

A Review on Phytochemical and Ethnomedicinal Profile of *Calotropis procera* Linn.

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ABSTRACT

Medicinal plant continues to provide newer lead compounds against various pharmacological targets and considered as the prime source of bioactive compounds for the new drug discovery. Due to the presence of active principles, interest in medicinal plants is undergoing in a renaissance. *Calotropis procera* Linn. (Family: Asclepiadaecae) is a common medicinal plant in Bangladesh, locally known as Akondo. The plant is reputed among the rural people due to its wide applications in traditional folk medicines. Considering its potential, the plant is used in the treatment of various respiratory and gastrointestinal disorders as well as ailments in headache, inflammation, fever, paralysis, rheumatism, vertigo, leprosy, dropsy, penile dysfunction, elephantiasis, helminthiasis, menorrhoea, snake poisoning, baldness, eczema and other skin diseases. Plant possesses significant amount of phytoconstituents like alkaloids, flavonoids, glycosides, phenolics, phytosterols, triterpenes, cardenolides and other promising phytoconstituents. Moreover, the plant has anti-inflammatory, anti-helminthic, anti-diarrhoeal, anti-dysenteric, antifertility, antimicrobial, antioxidant, antipyretic, spasmolytic, antiasthmatic, antimalarial, analgesic, antinociceptive, anticonvulsant, anti-tumor, antidiabetic, wound healing and hepatoprotective activities. The aim of the present study was to compile the geographical distribution, ethnomedicinal uses, phytoconstituents and pharmacological activities as well as to underscore the future prospects of the plant in isolating potential lead compounds for new drug discovery and development.

Keywords: Akondo, ethnomedicinal uses, cardenolides, calotropin, calotoxin.

1. INTRODUCTION

Affliction is as old as life itself and man has always been in search for agents to cure various ailments. Medicinal plants have been used as a potential source of medicinal agents and to alleviate human sufferings since antiquity. Even though modern medicine is the marvel of the world as well as blessings for human kind, a large number of people especially who are living in the rural areas depend solely on traditional medicine to eradicate their sufferings and relieve various diseases and disorders. This is due to the side effects of the synthetic drugs and also the glorious history of medicinal plants in curing various diseases and disorders. Plants, the molecular architect play an important role in identifying the lead compounds for new drug discovery through both synthetically and

from that of natural origin. Plants contain compounds having interesting skeleton and the bioactivity guided phytochemical investigation of medicinal plants may yield newer chemical constituents of remarkable therapeutic interest. Thus, phytotherapy laid the foundation stone of all form of medical treatment that are in practice today [1].

Calotropis procera Linn. is an important medicinal plants locally known as Akondo. Depending on different territories, it is also known as Sodom apple, desert apple, giant milkweed and Sodom's milkweed. It is a shrub or small tree attaining up to 3 to 5 m in height. It is native to the South Asia, Western Asia, North Africa, and Tropical Africa. The plant is widely disseminated throughout Bangladesh and India. In the indigenous

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system of medicine, different parts of the plant such as leaves, flowers, fruits, seeds, barks, roots, root bark and latex are used extensively to cure various diseases. Moreover, milky juice of the plant is used traditionally in the treatment of gastrointestinal, respiratory and sexual complications [2, 3]. It has attracted the attention of scientists due to its wide ethnomedicinal uses in various ailments by the rural people of Indian subcontinent. The plant possesses significant amount of phytochemical compounds like alkaloids, flavonoids, glycosides, terpenoids, saponins, tannins, steroids and other promising phytoconstituents [4]. Additionally, a large number of propitious bioactive compounds have been isolated from this plant. Several reports are available revealing anti-inflammatory, anti-helminthic, anti-diarrhoeal, anti-dysenteric, antifertility, antimicrobial, antioxidant, antipyretic, spasmolytic, antiasthmatic, antimalarial, analgesic, antinociceptive, anticonvulsant, anti-tumor, antidiabetic, wound healing and hepatoprotective activities of the plant [5-9]. This comprehensive review is a conglomeration of the geographical distribution, ethnomedicinal uses, isolated phytochemical constituents and pharmacological potentials of the species *C. procera*.

2. BOTANICAL FEATURE

2.1 Habitat

The generic name *Calotropis* comes from Kalos means beautiful and Tropis means keel indicating the beauty of the keel of flower [10]. It possesses about six species of shrubs. *C. procera* is a tropical plant growing wild in warm climate up to an altitude of about 1050 meters. It occurs in most parts of the tropical world, in waste lands, dry sandy and alkaline soils, and grows rampantly as a weed [11]. They are salt-tolerant, drought-resistant and seeds are dispersed through animals and wind. It grows well in sandy soil in the low rainfall territory. The plant is distributed widely throughout the road and riversides of Bangladesh and India and also occurs in China, Malaysia, Indonesia, Australia, Africa, Central and South America, Egypt, and Caribbean Island as wasteland weed [10]. The species grows in overgrazed pastures, beachfront dunes and roadsides. It occurs in dry territory nearly about 150 to 1000 mm precipitation and sometimes in highly drained soils in region with

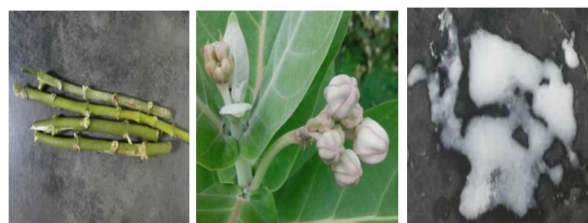
annual precipitation of about 2000 mm. It entrenches very deeply and sporadically grows in soils shallow over unfractured rock. It acts as soil binder and helps to meliorate the soil water conditions. The plant is a suitable indicator of debilitated soil.

2.2 Morphology

The plant is a highly branched small perennial shrub attaining up to 3 to 5 m in height. It is covered with soft tomentum. Leaves are stalkless, opposite, oblong-ovate covering with soft pubescent hair and about 7 to 18 cm long and 5 to 13 cm broad. Leaves possess 4 to 6 pairs of sub-opposite nerves visible on the dorsal surface, an acute apex, and sessile base [12]. They are pale green in color. They have a small pointed tip at the end and a heart-shaped base clasping the stem. Bark is corky, soft and light grey in color [13]. Flowers are umbellate-convex covering with densely matted filaments. They are more or less tubular having five lobes and 2-3 cm in diameter. Usually they are white to pink in color. Fruits are fleshy, grayish green in color and 8-12 cm long. They contain umpteen small, flattened seeds with long white hairs at one end. Seeds are brown in color and 8-10 mm long. Roots are bitter in taste, white-grey in color having wrinkles and curved woody appearance. The plant parts discharge white milky latex when cut [12]. Various parts of the plant are presented in (figure 1).



Whole plant with leaves



Twigs

Flowers

Latex

Figure 1: Various Parts of *C. procera*

3. ETHNO-MEDICINAL USES

Ethnomedicinal uses of medicinal plants is based on the addition of knowledge, skills, and traditional practices depending on the beliefs, theories, and experiences indigenous to a certain culture or community for the betterment of the health, and prevention of various ailments [14]. From decades to decades, man has used the medicinal plants for keeping better health and as the remedy of their sufferings. This knowledge of medicinal plants has been bequeathed generation to generation over the centuries. Use of medicinal plants as drugs in Traditional systems of medicine (TSM) has been of great implication because it provides as a great source of lead compounds for the discovery of new drugs. The lead compounds are isolated from the medicinal plants in crude or purified form by using various separation techniques. Thus, the ethnomedicinal uses of medicinal plants have been playing a remarkable role in the discovery of modern medicines over the centuries.

In the developing countries like Bangladesh where a large number of people live in rural areas are depending on the Traditional Health Practitioners (THPs) for their primary health care. THPs treat the rural people by using their knowledge, beliefs and experiences on medicinal plants. *C. procera* is a common medicinal plant to the rural people of Bangladesh. This plant is widely used by the rural people of Bangladesh and India in various disorders.

The plant has been used as purgative, digestive, emetic, expectorant, sedative, anthelmintic and blood purifier; also used as an antidote for snake poisoning as well as for the treatment of leprosy, ulcers, tumors, dysentery, boils, eczema, piles and diseases of liver, spleen and abdomen [15]. Leaves are used in cold, cough [16] and are applied warmly to the abdomen to mitigate pain inside [17]. In the treatment of migraine, tender leaves of the plant are used; to promote sexual health

including penile dysfunction; dried leaves are used and are reputed to be an aphrodisiac [2]. The dried leaves are used in the treatment of paralysis and rheumatic pains [18]. Powered obtained from leaves are used in fast wound healing as well as to treat liver problems, indigestion and skin disorders. Hot poultices are made from the leaves and applied to the stomach to mitigate pain and headaches and also applied to wrenches to ease the swelling and pain [2]. The pungent sap latex of the plant is used in the treatment of skin disorders such as boils, infected wounds of human and animals [19]. Latex is used in scorpion bite [16], dropsy, leprosy and taeniasis [20]. It is also used as a masticator [21]. In the treatment of hair fall, baldness, vertigo, intermittent fevers and rheumatoid swellings the latex of the plant is widely used in rural areas [19]. Moreover, it possesses antiseptic [22], laxative [23] and abortifacient properties [24]. The latex is used for treating ringworm, guinea worm blisters, scorpion stings, venereal sores and ophthalmic disorders; the local effect of the latex on the conjunctiva is congestion, epiphora and local anaesthesia [25].

The milky juice and caustic flowers are beneficial in indigestion and catarrh [26]. Bark and wood stimulate lactation in cattle [25]. The dried root is used to cure asthma, leprosy, eczema and elephantiasis. It is used as eye tonic and to cure hepatic and splenic enlargement [19]. Roots are beneficial in asthma, cough [27, 28], fever and swellings [29]. A root paste mixed with the leaves of *Ocimum sanctum* is taken orally to relieve menorrhoea [32]. Paste of root bark with rice vinegar is applied to elephantiasis of the scrotum, and legs [33]. The capsulated root bark powder is found to be effective against asthma, diarrhea [34].

After conducting a literature survey, a comprehensive list of the ethnomedicinal uses, along with their routes of administration and mode of preparation is presented in Table 1.

Table 1: Ethnomedicinal uses of *C. procera*

Part(s) Used	Mode of preparation	Mode of administration	Medicinal use (s) in Common diseases and features	Disease category	Ref.
Leaves	Decoction	Oral	Cold, Cough	Respiratory disorders	[16]
	Hot decoction	Topical	Abdominal pain	Inflammation and pain	[17]
	Powder	Topical	Wounds, Skin disorders	Dermatological problems	[2]
	Powder	Oral	Indigestion	Gastrointestinal problems	[2]
	Powder	Oral	Liver problems	Liver disorders	[2]
	Decoction	Oral	Penile dysfunction	Sexual complications	[2]
	Hot poultices	Topical	Stomach pain	Stomach disorders	[2]
	Hot poultices	Topical	Headaches, Swelling	Inflammation and pain	[2]
	Paste	Topical	Paralysis, rheumatic pain, and Pain	Inflammation and pain	[18]
	Tender leaves	Topical	Migraine	Inflammation and pain	[2]
Roots	Decoction	Oral	Bronchitis, cough, asthma	Respiratory disorders	[19,34]
	Paste	Topical	Leprosy, eczema	Dermatological problems	[19]
	Paste	Topical	Elephantiasis	Inflammation and pain	[19,20]
	Decoction	Oral	Hepatic and spleic enlargement	Hepatic disorders	[19]
Latex	Toothbrush	Oral	Toothaches	Oral infection	[16]
	Decoction	Oral	Rheumatoid / joints swellings, and paralysis, rheumatism	Inflammation and pain	[19,20]
	Paste	Topical	Boils, infected wounds, Parasitic skin infestation, Skin problems	Dermatological problems	[19,21,25]
Flowers	Milky juice	Oral	Indigestion, Lack of appetite	Gastrointestinal disorders	[26]
	Milky juice	Oral	Catarrh	Respiratory disorders	[2, 26]
	Juice	Oral	Abortion in women	Sexual complications	[3]
Twigs	Decoction	Oral	Edema	Inflammation and pain	[25]
	Decoction	Oral	Stomach disorders	stomach disorders	[25]
	Decoction	Oral	Diarrhoea	Gastrointestinal disorders	[25]

4. PHYTOCHEMICAL ANALYSIS

Mangroves are biochemically unique due to distinctive ecology and extreme tropical environmental conditions having multifarious bioactive compounds. These propitious compounds are mainly responsible for wide array of pharmacological activities exerted by the mangrove plants. In fact, mangrove plants contain secondary metabolites such as alkaloids, phenolic compounds, terpenoids, glycosides and steroids which could be the potential lead compounds facilitating new drug discovery.

α - and β -amyrin are pentacyclic triterpenes, widely

distributed in nature and have been isolated from a variety of plant sources. Several reports are available that revealed their anti-inflammatory effects. A study indicates that a mixture of α and β -amyrin might be beneficial in Inflammatory Bowel Disease (IBD). By modulating local cytokines and reducing COX-2 expression through the inhibition of NF- κ B and CREB-signaling pathways, α and β -amyrin exerts its anti-inflammatory effects [35].

α -Amyrin acetate (obtained from *Tylophora hirsuta*) exerted antispasmodic activity on spontaneous rabbits jejunum preparations while it can was tested positive also on KCl-induced contractions. Thus, the compound is proved to be beneficial against diarrhoea, dysentery and other gastrointestinal disorders [36]. Additionally, in STZ-induced diabetic rats, α -Amyrin acetate (isolated from *Ficus benghalensis*) lessened hyperglycemia and improved diabetic conditions [37].

The plant contains a novel dietary triterpene, lupeol which could be the possible compounds for which the medicinal plants exerted multifarious pharmacological activities. Lupeol is reported to have the potential to reduce IL-4 by T-helper type-2 [38]. In addition, another study suggested that it could act as a shield against metal toxicity leading to cancer [39]. By activating caspase-3 through down-regulation of death receptor 3, it also inhibits the growth of SMMC7721 cells along with apoptosis [40].

Compounds are isolated from various parts of the plants using different chromatographic techniques and spectroscopic methods like UV, IR, NMR and Mass. After conducting a literature survey, a number of phytochemical compounds including glycosides, flavonoids, triterpenes, triterpenoids, phytosterols, phenolics, saponins, alkaloids, cardiolides and other multifarious compounds have been found from the different parts of *Calotropis procera*. The isolated and characterized compounds are tabulated in Table 2 whereas structures of some selected phytochemical constituents are presented in Figure 2.

Table 2: List of some selected phytochemical constituents isolated from *C. procera*

SL.	Name of the Compounds	Parts Used	References
1	Acetic acid	Root bark	[41]
2	Akundarol isovalerate	Root	[42, 43]
3	Alactuceryl isovalerate	Flower	[44, 45]
4	α -Amyrin	Root bark	[41]
5	α -Amyrin acetate	Root bark, Root	[41]
6	α -Amyrin benzoate	Root bark, Sap	[41]
7	β -Amyrin	Root bark, Latex	[41]
8	β -Amyrin acetate	Root bark	[41]
9	β -Amyrin benzoate	Root bark	[41]
10	Asclepin	Root	[41]
12	1, 2-Benzene dicarboxylic acid, diisooctyl	Leaves	[4]
13	1, 2-Benzene dicarboxylic acid-dimethylester	Leaves	[4]
14	Bicycloheptane, 7-butyl	Leaves	[4]
15	Bis-(3, 5, 5-trimethylhexyl)-ether	Leaves	[4]
16	β -Bisabolene	Leaf essential oil	[49]
17	Butane, 2,2-dimethyl	Leaves	[4]
18	Calactin	Leaves, Latex	[35, 47]
19	Calotoxin	Leaves, Latex	[35, 47]
20	α -Calotropeol	Flower, Latex	[42]
21	Calotropin	Leaves, Latex, Seed	[35, 47]
22	Calotropriedelenyl acetate	Root	[41, 42]
23	Calotropursenyl acetate	Root	[42, 43]
24	Caryophyllene	Leaf essential oil	[46]
25	Caryophyllene oxide	Leaf essential oil	[46]
26	Caoutchouc	Latex	[46]
27	α -Cedrol	Leaf essential oil	[46]
28	L- glutamic acid	Leaves	[4]
29	Lupeol	Flower, Latex	[43]
30	Olean-5, 13(18)-dien-3 α -ol	Root	[43]
31	Olean-13(18)-en-9 α -ol	Root	[43]
32	Olean-13(18)-en-3 β -yl acetate	Root	[43]
33	Stigmasterol	Flower	[48]
34	Uscharin	Leaves, Latex	[2]

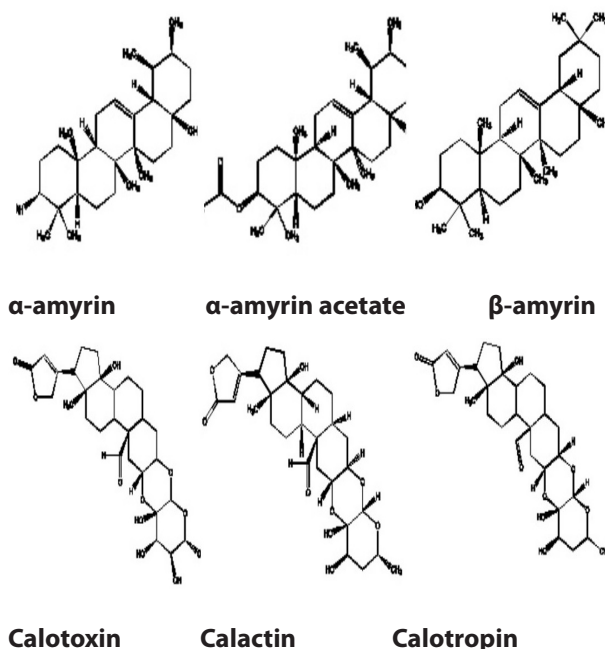


Figure 2: Some of the selected phytoconstituents isolated from *C. procera*

5. FUTURE PROSPECTS FOR MEDICINAL DISCOVERIES

C. procera contains a multitude of compounds, which can be potentially of therapeutic value, considering the various traditional uses of various parts of the plant. In the traditional medicinal system of the Indian sub-continent, namely Ayurveda, the plant is used for bronchial asthma, dyspepsia, flatulence, epilepsy, painful joints and swellings. Within the confines of Bangladesh, the plant is ethnomedicinally used mainly for treatment of pain [49, 50]. Thus the various components of the plant can be pharmacologically tested to validate the traditional uses of the plant.

A recent review has pointed out that lupeol has a potential to act as an anti-inflammatory, anti-microbial, anti-protozoal, anti-proliferative, anti-invasive, anti-angiogenic and cholesterol lowering agent [51]. Lupeol has also been reported to have antioxidant and antidiabetic properties [52]. Thus, the compound may prove to be a potential therapeutic agent for infectious diseases, cancer and diseases with oxidative stress like diabetes or diseases with chronic pain and inflammation like rheumatoid arthritis. Diseases like cancer, diabetes or rheumatoid arthritis are not curable

or difficult to cure with current allopathic drugs. Many infectious diseases are also getting difficult to cure with existing medicines, because of development of drug-resistant vectors. β -Sitosterol is a phytosterol, and such phytosterols reportedly may have a number of health and therapeutic benefits like treatment of benign prostatic hyperplasia [53], anticancer activities [54], protection against peptic ulceration [55] and atherosclerosis [56].

Taken together, *C. procera* can be considered as a plant from which many potential drugs can be discovered against various diseases like cancer, heart disorders, pain, helminthiasis, liver disorders, diabetes and inflammatory diseases like rheumatoid arthritis.

6. CONCLUSION

Various ethnomedicinal uses of the plant like against helminthiasis, liver diseases, pain, and as an abortifacient have already been validated by medical science. New uses have been suggested through reports on phytoconstituents of the plant and their anticancer and antidiabetic activities. Besides, the majority of the phytoconstituents of the plant remain to be scientifically studied regarding their bioactivity profiles. Since the plant contains numerous phytoconstituents, it is expected that in future, many more potentially therapeutic uses of the plant will be discovered. Modern scientists can also make use of traditional medicinal preparations containing the plant in Ayurvedic and Unani medicine and gather useful information on the pharmacological effects and efficacy of such drugs containing the plant.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

All authors participated in writing the manuscript through group discussions, searching data bases for available data, and confirming the accuracy of references. All authors edited the manuscript and read and approved the final manuscript.

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