ppm) caused larval mortality of 20–50% on 3rd instar larvae at 24 h and 90–100% during 7th day [57].

The insecticidal activity of essential oil of the leaves of *L. camara* was investigated against mosquito vectors. LD_{50} values of the oil were 0.06, 0.05, 0.05, 0.05, and 0.06 mg/cm^2, while LD_{90} values were 0.10, 0.10, 0.09, 0.09, and 0.10 mg/cm^2 against *A. aegypti*, *C. quinquefasciatus*, *Anopheles culicifacies*, *Anopheles fluviatilis,* and *Anopheles Stephensi,* respectively. KDT_{50} values of the oil were 20, 18, 15, 12, and 14 min and KDT_{90} values were 35, 28 25, 18, and 23 min against *A. aegypti, C. quinquefasciatus*, *A. culicifacies, A. fluviatilis,* and *A. stephensi*, respectively, on 0.208 mg/cm^2 impregnated paper. Studies on persistence of essential oil of *L. camara* on impregnated paper revealed that it has more adulticidal activity for longer period at low storage temperature [12].

Essential oils *L. camara* were also tested for insecticidal effect against *Sitophilus granarius* adults. Essential oils isolated at different times showed different activities on *S. granarius*. Exposure to April essential oil showed the highest activity after 24 h. Similar results were obtained for February and June essential oils after 48 h of exposure, while, December essential oil showed good fumigant activity after 96 h of exposure [24].

Lantana flower extract provided 94.5% protection from *Aedes albopictus* and *A. aegypti*. One application of flower extract gave more than 50% protection up to 4 h from the bites of *Aedes mosquitoes* [58].

The repellent effects of different fractions of *L. camara* flowers were evaluated against *A. mosquitoes*. The results revealed that the fraction eluted by chloroform produced maximum protection time (3.45 h). One application of this fraction showed 100% protection for 2 h and 75.8% at 7 h against the bites of *A. mosquitoes* [59].

The repellent properties of creams formulated from the methanol crude extract, hexane, and ethyl acetate fractions of *Ocimum gratissimum* and *L. camara* leaves were studied in single and combined actions against female *A. aegypti*. All formulations were applied to the human hands at a concentration of 2–8mg/cm^2. All the formulations revealed good protection against mosquito bites without any allergic reactions. The repellent effects were based on the strength of the extracts and fractions. Methanol crude extracts combination and hexane fractions mixtures from both plants showed synergistic effect [60].

The application of *L. camara* oil to the upper surface of the human forearms at the rates between 0.08 and 3.33 mg/cm^2 of skin possessed a significant repellent activity against mosquitoes (*A. aegypti*) [61].

Gastrointestinal effects

The antispasmodic effect of *L. camara* leaf constituents was studied on rat ileum. The methanolic leaves extract of *L. camara* showed promising antispasmodic action on excised rat ileum. When acetylcholine was given in the presence of methanolic leaves extract of *L. camara*, extract caused marked decrease in contraction of ileum, indicating that methanolic leaves extract of *L. camara* possessed anti-spasmodic activity by blocking cholinergic receptors [62].

The antimotility activity of *L. camara* leaf powder, *L. camara* methanolic extract, lantadene A, neostigmine (as promotility agent), and neostigmine + methanolic extract was evaluation in the intestine of mice. The intestinal transit with methanolic extract at a dose of 500 mg/kg was 26.46%, whereas the higher dose (1 g/kg) completely inhibited the transit of charcoal in normal mice. The percent of intestinal

transit in the group treated with neostigmine was 24 and 11 at the same doses, respectively. When the plant extracts (125 and 250 mg/kg) were administered ip, they were significantly reduced fecal output compared with castor oil-treated mice. At higher doses (500 and 1000 mg/kg), the fecal output was almost completely stopped [63].

The antidiarrheal activity of the aqueous stem extract (100, 200, and 400 mg/kg) of *L. camara* was evaluated in mice using castor oil-induced diarrhea, enteropooling, and small intestine transit models compared with positive controls received 3 mg/kg of loperamide and negative controls received 10 ml/kg of distilled water. In castor oil-induced diarrhea model, all doses of the extract significantly ($p<0.001$) prolonged diarrhea onset, decreased the frequency of defecation, and weight of feces. Furthermore, the extract produced a significant ($p<0.001$) decline in the weight and volume of intestinal contents at all tested doses. In addition, a significant ($p<0.001$) reduction in the gastrointestinal motility in charcoal meal test was also recorded in all doses of the extract [64].

The antidiarrheal activity of 80% methanol extract was evaluated using mice model of diarrhea. In the castor oil-induced diarrheal model, the 80% methanol extract delayed the onset of defecation, at 200 and 400 mg/kg, and reduced the number and weight of feces at all tested doses (100, 200, and 400 mg/kg) significantly. Furthermore, the methanol and aqueous fraction at all tested doses and chloroform fractions at 200 mg/kg and 400 mg/kg significantly reduced the number and weight of wet feces when compared with negative control. In the enteropooling test, the methanol and aqueous fractions significantly reduced the weight and volume of intestinal fluid at all tested doses, whereas the chloroform fraction significantly reduced the weight of intestinal content only at 400 mg/kg compared to negative control. Results from the charcoal meal test revealed that all the fractions produced a significant antimotility effect at all tested doses as compared to negative control [65].

The antiulcerogenic activity of the methanolic extract of *L. camara* leaves (250 and 500 mg/kg, orally) was evaluated in aspirin-induced gastric ulcerogenic in pyloric ligated rats, ethanol-induced gastric ulcer, and cysteamine-induced duodenal ulcer models. The lipid peroxidation reduced glutathione levels of ethanol-induced gastric ulcer model, and anti-*Helicobacter pylori* activity was also determined. *L. camara* extracts significantly ($p<0.01$) reduced ulcer index, total acidity and significantly ($p<0.01$) increased the gastric pH of aspirin+pylorus ligation-induced ulcerogenesis and ethanol-induced gastric ulcer models. The extract also significantly ($p<0.01$) reduced the ulcer index of cysteamine induced duodenal ulcers. The *L. camara* showed significant ($p<0.01$) reduction in lipid peroxidation and increase in reduced glutathione levels. The diameter of growth inhibition zone of the extract against *H. pylori* was 20 mm [66].

Antioxidant effects

The antioxidant activity, hydrogen peroxide radicals scavenging reducing power, the total phenolic, and flavonoids contents of *L. camara* leaves were studied. The total phenolic content was (40.859±0.017) mg gallic acid/g in the leaves of *L. camara*, while the total flavonoids were (53.112±0.199) mg/g dry weight. Leaf extract of *L. camara* showed good hydroxyl radical scavenging activities (45–73%) at a concentration of 0.2–0.8 mg/ml in the reaction mixture. Leaves extracts exhibited a concentration-dependent reducing ability. It induced the maximum reducing power at 0.8 mg/ml [39].

Antioxidant activity of *L. camara* of aerial parts methanolic extract, its fractions and purified compounds (lantadene A, oleanolic acid, and lantanilic acid) were determined using 1,1-diphenyl-2-picrylhydrazyl (DPPH). The methanolic extract showed 67% inhibition of DPPH free radical with EC_{50} value of 375 µg/ml, the three fractions were also active and exhibited 70%, 72%, and 65% inhibition, respectively, with EC_{50} value of 375 µg/ml [67].

The total phenolics, flavonoids, and the antioxidant activity of the methanolic extracts of leaves of four different varieties of *L. camara* (Chandigarh purple variety [CPV], Palampur red variety [PRV], Chandigarh yellow turning pink variety [YTPV], and Chandigarh yellow variety) were investigated using *in vitro* antioxidant models. The phenolic content was highest in the CYV extract (232.99±15.97 mg GAE/g extract). The contents of the flavonoids were in the order of YTPV, PRV, CPV, and CYV. The IC_{50} values for the DPPH radical scavenging test were in the order of CYV (33.30±2.39)<PRV (40.32±2.94)<YTPV (475.33±5.20)<CPV (927.16±2.88 µg/ml). The highest total antioxidant capacity was observed in CYV (222.20±5.05 mg AAE/g). The ferric ion reducing antioxidant potential values of the extracts were in the order of CYV>PRV>YTPV>CPV. The IC_{50} values of ABTS scavenging assay for CYV, PRV, YTPV, and CPV were 18.25±0.19, 18.24±1.82, 50.43±9.49, and 52.84±1.82 µg/ml, respectively. PRV extract showed the maximum *in vitro* lipid peroxidation inhibition with an IC_{50} value of 68.50 µg/ml [68].

The ethyl acetate extract of *L. camara* was studied for antioxidant properties by DPPH method. Furthermore, seven fractions obtained from the extract were also investigated for their antioxidant properties and total phenolic content. The results showed that IC_{50} of *L. camara* extract was 36.18 mg/l with a total phenolic content of 2419.6 GAE. IC_{50} value and total phenolic content of each fractions were found to be: 132.62 mg/l and 237.8 GAE, 113.51 mg/l and 589.4 GAE, 85.23 mg/l and 995.5 GAE, 81.26 mg/l and 1041 GAE, 24.83 mg/l and 3156 GAE, and 83.50 mg/l and 1037.8 GAE for fractions A-F, while IC_{50} value of G fraction was 806.71 mg/l. Antioxidant activity was correlated with the total phenolics [69].

Four extraction solvents including 80 and 100% methanol and 80 and 100% ethanol using stirring, microwave-assisted stirring, and ultrasonic-assisted stirring techniques were employed to extract the flowers of *L. camara*. The produced extracts contained total phenolics (8.28–52.34 mg GAE/100 g dry weight) and total flavonoids (1.24–7.88 mg CE/100 g dry weight) and possessed scavenging and antioxidant effects as tested by DPPH scavenging, inhibition of linoleic acid peroxidation and reducing power tests [70].

Various amounts of phenolics, flavonoids, and different antioxidants effects were recorded for different *L. camara* leaves extracts (ethyl acetate, methanol, acetone, and chloroform). The methanol solvent showed higher extractable compounds (14.4%) and contained the highest flavonoid (26.5 mgRE/g) and phenolic (92.8 mg GAE/g) content. DPPH radical scavenging assay showed IC_{50} value of 165, 200, 245, and 440 µg/ml for methanol, ethyl acetate, acetone, and chloroform extracts, respectively. The hydroxyl scavenging activity test showed IC_{50} value of 110, 240, 300, and 510 µg/ml for methanol, ethyl acetate, acetone, and chloroform extracts, respectively [46].

The antioxidant and DNA damage inhibition potential of the aqueous extract of *L. camara* leaves were studied *in vitro*. The extract exhibited high antioxidant activity in DPPH radical scavenging assay (IC50=42.66 µg/ml), metal chelating activity (IC50=1036.4 µg/ml) and reducing power assay. The extract also exhibited complete protection of pBR322 plasmid DNA during DNA damage inhibition assay [71].

The antioxidant activity of the methanolic extracts of *L. camara* various parts was screened for antioxidant activities by free radical scavenging activity (DPPH), xanthine oxidase inhibition activity, and Griess-Ilosvay method. The results showed that all the plant parts possessed antioxidant properties correlated with the total phenols. The leaves extract of *L. camara* was more effective than that of other parts [72].

Antioxidant activity of *L. camara* extracts was tested by the DPPH assay method. The methanolic extract from the stem of *L. camara* showed weak antioxidant activity, with values of 6.0 µg/ml [35].

The antioxidant activity of the leaves methanol extract was determined on DPPH radical, superoxide (O), hydroxyl (OH), and nitric oxide (NO)

radicals. The percentage inhibition of the methanol extract of *L. camara* leaves extracts on DPPH radical was concentration-dependent with EC_{50} of 27.56±0.02 µg/ml compared to standard (ascorbic acid) with EC_{50} of 1.07±0.03 µg/ml. The extract inhibited hydroxyl radical-induced 2-deoxy-ribose degradation, EC_{50} (22.18±0.02 µg/ml) compared to the standard (α-tocopherol) EC_{50} (18.60±0.02 µg/ml). The superoxide anion radical was inhibited in a concentration-dependent manner. The extract had a significant O_2 anion radical scavenging ability, EC_{50} was 27.94±0.03 µg/ml compared to ascorbic acid standard EC_{50} of 62.47±0.02 µg/ml. Studying of the overall scavenging activity of the extract on nitric oxide radical, showed that the extract at 500 µg/ml was most potent in scavenging nitric oxide radical compared to ascorbic acid standard at 500 µg/ml [22].

The antioxidant potential of the ethanolic extracts of leaves and stem of *L. camara* (0.2, 0.4, 0.6, 0.8, 1.0, and 1.2 µg/ml) was investigated using (DPPH), radical scavenging activity, NO scavenging activity, and H_2O_2 scavenging activity. The results showed that the extracts possessed antioxidant potential, DPPH activity (IC_{50}: 0.06 µg/ml), radical scavenging (IC_{50}: µg/ml), NO scavenging activity (IC_{50}: 0.41 µg/ml), and H_2O_2 scavenging activity (IC_{50}: 0.12 µg/ml). The leaf extracts showed high radical scavenging activity than that of the stem extracts [73].

The antioxidant activity of lantadene A, lantadene B, icterogenin, and lantadene C was examined using DPPH. Lantadene A and B possessed the highest scavenging activity, while icterogenin and lantadene C exhibited a lesser antioxidant effect [32].

The unsaponified terpene-rich extract of *L. camara* leaves was studied compared to petroleum ether extract for antioxidant activity, using DPPH radical scavenging model. The extract showed considerable antioxidant activity (IC_{50} value: 13 µg/ml) compared to standards [74]. Terpenes rich extract of *L. camara* leaves prepared for green synthesis of AgNPs exhibited dose-dependent antioxidant potential comparable with standard ascorbic acid [42].

Anticancer effects

The anticancer effects of *L. camara* root and leaf extracts were studied against Jurkat leukemia cell line by MTT assay. The extracts possessed statistically similar antineoplastic property (root: IC_{50}, 328.36±53.08 µg/ml and leaf: 394.41±99.73 µg/ml). Morphological examinations indicated apoptosis induction as the mechanism of anticancer activity on Jurkat cells [75].

The cytotoxicity of the methanolic extract of *L. camara* was evaluated in Vero cell line. The results showed that leaf extract at concentrations up to 500 µg/ml inhibited the growth of cells (2.5 times less than did Triton 100×1%). The cytotoxicity was declined when the concentrations of the extract were elevated [76].

Lantadene A, lantadene B, icterogenin, and lantadene C exerted a dose-dependent reduction in MCF-7 cell viability; however, lantadene B showed the highest anticancer activity, with an IC_{50} of 112.2 µg/ml. The results also confirmed a significant release of caspase 9 in a dose-dependent pattern following treatment of MCF-7 cells with a range of lantadene B concentrations. Lantadene B induced MCF-7 cell cycle arrest in G1 and blocking the G1/S transition. No significant changes were observed in S phase, but a decrease in the MCF-7 population was exhibited in G2/M phase [32].

An aqueous extract obtained from callus cultures of *L. camara* possessed dose-time-dependent cytotoxic effect on HeLa cells with an IC_{50} value of 1500 µg/ml in 36 h [77].

The anticancer effect of *L. camara* methanol leaf extract (400 mg kg twice a week, 1 week before and for 20 weeks thereafter) was investigated in 7,12-dimethylbenz[a]anthracene (DMBA)-induced skin cancer (twice-weekly topical application of 100 nmol for 8 weeks on the shaved backs) in Swiss albino mice. The results revealed significant decrease in incidence of skin papillomas in mice and reduced death rate in comparison with DMBA alone at the end of 20 weeks. The results were confirmed by histopathology. The skin section of *L. camara* methanol leaf extract-treated mice showed hyperplastic papillomatous lesions without the evidence of infiltration or cytological atypia [78].

The methanol leaf extract of *L. camara* showed *in vitro* cytotoxicity against human lung carcinoma cell lines (A-549) and mouse melanoma (B16F10). The human lung carcinoma cell line was found to be more susceptible with a CTC_{50} value of 48.1–58.5 mg/ml extract. In the short-term toxicity studies, the methanol extracts of the root with 191.5±5.1 µg/ml and leaf with 219.5±8.4 µg/ml, showed moderate activity against DLA cells after 3 h of exposure. The extracts of the stem, fruit, and flowers of *L. camara*, showed less activity with CTC_{50} values of 268.7±10.2, 492.7±14.4, and > 1000 µg/ml, respectively [79].

Oleanonic acid isolated from *L. camara* was tested for anticancer activity against a murine tumor (Ehrlich ascites carcinoma), and three human cancer cell lines (A375 [malignant skin melanoma], HEP2 [epidermoid laryngeal carcinoma], and U937 [lymphoma]). It exhibited promising cytotoxicity against A375 cells [80].

The extract of *L. camara* exhibited cell death properties on the human breast cancer cell line (MCF-7). The apoptosis induced by *L. camara* extract was regulated by the Bcl-2 family. Bid and Bax were increased, and Bcl-2 was decreased by *L. camara* extract. It modulated cleavage of caspase-8, and caspase-9, as well as poly (ADP-ribose) polymerase (PARP) [81].

Terpenes rich extract of *L. camara* leaves prepared for green synthesis of AgNPs was found to exhibit toxicity on Brine shrimp (*A. salinanauplii*) with LD_{50} value of 514.50 µg/ml [42].

The cytotoxicity of the methanol extract of various parts (root, stem, leaf, flower, and fruit) of *L. camara* was studied in *in vivo* brine shrimp lethality assay. All the tested extract showed very low toxicity on brine shrimp larva. The results showed that the root extract was the most toxic part of *L. camara* and may have potential as anticancer agent [82].

Extracts of the leaves, twigs, stems, and roots of *L. camara* were solvent-partitioned and screened for activity in the brine shrimp lethality test. The active fractions (oleanonic acid, lantadene A, and oleanolic acid) were very toxic to brine shrimp [83].

Anti-inflammatory and analgesic effects

The anti-inflammatory and antinociceptive activities of aqueous extract of *L. camara* (25, 50, and 100 mg/kg) were studied using animal models. The anti-inflammatory activity was studied using carrageenan-induced lung edema and pleurisy mice, while, the analgesic effect was studied using formalin pain test in rats. The administered doses showed significant ($p<0.05$) anti-inflammatory and analgesic activity and minimal toxic effects [84].

Methanolic extracts of the leaves and bark of lantana extract were screened for analgesic activity by acetic acid and hot plate, and anti-inflammatory activity by carrageenan and histamine-induced paw edema models. Methanolic leaf and bark extracts (100 and 200 mg kg body weight BW) possessed significant anti-inflammatory effects, and at 200 mg/kg dose, the extracts showed significant analgesic activity [85].

The anti-inflammatory activity of petroleum ether, ethanol, acetone, methanol, hydroalcoholic, and aqueous extracts (300 and 500 mg/kg BW, orally) of the leaves of *L. camara* was studied using carrageenan–induced paw edema test in rats. The results showed that treatment with aqueous extract of *L. camara* (300 mg/kg) exhibited mild decrease in paw volume, while, 500 mg/kg, possessed significant anti-inflammatory activity [86].

The analgesic activity of petroleum ether, ethanol, acetone, methanol, hydroalcoholic, and aqueous extracts (300 and 500 mg/kg BW, orally)

of the leaves of *L. camara* was studied using hot plate test in rats, the time for licking of the paws was recorded before, and 30 min after, the oral administration of the different extracts. The results showed that the latency time for licking was increased after treatment with the extracts [86].

Antiurolithiatic activity
The antiurolithiatic activity of the ethanolic extract of roots (200 mg kg) and oleanolic acid (60–100 mg/kg) isolated from roots of *L. camara* was studied in albino male rats using zinc disc implantation induced urolithiatic model. In the group of only zinc disc was implanted without any treatment, the calcium output was increased (23±2.7 mg/dl). Cystone receiving animals showed significant protection ($p<0.01$). Treatment with oleanolic acid and ethanolic extract of roots significantly reduced the calcium output at dose of oleanolic acid 60 mg/kg ($p<0.01$), oleanolic acid 80 mg/kg ($p<0.01$), ethanolic extract of roots 200 mg kg ($p<0.01$), and oleanolic acid 100 mg/kg ($p<0.001$), as compared with zinc disc implanted group. The rats received oleanolic acid, and ethanolic extract of roots also showed reduced formation of depositions around the zinc disc ($p<0.001$) [87].

Ethanolic extract of *L. camara* leaves was evaluated for antiurolithiatic activity against 0.75% v/v ethylene glycol and 2% w/v ammonium chloride-induced calcium oxalate urolithiasis and antioxidant activity against hyperoxaluria induced oxidative stress in male albino rats. The extract caused significant reduction in the deposition of calcium, oxalate, and also urinary excretion of calcium, oxalate, and creatinine, indicating its antiurolithiatic effect. It also decreased the extent of lipid peroxidation and enhanced the levels of antioxidant enzymes in the kidneys of urolithic rats, reflecting its antioxidant efficacy against hyperoxaluria induced renal oxidative stress [88].

Wound healing effects
The leaf extract of *L. camara* was investigated in wound healing in rats. Treatment of the wounds with extract significantly enhanced the rate of wound contraction (98%), synthesis of collagen, and decreased the mean of wound healing time [89].

The wound healing activity was assessed for both leaf juice and hydroalcoholic (ethanol 50% v/v) extract of the leaves of *L. camara* on excised rats. The leaf juice was more active than hydroalcoholic extract. The extract-treated group showed 87.13% healing and the leaf juice treated groups exhibited 94.32% wound healing at 14th day treatment [90].

The ethanolic extract of *L. camara* leaf was evaluated for their wound healing potential (dressed with a thin layer of placebo containing 5 and 10% *L. camara* extract) in rats. Wound dressed with placebo containing plant extracts significantly healed earlier than those treated with blank placebo. Placebo containing 10% extract significantly accelerated wound healing compared to those dressed with placebo containing 5% extract. Histologically, wounds dressed with placebo containing extracts showed large amounts of fibroblast proliferation and more mature and densely packed collagen with accompanying angiogenesis compared to wounds dressed only with blank placebo [91].

The wound healing activity of *L. camara* was studied by incorporating the hydro extraction in pure Vaseline at a concentration of 5% and 10% (w/w). The percentage of wound closure was increased in the group treated with 10% extract compared with 5% extract while control group takes more time for wound healing activity [10].

The efficacy of *L. camara* leaf extract ointment (5% and 10%) on the healing of the dermal wound infected with *S. epidermidis* was studied in rats. Wound healing was qualitatively better and bacterial colonies were lower in group treated with 5% leaf extract ointment, than group treated with 10% leaf extract ointment, fusidate 2%, and untreated group ($p<0.05$) [92].

Hypoglycemic effects
Oral administration of the methanol extract of the leaves of *L. camara* (200 and 400 mg/kg BW) in alloxan-induced diabetic rats, caused significant ($p<0.01$) reduction in the blood glucose concentration in dose-dependent manner. 400 mg/kg of the methanol extract of *L. camara*, decreased blood glucose level to 121.94 mg/dl. It was also effective in oral glucose tolerance test as it decreased the elevated glucose after 1 h. BW significantly ($p<0.05$) increased to normal after treatment with extract, which also found effective against diabetes-induced hyperlipidemia [93].

The hypoglycemic activity of the methanolic extract of *L. camara* fruits (100 and 200 mg/kg BW, orally) was evaluated in normal and streptozotocin-induced diabetic rats. Methanolic extract of *L. camara* fruit 200 mg/kg produced significant reduction in fasting blood glucose levels in the normal and streptozotocin-induced diabetic rats. Rats treated by the extract also showed improvement in BW, HbA1c profile as well as histopathological structures [94].

The antihyperglycemic activity of the aqueous extract of the leaves of *L. camara* was evaluated using both normoglycemic and alloxan-induced hyperglycemic rats. The aqueous extract caused significant reduction of blood glucose concentration between 2 and 4 h of administration in alloxan-induced hyperglycemic rats at the tested doses (200 and 400 mg/kg). However, in normoglycemic rats, the extract at 400 mg/kg produced significant reduction of blood glucose between 2 and 4 h of administration [90].

Reproductive effects
The hydroalcoholic extract from *L. camara* var aculeata leaves affected the fertility of male rats. It did not interfere with overall weight or internal organ weights, but interfered with sperm count, daily sperm production and sperm morphology in a dose-dependent manner [95]. The spermicidal potential of various *L. camara* leaf extracts (petroleum ether, chloroform, methanol, and water) was evaluated in healthy human spermatozoa. The results showed that methanolic and aqueous extracts possessed maximum spermicidal potential regarding sperm motility, sperm viability, sperm count, hypoosmotic swelling, acrosomal status, and function. Furthermore, methanolic and aqueous extracts were studied for *in vitro* pro-oxidant activity by detection of ROS generation using fluorescent probe detection method. Both methanolic and aqueous extracts of *L. camara* possessed pro-oxidant potential which could be attributed to their contact spermicidal activity [19].

The teratogenic effects of hydroalcoholic extract of *L. camara* var. aculeata leaves were studied in the rat. The extract caused skeleton anomalies in fetuses of dams treated with the extract. It also induced embryotoxicity, as indicated by post-implantation loss, without any signs of maternal toxicity [96].

Anxiolytic activity
The anxiolytic activity of the isolated compound (ursolic acid stearoyl glucoside [UASG]) from the leaves of *L. camara* was studied using elevated plus-maze, open field and light, and dark test. The UASG showed marked increased in (%) time spent and the number of frequent movements in open arm of elevated plus-maze apparatus. In light and dark models, UASG produced marked increase in time spent by animal, number of crossing, and reduced duration of immobility in lightbox [97].

Cardiovascular activity
The cardiovascular activity of the ethanolic extract of *L. camara leaves* was evaluated in different experimental models. The ethanolic extract of *L. camara leaves* produced negative inotropic and negative chronotropic effect, antagonized by atropine on isolated frog heart. The ethanolic extract caused dose-dependent ($p<0.05$) decrease in the mean arterial blood pressure in anesthetic chick. Salt treated rats displayed significant ($p<0.05$) increase in blood level of SGOT, SGPT, creatinine, and sodium, decrease in potassium levels in comparison with normal rats. Treatment with ethanolic extract (200 and 400 mg kg) significantly

balanced the ionic levels such as lower the sodium and elevate the potassium levels. Creatinine levels were significantly ($p<0.05$) reduced by ethanolic extract [98].

Hepatoprotective effect

The hepatoprotective effect of lantana camera dried rind extract was studied against carbon tetrachloride (CCl_4)-induced liver damage in male Wistar rats. Lantana camera extracts for 28 days significantly reduced the impact of CCl_4 toxicity on the serum markers of liver damage, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase. Lantana camera extract also caused marked increase in the levels of superoxide dismutase and catalase enzymes in rats. These results were further confirmed histopathologically [11].

Antihemorrhoidal activity

The antihemorrhoidal activity of *L. camara* was studied in 20 patients suffering from 1st to 2nd-degree hemorrhoids, using capsules prepared from dry aqueous extract of *L. camara* 500 mg/kg and lactose 100 mg kg. The results revealed significant reduction in signs and symptoms of acute hemorrhoidal attack (bleeding, anal discomfort, anal discharge, swelling, and pain at prolapse and proctitis) last week (on 28th day). No significant adverse effects were reported [86].

Antithrombin effects

Methanolic extracts prepared from the leaves of *L. camara* have been found to inhibit human thrombin [99].

SIDE EFFECTS AND TOXICITY

The most important toxic components present in the plant were lantadenes. Lantadenes are pentacyclic triterpenes that caused hepatotoxicity, photosensitization, and jaundice. The lantadenes were mainly present in the leaves of this plant. Other compounds such as naphthoquinones, oil constituents (citral), iridoid glycosides (Theveside), and some of the oligosaccharides were also (less importance) toxic compounds [100-102].

In acute toxicity study, a fixed large dose of 2 g/kg BW, orally of *L. camara* methanolic leaf extract showed no obvious acute toxicity within 2 weeks. However, female mice lost BW after being treated with a single dose of leaf extract in acute toxicity test, while, males lost organ mass, particularly for heart and kidney. The biochemical liver function tests showed significantly elevated TBIL and ALT in the *L. camara* leaf extract treated female mice group compared with the control group [76].

The toxin fraction (lantadene A and lantadene B) of the red variety of *L. camara*, administered orally (125 mg/kg, BW) to guinea pigs caused icterus and photosensitization within 48 h. All affected animals showed hepatomegaly with significant increases in conjugated and unconjugated bilirubin in plasma. The intoxicated animals of either sex had marked increases in acid phosphatase [103,104].

Methanolic extracts of the leaves and bark of lantana extract at a dose of 2000 mg/kg orally, do not exhibit any signs of toxicity in rats up to 14 days and no animal died [85].

The toxicity of the aqueous extract of *L. camara* was determined by intraperitoneal administration of 450, 670, and 1000 mg/kg daily for 28 days to rats. The histological, BW, hematological, and biochemical parameters were evaluated. The results showed that all doses of the extract were not toxic [84].

Once-daily administration of *L. camara* leaves juice at different dose levels (60, 300, 600, and 1500 mg/kg/day) for 14 days in rats resulted in alterations in various haemato and biochemical parameters. A significant increase in blood urea nitrogen was recorded at the doses of 600 and 1500 mg, and significant increase in the relative weights of adrenals was recorded at all dose levels. Total proteins, globulins, absolute lymphocyte count, and percent lymphocyte count were significantly decreased with 60, 600, and 1500 mg doses while a significant hypoglycemic effect was observed with 1500 mg only. 1500 mg dose did not exhibit any changes in alanine aminotransferase and aspartate aminotransferase activities and relative kidney and liver weights. In another set of experiments, once-daily oral administration of 1500 mg/kg/day for 14 days significantly inhibited the granulomatous tissue formation in rats [105].

Lantadenes possessed varying toxic effects among different species and strains of mammals/livestock. The toxic effects of this plant are evident both in ruminants and in non-ruminants. Among ruminants cattle, buffalo, and sheep were highly susceptible, while goats were little resistant to lantadene toxicity. The toxic effects of lantana were recorded in Kangaroos and Ostriches also. Green fodder scarcity was the major cause of lantana toxicity in animals [103,106].

L. camara mainly attacks liver and kidneys of ruminants and leads to photosensitization. Poisoned cattle may show signs of excessive skin sensitivity to sunlight (photosensitization), yellow discoloration (jaundice) of the whites of the eyes and gums. Skin of the nose and mouth, may become sun-sensitive and their skin may blister, reddening, and inflammation of unpigmented (white) skin; muzzle may become inflamed, moist, ulcerated and very painful (pink nose) and slough, swelling of ears and eyelids if unpigmented, reddening and discharge from the eyes (conjunctivitis), and ulceration of the tip and under surface of the tongue (if unpigmented). In chronic cases, affected skin may slough leaving raw ulcerated surfaces, the animal avoids sunlight (photophobia), stop eating, appear sluggish, weak and depressed, urinate frequently, become constipated (most commonly) or have diarrhea with strong-smelling black fluid feces in severely affected animals and become dehydrated. Histopathologically, lantadenes caused degeneration of the periportal parenchymal cells, distended bile canaliculi, fatty degeneration, portal fibrosis, hyperplasia of bile ducts, and edema of gall bladder walls in cattle. Hematological studies showed that lantadenes increased blood clotting time and hematocrit values and decreased erythrocyte sedimentation. Biochemical studies showed that lantadenes increased direct and total bilirubin, serum AST, ALP, GLDH, serum total protein, serum albumin, serum globulin, and decreased albumin/globulin ratio in cattle. A toxic dose for a 500 kg cow varied from about 5–20 kg of fresh leaf (1% or more of an animal's BW), depending on the toxin content of the lantana eaten [100,106-113].

Sheep gave powdered lantana leaf 4, 6, 8, and 12 g/kg BW developed jaundice and photosensitization after 3 days. At necropsy the severely intoxicated sheep showed liver and kidney necrosis, and pulmonary edema. Vacuolar or hydropic degeneration of the hepatic peripheral parenchymal cells, bile ductule hyperplasia, and slight portal cirrhosis were noted in less severely affected sheep. Myocardial necrosis and scarring were recorded in the hearts of some sheep. Hydropic and fatty degeneration of the tubular epithelium of the kidneys was seen in the acute phase, and cast formation, occlusion, and cystic dilatation of proximal tubules were seen in the more chronic stages associated with dehydration. The LD_{50} value of lantadene in sheep was 1–3 mg kg BW intravenously, and 60 mg/kg BW, orally. Administration of lantadene leaf powder in goats caused diarrhea, anorexia, and jaundice [106,113,114].

CONCLUSION

Human beings have depended on nature for their simple requirements as being the sources for medicines, shelters, foodstuffs, fragrances, clothing, flavors, and fertilizers. There is a promising future of medicinal plants as there are about half million plants around the world, and most of them are not investigated yet for their medical activities. *L. camara* possessed antimicrobial, antiparasitic, anxiolytic, gastrointestinal, hypoglycemic, cardiovascular, antioxidant, anticancer, anti-inflammatory, analgesic, wound healing, antiurolithiatic, hepatoprotective, reproductive, antihemorrhoidal, thrombin inhibition, and many other effects. Accordingly, it represents a promising medicinal plant with wide range of pharmacological activities which could be

utilized in several medical applications because of its effectiveness and safety.

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AUTHOR'S CONTRIBUTIONS

The author declares that this work was done by the author named in this article.

CONFLICTS OF INTEREST

There are no conflicts of interest. I am, alone responsible for the content and writing of this article.

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