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***Review Paper***

# The Genus *Calotropis*: An Overview on Bioactive Principles and their Bioefficacy

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## Abstract

*The herbal medicines occupy distinct position right from ancient period. Many higher plants accumulate extractable organic approaches substances in quantities sufficient to be economically management of diseases. The genus Calotropis possesses two species i. e. C. procera and C. gigantea .They contain many phytochemicals with potential pharmacological activities. C. procera has been investigated for many genes such as USBS1450 , expansin gene, Usp-like gene and MAPK-like gene. The most important of chemically active constituents of plants are alkaloids, tannin, flavonoid and phenolic compounds. Both species have been known to possess antimicrobial, analgesic, antitumor, antioxidant, anti-diarrhoeal, anti-malarial activity etc. They are also using as a source of methane, through anaerobic fermentation for bio fuel production.*

**Keywords**: *C. procera*, *C.* gigantea, phytochemicals, pharmacological activites.

## Introduction

From pre-historic times to the modern era in many parts of the world and India, plants, animals and other natural objects have profound influence on culture and civilization of man. The Indian subcontinent is rich in medicinal plants and is one of the richest countries in terms of genetic diversity of medicinal plants. It exhibits a wide range in topography and climate. Moreover the agro climatic conditions are conducive for introducing and domesticating new exotic plant varieties[1]. Plants have been a rich source of medicines because they produce wide array of bioactive molecules, most of which probably evolved as a chemical defence against predation or infection[2]. Natural products, which come out from medicinal plants are important for pharmaceutical research and for drug development as a sources of therapeutic agents. At presents the demand for herbal or medicinal plant products has increased significantly. The herbal medicines occupy distinct position right from ancient period. Many higher plants accumulate extractable organic approaches substances in quantities sufficient to be economically management of diseases. It is estimated that only one percent of 2,65,000 flowering plants on earth have been studied exhaustively for their chemical composition and potential against important medicinal value[3]. The most important of these chemically active constituents of plants are alkaloids, tannin, flavonoid and phenolic compounds. Many of these indigenous medicinal plants are also used for medicinal purposes[4,5]. *Calotropis* belongs to *Asclepiadaceae* or Milkweed or Aak family, contains many phytochemicals with potential pharmacological activities. They are commonly known as milkweeds because of the latex they produce. *Calotropis* species are considered common weeds in some parts of the world. It is represented in India by two species viz. *C. procera* and *C. gigantea*. In ancient ayurvedic medicine the plant *C. gigantea* is known as "Sweta Arka" and C. procera as "Raktha Arka". Both of them are often similar in their botanical aspects and also have similar pharmacological effects[6]. *Calotropis* is used as a traditional medicinal plant[7-12] with unique properties[13,14]. Traditionally *Calotropis* is used alone or with other medicines[15] to treat common disease such as fevers, rheumatism, indigestion, cough, cold, eczema, asthma, elephantiasis, nausea, vomiting, diarrhea[16]. The plant is poisonous can lead to blindness if its juice is put in to the eyes. The milky exudates from the plant are a corrosive. It is said to have mercury like effects on the human body and is sometimes referred as vegetable mercury. Calotropin a compound in the latex is more toxic than strychnine which is responsible for the cytotoxicity of *Apocynum cannabinum*[17]. Plant is also using as a source of methane, through anaerobic fermentation for bio fuel production[18]. *Calotropis procera*, a laticiferous arid plant has been identified as a potential petrocrop. It is a potential plant for bioenergy and biofuel production in semi arid regions of the country[19,20].

**Distribution**: *C. procera* is native to West Africa as far south as Angola, North and East Africa, Madagascar, the Arabian Peninsula, SW Asia (India, Pakistan, Afghanistan, Iran, Arabia, Jordan), and Indochina to Malaysia[21]. The species is now naturalized in Australia, many Pacific islands, Mexico, Central and South America, and the Caribbean islands. It is distributed in tropical and sub-tropical regions of India including Jammu Kashmir, Rajasthan, Gujarat, Tamil Nadu, Orissa, West Bengal,

Uttar Pradesh etc. *C. procera* is widely distributed in Western Rajasthan. *C. gigantea* is native to Cambodia, Indonesia, Malaysia, Philippines, Thailand, Sri Lanka, India and China. It is growing widely throughout the tropical and subtropical regions of Asia and Africa[6]. *C. gigantea* is found mostly under cultivated conditions near temples in Jaipur, Bharatpur, Udaipur, Bhilwara, Banswara division with relatively moderate climatic conditions[22].

## Biophysical limits

*C. procera* grows in dry habitat (150 to 1000 mm precipitation) and sometimes in excessively drained soils in areas with as much as 2000 mm of annual precipitation. Giant milkweed may be found in areas up to 1,000 m in elevation in India[23]. *C. gigantea* is drought resistant, salt tolerant to a relatively high degree, grows wild up to 900 meters throughout the country[24] and prefers disturbed sandy soils with mean annual rainfall: 300-400 mm.

Plants of the both species are soft-wooded, evergreen, perennial shrub[27]. *C. procera* is drought-resistant, salt-tolerant to a relatively high degree, and through its wind and animal dispersed seeds, it quickly becomes established as a weed along degraded roadsides, lagoon edges and in overgrazed native pastures . *C. procera* is well suited for intensive energy farming in arid or semi-arid regions where frost is not a limiting factor[6]. The botanical description is given below:

**Roots**: Giant milkweed has a very deep, stout tap root with few or no near surface lateral roots. Its roots were found to have few branches and reach depths of 1.7 to 3.0 m in Indian sandy desert soils[28].

**Shoots**: It has one or a few stems, few branches, and relatively few leaves, mostly concentrated near the growing tip. The bark is corky, furrowed, and light gray. A copious white sap flows whenever stems or leaves are cut.

**Leaves***:* The opposite leaves are oblong, obovate to nearly orbicular, short-pointed to blunt at the apex and have very short petioles below a nearly clasping, heart-shaped base. The leaf blades are light to dark green with nearly white veins. They are 7 to 18 cm long and 5 to 13 cm broad, slightly leathery, and have a fine coat of soft hairs that rub off.

**Flowers:** The inflorescence is an umbel-like cyme at or near the ends of twigs. Many flowers are borne on the inflorescence on pedicels that are about 1 inch long. Flowers are about 3/4 inch across. They consist of five sepals, approximately 1/4 inch long. The corolla is slightly succulent and is made up of five showy erect petals. The petals are about 3/4 inches long and are whitish and tinged with purple at the apex.

**Fruit***:* Flowers are replaced by kidney-shaped, recurved, inflated follicles. Immature fruits are green and become brown when mature. They are 3-4.5 inches long and 2-2.5 inches wide. Slightly fleshy, they split open on one side to reveal a rough fibrous interior. Most plants flower and fruit simultaneously throughout the year.

**Seeds:** Seeds are many, flat, brown, with tufts of long white silky hair (pappus) at one end.

***C. gigantea*** is a xerophytic, erect shrub[27]. It is a weed of roadsides and watercourses and commonly invades old cultivated land and heavily grazed areas where there is little competition from grass. It is drought resistant, salt tolerant to a relatively high degree[23]. The botanical description is given below:-

**Roots**: It roots very deeply and rarely grows in soils that are shallow over unfractured rock. Soils of all textures and derived from most parent materials are tolerated, as well as soils with high sodium saturation[29].

**Shoots**: The stem is woody with yellowish white bark, young stem and branches covered with soft, loosely apprised, whitish, waxy or sometime powdery pubescence[30].

**Leaves**: Leaves freshly, obovate, apex acute, rarely rounded, base cordate, 6-20 cm long and 3-8 cm wide[30].

**Flowers:** Flowers are lilac, pale rose or purple, rarely light greenish–yellow or white, inodorous[30].

**Fruit**: Fruits are inflated, obliquely ovoid follicles that split and invert when mature to release flat, brown seeds with a tuft of white hairs at one end[31].

**Seeds**: Seeds are many, small, flat, obovate, 6x5 mm, compressed with silky white pappus, 3 cm or more long[29].

## Phytochemistry

In *C. procera* genetic diversity has been investigated[32,33]. Many genes have been investigated in *C. procera* such as USBS1450[34], expansin gene[35,36], Usp-like gene[37] and MAPK-like gene[38]. Many proteins and enzymes have been studied at molecular level such as Procerain B[39], proteolytic and milk clotting enzyme[40], calotropin DI[41] and heat shock protein 70[42]. Phytochemical studies on *C. procera* have afforded several types of compounds such as flavonoids, cardiac glycosides, sterols, alkaloids cardenolide, triterpinoids, resins, anthocyanins, tannins, saponins, α- and β amyrin, teraxasterol, gigantin, giganteol, isogiganteol, β -sitosterol and a wax[43]. In *C. gigantea,* genetic characterization has been carried out[44,45]. Chemical investigations of *C. gigantea* report isolation of different types of phytochemicals such as flavonoids, glycosides, steroids, triterpenoids, cardiac glycosides, calotropin, calotoxin, syriogenin, proceroside, calctin. Calotrposide A, calotroposide, calotropin D1 and D2, procerosterol, taraxsterol *etc*.[46]. Chemical investigation of the plant has shown the presence of cardiac glycosides, saponins, flavonoids, steroids, terpenoids[47]. (table**-**2)

**Table-1**
**The synonyms /vernacular and common names of both species**

| **Synonyms /Vernacular names** | *Calotropis procera (L.) Dryand, C. heterophylla Wall., C. busseana K.Schum, C. syriaca Woodson, C. inflexa Chiov., Asclepias procera Aiton (basionym) and incorrectly C. procera (Willd.) R.Br. ex Aiton* [25] | *Asclepias gigentea* [26] |
|---|---|---|
| English | Sodom apple, calotrope, French cotton, small crown flower | Crown flower, giant Indian milkweed, King's crown |
| French | cotton-france, arbre de soie, and bois canon | Faux arbre de soie, mercure vegetal |
| Hindi | Arka, Madar,Arkaparna, Vikran, Raktapushpa, Sukhalphal, Ashphot | Aak, Mandar, (Kannada) Ekka, Ganrupa, Vasukh, Shvetapushpa, Sadapushpa, Alarka, Partapsh |

**Table-2**
**A comparative account of phytochemicals present in both seleced species**

| Plant Parts | *C. procera* | *C. gigantean* |
|---|---|---|
| Whole plant | Flavonoids, cardiac glycosides, sterols, teraxasterol, gigantin, giganteol, isogiganteol and β-sitosterol, alkaloids cardenolide, triterpinoids, resins, anthocyanins, tannins, saponins , α/β amyrin[48] | Cardiac glycosides, calotropin calotoxin, syriogenin, proceroside, sterols, calctin, calotroposide A, calotroposide, calotropin D1 and D2, procerosterol, taraxsterol, saponins and flavonoids[45,47,49, 50] |
| Root/root bark | Lupeol, β sitosterol, α-amyrin[51], β-amyrin[52], querctin-3-rutinoside, calotropterpenyl ester, calotropursenyl acetate, calotropfridelenyl acetate, akundarol isovalerate, mundarol isovalerate,quercetin-3-rutinoside[53-55] Procerursenyl acetate, proceranol N-dotriacont-6ene phosphate[56] | Calotroposide A and B, oxypregnane-digoglycosides[57], cardanolide glycosides such as calotropin, frugoside and 4-o-beta-D glucopyranosyl frugoside[58,59]. |
| Leaves | Amyrin, amyrin acetate, β -sitosterol, urosolic acid, cardenolides, calotropin, calotropagenin [60], alkaloids calotropin, calotaxein and uskerin[18]. | Isorhamnetin-3-o-rutinoside, isorhamnetin-3-o-glucopyranoside and taraxasteryl acetate, isorhamnetin-3-o[2-o-beta-D-galactopyranoside [57], ascorbic acid,o-pyrocatechic acid, β-amyrin, taxasterol, tarasterol, β-sitosterol, 19-Nor and 18, 20epoxy cardenolides,15 β hydroxy cardenolid-es, 16-hydroxy calactinic acid, Methylester[61]. |
| Latex | Caloptropaine[62], Caoutchouc, calotropin, calotoxin, calactin, uscharin trypsin, voruscharin, uzarigenin, syriogenin, proceroside[63]. | Carbohydrate, calotropain FI and FII[64], lupeol, calotropin, calotoxin, uscharidin[65]. |
| Flowers | Glucose, glucosamine, L-rhamnoseterpenes, multiflavenol, and cyclisadol[43], quercetin-3-ratinoside, sterol, calactin, calotoxin, calotropagenin, calotropin polysaccharides, giganteol, isogiganteol, glactuceryl acetate, uscharidin, 3-epimoretenol, uzarigenin, voruscharina-calotropeol, D-arabinose[66]. | Cardiac glycosides, caloropin, uscharin, calotoxin, calactin, uscharidin, gigantin, calotropin D1, DII, calotropin F1 and FII[67] |

## Antimicrobial and other biological activities

*C. procera* has potential antimicrobial properties against microbial infections[54] and insecticidal activities[68]. The extracts from roots show anti-malarial activity[23,69-71]. The latex has nematicidial activity[72], antimicrobial activity[62], insecticidal activity[73] and anti malarial activity[74]. The leaves are reported for antimicrobial activity[75], insecticidal activity[68] and nematicides[72]. The flowers show antimicrobial activity, larvicidal activity[76] and anthelmintic[77,78]. *C. gigantea* has also exhibited antimicrobial properties[79-82], antifungal activity[83], antiviral properties[84] and anthelmintic activity[85]. The root extracts show lavicidal[86], insecticidal activity[87,78]. Antimicrobial activity has been carried out in latex[7,80-82] and flowers[88]. In latex, antifungal[89] have been reported.

## Pharmacological study

All the parts, *viz.* root, stem, leaf and flowers of *C. procera* are in common use in indigenous system of medicine[88]. The roots are reported to have anti-fertility and anti-ulcer effects[75]. The latex of the plant is reported to possess analgesic and wound healing activity[90,91] and also exhibited local anesthetic activity[92]. Fewer reports are available with respect to the pharmacological properties of *C. gigantea*[93]. Different plant parts have shown biological activities *viz.* antitumor activity[94-96] anti-diabetic, analgesic and antinociceptive activity[97], anti-diarrhoeal[96], antifertility and emmenagogue[98], antipyretic, anti-inflammatory, wound healing, analgesic[99], antioxidant[100], anthelmintic activity[86], anticancer activity[101]. Ayurveda system of medicine recommends the use of *C. gigantea* in the treatment of cutaneous diseases, intestinal worms, cough, asthma[102,103], abortifacient[104], antidote for scorpion stings and insect bites[105], anxiety and pain[65], CNS activity[106], cold[15], expectorant[107], cytotoxic activity[108-111]. (Table-3).

## Significance

India has over 180 million of wasteland out of which 90 million ha is uncultivable. The degraded and denuded lands arise due to soil erosions as well as secondary salinizations. However *C. procera* is a potential plant for bioenergy and biofuel production in semi arid regions of the country because it is able to grow on such lands. The plant has a growth potential of 2 dry tones to 40 dry tons per ha depending on the agro climatic conditions of its growth. The plant has high level of regeneration potential and could be harvested up to 4 times a year. The plant yields valuable hydrocarbons which could be converted into diesel substitutes. The bio-diesel derived from *C. procera* is free from $NO_x$ gases, $SO_2$ and Suspended Particulate Matter (SPM) and has high cetane value. Due to its enormous potential for growth under adverse climatic conditions *C. procera* is suggested as potential plant for bio-diesel production under semi-arid and arid conditions. Almost all the parts of *C. procera* yield hydrocarbons. Biocrude obtained from this plant is reported to be a rich source of triterpenoid type of hydrocarbons. Hexane extract of different parts of *C. procera viz.* whole plant, stem, leaves and pods have been evaluated. Recently ethanol derived from renewable biomass has emerged as a major contender expected to replace liquid petroleum fuel. The potential of these flowers as a source of ethanol can further be studied.*C. procera* and *C. gigantea* have many curative principles and other economic values with the following features: perennial shrub, distributed up to 1000m elevation in the tropical and subtropical areas, growing in all types of soils and environmental conditions, requiring no cultivation practices.

A thorough review of the published literature on both species shows that phytochemical composition of these plant species exhibited the presence of various active principles justifies the use of these species for various ailments by traditional practitioners. This is probably due to the fact that each of the components identified has one therapeutic usage or another. For instance, plants rich in saponins have immune boosting and anti-inflammatory properties. Similarly tannins have been reported to have antibacterial potential due to their basic character that allows them to react with proteins to form stable water soluble compounds thereby killing the Bacteria by directly damaging its cell membrane. The antibacterial activities of alkaloids and flavonoids have been reported by a number of authors. However, higher doses cause vomiting diarrhea, bradycardia and convulsions These medicinal plants produce toxic effects on the animal system, if they are not used carefully or in regulated amount. These plant species are useful for find to increasing applications as source of direct therapeutic agents, models for new synthetic compounds and as taxonomic marker for the discovery of new compounds. The investigation carried out by us led to certain findings about the phytochemical features which no doubt can be proved beneficial and serve as scientific background for further isolation steps to obtain the lead compound.

## Conclusion

Through this review, the assessment of variation present for chemical composition will reflect the possibility of selecting more desired species for systematic exploitation at commercial level. At the same time it will lead to development of better methods of characterization and evaluation of germplasm collections, and to increase the utilization of plant genetic resources.

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**Table-3**
**A comparative account of pharmacological studies of both selected species**

| Plant parts | *C. procera* | *C. gigentea* |
|---|---|---|
| Whole plant | Anticancer[54], Antifertility, Molluscidal[87] and anti-ulcer[75]. | Antitumor[94,95,96], anti-diarrhoeal[96,111,112], analgesic[99], antipyretic[114], anticancer[101], wound healing[113], anti-inflammatory[114,16]. |
| Root/ Root Bark | Anti-inflammatory, analgesic activity[115] purgative[69,70,23,71,87] hepatoprotective effect[116], antiproliferative activity[117], cytotoxicity[118]. | Abortifacient, purgative, anti-diarrohoeal activity[86], antipyretic activity[119], pregnancy interceptive[120], cytotoxicity [58]. |
| Shoot | Analgesic[94] abortifacient, anthelmintic[102]. | Anti-diarrheal[111], hepatoprotective activity[122]. |
| Leaves | Anti-inflammatory, expectorant[123], antioxidant[124,42]. | Anti-inflammatory and antipyretic activity[16], hepatoprotective activity[125], cytotoxicity[61]. |
| Latex | Anti-inflammatory[126],antipyretic effect, analgesic and wound healing activity[91,92], antinociceptive activity[127],local anesthetic activity[78] laxative[75], antisperm activity[96], anti-arthritic activity[128]. | Anti-inflammatory[115], free radical scavenging activity[129], wound healing[93], procogulant activity[122]. |
| Flowers | Anti-inflammatory, antipyretic, analgesic activity[130,80,83] hepatoprotective activity[59,131], improve digestion, catarrh and increases appetite[72,132], astringent [77]. | Anti-inflammatory activity[50], antitumor[133], hepatoprotective, anticonvulsant, antiasthmatic and analgesic[83,134,135] |

## References


**1.** Mitchell R.N. and Cotran R.S. (2000). In: Robinsons Basic Pathology, 7th Ed, Harcourt Pvt. Ltd, New Delhi, India, 33-42.

**2.** Ramaprabha M. and Vasantha K. (2012). Phytochemical and antibacterial activity of *Calotropis- procera* (Ait.) R.Br. flowers, *Int. J. of Pharma and Biosciences,* 3(1), 1-6.

**3.** Cox P.A. and Balick M.J. (1994). The ethnobotanical approach to drug discovery. *Scientific American*, 270, 60-65.

**4.** Aiyelaagbe O.O. and Osamudiamen M.P. (2009). Phytochemical screening for active compounds in *Mangifera indica* leaves from Ibadan, Oya State, *Plant Sci. Res.*, 2(1), 11-13.

**5.** Edeoga H.O., Okwu D.E. and Mbaebie B.O. (2005). Phytochemical constituents of some Nigerian medicinal Plants, *African Journal of Biotechnology*, 4(7), 685-688.

**6.** Gamble J.S. (1935). Flora of the Presidency of Madras, Vol. I, b II, III, Botanical survey of India, Calcutta.

**7.** Rastogi R.P. and Mehrotra B.M. (1991). In: Compendium of Indian Medicinal Plants. Pbl. Central Drug Research Institute, Lucknow and Publications and Information Directorate, N. Delhi, 70-73.

**8.** Oudhia P. and Dixit A. (1994). *Weed News*. 1(2), 19-21.

**9.** Oudhia P. (1999a). *Int. Rice Res. Notes*, 24(1), 40.

**10.** Oudhia P. (1999b). Int. Chickpea and Pigeonpea Newslett., 6, 29-33

**11.** Oudhia P. Int. Arachis Newslett.,19, 62-64 (1999c)

**12.** Oudhia P. (1999d). Rachis, 18(1), 40-41.

**13.** Oudhia P. and Tripathi R.S. (1998). Proc. National Conference on Health Care and Development of Herbal Medicines, IGAU, Raipur, India 29-30 Aug. 1997. 71-78.

**14.** Oudhia P. and Tripathi R.S. (1999). *World Weeds,* 4, 109-119

**15.** Caius J.F. (1986). The Medicinal and Poisonous Plants of India, Scientific Publ., Jodhpur.

**16.** Das S., Das M.K. and Basu S.P. (2009). Evaluation of anti-inflammatory effect of *Calotropis gigantea* and Tridax procumbens on Wistar albino rats, *J. Pharm. Sci. and Res.*, 1(4), 123–12.

**17.** Pathyusha R.J.B. (2012). Potential of local anesthetic activity of *Calotropis procera* latex with epinephrine and pH in guinea pig. http//www.pharmatutor.org/ articles/ Pharmatutor-art-1043.

**18.** Ashwari K. (2009). Productivity of Calotropis procera and its use in renewable Energy, *Science Blogging*.http: //www.scientificblogging.com/humboldt_fellow_and_science/productivity_calotropis_procera_and_its_use_renewable_energy. retrieved on 5/01/2010.

**19.** Behera B.K., Arora M. and Sharma D.K. (2000). Studies on Biotransformation of *Calotropis Procera* Latex: A Renewable Source of Petroleum, Value-Added Chemicals, and Products, Energy Sources, 22(9), 781-807.

**20.** Rathore M. and Meena R.K. (2010). Potential of utilizing calotropis procera flower biomass as a renewable source of energy, *Journal of Phytology,* 2(1), 78–83.

**21.** Rahman M.A. and Wilcock C.C. (1991). A taxonomic

revision of *Calotropis* (Asclepiadaceae). *Nordic Journal of Botany*, 11(3), 301-308.

**22.** Kumar A. and Kumar V.R. (2002). Bioenergy potential of semi-arid regions of Rajasthan. In 12th European Conference on Biomass for Energy, Industry and Climate Protection, pp. 372- 374, eds. W. Palz, J. Spitzer, K. Maniatis, K. Kwant, P. Helm and A. Grassi (ETA-Florence and WIPMunich) Germany.

**23.** Parrotta J.A. (2001). Healing plants of Peninsular India. CAB International, Wallingford, UK and New York, 944.

**24.** Sharma A.P. and Tripathi B.D. (2009). Assessment of atmospheric PAHs profile through *Calotropis gigantea* R.Br. leaves in the vicinity of an Indian coal-fired power plant, *Environ Monit Assess*, 149, 477–482.

**25.** Forster P.I. (1992). A taxonomic account of the genus *Calotropis* R.Br. (Asclepiadaceae) in Australia, *Nuytsia,* 8, 201–208.

**26.** Gamble J.S. (1923). Asclepias *gigantea*n, L. Sp. Pl. 2, 832.

**27.** Watkins John V., Sheehan Thomas J. and Black Robert J. (2005). Florida Landscape Plants: Native and Exotic. University Press of Florida, Gainesville, Florida.

**28.** Sharma B.M. (1968). Root systems of some desert plants in Churu, Rajasthan, *Indian Forester*, 94(3), 240-246.

**29.** Carol J.P., Jignesh H.P., Mayuree A.P., Anar J.P. (2012). A comprehensive review on plant *Calotropis gigantea*. *International Journal of Institutional Pharmacy and Life Sciences*, 2(2). 463-470.

**30.** Sharma P.C., Yelne M.B. and Dennis T.J. (2002). Data base on Medicinal plant used in Ayurveda. Central Council for Research in Ayurveda and siddha, New-Delhi, I, 6-10.

**31.** Little E.L., Jr. Woodbury R.O. and Wadsworth F.H. (1974). Trees of Puerto Rico and the Virgin Islands.. Agriculture Handbook 449. U.S. Department of Agriculture, Washingtion, DC., 2(1), 24.

**32.** Pandeya S.C., Chandra A. and Pathak P.S. (2007). Genetic diversity in some perennial plant species with-in short distances, *Journal of Environmental Biology*, 28(1), 83-86.

**33.** Bekhit M.M.M., El-Shawaf I.I.S., Hassan A.M., El-Saied F.M. and Masoud I.M. (2008). Genetic distances between three Ushaar (*Calotropis procera* (Ait) f.) genotypes as measured by RAPD and ISSR techniques. The fourth conference of sustainab.

**34.** Juncker T., Schumacher M., Dicato M., Diederich M. (2009). UNBS1450 from *Calotropis procera* as a regulator of signaling pathways involved in proliferation and cell death, *Biochem. Pharmacol.* 78, 1-10.

**35.** Cheema H.M.N., Bashir A., Khatoon A., Iqbal N., Zafar Y., Malik K.A. (2010). Molecular characterization and transcriptome profiling of expansin genes isolated from *Calotropis procera* fibers. *Electron. J. Biotechnol.,* 13(6), 10-11.

**36.** Bajwa K.S., Shahid A.A., Rao A.Q., Kiani M.S., Ashraf M.A., Dahab A.A., Bakhsh A., Latif A., Khan M.A.U., Puspito M.A., Aftab A., Bashir A. and Husnain T. (2013). Expression of *Calotropis procera* expansin gene CpEXPA3 enhances cotton fibre strength, *AJCS*, 7(2), 206-212.

**37.** Shokry A.M., Al-Karim S., Ramadan A., Gadallah N., Al Attas S.G., Sabir J.S.M., Hassan S.M., Madkour M.A., Bressan R., Mahfouz M., Bahieldin A., Detection of a Usp-like gene in *Calotropis procera* plant from thede novo assembled genome contigs of the high-throughput sequencing dataset, *Molecular biology and genetics/Biologie et génétique moléculaires* (in press).

**38.** Ramadan A.M., Shokry A.M., Gadalla N.O.,Hassan S.M., Edris S., Al-Kordy M.A., Abuzinadah O.A., Sabir J.S.M., Alakilli S.Y.M., Al-Zahrani, H.S., Hussein R.M., El-Domyati F.M. and Bahieldin A. (2012). Detection of a MAPK-Like gene in *Calotropis procera* plant from the *de novo* assembled genome contigs of the high throughput sequencing dataset, *Life Science Journal*, 9(1), 157-166.

**39.** Singh A.N., Yadav P. and Dubey V.K. (2013). cDNA Cloning and Molecular Modeling of *Procera*in B, a Novel Cysteine Endopeptidase Isolated from *Calotropis procera, PLoS ONE*, 8(3), e59806.

**40.** Oseni and Ekperigin (2013). Partial Characterization of Proteolytic and Milk Clotting Enzymes in Sodom Apple *Calotropis procera* (Ait.) R.Br. (Asclepiadaceae) Plant, 3(2), 256-263.

**41.** Heinemann U., Pal G.P., Hilgenfeld R. (1982). Saenger W., Crystal and molecular structure of the sulfhydryl protease calotropin DI at 3.2 A resolution, *J. Mol. Biol.,*161(4), 591-606.

**42.** Hemalatha R.G. and Padmini E. (2011). Predictions for heat shock protein 70 related gene network and metabolite changes in *Calotropis* and/or fructose fed rats, *International Journal of Pharmaceutical Sciences Review and Research,* 10(1), 159-164.

**43.** Al-Yahya M.A., Al-Meshal I.A., Mossa J.S., Al-Badr A.A. and Tarig M. (1990). Saudi plants: A phytochemical and biological approach. Riyadh: King Saud university press, 31-34.

**44.** Mahmood T., Aslam R., Rehman S. and Naqvi S. M.A.S. (2013). Molecular markers assisted genetic characterization of different salt tolerant plant species, *The Journal of Animal and Plant Sciences*, 23(5), 1441-1447.

**45.** Dhivya R. and Manimegalai K. (2013). *In silico*

Molecular Docking and Molecular Dynamics applications in the Designing of a New Mosquito Repellent from the Plant *Calotropis gigantean* Targeting the Odorant Binding Protein of *Culex quinquefasciatus. Int. J. Pharm. Phytopharmacol. Res*., 3(2), 134 -138.

**46.** Murti P. and Seshadr T.R. (1945). Chemical composition of *Calotropis gigantea*n: Part VI. Flowers. A Comparison of the Composition of the Various Parts of the Plant, Proc. Ind. *Acad. Sci.*, 304–309.

**47.** Seniya C., Trivedia S.S. and Verma S.K. (2011). Antibacterial efficacy of *Calotropis gigantea, J. Chem. Pharm. Res.,* 3(6), 330-336.

**48.** Yoganarasimhan S.N. (1996). Medicinal Plants of India, Vol. 1, Interline Publishing Pvt. Ltd., Bangalore. 88.

**49.** Kumar S.S., Sivamani P., Baskaran C. and Mohamad M.J. (2012). Evaluation of antimicrobial activity and phytochemical analysis of organic solvent extracts of *Calotropis gigantean,IOSR Journal f Pharmacy*, 2(3), 389-394.

**50.** Jaiswal J., Srivastava S., Gautam H. and Sharma S. (2013). Phytochemical screening of *Calotropis gigantea*n (Madar) seeds extracts, *IJPRS*, 2(2), 235-238.

**51.** Saber A.H., Maharan G.H. and Rizkallah M.M. (1969). Sterols and pentacyclic triterpenes of alotropis *procera, Bull. Fac. Pharm Cairo Univ*, 7(1), 91-104.

**52.** Saxena V.K. and Saxena Y.P. (1979). Isolation and study of triterpenoids from *Calotropis procera, J. Res. Indian Med. Yoga Homeopathy*, 14, 152-154.

**53.** Lal S.D., Kumar P. and Pannu D.S. (1985). Quercetin-3-rutinoside in *Calotropis procera*, *J. Sci. Res.*, 7(1), 141-142.

**54.** Ansari S.H. and Ali M. (2001). Norditerpenic ester and pentacyclic triterpenoids from root bark of *Calotropis procera* (Ait) R. Br., *Pharmazie*., 56(2), 175-177.

**55.** Akhtar N. and Malik A. (1998). *Procera*genin, an antibacterial cardenolide from *Calotropis procera*, *Phytochemistry*, 31(8). 2821-2824.

**56.** Swpanali M.G., Patil M.V. and Mahajan R.T. (2012). Phytochemical screening and antimicrobial activity of *Calotropis procera* root, *Int. Res. Phytochem. Pharmacol.*, 2(3),143-146.

**57.** Kitagawa I., Zhang R.S., Park J.D., Baek N.I., Takeda Y., Yoshikawa M., Shibuya H. (1992). Indonesian medicinal plants. I. Chemical structures of calotroposides A and B, two new oxypregnane-oligoglycosides from the root of *Calotropis gigantea* (Asclepiadaceae). *Chem. Pharm. Bul*., 40, 2007-2013.

**58.** Kiuchi F., Fukao Y., Maruyama T., Obata T., Tanaka M., Sasaki T., Mikage M., Haque M.E., Tsuda Y. (1998). Cytotoxic principles of a Bangladeshi crude drug, akond mul (roots of *Calotropis gigantea* L.). *Chem. Pharm. Bull*. (Tokyo). 46(3), 528-30.

**59.** Balamurugan P., Muralidharan and Selvarajan S. (2009). Antiepileptic Activity of Poly Herbal Extract from Indian Medicinal Plants, *J. Sci. Res*., 1(1), 153-159.

**60.** Abbas B., El Tayeb A.E. and Sulleiman YR (1992). *Calotropis procera*: feed potential for arid zones, *Veterinary Record*, 131(6), 132.

**61.** Lhinhatrakool T. and Sutthivaiyakit S. (2006). 19-Nor- and 18,20-Epoxy-cardenolides from the Leaves of *Calotropis gigantea, J. Nat. Prod*., 69(8),1249-51.

**62.** Kishore N. and Chopra A.K. (1997). Antimicrobial properties of *Calotropis procera* Ait. In different seasons: A study *in vitro*. *Biological Memoirs*, 23(2), 53-57.

**63.** Atef G.H., Elgamal M.H.A., Morsy N.A.M., Duddeck H., Kovacs J. and Toth G. (1999). Two cardenolides from *Calotropis procera, J. Magn. Reson. Chem.,* 17, 754-757.

**64.** Abraham K.I. and Joshi P.N. (1979). Studies on proteinases from *Calotropis gigantea* latex. I. Purification and some properties of two proteinases containing carbohydrate, *Biochim Biophys Acta*, 568(1), 111-119.

**65.** Sharma V. (2001). Dravyaguna Vigyan, Chaukhambala Bharti Academy, Varanasi, 2,435.

**66.** Ansari S.H. and Ali M. (1999). New oleanene triterpenes from root bark of *Calotropis procera, Medicinal and Aromatic Plant Sci.,* 21(4), 978-981.

**67.** Kirtikar K.R. and Basu B.D. (1999). Indian Medicinal Plants. 2nd Ed, Vol. III, International Book Distributors, Dehradun, 191-192, 420-422, 993-994, 2045-2047.

**68.** Begum N., Sharma B. and Pandey R.A. (2010). Evaluation of insecticidal efficacy of *Calotropis procera* Linn., *Biokemistri*., 1(1), 1-6.

**69.** Mishra H.P. and Fridowich I. (1972). The role of super oxide anion in the autooxidation of epinephrine and a simple assay for superoxide dismutase, *J. Biol. Chem.* 247, 3170-3185.

**70.** Jain P.K., Kumar N. and Verma R. (1985). Clinical trials of Arka Mula Tuvaka, bark of Calotropios *procera* Ait. (R.Br.) on atisar and Pravihika- A preliminary study, *J. research in Aurveda and Siddha*, 6, 89-91.

**71.** Vohra R. (2004). *Calotropis* the medicinal weed. Online medicinal book store, India.

**72.** Anver S. and Alam M.M. (1992). Effect of late seed dressing on interacting root-knot and reniform nematodes, *Afro-Asian Journal of Nematology*, 2(1-2), 17-20.

**73.** Moursey L.E. (1997). Insecticidal activity of *Calotropis procera* extracts on the flesh fly, *Sarcophaga*

*haemorrhoidalis* Fallen, *Journal of the Egyptian Society of Parasitology*, 27(2)., 505-514.

**74.** Khory R.N., Katrak N. and Neeraj N. (1981). *Calotropis gigantea* and *Calotropis procera*. In Materia Medica of India and their Therapeutics, New Delhi, 395–396.

**75.** Mann A. and Abalaka M.E. (1997). The antimicrobial activity of the leaf extracts of *Calotropis procera*, *Biomedical Letters*, 55(219), 205-210.

**76.** Morcelle S.R., Caffini N.O. and Priolo N., Proteolytic properties of Funastrum clausum latex, *Fitoterapia,* 75(5), 480-493.

**77.** Agharkar SP (1991). Medicinal plants of Bombay presidency. *Scientific Publ.*, India. 48-49.

**78.** Mukherjee B., Bose S. and Dutta S.K. (2010). Phytochemical and pharmacological investigation of fresh flower extract of *Calotropis procera* Linn., *Int. J. of Pharmaceutical Sciences and Research,* 1(2), 182-187.

**79.** Ashraful M.A., Rowshanul M.H., Nikkon F., Rahman M. and Karim M.R. (2008). Antimicrobial activity of Akanda (*Calotropis gigantea* L.) on some pathogenic bacteria, *Bangladesh Journal of Scientific and Industrial Research*, 43, 397–404.

**80.** Nenaah E.G. and Ahmed M.E. (2011). Antimicrobial activity of extracts and latex of *Calotropis procera* and synergistic effect with reference antimicrobials, *Research journal of medicinal plants*, 5(6), 706-716.

**81.** Goyal M. and Mathur R. (2011). Antimicrobial Potential and Phytochemical Analysis of Plant Extracts of *Calotropis procera, International journal of drug discovery and herbal research*, 1(3), 138-143.

**82.** Sheth F.K. and Parabia M.H. (2011). Ethnobotanical studies and validation of lead: a case study on evaluation of *Calotropis* sp. on dermal fungal infections, *Int. J. of Pharm .and Life Sci. (IJPLS).* 2(6), 797-800.

**83.** Damayanti M., Susheela K. and Sharma G.J. (1996). Effect of plant extracts and systemic fungicide on the pineapple fruit-rotting fungus, Ceratocystis paradoxa, *Cytobios.* 86, (346). 155-65.

**84.** Locher C.P., Burch M.T., Mower H.F., Berestecky J., Davis H., Van Poel B., Lasure A., Vanden Berghe D.A. and Vlietinck A.J. (1995). Antimicrobial activity and anticomplement activity of extracts obtained from selected Hawaiian medicinal plants, *Journal of Ethnopharmacology,* 49, 23–32.

**85.** Iqbal Z., Lateef M. and Jabbar A. (2005). Muhammad G. and Khan M.N., Anthelmintic activity of *Calotropis procera* (Ait.) Ait. F. Flowers in sheep, *Journal of Ethnopharmacology*, 102, 256–261.

**86.** Singh V.P., Sharma S.K. and Khare V.S. (1980). Medicinal plants from Ujjain district, madhya pradesh Part II, *Indian Drugs Pharm. Ind*., 15(5), 7-12.

**87.** Alam P. and Ali Mohd (2009). Phytochemical investigation of *Calotropis* procer roots, *Indian Journal of Chemistry*, 48B(3), 443-446.

**88.** Larhsini M., Bousad M., Lazrek H.B., Jana M. and Amarouch H. (1997). Evaluation of antifungal and molluscicidal properties of extracts of *Calotropis procera*, *Fitoterapia*, 68, 371-373.

**89.** Kanimozhi D., Rathabai V. and Baskaran C. et al. (2012). Evaluation of antimicrobial activity of *Acalypha indica*. *International Journal of Research in Pharmacy and Science*, 2(1), 130-138.

**90.** Samvatsar S., Diwanji V.B. (2000). Plant sources for the treatment of jaundice in the tribals of Western Madhya Pradesh of India, *Journal of Ethnopharmacology*, 73, 313-316.

**91.** Raghubir R., Rasik M. and Gupta A.J. (1999). Healing potential of *Calotropis procera* on dermal wounds in guinea pigs, *J. Ethnopharmacol*., 68, 261-266.

**92.** Samar K.B., Arup B., Ayan M. and Prashant S. (2009). Ocular toxicity by latex of *Calotropis procera, Indian Journal of Ophthalmology*, 57, 232-234.

**93.** Cowan M.M. (1999). Plants products antimicrobial agents. *Clin. Microbial. Rev.*, 14, 564-584.

**94.** Blair T.S. (1907). A Practitioner's Handbook of Materia Medica and Therapeutics Based Upon Established Physiological Actions and The Indications In Small Doses.

**95.** Ghosh N.C. (1988). Comparative Materia Medica. Hannemann Publ. Co. Pvt. Ltd. Colicata, India.

**96.** Jayaweera D.M.A. (1982). Medicinal Plants (Indigenous and Exotic) Used in Ceylon, Vol. I-V, National Science Council of Sri Lanka, Colombo.

**97.** Nadkarni K.M. (1976). Indian Materia Medica, Popular Prakashan Pvt. Ltd., 3rd revised and enlarged edition, vol. 1, Mumbai, 237-246.

**98.** Patel N.K. and Patel K.B. (2004). Study of abortifacient plants used by Adivasi of Ambaji area in Danta taluka, *Advances in Plant Sciences*, 17(1), 37–40.

**99.** Pathak A.K. and Argal A. (2007). Analgesic activity of *Calotropis gigantea* flower, *Fitoterapia*, 78, 40–2.

**100.** Ahamed M., Rana A.C. and Dixit V.K. (2005). Plant Review *Calotropis* species (Ascelpediaceae): A comprehensive review, *Pharmacognosy Magazine*, 2, 48–52.

**101.** Choedon T., Mathan G., Arya S., Kumar V.L. and Kumar V. (2006). Anticancer and cytotoxic properties of the latex of *Calotropis procera* in a transgenic mouse model of hepatocellular carcinoma, *World J. Gastroenterol.,* 12,

2517–2522.

**102.** Roy S., Uddin M.Z., Hassan A. and Rahman M.M. (2008). Medico-Botanical report on the Chakma community of Bangladesh, *J. Plant taxon.,* 15(1), 67–72.

**103.** Saxena H.O. (1986). Observations on the ethnobotany of Madhya Pradesh, Bulletin of Botanical Survey of India, 28, 149–156.

**104.** Saha J.C., Savani E.C. and Kasinathan S. (1961). Ecbolic properties of Indian medicinal plants. Part 1, *Indian J. Med. Res.* 49, 130-151.

**105.** Hutt M.J. and Houghton P.J. (1998). A survey from the literature of plants used to treat scorpion stings, *Journal of Ethnopharmacology*, 60, 97–110.

**106.** Rama A.A.B. and Pathak A.K. (2006). CNS activity of *Calotropis gigantea* roots, *J. Ethnopharmacol.*, 106(1), 142-145.

**107.** Kirtikar K.R. and Basu B.D. (1975). Indian Medicinal Plants, Vol.2. International Book Distributors, Dehradun, 1606–1609.

**108.** Oliveira S., Bezerra D.P., Freitas C.D.T., Marinho-Filho J.D.B., Moraes O.M., Pessoa C., Costa-Lotufo L.V. and Ramos M.V. (2007). In vitro cytotoxicity against different human cancer cell lines of laticifer proteins of *Calotropis procera* (Ait.) R. Br., *Toxicology In Vitro*, 21, 1563–1573.

**109.** Ayoub S.M.H. and Kingston D.G. (1981). Screening of plants used in Sudan folk medicine for anticancer activity, *Fitoterapia*, 52, 281–284.

**110.** Kupchan S.M., Knox J.R., Kelsey J.E. and Renauld J.A.S. (1964). Calotropin, a cytotoxic principle isolated from Asclepias curassavica L. ,*Science*, 146, 1685–1686.

**111.** Chitme H.R., Chandra R. and Kaushik S. (2004). Studies on anti-diarrhoeal activity of *Calotropis gigantea* R.Br. in experimental animals, *J. Pharm. Pharmaceut. Sci* ., 7(1), 70-75.

**112.** Pratap B., Kumar R., Tiwari D., Yadav S. and Singh S. (2010). Evaluation of antidiarrhoeal property of the hydroalcoholic extract of roots of *Calotropis gigantea* R.Br. on Caster induced diarrhoea in rats, *Der Pharmacia Lettre*, 2(3), 309-314.

**113.** Nalwaya N., Pokharna G., Deb L. and Jain N.K. (2009). Wound healing activity of latex of *Calotropis gigantea*. *Int. J. of Pharmacy and Pharmaceutical Sciences,* 1(1), 176-181.

**114.** Adak M. and Gupta J.K. (2006). Evaluation of anti-inflammatory activity of *Calotropis gigantea* (AKANDA) in various biological system, *Nepal Med. Coll. J.,* 8(3), 156-161.

**115.** Basu A. and Nag Chaudhuri A.K. (1991). Preliminary studies on the anti-inflammatory and analgesic activities of *Calotropis procera* root extract, *J. Ethnopharmacology*, 31(3), 319-324.

**116.** Basu A., Sen T., Pal S. and Muscalo N. (1997). Capasso F. and Choudhuri A.K.N., Studies on antiulcer activity of the chloroform fraction of *Calotropis procera* root extract, *Phytother. Res.,* 11(1), 163-164.

**117.** Van Quaquebeke E., Simon G. and Andre A. et al. (2005). Identification of a novel cardenolides (2-oxovoruscharin) from *Calotropis procera* and the hemi synthesis of novel derivatives displaying potent in vitro antitumor activities and high in vivo tolerance, structure-activity relationship analyses, *J. Med. Chem.*, 48, 849–856.

**118.** Bhagat M., Arora J.S. and Saxena A.K. (2010). In vitro cytotoxicity of extracts and fractions of *Calotropis procera* (Ait.) roots against human cancer cell line. *International Journal of Green Pharmacy*, 36-40.

**119.** Chitme H.R., Chandra R. and Kaushik S. (2005). Evaluation of antipyretic activity of *Calotropis gigantea* (Asclepiadaceae) in experimental animals, *Phytotherapy Research*, 19(5), 454-6.

**120.** Srivastava S.R., Keshri G., Bhargavan B., Singh C. and Singh M.M. (2007). Pregnancy interceptive activity of the roots of *Calotropis gigantea* Linn. in rats. *Contraception*, 75, 318–322.

**121.** Qureshi M.A. and Qureshi N.M. (1991). A study on the antisperm activity in extracts from different parts of *Calotropis procera*, *Pakistan Journal of Zoology,* 23(2), 161-166.

**122.** Rajesh R., Raghavendra G.C.D., Nataraju A., Dhananjaya B.L., Kemparaju K. and Vishwanath B.S. (2005). Procoagulant activity of *Calotropis gigantea*n latex associated with fibrin (ogen) olytic activity, *Toxicon*, 46, 84–92.

**123.** Kapur S.K. and Sarin Y.K. (1984). Medico-botanical survey of medicinal and aromatic plants of Katra valley (J.K. State). India, *Indian Drugs*, 22(1), 4-10.

**124.** Yesmin M.N., Sarder N.U., Sanzida M. and Muhammad Ali A. (2008). Antioxidant and Antibacterial Activities of *Calotropis procera*Linn., *American-Eurasian J. Agric. and Environ. Sci.,* 4(5), 550-553.

**125.** Usmani S. and Kushwaha P.A. (2010). Study On Hepatoprotective Activity of *Calotropis Gigantea* Leaves Extract, *International Journal of Pharmacy and Pharmaceutical Sciences*, 2(3).

**126.** Majumdar P.K. and Kumar V.L. (1997). Antiinflammatory activity of fractions of latex of *Calotropis procera* in carrageenan induced rat Paw oedema, *Phytother. Res.* 11(2), 166-167.

**127.** Basu A. and Sen T. (1992). Hepatoprotective effects of *Calotropis procera* root extract on experimental liver

damage in animals, *Fitoterapia,* 63(6), 507-514.

**128.** Kumar V.L. and Roy S. (2007). *Calotropis procera* latex extract affords protection against inflammation and oxidative stress in Freund's complete adjuvant-induced monoarthritis in Rats, *Mediators Inflamm.,* 1, 1-7.

**129.** Mitra A., Chakrabortyd S., Auddyd B., Tripathia P., Senb S., Sahac A.V. and Mukherjee B. (2002). Evaluation of chemical constituents and free-radical scavenging activity of Swarnabhasma (gold ash). an ayurvedic drug, *Journal of Ethnopharmacology*, 80(2–3), 147–153.

**130.** Rastogi R.P. and Mehrotra B.N. (1993). Compendium of Indian Medicinal Plants. Lucknow: CDRI, 2, 174-551.

**131.** Setty S.R., Quereshi A.A., Swamy A.H., Patil T. and Prakash T. (2007). Hepatoprotective activity of *Calotropis procera* flowers against paracetamol-induced hepatic injury in rats, *Fitoterapia* , 78(7-8), 451-454.

**132.** Warrier P.K., Nambiar V.P.K. and Mankutty C. (1994). Indian medicinal plants, orient lonman; Chennai, India, 341-345.

**133.** Habib M.R. and Karim M.R. (2012). Antitumour evalution of di-(2- ethylhexyl) Phthalate (DEHP) isolated from *Calotropis gigantea* L. Flower, *Acta Pharm,* 62, 607-615.

**134.** Argal A. and Diwivedi A. (2010). Evaluation of Hepatoprotective Activity of *Calotropis gigantea* R.Br. Flowers. *Ethnobotanical leaflets*, 14, 427–34.

**135.** Joshi H., Gururaja M. P. and Suares D. (2011). *Calotropis gigantea* R.Br. (Asclepiadaceae) a review. *Int. J. of Pharmaceutials Res.,* 3(1), 10-14.