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CALOTROPIS GIGANTEA: A REVIEW ON ITS PHYTOCHEMICAL & PHARMACOLOGICAL PROFILE

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ABSTRACT *Calotropis gigantea* (Asclepiadacea) is a perennial herb with a long history of use in traditional medicines. A wide range of chemical compounds including cardiac glycosidis, flavonoids, terpenoids, alkaloids, tennins, & resins have been isolated from this plant. The plant has been used for various disease condition including leprosy, ulcers, tumours and piles. Various pharmacological activities reported like Analgesic activity, Antipyretic activity, Pregnancy interceptive activity, CNS activity, Anti-inflammatory activity, Procoagulant activity, Anti-diarrhoeal activity, free redical scavenging activity, Antimicrobial Activity, Anti-tumor activity, Antifungal activity, Antitussive activity, and Antifeedent activity.

INTRODUCTION This plant is distributed throughout India. It is popularly known as arka in Hindi. India being a tropical country is blessed with best natural resources and ancient knowledge for its judicious utilization. However, in order to make these remedies acceptable to modern medicine, there is a need to scientifically evaluate them to identify the active principles and understand the pharmacological action.[1] Humankind first utilized material found in environment on an empirical basis to cure various ailments. Natural products from plants and animals traditionally have provided the pharmaceutical industry with one of its important sources of lead compounds in search of new drugs and medicines. The search for new pharmacologically active agents from natural resources such as plants, animals and microbes led to discovery of many clinically usefuldrugs.[2]

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CALOTROPIS GIGANTEA (GIANT MILK-WEED)

Botanical name: *Calotropis gigantea* Linn.
Family : Asclepiadaceae

Hindi : Ag, Akan Ark, Madar
Sanskrit : Arka, Aditya, Mandara
Marathi : Akand, Lal
Part used : Leaves, root, root bark, latex, stem bark, flowers.

Fig. *Calotropis gigantea* Plant

DISTRIBUTION Throughout India, Ceylon-Malay Island, S. China.

BOTANICAL DESCRIPTION A tall shrub reaching 2.4-3m high; back yellowish white, furrowed; branches stout, terete, more or less covered (especially the younger ones) with fine appressed cottony pubescence. Leaves 1-20 by 3.8-10 cm., sessile or nearly so, elliptic-oblong or abovate-oblong, acute, thick, glaucous-green, clothed beneath and more or less above with fine cottony tomenum; base narrow, cordate. Flowers inodourous, purplish or white. Calyx divided to the base; sepals 6 by 4 mm, ovate, acute, cottony. Corolla 2cm long or more; lobes 1.3-1.6cm. long, deltoid-ovate, subacute, revolute and twisted in age; lobes of the corona1.3cm. long by 5mm. pubescent on the slightly thickened margin, the apex rounded with 2 obtuse auricles just below it. Follicles 9-10 cm. Long, broad, thick, fleshy, ventricose, green. Seeds numerous, 6 by 5 mm., broadly ovate, flattened narrowly margined, minutely tomentose, brown coma 2.5-3.2 cm long.[3,4]

CHEMICAL CONSTITUENTS

Root:cardiacglycosides, seven oxypregnane-oligo glycosides, calotroposides A-G. Rootbark:β-amyrin, two isomeric crystalline alcohols, giganteol, isogiganteol and cardenolides. Latex: akundarin, latex contins 0.45% uscharin, 0.15% calotoxin, 0.15% calactin, latex also contains α-calatropeol, β- calotropeol, β- amyrin and calcium oxalate, it also yields a nitrogen and sulphur containing fish and cardiac poison, gigantin. Latex also contins traces of glutathione and a proteoclstic enzyme similar to papain. Leaves: alkaloids, glycosides, mudarine. Stembark:β-calotropeol,β-amyrin, giganteol. Flower:nα-calatropeol,β-calotropeol,amyrin, cardioactive glycosides, mudarine, asclepin, bitter resins akundarin, calotropin. [4-8]

THERAPEUTIC USES The plant is purgative, anthelmintic, alexipharmic, cures leprosy, leucoderma, ulcers, tumors, piles, diseases of the spleen, the liver, and the abdomen; the juice is anthelminticand leucoderma, tumors, ascites, diseases of abdomen. The leaves are applied to paralyzed parts, painful joints, swellings; heal wounds. The tincture from the leaves used as antiperiodic in cases of intermittent fevers.[3, 4] Inflammations, tumors, rat-bite, good in ascites. The milk is bitter, heating, purgative;

Laxative; cures piles. The root bark is diaphoretic; cures asthma and syphilis. Flower is sweet, bitter, anthelmintic, analgesic, astringent, cures .

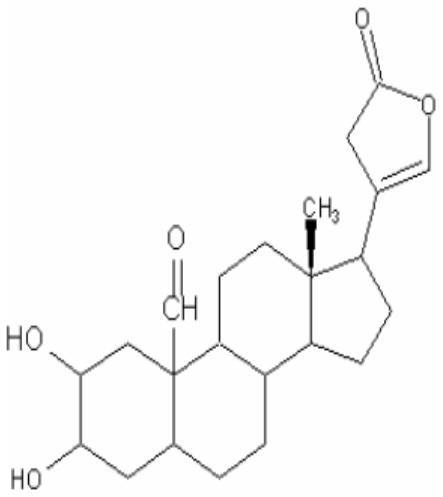
PHYTOCHEMISTRY Phytochemically the plants have been investigated for cardenolides from the latex and leaves,[9,10] triterpenoids,[10] anthocyanins from flowers[11] and hydrocarbons.[12] The leaves and latex of *Calotropis gigantea* were found to have cardiac glycosides, various glycosides were isolated and studies.[13] An active principle 'mudarine' was isolated from leaves of C. gigantean. Beside this, a yellow bitter acid and resin were also found. The cardiac glycosides were identified as Calotropogenjn (1), calotropin (2), Uscharin (3) and Calotoxin (4), Calactin (5).[10,14]

Threecardenolideglycosjdgs.Coroglaucigenn(6),frugoside(7),and40befaglucopyranosylfrugoside (8), were obtained as the cytotoxic principles of "akond mul" (roots of *Calotropis gigontea* L.). The cytotoxicity of these compounds against various cell lines of human and mouse origin was tested. They showed similar cell line selectivity to those of cardiac glycosides such as digoxin and ouabain. They are toxic to cell lines of human origin, but not to those from mouse Twonewoxypregnane-oligoglycosidesnamed calotroposides A (9) and (10) have been isolated from root of *C.gigantea*, an Indonesian medicinal plant, and their chemical structures have been elucidated by chemical and spectroscopic methos micrograms/ml.[15]

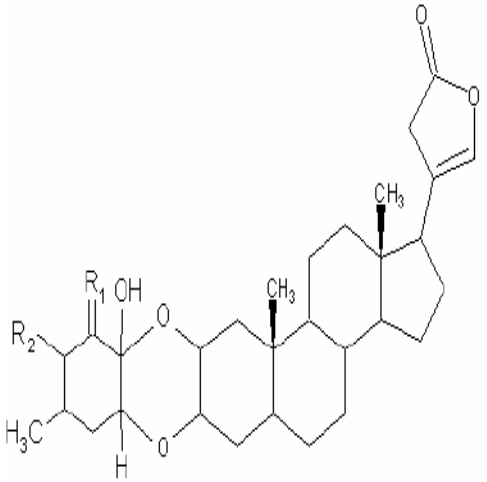
Pal studied crystallization, and properties of calotropins DI and DII from *C. gigantea.*[16]

12-0-benzoyl deacetyl metaplexigenin 3-0-beta-D-cymaropyranosyoleandropyranosyl(1-4)-beta-D-oleandropyranosyl(1-4)-beta-D-cymaro pyranosyl(1-4)-beta-D-pyranoside,respectively [17]. Besides isolation and characterization of isorhamnetin-3-O-rutinoside(11),isorhamnetin glucopyranoside (12) and taraxasteryl acetate, a new flavonol trisaccharide was isolated from the aerial parts of *C. gigantea*, and its structure was established as isorhamnetin-3-0-(2-0-beta-D-galactopyranosyl-6-O-alpha-L-rhamnopyranosyl)-beta- D-glucopyranoside (13) by a combination of fast atom bombardment mass spectroscopy, 'H and "C NMR spectra and some chemical degradations.[18]

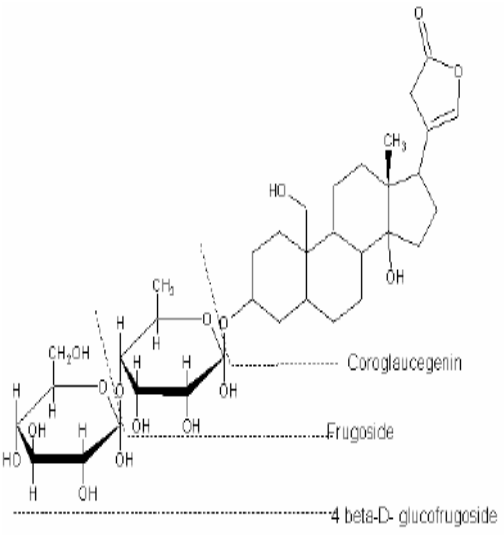
Giganticine, a novel non-protein amino acid, has been isolated from a methanol extract of the root bark of *Catotropis gigantea* and its structure established by spectroscopic methods. It exhibited a significant anti-feedant activity against nymphs of the desert locustSchistocercagregaria.[19] Two proteinase containing carbohydrate, called calotropain-FI and calotropain-FII, were purified from Calotropis gigantea latex by CM-Sephadex C-50 chromatography. Both calotropain-FI and Fll were found to homogeneous by rechromatography.[20]



(1) calotropoginin

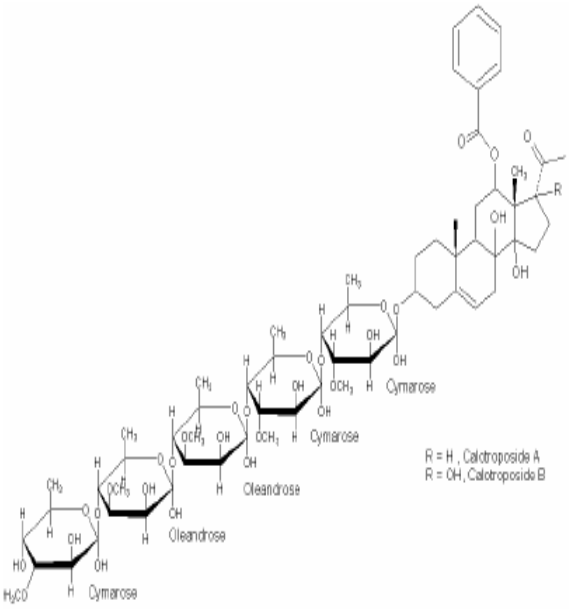


Structure No.	Nomenclature	R_1	R_2
2	Calotropin	α- OH, β- H	H
3	Uscharin	S- CH_2 / N-CH_2	H
4	Calotoxin	γ-H, γ-OH	H
5	Calactin	α- H, β- OH	H

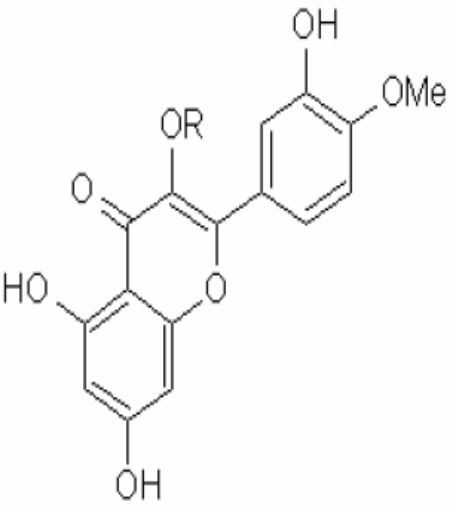


(6) Coroglaucegenin,

(7) Frugoside, (8) 4 beta-D-glucofrugoside,



(9) Clotroposide A, (10) Calotroposide B



Structure No.	Nomenclature	R
11	Isorhamnetin -3-O-rutinoside	Glu-ORha O Gal
12	Isorhamnetin 3-O-glucoside	Glucose
13	Isorhamnetin rhamnoglucoside	Glucose-O-Rhamnose

PHARMACOLOGICAL PROFILE

►**Studies on anti-diarrhoeal activity of *Calotropis gigantea* in experimental animals.** The anti-diarrheal effect of hydroalcoholic (50:50) extract of aerial part of *Calotropis gigantea* was studied against castor oil-induced-diarrhea model in rats. The gastrointestinal transit rate was expressed as the percentage of the longest distance traversed by the charcoal divided by the total length of the small intestine. The weight and volume of intestinal content induced by castor oil were studied by enteropooling method.[21]

►**Evaluation of antipyretic activity of *Calotropis gigantea* in experimental animals.** The roots of *Calotropis gigantea* have been used in leprosy, eczema, syphilis, elephantiasis, ulceration and cough in the Indian system of traditional medicin. The present communication

TAB (Typhoid) vaccine-induced pyrexia in rats and rabbits. In both yeast-induced and TAB vaccine-induced fever, the fever was significantly reduced and the body temperature was normalized by administration of 200 and 400 mg/kg dose intraperitoneally. Based on the results of the present study it can be concluded that the extract of *C.gigantea* has potential antipyretic activity against both yeast-induced and TAB vaccine-induced fever, indicating the possibility of developing *C.gigantea* as a cheaper and potent antipyretic agent.[22]

►**Procoagulant activity of *Calotropis gigantea* latex associated with fibrin (ogen)olytic activity.** The crude latex extract contained many proteins, which are highly basic in nature and exhibited strong proteolytic activity. The crude extract hydrolyses casein, human fibrinogen and crude fibrin clot in a dose-dependent manner. The hydrolyzing activity was completely inhibited by IAA indicating they belong to the super family, cysteine proteases. Crude extract hydrolyses Aalpha, Bbeta and gamma subunits of fibrinogen. Among all the subunits the preferential subunit to get hydrolyzed was Aalpha followed by Bbeta and gamma subunit is highly resistant and hydrolyzed at higher protein concentration or over a prolonged incubation time. The crude extract hydrolysis crude fibrin clot strongly compared to trypsin and papain. Pharmacologically the crude extract is hemorrhagic and induces skin hemorrhage at >75 microg and reduces coagulation time of citrated plasma from 150 to 47 s and promotes blood coagulation. [23]

►**Pregnancy interceptive activity of the roots of *Calotropis gigantea* Linn. in rats.** The ethanolic extract of the roots of *C.gigantea* Linn. exhibited 100% pregnancy interceptive activity in rats when administered as a single oral dose of 100 mg/kg on Day 1 postcoitum. The extract also exhibited 100% efficacy at the dose of 12.5 mg/kg when administered in the Days 1-5 and 1-7 postcoitum schedules. When administered during the peri-cum-early postimplantation period (i.e., Days 5-7 postcoitum at 250 mg/kg), most of the implantations showed signs of resorption. [24]

►**A Novel Insect Antifeedant Nonprotein AminoAcid from *Calotropis gigantea*** Giganticine (1), a novel nonprotein amino acid, has been isolated from a methanol extract of the root bark of *Calotropis gigantea* and its structure established by spectroscopic methods. It exhibited a significant antifeedant activity against nymphs of the desert locust Schistocerca gregaria. [25]

►**Cytotoxic principles of a Bangladeshi crude drug, akond mul (roots of *Calotropis gigantea* L.).** Three cardenolide glycosides, calotropin (1), frugoside(2),and4'-O-b Dglucopyranosylfrugoside (3), were obtained as the cytotoxic principles of "akond mul" (roots of *Calotropis gigantea* L.). The cytotoxicity of these compounds against various cell lines of human and mouse origin was tested. They showed similar cell line selectivity to those of cardiac glycosides such as digoxin and ouabain: they are toxic to cell lines of human origin, but not to those from mouse at 2 micrograms/ml. [26]

►**CNS activity of *Calotropis gigantea* roots.** Alcoholic extract of peeled roots of *Calotropis gigantea* R.Br. (Asclepiadaceae) was tested orally in albino rats at the dose level of 250 and 500mg/kg bodyweight for CNS activity. Prominent analgesic activity was observed in Eddy's hot plate method and acetic acid induced writhings. The paw licking time was delayed and the numbers of writhings were greatly reduced. Significant anticonvulsant activity was seen as there was a delay in the onset of pentylenetetrazole induced convulsions as well as decrease in its severity. The extract treated rats spent more time in the open arm of EPM showing its antianxiety activity. There was a decrease in the locomotor activity. The fall off time (motor coordination) was also decreased. A potentiation in the pentobarbitone-induced sleep due to the sedative effect of the extract was observed. No mortality was seen upto the dose of 1g/kg. These results show the analgesic, anticonvulsant, anxiolytic and sedative effect of the extract. [27]

►**Analgesic activity of *Calotropis gigantea* flower.** 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. [28]

►**Evaluation of anti-inflammatory activity of *Calotropis gigantea* in various biological systems.** The anti-inflammatory activity was evaluated using carrageenin-induced kaolin - induced rat paw oedema for acute and cotton-pellet granuloma, adjuvant-induced arthritis model for chronic inflammation. Antipyretic activity was carried out using yeast induced pyresis method. Phenylquinone--induced writhing method in mice was used for analgesic activity. Test compounds exhibited variable anti-inflammatory activity and peak activity of the test compounds were reached at 2 h. Alkaloid fraction possesses comparatively high initial anti-inflammatory activity. The residual anti-inflammatory activity of alkaloid fraction of *Calotropis gigantea* suggests either a greater malic enzyme of a filarial worm Setaria digitata: some properties and effects of drugs and herbal extracts. Mitochondrial malate dehydrogenase (mMDH) and malic enzyme (mME) of a filarial worm Setaria digitata were studied. The leaf extracts of *Ocimum sanctum, Lawsonia inermis* and *Calotropis gigantea* and leaf and flower extracts of *Azadirachta indica* were, however, found to inhibit both mMDH and mME. [32]

►**Effect of plant extracts and systemic fungicide on the pineapple fruit-rotting fungus, Ceratocystis paradoxa.** Antifungal activities of extracts of sixteen plants were tested against Ceratocystis paradoxa which causes soft rot of pineapples. Xanthium strumarium was the most effective followed by *Allium sativum*. The effectiveness of various extracts against C. paradoxa was in the decreasing order of *Meriandra bengalensis*, *Mentha piperita*, *Curcuma longa*, *Phlogacanthus thyrsiflorus*, *Toona ciliata*, *Vitex negundo*, *Azadirachta indica*, *Eupatorium birmanicum*, *Ocimum sanctum* and *Leucas aspera*. Extracts of *Cassia tora*, *Gynura cusimba*, *Calotropis gigantea* and *Ocimum canum* showed fungitoxicity. [33]

►**Evaluation of chemical constituents and free-radical scavenging activity of Swarnabhasma (gold ash), an ayurvedic drug.** In the present investigation, Swarnabhasma was prepared after proper purification and calcination as per Ayurvedic pharmacy which consisted of Realger (As(2)S(2)), Lead oxide (Pb(3)O(4)), Pure gold (Au) and Latex of *Calotropis gigantea*. [34]

►**Hepatoprotactive activity** Methanolic extract of*C.gigantea* leaf having good hepatoprotactive activity in dose dependant manner against CCl_4 induced hepatotoxicity in rats. [35]

►**Antitussive activity** Leaf extract showed antitussive activity due to presence of alkaloids and glycosides.[7]

►**Free redical scavenging activity** The ethanolic extracts of leaf and latex of *Calotropis procera* and *Calotropis gingantea* (Asciepadiacea) were tested of free radical Scavenging activity using 1,1 Dipthenyl Picryl hydrazyl radicas. The latex extracts of C. procera and C. gigeantea (10 mg/ml) exhibited greater capacity to scavenge DPPH radicals whereas leaf extract showed moderate free radical scavenging activity. [36]

►**Anti-inflammatory activity** To evaluate the effect of Calotropis *gingantea* in various experimental animal models. The anti-inflammatory activity was evaluated using carrageenin-induced kaolin-induced rat paw oedema for acute and cotton-pellet granuloma, adjuvant-induced arthritis model for chronic inflammation. Antipyretic activity was carried out using yeast induced pyresis method.[37]

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