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Pharmacological actions of *Euphorbia hirta*: A review

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Abstract
Euphorbiaceae is the family of Euphordia hirta. It is istributed throughout the indo-pak subcontinent, often found in waste places along the roadsides. The plant parts are widely used in traditional system of medicines, in the treatment of respiratory diseases, gastrointestinal disorders, wound healing, pulmonary disorders, urinogenital disorders, tumors, lactation in women etc. The plant has also been used as anti-inflammatory, antioxidant, antitumour, antidiabetic and free radical scavenging, anti allergic, analgesic and antianaphylactic, antioxytic, sedative, antiarthritic, antidiarrhoeal, spasmogenic, antithrombocytopenic, diuretic, GI tract, burn wound healing, immune stimulatory, sperm motility, genotoxic, synergic, antiviral, antihelmentic, immunoprohylatic, antimalarial, antimicrobial, herbicidal, antimolluscidal, larvicidal property and so on. In this report we explore investigations related to taxonomy, monographs, distribution, morphology, phytochemistry, traditional uses and pharmacological uses of the plant.

Keywords: Traditional uses, *euphorbia hirta* L, pharmacology, phytochemistry

Introduction

Taxonomy

Kingdom – Plantae
Subkingdom – Viridaeplantae
Infrakingdom – Straptophyta
Division – Tracheophyta
Subdivision – Spermatophytina
Infradivision – Angiosperms
Class – Magnoliopsida
Superorder – Rosanae
Order – Malpighiales
Family – Euphorbiaceae
Genus – Euphorbia
Species – hirta

Synonyms

Chamaesyce hirta (L) Millspaugh, *Euphorbia pilulifera* Linn.
English – Asthuma weed
Sanskrit – Dugdhika, Kshirini, Ksheerani, Svaduparni
Hindi - Dudhi
Telugu – Reddinanabrolu
Tamil – Amampatcharishi
Gujarat – Dudeli
Malayalam – Chittirappula, Nelapalai
Bengali – Barokheruie
Marathi – Dudhi, Mothidudhi
Malaysia – Ambin Jantin
Indonesia – Daun Biji Kcang
Philippines – Botobotonis
Thailand – Nam Nom Raatchasee
Sundanese – Nanangkaan, Nangkaan Javanese – Gelang Susu, Gendong Anak, Kukon-Kukon, Patican. *Euphorbia hirta* is commonly called as Australian asthuma herb,

Queensland asthuma weed, Pills bearing spurge, Cats hair, Hairy spruge, Spurge or milkweed, Garden spurge [1].

Morphology

The plant Dudhia/ *Euphorbia hirta* is a small annual herb, frequently seen occupying open waste spaces, roadsides, grasslands, pathways, rice field and as a weed of cultivation. The plant is a common herb, found in pan-tropic , partly subtropic areas and worldwide including Australia, Western Australia, Northern Australia, Northern territory, Queensland, New south wales, Central America, Africa, Indomalaysia, Philippines, China and India. It is native to Central America. It is usually erect, grows upto a height of 40cm tall and it can also be seen lying down [2]. The stem is slender, reddish in colour, covered with yellowish bristly hairs especially in young parts. Leaves – simple, arranged oppositely, distichous, leaf blades are lanceolate, unequal base, cuneate one side, round otherside, acute apex, finally toothed margins, dark green above, pale beneath, purple bloth in middle, measures about 1-2.5 cm long. Flower sunisexual, male flowers are sessile, linear bracteoles, fringed, single stamen, with absent perianth. Female flowers are short pedical, rimmed perianth, superior ovary, three-celled, three styles, minute, covered with short hairs, two-fid apex. Inflorescence – cluster of flowers called cyathium at terminal or auxillary. Several cyathia densely clustered into a cyme. Fruits – yellow, three lobed, three – seeded, keeled capsules, containing three brown, four- sided, angular, wrinkled seeds, base truncate, hairy, 1-2mm in diameter [2, 3, 4]. Seeds- oblong, four – sided, slightly wrinkled, pinkish brown, caruncle absent.

Fig 1

Chemical constituents

E. hirta has been studied by various workers and a number of active constituents have been isolated. Afzelin (I), quercitrin (II), and myricitrin (III) have been isolated from the methanolic extract of *E. hirta*. [5] The chemical investigation of *E. hirta* has led to the isolation of rutin (IV), quercitin (V), euphorbin-A (VI), euphorbin-B (VII), euphorbin-C (VIII), euphorbin-D (IX), 2, 4, 6-tri-*O*-galloyl-β-d-glucose, 1, 3, 4, 6-tetra-*O*-galloyl-β-d-glucose, kaempferol, gallic acid, and protocatechuic acid. [6, 7] *E. hirta* also contains β-amyrin, 24-methylenecycloartenol, β-sitosterol, heptacosane, *n*onacosane, [8] shikmic acid, tinyatoxin, choline, camphol, and quercitol derivatives containing rhamnose and chtolphenolic acid [9].

Traditional Uses

Plant is employed to cure several indications: gastro intestinal disorders (diarrhea, dysentery, intestinal parasitosis, bowel complaints, digestive problems), respiratory diseases (cough, cold, asthma, bronchitis, hay fever, emphysema), [10, 11] urinary apparatus (diuretic, kidney stones), genital apparatus (metrorrhagic, agalactosis, gonorrhoea, urethritis), various ocular ailments (conjunctivitis, corneal ulcer), [12, 13, 14] skin and mucous membranes problems (guinea worm, scabies, tinea, trush, aphtha) and tumour. In south india, it is used as ear drops, in the treatment of boils, score and wounds. [15] The latex of the plant is often used as warts and cuts to prevent pathogen infection. A decoction of leaves induces milk flow and the leaf chewed with palm kernel for restoration of virility. It is also effective in treating ulcers. The plant is also eaten as vegetables [16].

Pharmacological activity

Anti-inflammatory activity

Mei-Fen Shih *et al*., 2010 studied anti-inflammatory effect of ethanol extract of *Euphorbia hirta* (Eh) and active component β-amyrin against lipopolysaccharide (LPS) – activated macrophage cells (RAW 264.7). The extract and active component inhibited nitric oxide (NO) production and iNOS gene expression. Therefore, *Euphorbia hirta* and β-amyrin had potential arthritis inflammation treatment [17].

Mariano Martinez-Vazquez *et al*., 1999 isolated and identified triterpenes like β-amyrin, 24-methyl encycloartenol and β-sitosterol from n-hexane extract of *Euphorbia hirta*. The nhexane extract and triterpenes were evaluated for anti-inflammatory effects in mice. Both extracts and triterpenes exerted significant anti-inflammatory effects in TPA-induced ear model. The result also showed that dual and triplet combinations exerted higher activity than triterpene alone [18].

Anti-oxidation activity

Kumar *et al*., 2010 carried out antidiabetic and antioxidant effect in mice. The flower extracts, ethanol (250mg/kg) and petroleum ether (500mg/kg) of *Euphorbia hirta* were orally tested for 21 days alloxan induced diabetic mice. The serum cholesterol, triglycerides, creatinine, urea, alkaline phosphatase levels were reduced significantly. High density lipoprotein and total proteins were increased after treatments. The antioxidant assays of all extracts showed antioxidant activity. *Euphorbia hirta* flower extract posses both antidiabetic and antioxidant activity [19]. Abu Arra Basma *et al*., 2011 reported antioxidant activity of *Euphorbia hirta*. Methanol extract of four different parts of

plants, leaves, stems, roots and flowers were tested for invitro antioxidant activity. The IC50 for leaves, flowers, roots, stems and BHT were 0.803, 0.972, 0.989, 1.358 and 0.794 mg/ml. Butylated hydroxy toluene (BHT) acts as a standard. Leaves extract had highest total phenolic content, total flavonoid content, followed by flowers, roots and stem extracts. Phytochemical screening of *Euphorbia hirta* leaf methanol extract revealed the presence of reducing sugars, terpenoids, alkaloids, steroids, tannins, flavonoids and phenolic compounds. Based on data, it was suggested that *Euphorbia hirta* had a strong antioxidant activity [20].

Anti-tumour activity

Shao-Ming Chi *et al*., 2012 isolated a new cylclopentanone derivative (1'R,5'R)-5-(5'-carboxylmethyl-2'-oxocyclopentyl)-3Z-pentenyl acetate from *Euphorbia hirta*. Based on spectroscopic analysis 1D and 2D NMR the structure was elucidated. The cytotoxicity of ethanol extract was evaluated against K562 (human leukemia) and A549 (lung cancer) cell lines. From the data, the ethanol extract exhibited a weak activity against A549 cells (inhibition ratio 15.02 ± 11.60%) and inactive against K562cells [21].

Anti diabetic and free radical scavenging activity

Goldie Uppal *et al*., 2012 discussed anti-diabetic activity. The ethanol extract of *Euphorbia hirta Linn* was tested using animal screening models. Alloxan administered for 21 days, to induce diabetics. The ethanol extract showed a significant decreased blood glucose level (hypoglycemic effect) on alloxan-induced diabetic rats [22].

Invivo and invitro study of antidiabetic activity was done by Widharna *et al*., 2010. From the in vitro experiment, ethanol extract and ethylacetate fractions had α-glucosidase inhibition activity, while n-hexane, chloroform, butanol and water fractions had no α-glucosidase inhibitory effect. In vivo test, also had the same result. Based on in vitro and in vivo test, *Euphorbia hirta* L. ethanolic extract and ethylacetate extract exerted anti-diabetic mechanism and α-glucosidase inhibitory property [23].

Anti allergic activity

Singh *et al*., 2006 described a antiallergic reactions. 95% ethanolic extract prepared from whole aerial parts of *Euphorbia hirta* (EH A001). EH A001 significantly inhibited rat peritoneal mast cell degranulation triggered by compound 48/80, dextran-induced rat paw edema. It prevented eosinophil accumulation and eosinophil peroxidase activity and reduced the protein content in bronchoalveolar lavage fluid (BALF). Extract suppressed the CD4/CD8 ratio in peripheral blood. It also attenuated interleukin-4(IL-4) release and augmented interleukin –ϒ (IFN- ϒ) in ovalbumin-sensitized mouse splenocytes. The results of these findings compared with ketotifen, cetirizine and cyclophosphamide, known compounds and it proved that *Euphorbia hirta* possessed significant activity to prevent early and late phase allergic reactions [24].

Analgesic and anti anaphylactic activity

Euhorbia hirta ethanol extract (EH A001) administered orally (100 to 1000mg/kg) against compound 48/80 induced systemic anaphylaxis. The data showed that EH A001 inhibited passive cutaneous anaphylaxis (PCA) in rat and active paw anaphylaxis in mice. The result also showed a suppressive effect on TNF-α and IL-6 release from anti-DNP-HSA activated rat peritoneal mast cells. Thus, Youssouf *et al*., 2007 proved anti-anaphylactic effect of *Euphorbia hirta* [25].

Antioxytic and sedative

Anuradha *et al*., 2008 studied anxiolytic effect of hydroalcoholic extract of euphorbia hirta. Chronic immobilization (CIS) and forced swim stress (FSS) induced stress in rats. Eh (200mg/kg p.o) for seven days showed a marked anti-anxiety activity in CIS and a partially decreased activity in FSS. Cotreatment of rats with flumazenil (0.5mg/kg i.p), bicuculline (1mg/kg i.p) resulted in a significant reduction in anxiolytic effect of Eh.this indicates that anxiolytic activity are medicated through GABAA receptor, benzodiazepine receptor, Clchannel complex. Thus, result indicate that Eh acts as a potential anxiolytic drug, which might be beneficial in treatment of stress induced anxiety disorders. Marie-Claire Lanhers *et al*., 1990 found behaviroal effects of *Euphorbia hirta* L. in mice. Lyophilised aqueous extract does not show any mortality when administered i.p. and orally. Decrease and increased behavioural parameters were measured by a activitest and staircase test at a high (100mg of dried whole plant / kg) and lowest dose (12.5 and 25mg of dried whole plant/ kg). These findings support traditional use of *Euphorbia hirta* as a sedative and anxiolytic property [26].

Antiarthritic activity

Sheikh Fayaz Ahmed *et al*., 2012 investigated antiarthritic activity in animal model. Adjuvant arthritis induced by subplantar injection of 0.05ml freshly prepared suspension (5.0mg/ml) of steam killed *mycobacterium tuberculli* in liquid paraffin. Different doses 25, 50, 100 and 200mg/kg of ethanol extract were used for treatment. According to result, *Euphorbia hirta* significantly reduced IL-1β, TNF-α, IL-2 and IFN-ϒ in splenocytes of arthritic rats and down-regulated lipopolysaccharide (LPS)-induced nitric oxide production in peritoneal macrophages. These results suggest that *Euphorbia hirta* exhibits an improved adjuvantinduced arthritis [27].

Antidiarrhoeal and Spasmogenic activity

Kamgang *et al*., 2001 discussed the contractile activity of total aqueous extract of *Mallotus oppositifolium (MO)* and *Euphorbia hirta* (Eh) leaves in rat. *Mallotus oppositifolium* (1.32mg/ml) inhibited the stimulation of rat ileal contractions by acetylcholine (–9mm) and potassium chloride (–7mm) and also reduced faecal quantity (–11g, p<1%). *Euphorbia hirta* activated the stimulation of rat ileal contractions by acetylcholine (+148%) and potassium chloride (+381%).Eh aqueous extract also reduced the faeces quantity (–12g, p<5%). The result conformed that total aqueous extracts of *Mallotus oppositifolium* had antispasmodic effect, while *Euhorbia hirta* had spasmogenic effect in vitro and antidiarrhoeic effects in vivo [28].

Diuretic effect

Johnson *et al*., 1999 studied diuretic activity of *Euphorbia hirta* leaf extracts in rats using acetazolamide and furosemide, a standard diuretic drugs. A time – depended increase in urine output was observed with water and ethanol extracts (50 and 100mg/kg). From the result it was found that water extract increased the urine excretion of Na+, K+ and HCO3- and urine output as like

acetozolamide. Ethanol extract increased the excretion of HCO3-, decreased the loss of K+ and a little effect on Na+ removal. The standard drug, furosamide increased renal excretion of Na+ and Cl- but had no effect on K+ and HCO3- loss. Active component in aqueous extract of *Euphorbia hirta* had similar diuretic effect as acetazolamide, a standarad drug. These result, support traditional use of *Euphorbia hirta* as a diuretic agent by Swahilis and sukumus [29].

GI tract

Hore *et al*., 2006 studied gastrointestinal motility in rats and mice. Findings reported that aqueous leaf extract significantly and dose-dependently decreased gastrointestinal motility in rats and Castrol oil-induced diarrhoea in mice. These findings supported the traditional use of *Euphorbia hirta* in diarrhoea [30].

Sperm motility

Oyeyemi *et al*., 2009 utilized sexually mautured and healthy west African Dwarf (WAD) rams. The rams aged between 24 and 30 months were used for study. Experimental animals were orally dosed with 400mg/kg body weight for 14days. Semen samples were collected after a day and seven days after administration. Semen picture showed a significant reduction ($p<0.05$) of sperm motility from 80% to 47.5% and live – dead ratio from 90.75% to 32.5%. This result indicates that fertilization capacity and livability of spermatozoa were negatively affected. But no significant difference in values of body parameters. Thus *Euphorbia hirta* was not recommended for medicinal purpose in male animals [31].

Effect on CNS

Lanhers *et al*., 1996 evaluated lyophilized aqueous extract of *Euphorbia hirta* L. (Eh) for benzodiazepine-like properties, hypnotic, neuroleptic and antidepressant properties. The result showed that aqueous extract does not seem to possess benzodiazepine like properties hypnotic, neuroleptic effect. The plant extract caused a direct action on central nervous system and a slight depressant effect [32].

Effect on asthuma

Pretorius *et al*., 2007 made a comparative ultrastrctural analysis of platelets and fibrin networks using *murine Balb/c* asthma model. Ultrastrcture of fibrin networks and platelets of control compared with asthmatic mice, treated with two concentrations of hydrocortisone and one concentration of plant material. Control mice possess major, thick fibers and minor, thin fibres and tight round platelet aggregates with pseudopodia formation. Asthmatic mice have major fibers covered with a net like minor fibers and a loosely connected, granular aggregates of platelets. Hydrocortisone of both concentrations made the fibrin more fragile and more granular platelet aggregate, where as *Euphorbia hirta* have no impact on fragility of fibrin and prevented the minor fibers to form a dense netlike layer over the major fibers [33].

Toxicity

Sandeep *et al*., 2011 determined LC50 using shrimp lethality assay. Extracts of *Euphorbia hirta Linn* and *Euphorbia nerifolia Linn* were selected for brine shrimp lethality activity.

LC50 of ethylacetate, acetone extract of *Euphorbia hirta* and methanol extract of *Euphorbia nerifolia Linn* were found to be 71.15, 92.15 and 49.55µg/ml respectively. Among these two plants, the most active extract was methanol extract of *Euphorbia nerifolia* Linn. [34] Ram P. Yadav *et al*., 2011 studied the efficacy of binary and tertiary combinations of *Euphorbia hirta* latex powder with other active compounds like rutin, ellagic acids, teraxerol and betulin. Toxic effect of *Euphorbia hirta* latex and active compounds were evaluated against fresh water snails *Lymnaea* (Radux) *acuminate* and *Indoplanorbis exustus* in pond. Along with snails, fresh water fish *channa punctatus* (Bloch) was also lethal to high dose, while LC90 does not have apparent killing properties in fish populations [35].

Anti-bacterial / Anti-fungal activity

Chinwe *et al*., 2012 isolated Gram-positive *staphylococcus aureus*, and Gram negative *Escherichia coli*, *Salmonella typhi*, from degenerated wound, stool and a high vaginal swab. Total dehydrogenase activity assayed using 2,3,5-triphenyl tetrazolium chloride(TTC), ethanolic *Euphorbia hyssopifolia* and *Euphorbia hirta* inhibitory activity compared with standard antibiotics ciprofloxacin and gentamycin. A dose -depended inhibition was observed. *Euphorbia hyssopifolia* effective against gram-positive *staphylococcus aureus*, than gram-negative *salmonella typhi* and *Escherichia coli*. *Euphorbia hirta* effective against Gram-negative salmonella typhi and Escherichia coli, but not effective against *staphylococcus aureus*. Hence, *Euphorbia hirta* can be implicated against typhoid fever and urinary tract infections [36].

Kareem Kehinde Titilope *et al*., 2012 reported the antibacterial activity of dry and fresh leaf extracts (ethanol and water) against some pathogens, *Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa, Staphylococcus aureus, Slamonella typhi* and *Shigella dysenteriae*. Antibacterial sensitivity test indicated that *Euphorbia hirta* extracts had little or no zone of inhibition against *Haemophilus influenzae*. Hence, dry extract produced highest zone of inhibition on all pathogens than fresh extracts [37].

Conclusion

E. hirta is a popular herb among practitioners of traditional herb medicine in China and other counties and areas, such as Africa, India, Bangladesh, Phlippines, Australia, and Cambodia. It has long been used as a decoction or infusion for the treatment of various ailments, particularly intestinal disorders, diarrhea, amoebic dysentery, peptic ulcers, asthma, bronchitis, and skin diseases in China. However, in Australia, one of the most popular uses of *E. hirta* is for the treatment of hypertension. Thus, bioassay-guided isolation and identification of the bioactive components must be developed to reveal the structure-activity relationship of these active components. Several parts of the plant have interesting antidiabetic, anti-tumor, anti-oxidant and antimicrobial properties. Consequently, further studies on this plant should be considered by researchers in phytochemistry and pharmacology in discovering newer and potential bioactive compounds such as antidiabetic, antioxidants and anticancers.

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