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Review Article

Review of the phytochemical and pharmacological activities of *Euphorbia hirta* Linn.

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ABSTRACT

The use of plant extract to cure diseases has been the traditional way used in many parts of the world. The synthetic drugs used now are more prone to cause side effects than curing the disease. Hence, the use of plant extract has now emerged due to their effective action against the disease without causing any side effects. The plants belonging to the family called Euphorbia are widely used in medicine for its wide medicinal properties. The plant *Euphorbia hirta* has properties like anti-bacterial, anti-diarrheal, anti-allergic, diuretic, anti-oxidant, anti-tumor, anti-diabetic, anxiolytic and sedative activity. This review contains the detailed information about all the properties of *E. hirta*.

Key words: *Euphorbia hirta*, Anti-bacterial, Anti-oxidant, Diuretic, Sedative, Anti-apoptotic.

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INTRODUCTION

Euphorbia hirta, belongs to genus Euphorbia, and family Euphorbiaceae. It is widely used as an important medicinal plant and used for the treatment of various diseases like gastrointestinal disorders including intestinal parasites, diarrhea, peptic ulcers, heartburn, vomiting, and amoebic dysentery, inflammations of the skin and mucous membranes like warts, scabies, tinea, thrush, aphthae, fungal afflictions, and measles and respiratory system disorders like asthma, bronchitis, hay fever, laryngeal spasms, emphysema, coughs, and cold.[1,2] The plant is commonly found in China, India, Philippines, Australia, Africa, and Malaysia. According to the epidemiological survey, the increasing lifestyle in human causes more serious health issues like kidney and hepatic issues, which can be cured by the use of plant and weed extract.[3]

BOTANICAL DESCRIPTION

E. hirta is a plant that grows up to 80 cm in height with slender and erect stem. It is a broad leaf with hairy stem with leaves that are oblong, elliptical, opposite arrangement. It has a faint toothed margin with small flowers. The plant is usually found in grasslands, pathways, roadsides, and in areas rich in water. The fruits are yellow in color with 1-2 mm in diameter that has wrinkled seeds along the four sides with hairy capsules.[2]

PHYTOCHEMISTRY

E. hirta is composed of flavonoids, terpenoids, phenols, essential oil, and other compounds. Flavonoids include quercetin, quercitrin, quercitol, and its derivatives.[4] Terpenoids include triterpenes: α-amyrin, β-amyrin, friedelin, taraxerol, and its derivatives.[4-6] Tannins include the dimer rich hydrolysable dehydro-ellagi-tannins-euphorbins A, B, C, E, and terchebin, the monomeric hydrolysable tannins-geraniin.[7] Acids include ellagic, gallic, tannic, maleic and tartaric acid.[7] Various other compounds present in the plant contain saponins, amino acids, alkaloids and minerals.[8]

The ethyl acetate extract of the plant contain afforded quercetrin, dimethoxy quercetrin, and two new prenylated flavonosides known as hirtacoumaroflavonoside and hirtaflavonoside-B characterized as 7-O-(p-coumaroyl)-5,7,4'-trihydroxy-6-(3,3-dimethyl allyl)-flavonol-3-O-β-d-glucopyranosyl-(2″→1‴)-O-α-l-rhamnopyranoside and 5, 7, 3', 4'-trihydroxy-6-(3, 3-dimethyl allyl)-8-(iso-butenyl)-flavonol-3-C-β-d-glucopyranoside, respectively. All compounds extracted from the plant exhibited dose dependent inhibition of α-glucosidase. It was reported that 5,7,4'-trihydroxyflavone structure is imperative for the inhibitory activity. The rich flavonoids contents increase the potency and p-coumaroyl substitution at C-7 further enriched the α-glucosidase inhibition.[9] A Study conducted by Yvette Fofie reported that the leaf and stem extract of *E. hirta* contained mineral salts, bioactive secondary metabolites and various other trace elements which can be used as a therapeutic drug against diabetes mellitus.[10] Table 1 shows the different beneficial effects of different extracts of *E. hirta*.

ANTI-BACTERIAL ACTIVITY

The anti-bacterial activity of *E. hirta* was discovered and proven by using the methanol extract which showed the property against dysentery causing *Shigella* species in the Vero cell line.[11] The non-cytotoxic concentration of the plant extract was examined for anti-bacterial activity against the various doses of the pathogen. The extracts were thus proved to be non-cytotoxic and effective anti-bacterial agents.[11] The anti-microbial activity was tested using the nystatin and the methanol extract obtained from the leaves of *E. hirta* and examined on *Candida albicans*. The results obtained were favouring.[12]

It was reported that anti-microbial activity was attributed to tannins, flavonoids, alkaloids, glycosides, proteins, sterols, and saponins. The crude ethanolic extract of *E. hirta* exhibited anti-bacterial activity against the growth of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtilis*.[13] When compared to the anti-bacterial activity of the plant extract between the gram positive and gram negative bacteria the results were exhibited more promisingly in gram positive bacteria.[14]

The plant is found to be rich with caffeic acid and epicatechin 3-gallate acid, which are found to be anti-bacterial in nature. This is the reason for the plant to be traditionally used in Malaysia for the treatment of gastrointestinal, respiratory and bronchial ailments caused by nosocomial infectious agents. The plant extract also expressed inhibitory action against *P. aeruginosa* cells.[15] The flavonoids extracted from the roots of

the plant expressed activity against *C. albicans*, *Proteus mirabilis* and *S. aureus*.[16] Mir *et al.*[17] conducted study on dengue patients whose platelet count was extremely low and after treatment with the plant extract it was found that 70% patients showed improvement in platelet count, fever and flu-like symptoms.[17]

ANTI-DIARRHEAL ACTIVITY

The aqueous extract obtained from the leaves of *E. hirta* exhibited excellent effect by decreasing the gastrointestinal motility in normal rats and effect of castor oil-induced diarrhea in mice.[18] The anti-diarrheal activity was shown by Quercitin, a flavonoid extracted from the plant in crude form.[19] This quercitin acts by increasing the colonic fluid absorption showing anti-diarrheal activity in the presence of secretagogue compounds.[19]

ANTI-ALLERGIC ACTIVITY

The ethanolic extract of *E. hirta* showed effective anti-anaphylactic activity. *E. hirta* by inhibits the passive cutaneous anaphylaxis in rat and active-paw and anaphylaxis in mice. The extracts of *E. hirta* showed suppressive effects on the release of tumor necrosis factor-alpha (TNF-α) and interleuin-6 (IL-6) from anti-DNP-HAS activated rat peritoneal mast cells. Thus, it is reported that *E. hirta* is traditionally used as an herbal drug against Type I allergic disorders.[20] It was also found that the aqueous extract of the plant inhibited the stimulation of prostaglandin E2 from activated rabbit synovial fluid cells, HIG-82 cells upto a large extent. Bioactive compounds possessing anti-inflammatory activity was reported to be highly concentrated in the aqueous extract of the plant.[21]

DIURETIC ACTIVITY

The ethanolic and aqueous leaf extracts of *E. hirta* showed diuresis in rats. It was observed that the extract increased urine output and electrolytes.[22] Various experiments reported that the active components in the water extract of *E. hirta* leaf had similar property of diuretic just like acetazolamide thus proving the diuretic activity of *E. hirta*.

ANTI-OXIDANT ACTIVITY

The methanolic extract of the plant expressed similar anti-oxidant activity as that of green and black tea.[23] The phenolic acids extracted from the aqueous leaf solution showed the anti-oxidant activity. Ferric reducing antioxidant power (FRAP) and 1,1-Diphenyl-2-picryl-hydrazyl (DPPH) assays were conducted to ascertain the efficacy of phenolic extracts. The phenolic acid from *E. hirta* displayed enhanced, free radical scavenging activity, and exhibited protection against oxidative damage to protein.[23] Lipid peroxides, hydroperoxides and both enzymatic and non-enzymatic anti-oxidants express the anti-oxidant potential of the leaf extract.[24]

ANTI-TUMOR ACTIVITY

The anti-tumor activity of the *E. hirta* extract was studied on EL-4 cell lines in Swiss Albino mice. Significant in cell tumor mass was observed after treating it with the plant extract.[25] The methanol extract of the leaves of *E. hirta* showed anti-proliferative activity on Hep-2 cells from human epithelioma of the larynx.[26] It was also evaluated that the methanolic extract and quercetin exhibited mutagenic and anti-mutagenic activity.[27]

ANTI-APOPTOTIC ACTIVITY

In the studies conducted by Kwan *et al.*[28] it was revealed that *E. hirta* showed significant inhibition of the survival of breast cancer cell lines MCF-7 cells and the half inhibitory concentration (IC_{50}) values were 25.26 μg/mL at 24 h. Microscopic studies conducted expressed that *E. hirta* treated cells showed remarkable morphological characteristics of apoptosis. *E. hirta* extract also expressed an ignorable influence on the l*actate dehydrogenase* leakage. The flow cytometry study confirmed that *E. hirta* extract induced apoptosis in MCF-7 cells. *E. hirta* also induced DNA fragmentation in MCF-7 cells. Above all, *E. hirta* treatment resulted in the accumulation of cells at the S and G_2/M phases and apoptosis.[28]

ANTI-DIABETIC ACTIVITY

Ethanolic and ethyl acetate extracts of *E. hirta* were used to examine the anti-diabetic activity. Using the α-glusocidase inhibitor method the extract was assayed *in vitro*. A significant reduction in the blood glucose level was observed in streptozotocin induced diabetic mice on treatment with ethanolic extract of leaf, flower and stem of the plant.[29] Subramanian *et al.*[24] treated the experimental diabetic rats with the leaf extract of *E. hirta* and found the anti-diabetic property of the extract.[24]

ANXIOLYTIC AND SEDATIVE ACTIVITY

The hydroalcoholic extract of *E. hirta* was used to examine anxiolytic property of the plant in chronically stressed rats. To evaluate the mechanism for the anxiolytic action of the drug, antagonists of the GABAA receptor-benzodiazepine receptor-Cl channel complex with *E. hirta* were used together, showed marked anti-anxiety activity in chronic immobilization stress.[30]

ANTI-VENOM ACTIVITY

It is reported that the methanolic extract of *E. hirta* inhibited the venom enzymes under the *in vitro* conditions, thereby reducing the ration of edema in the mice. The evidences were collected by the histopathological analysis of the vital organs. The content of phenolic compound was also found to be quite elevated and the plant was found to be highly rich with the contents of ellagic acid, quinic acid and gallic acid. These compounds well known for their ability to inhibit venom proteases.[31]

IMMUNOSTIMULATORY ACTIVITY

Pratheepa and Sukumaran[32] worked with the leaf extract of *E. hirta* with the objective of studying its immunostimulatory activity. The study was conducted on a medicated fish which was infected with *Aeromonas hydrophila* pathogen. It was reported by them that the count of red blood cells and white blood cells gradually increased with the higher dose concentration of the plant leaf extract. The leaf extract was also able to induce immune response of antibodies. The extract also helped in the elimination of pathogens from the kidney and blood of the fish. Thus, their work suggested that *E. hirta* possessed immunostimulatory activity by stimulating both specific and non-specific immunity at elevated concentrations.[32]

WOUND HEALING ACTIVITY

Studies conducted by Upadhyay *et al.*[33] reveals that the methanol extract of the *E. hirta* possess wound healing activity as it showed potentially high anti-microbial activity against *Escherichia coli* and *Klebsiella pneumoniae* along with the fibroblast proliferating activity. In their study, they concluded that the wound healing activity and collagen production in wounded tissues is governed by the Smad-mediated proteins.[33] The triterpenes extracted from the stems, roots and leaves of *E. hirta* showed anti-microbial activity and are commonly used for wound healing and for the treatment of boils.[34]

ANTI-INFLAMMATORY ACTIVITY

Ahmad *et al.*[35] worked with the plant extract whose traditional use for the treatment of a variety of diseases drove their interest to check for the anti-inflammatory effect of it. They initiated the study with the aim

Table 1 Shows the several of activities of *Euphorbia hirta*

Activity	Action	Study done by
Anti-bacterial activity	Plant extracts were used to check the anti-bacterial activity in Escherichia coli, Staphylococcus aureus, Pseudomonas. aeruginosa, and Bacillus subtilis and the results showed reduced growth of these bacteria.	Vijaya *et al.*, 1995 Jackson *et al.*, 2009 Suresh *et al.*, 2008 Ogbulie *et al.*, 2007 Nelofar *et al.*, 2006
Anti-diarrheal activity	The flavonoid called quercitin present in the leaf extract showed anti-diarrheal activity by increasing the colonic fluid absorption in the presence of secretagogue compounds	Galvez *et al.*, 1993 Hore *et al.*, 2006
Anti-allergic activity	The ethanolic extract of E. hirta show suppressive effects on the release of TNF-α and IL-6 from anti-DNP-HAS activated rat peritoneal mast cells thus act as an anti-allergic agent.	Youssouf *et al.*, 2007
Diuretic activity	The ethanolic extract when given to rat showed increased urine output thus enhancing the diuresis.	Johnson *et al.*, 1999
Anti-oxidant activity	The methanolic extract showed the anti-oxidant activity. The FRAP and DPPH assays proved the activity of E. hirta extract acting against oxidative damage to protein.	Sharma and Prasad 2008
Anti-tumor activity	The methanol extract of the leaves of E. hirta showed anti-proliferative activity on Hep-2 cells from human epithelioma of the larynx thus proving its anti-tumor activity.	Sandeep and Chandrakant, 2011 Brindha *et al.*, 2010 Daphne *et al.*, 2009
Anti-diabetic activity	Reduction in the blood glucose level was observed in streptozotocin induced diabetic mice on treatment with ethanolic extract of leaf, flower and stem of the plant	Widharna *et al.*, 2010
Anxiolytic and sedative activity	The antagonists of the GABAA receptor-benzodiazepine receptor-Cl channel complex with E. hirta were used together, and anxiety in the EPM showed marked anti-anxiety activity in chronic immobilization stress	Anuradha *et al.*, 2008

of determining the anti-arthritic effects of *E. hirta* in the mouse models which were the adjuvant of arthritis. The effect of the plant extract was studied on the pro-inflammatory and anti-inflammatory cytokines. A substantial decrease was seen in the level of pro-inflammatory cytokines and an up-regulated anti-inflammatory cytokine effect was recorded. Thus, *E. hirta* is regarded as a promising treatment for arthritis and other inflammatory diseases.[35]

TOXICITY STUDIES

E. hirta is widely used as ethnomedicine due to its various benefits. Thus, the need of toxicity, check arose in the mind of various researchers and Yuet Ping *et al.*[36] went ahead with it. The conducted the study for evaluation of acute and subchronic toxicity on Sprague Dawley rats. The extract dose did not express any signs of acute toxicity or mortality on any of the rats. Long term oral administration of the plant extract showed no variation in the food or water consumption, body weight, biochemical and haemotological parameters etc. therefore, the team concluded that the plant extract does not possess acute or sub-chronic toxicity.[36]

CONCLUSION

In this review of *E. hirta,* a summary of its phytochemistry, anti-bacterial activity, anti-diarrheal activity, anti-allergic activity, diuretic activity, anti-oxidant activity, anti-tumor activity, anti-diabetic activity, anxiolytic and sedative activity were discussed in detail. Details furnished in this review will further help in exploring more about other properties associated with it.

CONFLICTS OF INTEREST

No funding source and there is no conflict of interest.

ABBREVIATION USED

DPPH: 1,1-Diphenyl-2-picryl-hydrazyl; **FRAP:** Ferric Reducing Antioxidant Potential; **IC_{50}:** Inhibitory Concentration; **IL-6:** Interleukin-6; **TNF-α:** Tumor Necrosis Factor-Alpha.

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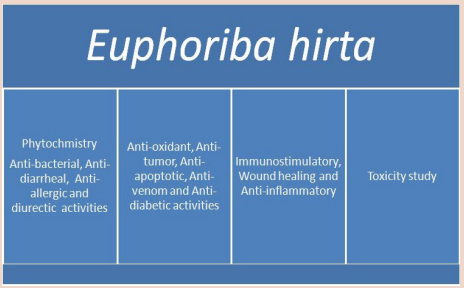
PICTORIAL ABSTRACT



SUMMARY

- *Euphorbia hirta* has been recognized as the medicinally essential phytoconstituents.
- These phytoconstituents have immense potential of this plant in the treatment of numerous diseases.

ABOUT AUTHOR

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