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Review

Insights into the therapeutic potential of the medicinal plant *Euphorbia hirta*

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ABSTRACT

Medicinal plants/herbs have evolved as one of the most essential preventive and therapeutic aid for various diseases. Extracts from medicinal plants have been traditionally used in different parts of the world to replace synthetic drugs, which may have side effects. Naturally occurring plant extracts have gained popularity because of their effectiveness against curing many diseases. The medicinal plant *Euphorbia hirta* has been widely used in traditional medicine because of its diverse medicinal properties such as antibacterial, anti-diarrheal, anti-allergic, diuretic, antioxidant, anti-tumor, anti-diabetic, anxiolytic, and sedative activity. In this review, we will delve insights the various medicinal uses of *Euphorbia hirta*.

Figure : 00 References : 49 Table : 00
KEY WORDS : Anti-bacterial, Anti-cancer, Anti-diabetic, Anti-fungal, *Euphorbia hirta* Linn.

Introduction

Euphorbia belongs to a genus of plants within the family Euphorbiaceace. Taxonomist and botanist Carl Linnaeus designated name Euphorbia to this entire genus in physician's honor[35]. In Manipur, it is known as Pakhangba-leiton. *Euphorbia hirta* Linn is also called as snake weed, pill-bearing spurge, asthma weed, and Ara Tanah. The plant has been used popularly in Manipur as a traditional medicine for the treatment of various diseases like skin problems, gastrointestinal disorders, especially intestinal parasitosis, amoebic dysentery, vomiting, diarrhea, and peptic ulcers and mucous membranes such as warts, scabies, fungal afflictions, and measles. The plant extract can treat respiratory disorders such as asthma, bronchitis, laryngeal spasms, hay fever, and colds[51]. The plant extract has the ability to cure complicated health issues involving kidney and hepatic problems. The plant is reported to be localized in India as well as in China, Africa, the Philippines, Malaysia and Australia[18]. The plant has popular diverse biological properties, being effective source of antioxidants, antibacterial, anti-fungal, antimalarial, larvicidal, diuretic, analgesic, and anticancer agents.[14,19,39].

Researchers have reported the phytochemicals of *Euphorbia hirta* Linn and its pharmacological activities. Among the phytochemicals, flavonoids, terpenoids, and phenols are found to be the major constitutents[5].

Botanical features

E. hirta Linn. can achieve maximum height of 80 cm with an erect and slender stem. The plant has broad leaves along with hairy stems and having elliptical and opposite arrangement. The flowers are small with a faint-toothed margin while the fruits are yellow (1-2mm), having hairy capsules with wrinkled seeds. The plant is abundantly located in roadsides, moist areas and grasslands.

Phytochemical analysis

E. hirta Linn. is a popular medicinal plant showing presence of therapeutically active/inactive constituents such as terpenoids, alkaloids, glycosides, flavonoids,

carbohydrates, essential oils, tannins, phenols, and other secondary metabolites[42]. Major flavonoids reported in *E. hirta* Linn. are quercetin, quercitrin, and their derivatives[47]. Many terpenoids are also synthesized in the plants such as taraxerol, alpha-amyrin, beta-amyrin and friedelin[47,12,2]. Other secondary metabolites are also found in *E. hirta* Linn.such as tannic, maleic, ellagic, gallic, and tartaric acid [24]. Several qualitative and quantitative chemical tests were reported by various research groups to create an ethanolic extract profile of the phytochemicals such as total flavonoids and total phenolic content [11,16,20, 26.] The ethyl acetate extract of the plant shows presence of other secondary metabolites such as quercetin, dimethoxy quercetin, and two new prenylated flavonoids known as hirtacoumaroflavonoside and hirtaflavonoside-B characterized as 7-O-(p-coumaroyl)-5,7,4'-trihydroxy-6-(3,3-dimethylallyl)-flavonol-3-O-â-d-glucopyranosyl-(2"'!1"')-O-á-1-rhamnopyranoside and 5, 7, 3',4'-trihydroxy-6-(3, 3-dimethyl allyl)-8-(iso-butenyl)-flavonol-3-C-â-d-glucopyranoside, respectively. Dose-dependent inhibitions of alpha-glucosidase were exhibited in the compounds extracted from *E.hirta* Linn. The 5, 7, 4'-trihydroxyflavone structure was reported as an imperative for the inhibitory activity[33]. The leaf and stem extract of the plant also demonstrated presence of mineral salts, bioactive secondary metabolites, and various other trace elements that can be used as anti-diabetic agents[50].

Bioactive properties of *E. hirta*

Antibacterial activity

The methanolic extract of the flower showed antibacterial activity against dysentery-causing *Shigella* species in the Vero cell line. Flower extracts of *E. hirta* Linn. were found to be non-cytotoxic and effective antibacterial agent[45]. The methanol extract from the leaves of *E. hirta* Linn. demonstrated activity against the fungus *Candida albicans*[15]. Bioactivity of the plant is demonstrated due to presence of alkaloids, glycosides, flavonoids, tannins, proteins, saponins, and sterols [2,3]. Organic extracts of *E. hirta* Linn. leaves were examined for *in-vitro* antibacterial activity against Gram-positive and Gram-negative bacteria. The methanolic extract of the leaf showed good inhibitory properties against Gram positive and Gram negative organisms such as *Staphylococcus aureus*, *Escherichia. coli*, and *Bacillus subtilis* to different extents[29,43]. The Minimum inhibitory concentration (MIC) of the extract against the test organisms like *Escherichia coli, Staphylococcus aureus*, and *Salmonella enteritis* were found to be in the range of 0.1mg/ml[43]. The antibacterial activity of plant was more in the gram-positive bacteria[22]. The plant extract also showed inhibitory activities against *Pseudomonus aeruginosa*[25]. Flavonoids extracted from the roots showed antibacterial activity against *Proteus mirabilis, Candida albicans*, and *Staphylococcus aureus*[38].

Anti-fungal activity

The ethanolic and aqueous extract of the aerial part of the plant showed antifungal activities against *Colletotrichum camellia* Mess., *Botryodiplodia theobromae* Patouiilard, *Pestalotiopsis theae* (Saw) Stey., and *Curvularia eragrostidis* (P. Hennings) Meyer[28].

Anti-dengue/anti-viral activity

The methanolic and dichloromethane extracts of *E. hirta* Linn. showed antiviral activity. The ethyl acetate fraction of *E.hirta* Linn. plant decreased (85%) the plaque forming capacity of dengue virus serotype 1. Altogether, nine (9) compounds were purified from the ethyl acetate fraction of the plant extract. Individually or synergistically, these compounds may have been involved in anti-Dengue activity [41].

Under *in vitro* conditions, the plant's ethanol extract showed 34.7% inhibition against virus serotype 2(DENV-2)[31]. Molecular docking studies using Lead IT (FlexX) and Maestro (Glide) software identified presence of various phytochemicals found in *E.hirta* Linn. such as myricetin, gallic acid, quercetin, rutin, protocatechuic acid, and kaempferol. Of all the phytochemicals, quercetin had the most potent binding with dengue targets such as Dengue methyl transferase (2P40) and Dengue protease (2FOM). *E. hirta* Linn. has potent activity against the Dengue virus[9].

Antioxidant activity

The methanolic extract of *E.hirta* Linn. as well as the phenolic acids extracted from the aqueous leaf extract showed antioxidant activity[32]. Phenolic acids protected against oxidative damage to protein and increased free radical scavenging activity. The leaf extract of *E.hirta* Linn.exhibited antioxidant potential mediated by lipid peroxides, hydroperoxides, as well as both enzymatic and non-enzymatic antioxidants[40].

Wound healing activity

The methanolic extract of the plant also demonstrated wound healing activity[44]. It helped in fibroblast proliferation and demonstrated anti-microbial activity against *Klebsiella pneumoniae* and *Escherichia coli*. Anti-microbial activity was also shown by the triterpenes extracted from stems, roots, and leaves of *E. hirta* Linn.[27].

Anti-allergic activity

The ethanolic extract of the plant inhibited active paw anaphylaxis in mice and passive cutaneous

anaphylaxis in rats. It also suppressed release of tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) from anti-DNP-HAS activated rat peritoneal mast cells. Traditionally, the plant is used as herbal drug against Type I allergic disorders[49]. The aqueous extract of the plant suppressed stimulation of prostaglandin E2 from activated rabbit synovial fluid cells[3].

Anti-inflammatory activity

The ethanolic extract of the plant and its active components were studied in lipopolysaccharide (LPS)-activated macrophage cells (RAW 264.7), a widely accepted inflammation model. The active components showed significant production of anti-inflammatory effect and a dose-related inhibition of LPS-induced nitric oxide production. This plant has potent inhibitory action of nitric oxide and demonstrated more efficacy as compared with indomethacin. However, less significant inhibitory action of *E.hirta* Linn. was revealed on other inflammatory molecules such as PGE_2, TNF alpha, and IL-6[34].

Anti-diabetic effects

Oral application of the ethanolic extracts of *E.hirta* Linn. for 21 days displayed a remarkable decline in blood glucose levels of streptozotocin induced diabetic mouse[17]. The ethyl acetate and ethanolic fraction showed anti-diabetic activity due to the inhibitory activity of alpha-glucosidase and more activity of insulin production from beta cells of islets of Langerhans[46].

Anti-cancer activity

The methanolic and aqueous extracts of *E.hirta* Linn. showed anti-mutagenic effects against the mutagenicity of 2-aminoanthracene as studied using S-9 metabolic activating enzymes. In *Salmonella typhimurium* TA98, the anti-mutagenic activity of methanol extracts and aqueous extracts of the whole plant of *E.hirta* Linn. was exhibited[48].

The anti-tumor activity of the plant extract showed decline in cell tumour mass in Swiss Albino mice [30]. Anti-proliferative activity was also shown by the methanolic leaves extract of *E.hirta* Linn. on Hep-2 cells from human epithelioma of the larynx[3]. The quercetin and methanolic extracts of the plant showed anti-mutagenic and mutagenic activity, respectively[6].

Anti-diarrhoeal effects

The aqueous extract of *E.hirta* Linn. reduced castor oil-induced diarrhea in mice and decreasing the gastrointestinal motility in normal rats[13]. Quercitin extracted in crude form from *E.hirta* Linn. showed anti-diarrheal activity. In the presence of secretagogue compounds, the quercitin enhanced the colonic fluid absorption[6].

Platelet augmentation effects

E.hirta Linn. demonstrated platelet increasing activity. Significant increase in platelet counts in ethanol induced thrombocytopenic Sprague –Dawley rats were observed. Decreased bleeding and clotting time in *E.hirta* Linn -treated rats were observed compared to ethanol induced thrombocytopenic rats.

Oral administration of aqueous extract of *E.hirta* Linn. on the dengue patients showed a significant increase in platelet number. Patients in the 30-35 age group showed a significant increase in platelet count compared to the 14-25 age group[21].

Endophytes associated with *E.hirta*

Various endophytic fungi are reported to be associated with *E.hirta*. An important example includes *Achaetomium sp.* belonging to the family Chaetomiaceae isolated from the roots of *E. hirta*. The fungal isolate produces a red-colored bioactive compound which demonstrated hepatoprotective activity on HepG2 cell lines[10]. The ethyl acetate extract of *Achaetomium* shows presence of flavonoids, phenolics, and tannins as major constituents which contributes to the antioxidant, hepatoprotective, and antibacterial properties[37, 36]. Another endophytic fungus *Nigrospora sphaerica* isolated from *E.hirta* shows antioxidant properties as well[8]. However, meagre studies have been done on endophytic bacterial isolation from *E. hirta*.

Conclusion

Our review gives glimpses of various pharmacoactive properties exhibited by the ethanolic, methanolic, and ethyl acetate extract of *E.hirta* Linn. such as antibacterial, anti-allergic, anti-fungal, anti-cancer, anti-diabetic, anti-inflammatory and wound healing effects.

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