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A Review on Phytochemical, Medicinal and Pharmacological Profile of *Euphorbia antiquorum*

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ABSTRACT

Euphorbia antiquorum is a fleshy shrub belonging to the family Euphorbiaceae. It is widely distributed in the hotter parts of India. *Euphorbia antiquorum* L. (Euphorbiaceae) has several therapeutic applications in folk medicine in curing or managing a wide range of diseases. The juice of the plant is acrid, and used as an anti-inflammatory, purgative, rheumatism, dropsy, gout, neuropathy, deafness, cough etc. The latex of EA contains insecticidal activity. The anti-inflammatory and anti-arthritic potential has been associated with aqueous and alcoholic extracts of EA.

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INTRODUCTION

Nature always stands as a golden mark to exemplify the outstanding phenomena of symbiosis. Natural products from plant, animal and minerals have been the basis of the treatment of human diseases. From the ancient time plants are acknowledged as a major resource for mankind. Plants are used as food material, in cosmetics and mostly in health care system. From human civilization up to date plants are primary resources of medicines. Different civilizations used plants in various ways for medicinal purposes. Traditional system of medicines particularly Ayurveda, Unani, Siddha, Naturopathy, Chinese system of medicine, European system of medicine, Homeopathy etc. are popular to treat different ailments, because these have faith in the mind of human being. These systems are based on time testing and expertise evolved on the use of plants as a source of safe medicine. The use of herbal medicine becoming popular due to toxicity and side effects of allopathic medicines, this led to sudden increase in the number of herbal drug manufactures. Herbal medicines as the major remedy in traditional system of medicine have been used in medical practices since antiquity. The practices continue today because of its biomedical benefits as well as place in cultural beliefs in many parts of world. Today about 80% of people in developing countries still relays on traditional medicine based largely on species of plants and animals for their primary health care. Herbal medicines are currently in demand and their popularity is increasing day by day. India is a country having biodiversity of 15 agro-climatic zones, 47000 plant species of which 15000 are reported to have medicinal properties^[1-2].

Euphorbia antiquorum L. (Euphorbiaceae) has several therapeutic applications in folk medicine in curing or managing a wide range of diseases. It is commonly found in village shrubberies throughout the tropical and warm temperate regions of India and Ceylon^[3]. It is a plant native to India, Sri Lanka and Southeast Asia, has various medicinal value^[4]. It can be found growing up to an altitude of 800 m^[5]. It looks like a large shrub or small tree. The juice of the plant is acrid, and used as an anti-inflammatory, purgative, rheumatism, dropsy, gout, neuropathy, deafness, cough etc. The juice, which flows from the branches, is a popular application to warts and other cutaneous infections^[6].

HABITAT

Euphorbia antiquorum Linn (EA) Euphorbiaceae is wide spread throughout peninsular India, it can be found growing up to an altitude of 800 m. It is easy to propagate from seed or

vegetatively in late spring to summer. It is found in shrubberies throughout the tropical and warm regions of Sri Lanka and Southeast Asia. One of the largest armed tree Euphorbia's with an average height of 5-7 m, stems are 5-7 cm thick, green, glabrous, branching from upper parts; upward curving, segmented. The odour of its latex is pungent and lingering. Ribs are 3 (or 4-5) prominent, wing like, up to 1-3 cm wide, 3-5 mm thick, prominently triangular toothed. Leaves are few, borne on the ridges, succulent, quite insignificant and fall off quickly, alternate, apically clustered, petiole very short, leaf blade obovate, to oblanceolate to spatulate in shape 2-5(-10) × 1-2 cm, base attenuate, margin entire. Apex rounded or obtuse with a small pointed projection, base gradually narrowing downward. Leaves are much more long in the young seedling, margins deeply sinuate. Flowers are cyathia yellowish-green to pinkish, subterminal, axillary, single or in triads or 3-4 individual cyathia together; peduncles reddish brown; primary peduncle 1 - 1.5 cm long, cyathia peduncle 2-3 mm; all cyathia bisexual; anthers pinkish. Male flower with only 1 stamen, filament short; female flower situated alone at the center of the cyathium, protruding beyond the involucre, styles 3, not joined to each other, each style forking towards the tip. They are full of honey that attracted bees. Blooming season of flowers and fruit is throughout the year. Fruit is capsules, glabrous, obscurely lobed, smooth about 8-10 mm in diameter and become deep red on maturity year [7,8].

SYNONYMS ^[9]

Arabic: Zaqqume hindi, Zekoom

Belgium: Tindarisend

Bengal: Bajvaran, Lariyadaona, Narasij, Shibgach, Tekatasij

Burma: Pyathal, Tazaung, Shazanvji

Cambodia: Chanlatday

Canarese: Bontekalli, Bontegalli, Chaturagalli

China: Huo Yu Jin

English: Triangular spurge

Deccan: Tidharisend, Tindharisend

Gujarat: Tandhari

Hasada: Siddaru

Indonesia: Sesuru

Hindi: Tridhara, Sehund

Malayalam: Chaturakalli, Kalli, Katakalli

Marathi: Naraseja, Narsej

Michi: Shidu

Mundari: Eteke, Etete, Siddaru

Sadani: Sid

Sanskrit: Simhunda, Snuhi, Tridharaka, Vajrakantaka, Vajri

Santal: Etkec

Tamil: Amudangam, Kalli, Kandirvam, Kaniravam

Telugu: Bommajemudu, Bontajensudu

Tulu: Darekalli

Urdu: Zakum

Uriya: Dokahanasiju

Taxonomical Classification ^[10]

Kingdom: Plantae

Phylum: Magnoliophyta

Order: Order

Class: Magnoliophyta

Family: Euphorbiaceae

Genus: Euphorbia

Species: Antiquorum

Botanical name: *Euphorbia antiquorum* Linn.

PLANT DESCRIPTION

EA is a member of the Euphorbiaceae family. It is a succulent plant which is usually leafless and can reach a height of up to 8 m with a stem diameter of 22 cm. The older stems are terete, with brownish bark while younger branches are smooth, green and distinctly angled, articulate with the segments 6–30 x 2–5 cm, drying greenish with shallow to hardly narrowed sinuses between the spine shields. Spine-shields are in rows, shallow, blackish and persistent. Stipules are transformed into spines. Leaves if present are alternate, caducous. Cyathia are axillary, yellow, solitary or in dichasia of 3, less than 2 cm long; basal peduncle is 4–6 mm long; bracts of branching 2 mm long; peduncle of individual cyathia is 1 mm long; involucre bracts are 1.5–2 mm long; cyathia are sessile in involucre; transversely elliptic, 1 x 2.5–3 mm, without appendages, interspersed with erect smaller lobes; pistillate flowers nearly sessile in

involucre. Fruits are yellow-orange on a pedicel which is 1 – 3 mm long; schizocarp is 4 – 4.5 x 6.5 – 7 mm deeply sulcate and sharply keeled. Seeds are 2.5 - 2 mm, pale to grey brown, ecarunculate^[11].

PHYTOCONSTITUENTS

Preliminary phytochemical investigation of EA shows the presence of triterpenoids and flavonoids, isolated compounds from the plant include euphol, antiquol A, euphorbol, isohelianol, camelliol^[6]. EA also contains Ingenol 3-angelate is one of the active compounds used as traditional medicines in treating a number of conditions, including warts, corns, waxy growths, skin cancer, asthma, and catarrh^[12]. Latex of the plant *Euphorbia antiquorum* contains eupa-7, 9(11), 24-trien-3beta-ol (antiquol C), 19(10-->9) abeo-8alpha, 9beta, 10alpha-eupa-5,24-dien-3beta-ol (antiquol B), and 24-methyltirucalla-8,24(24(1))-dien-3beta-ol (euphorbol), lemmaphylla-7,21-dien-3beta-ol, isohelianol, and camelliol C showed potent inhibitory effects on Epstein-Barr virus early antigen (EBV-EA) activation induced by the tumour promoter 12-O-tetradecanoylphorbol-13-acetate (TPA)^[13].

Chemical Structure of some important constituents of *Euphorbia antiquorum* Linn

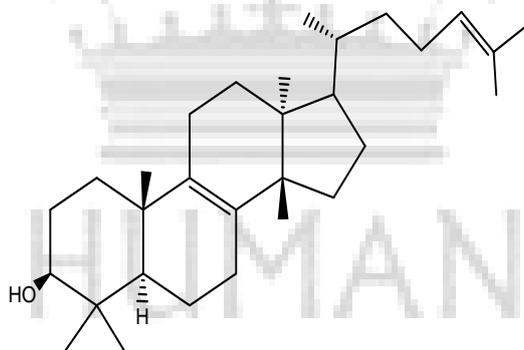


Figure 1: Euphol

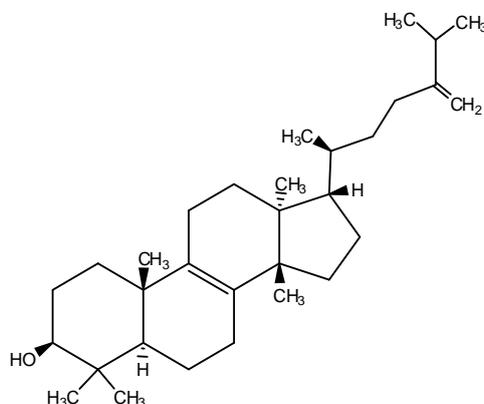


Figure 2: Euphorbol

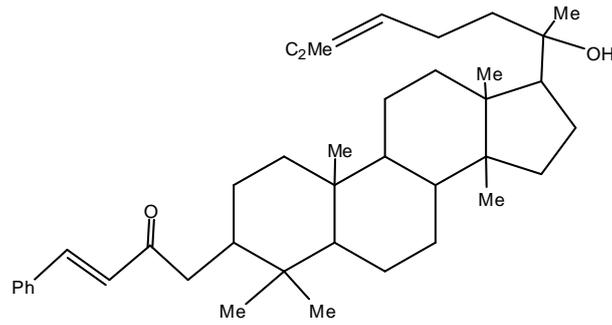


Figure 3: Antiquol A

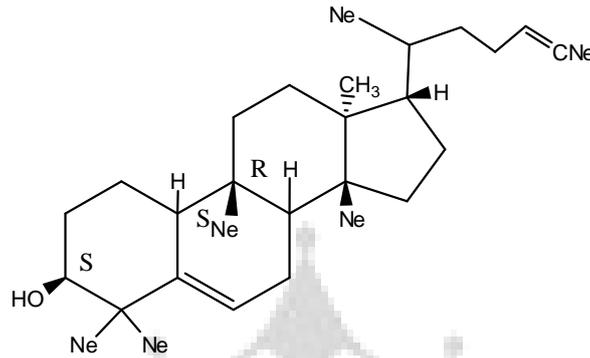


Figure 4: Antiquol B

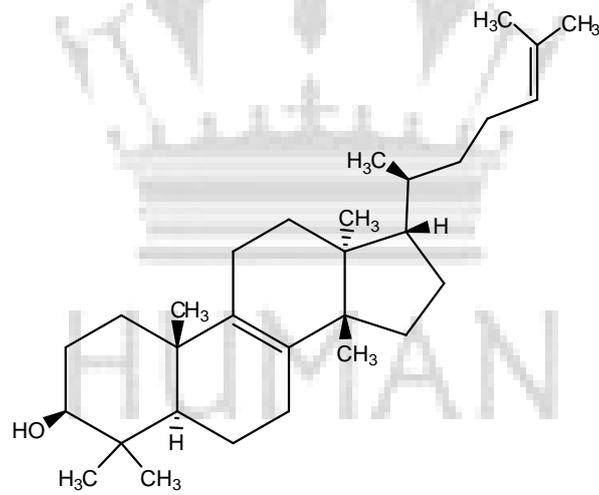


Figure 5: Antiquol C

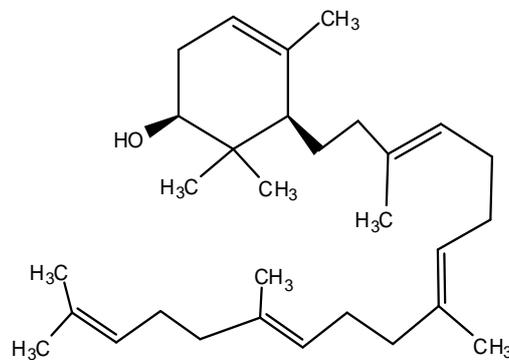


Figure 6: Camelliol C

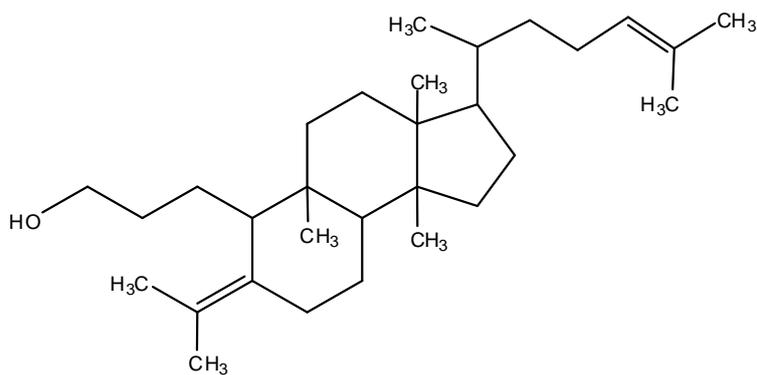


Figure 7: Isohelianol

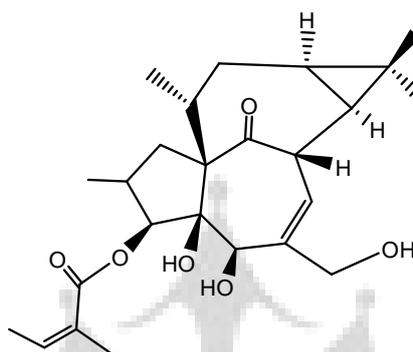


Figure 8: Ingenol 3-angelate

PHARMACOLOGICAL ACTIVITIES

The various parts of EA have been associated with a number of pharmacological activities which are enlisted below:

Cytotoxic activity

The latex can be effectively used along with chemotherapeutic drugs for cancer treatment, because the latex by itself is not cytotoxic and when given along with the standard chemotherapeutic drug etoposide, it was able to counteract the toxicity of the drug in normal chick embryo fibroblasts. The results also suggest its use in combination therapy along with chemotherapy to fight cancer ^[14].

Hepatoprotective and antioxidant activity

Aqueous extract of the aerial parts of EA has been reported to have hepatoprotective and antioxidant activity. EA extract exerted significant antioxidant activity (at 20 µg, 40 µg, 60 µg, 80 µg and 100 µg/ml *in-vitro*) as evidenced by its reducing power, hydroxyl and superoxide anion radical scavenging activities. The *in vitro* efficacy was reinforced by a

significant dose dependent hepato-protection (at 125 mg/kg and 250 mg/kg dose) by decreasing the activity of serum enzymes, bilirubin, cholesterol, triglycerides and lipid peroxidation while it significantly increased the reduced Glutathione levels of tissue in a dose dependant manner. The hepatoprotective and antioxidant activities of the extract have been found to be comparable to standards Silymarin and Sodium metabisulphite respectively. The hepatoprotective property was attributed to the antioxidant potential and the antioxidant principles of the plant which justifies the claim of the native practitioner that the decoction of the plant is useful in treating jaundice ^[6].

Insecticidal activity

The latex of EA contains insecticidal activity. It was tested against common and widely spread pest species of vegetables and rice and also against some of their natural enemies. These insects or pests are considered to be more resistant to synthetic insecticides. Results have revealed that the latex of EA is an effective insecticidal agent because both crude extract as well as partially purified extract caused more than 50% mortality of tested aphid populations. The observed LC₅₀ of *M. persicae* with EA latex extract (0.012%) was, however, greater than that with *Azadirachta* seed oil (0.0024%). EA latex extract was not effective against insects with thick cuticle covers. Although soft-bodied natural enemies like spiders are susceptible to the latex of EA, most common and important natural enemies like ladybird beetles are highly resistant ^[15].

Antihyperglycemic and *in silico* Aldose reductase inhibitory activity

The ethanol extract exhibited a drastic blood sugar level reduction after 1 hour of post treatment (30.11%). This effect was significant compared to standard drug Glibenclamide (23.36%). The petroleum ether extract and aqueous extract also showed a decrease in blood glucose but not in a significant manner. Whereas ethanol extract has showed significant anti-hyperglycemic activity on 8th hour of post treatment (69.22%). The level of glucose reduction at 8th hour of petroleum ether and aqueous extracts treated animals were found to be less than the reference standard, Glibenclamide (83.32% at 8th hrs). Both petroleum ether and aqueous extract both exhibited significant hypoglycemic level at 4th hour of post drug treatment 33.29% and 28.29% respectively. After fourth hour there was no significant reduction of blood glucose level was seen (38.76% and 33.82% at 8th hr). Three specific terpenoids

Antiquol A, Antiquol C, Zopolrestat, exclusively isolated from EA has been selected for aldose reductase docking studies ^[16].

Cancer

Latex of EA has inhibitory effects on several different cancer cell lines. EA induced apoptosis, which was characterized by morphological change, DNA fragmentation, increased sub-G1 population, and alterations in levels of apoptosis associated proteins. Treatment with EA increases cell death and expression levels of caspase-8, -9, and -3. EA suppressed expression of Bcl-2, increased Bax, and reduced cleavage of Bid and the translocation of t-Bid to the mitochondria and the release of cytochrome c from mitochondria. EA caused a loss of mitochondrial membrane potential and an increase in cellular reactive oxygen species (ROS). EA -induced ROS formation was suppressed by cyclosporine or allopurinol (an effective scavenger of ROS). EA also increased expression of Fas, FasL, and c-Jun N-terminal kinase (JNK), p38, and mitogen-activated protein kinase (MAPK) and decreased expression of extracellular signal-regulated kinase (ERK). Co-treatment with the JNK inhibitor SP600125 inhibited EA-induced apoptosis and the activation of caspase-8, -9, and -3. It could be hypothesised that EA causes cell death via apoptotic pathways in human cervical adenocarcinoma HeLa cells ^[17].

Anti-inflammatory and anti-arthritic activities

The anti-inflammatory and anti-arthritic potential has been associated with aqueous and alcoholic extracts of EA. It showed the presence of triterpenoids in the stem and diterpenoids in the latex. It was reported that the anti-inflammatory activity is a common property of many triterpenoids. The anti-inflammatory effects of triterpenes have been attributed to various mechanisms including inhibition of lipoxygenase and cyclooxygenase activities. Triterpenoids present in the extracts of EA might be responsible for anti-inflammatory and anti-arthritic effects ^[3].

Traditional uses of *Euphorbia antiquorum*

The literature reveals various traditional uses of *Euphorbia antiquorum* which are enlisted below:

- 1) Fresh milky juice or gum which flows from the branches is an acrid irritant applied externally to relieve warts and other cutaneous infections and also to relieve pain of gout, rheumatism and toothache.

- 2) Juice mixed with the flour of *Cicer arietinum* is administered in pills in gonorrhoea. When mixed with cantharides, it forms what is called gout-plaster, but it must be used with great caution as it is a dangerous irritant application.
- 3) Internally it is a powerful emetic and a violent purgative, even in very small quantities.
- 4) Mixed with burnt borax and common salt it is applied in painful joints swelling.
- 5) A plaster made from the root and mixed with asafoetida is applied externally to stomachs of children suffering from worms. Bark of the root is purgative and the stem in decoction is given in gout but with proper care.
- 6) When taken internally it acts as a purgative.
- 7) The stem fried, powdered and sprinkled over old ulcers promotes healing; the stem warmed and applied as a covering to whitlows or felon at the end of finger has the effect of fomentation and warm poultices rendering the nail and skin supple and favouring the formation and discharge of the matter.
- 8) Gum resin boiled in oil to form an effective application to scrofulous and other inveterate ulcer.
- 9) The drug is also used in enlargement of spleen in jaundice, leprosy and in snake bite^[18].
- 10) The entire plant parts of *Euphorbia antiquorum* have been used in the treatment of cancer. Extraction of stem cures joint pains and disorders of indigestion^[19].
- 11) *Euphorbia antiquorum* is used in wound healing^[20].
- 12) *Euphorbia antiquorum* is used as anti-microbial drug^[21].
- 13) Stem of *Euphorbia antiquorum* is used in treatment of gout^[22].
- 14) Stem of *Euphorbia antiquorum* is used as anti-hyperglycemic drug^[23].
- 15) Milk of *Euphorbia antiquorum* L. is applied on the neck and joints of the cattle to cure black quarter and also applied near the eyes of cattle to cure conjunctivitis and corneal opacity^[24].
- 16) *Euphorbia antiquorum* is used in phthisis^[25].
- 17) An herbal extract of *Euphorbia antiquorum* is used in liver cancer and colon cancer cytotoxicity^[26].
- 18) Its latex has been described as having emetic, purgative, diuretic and poisonous properties^[27].
- 19) It is used in relieving toothache and earache. It has also found uses in the treatment of nervous diseases, dropsy, palsy, deafness and amaurosis^[28].
- 20) The latex is also said to be an aphrodisiac^[29].

21) The latex is used in the preparation of surgical threads for use in the Kshara Sutra treatment, a surgical procedure of the Ayurveda for the treatment of fistula wounds [4].

The fresh stems are used in Chinese folk medicine for treatment of skin sores and scabies [11].

22) The juice of the plant is used in neuropathy, deafness and cough [9].

23) Whole part of the plant is used as anti-tussive [30].

CONCLUSION

Conventional treatment modalities are hindered by adverse effects and produce only a partial remission. Because of the limitations of the conventional treatment, there has been renewed interest in other alternative therapies with medicinal plants, which may have comparable efficacy to prescription medications while lacking their severe side effects. In recent years, medicinal plants have been significantly studied for their phytomedicinal properties which bring known and unknown medicinal virtues. Traditional uses, phytochemical screening and pharmacological activity of EA reveal it as a valuable medicinal plant with numerous medicinal properties. Many new drugs can be developed from EA to control numerous diseases with no or limited side effects. A typical research and development work findings should be carried out for the conservation of EA for their better therapeutic and commercial utilization.

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