

## REVIEW ARTICLE ON EUPHORBIA HIRTA

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## 1. INTRODUCTION

1.1 *Euphorbia Hirta* Synonyms and Taxonomy

*Euphorbia hirta* (*E. hirta*) L. belongs to the family Euphorbiaceae. It is a small annual herb common to tropical countries. It is usually erect, slender-stemmed; spreading up to 80 cm tall, though sometimes it can be seen lying down. The plant is an annual broad-leaved herb that has a hairy stem with many branches from the base to the top. The leaves are opposite, elliptical, oblong or oblong-lanceolate, with a faintly toothed margin and darker on the upper surface. The flowers are small, numerous and crowded together in dense cymes (dense clusters in

upper axils) about 1 cm in diameter. The stem and leaves produce a white or milky juice when cut. It is frequently seen occupying open waste spaces, banks of watercourses, grasslands, road sides, and pathways (*Rajesh et al., 2010 and Anonymous 2008*).

*Synonyms of Euphorbia Hirta* (Kumar et al., 2010)

Language	Vernacular name
English	Pill-bearing spurge, Asthma plant, Hairy spurge, Garden spurge, Pill pod sandman
Bengali	Boro-Keruie, Barokhervi
Gujarati	Dudeli
Hindi	Daridhudi, Dudhghas, Dudhi
Sanskrit	Chara, Amampatchairasi, Barokheruie
Tamil	Amampatchaiarisi
Telugu	Reddivarinanabalu, Reddinananbrolu, Bidarie
Urdu	LalDodhak

The photo Documentation of *Euphorbia hirta* as shown below:



## 1.2 Traditional Use

*E. hirta* is a very popular herb amongst practitioners of traditional medicine and is widely used as a decoction or infusion to treat various ailments including intestinal parasites, diarrhoea, peptic ulcers, heartburn, vomiting, amoebic dysentery, asthma, bronchitis, hay fever, laryngeal spasms, emphysema, coughs, colds, kidney stones, menstrual problems, sterility, and venereal diseases. Moreover, the plant is also used to treat affections of the skin and mucous membranes, including warts, scabies, tinea, thrush, aphthae, fungal afflictions, measles, and guinea-worm and as an antiseptic to treat wounds, sores, and conjunctivitis. The plant has a reputation as an analgesic to treat severe headache, toothache, rheumatism, colic, and pains during pregnancy. It is used as an antidote and pain relief of scorpion stings and snakebites (*Shih et al., 2012*).

*Euphorbia hirta* (Euphorbiaceae), commonly known as Dudhi is an annual hairy plant. Traditionally, it is used in treatment of gastrointestinal disorders, bronchial and respiratory diseases, kidney stones, diabetes and in conjunctivitis. It also exhibits antipyretic, analgesic, antibacterial, anxiolytic, anthelmintic, anti-fertility, antispasmodic, antifungal, and anti-inflammatory activities (*Elizabeth 2002*).

## 2. Phytochemistry

The aerial parts of plant are well investigated for chemical information (*Williams et al., 1997*).

**Flavonoids:** Euphorbianin, leucocyanidol, camphol, quercitrin and quercitol (*Gupta., 1966 & Blanc et al., 1972*).

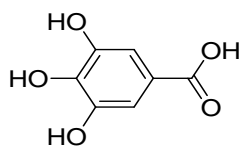
**Polyphenols:** Gallic acid, myricitrin, 3,4-di-Ogalloylquinic acid, 2,4,6-tri-O-galloyl Dglucose, 1,2,3,4,6-penta-O-galloyl- $\beta$ - D-glucose (*Aqil., 1999 & Chen., 1991*).

**Tannins:** Euphorbins A, B, C, D, E (*Joseph et al., 2002*).

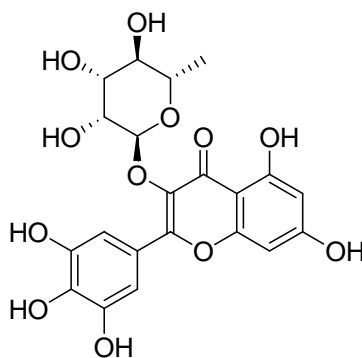
**Triterpenes and phytosterols:**  $\beta$ -Amyrin, 24- methylenecycloartenol, and  $\beta$ -Sitosterol (*Yoshida et al., 1989*).

**Alkanes:** Heptacosane, n-nonacosane and others (*Martinez et al., 1999*).

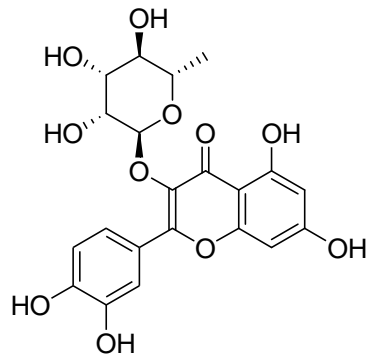
### Chemical Structure



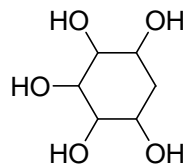
**Gallic acid**



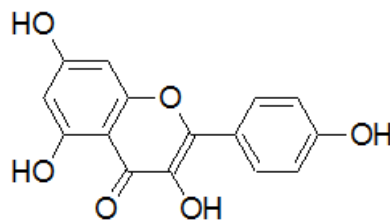
**Myricitrin**



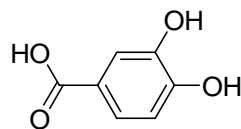
**Quercitrin**



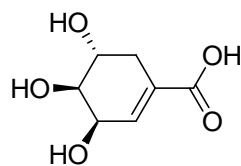
**Quercitol**



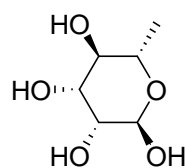
**Kaempferol**



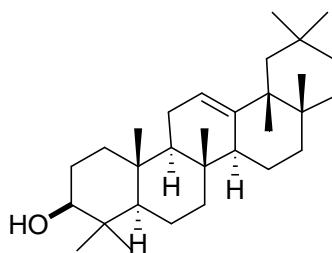
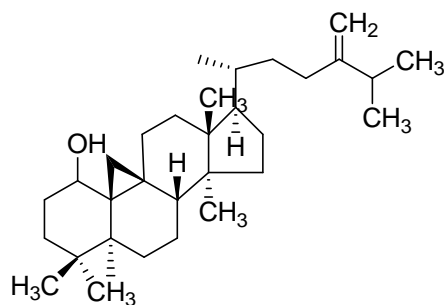
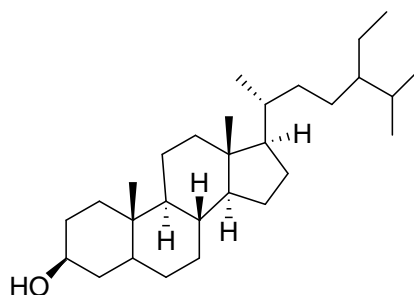
**protocatechuic acid**



**Chtolphenolic acid**



**Rhamnose**

 **$\beta$ -amyrin****24-methylenecycloartenol** **$\beta$ -sitosterol**

### 3. Geographical Distribution

*E. hirta* is distributed throughout the hotter parts of India and Australia, often found in waste places along the road sides. In India its native in Uttar Pradesh, Bihar, Gujarat, Madhya Pradesh, Himanchal Pradesh and West Bangol (*Sood et al.,2005*).

### 4. Pharmacological Activities Of Extracts, Fractions And Isolated Constituents

#### Anti-inflammatory activity

The n-hexane extract of the aerial parts of *E. hirta* and its main constituent triterpenes,  $\beta$ -amyrin, 24-methylenecycloartenol, and  $\beta$ -Sitosterol were evaluated for anti-inflammatory effects in mice. Both the extract and the triterpenes exerted significant and dosedependent anti-inflammatory activity in the model of phorbol acetate-induced ear inflammation in mice. The lyophilized aqueous extract showed analgesic, antipyretic and

anti-inflammatory activity in mice and rats. A central depressant activity, expressed by a strong sedative effect associated with anxiolytic effect, was also observed (*Lanhers et al., 1991*).

#### **Sedative and Anxiolytic activity**

Lyophilized aqueous extract of *Euphorbia hirta* L. (Euphorbiaceae) has been evaluated for behavioural effects in mice. Sedative properties could be confirmed with high doses (100 mg of dried plant/kg, and more), by a decrease of behavioral parameters measured in non-familiar environment tests, whereas anti-conflict effects appeared at lower doses (12.5 and 25 mg of dried plant/kg), by an enhancement of behavioural parameters measured in the staircase test and in the light/dark choice situation test. These findings validate the traditional use of *E. hirta* as a sedative and reveal original anxiolytic properties (*Lanhers et al., 1990*).

#### **Anticancer activity**

*Euphorbia hirta* possess anticancer activity. Cytotoxicity studies of the extracts were performed using the cell line and the non-cytotoxic concentration of the extract was tested for antibacterial activity against the cytopathic dose of the pathogen. These extracts were found to be non-cytotoxic and effective Anti-bacterial agents Extracts of *Euphorbia hirta* have been found to show selective cytotoxicity against several cancer cell lines. The plant is useful in effective treatment of cancers, particularly malignant melanomas and squamous cell carcinomas (*Mathur et al., 1995*).

#### **Anti-diarrhoeal activity**

*Euphorbia hirta* possess Anti-diarrhoeal activity. Their traditional medicinal use as antidiarrheal agents. Only 8 plant extracts (17.39%) proved as antidiarrheal agents by a triple pronounced antibacterial, antiamoebic and antispasmodic action. *Euphorbia hirta* whole plantare used(*Tona et al., 1999*).

#### **Antimalarial activity**

*Euphorbia hirta* posses antimalarial activity .*Euphorbia hirta* whole plant produced more than 60% inhibition of the parasite growth in vitro at a testconcentration g/ml. Extracts from *E. hirta* showedµ of 6 asignificant chemosuppression of parasitaemia in miceinfected with *P. berghei berghei* at orally given doses of 100-400 mg/kg per day(*Tona et al., 1999*).

**Antifertility activity**

*Euphorbia hirta* at a dose level of 50 mg/kg bodyweight reduced the sperm motility and density of caudaepididymal and testis sperm suspension significantly, leading eventually to 100% infertility (*Mathur et al., 1995*).

**Aflatoxin inhibition activity**

*Euphorbia hirta* aqueous extract significantly inhibited aflatoxin production on rice, wheat, maize and groundnut (*Singh et al., 1986*).

**Anti-platelet aggregation and anti-inflammatory**

Aqueous extracts of *Euphorbia hirta* strongly reduced the release of prostaglandins I<sub>2</sub>, E<sub>2</sub>, and D<sub>2</sub>. Additionally *Euphorbia hirta* extracts exerted an inhibitory effect on platelet aggregation and depressed the formation of carrageenin induced rat paw oedema. The chemical nature of the active principle of *Euphorbia hirta* could be characterized as (a) compound(s) of medium polarity in the molecular weight range of 1000 to 3000 Da (*Hiermann et al., 1994*).

**Immunomodulatory activity**

*Euphorbia hirta* aqueous and aqueous-alcoholic extracts, containing flavonoids, polyphenols, sterols and terpenes, demonstrated immunostimulant activity. The aqueous extract affected lectin-induced lymphoblast transformation *in vitro* (*Szenasi et al., 1992*).

**Antifungal activity**

An ethanolic extract of *Euphorbia hirta* displayed antifungal activity when tested against the plant pathogens *Colletotrichum capsici*, *Fusarium pallidroseum*, *Botryodiplodia theobromae*, *Alternaria alternata*, *Penicillium citrinum*, *Phomopsis caricae-papayae* and *Aspergillus niger* using the paper disc diffusion technique (*Mohamed et al., 1996*).

**Larvicidal activity**

Larvicidal activity of ethyl acetate, butanol, and petroleum ether extracts of Euphorbiaceae plants, *Euphorbia hirta*, was tested against the early fourth instar larvae of *Aedes aegypti* L. and *Culex quinquefasciatus* (Say). The larval mortality was observed after 24 h of exposure. The LC<sub>50</sub> value of petroleum ether extract of *E. hirta*, was 272.36 ppm against *A. aegypti* and 424.94 against *C. quinquefasciatus* (*Rahuman et al., 2007*).

### **Antioxidant activity**

Aqueous extract of *Euphorbia hirta* L. was prepared in hot water and crude extract yield (7% w/w) after lyophilization was used for antioxidant potential determination. The total antioxidant potential of crude extract was determined using phosphomolybdenum complex and ferric reducing power (FRAP) assays, which showed 185  $\mu\text{mol}$  of ascorbic acid and 398  $\mu\text{mol}$  Fe (II) equivalent per gram crude extract, respectively. The crude extract exhibited significant free radical scavenging activity of 247  $\mu\text{mol}$  Trolox equivalent per gram crude extract (*Sharma et al., 2007*).

### **Serum biochemistry**

The effects of the chromatographic fractions of *Euphorbia hirta* Linn were administered to rats in graded doses of 400 mg/kg, 800 mg/kg and 1600 mg/kg orally for fourteen days. After fourteen days the serum biochemical parameters total protein, albumin, globulin, alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), total bilirubin, creatinine, and blood urea nitrogen (BUN) showed a significant increase in rats (*Subramanian et al., 2011*).

### **Anti-anaphylactic activity**

The *Euphorbia hirta* ethanolic extract (EH A001) was found to possess a prominent anti-anaphylactic activity. A preventive effect of EH-A001 given by oral route at a dose from 100 to 1000 mg/kg was observed against compound 48/80-induced systemic anaphylaxis. At the same range of dose, EH-A001 inhibited passive cutaneous anaphylaxis (PCA) in rats and active paw anaphylaxis in mice. A suppressive effect of EH-A001 was observed on the release of TNF- $\alpha$  and IL-6 from anti-DNP-HAS activated rat peritoneal mast cells (*Youssef et al., 2007*).

### **Anthelmintic activity**

The anthelmintic efficacy of the aqueous crude extract of *Euphorbia hirta* Linn was studied in 20 Nigerian dogs that were naturally infected with nematodes. Results of this study show that the aqueous crude extracts of *E. hirta* after its administration in local dogs produced a significant increase ( $P < 0.05$ ) in PCV, RBC, Hb conc., TWBC and lymphocyte counts. The faecal egg counts also showed a remarkable and significant reduction in the levels of the identified helminths (*Duez et al., 1991*).



**Antidiarrhoeal activity**

The aqueous leaf extract of *E.hirta* significantly decrease the gastrointestinal motility and decrease the effect of castor oil induced diarrhea. These findings may lend support to the traditional use of *E.hirta* in diarrhea. It is also focused that the leaves of this plant possibly play a vital role in anti-diarrhoeic activity of the whole plant as reported earlier (*Hore et al., 2006*).

**Diuretic Activity**

The leaves extract of *E.hirta* increase the urine output and enhance the excretion of electrolytes i.e. Na<sup>+</sup>, K<sup>+</sup>, HCO<sub>3</sub><sup>-</sup>. The water and ethanol extracts of the plant produced time dependent increases in urine output. Electrolyte excretion was also significantly affected by the plant extracts. The water extract increase the urine excretion of Na<sup>+</sup>, K<sup>+</sup> and HCO<sub>3</sub><sup>-</sup>. In contrast the ethanol extract increased the excretion of HCO<sub>3</sub><sup>-</sup>, decreased the loss of K<sup>+</sup> and had little effect on renal removal of Na<sup>+</sup>. Acetazolamide, like the water extract, increased the urine output and enhance the excretion of Na<sup>+</sup>, K<sup>+</sup> and HCO<sub>3</sub><sup>-</sup>. The high – ceiling diuretic, furosemide, increased the renal excretion of Na<sup>+</sup>, and Cl<sup>-</sup>; but had no effect on K<sup>+</sup> and HCO<sub>3</sub><sup>-</sup> loss. These results validate the traditional use of *E.hirta* as a diuretic agent (*Johnson et al., 1999*).

**Antimicrobial activity**

The ethanolic extract of aerial parts of *E.hirta* was tested for anti microbial activity along with the ethanolic extracts of dry fruits of *Caesalpinia pulcherrima* and flowers of *Asystasia gangeticum*. The three plants exhibited a broad spectrum of antimicrobial activity particularly against *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* (*Sudhakar et al., 2006*).

**Molluscicidal activity**

The aqueous and serially purified latex extracts of *E.hirta* have potent molluscicidal activity. Sub lethal doses of aqueous and partially purified latex extracts of plant also significantly alter the levels of total protein, total free amino acid, nucleic acid and the activity of enzyme protease and alkaline phosphatase in nervous tissue of the snail *Lymnaea acuminata* in time and dose dependent manner. This is toxic effect of stem bark and leaf extract of *Euphorbia hirta* (*Duez et al., 1991*).

**Antibacterial activity**

The methanolic extract of *E.hirta* possesses the anti bacterial activity along with compounds extracted from *Camellia sinensis* were studied against dysentery causing *Shigella* species using the Vero cellline. These extracts were found to be non cytotoxic and effective anti bacterial agent (*Ajao et al., 1985*).

**Wound healing activity**

The ethanolic extract of whole plant of *E.hirta* possesses significant wound healing activity. The histopathological study, W.B.C. count and haemostatic activity were carried out to support its wound healing activity. The ethanolic extract of *E.hirta* has promoted wound healing activity and probable mechanism may be the promotion of collagen biosynthesis which further supports for increase in tensile strength of the granulation tissue. This evidence supports the use of *E.hirta* in the management of wounds (*Jaiprakash et al., 2006*).

**Antihepatotoxic activity**

The antihepatotoxic effect of *Euphorbia hirta* extracts were evaluated in experimental models of liver injury in rats induced by CCL4 or paracetamol. Hydroalcoholic extract (HE) from whole plant were tested. The Hepatic dysfunction was accessed by determining different biochemical parameters in serum and tissues. In serum, the activities of enzymes like Aspartate Aminotransferase (AST), Alanine aminotransferase (ALT), alkaline phosphatase (ALP), alkaline phosphate (ALP), Bilirubin were evaluated. Lipid peroxidation and reduced glutathione were also measured into control and treated rats. *E.hirta* whole plant (HE) showed hepatoprotective activities at doses 125 mg/kg and 250 mg/kg, since serum levels of ALT and AST in rats given the extracts were significantly low ( $p < 0.05$  and  $0.01$  respectively) When compare to control CCL4 or paracetamol-injured rats.

Furthered studies were carried on the HE from the whole part of both the plant by using the combination of the extract showed the highest level of antihepatotoxic activity with the hydroalcoholic extract which was effective at doses 75mg/kg and 150 mg/kg, for hepatoprotective activity in CCL4 and paracetamol injured rats. In experiments comparing the comprising the HE (125- 250 and 75- 150 mg/kg) to reference antihepatotoxic substance (silymarin) the HE exhibited a 70 and 80% hepatoprotection compared to the 80 and 90% one exhibited by silymarin in CCL4 or paracetamol -injured rats respectively. This study demonstrated that hydro alcoholic extract *Euphorbia hirta* and *Boerhaavia diffusa* was effective in protecting the liver from toxic hepatitis (*Brindha et al., 2010*).

### Antiviral activity

The antiretroviral activities of extracts of *Euphorbia hirta* were investigated in vitro on the MT4 human T lymphocyte cell line. The cytotoxicities of the extracts were tested by means of the MTT cell proliferation assay, and then the direct effects of the aqueous extract on HIV-1, HIV-2 and SIV (mac251) reverse transcriptase (RT) activity were determined. A dose-dependent inhibition of RT activity was observed for all three viruses. The HIV-1 inhibitory potency of *E. hirta* was studied further, and the activities of the aqueous and 50% methanolic extracts were compared. The 50% methanolic extract was found to exert a higher antiretroviral effect than that of the aqueous extract. The 50% MeOH extract was subjected to liquid-liquid partition with dichloromethane, ethyl acetate and water. Only the remaining aqueous phase exhibited significant antiviral activity; all the lipophilic extracts appeared to be inactive. After removal of the tannins from the aqueous extract, the viral replication inhibitory effect was markedly decreased, and it was therefore concluded that tannins are most probably responsible for the high antiretroviral activity (*Gyuris et al., 2009*).

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