A systematic review on *Calotropis gigantea* Linn.

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Abstract- **The giant calotropis Linn, often called milk weed or a popular restorative plant, has been used in Indian medicine for many years. The systematic position, background information on the plant, morphological analysis, phytochemistry, and economic benefits of the Calotropis gigantea are covered in this paper. It has a smooth stem and round, light green leaves. The plant may grow naturally in a variety of soils and environments and doesn't require any special gardening techniques. Numerous pharmacological effects have been reported, including antioxidant, anti-malarial, antimicrobial, cytotoxic, antipyretic, anti-asthmatic, anti-inflammatory, analgesic, insecticidal, wound healing, and anti- diarrheal effects. Furthermore, various pharmaceutical aspects have been reported in this paper.**

Keywords: Calotropis gigantea **Linn., milk weed.**

INTRODUCTION

The term “Medicinal plant” is typically used to describe plants that have curative benefits or have beneficial pharmacological effects on animal bodies. It has now been shown that plants with naturally occuring optional metabolites, such as alkaloids, glycosides, tannins, volatile oils, and nutrients and minerals, have healing qualities.(1)
The giant Calotropis Linn, Often called milk weed or a popular restorative plant, has been used in Indian medicine for many years. It has a smooth stem and round , light green leaves. The plant may grow naturally in a variety of solis and environments and doesn’t require any special gardening techniques. Numerous pharmacological effects have been reported, including antioxidant, anti-malarial, antimicrobial, cytotoxic, antipyretic, anti-asthmatic, anti-inflammatory,analgesic, insecticidal,wound healing, and anti-diarrheal effects.(2)
The plants *Calotropis gigantea* and *Calotropis procera* are referred to as "Sweta Arka" and "Raktha Arka," respectively, in archaic ayurveda medicine(3).Here we study about *Calotropis Gigantea. Calotropis gigantea* Linn is flowering plants belong to *Asclepidaceae* family. It is also known as Akada, Aak, Mandar, Aakh etc.(4)
Calotropis gigantea, sometimes known as gigantic milkweed, is a widespread weed in desert areas. This plant is indigenous to China, Indonesia, Malaysia, Pakistan, the Philippines, Thailand, Sri Lanka, Bangladesh, India, and Bangladesh. The plant has milky stems, waxy clusters of white or lavender blooms, and oval, light green leaves. The traditional medical system in India commonly uses *Calotropis gigantea* for a variety of therapeutic applications. Recently, various therapeutic characteristics of *Calotropis gigantea* have been scientifically described. The blooms have cytotoxic, antibacterial, and analgesic properties. Leaves and aerial parts of the plant have been reported for antidiarrheal activity, anti-candida activity and antibacterial activity, and antioxidant activity. The roots have been reported to have antipyretic activity, cytotoxic activity, antimicrobial activity, insecticidal activity, wound healing activity and CNS activity and load-blocking properties. Plant latex has been reported to have laxative properties, procoagulant activity, wound healing activity, and antimicrobial activity. Stem has been reported to possess hepatotoxic effects. The current review focuses ona general outline of the medicinal properties of *Calotropis gigantea* and its future prospects for further scientific research to develop effective therapeutic tablet formulation. (5)

Tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drugs or a mixture of drugs, with or without diluents. Tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. They vary in shape and differ greatly in size and weight, depending on amount of medicinal substancesand the intended mode of administration.(6)

Properties (6)

1) Should be elegant product having its own identity while being free of defects such as chips, cracks, discoloration and contamination.
2) Should have strength to withstand the rigors of shocks encountered in itsproduction, packaging, shipping and dispensing.

3) Should have the physical stability to maintain its physical attributes overtime.
4) Must be able to release the medicament agent(s) in the body in apredictable and reproducible manner.
5) Must have a suitable chemical stability over time so as not to allow alterationof the medicinal agent(s).

Advantages (6)

1) Tablets are unit dosage form and offer the greatest capabilities of all oral dosageform for the greatest dose precision and the least content variability.
2) They are easiest and cheapest to package and strip.
3) Low in cost.
4) Lighter and compact.
5) Having greatest chemical and microbial stability over all oral dosage forms.
6) Suitable for large scale production.
7) Easy to swallow with least tendency for hang-up.
8) Objectionable odour and bitter taste can be masked by coating technique.
9) Sustained release product is possible by enteric coating.
10) Easy to handling.

Disadvantages (6)

1) Difficult to swallow in case of children and unconscious patients.
2) Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.
3) Drugs with poor wetting, slow dissolution properties, optimum absorption highin GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.
4) Bitter testing drugs, drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating. In such cases, capsule may offer the best and lowest cost.
5) Irritant effects on the GI mucosa by some solids (e.g., aspirin).
6) Possibility of bioavailability problems resulting from slow disintegration and dissolution.

Plant profile

Table 1: Taxonomical classification of *Calotropis gigantea* Linn.(7)

Kingdom	Plantae
Order	Gentianales
Family	Apocynaceae
Subfamily	Asclepiadaceae
Genus	*Calotropis*
Species	*C.gigantea*

Vernacular names

Fig : *Calotropis gigantea* Linn.*(5)*

Table 2: Vernacular names of *Calotropis gigantea* Linn.(8)

Commonnames	Giant Milkweed, Crown Flower, Swallow Wort.
Hindi	Safed aak, Aak, Alarkh, Madar, Sveta Arka, Akanda, Bara Akand.
Gujarati	Aakando
English	Crown flower, giant Indian milkweed. Bowstring hemp, crownplant, madarMalaysia: Remiga, rembega, kemengu
Indonesia	Bidhuri (Sundanese, Madurese), sidaguri (Javanese), rubik (Aceh).
Philippines	Kapal-kapal (Tagalog).
Thailand	Po thuean, paan thuean (northern), rak(central)
French	Faux arbre de soie, mercure vegetal

LITERATURE SURVEY

Ethnobotanical Aspects

Chopra, R.N.et al. (1993) studied that the remote, primitive societies may only have oral tradition to pass on their knowledge of how to use medicinal herbs. Due to the significant deforestation, industrialization, and urbanization in the forest belts caused by these factors, research on ethnobotany in India appears to have captured the intellectual after independence who are eager to preserve all available information before the tribal culture in India completely fades..(9) Large, bushy, stout tomentose shrubs, 2 – 4 m high. Leaves sessile, decussate, ovate, obovate, ovate – oblong to elliptic – ovate, base cordate, ofter amplexicaul, apex obtuse or shortly acuminate, subglabrous above, cottony beneath, 8 – 20 * 5 – 7 cm cymes umbellate or sub-raceme, penducle lateral, cottony. Corolla obese spreading, recurved, ovate – lanceolate, uniformly coloured, light purple to white 2 – 5 cm dia.; Corona scales 5 narrow, adnate to gynostegium, shorter that the staminal column, back pubescent; apex entire with two obtuse auricles below it, vesicle recurved at the base, the spur upcourved, involute. Stigma depressed, 5 – angular (-lobed). Follicles 6 – 10 cm long, recurved, boat shaped, obtuse, pubescent.(9)

Mitte, V et al. (1981) told about the plant parts contain 23.38% ash, acid insoluble ash 5.08%,water soluble extractive 33.38% and alcohol soluble extractive 6.66%. Root bark : contains β-amyrin, 2-isomeric crystalline alcohols, giganteal (m.p.:2230 - 240) and iso-giganteol (m.p.1170 -780). A colourless substance (m.p.:1620) of Tetracyclic triterpene alcohol been obtained from unsaponifiable fraction o0.f the fatty matter. Leaf : contains an active principle

– Mudarine and three glycosides calotropin uscharin, calotoxin along with phenol. Latex: contains water and water solubles (86 – 95.5%) and caoutcohouc (.6 – 1.9%). The calcium consists of caoutchouch (5.5 – 18.6%), resin (73.6 – 87.8%) and insoluble matter (4.5 – 13.8%). Two isomeric resinols : - calotropeol (m.p.:2040 – 50) and β-calotropeol (m.p:2160

– 170) with ester combinations of acetic and isovaleric acids and β-amyrin with small amounts of unidentified tetracyclic compounds and calcium oxalate. Traces of glutathione and a proteoclastic enzyme similar to papain are also present. Seeds : contains moisture (7.4%), protein (27%), ether extracts (26.8%), crude fibre and nitrogen free extract (32.4%) and ash (6.55%). Oil extracted from seeds is an olive green liquid, acid fraction of which contains palmitic (15%), oleic (52%), linoleic (32%) and linolenic acid (0.9%). The unsaponifiable fraction (31%) of seed wax yields phytosterol (m.p.:1360), stigmasterol (m.p.:1700), melissyl alcohol and laurane (0.6%).(10)

Pharmacognostic Aspects (11)

Gharge VG et al. (2017) studied the pharmacognostic aspects as follows ,

Root: Simple, branched, woody at the base and covered with a fissured; corky bark; branches somewhat delicious and thickly white tomentose; early glabrescent. All parts of the plant exude white latex when cut or broken.

Leaves: Opposite-decussate, straight forward, subsessile, exstipulate; edge oval obovate to comprehensively obovate, 5-30X 2.5-15.5 cm, apex abruptly and shortly acuminate to apiculate, base cordate, edges whole, delicious, white tomentose when young, later glabrescent and glacouse.

Fruit: A basic, plump, swelled, subglobose to sideways ovoid follicle up to 10 cm or more in diameter.

Seeds: Many, small, flat, obovate, 6 × 5 mm, compacted with silky white pappus, 3 cm or more long.

Flowers: Bracteate, complete, sexually unbiased, actionmorphic, pentamerous, hypogynous, pedicellate, pedicel 1-3 cm long.

Calyx: Sepal 5, Polysepalous, 5 lobed, in a matter of seconds joined at the base, glabrescent, quincuncial aestivation Androecium: Stamens five, gynandrous, anther dithecous, sound.

Inflorescence: A thick, multi-bloomed, umbellate, peduncled cymes, emerging from the hubs and seeming axillary or terminal.

Gynoecium: Gynoecium: Bicarpellary, apocarpous, styles are joined at their peak, peltate disgrace with five parallel stigmatic surfaces. Anthers are adnate to the shame of framing a gynostegium.

Phytochemical aspects

Kumar D et al.(2015) studied about the phytochemical aspects about the *Calotropis giganteaLinn* as follows ,

Table 3: Various chemical constituents isolated from *Calotropis gigantea* Linn (12)

Class of Chemical Constituent	Name of ChemicalConstituent	Plant Part Used	Extract Taken
Triterpenoids	Di-(2-ethylhexyl) Phthalate	Flowers	Ethyl acetate extract
	Anhydrosophoradiol-3-acetate		
	Lupeol	Aerial parts	Latex
	α –Taraxerol	Root bark	Ethyl acetate extract
Triterpeneesters	γ-Taraxasterol	Aerial parts	Hexane and methanol soluble extract
	Lupenyl-1-acetate	Root bark	Petroleum ether extract
Flavonol	Isorhamnetin	Aerial parts	Methanol extract
Cardiac glycosides	Calotropone	Roots	Ethanol extract
	Gofruside		
Steroids	Stigmasterol	Root bark	Methanol extract
	β-Sitosterol		
	β−Sitosterolacetate		Ethyl acetate extract
Resin	β-Amyrin	Root bark	95 % Alcohol extract
	β-Amyrin acetate		
Fatty acids	Isovaleric acid	Root bark	95 % Alcohol extract
Miscellaneous	Asclepin	Roots	Latex

Pharmacological aspects

Antimicrobial Activity

Madhu Prakash Srivastav *et al*.(2020) was studied that the antimicrobial activity of aqueous,methanolic and ethanolic extract of leaves and flower of *Calotropis gigantea* Linn shows potent antimicrobial activity against Staphylococcus aureus.(13)

Cytotoxic Activity

S. Rajashekara *et al.* (2020) was studied that synthesized Zinc oxide nanoparticles from aerial (leaf) parts of *Calotropis gigantea* Linn showed a cytotoxic effect against MDAMB-231 cell lines. So, plant extract also shows cytotoxic effect. (14)

Antiasthmatic Activity

S. Sarkar *et al.* (2018) was studied anti asthmatic activity of *Calotropis gigantea* in ova albumin (OVA) induced asthma. The impact of *Calotropis gigantea* at 100, 200, 400 mg/kg, on various body cells, catalysts and histopathological changes were noticed. Along these lines, plant concentrate might help for treating asthma. (15)

Anti-Malarial Activity
Shripad M. Bairagi *et al*.(2018) was studied the mosquito repellent activity of *Calotropis gigantea* flower extract was studied. The distinctive extract of the plant was utilized for the investigation against the multi day blood starved female *Culex quinquefasciatus mosquito*. The alcoholic extract showed high mosquito repellent action against the female *Culex quinquefasciatus mosquito* as compared to the petroleum ether and chloroform extract. The dose dependent mosquito repellent activity of the extract was found.(16)

Antioxidant Activity
Mushir Ansari *et al*.(2016) was studied the *in vitro* antioxidant activity of *Calotropis gigantea* root extract by 2, 2-diphenyl- 1-picrylhydrazyl and fluorescence recovery after photobleaching assay. In both the method, extract possesses high antioxidant activity when compared with standard ascorbic acid due to presence of high content of various phytochemicals. (17)

Antipyretic Activity
Namrata Singh *et al.* (2014) was studied that root extract of *Calotropis gigantea* has expected antipyretic action against both yeast-induced and TAB vaccine-induced fever, showing the chance of creating *Calotropis gigantea* as a less expensive and intense antipyretic agent. (18)

Anti-Inflammatory Activity
V. A. Jagtap *et al*. (2010) was examined that ethanolic extract of leaves of *Calotropis gigantea* linn. On *in-vitro* models shows significant anti-inflammatory activity.(19)

Wound Healing Activity
Narendra Nalwaya *et al.* (2009) examined wound healing activity of latex of *Calotropis gigantea* Linn. in albino rats by using extraction and entry point wound model and the latex showed the significant wound healing activity. (20)

Insecticidal Activity
M. Rezaul Karim *et al*.(2009) was read for methanolic extract of root bark of *Calotropis gigantea* Linn. furthermore, its chloroform and petroleum ether soluble portions against several instar of larvae and adult of *Tribolium castaneum*. The methanol extracts and furthermore, its chloroform and petroleum ether soluble portions were repellent to *Triboliumcastaneum* in mild to moderate range. (21)

Analgesic Activity
A.K. Pathak *et al*.(2007) was studied the analgesic activity of alcoholic extractof *Calotropis gigantea* Linn. in acetic acid induced writhing test & hot plate technique in mice. In both the technique, extract has high analgesic activity.(22)

Pharmaceutical aspects
Herbal syrup
Amit G Nerkar et al (2023) focused on the formulation and evaluation of herbal medicinal syrups from *Calotropis gigantea*. Herbal syrup is prepared by the method of decoction. *Calotropis Gigantea* extract was obtained as a fine extract from Herbal Creations Pvt Ltd. The extract was prepared with an ethanol extracted by the Soxhlet extraction method.(23)

Mouthwash.
Diana setya ningish et al. (2022) prepared the ethanolic Calotropis gigantea leaf extract based mouthwash. The ethanolic *Calotropis gigantea* leaf extract (ECGLE) was taken from Ie Jue geothermal area, Aceh-Indonesia, and ECGLE based mouthwash formulation has been prepared. The formulation was prepared with various extract concentrations ranging from 0to 25% of ECGLE. Both the extract and formulation were evaluated for antibacterial and in vitro cytotoxic activity in order to determine their potential medicinal value in the oral cavity.Antibacterial tests were carried out against Gram-negative bacteria (Porphyromonas gingivalis), Gram-positive bacteria (Solobacterium moorei), and a mix of both Gram-negative and Gram-positive bacteria (P. gingivalis + S. moorei). The cytotoxic activity was evaluated against human dental pulp primary cells (hDPPC) by calorimetric assay using 3-(4,5-dimethylthiazol-2- yl)-2,5-diphenyltetrazolium bromide.(24)All formulations passed the stability test with a pH of 5.35–5.92. Antibacterial activity testing revealed that the higher the ECGLE concentration, the more effective it is against bacteria.(24)

In comparison with other formulations, formulation-3 containing 3 gr of ECGLE demonstrated the highest activity. The minimum inhibitory concentration (MIC) value and % inhibition of formulation-3 against P. gingivalis,

S. moorei, and a mix of both bacteria were 0.089, 0.075, and 0.083 µg/ml and 88.924%, 90.691%, and 89.72%, respectively. The cytotoxicity activities (IC50) for both ECGLE and a formulation containing ECGLE were 6.44 and 0.27 gr/ml, respectively. The ability of cells to undergo apoptosis showed a strong correlation between cell viability and the ECGLE extract (R2 = 0.973) as well as ECGLE- based mouthwash formulation (R2 = 0.897). The greater the concentration of ECGLE extract or ECGLE-based mouthwash formulation, the lower the viability of hDPPCs, but the greater the antibacterial activity.(24)

Hydrogel

Ramchandran AM et al. (2021) focused on the objective of present study was to develop hydrogel formulations loaded with *Calotropis gigantea* leaves extract.The prepared hydrogel formulations were compliance with their color, odor, homogeneity, pH, and spreadability.As all the formulations were complies with the all parameters and it can be suggest as a Good antibacterial gel. It is evident that, ethanolic extract of Calotropis gigantea showed a maximum inhibitory zone against bacteria associated with foot ulcer.The In vitro studies showed a quantity dependent increase in antibacterial activity against foot ulcer causing bacteria, a contraction which is higher than that produced by the control groups. These contractions were statistically significant ($p<0.05$), during the study with leave extract against foot ulcer causing bacteria in diabetes.(25)

Herbal cream

Ranjan Kumar Maji et al.(2021) studied this present research work to formulate and evaluate herbal cream. The herbal cream gives various types of advantages than any other creams. The aim of present study is to prepare the herbal cream for the use of wound healing activity, anti-inflammatory activity, analgesic activity, antifungal property and cure of various disease of the skin. Method of prepare herbal cream is very sample. At first oil phase are prepared, the mixtur e of stearic acid (48gm), potassium hydroxide (23gm), sodium carbonate (12gm), white soft paraffin (15gm) ware melted at 70°C. after that aqueous phase is prepared, ethanol (10ml), drug (latex of Calotropis Gigantea 1ml), glycerin (3ml), methyl paraben (1.5gm), perfume (1.5gm), distilled water (35ml), heated at 70°C. Then aqueous phase is added in to the oil phase at 70°C with continuous stirring. Then the mixture is put in room temperature with continuous stirring and added perfume and preservatives after that the product is transferred in suitable container. The physical parameter is determined such as pH, thermal stability, homogeneity, irritancy test, patch test, spreadability studies, accelerated stability testing etc.(26)

Transdermal Glycerogelatin In Situ Film Containing

Samad A et al. (2018) focuses on the aim of the study to design, optimize and evaluate transdermal glycerogelatin in situ film containing *Calotropis gigantea* leaves extract for the treatment of Arthritis. Skin is considered as an important route of administration for both local and systemic effects. Topical film forming systems are developing drug delivery system ment for topical application to the skin, which adhere to the body, forming a thin transparent elastic film which provide delivery of active ingredient to the body tissue. The formulation was optimized by mixture design (design expert software, version 11.03) with glycerin, gelatin, water as the factors and spreadability, elasticity, drying time, and tensile strength as the responses. *Calotropis gigantea* having significant anti-inflammatory potential and its ethanolic extract was incorporated into the optimized formula of glycerogelatin in situ film. The optimized formula contained 1.5% of drug extract and showed a drug release of 79% at 8th hour, and 96% in 24 hour time period.(27)

Conclusion

The plant Calotropis gigantea has several remarkable medicinal effects in addition to having a significant commercial worth. Excellent characteristics of the plant include its distributionin tropical and subtropical wastelands as a perennial shrub. Calotropis gigantea is a traditional medicinal plant with a wide range of phytochemical properties, including antioxidant, anti- malarial, anti-asthmatic, antimicrobial, cytotoxic, antipyretic, anti-inflammatory, analgesic, insecticidal, wound healing, and anti-diarrheal activity.

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