

Case Report

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Toxicological and Phytochemical Potentials of CALOTROPIS PROCERA

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Though literature searches reveal much work about ethnomedicinal uses, chemical composition and pharmacological activities, no recent papers are available that provide an overview of the toxicity and phytochemical potential of *Calotropis procera*. Hence, the insight of this review is to provide a systematic summary of toxicology, phytochemistry, and therapeutic potential of *Calotropis procera* and to highlight the gaps in the knowledge to offer inspiration for future research.

Calotropis procera is a species of flowering plant in the family Apocynaceae that is native to Northern and Tropical Africa, Western Asia, South Asia, and Indochina (mainland Southeast Asia).



Commonly known as *ashkhar* (Arabic: رخشا) in Arabic, it is a common desert shrub with a wide range of medicinal applications in traditional Bedouin medicine [1]. It has been linked to several cases of poisoning and corneal damage caused by children unknowingly touching its sap and then their eyes. Bedouins have long held that the plant causes blindness if contact is made with the eyes and any part of the plant. Its roots were traditionally burned and used as a component of gunpowder by Bedouins in the Trucial States [2].

Common names for the plant include apple of Sodom, Sodom apple, roostertree, king's crown, small crownflower, giant milkweed, rubber bush, and rubber tree [2-5]. The names "Apple of Sodom" and "Dead Sea Apple" stem from the ancient authors Josephus and Tacitus, who described the plant growing in the area of biblical Sodom [6]. Although not native to the New World, the plant (and other related milkweed species) has been cultivated and feeds monarch butterfly caterpillars, in places such as California,

Hawaii and the island of Puerto Rico [3,5]. In Arabic, it is known as *al-ashkhar* [7]. The ashkhar is listed in the Mishnah and Talmud. The fibers attached to the seeds may have been used as wicks. However, according to the Mishnah, it is one of the rabbinically prohibited activities of Shabbat [10,11].

The plant *Calotropis procera* is known by different name in different part of the world like Madar, French cotton, Alarka, or Rooster tree, and Widuri. The plant is poisonous can lead to blindness if its juice is put in to the eyes. The same plant is used for Ayurvedic medicines. The medicinal properties like Calotropin isolated from latex is used as remedy for painful tooth cavities rheumatism, syphilis, leprosy and edema, for ring worm, syphilitic soreness, and leprosy cutaneous dryness and toothache. Latex is also used in the treatment of gum bleeding and as odontagic. Flowers can all so be used for toothache, and ringworm infection. As the adage goes excess leads to distress, the judicious use of herbal medication is recommended otherwise it will lead to complication, as described in the case report.

Leaves are very much effective in decreasing inflammation, relieving pain when tied externally on joints [12]. Leaves contains Sapogenins, holarrhentine; cyanidin-3-rhamnoglucoside; taraxasterol isovalerate. Mudarine and three glycosides calotropin uscharin, calotoxin along with phenol [13]. Its green fruits contain a toxic milky sap that is extremely bitter and turns into a latex-like substance, which is resistant to soap.

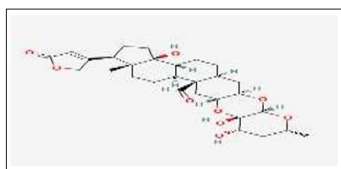
Toxicity

Every part of this plant is toxic, but stem (latex) and roots are more poisonous than leaves. The leaves of this plant have three toxic glycosides calotropin, calotoxin and us charin, whereas its latex contains calotropin, calotoxin and calactin, which are caustic and considered poisonous in nature. Besides this, the concentration of calactin, which is a toxic glycoside, gets increased as defense mechanism on encounter of grasshopper or insect attack and this is the rationale behind the plant not being consumed by cattles or other grazing animals. Other than this, osmotin, a laticifer protein purified from latex also provides protection to plant against phytopathogens. Its milk is irritant, neurotoxic and has anticholinergic activity, which causes toxicity and fatal complications. Madar juice and latex has bitter taste and a burning pain which causes salivation, stomatitis,

vomiting, diarrhoea, dilated pupils, titanic convulsion, collapse and death. The fatal period varies from half an hour to eight hours. If latex enters into the eye, it causes kerato-conjunctivitis, corneal edema and dimness of vision without any pain. Some cases showed permanent endothelial cell damage, which was evident after three weeks. *C.procera* was found toxic at the dose of 100 mg kg⁻¹ to chick embryo. Its toxicity caused hepatocellular degeneration in liver, brain congestion, dilation of central veins, sinusoids, underdeveloped lung and kidneys. Hence, bearing in mind the toxic effects of certain extracts and glycosides, further studies should be focused to explain toxicity and safe use of *Calotropis procera*.

The milky sap of *Calotropis* plants is a toxic substance that can cause irritation when it comes into contact with the skin or eyes [14,15]. The sap can be collected from various parts of the plant, including the flowers, stem, and leaves [16]. The sap is extremely bitter and turns into a gluey coating that is resistant to soap, therefore it has to be treated immediately once it has fallen into the eye [14].

Calotropis species are toxic plants; calotropin, a compound in the latex, is more toxic than strychnine [15]. Calotropin is similar in structure to two cardiac glycosides which are responsible for the cytotoxicity of *Apocynum cannabinum*. Extracts from the flowers of *Calotropis procera* have shown strong cytotoxic activity.



Calotropin

Cattle and other animals often stay away from the plants because of their unpleasant taste and their content of cardiac glycosides [16]. The toxic ingredients of *Calotropis* plants, including *Calotropis procera*, can be preserved in liquid form, and they naturally disintegrate over time [8]. *Calotropis* leaves are used as fodder for animals once they are dried [16,17].

Phytochemistry Chemical Constituents

Phytochemistry of *Calotropis procera* has always attracted the attention of researchers because despite its toxicity, it employs wide applications in traditional medicinal system till date. *Calotropis procera* contains flavonoids, cardenolides, sterols, oxypregnanes, triterpenoids, glycosides and other constituents as elaborated in different tables; Flavonoid and its glycosides (Figure 1) are the major compounds isolated from the leaves of *C. procera*. Steroids (Figure. 2) and cardenolides (Figure. 3) are the major secondary metabolites found in the latex. Cardenolides are C23 steroids with steroid nucleus having a glycoside moiety at C-3 and a lactone moiety at C-17.6 Cardiac glycosides can be novel antineoplastic agents as cancer cells are more prone to these compounds. Terpenoids (ursane, olenane type and pentacyclic triterpenes etc.) (Figure. 4) have been isolated from flowers, root bark and latex. Oxypregnane glycosides (Figure. 5) have recently been reported from root bark of this plant. They have a steroidal skeleton containing a 2-deoxy sugar moiety. These oxypregnanes have a benzoyl moiety at C-12 and a straight 5–7 units sugar chain connected to C-3 of the aglycone.6 Some glycosides (Figure. 6), lignan glycosides (Figure. 7), terpene glycosides (Figure. 8) and caffeic acid derivatives (Figure 9) have also been isolated from this plant.

Cardiac Glycosides (Cardenolides): The most notable compounds are concentrated heavily in the milky latex, roots, and leaves. Primary active cardenolides include calotropin, calotoxin, calactin, uscharin, and voruscharin. Derivatives like UNBS1450 (a semi-synthetic form of 2-oxovoruscharin) are studied for their anticancer potential. Triterpenoids and Steroids: Found in the roots, stem bark, and latex. Key isolates include β -amyrin, procroside, stigmasterol, and various calotropoleanylenyl esters. Phenolics and Flavonoids: Abundant in the flowers and leaves, offering strong antioxidant properties. Latex Specifics: The caustic, milky sap also contains caoutchouc (rubber), fatty acids, and proteolytic enzymes like trypsin. For comprehensive breakdowns of its medicinal and toxicological profiles, you can review this Phytochemistry of *Calotropis procera* and its Traditional Uses Study or the PMC Review on *Calotropis procera*.

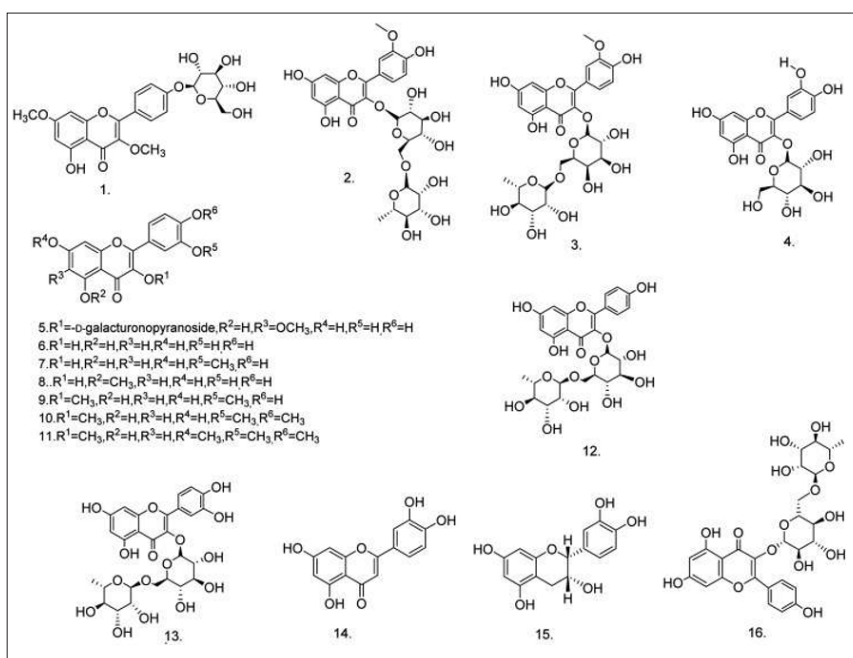


Figure 1: Chemical Structure of Flavonoids

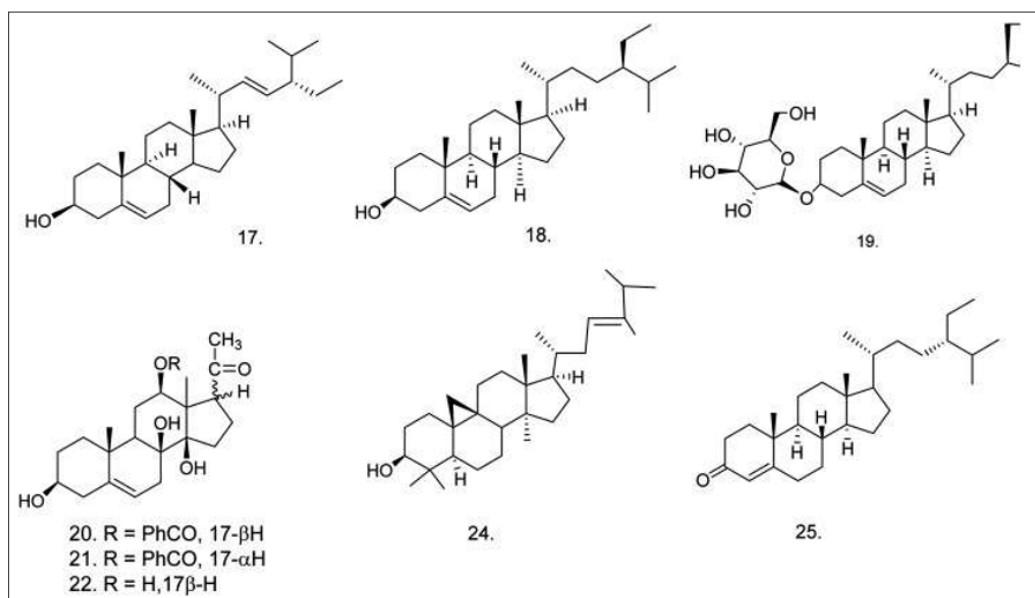


Figure 2: Chemical Structures of Steroids

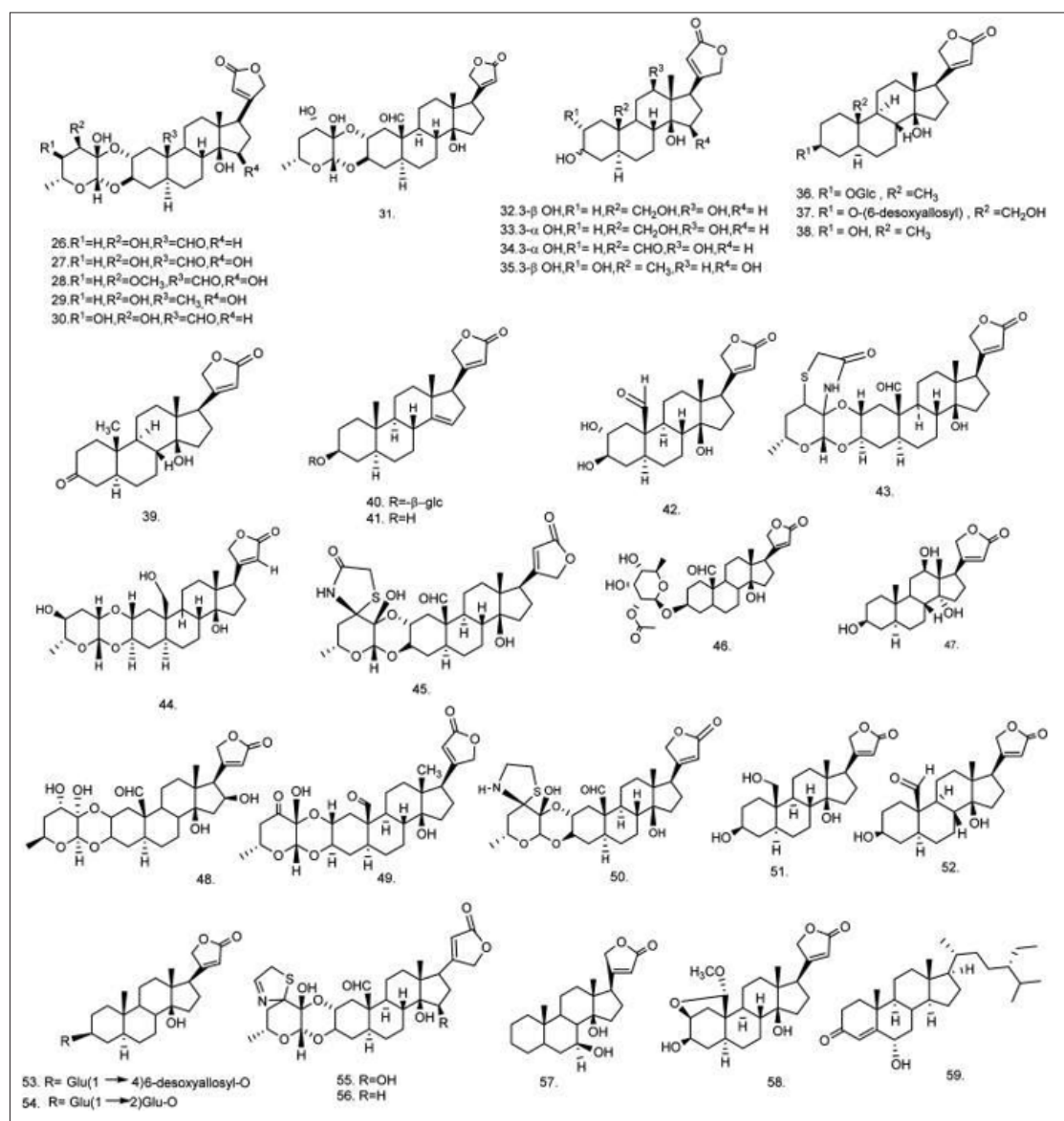


Figure 3: Chemical Structure of Cardenolides

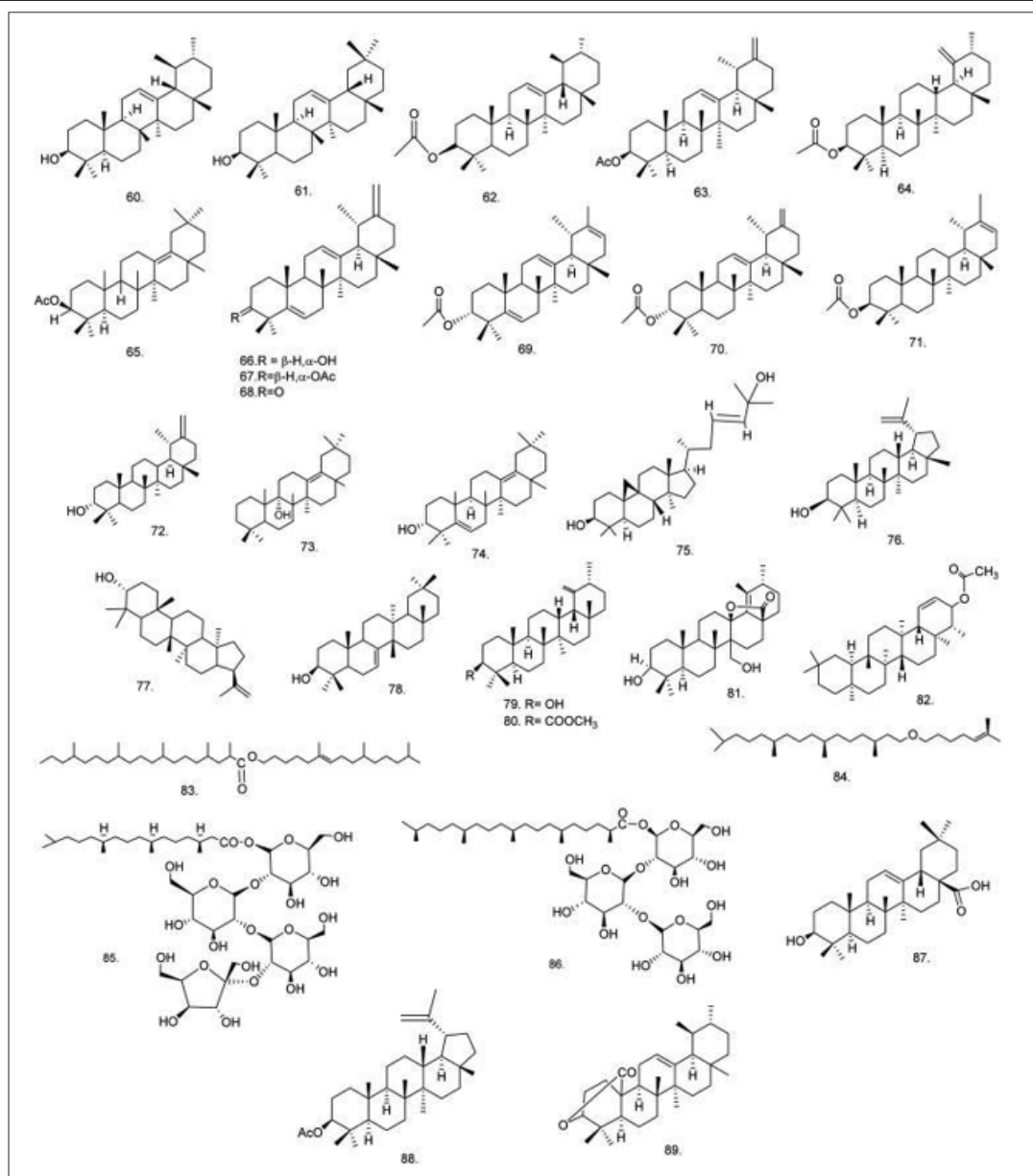


Figure 4: Chemical Structures of Terpenoids

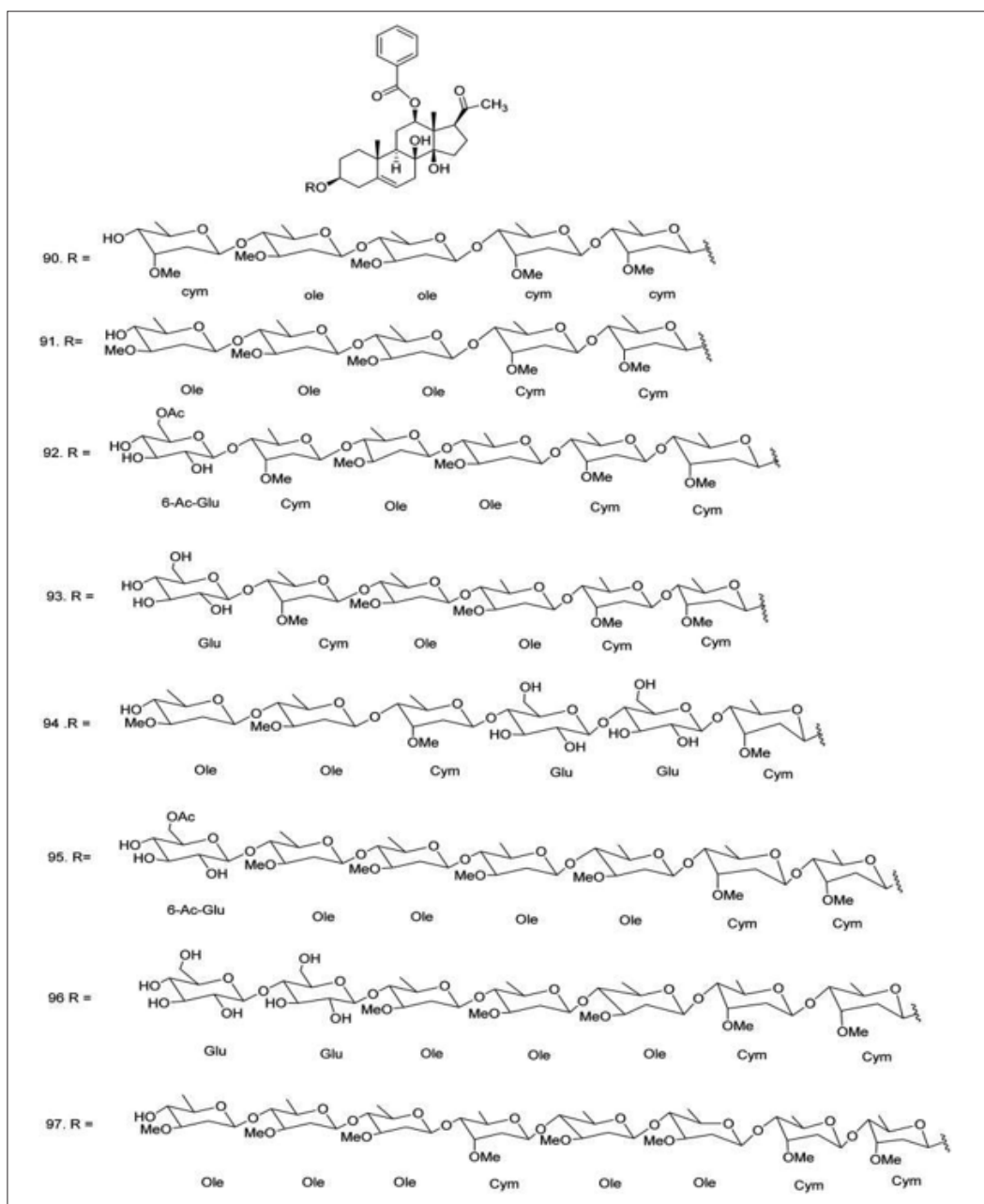


Figure 5: Chemical Structures of Oxypregnanes

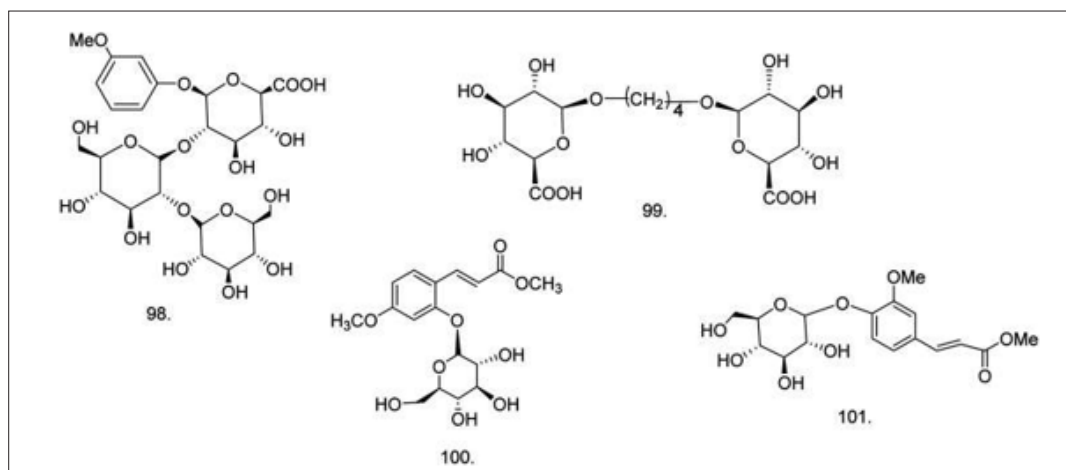


Figure 6: Chemical Structures of Glycosides

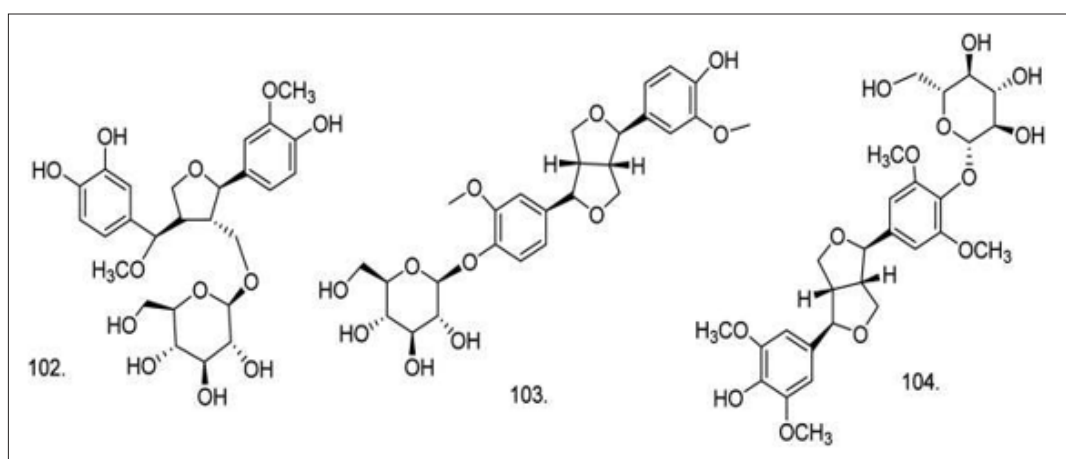


Figure 7: Chemical Structures of Lignan Glycosides

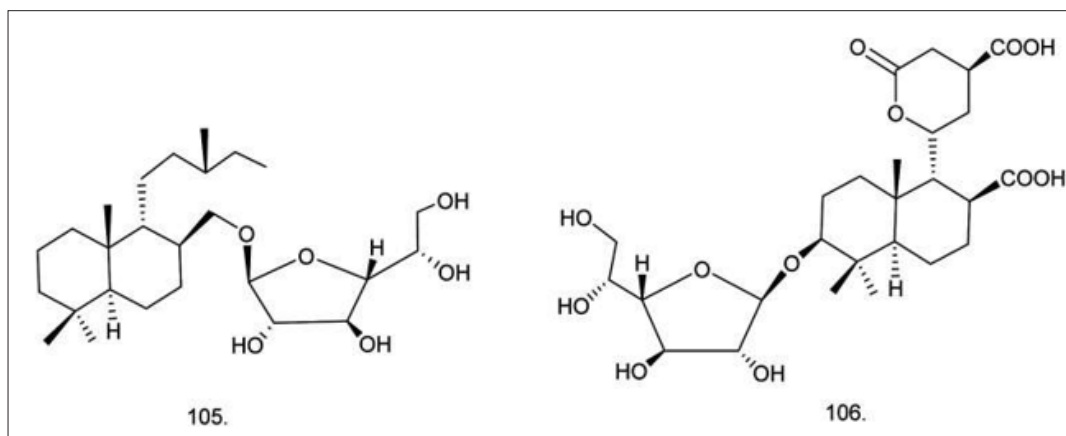


Figure 8: Chemical Structures of Terpene Glycosides

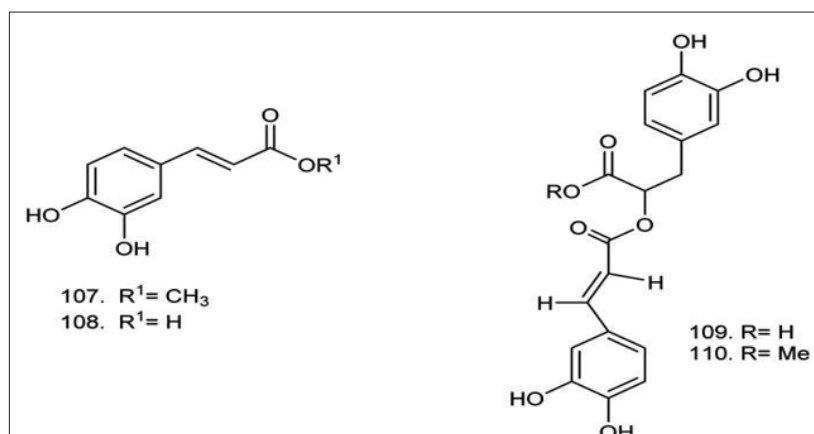


Figure 9: Chemical Structure of Caffeic Acid Derivatives

Therapeutic Potential: *Calotropis procera* has, has a wide range of therapeutic potential due to it rich phytochemical profile. Some of the key therapeutic properties are as follows:

- **Anti-inflammatory:** The plant has been used to treat inflammation and pain, making it beneficial for conditions like rheumatism and arthritis.
- **Antimicrobial:** *Calotropis procera* exhibits strong antimicrobial properties, which can be used to combat various infections.
- **Anticancer:** The plant's compounds have shown potential in inhibiting cancer growth and promoting cell death.
- **Neuroprotective:** It may have protective effects on the nervous system, potentially aiding in conditions like Alzheimer's disease.
- **Wound Healing:** The plant's constituents have been used to promote faster wound healing and reduce scarring.
- **Diuretic:** *Calotropis procera* can help in the removal of excess fluid from the body, which can be beneficial for conditions like edema.
- **Antioxidant:** The plant's compounds may help combat oxidative stress and prevent damage to cells.

Some studies suggest topical use of Madar plant on foot will help in controlling obesity, but no evidence based study or scientific study was available on the topical use of the raw leaves of this plant for topical application. If this plant would not have been poisonous, due to its toxicity it might cause contact dermatitis or redness and vesication [18-21].

The aforesaid properties make *Calotropis procera* a valuable plant in traditional medicine and a subject of interest in modern pharmacology. However, due to its potential toxicity, particularly at high doses, it is essential to use it under professional guidance and with caution.

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