Pharmacognosy Magazine
ISSN: 0973-1296

PHCOG MAG.
An official Publication of Phcog.Net

PHCOG MAG.: Plant Review

Calotropis Species (*Ascelpediaceae)*- A Comprehensive Review

K. K. Mueen Ahmed[a*], A. C. Rana[b] and V. K. Dixit[b]

[*a]*Dept. of Pharmacognosy, Al-Ameen College of Pharmacy, Bangalore 560 027, Karnataka, India*
[b]*Dept. of Pharm. Sciences, Dr. H. S. Gour Vishwavidyalaya, Sagar, Madhya Pradesh, India 470 003*
Correspondence: mueen.ahmed@phcog.net

Abstract: *Calotropis species* are perennial herb with a long history of use in traditional medicinal especially in the tropical and subtropical regions. A wide range of chemical compounds including cardiac glysocisdes, flavonoids, phenolic compounds, terpenoids have been isolated from this species. Extracts and metabolites from this plant have been found to possess various pharmacological activities. Comprehensive information on the chemical constituents and the biological activities of *Calotropis* species is presented in this review so as to potentially tap its medicinal properties.

Keywords: *Calotropis procera, Calotropis gigantea, Ascelpediaceae*, Pharmacology, Phytochemistry, Review.

Introduction

Humankind first utilized materials 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 useful drugs (1). Over the past two decades, researchers have also turned to many of the traditional folk medicines – invariably a "cocktail" of natural products to uncover the scientific basis of their remedial effects, which improves the efficacy as to enhance modern medical practices (2).

The growing awareness of the harmful side-effects of chemotherapy, has made people to explore the time tested remedies from traditional alternative medicine. India being a tropical country is blessed with vast 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 mechanism of action (3).

Of the large number of plant species reported on the ethnobotanical interest, the two species of *Calotropis* R.Br Viz., *Calotropis procera* and *Calotropis gigantea* in India holds a pride of place largely because of its other uses and economic values. The fibres extracted from the bark of the stem is white, silky, strong, flexible and durable and is used in making ropes for cots, gunny bags, fishing nets, and bow strings. The wood is used as cheap fuel and latex is used in tanning industries. The latex is used as wound healing agent by different traditional healers, It is also used as an abortificient in folk medicines.

The genus Calotropis R.Br (Asclepediaceae) is distributed in tropical and sub tropical regions of Asia and Africa (5). It is represented in India by two species viz, *C. procera* and *C. gigantea*. *C. procera* is more common in southwestern and central India and western Himalayas whereas *C. gigantea* is abundant through out India right from Himalayas to southern India. The species can be differentiated by the following floral characters, *C. gigantea* bears corolla lobes are spreading, uniformly coloured, pure lavender to white, coronal scales narrow truncate shorter than the staminal column with pubescent back, apex entire. Whereas the corolla lobes of *C. procera* erect while pink or purpled spotted on the lobes; corona scales equal or longer than the staminal column, glaburous on back apex bifid, auricles wanting. Gupta *et al.*, (6) suggested that the various leaf characters like leaf venation, anatomy, physical constants and fluorescence characteristics of leaf powders can also be used to differentiate them

Plant	*Calotropis procera*	*Calotropis gigantea*
Taxonamical classification		
Kingdom	Plantae, Plants;	Plantae, Plants;
Subkingdom	Tracheobionta, Vascular plants;	Tracheobionta, Vascular plants
Superdivision	Spermatophyta, Seed plants;	Spermatophyta, Seed plants;
Division	Magnoliophyta, Flowering plants;	Magnoliophyta, Flowering plants
Class	Magnoliopsida, Dicotyledons	Magnoliopsida, Dicotyledons
Subclass	Asteridae;	Asteridae;
Order	Gentianales;	Gentianales;
Family	Asclepiadaceae, Milkweed family	Asclepiadaceae, Milkweed family
Botanical description	Large, bushy, stout, tomentose shrubs 2-4 m height. Leaves are sessile, decussate, ovate, obviate, ovate – oblong to elliptic ovate, base cordate, apex obtuse, or shortly acuminate, subglaburous above, cottony beneath, 8-20 x 5-7 cm cymes umbelliate or a sub	Erect to sub erect perennial shrubs, 1- 1.5 m high, young parts floccusely white tomentose. Leaves are decussate, sub sessile, thick, ovate, obvate, oblong, elliptic to broadly ovate, base cordate, cottony beneath, glaburous with age. Cymer umbellate, penduncles stout,

	raceme, penducule lateral, cottony, corolla lobes, spreading, recurved, ovate lanceolate, uniformly coloured, light purple to white 2-5 cm ; Corona scales 5 narrow, adnate to gynostegium, shorter that staminal column, back pubescent, apex entire with two obtuse auricles below it, vesicle recurved at the base, the spur upcovered, involute, stigma depressed, 5 angular (lobed). Follicles 6-10 cm long, recurved, boat shaped, obtuse and pubescent. (5,7). laterally or auxiliary often paired and long. Flowers scented 1- 2.5 diameters. Corona lobes erect, white, pink or purple spotted, corona scales 5, fleshy, laterally, compressed, equal or larger than the staminal column. Follicles turgid, recurved to sausage shaped. (5, 7).
Parts Used:	Root, root bark, leaves, flowers and latex are used.
Ayurvedic description	In ancient Ayurvedic medicine the plant *C. gigantea* is known as "Sweta Arka" and *C. procera* as "Rakta Arka". Both of them are often similar in their botanical aspects and also have similar pharmacological effects. **Sanskrit:** *Arka, Alarka* **Synonyms:** *Sooryahawa, Sadaapushpi, Sooryapushpaka, aspota, jambala, ksheree, ksheeraparna, vikeerana, kshataksheree, dughdaanika, pushpee, tanuphala.* **Common general properties** *Rasa: Katu, tikat, madhura ;Guna : Sara, snigdha, laghu; Veerya: Ushna* *Vipaaka: Katu;* **Action/Uses** **General** *Krimighna, kushtagna, vranaghna, arshogana, gulmaghana, vishahara,* *Arka pushpa: Madhura, tikta, sangraahi, kushtagna, krimighna, arshogna, raktapitta, shamana, shophagna, gulmaghna.* **Alarkakusuma** *Laghu, deepana, paachana, arockshamana, praseekashama, arshogna, shwaasahara, kasaahara* **Arkasheera** *Sara, snighdha, laghu, katu, gulmaghna, kushtaghna, udaroraghana, virekashresta.*

Traditional Uses of Calotropis species

Phytochemistry

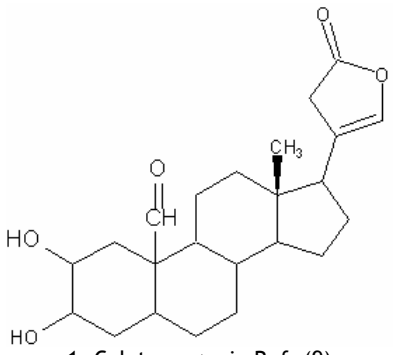
Phytochemically the plants have been investigated for cardenolides from the latex and leaves (8 & 9), triterpenoids (9), anthocyanins from flowers (10) and hydrocarbons (11). The leaves and latex of Calotropis species were found to have cardiac glycosides, various glycosides were isolated and studied (12). An active principle 'mudarine' was isolated from leaves of *C. gigantea*. Beside this, a yellow bitter acid and resin were also found. The cardiac glycosides were identified as Calotropogenin (1), Calotropin (2), Uscharin (3) and Calotoxin (4), Calactin (5) (9, 13). Three cardenolide glycosides, Coroglaucigenin (6), frugoside (7), and 4'-O-beta-D-glucopyranosylfrugoside (8), 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 (14). Pal, (15) studied on isolation, crystallization, and properties of calotropins DI and DII from *C. gigantea.*

Two new oxypregnane-oligoglycosides named Calotroposides A (9) and B (10) have been isolated from the root of *C. gigantea* (Asclepiadaceae), an Indonesian medicinal plant, and their chemical structures have been elucidated by chemical and spectroscopic methods as 12-O-benzoyllineolon 3-O-beta-D-cymaropyranosyl (1-4)-beta-D-oleandropyranosyl (1-4)- beta-D-oleandropyranosyl (1-4)-beta-D-cymaropyranosyl (1-4)-beta-D-cymaropyranoside and 12-O-benzoyl deacetyl metaplexigenin 3-O-beta-D-cymaropyranosyl(1-4)-beta-D-oleandropyranosyl (1-4)-beta-D-oleandro pyranosyl (1-4) -beta-D-cymaro pyranosyl (1-4)-beta-D- cymaro pyranoside, respectively (16). Besides isolation and characterization of isorhamnetin-3-O-rutinoside (11), isorhamnetin-3-O-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-O-(2-O-beta-D-galactopyranosyl-6-O-alpha-L-rhamnopy ranosyl)- beta-D-glucopyranoside (13) by a combination of fast atom bombardment mass spectroscopy, ^{1}H and ^{13}C NMR spectra and some chemical degradations (17).

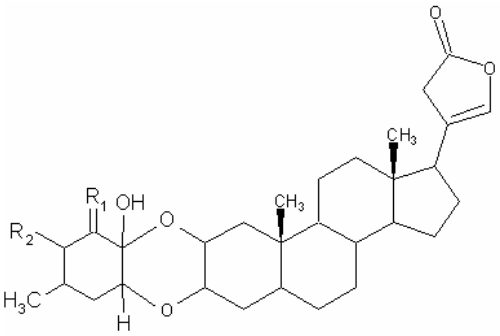
A new norditerpenyl ester, named Calotropterpenyl ester, and two unknown pentacyclic triterpenoids, namely calotropursenyl acetate and calotropfriedelenyl acetate have been isolated from the root bark of *Calotropis procera*. Their structures have been established as 6,10,14-trimethylpentadec-6-enyl-2',4',8',12',16'-pentamethyl nonadecane ester, urs-12,19(29)-diene-3 beta-yl acetate and friedelin-1-ene-3 beta-yl acetate, respectively, on the basis of spectral data analysis and chemical reactions (18). A powerful bacteriolytic agent capable of lysing *Micrococcus lysodekticus*, had been found to be present in latex of *C.procera*. The enzyme had a maximum activity at pH 5-5.4 at 45^{0}C (19). Asclepin, isolated from Calotropis species was found to be 3-O- acetyl- calotropin by various physical and chemical tests (20).

Giganticine, a novel non-protein 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 anti-feedant activity against nymphs of the desert locust *Schistocerca gregaria* (21). 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 FII were found to be homogeneous by rechromatography (22).

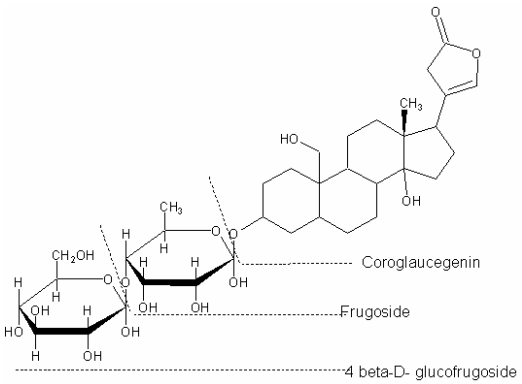


1. Calotropogenin Ref. (9)

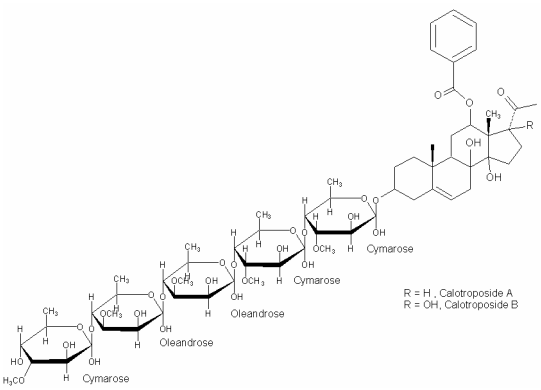


(2) : Ref (9)

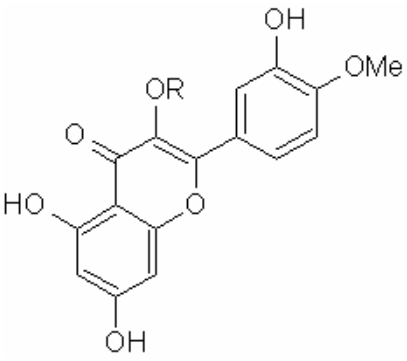
Structure No.	Nomenclature	R_1	R_2
2	Calotropin	α- OH, β- H	H
3	Uscharin	S- CH_2 / N-CH_2	H
4	Calotoxin	γ-H, γ-OH	H
5	Calactin	α- H, β- OH	H



6 - Coroglaucegenin, 7- Frugoside, 8- 4β-D-glucofrugoside Ref. (14)



9-Calotroposide A, 10- Calotroposide B Ref. (16)



Ref (17)

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 actions

Leaf, latex and roots of the plant *C. gigantea* are used as a remedy for snake bite or scorpion sting, but all parts are quite useless in the anti-dotal and symptomatic treatment of either snake bite or scorpion bite. Use of *C. procera* as a toothbrush enhances amylase activity, and also support in the use of root as digestive agent (23). Jain *et al.*, (24) prescribed capsulated root bark powder to patients suffering from diarrhoea and dysentery, and is an excellent substitute for ipecac. Traditionally bark is used to treat cholera, extracting guinea worms and indigestion. The drug is well known to enhance bile secretion and has sedative effect on the intestinal muscles. Ethanol extract of *C.procera* is applied to skin ulcers, which showed 60% cell regression. The tender leaves of *C. procera* are also used to cure migraine (23).

Calotropin isolated from latex and roots of *C. procera* inhibit spermatogenesis in male and induce abortion in female rats and rabbits. It is also used as a remedy for black scars of face, boils, cold cough, asthma, ear ache, eczema, skin eruptions, inflammatory lesions, pains of the body, rheumatism, syphilis, leprosy and oedema (23). Extracts from *C.gigantea* and *C.procera* caused marked contraction in isolated preparation of rabbit's duodenum, rat's ileum, and uterine horn from rat. Both

the extracts show vermicidal action on earthworms. The extracts were found to be non- toxic (25). The milky juice of *C.gigantea* exhibited marked stimulant action on the spontaneous activity of isolated non-gravid rat uterus (26). The alcoholic extracts of the root and leaves of *C. gigantea* and *C. procera* were found to have anti-cancer activity against human epidermal carcinoma of the nasopharynx tissue culture (27).

The anti-inflammatory property of the latex of *C. procera* was studied on carrageenan- and formalin-induced rat paw oedema model. A single dose of the aqueous suspension of the dried latex was effective to a significant level against the acute inflammatory response (28). A chloroform-soluble fraction from *C. procera* roots showed significant dose-related anti-inflammatory activity in rats using the pharmacologic models of carrageenan-induced paw oedema, cotton pellet granuloma and formaldehyde-induced arthritis. In addition, significant analgesic potential was demonstrated using acetic acid-induced writhing in mice (29). Dewan *et al.*, (30) evaluated the analgesic activity of dry latex (DL) of *C procera*. A single oral dose of DL ranging from 165 to 830 mg/kg produced a significant dose dependent analgesic effect against acetic acid induced writhing's in mice. An ethanolic extract of the flowers of *C procera* was investigated for anti-inflammatory, anti-pyretic, analgesic and anti-microbial activities. The plant extract reduced the paw swelling induced by carrageenan by 37%, fever in rats by 40% and showed some weak effect in rats on the writhing induced by acetic acid. The growth of both gram-positive and gram-negative bacteria was significantly inhibited. A dose-dependent effect on prostaglandin release was also observed (31).

Mossa *et al.*, (32) investigated the ethanolic extract of the *C procera* for its anti-pyretic, analgesic, anti-inflammatory, anti-bacterial, purgative and muscle relaxant activities. The results of this study showed a significant anti-pyretic, analgesic and neuromuscular blocking activity. On smooth muscle of guinea pig ileum, the extract produced contractions, which were blocked by atropine supporting its use in constipation. However, the extract failed to produce significant anti-inflammatory and anti-bacterial activities. Phytochemical studies on the aerial parts of *C. procera* showed the presence of alkaloids, cardiac glycosides, tannins, flavonoids, sterols and triterpenes. However, the chemical constituents responsible for the pharmacological activities remain to be investigated. The safety evaluation studies revealed that the use of extract in single high doses (up to 3 g/kg) does not produce any visible toxic symptoms or mortality. However, prolong treatment (90 days) causes significant mortality.

The dry latex (DL) of *C procera*, a potent anti-inflammatory agent has been evaluated for anti-diarrhoeal activity. Like atropine and phenylbutazone (PBZ), a single oral dose of DL (500 mg/kg) produced a significant decrease in frequency of defecation, severity of diarrhoea and afforded protection from diarrhoea in 80% rats treated with castor oil (33). The role of chloroform fraction of *C procera* root extract on different experimental ulcer models in rats was investigated. The extract demonstrated significant anti-ulcer activity against aspirin, indomethacin, ethanol, indomethacin + ethanol, or stress-induced ulcerations. Significant inhibition of gastric secretory volume and total acidity in pylorus-ligated rats were observed following treatment with the extract (17). Effect of ethanolic and aqueous extracts of *C procera* (Ait.) R.Br. roots have been studied on oestrous cycle and oestrogenic functionality in rats. Both extracts have been shown to interrupt the normal oestrous cycle by 60 and 80%, respectively, of rats treated (34). Sharma and Sharma (35) screened the ethanolic extracts of *C. procera* leaves, stems, roots, flowers and buds for anti-malarial activity against chloroquine (CQ)-sensitive and CQ-resistant Plasmodium falciparum strains.

The n-butanol extract of *C. procera* flowers and other 12 plant extracts were proved to be the most effective against the bacteria tested (36). Human erythrocytes were exposed in a dose dependent manner to various ethanolic extracts, and fractions obtained from plant parts of *C procera* (Ait.) R. Br. and the gum-oleo resin of *Commiphora wightii* (Arnott.) Bhand. These have been screened for *in vitro* schizontocidal activity and graded with respect to their 50% inhibitory concentration (IC_{50}) derived from the twofold serial dilution of the dose range 0.0625-2 mg/ml. An attempt had been made to relate their anti-plasmodial activity with their cytotoxicity as represented by the *in vitro* rate of hemolysis (35). Rasik *et al.*, (37) selected *C. procera* for evaluation of its wound healing potential. Topical application of 20 micro litres of 1.0% sterile solution of the latex of *C. procera* twice daily was followed for 7 days. Wherein the latex significantly augmented the healing process by markedly increasing collagen, DNA and protein synthesis and epithelization leading to reduction in wound area.

Sharma and Sharma (38) also reported the effect of crude fractions of flower, bud and root of *C procera* against a chloroquine (CQ) sensitive strain, MRC 20 and a chloroquine resistant strain, MRC 76 of *Plasmodium falciparum* using the Desjardins method and the effectiveness of its fractions compared better with the CQ sensitive strain than the CQ resistant strain *in vitro*. The insecticidal activity, expressed by LD_{50} values, of acetone, ethanol, petroleum ether and water extracts of *C procera* leaves against the flesh fly, *Sarcophaga haemorrhoidalis* Fallen was evaluated. Findings suggest that *C. procera* extracts may produce larvicidal, pupicidal and adulticidal effects, (behaving like general toxicants) against the flesh fly, *S. haemorrhoidalis* (39). *C. procera* latex showed anti-oxidant activity using DPPH model (39) and also reduced increased enzyme levels in isoproterenol induced myocardial necrosis (40, 41).

Conclusion

The literature supports the medicinal value of calotropis species, considering its various pharmacological activities. Although the plant contains cardiac glycosides and other constituents, a systematic screening of these plants with special reference to its active principles has not been scientifically studied. Hence phytochemical and pharmacological evaluation of these plants will enable to exploit its therapeutic use in traditional medicine.

References

1. Edwin Haslam, ***J. Nat. Prod.***, 59, 205-215, (1996).

2. Varro, E, Tyler, ***J. Nat. Prod.***, 62, 1589-1592 (1999).
3. Ashok, Vaidya, ***Pharm. Res. India (Pharma Pulse – suppl)***, 44-45 (1998).
4. K. K. Bhutani, ***East. Pharm.***, 21-37 (2000).
5. ***The Wealth of India***, Raw Materials, Vol II, CSIR, New Delhi, 20-23 (1959).
6. R.C Gupta, P.C. Sharma and L.D. Kapoor, ***J. Res. Ind. Med.***, 6(2), 167-172 (1971).
7. K. R. Kirthikar and B.D Basu, ***Indian Medicinal Plants***, Vol. III, Bhushen Singh and Mahendra Pal Singh, Dehradun, 1606-1611 (1933).
8. H.G. Crout, et al., ***Tetrahedron***, 26, 1281-1285 (1962).
9. N. Seiber, James Carolyn, J. Nelson and S. Mark Lee, ***Phytochemistry***, 9, 2343-2348 (1982).
10. Tiwari et al., ***Vigynan Parishad Anusandhan Patrika***, 21, 177-178 (1978).
11. I.B Carruthers, et al., ***Biomass***, 4, 275-282 (1984).
12. Yamouchi tatsuo and Abu Fumiko, ***Tetrahedron Letters***, 1852-28 (1978).
13. H.N. Chaudhari Rai, ***Bull. Bot. Surv. India***, 3(2), 171-173 (1961).
14. F. Kiuchi, Y, Fuakao, T. Maruyoma, T. Obata, M.Tanaka, T.Sasaki, M.Mikage, M.E. Haque and Y. Tsuda, ***Chem. Pharm. Bull.***, 46(3), 528-530 (1998).
15. G. Pal and N.K Sinha, ***Arch. Biochem. Biophys.***, 202(2), 321-329 (1980).
16. J. Kitagawa, R.S Zhang, J.O Park, N.L Beek, Y.Takeda, M.Yoshikawa and H. Shibuya, ***Chem. Pharm. Bull.***, 40(8), 2007-2013 (1992).
17. Sucharita Sen, Niranjan, P. Sahu and Shashi, Mahato, ***Phytochemistry***, 31(8), 2919-2921 (1992).
18. H. Ansari and M. Ali, ***Pharmazie***, 56(2), 175-177 (2001).
19. O. P Shukla and C.R Krishnamurthy, ***J. Sci. Ind. Res.***, 20C, 109 (1961).
20. B. Singh and R. P. Rastogi, ***Phytochemistry***, 11, 757 (1972).
21. K. Pari, P. J Rao, C. Devakumar and J. N Rastogi, ***J. Nat. Prod.***, 23(61), 102-104 (1998).
22. S.K. Abraham and L. Joshi, ***Anal Biochem***, 4: 341-345 (1979).
23. H. Misra and I. Fridowich, ***J. Biol. Chem.***, 247, 3170-3185 (1972).
24. P. K Jain et al., ***J. Res. Ayur. Sid.***, 6, 88-91 (1985).
25. H. R Derasari and G.G Shah, ***Ind. J. Pharmacol.***, 27,278 (1995).
26. B. N Dhawan and P. N. Saxena, ***Ind. J. Med. Res.***, 46,808 (1968).
27. M. L Dhar et al., ***Ind. J. Exp. Biol.***, 6, 232 (1968).
28. V. L Kumar and N. Basu, ***J. Ethnopharmacol.***, 123-125 (1994).
29. A. Basu and A. K Chaudhari, ***J. Ethnopharmacol.***, 31(3), 319-324 (1991).
30. S. Dewan, H. Sangruala and V. L Kumar, ***J. Ethnopharmacol.***, 73(1-2), 307-311 (2000).
31. N. Mascolo, P. Sharma, S.C Jain and F. Capasso, ***J. Ethnopharmacol.***, 1988, 22(2), 211-221 (1998).
32. J. S. Mossa, M. Tariq, A. Mohsin, A. M Aqeel, M. A Al-Yahiya, M. S. Al-Said and S. Rafatullah, ***Am. J. Chin. Med.***, 19(3-4), 223-231 (1991).
33. (Kumar *et al.*, 2001)
34. C. Circosta, R. Sanogo and Ochusto., ***Farmaco***, 56(5-7), 373-38 (2001).
35. P. Sharma and J. D Sharma, ***Fitoterapia***, 71(1), 77-79 (2000).
36. Larhsini et al., ***Phytother. Res.***, 15(3), 250-252 (2001).
37. M. Rasik, R. Raghubir, A. Gupta A. Shukla, M.P Dubey, S. Srivastava, H. K Jain and D. K Kulshreshta, ***J. Ethnopharmacol.***, 68(1-3), 261-266 (1999).
38. P. Sharma and J. D Sharma, ***J. Ethnopharmacol.***, 68(1-3), 83-95 (1999).
39. K. K. Mueen Ahmed, A.C.Rana and V.K.Dixit. In-vitro free radical scavenging activity of calotropis species- ***Indian drugs***, 40 (11), 654-655 (2003).
40. K. K. Mueen Ahmed, A.C.Rana and V.K.Dixit, Effect of *Calotropis procera* latex on isoproterenol induced myocardial infarction in albino rats- ***Phytomedicine***, 11 (4), 327 -330 (2004).
41. K. K Mueen Ahmed, A.C.Rana and V.K.Dixit. Studies on Calotropis species for antimyocardial infarction activity in albino rats- ***Indian drugs***, 39 (11), 613-615 (2002).