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E: ISSN NO.: 2349-980X **Shrinkhla Ek Shodhparak Vaicharik Patrika**

Anti-microbial and Anthelmintic Activities of *Calotropis procera*: An Overview

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Abstract

Herbal medicines have been used from the earliest times to the present day which shows a remarkable therapeutic diversity. Nowadays, its importance is increasing nowadays at global level because of its negligible side effects. *Calotropis procera* (Asclepiadaceae), commonly known as a giant milk weed is a renowned Ayurvedic plant and used in the Indian traditional medicare practices since ancient time. The extracts from different parts of the plant have significant therapeutic value which is used in several traditional medicines to cure various diseases. The plant is a very promising source of anticancerous, ascaricidal, schizonticidal, anti-microbial, anthelmintic, insecticidal, anti-inflammatory, anti-diarrhoeal, larvicidal actvities with many other beneficial properties. Numerous active phytochemicals including calotropin, calotropagenin, calotoxin, calactin, uscharin, amyrin, amyrin esters, uscharidin, coroglaucigenin, and calotropagenin extracted from different parts of the plant and used in many therapeutic applications and made this plant of scientific attraction for centuries. In present communication efforts have been made to overview the antimicrobial and anthelmintic activities of the plant in view to arrange the scattered information to a single place which will ultimately be convenient to further study.

Keywords: Antimicrobial and anthelmintic activities, *Calotropis procera*, Ethnomedicine, Pharmocological properties, Phytochemicals.

Introduction

The human race started using plants and plant products as a mean of treatment of diseases as useful and effective therapeutic tools from the early days of civilization (Ghani, 2003). In recent years, a gradual revival of interest in the use of traditional herbal medicines has been shown all over the world as these are reported to have negligible adverse effect in comparison to synthetic drugs (Shaikh et. al. 2016)**.** According to an estimate around 70,000 plant species, from lichens to tall trees have been used for medicinal purposes; among them higher plants play a significant role since ancient times (Farombi, 2003). Ayurveda, the most ancient and scientific treaties on medicines and diseases which dates back to 1500-800 BC has mentioned the role of plants in treating diseases (Manoharachary and Nagaraju, 2016). As per an estimate, today about 80 % population of the world rely on the use of traditional medicines for the treatment of several diseases because of its safe nature in comparison to synthetic drugs that are regarded unsafe to human and environment in long terms of use (WHO, 2002). There are about 45,000 plant species in India. The officially documented plants with medicinal potential are 3000 but traditional practitioners use more than 6000. India is the largest producer of medicinal herbs and is appropriately called as the Botanical Garden of the World (Ahmedullah and Nayar 1999). In rural India, 70% of the population is dependent on the traditional system of medicine (Farombi, 2003). In fact, plants are reported to possess diverse range of bioactive phytochemicals which are responsible for biological activities such as antioxidant, antimicrobial, anticancer, anti-diorrehal, anti-inflamatory and anti-HIV activities (Pandey et. al. 2012). It is estimated that approximately one quarter of prescribed drugs contain plant extracts or active ingredients obtained from plants. Many medicinal products derived from plants are easily available in the market such as aspirin, atropine, artimesinin, colchicine, ephedrine, morphine, quinine, reserpine, taxol, vincristine and vinblastine (Sekar et. al. 2010).

Calotropis procera (C. procera) belongs to angiospermic family Asclepiadaceae, known by various vernacular names as “Swallow wort in English, madar in Hindi, and Alarka in Sanskrit is well known for its high medicinal properties. It is found in most parts of the world with a warm climate in dry, sandy and alkaline soils. It is commonly referred to as ark, swallow-wart or milkweed and it occurs frequently in Indonesia, Malaysia, China, and the Indian subcontinent as wasteland weed. In India, it is found from the Punjab and Rajasthan to Assam and Kanyakumari up to an altitude of 1050 m. It grows abundantly in Rajasthan. It is found in waste lands and grows as a weed in cultivated areas. It also grows well on rubbish heaps, waste and fallow land, by the roadside and in sand dunes. *Calotropis* is primarily harvested because of its distinctive medicinal properties. The inner bark of *Calotropis* is used to make strong fibers called madar which are used in the manufacture of weave carpets, ropes, sewing thread and fishing nets. It is a xerophytic, erect shrub about 6m high, growing widely throughout the tropic of Africa and Asia. It is grown abundantly in arid and semi-arid regions without any agricultural practices. *C. procera* is a highly effective bio-indicator to monitor pollution in varying concentrations of Br, Mn, Se, Cr and Zn between urban and suburban samples. For centuries, different parts of the plant have been reported to possess a number of biological activities such as proteolytic, antimicrobial, larvicidal, nematocidal, anticancer and anti-inflammatory. Its flowers possess digestive and tonic properties. On the contrary, the powdered root bark has been reported to give relief in diarrhoea and dysentery. The root of the plant is used as a carminative in the treatment of dyspepsia. The root bark and leaves of *C. procera* are used by various tribes of central India as a curative agent for jaundice and many other beneficial properties make this plant as a golden gift for human kind (Meena 2010). The leaf biomass of the plant is potentially a good adsorbent for the removal of crystal violet (a cationic dye) from aqueous solution and is being used in textile industry. The giant milk weed is an important source for plant hydrocarbons used for testing various drugs against anti-inflammatory and antinociceptive activity (Sharma, 2012) Present review discusses the biopharmaceutical prospective future potential of *C. procera*.

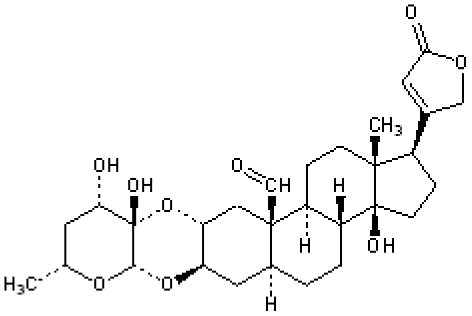
Aim of the Study

In present communication, efforts have been made to overview the phytochemical properties of *C. procera* with the aim to highlight the significance of the plant for human being and also provide new area of research to develop the compounds synthetically.

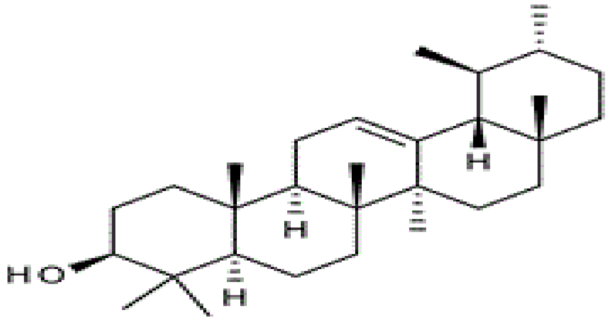
Active Constituents

C. procera is considered as a pool of various active compounds those are responsible for its diverse pharmacological activities**.** The phytochemical studies of the extracts of *C. procera* in different solvents were extensively studied by various researchers and revealed that leaves, stem, roots, flower, seed showed the presence of significant amount alkaloids, cardiac glycosides, tannins, flavonoids, sterols and triterpenes (Mossa et. al. 1991; Ansari and Ali, 1999, 2001, Gupta et al. 2003, Kutama et. al. 2018). The presence of D-glucose, D-arabinose, D-glucosamine and α-rhamnose in the aqueous extract of the leaves of *C. procera* were reported while α- and ß-amyrin and ß-sitosterol were identified in the unsaponifiable matter of the petroleum ether extract of same species (Sharma et. al. 2012). Fatty acid composition of the extract of this plant has also been studied which showed the presence of 7 saturated and 11 unsaturated fatty acids (Khanzada et. al. 2008). The essential elements Al, As, Cu, Ca, Cr, Cd, Fe, K, Mn, Na, Pb, and Zn have been reported from this medicinal plant in variable range with 27-32% of the total protein. Pharmacologically active substances such as calotropin, uscharine, calotoxin, calctin, uscharidin and calotropagenin, amyrin etc. are some important chemicals obtained from the leaves and latex of *C. procera* plant (Sharma et. al. 2012). Besides uscharine another cardenolide namely voruscharine was identified in the latex of *C. procera.*. In the leaves, mudarine is the principal active constituent as well as a bitter yellow acid, resin and 3 toxic glycosides calotropin, uscharin and calotoxin. The latex contains a powerful bacteriolytic enzyme, a very toxic glycoside calactin (the concentration of which is increased following insect or grasshopper attack as a defense mechanism). The chemical constituents of the seeds of *C. procera* were also investigated and reported the presence of coroglaucigenin, frugoside, corotoxigenin and calotropin. There is hardly any doubt that *C. procera* is a recommended natural source of phytochemicals having a good sign for future biopharmaceutical prospect. The chemical structures of few important phytochemical are shown in figure-1.

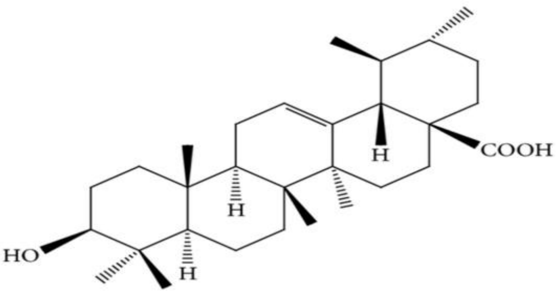
Figure-1: Molecular structure of some phytochemicals isolated from various parts of *C. procera*
(Source: Meena et. al. 2010; Yogi et. al. 2016)



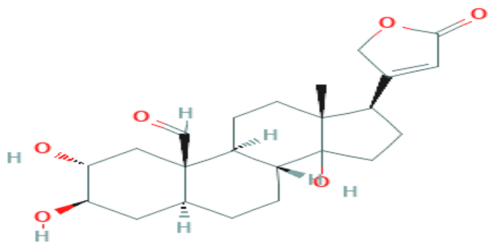
Calotropin



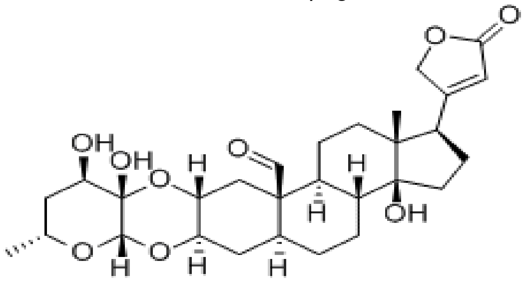
α-amyrine



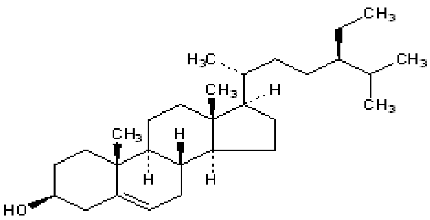
Urosolic acid



Calotropagenin



Calactin



ß- Sitosterol

Ayurvedic uses

C. procera is a traditional medicinal plant growing wild from West Africa to South East Asia. Almost all the parts of the plants are used in Ayurvedic medicines including root bark and flowers. The powdered of the leaves are used for the fast healing of wounds, as a purgative and to treat indigestion. They are also used to treat skin disorders and liver problems. The dried leaves are used to treat various sexual problems which include penile dysfunction. Hot poultices made from the leaves are applied to get the relief from stomachaches, headaches and also applied to the area of sprains to ease the swelling and pain. The flowers of the *C. procera* are used as a milk drink to treat a variety of complaints including coughs, asthma, indigestion, cholera and also reported to have an anti-asthmatic effect. Traditionally, the plant has been used as an antifungal, antipyretic and analgesic agent. The dried leaves are used as an expectorant, and anti-inflammatory for the treatment of paralysis and rheumatic pains (Meena et. al. 2011). The dried latex and dried root are used as an antidote for snake poisoning. It is also used as an abortifacient for the treatment of piles and intestinal worms. The tender leaves of the plant are also used to treat migraine. The capsulated root bark powder is effective against diarrhoea and asthma. The root of *C. procera* is used as carminative in the treatment of dyspepsia. The root bark is useful in various ailments like skin diseases, enlargement of the abdominal viscera, intestinal worms and ascites. Further, the root bark is used by various tribes in central India as a curative agent for jaundice (Khan and Malik, 1989, Yogi et. al. 2016)

Antimicrobial activity

It is well known fact that infectious diseases account for high proportion of health problems, especially in the developing countries. The excessive use of antibiotics has contributed to the emergence and spread of antibiotic- resistant bacteria in communities. Microorganisms have developed resistance to many antibiotics, and this has created immense clinical problem in the treatment of infectious diseases (Evans, 1996) and this resistance further aggravated due to indiscriminate use of commercial antimicrobial drugs commonly used in the treatment of infectious diseases. This situation forced scientists to search for new antimicrobial substances from various sources and one of these is medicinal plants (Karmaan, 2003). The medicinal plants are known as antimicrobial agent that kills or inhibit the growth of microorganisms. Medicinal plants were used as antimicrobial agents to avoid the development of multi-drug resistant bacteria. Medicinal plants can exert antibacterial activities through multiple mechanisms, such as disruption of cytoplasmic membrane, inhibition of cell wall synthesis, inhibition of cell membrane synthesis, inhibition of nucleic acid synthesis, inhibition of energy metabolism, as well as inhibition of bacterial virulence factors, including quorum-sensing signal receptors, enzymes and toxins (Al-Snafi, 2019). Several workers have reported antimicrobial activities of different extracts of various plants against different species of bacteria. The antimicrobial effect of ethanol, aqueous and chloroform extracts of leaf and latex of *C. procera* on six bacteria, three fungi, *one yeast Candida albicans* were evaluated using agar well diffusion and paper disk methods (kareem et al. 2008). Ethanol extract was found to be the best for antimicrobial properties of leaf and latex of *C. procera* followed by chloroform and aqueous ($P<0.05$). It was further noted that the ethanolic extracts of *C. procera* latex gave the widest zone of inhibition (14.1mm) against *Escherchia coli* using agar well diffusion while 9.0 mm was recorded for the same organism in the disc plate method. The results also revealed that the growth of six bacterial isolates was inhibited by the three extracts except *P. aeruginosa* and *S. pyogenes* that were not inhibited by the aqueous extracts of both leaf and latex of *C. procera*. In the same way, the growth of four test fungi were inhibited by ethanol and chloroform extracts while the aqueous extract was found to be the least effective on the test fungi. The best antifungal activity was recorded in ethanol extract of *C. procera* latex against *Candida albicans* (Meena, 2011)

In another study, antimicrobial activities of chloroform and methanol extracts of seeds of *C. procera* were performed which was obtained from plants located in the forest area of Ghaziabad, India. The results reveal that the chloroform extract of *C. procera* seeds exhibited better antimicrobial activity while the extracts obtained from *C. procera* seeds were evaluated for their possible in vitro antibacterial activities using the paper disc method. (Quazi et. al. 2013, Leonard et. al. 2013) In another study, They tested the antimicrobial potential and minimum inhibitory concentrations (MICs) of aqueous, chloroform and ethanol extracts of *Jatropha curcas* and *C. procera* leaves against *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Aspergillus niger*, *Penicillum fellutanum* and *Candida* sp. isolated from commercial motorcycle helmets in Lagos metropolis using agar well diffusion technique and the Clinical and Laboratory Standard Institute guidelines respectively. They observed that aqueous and ethanol extracts of *C. procera* and *J. curcas* showed antimicrobial activity against almost all test isolates, while the chloroform extracts generally had lower antimicrobial activities. MICs of aqueous extracts of both plants was between 12.5 and 50 mg/ml of extract in all susceptible isolates, while MICs of ethanol extracts was between 12.5 and 100 mg/ml. The MICs of chloroform extracts was between 50 and 100 mg/ml for most test isolates, while failing to inhibit *S. aureus* and *E. coli* at the highest concentration tested. The ethanol extract of *C. procera* had the highest antimicrobial activity of all the extracts, indicating it is the most potent antimicrobials for motorcycle helmet disinfection. Yesmin et. al. (2008) studied the crude methanol extract of *C. procera which* showed the antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis, Plesiomonas shigelloides, Shigella dysenteriae, and Vibrio cholerae* on the other hand aqueous extract showed antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis, Staphylococcus saprophyticus*, *Streptococcus pyogenes Plesiomonas shigelloides, Shigella dysenteriae, Vibrio cholerae, Shigella Flexner, Shigella sonnei and Pseudomonas aeruginosa.* Both extracts did not show any activities against *Salmonella typhi and Shigella boydii.* In fact, both methanol and aqueous extract of *C. procera* showed significant antibacterial activity against few gram positive and gram negative bacterial strains. The reputation of *C. procera* as a remedy for different microbial diseases traditionally including diarrhoea and dysentery was supported by the antibacterial screening tests.

Anthelmintic Activity

Although the latex of *C. procera* possesses various medicinal properties, it is also known for its toxic, bactericidal, larvicidal and cytotoxic effects (Smit et al., 1995; Markouk et al., 2000; Srinivasan et. al., 2001). Recently, the latex has been reported to produce an anthelmintic effect against *Haemonchus contortus* infection in Najdi sheep, in which it decreases the egg production and the number of worms in the abomasum (Al-Qarawi et al., 2001). Vitro and in vivo studies were done to evaluate the anthelmintic activity of *C. procera* flowers in comparison with levamisole (Iqbal et al, 2005). In vitro studies revealed the anthelmintic effects ($P < 0.05$) of crude aqueous extract (CAE) and crude methanolic extracts (CME) of *C. procera* flowers on live *Haemonchus contortus* which was based on their mortality or temporary paralysis. For in vivo studies, *C. procera* flowers were administered as crude powder (CP), CAE and CME to sheep naturally infected with mixed species of gastrointestinal Nematodes (Iqbal and Jabbar, 2005). Egg count percent reduction (ECR) was recorded as 88.4 and 77.8% in sheep treated with CAE and CP at 3 g kg-1 body weight on day 7 and 10 post-treatment (PT), respectively. CME was least effective resulting in 20.9% reduction in ECR on day 7 PT. It was found that *C. procera* flowers possess good anthelmintic activity against nematodes, yet it was lower than that exhibited by levamisole (97.8–100%). The ethanolic extracts of *C. procera* leaves were separated into n-butanol and water fractions. The n-butanol fraction was subjected to column chromatography. Indian earthworm, *Pheretima posthuma* as an experimental model has been evaluated by using ethanolic extract, n-butanol, and water fractions as well as n-hexane, chloroform, chloroform: methanol (9:1); chromatographic elutes of n-butanol fraction for in-vitro anthelmintic activity. The results revealed that ethanolic extract, water fraction, n-hexane, and chloroform elute showed better activity as compared to n-butanol fraction and chloroform:methanol (9:1) elute of *C. procera* leaves [Murti et. al. 2015, Mali 2019]. It is suggested that further research on large scale be carried out involving a large number of animals, doses higher than those used in the current study, identification of active principles, and standardization of dose and toxicity studies for drug development (Sivakar and Kumar, 2003; Iqbal and Jabbar, 2005).

Conclusion and Prospects

In present communication effort has been made to overview the medicinal significance of *C. procera* with special reference to antimicrobial and anthelmintic activities. It has been concluded from the above discussion that different parts of *C. procera* show the significant antimicrobial and anthelmintic activities. Almost all the parts of this plant such as leaf, flower, seed, bark and root are used to cure a variety of diseases. As the pharmacologists are looking forward to develop new medicinal recipes from the natural origins, active phytochemicals of *C. procera* can play a very viable role for these drives.

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