

Footslog of a wild weed to pharmacy-a methodical review on traditional herb *Euphorbia hirta* linn

RAMPRIYA. A. R *, ELANGO VAN. B, MOHANKUMAR. M and FATHIMA BASHEERA. M

Department of Pharmacology, Arulmigu Kalasalingam College of Pharmacy, Krishnankovil -626126, India.

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Abstract

Euphorbia hirta is a funeral herbal medicine widely used in traditional remedies for various ailments like asthma, skin diseases, hypertension, jaundice, gonorrhoea and dengue. Many researchers proposed the medicinal properties of *E. hirta* in various aspects. A detailed study shows the different pharmacological activities like anti-inflammatory, anti-biotic, anti-malarial, anti-bacterial and anti-ulcer efficacy. Previous studies showed that *Euphorbia hirta* possess the activity as like quinolone activity. Improved microcirculation and increasing capillary resistance has been achieved by the flavonoids present in this folklore herb protects gastric damage. The latex exudate has been reported for treatment of conjunctivitis as eye drops. High anti-oxidant level in this weed synergizes the therapeutic effects. This comprehensive review describes about the properties, ethno pharmacology, chemical constituents and various concepts of *E. hirta*. Furthermore, this will paves the way for accounting the study in different angles and for the development of new lead compounds with multiple pharmacological actions.

Keywords: Ruderal herb; Anti-inflammatory; Antibiotic; Flavonoids; Conjunctivitis; Dengue; Gonorrhoea

1. Introduction

In the indigenous system of medicine herbs plays effective role in controlling various diseases. Herbals are the provender for the production of more conventional drugs. The complex chemical nature of the medicinal plants is the rationale for preventive and curative nature of the diseases. In India more than 2500 species of plants were recognized for its medicinal value [1]. Some of the bright outlooks of the medicinal herbs are highly tolerable, easily approachable, economically low-cost, readily procurable, strongly potent and relatively prudent [2]. Recently, tremendous surge of engrossment in herbal medicines therapy has seen in developing and developed countries. World Health Organization predicts about more than 80% of the world population showing their interests on natural herbal source for their primary health care. The secondary metabolite of the plant restores human health and cures lots of diseases. So they were vital and immanent part in alterative medicines [3].

Euphorbiaceae is a largest family containing about 1600 species of plants. About 5% of this family is used as a folkloric medicine. Smattering species of this family has been approved by Food and Drug Administration in the countries like southwest of US and in Northern Mexico. *Euphorbia hirta* is also termed as Australian asthma herb ubiquitously used in India. It is an important herbal remedy for diverse range of diseases like asthma, dengue, malaria, jaundice and some venereal disease. This is because of the presence of intense phytochemical and nutrient constituents [4]. Flavonoids, terpenoids, tannins, saponins, amino acids and polyphenols present in this herbal plant have great biological effect in human system. Several ethnobotanical researches show the presence of anti-inflammatory, anti-malarial, anti bacterial and anti asthmatic activity of *Euphorbia hirta*. Superabundant antioxidant property shows folkloric utility for various skin diseases [5]. In the modern enlightenment *E. hirta* is one of the panacea for various diseases. This review designated

* Corresponding author: RAMPRIYA. A. R

to highlight the scientific aspects such as taxonomical, morphological, monographical, phytochemical evaluation, traditional and pharmacological effects of the plant *E. hirta*. Furthermore, it also signifies the extraction process of the plant. We hope this review will provide resourceful reference for the future research on the plant and plant based formulations [1, 3, 6].

2. *Euphorbia hirta*

2.1. Synonyms

Chamaesyce hirta linn, *E. pilulifera* linn

2.2. Vernacular names

- English – Asthma herb, snake weed
- Hindi – Dudhei
- Marathi – Govardhan
- Tamil – Ammumpatchaiyarissi
- Telugu – Nanabala
- Sanskrit - Dugadhika

2.3. Plant taxonomy

- Kingdom- Plantae
- Division – Tracheophyta
- Class – Magnoliopsida
- Suborder- Rosanae
- Order – Malphigiales
- Family – Euphorbiaceae
- Genus – *Euphorbia*
- Species – *hirta*
- Botanical name – *Euphorbia hirta*

2.4. Geographical description

Central America is the native of the medicinal plant *Euphorbia hirta* that scatter throughout the tropical parts of India, usually seen as weeds in the wayside. It often grows in the paddy fields, gardens and lowland which prefer dry and humid climatic conditions [7]. The altitude of 2200 meters from the sea level promotes the growth [8, 9].

2.5. Morphological studies

Euphorbia hirta is a slim-hairy stemmed, annual herb with numerous branches spreads up to 40 cm in height. Leaves of the plant are elliptically oblong, arranged opposite in a terrible pattern. Dark green leaves measures about 1-2.5 cm long and has purple blotches in the middle. Three celled hairy yellow fruits of about 1-2 mm diameter having creased seeds are present [1].

2.6. Histological evaluation

Histological evaluation of the leaf shows dorsiventral pattern with non prominent cuticle. Adaxial midrib measures about 300µm thick and 390µm width with thick cylindrical epidermal layer has been seen. Kranz tissue a specialized epidermal cells is seen in both leaf and stem. Lignified vascular bundles were seen in stem. Powdered microscopy intimate the presence of starch, lignified fibres, kranz tissues, pericyclic fibres and epidermal cells with trichomes. Stomatal number and index had been determined by quantitative microscopy as 16.66 and 6.391 respectively [3].

2.7. Physicochemical evaluation

Physicochemical studies results various parameters like total ash value, moisture content, sulphuric acid content and insoluble ash content. Qualitative analysis has been performed and reported the presence of phenols, tannins, saponins, flavonoids, alkaloids and proteins in the methanolic extract [10, 11].

2.8. Ethnopharmacology

Medicinal herb *E.hirta* is widely used for various diseases as different formulations like crude drug, decoction, lotion, infusion and powders. The decoction of whole plant is used for the treatment of bronchitis whereas the latex is applied for conjunctivitis. Aqueous extract shows anxiolytic, analgesic, antipyretic and anti-inflammatory effects. Methanolic extract of leaves exhibits antifungal and antibacterial properties. Cytotoxic property against human epidermoid carcinoma is observed in the methanolic extract. The decoction obtained from leaves induces the milk secretion and the virility is restored when the leaf is chewed with palm kernel. Alcoholic extract from the entire plant possess hypoglycemic activity in rats. Decoction from the root is used to treat snake bites. The crude extract has been reported to have anti-diarrheal activity mediated by calcium channel antagonist. In folklore medicine, the crude extract is used as veterinary medicine to treat esenteritis and diarrhea in pig, fish, horse, and sheep [8, 12, 13, 14, 15].

2.9. Phytochemical studies

Euphorbia hirta had reported to possess varied quantity of bioactive compounds like polyphenols, antioxidants, flavonoids, terpenoids, volatile oils and tannins [8, 16].

2.9.1. Nutritional value

The excellent nutritional source of the plant includes carbohydrate and proteins. Aspartic acid, threonine, serine glycine and some other aminoacids are rich in *Euphorbia hirta*. Fatty acids like myristic acid, palmitic acid, stearic acid, etc also abundantly in this herbal plant. Crude lipids and crude fiber are also rich in the plant. Beta carotene and vitamin-C are the anti-oxidants were present in aerial parts of the plant. Sodium, potassium, calcium, copper, iron and cobalt are the minerals (spark plugs of life) present in the aerial parts of the plant. Ubiquitously, polyphenols are the natural source of plants hence it serves as an ingredient for functional foods and for pharmaceutical utilization [4, 17, 18].

2.10. Pharmacological effects

2.10.1. Anti-infective effect

The extract of *E.hirta* possesses better anti-bacterial action against various micro organisms. The growth of *E.coli*, *S.aureus*, *P.aeruginosa*, *B.subtilis* is inhibited by the ethanolic extract whereas aqueous and chloroform inhibits Klebsiella pneumonia. This plant has been recommended for the management of burn wounds due to its wound healing property. It is highly effective against gram negative bacteria and so used to treat urinary tract infection and typhoid fever. Effective zone of inhibition is observed in dry extract. Anti-fungal activity has been reported high in leaf extract. Citronellal is responsible for anti-bacterial activity [1, 13]. A novel protein isolated from this plant shows potent anti-microbial and immuno-modulatory activity [19]. The anti-bacterial activity has been performed by comparing whole plant materials *Euphorbia hirta* and *Tephrosia purpurea* which confirms better zone of inhibition (14mm) present in *E.hirta* [11]. Extract obtained from ethanol has maximum inhibitory concentration of 31µg/ml against *Salmonella typhi* [20].

2.10.2. Anti-viral effect

Aqueous and methanolic extracts of *E.hirta* drop off the replication of most pathogenic viruses like Japanese encephalitis virus, respiratory syncytial virus, HIV, SIV, and mac 251. This is due to generous phytochemical constituents quercetin and gallic acid. This is achieved by different pathway of mechanism including DNA polymerase enzyme inhibition and inhibition of viral protein synthesis. A combination therapy including *Allium sativum*, *Zingiber officinales*, *Acalypha indica*, *Musa paradisiacal* and *Euphorbia hirta* is used in the form of paste to treat various types of Bovine papilloma viruses in cattle [21,22].

2.10.3. Anti-malarial action

Flavonol glycosides like afzelin, quercitrin and myricitrin shows inhibition of *Plasmodium falciparum* proliferation that reveals anti-malarial activity at a dose range of 5µg/ml. It is effective against dengue by significantly increasing the platelet count and inhibits the virus serotype DENV-2. Anti-malarial activity is due to the presence of saponins. Essential oil present in the plant is used as a mosquito repellent. As a supportive therapy in case of dengue it increases platelet count by restoring of platelet from the spleen. It also has the ability to increase the platelet count in case of dengue patients at an age group 30-55 and alleviate flu-like symptoms. Simultaneously, the hemostatic effect of *Euphorbia hirta* prudently manages the dengue symptoms [12, 13, 20, 23].

2.10.4. Anti-ulcer activity

Methanolic extract of *Euphorbia* combined with honey shows anti-ulcer activity and also increases the mucus secretion in the stomach. It has better gastro-protective and anti-secretory action synergized with honey. It shows decreased gastrointestinal motility in rats induced diarrhea using castor oil. The phytochemicals in this folklore herb has ulcer wound healing activity. Gastro-protective and gastro-therapeutic activity is achieved by inducing prostaglandin bicarbonate and mucus secretion over the gastric mucosa [2, 13].

2.10.5. Anti-inflammatory activity

Ethanol decoction shows maximum anti-inflammatory action in rats induced edema using carrageenan. This effect is due to the presence of flavonoids, quercitrin and myricitrin. Selectively it inhibits Nitric oxide and so used to treat arthritis for reducing inflammation. Studies on inflammatory markers like serum tumor necrosis factor (TNF- α) and interleukin-6 has been reduced in neonatal asthmatic rats treated with *E.hirta* [7, 8, 24].

2.10.6. Diuretic activity

The aqueous extract of *Euphorbia hirta* significantly increases the urine output in rats. Aqueous extract enhances the excretion of Na^+ , K^+ and HCO_3^- whereas ethanolic extract increases HCO_3^- only. This shows that the mechanism of diuresis is that of standard drug Acetazolamide [13].

2.10.7. Anti-diarrheal activity

High concentration of quercetin in the crude plant is reported to have 70% of protective action against castor oil and PGE2- induced diarrhea in rats. This effect is mediated via calcium antagonistic mechanism [15].

2.10.8. Anti-gout activity

Flavonoids and phenolic compounds present in this herb shows xanthine oxidase (XO) inhibitory mechanism has significantly used to treat gout [18].

2.10.9. Anti-asthmatic activity

Effect of *Euphorbia hirta* against asthmatic rats shows curative property. Ultimately it reduces the levels of WBC's (neutrophils, basophils and eosinophils) that are increased as a result of inflammatory response. Furthermore, review shows that it acts on the dense fibrin network and render it into a fragile form. It is reported as a bronchial tubes relaxant property due to the presence of the flavonoid and Quercitrin [25].

2.10.10. Anti-oxidant property

Ethyl acetate extract of *E.hirta* has strongest free radical scavenging and antioxidant effect. Phenolic acids present in *E.hirta* shows free radical scavenging property experimentally reported by various in vitro like ABTS, DPPH and hydroxyl radical scavenging assay. Significant reduction of the oxidation marker malondialdehyde (MDA), whereas elevated levels of enzymes such as glutathione (GSH), superoxide dismutase (SOD), catalase, glutathione peroxide (Gpx), and acetylcholinesterase (AChE) were observed spectrophotometrically [24, 26, 27].

2.10.11. Anti-cancer activity

The flavonol glycosides namely Afzelin, Quercitrin and Myricitrin from the methanol decoction of the leaves has been reported to have cytotoxic activity against human epidermoid carcinoma KB 3-1 cells. Furthermore, the methanolic decoction from leaves shows reduced proliferation of Hep-2 human epithelioma of larynx. Concurrently, the solid tumour mass is reduced in EF-treated tumor induced animals. Evidently, it is proved that the polyhydroxy triterpenoids (25-hydroperoxycycloart-23-en-3 β -ol) in the plant shows cytotoxic effect in human cancer cells. The latex obtained from *E.hirta* had been used to treat warts that is recently associated with cancer and immuno suppressing condition [16, 22, 28]

2.10.12. Anti-venom effect

The methanolic extract of the plant contains Ellagic acid, quinic acid and gallic acid that are major phenolic acids sources shows the effect of inhibition in venom proteases. Prevention of hemolysis was observed in the venomous rat treated with the plant extract. Significantly, zero death rates have been observed in the group treated with herbal extract [6, 27].

2.11. Toxicological studies

The aqueous extract of *E.hirta* shows slight toxic effect in reproductive system of male rats by retrogression and reducing the mean diameter of seminiferous tubules. The Shrimp lethality assay results the toxic level LC₅₀ values almost 1mg/ml and so great vigilance should be taken while administering the herbal drug. It is possibly unsafe for pregnant and lactating condition as it might cause contraction of uterus [8, 29]. Overdose of *E.hirta* shows increased biochemical factors (ALT, AST, BUN, total bilirubin and creatinine) levels in rats. Deleterious effect on grazing rats shows the source for toxicosis. *Allium cepa* test shows genitor-toxic and mitodepression effect of *E.hirta* in the methanolic extract [7, 30]. Histo-pathological report shows Damage of murine liver, kidney and aorta has been reported with increased biomarkers [ALT & AST] level at toxic dose. Crude extract shows more toxic in kidney cell lines of monkey [31, 32].



Figure 1 Roadside weed- *Euphorbia hirta*

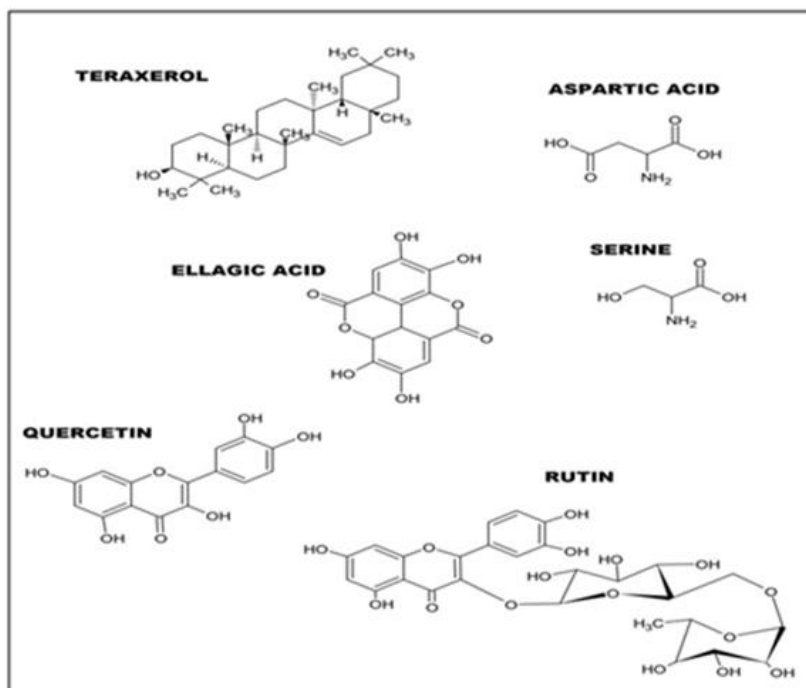


Figure 2 Structure of the Phytochemical constituents

Table 1 Chemical Classification of the Phytoconstituents [38,39]

S.no	Chemical class	Active constituents
1	Flavonoids	Quercetin Quercitrin Quercitol Rutin Kaempferol
2	Terpenoids	α - Amyrin β - Amyrin Friedelin Teraxerol
3	Tannins	Euphorbins A,B,C,E Terchebin
4	Essential oils	Hexaecanal Phytol n-Hexadecanoic acid
5	Amino Acids	Aspartic acid Therionine Serine Glutamic acid Glycine Alanine Valine
6	Acids	Ellagic acid Gallic acid Tannic acid Maleic acid Tartaric acid
7	Other compounds	Alkaloids Saponins Minerals

Table 2 Preliminary Phytochemical screening of *Euphorbia hirta* in various solvents

PHYTO CONSTITUENTS	DP	AQ	ETH	P.ETH	MET	CHCL ₃	REF
Sterols	+++	+++	+++	+++	+++	+++	[33,34,35,39]
Terpenoids	+++	+++	+++	-	+++	+++	
Carbohydrates	-	+++	-	+++	-	+++	
Proteins/Amino acid	+++	+++	-	-	-	-	
Flavonoids	+++	+++	+++	+++	+++	+++	
Saponins	+++	+++	+++	+++	+++	-	
Alkaloids	+++	+++	+++	-	+++	+++	
Cardiac Glycosides	+++	+++	+++	+++	+++	+++	
Tannins	+++	+++	+++	+++	+++	+++	
Resins	-	-	+++	-	+++	-	
Coumarins	-	-	+++	-	+++	-	
Anthraquinones	+++	-	-	-	-	-	

DP- Drug Powder; AQ-Aqueous; ETH-Ethanol; P.ETH-Petroleum Ether; CHCL₃-Chloroform;

Table 3 *In-vitro* parameters of *Euphorbia hirta*

S.NO	PARAMETERS	ME.OH	ET.OH	PET. ETHER	CHCL ₃	AQUEOUS	REF
1.	Extractability (%)	12.2	11.2	3.2	2.43	16.6	[31]
2.	Thrombolytic percent (Mean ±SD)	-	25.81 ±4.22	-	-	30.48 ±5.51	[36]
3.	Zone of inhibition(mm) Anti-diarrheal property	<i>E. coli</i>	17	-	-	18	-
		<i>S. aureus</i>	18	-	15	14	-
		<i>S. typhii</i>	-	-	-	-	-

3. Conclusion

Proteins isolated from *E.hirta* shows anti-fungal activity against non dermatophytic molds and also exhibit strong immune-modulatory effect. Optimized phytochemicals of the plant evidently shows Anti-gout and Anti-inflammatory properties by inhibiting inflammatory mediators like IL-1 β and TNF- α . Due to its action as free radicals scavenging, the proteins hydrolysed from *E.hirta* show excellent selectivity for chemotherapeutic against cell lines of gastric cancer. This weed is an excellent phytochemical source for increasing the milk secretion in rats and thus it has traditionally been used to treat insufficient milk production. Preliminary phytochemical evaluation shows wide range of chemical constituents present in this plant possess thrombolytic activity as like Streptokinase. This clinically proven thrombolytic activity hikes the weed to pharmacy level. In Cosmeceuticals, the serum prepared from the ethanolic extract of *E.hirta* is used to treat skin Acnes because of its Anti-bacterial activity against *Propionibacterium acnes*. Methanolic extract of *Euphorbia hirta* shows hermetic Anxiolytic and sedative property by acting on GABA and Dopaminergic receptors. The rich source of flavonoids in this herb produces ant-hypertensive activity and anti-oxidant property. This study may drive my research to a patentable formulation in future.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors state that this review was conducted without any conflict of interest.

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