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Calotropis gigantea: An in-depth review of its therapeutic potential

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Abstract

Background: *Calotropis gigantea*, belonging to the *Asclepiadaceae* family, is a perennial herb in question that has been used in the field of traditional medicine for an extensive duration. The botanical specimen in question has been shown to produce a wide array of chemical compounds, including but not limited to cardiac glycosides, flavonoids, terpenoids, alkaloids, tannins, and resins seen in the management of a diverse range of medical conditions, including leprosy, ulcers, tumors, and piles.

Objectives: The compounds under investigation exhibit various pharmacological activities, including analgesic, antipyretic, pregnancy interceptive, central nervous system (CNS), anti-inflammatory, procoagulant, anti-diarrheal, free radical scavenging, antimicrobial, anti-tumor, antifungal, antitussive, and antifeedant activities are among the pharmacological activities reported. It is a weed plant usually known as enormous milkweed. It contains one of the most essential traditional remedies for treating various diseases. The primary goal of this research on *Calotropis gigantea* is a plant that may be identified as an example in this context. The present study investigates the systematic categorization, introduction of plants, investigation of morphological characteristics, composition of phytochemicals, and economic importance of *Calotropis gigantea*. *Calotropis gigantea*, a shrub or small tree, has a bare or hoary characteristic and possesses laticiferous properties. It is well recognized by the popular names "swallow-wort" or "milkweed." *Calotropis* is a botanical species often used in traditional medicine. Cardenolides, flavonoids, terpenes, pregnanes, and nonprotein amino acids are chemical components of *C. gigantea*. The latex, leaves, blossoms, bark, and root are also used as a caustic, acrid, expectorant, depilatory, and anthelmintic, and are beneficial in leprosy, scabies, and ringworm of the scalp, piles, and other conditions.

Conclusion: The review focuses on the pharmacokinetic and pharmacotherapeutic approaches of the herbs and primarily studies the parameters hepatic protectant effect of the substance.

Keywords: *Calotropis gigantea*, hepatoprotective, milkweed, pregnanes, Pharmacological profile

Introduction

Fig 1: *Calotropis gigantea* (L). Br

Throughout several regions around the globe, including India, spanning from antiquity to the present day, the influence of flora, fauna, and other elements of the natural world on human ancient civilizations and cultures has been of considerable importance ^[1]. Throughout human history, plants have been held in high esteem by many civilizations ^[2].

The genetic resources that are being safeguarded and used for various reasons include those pertaining to food, fibre, fuel, fertiliser, febrifuges, and several other applications [3].

Ethno botanical Description

A tall shrub that can reach heights of 2.4 to 3 metres; its back colour of the object in question is a shade of yellowish white, and its surface exhibits a wrinkled texture. Additionally, the branches of this object are robust and possess a cylindrical shape and mostly (Particularly the younger individuals, they are covered in a delicate layer of closely pressed cotton-like hairs. The dimensions of the leaves range from 1 to 20 centimetres in length and 3.8 to 10 centimetres in width. The leaves are sessile, without a stalk or petiole or approximately so, oval and elongated or superficially elongated and pointed; Thick, glaucous-green, with delicate cottony to mentum underneath and more or less above; thin, cordate base. Flowers that is odourless, purple, or white. Calyx split to the bottom; sepals oval, acute, cottony, the dimensions of the object are 6 by 4 millimetres. The corolla is at least 2 cm in length, with segments ranging from 1.3 to 1.6 cm. These segments are deltoid-ovate in shape, sub-acute at the tip, and exhibit revolute and twisted characteristics as they mature. The coronal lobes are 3 cm long and have a pubescent surface along the slightly thickened border. The apex of the lobes is rounded, with two obtuse auricles located directly below it. Follicles are 9-10 cm long. Green, long, wide, thick, meaty, ventricose. Seeds are abundant, 6 by 5 mm in size, roughly oval, flattened, thinly margined, tomentose, and brown in colour. 2.5–3.2 cm in length [5, 6].

Table 1: Morphological Classification

Kingdom	Plantae
Order	Gentianales
Family	Asclepiadaceae
Subfamily	Asclepiadoideae
Genus	<i>Calotropis</i>
Species	<i>gigantea</i>

Table 2: Nutritive and growth contrasted morphological analysis of selected plant

Habit	The plant in question is a miniature tree or shrub that has the potential to reach a maximum height of 2.5 metres, with some specimens perhaps reaching up to 6 metres tall.
Roots	The plant has a straightforward growth pattern, with several branches originating from the base. The bark is deeply fissured and possesses a cork-like texture. The branches are somewhat fleshy and covered in a dense layer of white hairs. Over time, the plant gradually loses these hairs and becomes smooth. The plant emits a white latex secretion from each component that is cut or damaged.
Leaves	The blade of the leaf is ovate-ovate to ovate, measuring 5-30X2.5-15.5 cm. The apex is abruptly and momentarily sharp, while the base is cordate. The edges of the leaf are whole, and the leaf itself is fleshy. When young, it is covered in a white tomentose layer, but as it matures, it becomes glabrous and glaucous.
Flowers	The specimen exhibits bractation, hermaphroditism, actinomorphy, pentamerism, dioecy, petiolation, and has stalks of 1 to 3 cm in length.
Floral Characteristics	The inflorescence is characterised by its dense arrangement of several flowers, forming an umbellate structure. It is attached to the nodes and may be seen either at the axillary or terminal positions.
Calyx	The sepals are polysepalous, consisting of five lobes that are temporarily fused at the apex. They have a glabrescent characteristic and display quincuncial aestivation. The total number of sepals is five.
Corolla	Aestivation with five petals, gamopetalous, five lobed, and twisted.
Androecium	The stamens are five and gynandrous, and the anthers are ditheous while coherent.
Gynoecium	The bicarpellary nature of the structure is illustrated by the fusion of apocarps and styles at the apex, while the stigma bears a peltate form with five longitudinal stigmatic surfaces. The fusion of anthers with the stigma results in the formation of a gynostemium.
Fruits	A sub globose to obliquely oval follicle that is straightforward, fleshy, inflated, and has a diameter of at least 10 cm.
Seeds	The specimen consists of many small, flattened, obovate structures measuring 6 × 5 mm. These structures are densely packed and adorned with elongated, silky white pappus.

Numerous phytochemical components have been found in *Calotropis gigantea*'s numerous sections, particularly in the

Nutritive and growth contrasted analysis: *Calotropis* has a high level of drought tolerance and demonstrates a certain degree of salt resistance [7]. It thrives in its natural habitat at elevations of up to 900 metres above mean sea level (msl) over the whole country. The species prefers sandy soils that have been disrupted, and thrives in regions with an annual precipitation range of 300-400 mm. The plant in question readily establishes itself as a source of annoyance in areas characterised by deteriorated roadsides, margins of lagoons, and overgrazed native grasslands, mostly owing to the dispersal of its seeds by wind and animals. This particular species prefers and tends to dominate in locations characterised by abandoned agricultural practises, namely in areas with unsettled sandy terrain and little precipitation. The phenomenon is often seen as indicative of excessive cultivation practises.

Phytochemical Parameters

Calotroposides A-G seven the compounds under investigation include oxypregnane-oligo glycosides and cardiac glycosides. The root and bark, two isomeric crystalline alcohols, namely giganteol and isogiganteol, together with cardenolides, have been identified [9]. Akundarin is present in latex, which also includes 0.45% uscharin, 0.15 calotoxin, and 0.15 calactin. Moreover, latex is composed of many compounds such as calatropeol, calatropeol, amyrrin, and calcium oxalate [10]. Furthermore, it exhibits the ability to generate nitrogen and sulphur when interacting with fish, as well as the production of the cardiac toxin gigantol [11]. Glutathione and an enzyme that breaks down proteins related to papain are also found in tiny amounts in latex. Leaves: mudarine, alkaloids, and glycosides. Stembark: giganteol, amyrrin, and calatropeol [12]. Calatropeol the compounds incorporated throughout the botanical structure *Calotropis procera* is known to contain many chemical compounds, including n-calatropeol, amyrrin, cardioactive glycosides, mudarine, asclepin, bitter resins akundarin, and calotropin. All of these components are included inside the structure of flowers [8].

leaves, according to earlier researchers [9]. Further analysis revealed the presence of terols, giganteol, alpha and beta-

calotropeol, beta-amyrin, saturated and unsaturated fatty acids, hydrocarbons, acetates, benzoates, and a combination of tetracyclic triterpene molecules [10, 11]. Beta-amyrin, beta-amyrin, taraxasterol, sitosterol, beta-amyrin methylbutazone, beta-amyrin methylbutazone, usharin, gigantol, calcium oxalate, alpha and beta-calotropeol, beta-amyrin, beta-amyrin, Amyrin acetate, taraxasteryl acetate, lupeol acetate B, gigantursenyl acetate A, and gigantursenyl acetate B are among the substances discussed [12, 13]. The activities of the subject are often ascribed to many compounds, including flavonol glycosides, akundarol, uscharidin, calotropin, frugoside, and Calotroposides A through G [14]. The scientific research also describes calactin, calotoxin, calotropagenin, proceroside, syriogenin, uscharidin, Uscharin, uzarigenin, and voruscharin [15].

Calotropis gigantea has yielded flavonoids [16], triterpenoids are, alkaloid substances, the compounds included in the material include steroids, glycosides, saponins, terpenes,

enzymes, alcohol, resin, fatty acids and esters of calotropeols, volatile fatty acids with long chains, glycosides, and proteases [17, 18]. Enzymes called cysteine proteinase and aspartic proteinase were discovered in the laticifer fluid of *Calotropis* [19, 20].

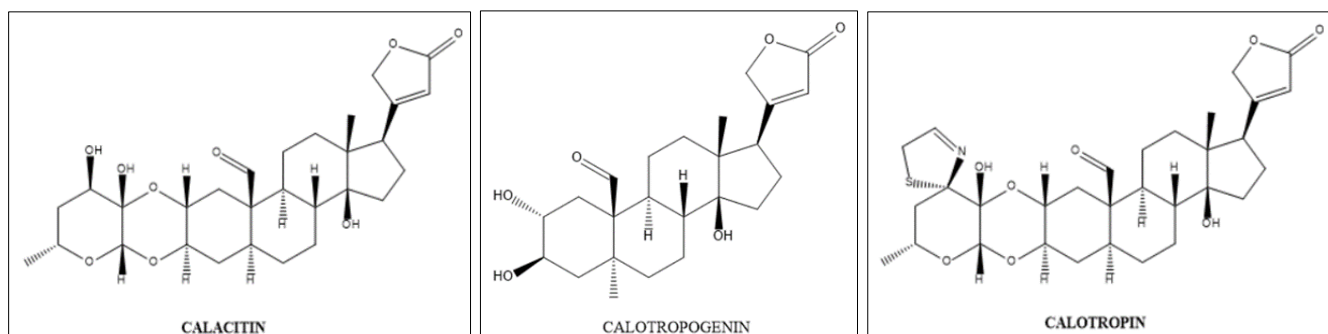
Because of the existence of these elements, the plants are resistant to pathogenic organisms. Insects, specifically found in the leaves, are known to have a high presence due to the abundant flow of latex. The latex of the plant has a significant concentration of lupeol, calotropin, calotoxin, and uscharidin, which includes a protein component. [21] In the study, conducted a comprehensive analysis of the primary phytochemical constituents present in several parts of the *Calotropis* plant, namely the flower, bud, and root [22]. The researchers examined a range of chemical classes, including alkaloids, carbohydrates, glycosides, phenolic compounds/tannins, proteins and amino acids, flavonoids, saponins, sterols, acid compounds, and resins [23].

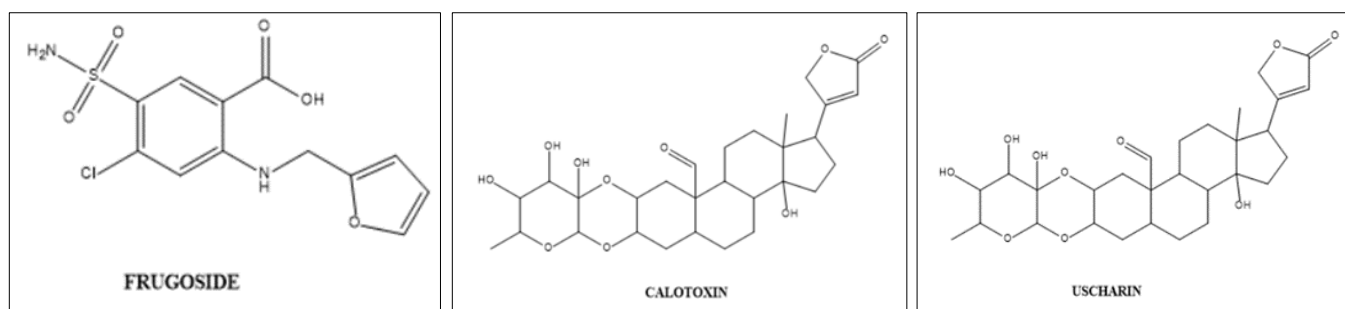
Table 3: Phytochemical components in *Calotropis gigantea*

S. No.	Class of Compounds	Plant Part			Tests performed
		Flower	Bud	Root	
1.	Alkaloids	✓	✓	✓	Dragendorff's test, Mayers test
2.	Carbohydrates	✓	✓	✓	Molish test, Fehling test
3.	Glycosides	✓	✓	✓	Keller killiani test
4.	Phenolic compounds/tannins	✓	✓	✓	Ferric chloride test
5.	Proteins and amino acids	✓	✓	✓	Xantho protein test
6.	Flavonoids	✓	✓	✓	Ammonia test
7.	Saponins	✓	✓	✓	With water With Na ₂ CO ₃
8.	Sterols	✓	✓	✓	Liebermann-Burchard test, Salkowski reaction, Hesse's reaction
9.	Acid compounds	✓	✓	✓	With Na ₂ CO ₃ , With litmus paper
10.	Resins	✓	✓	✓	With double distilled water, With acetone, and conc. HCl
11.	Peroxides	×	×	×	Potassium Iodide test

The floral specimens have been found to include cardenolides obtained from the mucus and foliage, triterpenoids, pigments generated from the flowers, and hydrocarbons. [24] *Calotropis gigantea* leaves and latex were discovered to contain cardiac glycosides; several glycosides were extracted and studied. *C. gigantea* leaves were used to extract an active component called "mudarine" [25]. Additionally, a yellow noxious acid and latex were identified. Calotropogenin (1), calotropin (2), Uscharin (3), calcotoxin (4), and Calactin (5) were found as cardiac glycosides [26]. Three cardenolide glycosides, namely coroglucigenin (6), frugoside (7), and 40 befagluopyranosylfrugoside (8) were isolated as the cytotoxic constituents from the roots of *Calotropis gigantea* L.,

often known as "Akond Mul". The study focused on assessing the detrimental impact of these components on the human organism and mouse cell lines [27, 28]. The numerical range of the observed selectivity of the cell line showed similarities to the selectivity of cardiopulmonary glycosides, namely digoxin and ouabain. The observed effects of these substances on human cell lines indicate their potential for posing a risk, but no such effects have been seen on mouse cell lines. [29] Calotroposides A are newly discovered oxy pregnane-aminoglycosides that have been extracted from the source of *C. gigantea*, a medicinal plant indigenous to Indonesia. The chemical structures of these compounds have been successfully identified [30].



Chemical structure derived from the *Calotropis gigantea***Pharmacological Profile**

- **Experimental animal studies have been conducted to investigate the antidiarrheal impact of *Calotropis gigantea*:** The anti-diarrheal activity of a hydroalcoholic (50:50) extract of *Calotropis gigantea* aerial portion against a castor oil-induced diarrhea model in rats was investigated. [31] The gastrointestinal transit rate was calculated by dividing the largest distance traveled by the charcoal by the entire length of the small intestine. [32] The enteropooling method was used to investigate the weight and volume of intestinal content caused by castor oil [33]
- **Evaluating *Calotropis gigantea*'s Antipyretic Effect in Animals:** *Calotropis gigantea* roots have been used in traditional Indian medicine to treat leprosy, eczema, syphilis, elephantiasis, ulceration, and cough. [34] The current study looked into TAB (Typhoid) vaccine-induced pyrexia in rats and rabbits. [35] The injection of 200 and 400 mg/kg doses intraperitoneally effectively decreased fever and normalized body temperature in both yeast-induced and TAB vaccine-induced fever. [36]
- Based on the findings of this investigation, it is possible to conclude that *C. gigantea* extract has potential antipyretic action against both yeast-induced and TAB vaccine-induced fever, implying a chance of developing *C. gigantea* as a less expensive and more effective antipyretic medication. [37]
- ***Calotropis gigantea* latex has procoagulant activity (Olytic) Activity Associated with Fibrin (ogen):** A significant number of proteins included in the unrefined latex extract exhibited a high degree of alkalinity and had notable proteolytic capabilities. The crude extract exhibits a dose-dependent manner of hydrolyzing casein and human proteins fibrinogen, and crude fibrin clot. [38] IAA fully reduced the hydrolyzing activity, indicating that they belong to the cysteine proteases superfamily. The crude extract hydrolyses the fibrinogen Alpha, Beta, and Gamma subunits. [39] The Alpha subunit was the most resistant to hydrolysis, followed by Beta, while the Gamma subunit was very resistant and only hydrolysed at greater protein concentrations or after a longer incubation period. [40] When contrasting with trypsin and papain, crude extract hydrolysis crude fibrin clots significantly. [41]
- **Pregnancy Interceptive Activity of *Calotropis gigantea* Linn. Roots in Rats:** When delivered as a single oral dosage of 100 mg/kg on Day 1 postcoitum, an ethanolic extract of the roots of *C. gigantea* Linn displayed 100% pregnancy interceptive action in rats. [42] When delivered in the Days 1-5 and 1-7 postcoitum regimens, the extract likewise demonstrated 100% effectiveness at a dosage of 12.5 mg/kg. Most implantations exhibited evidence of resorption when provided during the pericumearly post-implantation period (i.e., Days 5-7 postcoital at 250 mg/kg) [43]
- ***Calotropis gigantea* Non-protein Amino Acid as an Insect Anti-feedant:** Giganticine (1), a new non-protein amino acid, was isolated from an extract made from methanol of *Calotropis gigantea* root bark and its structure determined using spectroscopic techniques. [44] It had substantial antifeedant efficacy against desert locust nymphs *Schistocerca gregaria*. [45]
- **Cytotoxic Principles Extracted from Akond Mul (Roots of *Calotropis gigantea* L.):** As the cytotoxic components of "akond mul" (*Calotropis gigantea* L. roots), three cardenolide glycosides, calotropin (1), frugoside (2), and 4'-O-b Dglucopyranosylfrugoside (3), were produced. [46] These chemicals were investigated for cytotoxicity against human and animal cell lines. They exhibited cell line selectivity comparable to that of cardiovascular glycosides such as digoxin and ouabain: at 2 micrograms/ml, they are lethal to human cell lines but not to mouse cell lines. [47]
- **CNS Activity of *Calotropis gigantea* Roots:** CNS activity was investigated orally in albino rats at dosage levels of 250 and 500 mg/kg body weight using an alcohol extract of peeled roots of *Calotropis gigantea* R.Br. (Asclepiadaceae). Eddy's hot plate technique and acetic acid-induced writhings both shown significant analgesic effect. [48] The paw-licking duration was extended, and the quantity of writhings was drastically reduced. Significant anticonvulsant action was seen as there was a delay in the start and a decrease in the severity of pentylenetetrazole-induced convulsions. The rats given the extract spent more time in the open arm of EPM, demonstrating its antianxiety action. There was a reduction in locomotor activity. [49] The time it took to fall off (motor coordination) was also reduced. There was a reduction in locomotor activity. The time it took to fall off (motor coordination) was also reduced. [50] The extract's sedative action resulted in a potentiation of pentobarbitone-induced sleep. [51] There was no mortality up to a dosage of 1 g/kg. These findings demonstrate the extract's analgesic, anticonvulsant, anxiolytic, and sedative properties. [52]
- ***Calotropis gigantea* Flower Analgesic effect:** A distillate of *Calotropis gigantea* grown in alcohol flowers was provided orally and tested for analgesic effect in chemical and thermal models in mice. In an acetic acid-induced writhing test, dosages of 250 and 500 mg/kg reduced the number of writhes by 20.97% and 43.0%, respectively. [53] The paw licking period was delayed in the hot plate procedure. The relief of pain was found after

30 minutes after dosage administration and peaked after 90 minutes^[54].

- **The Influence of Pineapple Fruit-Rotting Fungus, *Ceratocystis paradoxa*, on Pineapple Fruit-Extracts and Systemic Fungicides:** Extracts from sixteen distinct species were examined for their ability to inhibit the growth of the fungus *Ceratocystis paradoxa*, which is responsible for the soft rot that occurs in pineapples.^[55] It turns out that *Xanthium strumarium* was the most effective, subsequent to *Allium sativum*. *Meriandra bengalensis*, *Mentha piperita*, *Curcuma longa*, *Phlogacanthus thyrsoiflorus*, *Toona ciliata*, *Vitex negundo*, and *Azadirachta* extracts were used in the current investigation.^[56] *Indica*, *Eupatorium birmanicum*, *Ocimum sanctum*, and *Leucas aspera* shown to be the most effective plant species in the fight against *C. paradoxa*. The fungitoxic properties of *Cassia tora* and *Gynura cusimba* have been identified in their respective extracts. *Calotropis gigantea* and *Ocimum canum* are the species in question.^[57]
- **Hepatoprotective effect:** The hepatoprotective activity of the methanolic extract derived from the leaves of *C. gigantea* has been shown to be significant in rats, particularly in mitigating hepatotoxicity produced by CCl_4 .^[58]
- ***Calotropis gigantea*'s anti-inflammatory activity** will be evaluated in numerous experimental animal models. Carrageenan. The experimental model of kaolin-induced rat paw edema was used to study acute inflammation, whilst the cotton-pellet granuloma and adjuvant-induced arthritis models were utilized to investigate chronic inflammation. The yeast-induced pyresis technique was used to test antipyretic activity^[59].

***Calotropis gigantea* as potent hepatoprotective agent**

Calotropis gigantea flower hydro-ethanolic extract (70%) was produced and evaluated in rats for its hepatoprotective efficacy against paracetamol-induced hepatitis. The present study investigated to evaluate the levels of various biochemical markers linked to liver damage, such as SGPT, SGOT, ALP, bilirubin, cholesterol, HDL, and tissue GSH, in both the treated and untreated cohorts.^[60] The administration of paracetamol as at a dosage of 2 grams per kilogram has led to increased amounts of SGPT, SGOT, ALP, bilirubin, and cholesterol, while simultaneously decreasing blood levels of HDL and tissue levels of GSH. The hydro-ethanolic instillation of *C. gigantea* flowers displayed a dose-dependent response, with the infusion of doses at 200 mg/kg and 400 mg/kg showing the ability to bring abnormal levels of biochemical markers back to a range that closely resembles the normal range^[61].

Toxicological Study

Calotropis gigantea (giant milkweed) has been claimed to offer several therapeutic and economic benefits, but it has also been shown to be potentially harmful to the body, particularly after extended or chronic usage.^[62]

Calotropin, which is contained in latex, causes cardiac slowing and gastroenteritis when injected into a frog's lymph sac 59. If more than 0.12 mg/kg is administered, it is expected to result in death.^[63] Latex is a skin and mucous membrane irritant that has been linked to blindness. A dose of 4-5 mL of latex may be fatal. It has the potential to tear the muscle of the gut and colon, resulting in death^[64]. The plant can induce severe bullous dermatitis, delayed yet stronger heartbeats,

labored breathing, high blood pressure, convulsions, and death.^[65] Latex is very hazardous to human eyes, causing rapid painless dimness and photophobia^[66].

Conclusion

Calotropis gigantea is an herb that has numerous medicinal principles and economic values this particular entity possesses distinct qualities. It is classified as a perennial shrub, capable of thriving in many soil compositions and environmental circumstances, without necessitating any cultivation practises. This particular plant, characterized by its high hydrocarbon content, needs more investigation in the field of energy conversion.

The potency and abundance of bioactive compounds, crucial for the treatment of several ailments, are influenced by a range of factors including climatic conditions, soil composition, and other relevant variables. The standardization of phytochemicals based on these factors is of utmost importance in order to effectively build plant applications. The above-mentioned information about the use of *Calotropis gigantea* around the world is corroborated by existing literature. The usage of this plant implies that the plant in question should be preserved. Furthermore, the human-unknown applications of this plant should be extensively publicized in the globe under study so that people might utilize its applications for their well-being in everyday life.

Calotropis gigantea is one of the prospective performing possibilities. Hydrocarbons may be extracted from latex derived from *Calotropis gigantea*. More studies on *Calotropis gigantea* are required to acquire petroleum products. It also concluded the various pharmacological hepatoprotectant effects of the herb natural extract which shows the potent hepatic treatment characteristics.

Conflict of Interest

No Conflicts of interest were raised by any of the authors about the publication/investigation.

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