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CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL EFFECTS OF *Clerodendrum inerme*- A REVIEW

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ABSTRACT

Clerodendrum inerme contained cardiac glycosides, anthraquinones, proteins, phenolics, flavonoids, saponins, tannins, iridoids, diterpenes, triterpenes, sterols, steroids, carbohydrates, fixed oils, volatile oils and lignin. It exerted many pharmacological effects including anti-inflammatory, analgesic, antipyretic, neural and smooth muscle effects, antimicrobial, antidiabetic, antioxidant, antiparasitic, insecticidal, antiallergic, anticancer, protective and many other pharmacological effects. This review will highpoint the chemical constituents and pharmacological effects of *Clerodendrum inerme*.

Keywords: *Clerodendrum inerme*, Pharmacology, Phytochemistry.

INTRODUCTION

World Health Organization survey indicated that about 70-80% of the world's population rely on nonconventional medicine, mainly of herbal sources, in their primary healthcare. This is especially the case in developing countries where the cost of referring a western style doctor and the price of medication is beyond the means of most people [1-2]. During the last few decades, there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world [3]. Recent reviews showed that there were hundreds of significant drugs and biologically active composites extracted from the medicinal plants [4-45]. *Clerodendrum inerme* belong to the family Verbenaceae, contained many biologically active metabolites, including cardiac glycosides, anthraquinones, proteins, phenolics, flavonoids, saponins, tannins, iridoids, diterpenes, triterpenes, sterols, steroids, carbohydrates, fixed oils, volatile oils and lignin. It exerted many pharmacological effects such as anti-inflammatory, analgesic, antipyretic, neural and smooth muscle effects, antimicrobial, antidiabetic, antioxidant, antiparasitic, insecticidal, antiallergic, anticancer, protective and many other pharmacological effects. This review will highlight the chemical constituents and pharmacological effects of *Clerodendrum inerme*.

Synonyms: *Volkameria inermis L* [46]

Nomenclature and common names

The name *Clerodendrum* is derived from the Greek kleros, meaning chance or fate, and dendron, meaning tree, in reference to the

uncertain medicinal qualities of some of the plants. The common names are: Arabic: Yasamen katheb, Yasamen Zefar, Shajar khat; Bengali: Banajai; Chinese: Ku lang shu, English: Seaside *Clerodendrum*, Wild Jasmine, Sorcerers Bush, Indian privet, Garden quinine, Embrert; Hindi: Sankuppi; Sanskrit:Kundali; Tamil: Sangam, Peechangu; Urdu: Guldamdam[47-48].

Taxonomic classification

Kingdom: Plantae, **Subkingdom**: Tracheobionta**, Superdivision**: Spermatophyta, **Division:** Magnoliophyta, **Class**: Magnoliopsida, **Subclass**: Asteridae, **Order**: Lamiales, **Family:** Verbenaceae, **Genus**: *Clerodendrum* L., **Species**: *Clerodendrum inerme* (L.) *Gaertn* [49].

Distribution

Clerodendrum inerme is widely distributed tropical plant, it is mainly found in India, Nepal, Bangladesh, Sri Lanka, Southeast Asia and Mediterranean [50].

Description

Evergreen extensive shrub 1-1.8 m tall. Stems woody, smooth. Leaves ovate to elliptical (5-10 cm) long, acute to acuminate tip, green, smooth, slightly shiny upper 2 surface, pinnate venation, margins entire, leaves opposite, simple. Cyme or umbel usually comprised of 3 flowers joined at a common base point; corolla white, fused, with 5 lobes; stamens 4, reddish to purple and upwardly curved. Fruit green turning black, 1 – 1.5 cm long, obovoid [51-52].

Traditional uses

Clerodendron inerme was used as a febrifugal and uterine stimulant, a pest control agent and antiseptic, to arrest bleeding, treatment of asthma, hepatitis, ringworm and stomach pains [53]. The plant was also used in the treatment of scrofulous and venereal infections, and also as an antidote for poisoning from fish, crabs, and toadstools [54]. The fresh leaf juice was used externally for treating skin diseases. The roots are boiled in oil and used in rheumatic affections [55-56]. Part used: Roots and leaves [53-56].

Physicochemical parameters

Physicochemical characteristics of *Clerodendron inerme* (%) were: total ash: 11.7, water soluble ash: 5.49, acid insoluble ash: 4.68, crude fiber content: 17.6, moisture content: 5.5, volatile oil content: Nil, alcohol extractive value: 26.7, water extractive value: 10.8 and foaming index: Up to 1000 [57].

Chemical constituents

Clerodendrum inerme contained cardiac glycosides, anthraquinones, proteins, phenolics, flavonoids, saponins, tannins, iridoids, diterpenes, triterpenes, sterols, steroids, carbohydrates, fixed oils, volatile oils and lignin [57-60]. A new triterpenic glucoside, lup-1,5,20(29)-trien-3-O-β-D-glucopyranoside, n-octacosane, friedelin and β-amyrin, has been isolated from the leaves of *Clerodendrum inerme* (L.) Gaertn. (Verbenaceae) [61]. A watery soluble bitter principle, alkaloidal was also isolated from the leaves of *Clerodendron inerme*. The unsaponifiable fraction of the fat afforded some sterols, one of them is a mixture of two isomers of C27H46O, which indicates the probable presence of cholesterol. An aliphatic alcohol C15H32O and an alphatic ketone C24H48O were also isolated. Glucose, fructose and sucrose were indentified to be present in the leaves of the plant as free sugars [62]. The leaves yielded the flavanolid, friedelin, salvigenin (5-hydroxy-6, 7, 4'- methoxy flavones), acacetin, cirisimaritin, pectolinarigenin, apigenin (5, 7-dihydroxy-4' mathoxy flavaone) and amethyl flavones, cleroflavone (7-hydroxy 5, 4' dimethoxy-6-methyl flavanone) [63].

Three neo-clerodane diterpenoids, inermes A, B and 14,15-dihydro15b-methoxy-3-epicaryoptin, have been isolated from the hexane extract of the leaves of *Clerodendrum inerme*, in addition to an epimeric mixture of 14,15-dihydro-15- hydroxy-3-epicaryoptin [64]. Phenylethanoid glycoside, 2-(3-methoxy-4-hydroxyl phenyl) ethyl-O-2″,3″-diacetyl-α-L-rhamnopyranosyl-(1→3)-4-O-(E)-feruloyl-β-Dgluco-pyranoside, monomelittoside, melittoside, inerminoside A1, verbascoside, isoverbascoside, campneoside I was isolated

from the aerial parts of *Clerodendrum inerme* (L.) *Gaertn* [65]. B-friedoolean-5-ene-3-β-ol, β-sitosterol, stigmasta-5,22,25-trien-3-β-ol, betulinic acid, and 5-hydroxy-6,7,4′-trimethoxyflavone were isolated from the aerial parts of *Clerodendrum inerme* [66]. Volatile constituents such as 5-Oethylcleroindicin D, linalool, benzyl acetate and benzyl benzoate, have been isolated from *C. inerme* [67]. Anandhi and Ushadevi isolated 21 compounds from the ethanolic extract of the leaves of *Clerodendron inerme* including: p-Xylene, Cyclohexane, nitro- , Decane, Limonene, Undecane, 1-Heptanol, 2-propyl-, Tetradecene, (E)-, Decane, 2,3,5,8-tetramethyl-, Hexadecane, Dodecanoic acid, Nonadecane, Eicosane, Tetradecanoic acid, 1,2-Benzenedicarboxylic acid, bis (2- methylpropyl) ester, nHexadecanoic acid, 9,12-Octadecenoic acid, methyl ester, (E,E)-, 9-Octadecenoic acid (Z)-, methyl ester , Oleic acid, Eicosane, Heptacosane and Squalene [68].

Pharmacological effects

Anti-inflammatory, analgesic and antipyretic effects

The alcoholic and aqueous extracts of the leaves of *C. inerme* showed significant antinociceptive activity in analgaesiometer tests [61]. The methanol extract of aerial part of *Clerodendrum inerme* were examined for anti-inflammatory and analgesic effects at the dose 200 mg/kg body weight. The experimental models used were carrageenan, induced pedal edema for anti-inflammatory activity and acetic acid induced writhing methods to assess analgesic activity. In acute phase inflammation, a maximum inhibition 60.17% % ($P<0.01$) was recorded at the dose of 200 mg/kg of

treatment with methanol extract of *Clerodendrum inerme* (MECI) after 3 h in carrageenan, induced pedal edema. The extract also produced significant ($P<0.01$) analgesic activity in both models [69]. The total methanolic extract (TME) of the aerial parts, exhibited anti-inflammatory activity. Hind paw edema model was carried out by injection of 4% formalin (20 µl) solution into the subplanter region of the left hind paw of adult male albino rats. The total methanolic extract was administered as 50, 100, and 200 mg/kg hypodermically. It showed anti-inflammatory activity more than indomethacin at a dose of 200 mg/kg after 4 hours [66].

The leaves of *Clerodendrom inerme* were subjected to In vitro Anti-inflammatory activity by HRBC membrane stabilization method in various concentration 10, 50, 100, 200, 400, 800 and 1000µg/ml. All the excerpts showed positive response as compared to standard Diclofenac sodium. The Ethyl acetate and ethanol extracts showed the maximum activity. The order of effect of different extracts were represented as follows Ethyl acetate> Ethanol >Water> Chloroform> Petroleum ether. The Petroleum ether, Chlorofrom, Ethyl acetate, Ethanol and water fractions of the leaves of *Clerodendrom inerme* were subjected to in vitro anti-arthritic activity by protein denaturation method. All the extracts showed positive response. The effect was represented as follow: Ethyl acetate> Chloroform>Ethanol> Water> Petroleum ether [60]. Anti-inflammatory and analgesic effect of methanol extract of *Clerodendrum inerme* (MECI) was also evaluated in animal models. Pre-treatment with methanol extract of *Clerodendrum inerme* (MECI) (125, 250 and 400 mg/kg) prevented acetic acid induced writhing movements in mice. However, the inhibitory effect of diclofenac sodium (10 mg/kg) on acetic acid induced writhing was greater than MECI (500 mg/kg). In subchronic rat model of inflammation (cotton pellet granuloma), MECI inhibited the granulator phase of inflammation in a dose related manner [70].

Adjuvant induced arthritic rats showed a significant decrease in body weights, organ weights, liver glycogen and serum ionic levels. But treatment with the effective fraction (apigenin, scutallarin and pectinolinergenin) of *C. inerme* for 15 days, produced a very good relief from the arthritic conditions by increasing the body weight by 18% and increasing serum ionic levels (copper 5.8%; zinc 49%, and iron 10%). Furthermore, increased liver glycogen content by 35% was noted after treatment with the effective fraction. Moreover, the X-ray analysis at the 30th and 49th days of untreated

arthritic rats showed sever periostitis and other degenerative changes in the bone. Radiological scores of *C. inerme* treated rats showed little progressive changes in the bones suggesting the longterm effect of effective fraction. The authors concluded that the flavonoidal glycosides of the *C. inerme* may confer long term relief for arthritis without any side effects [71].

The petroleum ether, Chlorofrom, Ethyl acetate, Ethanol and water fractions of the leaves of *Clerodendron inerme* were subjected to in-vitro anti-arthritic activity by protein denaturation method. It appeared that all the extracts of *Clerodendron inerme* leaves are capable of controlling the production of autoantigen and thereby, they inhibited the denaturation of proteins, and their effects were comparable with the standard drug diclofenac sodium. The percentage protection was found to be 78.94% (Petroleum ether extract), 88.46 % (Chloroform extract), 89.25% (Ethyl acetate extract), 87.10% (Ethanol extract), 82.31% (Water extract) and 92.20% (Diclofenac sodium). All the extracts showed dose dependant effect [60].

The analgesic, and antipyretic effects of aqueous extract obtained from *Clerodendrum inerme* leaves (AECI) was investigated in rats and rabbits. Analgesic effect of AECI was evaluated by Hot plate, Tail Flick and Tail immersion methods in albino rats. Antipyretic activity of AECI was evaluated by milk-induced hyperpyrexia in rabbits. The AECI produced significant ($P<0.001$) painkilling activity in all models. Furthermore, the AECI potentiated the Diclofenac sodium-induced analgesic effect in albino rats. Treatment with AECI showed a significant ($P<0.001$) dose-dependent reduction of pyrexia in rabbits [72].

Neural effects

Tics are characterized by involuntary, sudden, rapid, repetitive, non-rhythmic, stereotyped movements or phonic productions. A report of a 13-year-old girl, with chronic motor tic disorder refractory to multiple anti-tic therapies, showed dramatic improvement and remission after taking the crude leaf extract of *Clerodendrum inerme* (L) *Gaertn*. No side effects were observed during a follow-up of more than 2 years [73].

The effect of the ethanol extract of *Clerodendrum inerme* leaves was evaluated in animal behaviors mimicking Tourette syndrome (TS), hyper-locomotion, and sensori-motor gating deficit. The latter is also observed in schizophrenic patients and can be reflected by a disruption of prepulse inhibition of acoustic startle response (PPI) in animal models induced by methamphetamine and NMDA channel blockers (ketamine or MK-801), based on hyperdopaminergic and hypoglutamatergic hypotheses, respectively. *Clerodendrum inerme* extract (10–300 mg/kg, ip) dosedependently inhibited hyperlocomotion induced by methamphetamine (2 mg/kg, ip) and PPI disruptions induced by methamphetamine, ketamine (30mg/kg, ip), and MK 801 (0.3 mg/kg, ip) but did not affect spontaneous locomotor activity, rotarod performance, and grip force. Accordingly, *Clerodendrum inerme* extract can relieve hyperlocomotion and improve sensorimotor gating deficit, supporting the therapeutic potential of *Clerodendrum inerme* for TS and schizophrenia [74].

Antidiabetic effect

The anti-diabetic activity of *Clerodendrum inerme* was evaluated using in vivo streptozotocin-induced diabetes in mice, and in vitro studies. The leaves of *C. inerme* were extracted in petroleum ether, methanol followed by aqueous solvent. Methanolic extract of leaves of *Clerodendrum inerme* at 200 mg/kg showed a very significant and progressive reduction in glucose level [75].

Antimicrobial effect

When *Clerodendrum inerme* tested against S. typhi, K. pneumonia, S. aureus, Proteus sp. and B. subtilis, Iso amyl alcohol extract showed antibacterial activity against all the bacterial species, propanol extracts also active against all species except Proteus sp., while ethanol, methanol and chloroform extracts exerted activity against Proteus sp. and S. aureus only [58]. The antibacterial studies of *Clerodendrum inerme* were carried out by disc diffusion technique against Shigella sonnei,

Klebsiella pneumoniae, Bacillus subtilis, Salmonella typhi, Pseudomonas aeruginosa, Pseudomonas solanacerum and Xanthomonas citri. The maximum antibacterial activities were observed in ethanol extract (0.30 ± 0.10). Among the seven bacterial organisms, growth suppression was observed in Pseudomonas solanacearum, Xanthomonas citri and Klebsiella pneumonia only [68].

The antimicrobial activity of *Clerodendrum inerme* was investigated against E. coli, Shigella flexneri, Shigella dysenteriae, Vibrio cholerae, Salmonella paratyphi, Proteus spp., Staphylococcus aureus and Staphylococcus epidermis using disc diffusion assay. The chloroform bark extract of of C. inerme showed excellent performance against all tested bacteria except Staphylococcus epidermis [76]. The effectiveness of the crude extracts of *Clerodendrum inerme* (L.) *Gaertn*. was studied against some of the human pathogenic bacteria, Gram positive (Staphylococcus aureus, Staphylococcus aureus ATCC 25953, Staphylococcus albus, Streptococcus haemolyticus Group-A, Streptococcus haemolyticus Group-B, Streptococcus faecalis and Bacillus subtilis) and Gram negative (Escherichia coli, Edwardsiella tarda, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Salmonella typhi, Shigella boydii, Shigella dysenteriae, Shigella flexneri and Plesiomonas shigelloides). Five plant extracts (Petrol, Benzene, Methanol, Ethyl acetate and Aqueous) under six different concentrations (500 mcg, 1mg, 2mg, 5mg, 10mg and 15mg/ml) were tested by disk diffusion method. Methanol, Ethyl acetate and Aqueous extracts of the plant showed significant inhibition against fifteen of the eighteen tested bacteria [77].

The antimicrobial activities of different extracts (ethanol, benzene and aqueous) of *Clerodendrum inerme* plant parts were evaluated in vitro by disc diffusion method against Gram positive - Bacillus subtilis (ATCC 6633), Staphylococcus aureus (ATCC 25923), Gram negative- Escherichia coli (ATCC 25922), Psedomaonas aeruginosa (ATCC 27853) and fungal strains Aspergillus niger (ATCC 16404), Aspergillus flavus (ATCC 9807), Candida albicans (ATCC5027) and Candida glabrata (ATCC 66032). The methanol leaves extract exhibited highest zone of inhibition against S. aureus and A. niger (16.67 ±0.47 and 15.0±0.0 mm, respectively) with low MIC values (0.78 mg/ml for each). However, no activity was shown by aqueous extract against the tested pathogenic strains [78].

The ethyl acetate and hexane extracts of leaves and stems of *Clerodendrum inerme* were screened for antifungal activity. The tested fungi were included clinical isolates of dermatophytes such as pidermophyton floccosum, Trichophyton mentagrophytes, Trichophyton rubrum and Trichophyton tonsurans, and plant pathogens such as Aspergillus niger, Aspergillus flavus, Curvularia lunata, Botrytis cinerea and Fusarium oxysporum. Leaf hexane extract (1 mg/ml) of *C. inerme* inhibited the plant pathogenic fungi better than the human dermatophytes [79]. Clerodendrum inerme showed antiviral activity against Hepatitis B virus with ED50 value of 16 mg/ml [80].

Antioxidant effect

All *Clerodendrum* species showed antioxidant potential by all the antioxidant assays tested (DPPH Assay, Reducing Power Assay and Total Antioxidant Activity). For DPPH assay maximum antioxidant activity, Reducing Power Assay and Total Antioxidant Activity, *C. inerme* showed nearly the maximum activity among *Clerodendrum* species [58]. Study of methanolic extract of leaves of *C. inerme* showed free radical scavenging activity increasing with concentration, with maximum activity at 2500 mg/ml. This antioxidant activity may be attributed to phenolic compounds [81]. The total methanolic extract (TME) of the aerial parts, and compound - hydroxy-6,7,4′-trimethoxy flavone showed scavenging activity with maximum inhibition of 61.84% for TME (100 µg/ml) and 37.19% for -hydroxy-6,7,4′-trimethoxy flavone (20 µM), using DPPH assay [66].

Antiparasitic and insecticidal effects

Leaf extracts were evaluated for their nematicidal efficacy against root-knot

nematodes. In the juvenile mortality assay against egg masses, leaf extracts of C. inerme significantly inhibited the development [82]. The aqueous extract of *Clerodendron inerme* plant leaves was evaluated against laboratory strain Aedes aegypti larvae. The extract elucidated 100% inhibition of adult emergence at 2% concentration of extract, and concentrations above 4% led to prolongation of larval developmental period without moulting leading to death during larval stage. Mortality during larval stage was found to be dose-dependent elucidating 100% mortality at 16% concentration. It is apparent that the extract interferes in the developmental process affecting larval developmental period and disruption of larval-pupal moult [83].

Laboratory and field investigations have been made to evaluate the combined effect of *Clerodendron inerme* and Acanthus ilicifolius on three species of mosquito vectors, Anopheles stephensi, Aedes aegypti and Culex quinquefasciatus. Different concentrations of *Clerodendron inerme* and Acanthus ilicifolius have been tested on the various stages of species of mosquito vectors. They were active against different larval stages of mosquitoes. The lethal effect on mosquito larvae may be due to the active plant compounds on the gut lining of the mosquito larvae. The larval density was decreased after the treatment with the *Clerodendron inerme* extracts at the breeding sites (drinking water and ditches water) [84]. The dry powder of *Clerodendrum inerme* leaves was tested (10 to 60 mg) against freshly moulted fourth instar larvae of dengue mosquito vector Aedes aegypti. The results revealed that there was no larval mortality in the treated larvae and they moulted to pupae after 60h from the start of the experiment and the process was completed by 72h. Control larvae also required 60–72h to pupate. There were no visible behavioural changes in the treated larvae, except for the fact that they were not as active as those of control ones after 24h of treatment.

During pupal stage also, the pupae in treated flasks were not as active as control groups. Flasks containing 40, 50 and 60 mg powder showed pupal mortality after about 18-20h. At the end of 72h, the percent pupal mortality in the same treated groups was 48, 74 and 96 respectively. Flasks containing 20 and 30 mg of powder exhibited less than 10% pupal mortality. In order to determine the quantity of powder required to cause larval mortality, the quantity of powder was increased from 100 to 200 mg with 20 mg increment between the treatments. The results showed dose-dependent larval mortality. As much as 85% larval mortality was seen when the powder quantity was increased to 160 mg. It was further noted that the fourth instar larvae that moulted to pupae died during the early pupal stage. The final analysis of results revealed 100% mortality in all the experimental flasks, which included larval as well as pupal mortality. Microscopic examination of dead larvae revealed that the larval cuticle had started sclerotization, which appeared to be a characteristic feature of the pupal cuticle. The dead pupae on the other hand, showed less sclerotization of the cuticle compared to untreated ones, and in majority of the pupae, the head capsule remained attached to the pupal head [85]. It was stated that petroleum ether extract of *Clerodendrum inerme* gave 3h protection against mosquitoes at 9% concentration [86].

The Petroleum ether, Chlorofrom, Ethyl acetate, Ethanol and water fractions of the powdered leaves of *Clerodendrum inerme* were tested for their efficacy against the stored grain insect pest Corcyra cephalonica (Stainton) (Lepidoptera Pyralidae). Seven different doses (0.05, 0.1, 0.15, 0.5, 1.0, 1.5, and 2.0 g) per 20.0 g of rice were tested against this common insect pest of rice to evaluate their effect on its life cycle and mortality. Three higher doses were further tested for their effect on physiological parameters like total haemocyte count (THC), total protein content and glycogen level along with starved insects. *C. inerme* exhibited biopesticidal activity as evidenced by the high mortality rate in treated insects. There was also a significant reduction in the THC (39-53%), protein (30-38%) and glycogen (40-61%) content in *C. inerme* treated larvae with respect to their controls [87].

The efficacy of *Clerodendron inerme* leaf extract was evaluated against Pieris brassicae. Larva, pupa and adult of P. brassicae

have been treated with the aqueous extract of *C. inerme* leaf of different concentration. The results show that extract was quite effective against all the three stages in general, and pupa in particular. A typical extract with 12.5% concentration showed a mortality rate of 20% for larvae which rises to 55% for pupa. The mortality rate generally increases with increase in the concentration, reached to its maximum at 10% to 17.5% of concentration and then decreased or became constant for different developmental stages [88].

Antiallergic effect

The G7, a Siddha medicine [herbal mixture (500mg capsule) contained 100 mg *Clerodendrum inerme*] moderated the release of histamine, IL1α and IL8 in vitro and therefore it is a promising alternative for the management of allergic disorders [89].

Effect on muscle contraction

Clerodendrum inerme methanolic extract did not demonstrate any contracting, relaxant or blocking effects on frog rectus abdominus muscle and rat aortic strip preparations. The extract produced a concentration-dependent ($p<0.05$) decrease of the normal rhythmic contraction of rabbit jejunum, however, this effect was reversed by prior addition of cyproheptadine (non-specific 5-HT antagonist). In addition, *Clerodendrum inerme* methanolic extract also produced a stimulant activity on rat uterus which was blocked by cyproheptadine [90]. The alcoholic extract of the leaves of *Clerodendron inerme* and the bitter principle enormously stimulated the pregnant uterus, raised the blood pressure and increased the intestinal movements. The plant possessed, ecbolic, hypertensive and laxative effects [55].

The hypotensive effect of dried leaves of *Clerodendrum inerme* was evaluated in rabbits. Rabbits were injected with 10 ml of ethyl uretane, intraperitoneally. The saphenous vein was intubated with a catheter attached to a syringe allowing the injection of different doses of *C. inerme* and Acetylcholine. The physiological records made on rabbits revealed that *C. inerme* has no effect on the blood pressure, at low doses (≤ 10-4 mg/ml). For doses ranging from 10-3 mg/ml to 10 mg/ml, it developed a gradual and reversible hypotension; so a lowering of the normal pressure level and a decrease in the power of systoles was recorded. At 20 mg/ml, the hypotension remains steady [91].

Protective effects

The potential genomic stability and tissue protection of petroleum ether and methanolic extract of *Clerodendron inerme* (L.) *Gaertn* leaves were studied using F1 hybrid mice (C57BL male and Swiss albino female). Results revealed that when the *Clerodendron inerme* methanolic extract (CIME) was given alone and with radiation therapy (4 Gy), the intestinal tissues were protected better by methanolic extract 500mg/kg bw orally in mice as compared to test groups and radiation control group. Methanolic extract showed good results in intestinal tissue protection but the percentage of the chromosomal aberration was not well appreciated in comparison to petroleum ether extract which showed good activity in reducing percentage of chromosomal aberration [92]. The ethanolic extract of *Clerodendrom inerme* leaves were screened for its hepatoprotective activity in paracetamol induced liver damage in Swiss albino rats at a dose of 200 mg/kg bw. The ethanolic extract exhibited a significant protective effect by lowering serum levels of glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase and total bilirubin [50].

Anticancer effect

The modifying effects of ethanolic extract of *Clerodendrum inerme* leaves on membrane integrity was investigated by measuring the levels of plasma and erythrocyte membrane glycoconjugates and red blood cell osmotic fragility during 7,12-dimethylbenz(a)anthracene (DMBA) induced skin carcinogenesis in Swiss albino mice. The skin squamous cell carcinoma was induced in the shaved back of mice, by painting with DMBA (25 µg/0.1 ml acetone) twice weekly for 8 weeks. 100% tumour formation was recorded in the fifteenth week of experimental period.

The status of glycoconjugates in plasma and erythrocyte membrane and red blood cell osmotic fragility was assayed by using specific colorimetric methods. The levels of glycoconjugates were increased in plasma whereas decreased in erythrocyte membrane of DMBA treated animals as compared to control animals. Red blood cells from tumour bearing animals were more fragile than those from control animals. Oral administration of ethanolic leaf extract of *Clerodendrum inerme* (CILEE) 300 mg/kg significantly prevented the tumor formation as well as restored the status of glycoconjugates and red blood cell osmotic fragility in DMBA treated animals [93].

The chemopreventive and anti-lipidperoxidative effect of the ethanolic extract of *Clerodendrum inerme* leaves were studied in 7,12-dimethylbenz(a) anthracene (DMBA) induced skin carcinogenesis in Swiss albino mice. The skin squamous cell carcinoma was induced in the shaved back of mice by painting with DMBA (25 µg/0.1 ml acetone) twice weekly for 8 weeks. 100% tumor formation was recorded in the fifteenth week of experimental period. Elevated lipid peroxidation and decline enzymatic and non-enzymatic antioxidant status was observed in tumor bearing mice. Oral administration of the ethanolic extract of *Clerodendron inerme* leaves (300 mg/ kg bw) for 25 weeks significantly prevented the tumor incidence, volume and burden of tumor. The ethanolic extract of *Clerodendron inerme* leaves also showed potent antilipidperoxidative effect as well as enhanced the antioxidant defense mechanisms in DMBA painted mice [94].

The chemopreventive potential of the aqueous leaf extract of *Clerodendron inerme* (CiAet) was investigated in 7,12-dimethylbenz(a) anthracene (DMBA)- induced hamster buccal pouch carcinogenesis. Oral squamous cell carcinoma was developed in the buccal pouch of male Syrian golden hamsters by painting them with 0.5% DMBA in liquid paraffin thrice a week for 14 weeks. The tumour incidence, tumour volume and tumour burden that were formed in the hamster buccal pouches were determined. Oral administration of CiAet at a dose of 500 mg/kg body weight to DMBA-painted animals on days alternate to DMBA painting for 14 weeks significantly prevented the tumour incidence, and decreased tumour volume and tumour burden. CiAet also exerts potent antilipidperoxidative effect and improved the antioxidant defence system in DMBA-painted animals. The chemopreventive efficacy of CiAet was evident by inhibition of tumour formation (80%) in DMBA-painted animals [95].

Diuretic effect

The diuretic activity of chloroform and ethanolic extract of leaves of *Clerodendrum inerme* was investigated in rats. The effect of 200 and 400mg/kg of both extracts were evaluated on urine volume and electrolyte concentration. Both extracts showed good diuretic activity after 24 hr [96].

Side effects and toxicity

The ethanolic extract of *Clerodendrum inerme* leaves did not show any mortality up to a dose of 2000g/kg bw in Swiss albino rats [50]. The plant proved to be nontoxic, since it does not produce ill effects with doses as large as 8 g/kg body weight of the powdered plant [55]. Acute oral toxicity was performed in rats. Before study the rats were fasted overnight with free access to water. They were received ethanolic and chloroform extract with a single oral dose (2000mg/kg body weight). Animals were observed individually at least once during first 30 min. after dosing, periodically during first 24h (with special attention during first 4h) and thereafter once daily for a period of 14 days for major behavioral changes and mortality. Both the extracts of *C. inerme* were found to be safe up to 2000 mg/kg body weight [96].

Conclusion

The paper reviewed *Clerodendrum inerme* as 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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