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Pharmacological actions and therapeutic uses of *Aak* (*Calotropis procera*): A Review

Shamim, Saad Ahmed and Lubna Fatima

Abstract
Aak (*Calotropis procera*) is a drug of herbal origin, which has been in use for medicinal purpose since time immemorial. *Aak* was first described by Abu Hanifa (circa 270 A.H) in his book of plants. According to Burhan, *Usher* is a Persian name for all plants having a milky juice and specially plants known in India as *Aak.* It is found more or less throughout India, in warm and dry places. It is a native of China and Malaysia and distributed in many countries all over world. IT has *Mohallil* (Resolvent), *Akkal* (Corrosive), *Jali* (Detergent), *Mus'hil* (Purgative), *Munaffis-e-Balgham* (Expectorant) and *Musakkin* (Analgesic) etc. properties. Pharmacological studies have revealed that the drug has effectively been employed for the treatment of various ailments like *Waja-Ul-Mufasil* (arthritis), *Istisqa* (ascites), *Iltehab* (inflammatory conditions), *Juzam* (leprosy) and *Zeeq-Un-Nafs* (asthma) etc. In this paper, an effort has been made to compile the actions and therapeutic uses of *Aak* (*Calotropis procera*).

Keywords: *Aak, Madar, Calotropis procera, Iltehab,* antinfalmmatory and analgesic herb etc.

Introduction
Aak (*Calotropis procera*) is a drug of herbal origin, which has been in use for medicinal purpose since time immemorial. Although comparatively toxic, the drug has effectively been employed for the treatment of various ailments like *waja-ul-mufasil* (arthritis), *istisqa* (ascites), *iltehab* (inflammatory conditions), *juzam* (leprosy) and *zeeq-un-nafs* (asthma) etc. It belongs to the family of Asclepedaceae and genus *Calotropis*. There are four (4) species of this genus, but only *Calotropis procera* and *Calotropis gigantea* are well recognized for their medicinal properties (Anonymous, 2007; Yogi *et al.*, 2016) [6, 57].

Fig 1: Leaf of *Aak*

Vernacular Names

Afghani	:	Spalwakka
Arabic	:	Usher, Ochar, Osher
Burmese	:	Mayopin, Mehobin
English	:	Swallow wart
Gambia	:	Fouftan
Gold coast	:	Sodom apple
Hindi	:	Ag, Ak, Akada, Madar, Safeda

Kannad	:	Ekka, Ekkagida
Kumaon	:	Ak
Malayalam	:	Bukam
Marathi	:	Mandara
Persian	:	Usher
Punjabi	:	Ak, Shakrallighal, Shakarulushar
Sanskrit	:	Alarka, Arka, Bimbora, Mandarapratapa
Sindhi	:	Aak
Sudanese	:	Usher
Tamil	:	Velleruku
Telugu	:	Jilledu, Mandaramu
Uriya	:	Orko, Arakka
Urdu	:	Aak

(Kirtikar and Basu, 2005; Anonymous, 1992; Ghulam, 2007; Kabiruddin, 2000; Nadkarni, 2007; Ibn Baitar, 1999) [33, 3, 20, 25, 42, 12].

Description according to unani classical literature

Madar (*Calotropis procera*) was first described by Abu Hanifa (circa 270 A.H) in his book of plants. According to Burhan, *Usher* is a Persian name for all plants having a milky juice and specially plants known in India as *Aak* (Anonymous, 1992) [3].

The author of *Khazainul Advia*, *Najmulghani* mentions about three varieties of the drug:

i. Large tree with large leaves and white flowers and profuse latex secretion.
ii. Comparatively smaller tree with flowers white externally and purplish inside.
iii. Smallest tree with pale, yellowish green flowers.

Parts Used

Leaves, Flowers, Flower buds, Latex of tree, Salt of the leaves, Bark of the root.

(Ibn Baitar, 1999; Kabiruddin, 2000; Kirtikar and Basu, 2005; Khan, 1313; Ghulam, 2007; Anonymous, 1992; Nadkarni, 2007; Khare, 2007; Khan, 1273) [12, 25, 33, 28, 20, 3, 42, 31, 30].

Mizaj

Latex	: Hot 4^0 and Dry 4^0	(Ghani, ynm; Ghulam, 2007; Hakeem, 2002; Kabiruddin, 2000) [20, 22, 25].
Leaves	: Hot 3^0 and Dry 3^0	(Anonymous, 1992; Ghani, ynm; Hakeem, 2002; Kabiruddin, 2000) [3, 22, 25].
Flowers	: Hot 3^0 and Dry 3^0	(Ghani, ynm; Hakeem, 2002; Kabiruddin, 2000) [22, 25].
Root bark	: Hot 3^0 and Dry 3^0	(Anonymous, 1992; Ghani, ynm; Hakeem, 2002) [3, 22].

DOSE

Latex	250 mg	(Kabiruddin, 2000) [25].
	1-1.5 grams	(Ghani, ynm)
	3 grams	(Ghulam, 2007) [20].
Leaves	250 mg -1gram	(Anonymous, 1992; Kabiruddin, 2000) [3, 25].
Root bark	250 mg -650 mg	(Kabiruddin, 2000) [25].
	9 grams	(Ghani, ynm)
	5-10 grams	(Anonymous, 1992) [3].
Flowers	125 mg -375 mg	(Kabiruddin, 2000) [25].

Table 1: Actions

Action	Reference
Akkal (Corrosive)	Kabiruddin, 2000; Anonymous, 1992; Ghani,ynm; Ghulam, 2007; Khan, 1313 [25, 3, 20, 28].
Haliq (Epilant)	Anonymous, 2006; Hakeem, 2002; Ghani, ynm [22].
Hazim (Digestive)	Ghani, ynm; Ghulam, 2007; Nadkarni, 2007; Kabiruddin, 2000; Kirtikar and Basu, 2005 [42, 20, 25, 33].
Jazib (Absorbant)	Kabiruddin, 2000; Hakeem, 2002; Khan, 1273 [25, 22, 30].
Jali (Detergent)	Ghulam, 2007; Kirtikar and Basu, 2005; Hakeem, 2002; Nadkarni, 2007 [20, 33, 22, 42].
Kasir-e-Riyah (Carminative)	Kirtikar and Basu, 2005; Anonymous, 1992 [33, 3].
Muqawwi-e-Meda (Gastric tonic)	Nadkarni, 2007; Ghulam, 2007; Kabeerudin, 2000 [42, 20].
Mulayyin (Laxative)	Kirtikar and Basu, 2005; Anonymous, 1992 [33, 3].
Muqawwi-e-*Bah* (Aphrodisiac)	Ghani, ynm
Mohallil (Resolvent)	Anonymous, 2006; Khan, 1313; Hakeem, 2002; Ghani, ynm; Ghulam, 2007; Anonymous, 1992; Kabiruddin, 2000; Kirtikar and Basu, 2005; Basu *et al.*, 1991; Khan, 1313; Khan, 1273 [28, 22, 20, 3, 25, 33, 13, 28, 30].
Muqarreh (Ulcerative)	Hakeem, 2002; Ghani,ynm; Ghulam, 2007; Kabiruddin, 2007 [22, 20, 25].
Mus'hil (Purgative)	Hakeem, 2002; Ghani, ynm; Anonymous, 1992; Kabiruddin, 2000; Ibn Baitar, 1999 [22, 3, 25, 12].
Moarriq (Diaphoretic)	Anonymous, 1992; Kabiruddin, 2000 [3, 25].
Munaffis-e-Balgham (Expectorant)	Anonymous, 1992; Ghulam, 2007; Kabiruddin, 2000; Kirtikar and Basu, 2005 [3, 20, 25, 33].
Muqawwi (Tonic)	Nadkarni, 2007; Kirtikar and Basu, 2005 [42, 33].
Munaffit (Blistering agent)	Kirtikar and Basu, 2005; Nadkarni, 2007; Ghani, ynm [33, 42].
Mujaffif (Desicant)	Khan, 1313 [28].
Muqi (Emetic)	Nadkarni, 2007; Anonymous, 1992 [42, 3].
Mushtahi (Appetiser)	Anonymous, 2006; Nadkarni, 2007 [42].
Mudir-e- Haiz (Emmenogogue)	Ghani, ynm; Khan, 1313 [28].
Mukhaddir (Anaesthetic)	Kabiruddin, 2000; Khan, 1313 [25, 28].
Musakkin (Analgesic)	Khan, 1313; Hakeem, 2002; Kirtikar and Basu, 2005; Ghani, ynm; Kabiruddin, 2000 [28, 22, 33, 25].

Qatil-e-Deedan (Anthelmentic)	Ghani, ynm; Ghulam, 2007; Kirtikar and Basu, 2005; Anonymous, 1992 [20, 33, 3].
Qatai wa mukhrij-e-Balgham	Hakeem, 2002; Ghani, ynm; Ghulam, 2007; Kabiruddin, ynm [22, 20].
Qatil-e-Janeen (Abortificient)	Anonymous, 1992; Kabiruddin, 2000; Kirtikar and Basu, 2005; Nadkarni, 2007 [3, 25, 33, 42].

Table 2: Therapeutic uses

Clinical Indication	Reference
Aatishak (Syphilis)	Ghani, ynm; Kabiruddin, 2000 [25].
Atash (Thirst)	Anonymous, 1992 [3].
Amraz-e-Meda (Gastric disorder)	Ghani, ynm; Ghulam, 2007; Kabiruddin, 2000 [20, 25].
Amraz-e-Jild (Skin diseases)	Anonymous, 2006; Ghani, ynm
Amraz-e-Kabid (liver diseases)	Khan, 1313; Ghani,ynm [28].
Bars (Leucoderma)	Ghani, ynm
Bawaseer (Haemorrhoids)	Hakeem, 2002; Ghulam, 2007; Anonymous, 1992; Kabiruddin, 2000; Kirtikar and Basu, 2005; [22, 20, 3, 25, 33].
Badhazmi (Indigestion)	Anonymous, 2006; Ghani,ynm; Kirtikar and Basu, 2005 [33].
Dard-e-Sar (Headache)	Kirtikar and Basu, 2005 [33].
Daad wa Ganj	Ibn Baitar, 1999; Ghani,ynm; Kabiruddin, 2000 [12, 25].
Faliz (Paralysis)	Hakeem, 2002; Khan, 1313 [22, 28].
Haiza (Cholera)	Nadkarni, 2007; Ghulam, 2007; Kabiruddin, 2000 [42, 20, 25].
Humma (Fever)	Ghani, ynm
Istisqa (Sciatica)	Anonymous, 1992; Anonymous, 2006; Hakeem, 2002; Khan, 1313; Kabiruddin, 2000; [3, 22, 25, 28].
Jarb (Scabies)	Khan, 1313 [28].
Juzam (Leprosy)	Ghani,ynm; Hakeem, 2002; Khan, 1313 [22, 28].
Kharish (Itching)	Ghani,ynm; Kabiruddin, 2000 [25].
Khadar (Anaesthetic)	Kabiruddin, 2000; Khan, 1313 [25, 28].
Khansi wa Nazla (Cough and Cold)	Ghani,ynm; Kabiruddin, 2000 [25].
Mouch (Sprain)	Kritikar and Basu, 2005 [33].
Niqrus (Gout)	Ghani,ynm; Kabiruddin, 2000 [25].
Nazaf-ud-dam (Haemorhage)	Kabiruddin, 2000 [25].
Pechish (Dysentary)	Nadkarni, 2007 [42].
Deedan-e-Am'a (Intestinal worms)	Anonymous, 2006; Ghulam, 2007; Kabiruddin, 2000 [20, 25].
Qarah Medi (Gastric ulcer)	Kiritikar and Basu, 2005 [33].
Qulai-e-Dahan (Stomatitis)	Hakeem, 2002; Khan, 1313 [22, 28].
Qooba (Tenea)	Khan, 1313 [28].
Sara (Epilepsy)	Anonymous, 2006
Suaal-e-Balghami (Cough)	Anonymous, 1992 [3].
Tashannuj (Convulsions)	Hakeem, 2002; Khan, 1313 [22, 28].
Waja-ul-Mufasil (Arthralgia)	Anonymous, 1992; Ghani,ynm; Kabiruddin, 2000 [3, 25].
Waja-ul-Uzn (Otalgia)	Anonymous, 2006
Waja-ul-Asnan (Toothache)	Ghani,ynm; Hakeem, 2002; Kritikar and Basu, 2005; Nadkarni, 2007 [22, 33, 42].
Waja-ul-Meda (Stomachic)	Nadkarni, 2007 [42].
Yarqan (Jaundice)	Ghani, ynm
Zeequnnafs (Asthma)	Anonymous, 1992; Ghani,ynm; Hakeem, 2002; Kabiruddin, 2000; Nadkarni, 2007 [3, 22, 25, 42].
Zof-e-Ishteha (Loss of Appetite)	Anonymous, 2006; Nadkarni, 2007 [42].

Botanical Description

Habit and Habitat

It is found more or less throughout India, in warm and dry places. It is a native of China and Malaysia and distributed in the following countries: Afghanistan, Algeria, Burkina Faso, Cameroon, Chad, Cote d'Ivoire, Democratic Republic of Congo, Egypt, Eritrea, Ethiopia, Gambia, Ghana, Guinea-Bissau, India, Iran, Iraq, Israel, Kenya, Kuwait, Lebanon, Libyan, Arab Jamahiriya, Mali, Mauritania, Morocco, Mozambique, Myanmar, Nepal, Niger, Nigeria, Oman, Pakistan, Saudi Arabia, Senegal, sierra Leone, Somalia, Sudan, Syrian Arab Republic, Tanzania, Thailand, Uganda, United Arab emirates, Vietnam, Yemen, Republic of Zimbabwe, Exotic: Antigua and Barbuda, Argentina, Australia, Bahamas, Barbados, Bolivia, Brazil, Chile, Colombia, Cuba, Dominica, Dominican Republic, Ecuador, French Guiana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Montserrat, Netherlands Antilles, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, StKitts and Nevis, St Lucia, St Vincent, and the Grenadines, Surinam, Trinidad and Tobago, Uruguay, Venezuela and Virgin Islands **(**Quazi *et al.*, 2013; Sharma *et al.*, 2011; Dwivedi *et al.*, 2010; Anonymous, 1992) [45, 51, 18, 3].

Plant Description

Large shrub or small tree up to 4-10 m tall, much-branched at base, stems erect, up to 20 cm in diameter; bark pale gray, longitudinally cracked; young shoots woolly hairy; latex in all parts.

Leaves: A twig with oppositely arranged sub sessile leaves, decussate, blade broadly ovate to oblong-obovate, or elliptical, 9.5–20 cm × 6–12.5 cm, base cordate with semiamplexicaule lobes, cottony, pubescent when young and glabrous on maturity.

Apex: Almost acute, short-hairy beneath. Inflorescence is an axillary, umbellate to almost corymbose cyme up to 12.5 cm in diameter, peduncle 6–12 cm long, stout, secondary branches up to 2 cm long.

Flowers: Flowers bisexual, regular, 5-merous, white, cream, lilac or purple; pedicel 2.5–7.5cm long, lateral pedicles 6 mm long densely woolly hairy, Flowers consist of 5 small triangular dirty white sepals, 5 thick ovate petals (1cm x 1cm) which are white at the base and purple at the tips and 5 purple tipped stamens, which surround a white 5 lobed stigma. Calyx divided to the base, glabrous, sepals 5-2.5 mm ovate acute. Corolla glabrous, about 2.5 cm across divided about 2/3 of the way down, lobes usually erect, ovate, acute, 1 cm long lobes of corona 6 by 4.5 mm, compressed equaling or exceeding the stamina column, the bark nearly straight or something slightly curved away from the column above the upcurved subacute spur, usually glabrous but sometimes slightly scabrous – pubescent along the outer margin.

Fruits: Consist of green, spongy ovoid fruits (follicles), up to 15 cm long by 10 cm wide. They split open to release plumed, papery light brown seeds with a pappus of white filaments up to 6 cm long on one side. The main flowering period would be from March to October.

Follicles: 7.5-10 by 5-7.5 cm, sub globose, ellipsoid or ovoid.

Seeds: 6 by 4 mm broadly ovate, acute, flattened, narrowly margined, minutely tomentose, light brown (Sharma *et al.*, 2011; Kritikar and Basu, 2005; Murti *et al.*, 2010) [51, 33, 42].

Table 3: Scientific Classification

Kingdom	Plantae
Class	Magnoliopsida
Order	Gentianales
Family	Asclepiadaceae
Genus	*Calotropis*
Species	*Procera*

Microscopic examination

Microscopic examination of vertical section of leaf shows that it is dorsiventral and the mid rib is much elevated on the lower side but the wing region are uniformly thickened. Both the upper and lower epidermis is thicky cuticulised and bears small cubical cells the upper epidermis is also characterized by the presence of striations and rubiaceous type of stomata. The collenchymatous hypodermal region are found only in the mid rib. The mesophyll is well differentiated into upper palisade region and lower spongy. The palisade is 3-4 layer consisting of the compactly arranged cells which contains chloroplast. They are small and numerous in wing region but one big vascular bundle of arch shaped is found in the mid rib region. Another diagnostic feature of leaf is presence of laticiferous canals which contains the white, milky secretions. Some unseriate trichomes are also found which are observed easily in epidermal peeling which seen in surface view, oxalate of lime occurs in form both solitary and clustered crystals.

The petiole on the other hand contains single, large, bicollateral, an arc shaped vascular bundle while the epidermal and ground tissues are an usual parenchymatous in nature.

Stem bark shows exfoliated cork, consisting of 6-8 layers of tangentially elongated, thick-walled cells; where cork has not developed, epidermis present consisting of a single layered rectangular cells covered externally with striated cuticle; secondary cortex composed of tangentially elongated, oval, rounded or rectangular thin-walled parenchymatous cells having intercellular spaces, some cells contain rosette crystals of calcium oxalate, a number of rounded, oval to elongated, single or groups of stone cells and latex cells also found scattered in this region; pericyclic fibers numerous, lignified; secondary phloem composed of sieve elements, phloem parenchyma, phloem fibers and phloem rays; phloem parenchyma rectangular to polygonal in shape having rosette crystals of calcium oxalate, latex cells and stone cells similar to those found in secondary cortex; phloem fibers aseptate with bordered pits; phloem rays mostly uniseriate and straight (Anonymous, 1992) [3].

Identity, Purity and Strength

Foreign matter: Not more than 2 per cent
Total Ash: Not more than 21 per cent
Acid-insoluble Ash: Not more than 5 per cent
Alcohol-soluble extractive: Not less than 5 per cent
Water soluble extractive: Not less than 24 per cent (Anonymous, 2007) [7].

Phytochemical Studies

Calotropis procera have several types of compounds such as Cardenolides, triterpinoids, alkaloids, resins, anthocyanins and proteolytic enzymes in latex, flavonoids, tannins, sterol, saponins, and cardiac glycosides. Flowers contain terpenes, multiflorenol, and cyclisadol.

Leaves: In the leaves, mudarine is the principal active constituent as well as a bitter yellow acid, resin and 3 toxic glycosides calotropin, uscharin and calotoxin. The leaves contain mainly the amyrin, amyrin acetate, ß-sitosterol, urosolic acid, cardenolides, calotropagenin.

Latex: The latex contains caoutchouc, calotoxin 0.15%, uscharin 0.45%, trypsin, voruscharin, uzarigenin, syriogenin and proceroside 18. The latex contains a powerful bacteriolytic enzyme, a very toxic glycoside calactin 0.15% (the concentration of which is increased following insect or grasshopper attack as a defense mechanism), calotropin D I, calotropin D II, calotropin-F I, calotropin F II and a non-toxic protealytic enzyme calotropin (2 %-3 %). This calotropin is more proteolytic than papain, and bromelain coagulates milk, digests meat, gelatin and casein.

Flower: The flower contains the flavonoids, queretin- 3-ratinoside, sterol, calactin, calotoxin, calotropagenin, calotropin, and polysaccharides with D-arabinose, glucose, glucosamine and L-rhamnose. Flowers also contain enzymes 3-proteinase and calotropain (protease) lupeol, uscharin, proceroside, proceragenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3-pentenoate), 3-thiazoline cardenolide, gigantin, giganteol, isogiganteol, uscharidin, uzarigeninvoruscharin a-calotropeol, 3-epimoretenol, alactuceryl acetate and a-lactucerylisovalerate.

Bark Root: Phytochemical investigation of the roots of *Calotropis procera* Linn yields two new phytoconstituents, procerursenyl acetate and proceranol, together with the known compounds N-dotriacont-6-ene, glyceryl mono-oleolyl-2-phosphate, methyl myrisate, methyl behenate and glyceryl-1, 2-dicapriate- 3-phosphate. The structures of the new compounds have been identified as urs-18 alpha-II-12, 20 (30)-diene-3 beta-yl acetate and n-triacontan-10 beta-ol on the basis of spectral data analysis and chemical reactions. The

root bark has also been found to possess α-amyrin, β-amyrin, lupeol, β-sitosterol and flavanols like quercetin-3-rutinoside. (Quazi, *et al.*, 2013; Sharma *et al.*, 2011; Tiwari, 2014; Shrivastava *et al.*, 2013; Mainasara *et al.*, 2011; Anonymous, 1992; Ansari *et al.*, 1999; Aansari *et al.*, 2001; Akhtar *et al.*, 1998; Mahran *et al.*, 1971; Atef *et al.*, 1995, Khan *et al.*, 1988; Alam *et al.*, 2008; Ramaprabha *et al.*, 2012; Quazi *et al.*, 2013; Seiber *et al.*, 1982) [45, 51, 56, 13, 37, 3, 8, 9, 1, 2, 46, 36 45, 48].

Pharmacological Studies

Antimicrobial study

i. Mainasara *et al.*, (2011) [37] showed the result of the antibacterial activity measured in term of diameter of zone of inhibition, the antibacterial activity of *Calotropis procera* on the test organisms using water, methanol and ethanol extracts of fruit and bark exhibited antibacterial activity against both the Gram positive and Gram negative bacteria.
ii. Mann *et al.*, (1997) [39] showed that *in vitro* antibacterial activity of methanol extract of the leaves against gram negative bacteria such as Salmonella typhi, Pseudomonas fluorescens, Pseudomonas aeruginosa and Escherichia coli.
iii. The antimicrobial effect of ethanol, aqueous and chloroform extracts of leaf and latex of *Calotropis procera* on six bacteria namely, Escherichia coli, Staphylococcus aureus, Staphylococcus albus, Streptococcus pyogenes, Streptococcus pneumonia. The results revealed that ethanol was the best extractive solvent for antimicrobial properties of leaf and latex of *Calotropis procera* followed in order by Chloroform and aqueous. The growth of six bacterial isolates were inhibited by the three extracts except P.aeruginosa and S.pyogenes that were not inhibited by the aqueous extracts of both leaf and latex of *Calotropis procera* (Kareem *et al.*, 2008; Jain *et al.*, 1996; Kishore *et al.*, 1997; Malik *et al.*, 1979; Goyal and Mathur, 2011; Hassan *et al.*, 2006) [26, 24, 34, 38, 21, 23].
iv. The antimicrobial activities of water, methanol and ethanol extracts were determined by using disc diffusion method. The study shows that plant extracts crude and aqueous, methanolic and ethanolic with antibiotics, provide evidence that *Calotropis procera* extracts has the similar antibacterial activity as these antibiotics against test pathogens i.e. Salmonella Typhi, E.Coli (Muzammal, 2014; Kawo *et al.*, 2009; Nenaah *et al.*, 2011) [41, 27, 43].
v. Ghiasuddin *et al.*, (2012) studied that the antibacterial activity was done using modified agar well diffusion method according to standard protocol. The crude methanolic extract and Milky latex extracted from *Calotropis procera* were also screen for antibacterial properties and result showed that *Calotropis procera* has potent antimicrobial activities.
vi. In another study Shobowale *et al.*, (2013) [52] Plant extracts have been reported to be active against both gram positive and gram negative bacteria.
vii. Shobowale *et al.*, (2013) [52] studied that the aqueous and ethanol extracts were tested for antifungal activities and showed antifungal activity against C. albicans and A. Niger.

Antiinflammatory and analgesic study

i. Saba *et al.*, (2011) [47] studied that ethanolic extract of the leaf of *Calotropis procera* was investigated for its antiinflammatory and analgesic activities, results showed ethanolic extract of the leaf of *Calotropis procera* had potent antiinflammatory and analgesic activities.
ii. The methanolic extract of plant *Calotropis procera*, has been reported to exhibit potent antiinflammatory activity against carrageenan induced paw oedema and cotton pellet induced granuloma in albino Wistar rats (Basu *et al.*, 1991; Dewan *et al.*, 2000) [14, 16].
iii. The ethanolic extract of root bark of *Calotropis procera* was investigated for its anti-inflammatory activity at different dose in the different animal models. The experimental paradigms used were Complete Freunds Adjuvant (CFA) induced arthritis (chronic inflammation), acetic acid induced vascular permeability model in mice for anti-inflammatory activity (Parihar *et al.*, 2011) [44].
iv. The latex of the plant *Calotropis procera* has been reported to exhibit potent anti-inflammatory activity against carrageenin and formalin that are known to release various mediators (Arya *et al.*, 2005; Kumar *et al.*, 1994) [10, 35].
v. Studied carried out with the chloroform fraction of *Calotropis procera* root showed that this structure has potent antiinflammatory activity against the exudative and proliferative phases of inflammation, and presents potential analgesic properties through tests assessing changes induced by acetic acid in rats (Parihar *et al.*, 2011) [44].
vi. The crude dry latex of the plant *Calotropis procera* has been reported to exhibit potent anti-inflammatory activity. The antiinflammatory activity of petroleum ether, acetone, methanol and aqueous extracts of dry latex of *Calotropis procera* was tested in the carrageenan induced rat paw oedema model (Gupta *et al.*, 2012).
vii. The latex of *Calotropis procera* is well known for its medicinal and toxic properties. When administered locally, it induces an intense inflammatory process that can be characterized by increased vascular permeability, edema and increased cellular infiltration. This inflammation produced by latex involves the release of histamine from mast cells and the presence of histamine in the latex itself. Thus, it appears that antihistamine drugs can be effectively used in the treatment of inflammation induced by the latex of this plant (Silva *et al.*, 2010) [54].
viii. A single oral dose of dry latex ranging from 165 to 830 mg/kg produces a significant dose dependent analgesic effect against acetic acid induced writhing. The effect of dry latex at a dose of 415 mg/kg is more pronounced than a 100 mg/kg oral dose of aspirin (Quazi *et al.*, 2013) [45].

Wound Healing study

In an study by Sharma *et al.*, (2012) [50], *Calotropis procera* was selected for evaluation of its wound healing potential in guinea pigs for this purpose four full thickness excision wounds of 8.0 mm diameter were inflicted on the back of guinea pigs. Topical application of 20 µl of 1.0% sterile solution of the latex of the plant, twice daily was followed for 7 days. The latex significantly augmented the healing process by markedly increasing collagen, DNA and protein synthesis and epithelization leading to reduction in wound area. Thus the result provided a scientific rationale for the traditional use of this plant in the management of wound healing (Sharma *et al.*, 2012) [50].

Anti-cancerous study

i. *In vitro* assay for cytotoxic activity of the stem-leaves of *Calotropis procera* was carried out against human cancer cell lines at the concentration of 10, 30 and 100 mg/ml. Results revealed that the extracts of the plant possessed *in vitro* anticancer potential against HCT-15 (colon) cancer cell line at different concentrations. Further, the fractionation of the extracts was carried out and the fractions were tested on the same human cancer cell line. It was found that all the fractions inhibited the growth of HCT-15 at 100 g/ml except water soluble fractions, but the significant growth inhibition was shown by the chloroform-soluble fractions of the ethanolic extract and 50% ethanolic extract.
ii. Anticancer and cytotoxic properties of the latex of *Calotropis procera* in a transgenic mouse model of hepatocellular carcinoma result showed *Calotropis procera* have anticancer properties (Choedon *et al.*, 2006) [15].
iii. The antitumor potential of the root extracts of *Calotropis procera* was investigated using the methanolic, hexane, aqueous and ethyl acetate extract and its possible mechanism against Hep2 cancer cells was studied and the result showed extracts having potent action against Hep2 cancer cells (Quazi *et al.*, 2013) [45].

Mosquito larvicidal and repellent study

Singhi *et al.*, (2004) [55] studied on *Calotropis procera* as larvicide and repellent plant against vectors of Dengue and DHF. The latex of *Calotropis procera* has shown larvicidal efficacy against all three important vector species *viz*, aedes aegypti, anopheles stephensi and culex quinqefaciatus, vectors of dengue, malaria and lymphatic filariasis respectively.

Anti-fertility study

Sharma *et al.*, (2012) [50] studied that the effect of an ethanolic extract of the roots of *Calotropis procera* had been studied in albino rats to explore its antifertility and hormonal activities. Strong anti-implantation (inhibition 100 %) and uterotropic activity was observed at a dose of 250 mg⁄kg (1⁄4 of LD50).

Anti-helmintic study

i. In a study by Quazi *et al*, (2013) [45] antihelmintic activity of *Calotropis procera* methanolic extract of Flowers, in comparison with levamisole, was evaluated in a series of *in vitro* and *in vivo* studies the result showed methanolic extract had antihelmintic activity.
ii. In an another study the antihelmintic activity using adult earthworms from the crude latex of *Calotropis procera* was evaluated Both fresh as well as aqueous extracts of dried latex exhibited a dose-dependent inhibition of spontaneous motility (paralysis) and evoked responses to pin-prick. (Sharma *et al.*, 2012) [50].

Anti-diarrhoeal study

The dry latex of *Calotropis procera*, a potent antiinflammatory agent, was evaluated for its antidiarrhoeal activity. Like atropine and phenylbutazone, a single oral dose of dry latex (500 mg/kg) produced a significant decrease in the frequency of defecation and the severity of diarrhoea as well as protecting from diarrhoea in 80 % rats treated with castor oil (Zafar *et al.*, 2005) [58].

Oestrogenic study

The effects of ethanolic and aqueous extracts of *Calotropis procera* roots were studied on the oestrous cycle and on some parameters of Oestrogenic functionality in rats. Both extracts were found to interrupt the normal oestrous cycle in 60 % and 80 % of rats treated (Zafar *et al.*, 2005) [58].

Spasmolytic study

Spasmolytic is referred as a muscle relaxant, is a drug which affects skeletal muscle function and decreases the muscle tone. It may be used to alleviate symptoms such as muscle spasms, pain, and hyper reflexia. The aqueous extract of *Calotropis procera* was evaluated for its spasmolytic effect using *in vitro* trachea smooth muscle chain of Guinea-pig. The extract (50, 100 and 200 µg/ml) showed a dose-dependent relaxant activity probably exhibited through the direct relaxant action on the smooth muscle (Sharma *et al.*, 2012) [50].

Anti-convulsant study

The anticonvulsant activity of different root extracts of *Calotropis procera* was studied in rats in order to evaluate the traditional use of this plant. The anticonvulsant activity of different extracts of *Calotropis procera* roots was studied using seizures induced by maximal electroshock seizures (MES), pentylenetetrazol (PTZ), lithium-pilocarpine and electrical kindling seizures (Quazi *et al.*, 2013) [45].

Anti-pyretic study

Antipyretic effect from aerial parts of *Calotropis procera* was reported. Similarly, the ethanolic extract of *Calotropis procera* latex to possess antipyretic effect against yeast induced fever in rats was also reported four hours after administration of yeast, either dose of 250 or 500 mg/kg, aspirin (200 mg/kg) or saline were administered orally in 1 ml volume. Body temperature (ºF) was measured at 0, 3, 4 and 6 hours through rectal route using a digital thermometer (Sharma *et al.*, 2012; Dewan *et al.*, 2000) [50, 17].

Hepato-protective study

Hydro-ethanolic extract of *Calotropis procera* flowers was prepared and tested for its hepatoprotective effect against paracetamol-induced hepatitis in rats, result showed extract of *Calotropis procera* flowers has Hepatoprotective Activity (Sharma *et al.*, 2012; Setty *et al.*, 2007) [50, 49].

Anti-ulcer study

The antiulcer activity of *Calotropis procera* using different *in vivo* ulcer models were reported. The results of the study revealed that it significantly inhibited aspirin, reserpine, absolute alcohol and serotonin induced gastric ulcerations in rats and also protecting the gastric mucosa from aspirin-induced ulceration in pyloric-ligated rats and significant protection was observed in histamine-induced duodenal ulcers in guinea-pigs (Sharma *et al.*, 2012) [50].

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