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Moumita Saha

Department of Pharmacy,
BRAC University, Mohakhali,
Dhaka, Bangladesh

Moni R Saha

Masters of Public Health
Program, Torrens University
Australia

Taslima Begum

Department of Pharmacy,
Primeasia University, Banani,
Dhaka, Bangladesh

Rayhana Begum Department
of Pharmacy, Primeasia
University, Banani, Dhaka,
Bangladesh

Pritesh Ranjan Dash

Department of Pharmacy,
Primeasia University, Banani,
Dhaka, Bangladesh

Corresponding Author:

Pritesh Ranjan Dash

Department of Pharmacy,
Primeasia University, Banani,
Dhaka, Bangladesh

Phytoconstituents and biological activities of *calotropis gigantea*: A review

Moumita Saha, Moni R Saha, Taslima Begum, Rayhana Begum and Pritesh Ranjan Dash

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Abstract

Calotropis gigantea (CG) widely known as milk weed, is a valuable Apocynaceae medicinal herb that is still underutilized despite its wide range of pharmacological effects. Its traditional therapeutic virtues have made it popular in Southeast Asian countries. It is commonly used to treat inflammation as a traditional medication, analgesic, mosquito repellent, antimicrobial, antioxidant, diabetes mellitus, cancer and the ability to cure wounds we analyzed all of the published information on the phytoconstituents isolated from the plant, as well as the pharmacological qualities of this remarkable herb, in order to emphasize its efficacy and potential.

Keywords: *Calotropis gigantea*, phytochemical compounds, pharmacological properties

Introduction

Calotropis gigantea (CG), an Apocynaceae family member, is known in English as giant caltrops or crown flower and in Bengali as Dudh akond. It is native to Bangladesh and is found mainly in India, Southeast Asia, Malaysia, the East Indies, Thailand, Asia, China, Nepal, Pakistan, and tropical Africa (Haque *et al.*, 2012). CG grows up to 3–4 m tall with a shrub and has smooth latex and fiery debris colored bark. The leaves are opposite, decussate, sessile or sub sessile. The blossom is 2–4 cm in diameter, purplish white, with natural product follicles that are 9–10 cm in length, broad, thick, and succulent, as well as seeds that are abundant and 6 by 5 mm in size, broadly oval. Plano-convex (Ishnava *et al.*, 2011).

Medicinal plants or medicinal herbs are consisting of bioactive phytochemical constituents that deliver unequivocal physiological and pharmacological activities on human body or creature body. They provide health promoting characteristics, transitory help from symptomatic issues or healing properties based on a few ethno botanic information's, auxiliary metabolites are dynamic substance with natural movement. CG is traditionally being applicable to treat conditions such as viral infection, arthritis, acid reflux, snuffle, cold, dermatitis, respiratory problems, tonsillitis, drowsiness, nausea, and diarrhea. Numerous plant parts of CG were used in the folk medicine of Bangladesh to treat of ailments such as leaves for high blood sugar in diabetic patients or to relieve pain. The flowers are used for analgesic activity as well as antimicrobial and cytotoxic activity, anti-diarrheal, anti-candida, anti-bacterial, and anti-oxidant activities also anti-pyretic activity, insecticidal activity, wound healing activity, CNS activity, and pregnancy interceptive properties have been reported for roots. The Stem of this plant reportedly possess hepatoprotective effects as demonstrated by protection of liver of rats against carbon tetrachloride induced liver injury. The latex of this plant contain purgative properties, pro-coagulant activity, wound healing activity, as well as anti-microbial activity (Haque *et al.*, 2012). According to Ayurvedic studies, unani, siddha, or Sweta arka has been used as an elixir, cough suppressant, antidiarrheal, and antiparasitic since ancient times, and the powdered stem is used in asthma, bronchitis, and dyspepsia (Amutha *et al.*, 2018).

The CG plant produces a variety of phytochemical compounds such as and Calotropeol, amyirin, essential fats, crude oil, a combination of triterpenoid, polyphenols, calotropin amyirin, amyirin, taraxasterol, sit sterol, amyirin methylbutazone (Amutha *et al.*, 2018). The hereunder overview about the origins, photocatalysis, potency and medicinal properties of

CG with a desire of further developments in the pharmacological activities of the plant globally.

History:

The plant has been noticed as a rapidly expanding, drought resistant, salt tolerant plant native to the Asian continent and been presented as an ornamental herb in the Island Nations, Australia, Northeastern, and Latin America. Furthermore, milk weed is a common weed in poor waste areas, hillsides, railway tracks, and rural environments (Kumar *et al.*, 2010, Biswasroy *et al.*, 2020). Its flowers

are aromatic, and in some mainland Southeast Asian cultures, they are being used to produce 'floral tassels.' These plants' fibers are known as mudar or mader. In Ayurveda, the plant is known as aak. Calotropis plants are typically found in abandoned farmland. Cattle frequently avoid the plant due to its unpleasant taste and presence of Cardiac Glucosides in its sap (Palejkar *et al.*, 2012). In recent years, the plant has stimulated the interest of the research community as an origin of several effective phytochemicals, as well as a treatment for common ailments, and so on.

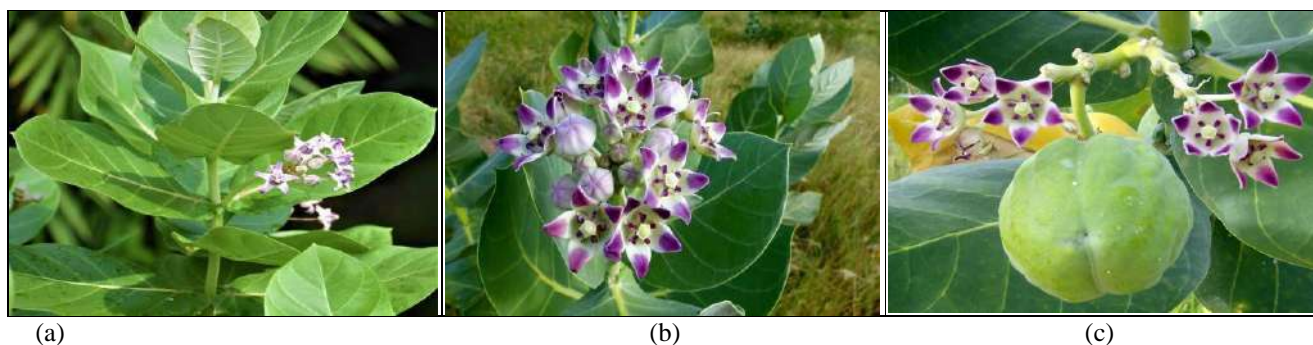


Fig 1: (a) Plant, (b) Flowers, (c) Fruit of *calotropis gigantea*

Taxonomical classification

Binomical name: *Calotropis gigantea* (L.) Dryland.

Scientific categorization:

Kingdom: plantae

Unranked: angiosperms

Unranked: Eudicots

Unranked: Asteroids

Order: Gentian ales

Family: Apocynaceae

Genus: *Calotropis*

Species: *C. gigantea*

Phytochemical constituents

A substantial amount of work has been utilized to find and extract the bioactive components of various CG extracts. Research has indicated that numerous compounds of the CG plant contain multiple active chemical constituents such as alkaloids, glucosinolates, saponins, phenolic, polyphenolic compounds, cardenolides 20, 21, flavones, terpenes 23, 24, sterols 25, proteolytic enzymes, also no protein (Kumar *et al.*, 2011, Supawadee *et al.*, 2016, Islam *et al.*, 2012). Table 1 lists some of the bioactive molecules discovered in the three different parts of CG (Kumar *et al.*, 2011).

Table 1: Important Phytoconstituents Isolated and Biological Activities of *Calotropis gigantea*

Plant parts	Chemical constituents	Chemical nature
Arial parts	Isorhamnetin-3-O-rutinoside, Isorhamnetin-3-O-Glucopyranoside	Flavonol
Latex	Glycosides 22, 23, 29 18-Norclerodane glucoside, Furanoid diterpene glucoside, Tinocordiside, Tinocordifolioside, Cordioside, Cordifolioside Syringin, Syringinapiosyl glycoside, Pregnane glycoside, Palmatosides, Cordifolioside A, B, C, D and E	Proteinases Triterpene esters
Flowers	Di-(2-ethylhexyl) Phthalate, Anhydrosophoradiol-3-acetate	Triterpenoids
Leaves	19-Nor- and 18,20-Epoxy cardenolides 15beta-hydroxycardenolides 16alpha-hydroxycalactinic acid methyl ester	Cardenolides
Root barks	Stigma sterol, β -sit sterol, Giganticness	Sterols Non protein amino acids

Pharmacological properties

Anti-cancer and Cytotoxic activity:

The anti-cancer, and cytoprotective ability of CG isolated from its flower and root is attributed to ethyl acetate, methanol, and ethanoic extracts of CG (Biswasroy *et al.*, 2020). Three cardenolide glycosides were isolated as cytotoxic principles from "Akond mul" (roots of *Calotropis gigantea* L.) calotropin (1), frugoside (2), and 4'-O-b D glucopyranosylfrugoside (3). The cytotoxicity of these compounds was tested against a variety of human and mouse cell lines. They indicate consistent cell line sensitivity to beta blockers such as statins and available resources: at 2 micrograms/ml, they are extremely poisonous to cell cultures but does not mouse cell lines. *Calotropis gigantea* sterols are extremely beneficial in the treatment of fatal ovarian cancer. Anticancer and cytotoxic

activity of *Calotropis gigantea* latex against renal cell carcinoma (Kumar *et al.*, 2012). This same water-soluble protein fraction of latex was tested and discovered to have potential antitumor effects against several cancerous cell lines. In an *in vivo* ehrlich ascites carcinoma study, the anticancer activity of this crude sample was taken. The highest inhibition of Ehrlich's melanoma cell growth was seen at 200 mg/kg (71.24%) (Kumar *et al.*, 2012, Habib *et al.*, 2011). New research has discovered, a *Calotropis gigantea* extract causes bactericidal activity in BT-549 cells in response to multiple other Human cell lines. Additionally, biomarker modification of such BT-549 specific supplement produced nine cardenolides, which are liable for the partial action (Pederson *et al.*, 2020). A further study found that CG waxy flower causes apoptotic cell death in A549 and NCI-H1299 leukemia cells by activating internal and external pathways, cell cycle progression, and oxidative

stress. As a result, CG could be used for the treatment of lung cancer (Jiyon *et al.*, 2019).

Anti-inflammatory activity

In the body, CG has anti-inflammatory properties. Its natural detoxification and purgative activity promote initial wound healing, pruritus, and epidermis and gall bladder abnormalities. In the body, CG has anti-inflammatory properties. Its natural detoxification and purgative activity promote initial wound healing, pruritus, and epidermis and gall bladder abnormalities. It has been reported that chloroform and ethanol extracts derived from the flower of CG have anti-inflammatory activity against sodium alginate oedema in Transgenic mice (Sarkar *et al.*, 2014, Kumar *et al.*, 2011). Its alkaloid fraction exhibits moderate inflammatory activity. The dairy obtained from plants as well as stem bark is effective for treating corn on the skin completely (Martha *et al.*, 2018). Besides that, the anti-inflammatory activity of the test compounds varied, with the highest activity occurring at 2 h. The anti-inflammatory activity of 400mg/kg of CG was greater than that of 100mg/kg of Ibuprofen when administered orally (Kumar *et al.*, 2011). The anti-inflammatory activity was evaluated in an in-vivo carrageen-induced rat paw-edema model for systemic infection, a cotton pellet-induced granuloma model for chronic inflammation, and an adjuvant-induced arthritis model (Singh *et al.*, 2014, Biswasroy *et al.*, 2020, Madhuri *et al.*, 2013).

Analgesic activity

An ethanol extract of CG flower along with bark has been shown to have analgesic activity against chemical and heat designs in rats (Biswasroy *et al.*, 2020, Singh *et al.*, 2014)^[9]. The anxiolytic activity was assessed for 90 minutes using an in-vivo ethanoic acid-induced convulsing test and thus the heating plate technique (Biswasroy *et al.*, 2020). The Oral treatment of 250 and 500 mg/kg of CG flower resulted in 20.97% and 43% analgesia, respectively (Biswasroy *et al.*, 2020).

Anti-diabetic activity

A study on CG leaves extract found that it significantly reduced blood glucose levels throughout glucose tolerance test with glucose-loaded mice. Oral doses of 100, 200, and 400 mg extract per kg body weight show more significant antihyperglycemic activity. The study also found that at these doses, the percent reduction in blood glucose levels was 21.35, 25.39, and 28.54 in comparison to control animals (Haque *et al.*, 2012). The chloroform extract derived from the CG flower and leaf substantially decreased LPO, SGPT, SGOT, alkaline phosphatase, cholesterol, and triglyceride levels. The Streptozotocin (STZ) induced model supported this study (Biswasroy *et al.*, 2020, Jaiswal *et al.*, 2014).

Hepatoprotective

The ethanolic extract of CG flower has significantly decrease the serum enzyme levels, when animal was treated with ethanol extract. The experimental design was done by in-vitro paracetamol induced hepatotoxicity (Biswasroy *et al.*, 2020).

Anti-nociceptive activity

The anti-nociceptive constituents were actively present in the methanolic extract of CG leaves which exerts same activity as aspirin (Haque *et al.*, 2012, Rahman *et al.*, 2015).

Antimicrobial activity

The CG leaf water - soluble, methanol, ethanol, and petroleum ether extracts have significant anti-candida activity against *C. albicans* and *Typhi*. The crude extracts anti-Candida activity was determined using the sodium alginate dilution method with some modifications. Its MIC values for *C. tropicalis*, *C. krusei*, *C. albicans*, and *C. parapsilosis* were 125, 250, 500, and 1000 g/ml, respectively. Methanol extracts had MIC values of 500 g/ml for *C. tropicalis* and *C. krusei* and 1000 g/ml for *C. albicans* and *C. parapsilosis*. Petroleum ether extracts had MIC values of 500 g/ml for *C. tropicalis* and 1000 g/ml for *C. albicans* and *C. krusei*, respectively. The aqueous extract of CG leaves also has bactericidal property against *Staph*, *Escherichia*, *Cereus*, *Pseudomonas*, *Micrococcus luteus*, and *Pneumonia*. The antibacterial activity of CG root bark methanol extract and fractions of petroleum ether, chloroform, and ethyl acetate has been demonstrated. The activity is measured using the in-vivo disk assay, in-vitro agar well, and agar wall diffusion methods. The zone of inhibition for *Escherichia coli*, *Bacillus subtilis*, and *Staphylococcus aureus* was found to be 23.5, 12.5, and 16.5 mm for the highest inhibition (14 mm), *Salmonella typhi* (14 mm), and *Shigellasonnei* (11mm). Methanol extract and its chloroform fraction were found to be active against *Sarcina lutea*, *B. megaterium*, and *P. aeruginosa*. Then, the petroleum ether fraction inhibited *B. subtilis* and *Shigella sonnei*, whereas the ethyl acetate fraction inhibited *P. aeruginosa* and *E. coli*. Furthermore, CG has been shown to have antifungal activity against plant pathogenic fungi such as *Fusarium mangiferae*, a serious threat to mango cultivation. *Candida Albicans* (3mg/disc.) and *Saccharomyces cerevisiae* (8mg/ml) demonstrated the highest antifungal activity and MIC, respectively, while *Candida Albicans* (1g/ml) demonstrated the lowest. Ethanolic extract inhibited the growth of *Aspergillus Niger* and *Trichoderma harzianum* (Kumar *et al.*, 2010; Biswasroy *et al.*, 2020; Kumar *et al.*, 2011; David *et al.*, 2011; Sarkar *et al.*, 2014; Ishnava *et al.*, 2011; Jp *et al.*, 2000).

Pregnancy interceptive properties:

The CG leaf extracts had 100% pregnancy interceptive activity at a dose of 100 mg/kg. The extract already illustrated guaranteed efficacy at a dose of 12.5 mg/kg when given on Days 1-5 and 1-7 postcoitum (Singh *et al.*, 2014, S.R *et al.*, 2007).

Procoagulant activity:

Procoagulant activity is attributed to CG latex. Furthermore, the proteins found in CG latex are highly proteolytic and are responsible for procoagulant activity (Kumar *et al.*, 2011, Singh *et al.*, 2014, Ravi *et al.*, 2005).

Antioxidant activity

CG leaf hydroalcoholic extract inhibits free radicals in DPPH (85.17 percent), nitric oxide scavenging (54.55 percent), TPC (6374.17 mg Gallic acid approximate weight), tannins (0.52 percent mg Gallic acid equivalent/dry weight), and flavonoids (46.9771.95 mg quercetin equivalent/dry weight) (Biswasroy *et al.*, 2020). The experimental design was carried out using an in DPPH free radical scavenging, Nitric oxide scavenging, reducing power assay, and in-vitro assay for total phenolic, flavonoids, and tannin contents

(Biswasroy *et al.*, 2020, Kumar *et al.*, 2011).

Anti-pyretic activity

In Albino Swiss rats and rabbits, a moisture: alcohol (50:50) concentrate of CG root was found to be effective against bacteria and TAB (Typhoid) vaccine stimulated anorexia. At doses of 200 and 400 mg/kg body weight (intraperitoneal injection), the extract drastically decreased fever and relatively stable body temperature (Biswasroy *et al.*, 2020, Carol *et al.*, 2012).

Treating Covid -19

Using the GC – MS technique, several phytoconstituents were isolated, including Juniper essential oils, Ethanol 4-fluoro-1-methyl-1H-imidazole-5-carboxylate, Bicyclo [4.3.0] nonane, 1-isopropenyl-4,5-dimethyl-5-phenylsulfonylmethyl, and Olean-12-en-3-ol, acetic acid and all these four could be prospective suppressors for Covid -19, necessitating further investigation

Conclusion

According to CG's literature review, that has wide - ranging therapeutic potential that effectively treat a variety of disorders. Table 1 summarized the plant's various parts and active constituents. Significant progress has already been made in the isolation and pharmacological evaluation of various constituents from CG extracts. Water, for example, is responsible for this plant's anti-pyretic, hepatoprotective, analgesic, and anti-inflammatory effects: ethanol, ethanoic acid, chloroform, and ethanol, respectively. Furthermore, CG is expected to play a significant role in the treatment of SARS-CoV-2. The presence of major bioactive secondary molecules in the leaves extract of CG, such as alkaloids, tannins, saponin, flavonoids, and glycosides, provides several medicinal potentials. The research on its photochemistry and various pharmacological properties of the extracts and constituents may provide an incentive for a more thorough evaluation of the plant's use in medicine.

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