



Review Article

THERAPEUTIC POTENTIAL OF *EUPHORBIA FUSIFORMIS* BUCH. -HAM. EX. D. DON

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ABSTRACT

Nature has gifted widest range of plant diversity to India for the welfare of mankind. Plants have been utilized for various purposes by the human beings since the time immemorial. Plants have been the basic source for therapeutic preparation in the indigenous system of medicine, the Ayurveda. With the recent changes in the life style of human being, over exploitation of natural resources has put a large number of plant species to the verge of extinction. *Euphorbia fusiformis* Buch. -Ham. ex D. Don (Euphorbiaceae), botanical source for the classical drug *Adhoguda* is one among plant species threatened with the extinction (endangered). It is a plant having potential pharmacological properties and actions. Traditionally, tribal communities have been using this plant in ethnomedicine to treat headache, arthritis, gout, paralysis, diarrhoea, abdominal diseases, abdominal tumour, liver disorders, urinary stones, chronic wounds, cracks, skin disease, eczema and poor lactation, scorpion and snake bites and plant latex as an antidote.

E. fusiformis is reported to possess variety of pharmacological activities like antioxidant, antifungal, diuretic, anti-inflammatory, antibacterial, hepatoprotective, antinociceptive and galactagogue. Also, the plant has been evaluated for its use in female infertility. Present paper is an attempt to review therapeutic potential of this underexplored drug *E. fusiformis*.

INTRODUCTION

India is very rich in plant biodiversity ranging from alpine vegetation to deep sea vegetation. A large number of plants have potential to be used for medicinal purposes. In recent past, a surge in the demand of medicines of herbal origin has been observed world over which has triggered non-judicious over exploitation of herbs from natural sources. The rich herbal resources are disappearing at an alarming rate. Therefore, the conservation of traditional medicinal plant resources has become a matter to be addressed urgently. An ever-increasing demand of medicines based on herbs is difficult to be met from natural resources without any alternative arrangement.

Therefore, along with the conservation of rare herbs, it is the high time for stressing upon the cultivation of medicinal plants^[1]. Many potential medicinal plant species are almost un-explored because of their limited geographical distribution. *Euphorbia fusiformis* Buch. -Ham. Ex D. Don (Euphorbiaceae) is one of such species.

Morphology

Euphorbia fusiformis is dwarf, glabrous herb, with stout, underground cylindrical rootstock. Leaves radical, subsessile, 9-15cm long and 2.5-5cm in diameter; generally, 1-12 in number, oblanceolate, base cuneate, margin curled. Cyathia yellow, arranged in cymes on long peduncle, arising from the rootstocks. Involucres subsessile, greenish, lobes spatulate^[2].

Geographical Distribution

Euphorbia fusiformis Buch. -Ham. ex D. Don has endemic distribution in India, Nepal China and Africa^[3,4]. In India it is limited to few localities of Uttar Pradesh, Maharashtra, Karnataka, Tamil Nadu, Nagar Haveli, Telangana, Andhra Pradesh and West Bengal.^[5] It has also been found growing in Tropical Himalayas up to 1500 feet from Garhwal to Nepal^[6,7]. It is

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reported growing in some Ranges of Dudhwa Tiger Reserve in Kheri District of Uttar Pradesh, locally known with the name of 'Banmuli' by the tribal people and used in ethnomedicine.

Synonyms of *Euphorbia Fusiformis* [8,9]

1. *Euphorbia acaulis* Roxburgh
2. *E. nana*
3. *E. humilis*
4. *E. seshachalamensis*

Varieties of *Euphorbia fusiformis*

- *Euphorbia fusiformis* var. *khandalensis*
- *Euphorbia fusiformis* var. *panchganiensis*

Vernacular Names [10,11]

Uttar Pradesh - *Banmuli*

West Bangal - *Dhudhmul*

Madhya Pradesh - *Khargoni*

Maharashtra - *Bhuiphod, Chirkandichakanda*

Gujarat - *Khurkund*

Andhra Pradesh- *Barrasapugaddalu, Palachepugaddalu*

Euphorbia Fusiformis in Classical Texts

In first chapter of *Charaka Samhitā Sutra sthāna*, Āchārya Charaka has classified drugs into three groups according to the source of origin i.e., drugs of animal origin (*Jāngama*), drugs obtained from earth (*Khanij/Bhaum*) and drugs of plant origin (*Sthāwar*). In the same context Āchārya Charaka has mentioned two groups of plant drugs viz^[12]:

1. *Mulinī*- Having roots as their therapeutically useful plant parts.
2. *Phalinī*- Having fruits as therapeutically used plant parts.

In the group of *Mulinī* drugs, Acharya Charak has mentioned sixteen plant drugs having roots as therapeutically used plant parts along with their therapeutic application for purification therapy (*Samshodhana Chikitsā*). Maximum drugs included under *Mulinī* group of drugs are either unidentified or controversial. Probable specifications of botanical sources of drugs of *Mulinī* group of drugs accepted by scholars are as under.

Therapeutic Application of the *Moolinī* Drugs

Shanpushpī, Bimbī, Hemvatī- Emesis (*Chardan/Vaman*).

Shwetā, Jyotishmatī - *Shirovirechana* (Errhine).

Rest eleven drugs including *Adhogudā* (*Euphorbia fusiformis* D. Don. syn. *E. acaulis* Roxb^[13] Euphorbiaceae) have been indicated for *Virechana* i.e., purgation^[12].

Adhogudā: Specification of Botanical Source

From the therapeutic indications, it is evident that Charaka has indicated *Adhogudā* for *Virechan* (purgation). The word "*Gudā*" is considered as

synonym of *Snuhī* [14]. Scholars of Āyurveda assumed resemblance of the *Mulinī* drug *Gudā* in morphology or therapeutic potential to that of *Snuhī*. *Snuhī* contains plenty of latex which is said to be best among drastic purgatives (CS.Su.25). Term *Adhogudā* may be literally interpreted as *Snuhī* found under the ground. Commenting on the term *Adhogudā*, Chakrapani Dutta has identified it as *Vridhdārūka*^[14] which etymologically means "it delays old age or kills the old or advancing age". This observation means that it is used as *Rasāyan* or rejuvenating agent. In some other references, it is mentioned as good aphrodisiac. Botanical source of drug has been considered to be *Ipomoea petaloidea* Choisy^[15]. Leaves of *Argeria speciosa* Linn. f. (*Vridhdārūka*) has been used in wound healing in local health traditions. Its root is used in constipation, also used as nutritious agent in Bengal. Leaves are used in rheumatic arthritis, abdominal pain, cough, ascites, headache. Morphological features of classical drug *Vridhdādaruk* have been clearly mentioned by the commentator of *Siddhamantra* in Ashtānga Sangraha. None of the classical indications of *Vridhdādaruk* establish its use as a purgative drug. Therefore, *Vridhdādarūka* can't be considered to be *Adhogudā* included in *Mulinī* drugs. Therefore, idea of Chakrapani Dutta considering *Vridhdārūka* as *Adhogudā* is not appropriate.

Tribal communities in some parts of Bihar and Uttar Pradesh, in their local health traditions use a plant in the name of *Vanamulī*. Plant belongs to family Euphorbiaceae and has plenty of latex present in all parts. Thakur Balvant Singh and Prof. K.C. Chuneekar, on the basis of field survey, have equated *Vanamulī* of tribes with *Mulinī* drug *Adhogudā* and identified it taxonomically as *Euphorbia fusiformis* Buch. -Ham.ex D.Don. Syn. *Euphorbia acaulis* Roxb.^[13] This identity has been accepted by other scholars also. Root of *Vanamulī* has latex like *Snuhī*^[14] and is used by tribal medicine men for purgation in severe constipation. Therapeutic use of *Vanamulī* by the tribe and its pharmacological properties strongly suggest that *Vanamulī* is *Adhogudā*. Tuberos root of *Adhogudā* has been reported to be used for the management of constipation by the Tharu tribe in Kheri district of U.P. and in other parts of country. The drug is also reported to be used for the management of various other ailments especially joint pain and inflammation.^[16]

Therapeutic potential of *e. Fusiformis*

Classical Indications

Acharya Charak has indicated it for purgation. Thus, *E. fusiformis* can be used in the diseases where purgation is the method adopted for purification therapy like *Pakshaghat* (paralysis), *Pandu* (anaemia), *Kamla* (jaundice), *Kustha* (skin diseases), *Unmad* (insanity), *Amlapita* (acidity), *Urdhag raktapitta*, *Tamak swash* (respiratory disorder).

Ethnomedicinal Uses

E. fusiformis has ethnomedicinal importance as it serves as a remedy for several diseases in local health traditions.

Root

- The pulp of the tuber is used for relieving pain and inflammation in arthritis.^[5]
- The rootstock paste admixed with mustard oil as the external application is the potential remedy for arthritis, paralysis and gout.^[17,18]
- Root powder is eaten to get relief from constipation.^[19]
- The root paste is given orally to animals to cure dysentery and fever for two times a day for 3 to 5 days.^[20]
- The tuberous root of this plant is used by *Bhagats* (tribal physicians) of *Dangs* Forest for the treatment of various abdominal disorders, especially for tumours of abdomen and urinary stones.^[2]
- In some region of Ramanagara district at Karnataka state *Vaidyas* use aqueous solution of tuberous root of *E. fusiformis* to increase the milk production in lactating mothers.^[4,21]
- Mustard oil cooked with *Banmūlī* alone or with *Calotropis procera* R. Br. root, pulp of *Aloe vera* Tourn. Ex.Linn., *Alium sativum* Linn., *Urginea indica* Kunth. and *Curcuma aromatica* Salisb. is used for massage in arthritis and tendonitis.^[16]
- Powder of dried *banmūlī*, honey, black chilly (*Piper nigrum* Linn.) along with mustard oil is used for massage in Rheumatoid arthritis.^[16]
- *Banmūlī* pounded with *Banpyāj* (*Urginea indica* Kunth) is applied to the joint inflammation in rheumatoid arthritis. Dressing changed after 24 hrs.^[16]
- *Banmūlī* (*E. acaulis*) (1gm approx.) with sugar (1 tsf) is given in constipation and pain abdomen with lukewarm water.^[16]

Latex

- The latex of this plant acts as an antidote and it is used to counteract the poisoning caused by snake or scorpion bites.^[22]
- It is used to treat liver disorders, diarrhoea, chronic wounds and skin diseases.^[4,22]
- It is helpful for burning off warts and eczema.^[23]

Leaves

- Paste of the leaves, when applied to the forehead, provides relief from acute headaches.^[23,24]
- The roots and leaves of this plant can be used to treat ephemeral fever.^[17,25]
- Leaf Juice is used for the treatment of burn.^[26]

Biological Activities Demonstrated

Diversified biological activities have been reported in *E. fusiformis*. Biological activities exhibited in the plant are being listed below.

General Pharmacology/Safety Profile: Analgesic, antipyretic activities and gross behavioral effects not demonstrated in experimental animals. LD₅₀ of the extract by oral route in mice 1200mg/kg.^[27]

Antioxidant Activity

- Vitamin E and Vitamin C demonstrated in *E. fusiformis* which are protecting agents against oxidative stress.^[5,28]
- Phenolic compounds present in *E. fusiformis* may have protective role against oxidative stress.^[29] DPPH free radical scavenging activity demonstrated in *E. fusiformis* tuber extracts. Free radical scavenging activities of water extract and methanol extract found to be comparable. Results of study reveal a positive relationship between phenolic compounds, flavonoids and vitamin E contents in tuber and anti-oxidant activity.^[5]
- Antioxidant activities of n-hexane, ethyl acetate extracts and different phytoconstituents demonstrated in tubers of *E. fusiformis* were demonstrated using ascorbic acid as standard drug. Ethyl acetate extract exhibited promising anti-oxidant activity. Caudicifolin, a compound isolated from tubers of *E.fusiformis* exhibited moderate antioxidant activity.^[30]
- Different leaf extracts of *E. fusiformis* demonstrated free radical scavenging activity against hydrogen peroxide radical, superoxide radical, DPPH radical, nitric oxide radical, and ferrous ion chelating activity.^[23]
- *Euphorbia fusiformis* leaf and rhizome solvent extracts (chloroform, acetone, and ethanol) exhibited strong hydroxyl radical scavenging activity strongest in ethanol extract.^[31,32]
- In a study carried out for evaluation DPPH radical scavenging activity in methanol and acetone extracts of *Euphorbia fusiformis* roots, strongest radical scavenging activity was demonstrated in acetone extract perhaps because of high concentration of phenolic compounds.^[4]

Anti-inflammatory Activity

Anti-inflammatory activity in tubers of *E. fusiformis* was evaluated using carrageenan-induced edema model in experimental animals. n-hexane fraction of tuber exhibited a dose dependent inhibition of oedema which was comparable to phenylbutazone. The activity was more profound when the drug was administered by i.p. route.^[27]

Anti-Arthritic Activity

In chronic models of formaldehyde induced and adjuvant arthritis, anti-arthritic activity of *E. fusiformis* extract was found to be superior to that of phenylbutazone.^[27]

Diuretic Activity

Diuretic activity in *E. fusiformis* root powder was evaluated in rats. Trial drug administered by oral route exhibited significant diuretic activity in terms of increased urine volume as well as urinary excretion of Sodium and potassium. The diuretic activity was evaluated in rats.^[33]

Anti-bacterial activity

Anti-bacterial activity of *Euphorbia fusiformis* tuber and leaves was investigated using disc diffusion and well-in agar methods. Tuber extracts demonstrated good anti-bacterial activity as compared to leaf extracts. Although methanol extract demonstrated strongest anti-bacterial activity against Gram positive (*Bacillus subtilis* and *Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli*, *Klebsiella pneumoniae*, *salmonella typhi* A and B) followed by acetone and chloroform extract, a broad-spectrum antibacterial activity was demonstrated in all extracts.^[34,17]

Anti-microbial Activity

Acetone, chloroform, methanol, isopropyl alcohol and water extracts of tubers of *E. fusiformis* screened for their anti-microbial potential against isolated bacterial and fungal strains. In study methanolic and aqueous extracts demonstrated moderate activity against microbial strains tested. acetone, chloroform and isopropyl alcohol (IPA) extracts demonstrated no activity against microbial strains tested.^[5]

Antifungal Activity

- Ethyl acetate extract showed significant reduction in growth of *Candida albicans* and *Aspergillus niger* comparable to fluconazole.^[30]
- Antifungal activity in tuber and Leaf extracts of *E. fusiformis* was tested against *Candida albicans*, *Cryptococcus neoformans* and *Aspergillus Niger*. Aqueous extracts devoid of antifungal activity whereas ethanolic leaf extract and chloroform extracts demonstrated strong antifungal activity against *C. neoformans* and *C. albicans*. Activity of combined extracts was found to be better against *C. albicans* than *C. neoformans*.^[35,36]

Hepatoprotective Activity

Ethanol extract of tubers of *Euphorbia fusiformis* was evaluated for hepatoprotective potential against liver damage caused by rifampicin in animal models. Ethanol extract of tubers of *Euphorbia fusiformis* demonstrated promising hepatoprotective activity by restoration of gamma-glutamyl

transpeptidase (GGTP), serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP), total bilirubin and total protein to normal levels.^[24]

Antinociceptive (Analgesic) Activity

Euphorbia fusiformis root powder was investigated for antinociceptive activity by tail flick, paw licking model (formalin-induced) and acetic acid induced writhing models. Oral administration of drug has no significant effect on acetic acid induced writhing. A significant rise in pain threshold was observed in tail-flick test. At a higher dose level, formalin induced paw licking responses were significantly inhibited.^[7,37]

Galactagogue Activity

Ethanol extract of *E. fusiformis* was evaluated for Galactagogue activity in pup and mother rats. Trial drug exhibited significant galactagogue activity measured indirectly by pup's body weight (or growth) in respect to untreated pups, bodyweight of lactating mothers remained unaltered; in mother rats, serum prolactin level, protein and glycogen concentrations in the tissues of the mammary glands was found to increase as compared to control. Mammary glands of treated rats, in histological studies, demonstrated increase in the propagation of acini and lobuloalveolar size in the duct.^[4]

Hypotensive Activity

Euphol (8, 24-euphadien-3 β -ol), isolated from *E. fusiformis*, exhibited hypotensive activity which varied from a slight to a marked degree depending upon the dose in normotensive anesthetized dogs and rats by i.v. route without any significant effect on respiration. In rats, higher dose of Euphol was required to produce hypotensive effect similar dogs. The hypotensive effect was not affected in dogs pretreated with atropine, antistine and β blockers and in bilaterally vagotomised and carotid sinus denervated animals. The fall in blood pressure was enhanced in spinal transected and eviscerated dogs and after ganglion blockade with hexamethonium. LD₅₀ was found to be 1500mg/kg i.p. in dogs and 2g/kg p.o. in mice.^[38]

Action on Female Infertility

Anti-infertility activity of *E. fusiformis* was evaluated using infertile female obese rats. Parameters selected for evaluation were number of days taken for the vaginal opening, duration of oestrus cycle, weights of reproductive organs like ovaries, uterus and length of fallopian tubes. The histopathological analysis did not show any toxicological effect in experimental animals. Results of the study revealed infertility reversing potential of *Euphorbia fusiformis* in animal models.^[39]

Effect on Intestinal Transit Time

Effect of *E. fusiformis* on intestinal transit time was evaluated in Swiss albino mice. *Euphorbia fusiformis* root powder at doses 130mg/kg and 260mg/kg powder significantly shortened the time required for expulsion of kaolin in dose-dependent manner. From the study it may be concluded that *Euphorbia fusiformis* increases intestinal motility.^[37]

Clinical Studies: Eczema

In a placebo control clinical study carried out in 38 subjects of dry and wet eczema administered with powder of *E. fusiformis* root powder, the drug was found efficacious in both dry and wet eczema with 18 subjects having complete cure, 3 subjects having 75 percent cure and 01 subject having 50 percent cure.^[38,40]

Toxicity Studies

- In acute toxicity screening, ethanolic extract of *E. fusiformis* leaves and tuber, orally in mice, produce no mortality up to 10,000mg/kg bw.^[31,41]
- In sub-chronic oral toxicity studies in rats, no changes were observed in body weight, body temperature, normal behaviour and food intake at 125, 250, and 500mg/kg bw oral dose. The ethanolic extract did not exhibit any remarkable change in haematological, biochemical and electrolyte parameter. Histological profile of liver and kidney also remained unchanged.^[24]
- In another toxicity screening study in Wistar rats, ethanolic extract of *E. fusiformis* given orally in graded fashion, i.e., lower to higher doses (100 to 2000mg/kg) for three consecutive days, no mortality or morbidity up to the dose of 2000mg/kg was observed.^[4]

Phytochemistry

E. fusiformis is known to be rich source of a variety of secondary metabolites such as terpenoids, alkaloids, flavonoids, phenols, steroids, glycosides, saponins, tannins and volatile oils. Vitamin E and vitamin C have also been reported to occur in the plant.^[5] Its rich phytochemical constitution is the factor responsible for its multidimensional biological activities.

Conservation and Domestication for Sustainable Utilization

Loss of habitat along with over-harvesting from natural resources has threatened the survival of many plant species. *E. fusiformis* is one among such plant species. For sustainable utilization of such plant species all the possible efforts must be undertaken before it is too late. *Euphorbia fusiformis* variety *panchganiensis* Blatt. & McCann, family *Euphorbiaceae* is considered as rare plant.^[42] First red list of medicinal plants of Andhra Pradesh, India considered *Euphorbia fusiformis* in Vulnerable group.^[43]

Possible Conservation Strategies

Effective conservation strategy for medicinal plants should include four main areas: in-situ conservation, ex-situ conservation, education and research.^[44]

1. **In-situ conservation:** This process is also known as on-site conservation. It's protecting the endangered species in their natural habitat by the conservation of their ecosystem and natural habitats. Its examples are natural reserves and wild nurseries. This strategy may prove effective for the conservation of genetic material of naturally growing *E. fusiformis*. Extraction of plant species from natural resources must be strictly prohibited.
2. **Ex-situ conservation:** In this process, endangered species are protected outside their natural habitat. Examples include botanical gardens and seeds banks. This may be one strategy for the conservation of *E. fusiformis* for the purpose of teaching and research.
3. **Cultivation for Conservation:** Apart from in-situ and ex-situ conservation, good agricultural practices (GAP) are another approach to conserve plant species by providing alternative source for crude drug. For improved yields and quality of target products, these practices provide the appropriate levels of water, nutrients, optional additives and environmental factors including temperature, light and humidity.^[45] Domestication of *E. fusiformis* on large scale may prove the best strategy for conservation. Modern micropropagation techniques may be adopted for better results.

CONCLUSION

Form the facts mentioned above, it may be concluded that *E. fusiformis* is an important medicinal plant with promising therapeutic potential. Main streaming this herb in therapeutics will certainly open new areas for the management of certain tough pathological conditions. There is a need of detailed clinical evaluations of therapeutic potential of the drug.

Conservational approach towards utilization of medicinal plants is the need of the day. Cultivation of medicinal plants may provide a solution to relieve stress on natural resources and meet the increasing demand of crude drugs. A concrete step needs to be taken by the governments to promote cultivation of medicinal herbs including special incentives to the farmers, establishment of supply chain for agricultural produce and a policy of minimum support price for crude herbs.

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