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EUPHORBIA HIRTA LINN - A REVIEW ON TRADITIONAL USES, PHYTOCHEMISTRY AND PHARMACOLOGY

Asha.S[1], Deevika.B[2], Mohamad Sadiq.A[3*]

[1]Department of Biochemistry, D.K.M. College For Women, Sainathapuram, Vellore, Vellore DT, Tamilnadu-632001.

[2]Department of Biochemistry, Indo-American college, Vallarpuram, Cheyyar, Tiruvannamalai DT, Tamilnadu-604407.

[3]Department of Biochemistry, Adhiparasakthi College Of Arts and Science, G.B.Nagar, Kalavai, Vellore DT, Tamilnadu-632506.

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***Correspondence for Author**
A. Mohamad Sadiq
Principal, Adhiparasakthi College of Arts and Science,G.B.Nagar, Kalavai, Vellore DT, Tamilnadu - 632506.

ABSTRACT

Euphorbia hirta Linn. is a small herb, belongs to family Euphorbiaceae , distributed throughout the hotter part of India, 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.

KEY WORDS: *Euphorbia hirta L*, traditional uses, phytochemistry, pharmacology.

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.

Monographs

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 *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. Flowers- unisexual, 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.[3,4,5] Seeds- oblong, four – sided, slightly wrinkled, pinkish brown, caruncle absent.

PHYTOCHEMISTRY

Euphorbia hirta contains flavonoids, terpenoids, phenols, essential oil and other compounds.

Flavonoids:- Quercetin, quercitrin, quercitol and derivatives containing rhamnose, quercetin-rhamnoside, a chlorophenolic acid, rutin, leucocyanidin, leucocyanidol, myricitrin, cyaniding 3,5-diglucoside, pelargonium 3,5-digucoside and camphol, flavonol glycoside xanthrhamnin, hentriacontane , myricyl alcohol, inositol, tetraxerol, friedelin, β-sitosterol, ellagic acid, kaempferol.

Terpenoids:- Titerpenoids, α-amyrin, β-amyrin, friedelin, teraxerol, and its esters-taraxerone, 11α, 12α-oxidoteraxerol, cycloartenol, 24-methylene-cycloartenol, euphorbol hexacosonate. Diterpene esters of phorbol type and ingenol type including 12-deoxy phorbol-13-

dodecanoate – 20-acetate, 12-deoxy phorbol -13-phenyl acetate-20-acetate, ingenol triacetate, higly toxic tinyatoxin, a resiniferonol derivative. 2-beta, 16-α, 19- trihydroxy – ent-kaurane, 16-alpha, 19-dihydroxy-ent-kaurene. Other isolated terpenoids are sterols, including β-sitosterol, campestrol, cholesterol and stigmasterol.

Tannins:- Dimeric hydrolysable dehydro ellagic tannins, euphorbins A, B, C, E and terchebin, the monomeric hydrolysable tannins geraniin, 2,4,6-tri-o-galloyl-β-D-glucose and 1,2,3,4,6-penta-O-galloyl-β-D-glucose and the esters 5-O-caffeoyl quinic acid (neo chlorogenic acid), 3,4 –di-o-galloyl quinic acid and benzyl gallate.

Acids:- Ellagic, gallic, tannins, maleic and tartaric acids.

Essential oil:- Major constituents include 3,7,11,15-tetra methyl-2-hexadecon-1-ol, 6,10,14-trimethyl-2-pentadecanone,hexaecanal, phytol and n-hexadecanoic acid. Minor constituents include 2-butoxyethanol, tetradecane, phtalic acid, butyl tetradecyl ester, oleic acid, 13-hepta decyl-1-ol, 2-methyl-1-hexadecanol and 1,2 – benzene dicarboxylic acid diisocylester.

Other compounds:- Alkaloids, saponins, amino acid and mineral. Two new compounds n-butyl-1-0-L-rhamno pyranoside and n-butyl-1-0-L-rhamnopyranoside.

TRADITIONAL USES

Traditionally, 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), [6,7] urinary apparatus (diuretic, kidney stones), genital apparatus (metrorrhagic , agalactosis, gonorrhoea, urethritis), various ocular ailments (conjunctivitis, corneal ulcer), [8,9,10] 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. [11] 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.[12]

PHARMACOLOGICAL ACTIVITY

Wu yi et al., 2012 investigated chemical constituents from aerial part of *Euphorbia hirta Linn*. These chemical constituents were isolated , purified by chromatographic techniques and structural elucidation based on spectroscopic analysis. Nine compounds were isolated and

identified. The nine compounds were scopoletin (1), scoparone (2), isoscopoletin (3), quercetin (4), isorhamnetin (5), pinocembrin (6), kaempferol (4), luteolin (8), gallic acid (9). Among these compounds 1-3, 5-8 were identified for the first time from this plant.[13] Abha Singh et al., 2012 isolated , screened and characterised a bacterial strain from rhizospheric soil of *Euphorbia hirta*. The strain was screened as a gram positive motile rod bacteria with terminal spore. It showed >98% similarity with reference strains in Gen bank. The 16srRNA gene sequence construction identified the strain as *Bacillus subtilis KC3*. The maximum enzyme production was achieved after 48h (22.92U/ml at 40^0c at P^H 7. The optimum temperature and pH for enzyme activity were 50^0c and 6.5 respectively. Barley starch (27.27 U/ml), corn starch (24.30 U/ml) and maltose (19.10 U/ml) were the inducers for α-amylase production. Glucose (5.45 U/ml) acts as a repressor for α-amylase synthesis. These properties suggest that *Bacillus subtilis KC3*, could be commercially exploited for production of α-amylase in starch and various biotechnological processes.[14]

Girijesh kumar patel et al., 2012 purified a 34 KDa serine protease , hirtin, with fibronolytic activity by combination of ion exchange and gel filteration chromatography. YAVYIGLILETAA/NNE found at N-terminal sequence of hirtin. Hirtin contains esterase and amidase activities along with azocaseinolytic, gelatinolytic, fibrinogenolytic and fibrinolytic activities. For enzyme activity, the optimum pH and temperature was found to be 7.2 and 50^0c. Enzyme activity was significantly inhibited by PMSF and AEBSF. The specific synthetic substrate for hirtin was P-tos-GPRNA. Hirtin hydrolysed Aα and α-chains, followed by Bβ and β, and ϒ and ϒ-ϒ chains of fibrinogen and fibrin clot. The result indicated that hirtin has thrombin-like serine protease and have potential industrial and therapeutic applications.[15] Shijun yan et al., 2011 isolated , structural elucidated a new ent-kaurane diterpenoid from *Euphorbia hirta* ethanol extract. 2β, 16α,19-trihydroxy-ent-kaurane a new compound and two known ent-kauranes, 2β, 16α-dihydroxy-ent-kaurane and 16α, 19-dihydroxy-ent-kaurane compounds.[16] Mallavadhani et al., 2009 isolated and structural elucidated two new novel butanol rhamnopyranosides and nine known compounds from n-hexane, ethylacetate, methanol and aqueous extracts of *Euphorbia hirta*. The two new novel compounds were n-butyl-1-0-β-L-rhamnopyranoside and n-butyl-l-0-α-L-rhamnopyranoside.[17]

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.[18]

Prabhat Das et al., 2010 carried out an carragenan induced inflammation model. Diclofenac sodium 50mg/kg served as reference standard. The petroleum ether, chloroform, methanol, ethanol and aqueous fruit extracts of *Euphorbia hirta* were tested for anti-inflammatory activity. The aqueous and ethanol extract showed a maximum percentage of protection towards inflammation compared to other extracts. Thus , the plant *Euphorbia hirta* reduces and prevents experimentally induced inflammation in rats.[19]

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 n-hexane 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.[20]

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.[21] 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.[22]

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.[23]

Antitumour activity of *Euphorbia hirta linn* was studied by Sandeep et al., 2011. Aerial parts of the plant, *Euphorbia hirta* were extracted with ethanol, chloroform and petroleum ether. All the extracts showed positive result for tannin, saponin , alkaloids and flavonoids. Chloroform, ethanol extract enhanced mean survival time and reduced solid tumor mass tumour bearing mice. This antitumour activity due to presence of flavonoids.[24]

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.[25]

Invivo and invitro study of antidiabetic activity was done by Widharna et al., 2010. From the invitro 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.[26]

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.[27]

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*.[28]

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 $GABA_A$ receptor, benzodiazepine receptor, Cl^- channel complex. Thus, result indicate that Eh acts as a potential anxiolytic drug, which might be beneficial in treatment of stress induced anxiety disorders.[29] 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.[30]

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 adjuvant-induced arthritis.[31]

Kan Heng Lee et al., 2008 induced arthritis in rats using freund's complete adjuvant containing heat- killed mycobacterium tuberculosis 50,100, 500 mg/kg of water extract of *Euphorbia hirta*. High dose of *Euphorbia hirta* had greater extend of cartilage degeneration, while, intermediate and low doses showed improved histology. Decreased MMP – 13 and increased TIMP – 1 levels were found with low dose of *Euphorbia hirta*.[32]

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.[33]

Antithrombocytopenic activity

Antithrombocytopenic effect of lyophilized decoction of *Euphorbia hirta Linn* was studied by Jovencio G Apostol et al.,2012 in Sprague-Dawley rats. Ethanol induction induced thrombocytopenia within 7days in rats. Platelet count, bleeding time and clotting time were assayed in four groups of rats. A significant increased platelet count, decreased bleeding and clotting time observed after *Euphorbia hirta* treatment. Histopathological studies showed a decreased liver sinusoidal dilation in *Euphorbia hirta* treated groups. *Euphorbia hirta* decoction, thus, acts as potential antithrombocytopenic.[34]

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 HCO_3^- and urine output as like acetozolamide. Ethanol extract increased the excretion of HCO_3^-, 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 HCO_3^- 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.[35]

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.[36]

Burn wound healing

Akinrinmade et al., 2010 reported antimicrobial effect and tissue reaction of crude ethanol extract of *Euphorbia hirta* in canine infected incised wounds. 72h after treatment, gross appearance and histopathological reactions were examined. Ethanol extract had a positive effect on *staphylococcus aureus* growth in canine wound but the extract had not provoked cutaneous tissue reaction in canine wounds. Thus, *Euphorbia hirta* can be recommended for wound management.[37] Jaiprakash et al., 2006 studied burn wound healing activity of *Euphorbia hirta*. The result concluded that 2% W/W cream of ethanol extract of whole plant of *Euphorbia hirta* in rats showed significant burn wound healing activity.[38]

Immunostimulatory activity

Bronchodilator effect of alcoholic extract of *Euphorbia hirta Linn* evaluated by Karpagam Kumara Sundari et al., 2004. Different doses 50,100, 200mg/kg, p.o. extracts, tested against histamine aerosol induced bronchoconstriction. Dose at 200mg/kg was found to be more effective as bronchodilator with a significance of $p<0.001$.[39]

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.[40]

Genototoxic effect

Kwan Yuet Ping et al., 2012 investigated genotoxic effect of methanol extract of *Euphorbia hirta* using *Allium cepa* assay. The extracts 125, 250, 500 and 1000 µg/ml were tested on root meristems of *Allium cepa*. Ethylmethane sulfonate and distilled water served as positive control and negative control. A decreased mitotic index and a increased chromosome aberrations were observed as the concentrations of *Euphorbia hirta* extract increased. Some abnormalities like stickiness, c-mitosis, bridges and vagrant chromosomes were also observed. At interphase stage, micronucleated cells also observed.This result confirmed that *Euphorbia hirta* methanol extract (1000 µg/ml) exerted a significant genotoxic and mitodepressive effect.[41]

Synergistic activity

Michel Adikwu et al.,2010 illustrated in vitro Combined effects of erythromycin and *Euphorbia hirta* leaves methanol extract against *staphylococcus aureus* using checker board technique. The results indicate that some combination of *Euphorbia hirta* leaf and erythromycin at a given ratio 9:1, 8:2, 6:4, 3:7, 2:8, 1:9 Showed synergistic activity, while other ratios 5:5, 4:6 showed indifference.[42]

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.[43]

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 controlmice 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.[44]

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*.[45] 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 LC_{90} does not have apparent killing properties in fish populations.[46]

Antiviral activity

In vitro antiretroviral activities of aqueous and methanol extracts of *Euphorbia hirta* were compared against SIV_{mac251}, HIV-1 and HIV-2 viruses on MT_4 human T lymphocyte cell line. A dose dependent inhibition of RT activity was determined. 50% methanol extract exerted a high antiretroviral effect than aqueous extract. The 50% MeOH extract subjected to liquid - liquid partition with dichloromethane, ethyl acetate and water. The remaining aqueous phase with tannin exhibited significant viral replication inhibitory effect (antiviral activity), while, all other lipophilic extracts were inactive. From the result it was confirmed that high antiretroviral activity of *Euphorbia hirta* extract was mainly due to the presence of active compound tannin.[47]

Antihelminthic and Immunoprophylactive activity

Pratheepa et al., 2012 investigated enzymatic and survival effect of *Pseudomonas fluroescens* pathogen infected *cyprinus carpio* (fish). About 50 days, different concentrations of leaf

extract of *Euphorbia hirta* (0,5,10,20,25 and 50g/kg) was administered with feed. Leaf extract (50g/kg) fed through feed continuously increased acid phosphatase, alkaline phosphatase, serum peroxidase activity and pathogen clearance through blood and kidney. Results showed at higher concentrations 50g/kg of *Euphorbia hirta*, a improved survival rate of *pseudomonas fluorescencs* infected fish with a effective elimination of pathogen, from *cyprinus carpio,* fish. These results agree that *Euphorbia hirta* can be used as an immunoprophylatic.[48]

Antihelmintic efficacy of aqueous *Euphorbia hirta* extract in 20 nigerian dogs were studied by Adeolu Alex Adedapo et al., 2005. Nigerian dogs naturally infected with nematodes. Group A (untreated), Group B (mebendazole treated), Group C and Group D served as treated (aqueous extract of *Euphorbia hirta*, intramusucular and oral route administration). After two weeks, blood and faecal samples were collected. Results showed a significant increase in PCV, RBC, Hb conc, TWBC and lymphocyte counts. Also encountered a reduced faecal egg counts. Oral route pronounced more effect on faecal egg count than intramusucular administration.phenolic compound in aqueous extract was responsible for reduction in worm load. Thus aqueous crude extract of *Euphorbia hirta* could serve as anthelmintic agent.[49]

Anti-malarial activity

Neetu arya et al., 2011 isolated mosquito larvicidal bioactive saponin from indigenous plant, *Euphorbia hirta*. The isolated bioactive saponin was tested against *culex quiquefasciatus*. IInd and IV instar larvae of mosquito was exposed to four different concentration of bioactive saponin. 24hrs LC50 and LC90 values were determined using probit analysis method. Obtained result suggest that bioactive compound of *Euphorbia hirta* were more susceptile to IVth instar larvae than II instar larvae.[50]

Modupe Ogunlesi et al., 2009 extracted essential oil from dried leaves of *Euphorbia hirta*. Both major and minor components were identified on oil analysis. Major components identified includes 3,7,11,15-tetramethyl -2-hexadecon-1-ol, 6,10,14-trimethyl-2-pentadecanone, hexadecanal, phytol and n-hexadecanoic acid. Identified minor components includes 2-butoxyethanol, tetradacane, phthalic acid, butyl tetradecyl ester , oleic acid, 13-heptadecyn-1-ol, 2-methyl-1-hexadecanol and 1-2 benzene dicarboxylic acid diisooctylester. The role of components in treatment of asthma and other diseases were also discussed. The oil has potential repellent function against *anopheles* mosquito species due to presence of 6,10,14-trimethyl-2-pentadecanone and thus it can be useful for malaria control.[51]

Tona et al., 2004 made a comparative study among seven African medicinal plants, used in Democratic Republic of Congo, for malaria treatment. The ethanol extract (IC50<3µg/ml) and petroleum ether fractions (IC50<3µg/ml) of *cassia occidentalis* leaves, *Euphobia hirta* whole plant, *Garcinia Kola* stem back and *phyllanthus niruri* whole plant were most active. The ethanol extract of *venonia amygdalina* leaves, *Tetracera poggei* leaves, *morinda morindoides* leaves showed less active while petroleum ether fractions exhibited a pronounced antiplasmodial activity (IC50<3µg/ml). Isoamyl alcohol fractions from *Euphorbia hirta, phyllanthus niruri and vernonia amygdalina* showed IC50 values less than 3µg/ml and from *cassia occidentalis, Garcinia kola, Morinda morindoides* and *Tetracera poggei* IC50 value was between 10 and 50µg/ml. These antiplasmodial activity may be due to presence of terpenes, steroids, coumarins, flavonoids, phenolic acids, lignans, xanthones and anthraquinones.[52]

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.[53]

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.[54]

Qualitative and quantitative, antibacterial activity of ethanolic, aqueous extracts of *Sida acuta* and *Euphorbia hirta* was carried out by Ibrahim et al., 2012. The phytochemical analysis showed the presence of alkaloids, tannins, saponin, reducing compounds, flavonoids, terpenoids, phenolic compounds and glycosides in moderate amounts. The antibacterial activity was determined against isolates *Staphylococcus aureus*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Streptococcus faecalis* and *Escherichia coli*. Among the tested isolates *Escherichia coli* , *Streptococcus faecalis* were most susceptile while *Klebsiella pneumonia* was most resistant to extract.[55]

Shanmuga priya perumal et al., 2012 evaluated antimicrobial and cytotoxic activity of various extracts (hexane, dichloromethane, ethylacetate, ethanol) of *Euphorbia hirta*. Gram-negative species, Enterobacter aerogens, *Escherichia coli*, *Klebsiella pneumonia*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Shigella dysenteriae* and Gram-positive species, *Staphylococcus aureus* and *Bacillus subtilis*. Ethanol extract exhibited strongest antimicrobial activity against *Salmonella typhi* with MIC value 0.031mg/ml. Dichloromethane and ethyl acetate extracts had moderate activity with MIC value 1-0.5mg/ml. Hexane extract appeared to have least activity. All the extracts had no cytotoxic effect against vero ell line. The result confirmed that *Euphorbia hirta* extract possess only antimicrobial property and no cytotoxic effect.[56]

Rajendran Darling Anpin Raja et al., 2011 screened antimicrobial potential of three plants, *Chassalia curviflora Thw (c.curviflora)*, *Cyclea peltata Hook. F* and Thomson *(c.peltata)* and *Euphorbia hirta* against human bacterial pathogens. Pathogens were *Escherichia coli* (E.coli) (ATCC 35218), *Staphylococcus aureus (S.aureus)* (ATCC 6538), *Salmonella typhi* (S.typhi) (MTCC733), *Proteus vulgaris* (P.vulgaris), *Proteus mirabilis* (P. Mirabilis) and *Streptococcus pyogenes* (S.pyogenes). Methanol extract of *C.peltata* showed antibacterial activity against three pathogens, *S.pyrogenes*, *P.vulgaris* and *E.coli*. The hexane extract of C.Peltata was active against *P.vulgaris* and *P.mirabilis*. The methanol and hexane extracts of *C.curviflora* exhibited antibacterial activity against *P.vulgaris* and *S.typhi* each respectively. The ethanol and hexane extract of Euphorbia hirta showed antibacterial activity against only one bacterium S.pyogenes. A maximum degree of antibacterial activity was observed in *C.peltata* , followed by *C.curviflora* and a low degree of activity by *Euphorbia hirta*. The results revealed that *C.curviflora*, *C.peltata* and *Euphorbia hirta* had potential antibacterial activity.[57]

Singh et al., 2011 carried out a study on taxonomy ethnobotany and antimicrobial activity of three plants, *Croton bonplandianum*, *Euphorbia hirta* and *Phyllanthus fraternus* etc. Extracts tested were three different solvents -water, methanol and petroleum ether. Four bacteria (*Bacillcs macerans, Staphylococcus aureus, Pseudomonas aeruginosa, Pseudomonas striata*) and one fungal species (*Aspergillus niger*) were used. Agar well diffusion method adopted to evaluate antimicrobial activity. Among the three plant studied, methanol extract of *Euphorbia hirta* found to possess potent antimicrobial activity against gowth of bacterial strains. It also found, none of the three plants provided antifungal activity.[58]

Aniel kumar et al., 2010 examined antibacterial acvtivity of snake weed, *Euphorbia hirta Linn*. Ethanol, methanol, chloroform and Aqueous extracts of leaf, stem, root and whole plant were used for antibactecial activity. Gram positive (*Bacillus Subtilis* and *Staphylococcus aureus*) and Gram negative (*Escherichia coli, Klebsiella pneumoniae* and *Proteus Vulgaris*) assayed by agar-well diffusion method. Aqueous and chloroform extracts of stem and root had no inhibitory activity. Ethanol and methanol extracts of leaf and whole plant were more effective and significant than aqueous and chloroform extracts. Phytochemical screening revealed the presence of tannins, flavonoids, alkaloids, glycosides and saponins.[59]

EI-Mahmood Muhammad Abubakar 2009 discussed the antibacterial activity of three different extracts of *Euphorbia hirta*. Methanol, hexane and distilled water were employed against *Escherichia coli, Klebsiella pneumoniae, Shigella dysentriae, Salmonella typhi* and *Proteus mirabilis*, cause enteric infections in humans. Phytochemical screening revealed the presence of tannins, saponins, phenolics, flavonoids, cardiac glycosides, anthroquinones and alkaloids.Growth of bacteria especially *Escherichia coli* and *Salmonella typhi* more susceptible to plant material. The herb *Euphorbia hirta* used as a oral drugs to fight bacterial infections.[60]

Mohammad Abu Basma Rajah et al., 2010 reported antimicrobial activity of methanol extracts of *Euphorbia hirta* L leaves, flowers, stems and roots against some medically important bacteria and yeast using the agar disc diffusion method. Four gram positive bacterias (*Staphylococcus aureus, Micrococcus sp, Bacillus subtilis* and *Bacillus thuriengenesis*) four gram negative bacteria (*Escherichia coli, Klebsiella pneumonia ,Salmonella typhi* and *Proteus mirabilis*) and one yeast (*Candida albicans*) species were screened for antibacterial and antifungal activity. The inhibition zone of leaves extract had

greater growth inhibition than flowers. The root extract displayed high zone of inhibition compared to stem extract. LC50 value of all extracts of *Euphorbia hirta* were determined in *Artemia salina* cysts (brine shrimp eggs 0.1g). The LC50 value of stems, leaves, roots and flowers were 0.71, 0.66, 0.41 and 0.03mg/ml. Thus, the LC50 value was found to be less than 1mg/ml.[61]

Ahmad Zorin sahalan et al., 2007 screened two species of plants, *Andrographis paniculata* and *Euphorbia hirta* for antibacterial activity against three Gram positives (*Staphylococcus aureus, Bacillus subtilis, Streptococcus epidemidis*) and three gram negatives (*Escherichia coli klebsiella pneumonia* and *pseudomonas aeruginosa*) bacteria. The leaves from both plants were extracted by methanol extraction. Minimum inhibitory concentration (MIC) value of *Andrographis paniculata* ethanol extract for both gram positive and gram negative bacteria ranges between 1.56mg/ml to 12.5mg/ml and for *Euphorbia hirta* 3.13mg/ml to 12.5mg/ml. Gram negative bacteria showed higher MIC value than gram positive bacteria due to presence of cell wall.[62]

Shanmugaraju et al., 2007 reported and isolated a compound for antibacterial activity. Ethanol and aqueous extracts of *Euphorbia hirta* tested against *E.Coli, Klebsiella pneumonia, Proteus species, Pseudomonas aeruginosa, Salmonella typhi, Staphylococcus aureus, Streptococcus* species. For *Klebsiella pneumonia, Streptococcus species, pseudomonas aeruginosa* and *Staphylococcus aureus* ethanol extract alone exhibited antibacterial activity. A maximum antibacterial activity was achieved by aqueous extract on *protease* and *salmonella typi*. Both ethanol and aqueous extracts inhibited growth of *E.Coli*. Thus, ethanol extract posses more antibacterial activity than aqueous extract. Gas chromatography analysis of ethanol extract of plant showed the presence of citronellal, a compound responsible for antibacterial activity of *Euphorbia hirta*.[63]

Sudhakar et al., 2006 compared the antimicrobial activity among three plants. Dry fruits of *caesalpinia pulcherrima*, aerial parts of *Euphorbia hirta*, flowers of *Asystasia gangeticum* were tested against *Escherichia coli* (enteropathogen), *Proteus vulgaris, Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans, Aspergillus niger* and *Rizopous oligosporus*. Ethanolic extracts of all plants exhibited significant antimicrobial activity against *Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Caesalpinia pulcherrima* only exhibited significant antifungal activity against *Candida albicans, Aspergillus niger* and *Rhizopus oligosporus*.[64]

Emele et al.,1998 cultivated fungi on sapientum glucose agar medium and sabouraud glucose agar, a standard medium. Sporulation and pigment formation of mycelium was stronger on sapientum glucose agar medium than other medium. *Euphorbia hirta* leaves and *musa sapientum* fruit extract added to mycological medium. Addition of *Euphorbia hirta* extract remarkably enhanced fungal growth and suppressed bacterial growth as like as antibiotics. The result suggest that *Euphorbia* sapientum glucose agar could be used as a cheap and efficient medium for fungal isolation in clinical and general mycological studies.[65]

Vijaya et al., 1995 studied antibacterial activity of compounds theaflavin, polyphenon 60 from *camellia sinensis L*. and methanol extract of *Euhorbia hirta* L. against *shigella spp*, a dysentery causing organism, using vero cell line. Cytotoxicity study and antibacterial study were tested using cell line and pathogen. The compounds and extract were found to be non-cytotoxic and effective anti-bacterial agents.[66]

Anti-molluscicidal activity

Potent molluscicidal activity of plant *Euphorbia hirta* was studied by Sunil kumar singh et al., 2005. The aqueous stem, bark, and leaf extracts were choosen for study. Vector snail *Lymnaea acuminate* were exposed to sub-lethal doses (40% and 80% of LC50). A significant ($p<0.05$) altered levels of total protein, total free aminoacid, nucleic acids (DNA and RNA) and activity of enzyme protease, acid and alkaline phosphatase in various tissues was obtained. *Euphorbia hirta* showed a time and dose dependent mollusicicidal activity.[67]

Molluscicidal activity of *Euphorbia pulcherima* and *Euphorbia hirta* was discussed by Sunil kumar Singh et al., 2003. LC_{50} 40 and 80% of aqueous and partially purified (chloroform, carbon tetrachloride, acetone, diethyl ether, ethyl acetate) ;latex extracts of both plants significantly altered the levels of total protein, total free aminoacid, nucleic acid (DNA and RNA), protease enzyme, acid and alkaline phosphatase in snail *Lymnaea accuminata*.[68]

Larvicidal activity

Karthikeyan Agalya priyadarshini et al., 2012 synthesised sliver nanoparticles (AgNPs) *Euphorbia hirta* leaf extract concentration range of AgNps (3.125, 6.25, 12.5,25 and 50PPm) and methanol crude extract (50,100,150, 200 and 250PPm) were tested against malarial vector *Anopheles stephensi*. The synthesized AgNps exhibited a highest larval mortality

against first to fourth instar larvae and pupae. Methanol extract exhibited a lowest larval mortality than the synthesized silver nanoparticles can be potential mosquito larvicidal agents.[69]

Larvicidal property of *Amaranthus oleracea* and *Euphorbia hirta* extract against third instar larvae of *Anopheles stephensi*, malaria vector was studied by Preeti Sharma et al., 2009. LC50 value of both plant extracts, carbon tetrachloride extract, methanol extract, petroleum ether extract after 24 and 48h of exposure showed a potential larvicidal property. Among the extracts, petroleum ether extract fractions were more potent compared to other crude forms.[70]

Herbicidal activity

Martha Leema Rose et al., 2012 studied the effect of leaf, stem and root extracts of *Euphorbia hirta* L. on germination and seedling growth of groundnut. Higher concentration significantly inhibited germination than lower concentration. Root extract caused more inhibition than the stem and leaf extracts. A significant decrease in root length and shoot length of groundnut was also found in *Euphorbia hirta* infested soil.[71]

Corrosive activity

Anozie et al., 2011 discussed the corrosion inhibition effect of plants. A gravimetric technique (30^0c and 60^0c) was used to study. The leaf extract of euphorbia hirta and dialum guineense on aluminium alloy (AA8011) in 0.5M HCl solution. Based on physical adsorption phenomenon, both extracts acted as good inhibitors and also inhibited corrosion process in medium. [72]

Other activities

Arya et al., 2009 compared TLC of ethanol extract of plants, *Euhorbia hirta* L. (Euhorbiaceae) and *Gomphrena celosioides Mart*. (Amaranthaceae) individually and combination *Euphorbia hirta* + *Gomphrena celosioides* 4:1) with homeopathic drugs (Aesculus, Aloes, Arnica, Hamamelis, Nuxvomica, Lycopodium, Pulsatilla) for piles. Comparative chemoprofiling showed that homeopathic drugs major components were also found in *Euphorbia hirta* , *Gomphera celosioides* and incombination form. This report suggest that *Euphorbia hirta* and *Gomphera celosioides* acts as a folk remedy for piles. On microscopical identification, *Euhorbia hirta* showed the presence of various types of simple, multicellular, uniseriate , warty and smooth trichomes and latifers in traverse section (TS) of

root, stem and leaves. G.celosides showed the presence of long mulitcellular simple trichomes, anamalous secondary growth and pith in traverse section (TS) of root.[73]

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