RESEARCH REVIEW

Discovery Phytomedicine 2016, Volume 3, Number 2: 15-21

A review on phytochemical and biological properties of *Calotropis gigantea* (Linn.) R.Br.

Ansari Mushir,[1] Nasreen Jahan,[*1] Aziz Ahmed[2]

ABSTRACT

Calotropis gigantea Linn is a well known medicinal herb commonly known as milk weed and has been used in Unani, Ayurveda and Siddha system of medicine for years. It is a native of India, China and Malaysia and it is distributed in almost all over world. All parts of the plant have been used as medicine as well as an important ingredient in a number of Unani formulations used for the treatment of various ailments. In classical Unani literature it is mentioned to have anthelmintic, appetizer, anti flatulence, astringent, tonic, expectorant, emetic, diaphoretic, anti inflammatory, sedative, wound healer, antidote and digestive properties and used in asthma, stomach ache, cholera, amenorrhea and toothache. Phytochemical constituents include giganteol, α and β calotropeol, β-amyrin, giganteol and isogiganteol etc. *Calotropis gigantea* has been reported for its anti asthmatic, antioxidant, antibacterial, antiviral, wound healing, antiinflammatory, antidiarrhoeal, hepatoprotective and hypoglycemic activities. In this manuscript the articles published from 2004-2016 were reviewed. Well known scientific search engines *viz*. Pub med, Medline, Google scholar, and Science Direct were used to retrieve online literature. All referred studies published in peer reviewed indexed journals were included. For Unani literature classical text and manuscripts were referred.

Key words: Milk weed; Phytoconstituents; Therapeutic uses; Pharmacological studies; Traditional medicine.

*Corresponding Author: Nasreen Jahan, Dept. of Ilmul Advia, National Institute of Unani Medicine, Bangalore, India
Email: nasreen2000@yahoo.com

Cite this Article: Jahan, N., Mushir, A., Ahmed, A. 2016. A review on Phytochemical and biological properties of Calotropis gigantea (Linn) R.Br.. Discovery Phytomedicine 3(3): 15-21. DOI:10.15562/phytomedicine.2016.32

INTRODUCTION

Calotropis gigantea Linn belongs to the family Asclepiadaceae which includes more than 280 genera and approximately 2,000 species. *Calotropis gigantea* (Linn) R.Br. and *Calotropis procera* (Ait) R.Br. are the two common and closely related species. *Calotropis gigantea* is a well known medicinal herb commonly known as *Madar* has been used in Unani, Ayurveda, and Siddha system of medicine for years.[1] The drug *Calotropis gigantea* Linn has different names in different languages. In Arabic it is called as "Ashur"; in English "Gigantic" or "Swallow wort" or milk weed; in Hindi, "Ak" or "Ark" or "Madar"; in Kannada, "Arkagida"; in Malayalam, "Bukam" or "Dinesam"; in Marathi, "Akanda" "Lalakara".

To date, there have been several reviews detailing *Calotropis gigantea*. However, none of them details the Unani description of plant and therapeutic uses. This review included 25 different pharmacological studies on *Calotropis gigantea* published in last 12 years (2004-2016). In this review, we have made an attempt to bring together recent works and current trends about *Calotropis gigantea's* phytochemistry and pharmacology in the field of modern phytomedicine from different parts of the world.

GEOGRAPHICAL DISTRIBUTION

It is a native of India, China and Malaysia and distributed in almost all over the world. In India found chiefly in lower Bengal, Himalya, Punjab, Assam, Madras and South India. Common in waste land, road sides, railway embankments, ascending to about 1000 m in the Himalayas from Punjab to Assam.[2]

BOTANICAL DESCRIPTION

Macroscopic features

Calotropis gigantea is an erect, much branched shrub about 1-5 m tall. The roots are cylindrical, tortuous and often branched, externally yellowish grey while internally ceramic white and about 90 cm in length and 2.5-10 cm in diameter. Root bark is short, curved and is more rarely quilled pieces, 2-5 mm thick and 3-5 cm broad and has distinctly mucilaginous, bitter taste. Leaves are simple, opposite-decussate, sub sessile, extipulate; blade-oblong obovate to broadly obovate, 5-30 × 2.5-15.5. Flowers are complete, bisexual, bracteate, actinomorphic, pentamerous, hypogynous and pedunculate; Calyx has five sepals and lobe, shortly united at the base; Corolla is gamopetalous. Fruit is simple, fleshy, inflated, subglobose to obliquely ovoid. Seed is about 6 × 5 mm, flat compressed with silky white pappus.[3-5]

Microscopic features

The transverse section of the root shows the presence of cork as the outermost layer, regularly arranged with 15-20 layers of rectangular cells without any

[1]Dept. of Ilmul Advia, National Institute of Unani Medicine, Bangalore, India; [2]Dept. of Ilmul Advia, Dr. Abdul Haq Unani Medical College and Hospital, Kurnool, India.

intercellular space. The cells in the cortex region consist of abundant number of starch grains. These cells were consists of irregularly shaped parenchymatic cells and contains laticiferous tubes and rosette of calcium oxalate.[5] Transverse section through midrib of leaves shows an upper and lower single layered epidermis externally covered with thick striated cuticle and few epidermal cells on both surface of leaf elongated to form uniseriate 2-3 celled trichomes. Xylem consists of mostly vessels and tracheid.[6]

DESCRIPTION OF PLANT IN UNANI SYSTEM OF MEDICINE

Dioscorides (78A.D.) has mentioned *Calotropis gigantea* in his noteworthy book "*Kitabul–Hashaish*".[7] It is thorny tree with broad leaf and at the site of flowers and stem it oozes milk which is called as "*sukr*" which is also obtained from different parts of plant. The wood is fragile, delicate and leaves are soft. In some part of the world the milk is used in leather cleaning.[8] In "*Makhzan-al-Advia*" it is mentioned that there are three varieties of *Madar* first is a large with white flowers, large leaves, and much milky juice. It is found near towns and the habitations of man; Second variety is smaller with small leaves, the flowers are white externally lilac within. Third is a still smaller plant, with pale yellowish green flowers.[9, 10]

Pharmacological actions and therapeutic uses in Unani system of medicine

In Unani literature the root of *Calotropis gigantea* has been described to possess numerous pharmacological actions viz. *Qabiz* (Astringent),[11] *Muqawwi* (Tonic), *Qate wa Mukhrije Balgham* (Expectorant), *Moarrique* (Diaphoretic), *Qatile deedan* (Anthelmintic),[10] *Muhallil* (Anti inflammatory), *Musakkin* (Sedative), *Mundamile qurooh* (wound healer), *Tiryaq* (anti dote) and *Hazim* (Digestive). On the basis of these actions milk weed is used therapeutically in a variety of ailments. Najmul Ghani (1902 AD) has reported that root bark is very effective in treatment of diarrhoea, dysentery and cholera, if used with black pepper and ginger water in equal amount. Root bark with goat milk is found useful in epileptic attack. Decoction of root bark is used in the treatment of amenorrhoea and it is also used to relieve toothache. Two parts of root bark, one part black pepper and goat milk 1 part is used in treatment of fever. Root bark and *Kanji* is used in treating elephantiasis.[9]

Flowers are digestive, anti flatulence and work as appetizer. Flower buds are effective in asthma, with black pepper and rock salt useful in digestive disturbances and stomach ache. Leaves after crushing when applied externally cleanse wound and stop recurrence.[9, 12] Leaves along with the milk and *Dare Hald* (*Berberis aristata*) are used to treat fistula in ano. If leaves are burnt with salt in closed container and the ash which obtained after incineration is useful in ascites and splenomegaly.[9] Leaves are very much effective in decreasing inflammation, relieving pain when tied externally on joints.[12] The various part of the plant are used as an ingredient in many of Unani formulations such as *Johar Madar, Habbe Madar, Roghane Madar, Sufoofe Madar, Habbe Gule Akh* etc.[13]

ETHNOPHARMACOLOGICAL REPORTS

All parts of the plant are used in the treatment of bronchitis and asthma. Milky juice is used as purgative (gastrointestinal irritant).[3] Roots are used in the management of lupus, tuberculous leprosy and syphilitic ulceration.[3] Leaf-juice is used to relieve external swellings. In Java, roots are used to treat scabies.[3] Preparation of roots and leaves in the form of powders, balms, enemas and ghee or clarified butter used to resolve abdominal tumours.[14] Powdered root with milk is used for the treatment of ear trouble and boils.[14] The root bark and especially the inspissated juice are used as powerful alterative and purgatives.[15] The root bark and dried milk in small doses is used in treatment of certain cutaneous affections, such as leprosy and secondary syphilis.[2] Root bark reduced to a paste with sour rice-vinegar is applied to treat the elephantiasis.[2] The root bark is also useful in scorpion bite,[16] in treatment of earache, body ache, mumps, headache, joints pain, swellings, tooth decay, ring worm and cuts. Roots paste is applied on head and few drops of diluted solution are poured in the anus to expel worms in infants.[17] Powdered root bark gives relief in diarrhoea and dysentery.[3, 18] Soak the powdered root bark in its own milky juice and dry, bougies are then prepared from the powder and their fumes are inhaled; it is very effective in cough.[19]

PHYTOCHEMISTRY

Different parts of *Calotropis gigantea* is reported to have abundant phytochemical constituent as mentioned in table.

PHARMACOLOGICAL STUDIES

Anticancerous activity

Treatment with anhydrosophoradiol-3-acetate (A3A) isolated from the flower of *Calotropis gigantea* decreased the viable tumor cells and body weight gain, altered hematological (Hb, RBC and WBC) and biochemical parameters more or less

Plant parts	Chemical constituents
Stem Bark	Giganteol, α and β calotropeol, β-amyrin.[20]
Root	Calotropnaphthalene [naphthalenederivative], calotropisesquiterpenol, calotropisesterterpenol [terpene derivatives], calotropbenzofuranone [aromatic product] and sucros.[21]
Seed	Oil extracted from seeds contains palmitic, oleic, linoleic and linolenic acid. The unsaponifiable fraction contains phytosterol, stigmasterol , melissyl alcohol and laurane.[22]
Flower	Ester of α-and β-calotropeols.[22]
Leaves	Sapogenins, holarrhetine; cyanidin-3-rhamnoglucoside; taraxasterol isovalerate. mudarine and three glycosides calotropin uscharin, calotoxin along with phenol.[4]
Latex	Water and water soluble substance (86-95.5%) and caoutchouc (0.6-1.9%). The coagulam consist of caoutchouc (5.1-18.6), resin (73.6-87.8) and insoluble matter (4.5-13.8%).[18]
	α- and β-calotropeols (also in latex); latex-protease, calotropains FI & FII, flower β-amyrin, stigmasterol.[17] Calotoxin, uscharin, and calactin.[23]
	Two new Triterpine ester-3'-methyl butanoates of α-amyrin and Ψ taraxasterol–isolated from latex.[24]
Root Bark	Root bark contains β-amyrin, two isomeric crystalline alcohols, giganteol and isogiganteol.[20]

to normal level thereby increasing the life span of Ehrlich's ascites carcinoma (EAC) bearing mice. Results of this study conclude that *in vivo,* the A3A was effective in inhibiting the growth of EAC with improving in cancer induced complications.[25]

Wound healing activity

Calotropis gigantea latex showed wound healing activity in albino rats using excision and incision wound models. Latex treated animal exhibited 83.42% reduction in wound area when compared to controls which was 76.22%. The framycetin sulphate cream 1% w/w was used as standard. The extract treated wounds were found to epithelize faster as compared to controls. Significant ($p < 0.001$) increase in granuloma breaking strength was observed.[26]

In another study in streptozotocin (50 mg/kg) induced diabetic rats, 2 cm diameter excision wounds were created under anaesthesia. *Calotropis gigantea* latex extract ointment (2%) for 14 days were applied as a treatment. The rate of wound contraction had increased and time of epithelisation had decreased significantly ($p < 0.05$) in test drug treated rats. The volume density of collagen fibers, numerical density of fibroblasts, and length density of vessels were also significantly ($p < 0.05$) increased. This study discovered that *Calotropis gigantea* promotes diabetic wound healing by stimulating collagen synthesis and enhancing histological processes central to normal wound healing.[27]

Antiasthmatic activity

Calotropis gigantea showed anti asthmatic activity in ova albumin (OVA) induced asthma. Rats were sensitized and challenged with OVA. The effect of *Calotropis gigantea* at 100, 200, 400 mg/kg, p.o. on different body cells, enzymes and histopathological changes were observed. *Calotropis gigantea* at 200, 400 mg/kg showed significant inhibition of eosinophils, neutrophils, lymphocytes and total leukocyte counts in bronchoalveolar lavage fluid ($p < 0.05$). These results suggest that plant may prove to be potential therapeutic drug for treating asthma owing to its antiinflammatory, antilipoxygenase and antioxidant activities.[28]

Ovicidal activity

Different parts viz. leaves, stem, flower, roots and whole plant of *Calotropis gigantea* at 2, 4, 6, 8 and 10 per cent concentrations tested for ovicidal activity on *Helicoverpa armigera.* Leaf extract caused 100 per cent inhibition of egg hatchability followed by flower (90%) extract. It was also observed that as the dosage increased there was higher percentage of inhibition in egg hatchability and the early stage of eggs (24-48 h old eggs) were found to be highly susceptible at all the concentrations. These results indicate that the milkweed plant possesses ovicidal activity and could be used for the management of *Helicoverpa armigera*.[29]

Hair growing activity

Calotropis gigantea with *Hibiscus rosa sinensis* (HRSF), and polyherbal formulation (HCF) in combination of both the plants were aimed for revealing effect on hair growth initiation and promotion in albino rats. The study observations and results were compared with Minoxidil. *Calotropis gigantea* showed potential hair growth activity but less in comparison with other treatment.[30]

Antibacterial activity

Well plate method was employed on leaf extract of *Calotropis gigantea* against certain Gram positive (*B. subtilis, M. luteus, S. aureus*) and Gram negative (*K. pneumoniae, P. vulgar* and *E. coli*) bacteria. Ethyl acetate and dichloromethane extracts showed better and broader spectrum of activity when compared to other extracts.[31]

The aqueous extract of leaf was studied for *in vitro* antimicrobial activity by well diffusion method in MH agar. The extract showed maximum zone of inhibition against *E. coli* whereas, lowest against *K. pneumoniae.* Crude extract showed maximum relative percentage inhibition against *B. cereus* and lowest relative percentage inhibition against *M. luteus.* Minimum inhibitory

concentration (MIC) was measured by modified agar well diffusion method. Extract showed 50, 25, 6.25, 3.1, 1.5 and 12.5 mg/ml MIC values for *S. aureus, K. pneumoniae*, *B. subtilis, P. aeruginosa, M. luteus and E. coli,* respectively.[32]

The leaves extraction was done in n-hexane, ethanol, methanol, chloroform, water and ethyl acetate and tested against *B. cereus*, *B. subtilis, E. coli*, *K. pneumoniae*, *S. aureus*, *S. typhi* and *M. luteus* for its antibacterial activity. Ethyl acetate extract was found to be most effective with MIC value also ranging from 0.25 to 1.0 mg/ml. Aqueous leaves extract showed weak antibacterial activity.[33] The crude n-hexane, carbon tetrachloride, chloroform, ethanol and water extract of leaves were evaluated against 16 microorganisms including Gram positive, Gram negative and fungi. The carbon tetrachloride and ethanolic fraction showed little antimicrobial activity with average zone of inhibition 9.5 mm and 8.4 mm respectively at a concentration of 400 µg/ disc. The antimicrobial activities were compared with doxycycline (30 µg/ disc) which showed an average zone of inhibition of 40 mm.[34]

Calotropis gigantea latex was evaluated for its potential antibacterial activity against six bacterial species and two species of fungi. The result showed that *S aureus, B. cereus* and *E. coli* was the most susceptible bacterium, while *C. krusei* moderate susceptible whereas, no effect were observed on *M. luteus, K. pneumonia*, *P. aeruginosa* and *A. niger*.[35]

Antioxidant activity

The *in vitro* antioxidant activity of *Calotropis gigantea* root extract was investigated by 2, 2-diphenyl-1-picrylhydrazyl and fluorescence recovery after photobleaching method. In both the method, extract possesses high antioxidant activity when compared with standard ascorbic acid due to presence of high content of various phytochemicals.[36]

Anti-inflammatory activity

The anti-inflammatory activity of *Calotropis gigantea* was proved against albumin denaturation technique. The Percentage inhibition of denaturation produced by test drug was comparable with that produced by Ibuprofen (85.71%) which indicates that test drug possesses significant anti-inflammatory activity.[37]

Cytotoxic activity

Brine shrimp lethality bioassay (BSLB) and *Allium cepa* root meristem (ACRM) models were used to assess cytotoxic property of root extract of *C. gigantea*. ACRM growth inhibition was highest ($p < 0.01$) at 10 mg/ml concentration after 48 h incubation for ethanolic root extract. Extract produced dose and time dependent growth inhibition. *Calotropis gigantea* exhibits potent cytotoxic property comparable to that of standard drug.[38]

Vasodilatation activity

Calotropis gigantea latex extract was studied in the green frog (*Rana hexadactyla*) for Vasodilatation effect. The diluted crude extract with distilled water in 1:10 and 1: 100 concentrations produces percentage increase in the cardiac output. Higher dilution factor increase the cardiac output 66% where as 1:10 produces 50% cardiac output. This reveals that the latex produces vasodilatation effect at fixed dose concentration.[39]

Hepatoprotective activity

Acetaminophen induced hepatotoxicity models were used to evaluate hepatoprotective activity of leaf extracts of *Calotropis gigantea* in various solvents viz. petroleum ether, acetone, chloroform and methanol in increasing polarity. Chloroform and methanolic extract showed very significant reduction in SGPT level whereas, methanolic extract and Silymarin showed very significant reduction in SGOT level. The methanolic and chloroform extract of leaves showed significant hepatoprotective activity. However, acetone and petroleum ether extracts showed either no reduction or very slight reduction in various liver enzymes.[40]

Insecticidal activity

The residual film toxicity, fumigant toxicity and repellent effect of methanol extract of root bark of *Calotropis gigantea* and its chloroform and petroleum ether soluble fractions were evaluated against several stages of larvae and adult of *Tribolium castaneum*. In residual film toxicity, methanol extract and its chloroform and petroleum ether fractions showed insecticidal activity. Methanol extract showed lowest LD50 values against several inster of larvae and adult which indicates highest toxicity or insecticidal activity. The order of toxicity on *T. castaneum* was methanol extract > petroleum ether fraction > chloroform fraction. No fumigant toxicity of test samples was found. In the treated filter paper repellency test, methanol extracts and also its chloroform and petroleum ether soluble fractions were repellent to *Tribolium castaneum* in mild to moderate range.[41]

Sedative and anxiolytic activity

Ethanolic extract of *Calotropis gigantea* was tested in Swiss mice against Hole cross test, Open field test, Elevated plus maze (EPM) test and Thiopental

sodium induced sleeping time test. Extract showed significant decrease of movement from its initial value at 0 to 120 min which was comparable with that of the group treated with diazepam (1 mg/kg). In the open field test, the number of squares travelled by the mice was suppressed significantly ($P < 0.05$, $P < 0.001$) from its initial value at 0 to 120 min. that ethanolic extract of *Calotropis gigantea* leaves induced sleep at an earlier stage, i.e. it had a good effect on the onset of thiopental sodium induced sleep and also lengthened the duration of sleeping time in test animals compared to control. EPM test showed significant ($P < 0.05$-0.001) reduction in the percentage of entries of mice into the open arms and the percentage of time spent in the open arms of the EPM.[42]

Hypoglycemic activity

Hypoglycaemic activity of chloroform extracts of *Calotropis gigantea* leaf and flower 10, 20 and 50 mg/kg were evaluated in Streptozotocin induced diabetic rats and compared with glibenclamide. The leaves and flower extracts were effective in lowering serum glucose levels in normal rats. Improvement in oral glucose tolerance was also registered by treatment with test drug. The administration of leaf and flower extracts to streptozotocin induced diabetic rats showed a significant reduction in serum glucose levels.[43]

Analgesic activity

The alcoholic extract of the flowers of *Calotropis gigantea* was administered orally and explored for its analgesic activity in chemical and thermal models in mice. In acetic acid induced writhing test, an inhibition of 20.97% and 43.0% in the number of writhes was observed at the doses of 250 and 500 mg/kg, respectively. In the hot plate method the paw licking time was delayed. The analgesic effect was observed after 30 min of dose administration which reached its maximum after 90 min.[44]

Antidiarrhoeal activity

Antidiarrhoeal effect of hydroalcoholic extract of aerial part of *Calotropis gigantea* were assessed in castor oil induced diarrhoea model. The weight and volume of intestinal content induced by castor oil were studied by enteropooling method. The dose 100 ($P < 0.01$), 200 and 400 mg/kg significantly ($P < 0.001$) inhibited weight and volume of intestinal content in the same way as atropine (3 mg/kg IP), there were significant reductions in faecal output and frequency of droppings when the plant extracts of 200 and 400 mg/kg IP compared with control rats.[45] Another study was carried out by using aqueous extract of root bark of *Calotropis gigantea* in two doses (73 mg) and (125 mg/kg), in adult Wistar rats. Number of diarrhoea in different groups and the purging index was calculated in castor oil induced diarrhoea while the volumes of intestinal content in the castor oil induced enteropooling test. This study revealed that the aqueous extract has significant antidiarrhoeal effect at both the doses as the mean number of defecation was reduced significantly in treated group in comparison to control. Inhibitory activity against castor oil induced enteropooling was also found to be significant as compared to control group.[46] One more study was done on aqueous extract (73 mg) and (125 mg/kg), against charcoal induced gut motility. The distance travelled by charcoal was found to be reduced significantly in treated groups at both the doses when compared to control. The study suggests that *Calotropis gigantea* root bark possesses significant antidiarrhoeal activity.[47]

Antivenom activity

The methanolic extract of *Calotropis gigantea* was evaluated for its efficacy to neutralize various effects of the venom (*Vipera russelli*) like lethality, necrotizing activity, edema and haemorrhagic activity. Oral administration of extract at 200 and 400 mg/kg effectively neutralized the lethal effect of 2LD50 and 3LD50 of venom in mice (*in-vivo* neutralization). In *in vitro* studies, the plant extract at 100, 200 and 400 mg/kg effectively neutralized 2LD50 and 3LD50 of venom. Effective inhibition of induction of haemorrhage and necrosis was also observed. At doses 200 and 400 mg/kg, the antinecrotic effect of plant extract was significant. The effect of methanolic extract against edema induced by viper venom was studied at 60, 120, 180 and 240 minutes. Plant extract at dose levels 200 mg/kg and 400 mg/kg showed significant anti-inflammatory activity at 240 min, and effect was comparable with that produced by the standard antivenom.[48]

Anthelmintic activity

Aqueous and alcoholic extracts (20, 40, 80 and 100 mg/ml) of peeled roots of *Calotropis gigantea* were tested in *Pheretima posthuma* for paralysis and death time of individual earth worm. The observation shows that the test drug were able to produce dose related paralysis and death in earth worms. The effect of 20, 40, and 80 mg/ml was quite close to that of standard drug albendazole. At the same time 100 mg/ml had almost same effect as that of 80 mg/ml albendazole. Moreover, the study revealed that the aqueous extract was found to be more effective than alcoholic extract.[49]

Anti viral activity

A new lignan glycoside isolated from the latex of *Calotropis gigantea* viz. (+)-pinoresinol 4-O-[60-O-vanilloyl]-b-D-glucopyranoside (1) and two known phenolic compounds, 69-O-vanilloyltachioside (2) and 69-O-vanilloylisotachioside (3) and one authentic compound, (+)-pinoresinol 4-O-b-D-glucopyranoside, were screened for A/PR/8/34 (H1N1) inhibitory activity by cytopathic effect (CPE) inhibition assay on MDCK cells. Compound 1 showed inhibitory activity against A/PR/8/34 (H1N1). This was further evaluated for *in vitro* inhibitory activities against a panel of human and avian influenza viruses by CPE inhibition assay. It showed inhibitory effect against human influenza viruses also in both subtypes A and B while had no effect on avian influenza viruses. Additionally its activity against human influenza viruses subtype A was further confirmed by plaque reduction assay. The time course indicated by assay showed that compound 1 exerts its antiviral activity at the early stage of viral replication. A mechanistic study showed that compound 1 efficiently inhibited influenza virus-induced activation of NF-kB pathway in a dose-dependent manner, but had no effect on virus-induced activation of Raf/MEK/ERK pathway. Further studies demonstrated that nuclear translocation of transcription factor NF-kB induced by influenza virus was significantly blocked by 1, meanwhile, nuclear export of viral ribonucleoproteins was also effectively inhibited.[50]

Toxicity

If taken orally above the therapeutic dose causes nausea, vomiting and diarrhoea. Prolonged higher doses cause headache, burning micturition[3] and weakens the intestine.[7] In pregnant women it may lead to abortion, injurious to liver and lungs.[9, 51]

CONCLUSION

The various parts of *Calotropis gigantea* Linn. Plant viz. root, root bark, leaves, flower, milk are used ethnomedicinally as a remedy for various diseases of human beings. The present review tries to collect the morphological description, therapeutic uses mentioned in Unani system of medicine, ethnopharmacological reports and all the pharmacological studies conducted on the plant along with its phytochemistry. These findings justify the relevance of plant in traditional medicine and also provide a platform for further investigations to investigate the pharmacological and therapeutic potential of the plant.

CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest.

REFERENCES

1. Singh U, Wadhwani AM, Johri BM. Dictionary of Economic Plants of India. New Delhi: Indian council of Agricultural Research; 1996:38-39.
2. Chatterjee A, Pakrashi SC. The Treatise on Indian Medicinal Plants. V-IV. New Delhi: National Institute of Science Communication and Information Resources; 2003: 128-129.
3. The Wealth of India. Council of Scientific & Industrial Research New Delhi. A dictionary of Indian Raw materials & Industrial products Raw materials, Ca-Ci, (Revise). V-III. New Delhi: 1992: 79-80.
4. Misra MK, Mohanty MK, Das PK. Studies on the method – ethnobotany of *Calotropis gigantea* and *C. procera*. *Ancient science of life.* 1993; Xiii (1 & 2): 40-56.
5. Sharma N, Shankar R, Gupta N, Prakash P. A preliminary phyto-pharmacognostical evaluation of *Calotropis gigantea* (L.) R. Br. (Alarka or Mandara) Root. *International Journal of Ayurvedic Medicine.* 2016; 7(1): 44-48.
6. The Unani pharmacopoeia of India. V-I, Part 1. New Delhi: CCRUM; 2007: 3-4.
7. Dioscroides. Kitabul Hashaish. (Manuscripts). Patna Khuda Baksh library. V-II. 305, 1080.
8. Ibne Baitar. Al-Jam ul Mufridate Al Advia wa Al-Aghzia.V-III. New Delhi: CCRUM; 1999: 275-276.
9. Najmul Ghani. Khazainul Advia. New Delhi: Idara Kitabul Shifa; (YNM): 175-178.
10. Kabiruddin H. Makhzanul Mufridat. New Delhi: Aijaz Publishing House; (YNM): 49-52.
11. Ibne Sina. Al Qanoon Fil Tib Book II. New Delhi: Jamia Hamdard; 1998: 42, 49, 51, 75, 81, 417.
12. Hakeem A. Bustanul Mufridat. New Delhi: kitabul Shifa; 2002: 78.
13. Zakai I. Encyclopedia of Unani Mufrida. V-1. New Delhi: Aijaz Publishing House; 2000: 14-15.
14. Asolkar LV, Kakkar KK, Chakre OJ. Glossary of Indian Medicinal Plants with active Principles (Second supplement). Part-1. New Delhi: (A-K), (1965-1981) National Institute Of Science Communication and Information Resources (CSIR); 2005: 157.
15. Lindley J. Flora Medica. A Botanical Account of All the more important Plants Used in Medicine. Delhi: Ajay Book Service India; 2001: 540.
16. Bhat HR. A field guide to the Medicinal Plants of Devarayanadurga State Forest. Karnataka Forest Department, Tumkur; 2000; 37.
17. Medicinal Plants in Folklores of Bihar and Orissa. CCRUM, Ministry of Health & Family Welfare, Govt of India. Department of Indian system of Medicine and Homeopathy; 2001: 119-120.
18. Medicinal Plants of Andhra Pradesh. Part. I. CCRUM, Ministry of Health and Family Welfare, Govt. of India; 1999: 28.
19. Dymock W, Warden CJH. Hooper D. Pharmacographica Indica. V-II. New Delhi: Srishti Book Distributors; 2005: 429-436.
20. Chopra RN. Glossary of Indian Medicinal Plant. New Delhi: National Institute Science communication and information Resources (CSIR); 2002: 46.
21. Gupta J, Ali M. Faculty of Pharmacy. Jamia Hamdard, P.O. Hamdard Nagar. New Delhi 2000; 62 (1); 29-32.
22. Daniel M. Medicinal plants: chemistry and properties. Oxford & IBH publishing: New Delhi; 2006: 131.
23. Rastogi Ram. P. Compendium of Indian Medicinal Plants. V-III. Lucknow: Central Drug Research Institute & National Institute of Science Communication; 2001: 118.
24. Rastogi Ram. P. Compendium of Indian Medicinal Plants. V-IV. Lucknow: Central Drug Research Institute & National Institute of Science Communication; 2002: 137.
25. Habib MR, Karim MR. Effect of anhydrosophoradiol-3-acetate of *Calotropis gigantea* (Linn.) flower as antitumoric agent against Ehrlich's ascites carcinoma in mice. *Pharmacological Reports*. 2013; 65: 761-767.

26. Nalwaya N, Pokharna G, Deb L, Jain NK. Wound healing activity of latex of *Calotropis gigantea. International Journal of Pharmacy and Pharmaceutical Sciences.* 2009 July-Sep; 1(1): 176-181.
27. http://gyti.techpedia.in/project-detail/effect-of-latex-from-calotropis-gigantea-on/237.
28. Bulani V, Biyani K, Kale R, Joshi U, Charhate K, Kumar D, Pagore R. Inhibitory effect of *Calotropis gigantea* extract on Ovalbumin-induced airway inflammation and arachidonic acid induced inflammation in a murine model of asthma. *Int J Cur Bio Med Sci*. 2011; 1(2): 19-25.
29. Prabhu S, Priyadharshini P, Veerave R. Effect of aqueous extracts of different plant parts of milkweed plant (*Calotropis gigantea* R. Br.) against ovicidal activity on *Helicoverpa armigera* (Hubner). *International Journal of Advanced Life Sciences.* 2012 Feb-April; 2: 39-44.
30. Pathan AK, Pathan MK, Garud N, Garud A. Effect of some novel medicinal plants and polyherbal formulation on stress induced alopecia. *Pharmacologyonline*. 2012; 3: 150-157.
31. Bharathi R, Thomas A, Thomas A, Krishnan S, Ravi TK. Anti bacterial activity of leaf extracts of *Calotropis gigantea* Linn. against certain gram negative and gram positive bacteria. *Int. J. Chem. Sci.* 2011; 9(2): 919-923.
32. Kumar G, Karthik L, Rao KV. Antibacterial activity of aqueous extract of *Calotropis gigantea* leaves – an *in vitro* study. *International Journal of Pharmaceutical Sciences Review and Research*. 2010 September-October; 4(2): 141-144.
33. Seniya C, Trivedia SS, Verma SK. Antibacterial efficacy and phytochemical analysis of organic solvent extracts of *Calotropis gigantean*. *Chem. Pharm. Res.* 2011; 3(6): 330-336.
34. Hossain SF, Islam MS, Parvin S, Shams T, Kadir MF, Islam SMA, et al., Antimicrobial screening and brine shrimp lethality bioassay of *Calotropis gigantea* (Fam: Asclepiadaceae). *J. Nat. Prod. Plant Resour*. 2012; 2(1): 49-59.
35. Kumar G, Karthik L, Rao KVB. Antimicrobial activity of latex of *Calotropis gigantea* against pathogenic microorganisms-an *in vitro* study. *Pharmacologyonline.* 2010; 3: 155-163.
36. Elakkiya LP and Prasanna G. Study on phytochemical screening and *in vitro* antioxidant activity of *Calotropis gigantea*. *IJPRIF*. 2012; 4(4): 1428-1431.
37. Jagtap VA, Usman MRM, Salunkhe PS, Gagrani MB. Anti-inflammatory activity of *Calotropis gigantea* Linn. leaves extract on *In vitro* models. *IJCPR*. 2010; 1(2):1-5.
38. Ravi RG, Harikesh D, Chandrasekhar TR, Pramod YG, Angad PM. Cytotoxic activity of ethanolic root extract of *Calotropis gigantea* Linn. *Int. J. Drug Dev. & Res.* Oct-Dec 2011; 3(4): 101-108.
39. Sheelaa B, Hussain SM, Kumar PS, Kalaichelvam VK, Venkatachalam VK. Vasodilatation Effect of Latex from *Calotropis gigantea* in Green Frog *Rana hexadactyla. Asian Journal of Medical Sciences.* 2010; 2(1): 22-24.
40. Usmani S and Kushwaha P. Hepatoprotective activity of extracts of leaves of *Calotropis gigantea*. *Asian Journal of Pharmaceutical and Clinical Research.* 2010; 3(3): 195-196.
41. Alam MA, Habib MR, Nikkon F, Khalequzzaman M, Karim MR. Insecticidal activity of root bark of *Calotropis gigantea* L. against *Tribolium castaneum* (Herbst). *World Journal of Zoology*. 2009; 4(2): 90-95.
42. Khan IN, Sarker MMI, Ajrin M. Sedative and anxiolytic effect of ethanolic extract of *Calotropis gigantean* (Asclepiadaceae) leaves. *Asian Pac J Trop Biomed*. 2014; 4: S400-S404.
43. Rathod NR, Chitme HR, Irchhaiya R, Chandra R. Hypoglycemic effect of *Calotropis gigantea* Linn. leaves and flowers in streptozotocin-induced diabetic rats. *Oman Medical Journal.* 2011; 26(2): 104-108.
44. Pathak AK, Argal A. Analgesic activity of *Calotropis gigantea* flower. *Fitoterapia* 2007 Jan; 78(1): 40-42.
45. Chitme HR. Chandra R. Kaushik S. Studies on anti-diarrhoeal activity of *Calotropis gigantea* R.BR. in experimental animals. *J Pharma Pharmaceutical sci*. 2004; 7(1): 70-75.
46. Ali R, Amin KMY, Ahmad G, Wadud A, Jahan N. Efficacy of post *Beekhe Madar* (*Calotropis gigantea*) root bark in experimentally induced diarrhoea. *Hippocratic journal of Unani medicine.* 2010 July September; 5(3): 1-8.
47. Ali R, Jahan N, Amin KMY. Anti diarrhoeal activity of *Calotropis gigantean* root bark in experimental animals. *Journal of research in Unani medicine*. 2012; 1(1):1-5.
48. Chacko N, Ibrahim M, Shetty P, Shastry CS. Evaluation of antivenom activity of *Calotropis gigantea* plant extract against *Vipera russelli* snake venom. *IJPSR*. 2012; 3(7): 2272-2279.
49. Argal A, Sachan R. Anthelmintic activity of *Calotropis gigantea* roots. *Journal of Pharmacy Research.* 2009; 2 (6): 1085-1086.
50. Parhira S, Yang ZF, Zhu GY, Chen QL, Zhou BX, et al. *In vitro* anti-influenza virus activities of a new lignan glycoside from the latex of *Calotropis gigantea*. PLOS ONE. 2014; 9(8): 1-13.
51. Husain SG. Tarjumae Qanoon Sheikh Abu Ali Sina. Lucknow: Munshi Naval Kishore. YNM; 178.