Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2016, 8(1):351-355

Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Hybanthus enneaspermus (L) F. Muell: A phytopharmacological review on herbal medicine

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ABSTRACT

Phytotherapy has proved to be an effective method to treat several health disorders. Hybanthus enneaspermus (L) F. Muell is a perennial medicinal herb which is used in traditional medicine for treating diarrhoea, urinary infections, leucorrhoea, dysuria, inflammation, cholera and sterility. A number of active compounds like alkaloids, dipeptide, isoarborinol, sitosterol, flavonoids, sugars, tannins, etc., are present in this plant. In this review, the phytopharmacological activities of the plant such as antimicrobial, antioxidant, antidiabetic, anti-arthritic, antinociceptive, anti-allergic, anticonvulsant, antihyperlipidemic, nephroprotective, cardioprotective and neuroprotective activities were discussed. Since the plant possess many pharmacological activities, further research work in the field of drug discovery could be carried out on the active compounds isolated from this divine herb.

Keywords: *Hybanthus enneaspermus*, medicinal plant, pharmacological activity

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INTRODUCTION

Medicinal plants play a major role in healthcare and they are recognised by WHO as a key factor in world health. They exhibit a wide range of therapeutic properties. Several medicinal plants are available especially in developing and underdeveloped countries, which are used by the rural individuals. In India, thousands of medicinal plants were used from ancient days for treating diseases. Medicinal plants act as chemical factories, which are capable of synthesising unlimited number of highly complex and active phytochemicals. These plants are constantly screened for their pharmacological activities. The bioactive components present in the plant are further isolated, characterised and formulated as drugs for therapeutic purposes. About hundreds of natural bioactive compounds have been identified and used worldwide [1].

Hybanthus enneaspermus (L) F. Muell (Syn. *Ionidium suffruticosum*), belonging to Violaceae family is an important medicinal herb used from ancient times. The plant is native to Himalayan region and warmer parts of India. It is also distributed in Sri Lanka, tropical Asia, Africa and Australia. It is commonly found in river banks, open grass lands, sandy regions and waste lands. It is a perennial small herb which is used in Ayurveda, Siddha and other traditional medicines for treating ailments. It is also known as “spade flower” and “pink ladies slipper”. In Ayurveda, it is called as “Sthalakamala”. Other names are Ratan purush (Hindi), Nunbora (Bengali), Purusharathna (Kannada), Orithalthamara (Malayalam), Orilai thamarai (Tamil), Rathnapurusha (Sanskrit) and Rathanparas (Marathi).

The phytocompounds present in the plant include alkaloids, dipeptide, isoarborinol, sitosterol, flavonoids, sugars, tannins, etc. Recent research work proved that the plant possess medicinal activities against number of dreadful diseases. In the present review, the morphological characteristics, phytochemical constituents and phytopharmacological activities of *H. enneaspermus* were reported.

Taxonomic Classification of *Hybanthus enneaspermus*

Kingdom	-	Plantae
Phylum	-	Tracheophyta
Class	-	Magnoliopsida
Order	-	Malpighiales
Family	-	Violaceae
Genus	-	*Hybanthus*
Species	-	*enneaspermus*

Morphological Characteristics

The perennial herb *H. enneaspermus* grows up to 15-30 cm height with many ascending branches (Figure 1). Roots are spindle shaped, rough and have sparingly branched stem which is woody at the base. The leaves are linear, lanceolate, margin serrate, stipules acuminate and 4-5 cm long. The flowers are pink-purple spade shaped, axillary, solitary and zygomorphic. The fruits are capsule (5-8 mm) and sub-globose with 5-12 seeds. Sepals are five, lanceolate, acute and ciliate. Petals five, pink coloured and unequal. Stamens are five, connate and puberulous [2].

Figure 1: *Hybanthus enneaspermus* plant

Phytochemical Constituents

The phytocompounds present in *H. enneaspermus* have been extensively investigated. The chief chemical constituents include alkaloids, flavonoids, steroids, terpenoids, phenols, dipeptide, isoarborinol, sitosterol, sugars and tannins. Awobajo *et al* [3] reported the presence of flavonoids, cardiac glycosides, cyanogenic glycosides, anthraquinone glycosides, saponins, tannins and hexose sugar in the aqueous leaf extract of *H. enneaspermus*. The GC-MS analysis of *H. enneaspermus* revealed the presence of more than 10 compounds such as D-mannitol, tetradecanediol, phytol, 2-piperdinone, cedarn-diol, 2-mono linoleo glycerol trimethyl silyl ether and silane [4]. Ghani reported the presence of higher amount of amino acids like valine, leucine and glutamic acid in nectar of *H. enneaspermus* [5]. These active phytocompounds are mainly responsible for the pharmacological activity of the plant.

Traditional Uses

In traditional medicines, *H. enneaspermus* is used for the treatment of diarrhoea, urinary infections, leucorrhoea, dysuria, inflammation, cholera and sterility [6]. The whole plant is used as a general tonic for pregnant women. The root infusion is used as a diuretic for gonorrhoea and urinary infections. The decoction of leaf and tender stalks are used as a demulcent. Leaves are traditionally used as an external application for the treatment of wounds. Dried leaf powder is used to treat asthma. The fruit possess antivenom activity against snake and scorpion sting [7].

In Ayurvedic literature, the plant is used to treat ailments such as, urinary calculi, painful dysentery, vomiting, burning sensation, blood troubles, asthma, epilepsy and breast tone [8]. In Siddha medicine, it is used to enhance milk secretion in women. External application of the herb relieves ulcer and head ache. It increases libido and used to treat stress-related disorders.

Pharmacological Aspects of *H. enneaspermus*

Antimicrobial activity

Microorganisms are major disease-causing agents which infect both animals and plants. Antimicrobial agents act on infections caused by the microbes. Plant-based antimicrobial drugs are more efficient when compared with synthetic drugs. Secondary metabolites produced by the plants possess more bioactive compounds which can be effectively used as antimicrobial agents.

Antibacterial activity

Sahoo *et al* [9] reported the antibacterial activity of different solvent extracts of *H. enneaspermus* against urinary tract pathogens (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis* and *Staphylococcus aureus*). In disc diffusion assay, ethanol and aqueous extracts showed broader spectrum of inhibition at lesser concentration, when compared with chloroform and petroleum ether extracts. The aqueous herbal extract of *H. enneaspermus* inhibited the most resistant root canal organism *E. faecalis* at 50% concentration [10].

Antifungal activity

The antifungal activity of different extracts of *H. enneaspermus* was reported in *Aspergillus niger*, *Aspergillus flavus* and *Aspergillus fumigatus*. The fungal spots isolated from wet clothes were cultured and the zone of inhibition was determined by disc diffusion assay. Maximum inhibitory effect was seen in methanol extract followed by petroleum ether and chloroform extract [11]. The *in vitro* study of *H. enneaspermus* extracts against aflatoxin-producing fungi (*A. flavus* and *A. fumigatus*) and human pathogenic fungi (*Candida albicans* and *Candida tropicalis*) exhibited significant antifungal activity [12]. In another study, the ethanolic extract of *H. enneaspermus* showed significant antifungal activity against *C. albicans* and *A. niger* [4]. The antimicrobial activity might be due to the presence of biologically active components like alkaloids, flavonoids, etc.

Antiviral activity

The human immunodeficiency virus (HIV) infection is a fatal disease spreading rapidly throughout the world. As there is no satisfactory curative drug, more research work has been carried out in plant-based products. Recently, Anbalagan *et al* [13] reported the anti-HIV activity of *H. enneaspermus* leaf extract by reverse transcriptase inhibition assay. The methanol and hexane extracts showed positive result and ethanol, chloroform and petroleum ether extracts showed no inhibition.

Antioxidant activity

More than hundred disorders in humans including cancer, arthritis, gastritis, etc., are due to accumulation of free radicals in the body. They are produced by various chemical and physical factors. Antioxidants act as potential agents to treat the free radical-mediated diseases. The hydroethanolic extract of *H. enneaspermus* along with paracetamol exhibited significant antioxidant activity and decreased lipid peroxidation activity in rats [14]. The *in vitro* study of alcoholic extract of *H. enneaspermus* showed higher antioxidant activity with good reducing power against reactive oxygen species like DPPH radical, nitric oxide, hydrogen peroxide and deoxyribose [15]. The ethyl acetate extract of *H. enneaspermus* showed strong antioxidant activity due to the presence of phenolic compounds. In another study, the antioxidant potential of field-grown plant was compared with *in vitro* grown calli of *H. enneaspermus*. In all the free radical scavenging assays, the *in vitro*-cultured samples showed increased activity than the field-grown plants [16].

Antidiabetic activity

Diabetes mellitus is a metabolic disorder which occurs worldwide due to defect in insulin production. Under severe conditions, it leads to complications in kidney, eye, nervous system and heart. Recently, more research work has been focussed on the treatment of diabetes by phytodrugs. Vennila and Pavithra evaluated the alpha-amylase and alpha-glucosidase inhibitory activity of various solvent extracts of *H. enneaspermus*. Ethanol extract showed maximum inhibitory effect for both the enzymes (alpha-amylase: 200 µg-84.61%; alpha-glucosidase: 200 µg-83.02%) when compared with petroleum ether, aqueous and acetone extracts [17]. Patel *et al* [15] reported the antidiabetic potential of alcoholic extract of *H. enneaspermus* in rat hemi-diaphragm. Blood glucose level was reduced in streptozotocin-induced diabetic rat model. Moreover, improvement in body weight was observed which indicated its ability to reduce hyperglycemia.

Anti-arthritic activity
Rheumatoid arthritis is an autoimmune disorder which causes inflammation in a joint. Since the side effects and toxicity of synthetic drugs are higher, more effective natural drugs are required. Tripathy *et al* [18] evaluated the anti-arthritic potential of alcoholic and aqueous extracts of *H. enneaspermus* on Freund's adjuvant-induced arthritis in albino rats. The paw thickness decreased for the rats treated with both the extracts. In chronic phase, alcoholic extract (59.4%) exhibited more activity than the aqueous extract (57.4%).

Antinociceptive activity
The commercially available synthetic analgesic drugs cause several side effects such as kidney damage, constipation, gastrointestinal irritation, etc. Use of plant-derived products reduces the harmful side effects and cost of medication. Afolabi *et al* [19] evaluated the antinociceptive effect of ethanolic extract of *H. enneaspermus* in albino rats by tail immersion and formalin test. The animals treated with 500 mg/kg and 1000 mg/kg doses of *H. enneaspermus* extract showed increased tail flick latency when compared with the animals treated with the standard drug, acetaminophen. In formalin test, the animals treated with 1000 mg/kg dose of *H. enneaspermus* extract significantly reduced the paw licking time when compared with acetaminophen. In another study, the analgesic activity of *H. enneaspermus* extract was proved by hot plate, radiant heat tail flick and tail immersion methods. In all the tests, ethanol and petroleum ether extracts at 200 mg/kg doses showed more significant antinociceptive activity. The plant extracts increased the stress tolerance capacity of the animals [20].

Anti-allergic activity
Allergy is an exaggerated response of the immune system when it encounters a foreign antigen like dust, pollen, mold spores and chemicals. The physiological effects due to allergic reactions lead to various diseases. The *in vitro* study of ethanol and petroleum ether extracts of aerial parts of *H. enneaspermus* in albino mice proved the anti-allergic activity by milk-induced leucocytosis and eosinophilia methods. In both the tests, ethanolic extract exhibited higher level of inhibition at a dose of 200 mg/kg when compared with the petroleum ether extract. The flavonoids and polar constituents in the plant mainly contribute for the anti-allergic activity [20].

Anticonvulsant activity
The conventional anticonvulsant drug used for neurological disorder, epilepsy causes adverse side effects and neurotoxicity. The plant *H. enneaspermus* has been traditionally used for the treatment of epileptic fits. Hemalatha *et al* [21] reported the anticonvulsant activity of aqueous and ethanolic extracts of *H. enneaspermus* using maximal electrical shock and strychnine-induced convulsion models. Aqueous extract at the doses of 200 mg/kg and 400 mg/kg showed 50% and 80% protection respectively. The percentage of mortality was decreased and no neurotoxicity was observed in animals.

Antihyperlipidemic activity
Hyperlipidemia is the increased level of lipid including cholesterol and triglycerides in the blood. It increases the risk of cardiovascular diseases, diabetes, hypertension, stroke, and kidney damage. Hyperlipidemia was induced by feeding the wistar albino rats with high-fat diet. The hydroalcoholic extract of *H. enneaspermus* exhibited antihyperlipidemic activity at 400 mg/kg dose. In acute toxicity study, no sign of toxicity and mortality was observed in animals treated at a dose of 2000 mg/kg [22].

Nephroprotective activity
The kidneys are the most important organ which removes the waste from the body. If there is any defect in the removal process, the wastes would accumulate in the blood and leading to renal damage. Excretion of many drugs and their metabolites through kidney also leads to nephrotoxicity. The *in vitro* study of alcoholic and aqueous extracts of *H. enneaspermus* in cisplatin-induced rat models proved the nephroprotective activity. The alcoholic (250 mg/kg and 500 mg/kg) and aqueous extracts (500 mg/Kg) normalised the raised blood urea, blood protein and serum creatinine. Extracts protected the kidney from lipid peroxidation damage and increase in body weight was observed. The activity of alcoholic extract was more potent than the aqueous extract [23].

Cardioprotective activity
Cardiovascular disease which arrests the cardiac function is the leading cause of death worldwide. Many research works has been focussed on an alternative medicine without side effects for this defect. Medicinal plants rich in polyphenols may act as potential agents to reduce the risk for heart disease. Radhika *et al* [24] reported the cardioprotective activity of *H. enneaspermus* in isoproterenol-induced rats. Myocardial infarction was induced in rats by administration of isoproterenol. When the myocardial infarcted rats were treated with ethanolic extract of *H. enneaspermus*, it reduced the oxidative stress by decreased lipid per oxidation, reduced glutathione and normalised the levels of cardiac marker enzymes like creatine kinase, lactate dehydrogenase, serum glutamic oxaloacetic transaminase, serum glutamate pyruvate transaminase and cardiac protein troponin I in the histological studies.

Neuroprotective activity

Plant-based products like essential oils have been used traditionally for treating central nervous system (CNS) disorders. Most of the depressant drugs cause unavoidable side effects which affect the other vital organs. Kar *et al* [25]reported the CNS activity of ethanolic and aqueous extracts of *H. enneaspermus* in mice models by maze test (plus, Y-maze), barbiturate and alcohol-induced sleeping time, tail suspension test, despair test, head dip test, locomotor activity and motor coordination test. The mice were administered orally with doses of 250 and 500 mg/kg of each of the extract. Diazepam (1mg/kg), chlorpromazine (5 mg/kg) and imipramine (30 mg/kg) were administered intraperitoneally as standard drugs. In all the tests, the animals treated with *H. enneaspermus* extract exhibited significant activity than the animals treated with standard drugs.

CONCLUSION

Plants have been used by humans and animals for their food and health purposes from ancient days. The medicinal plant, *H. enneaspermus* is widely used as a folk medicine to treat number of ailments. The pharmacological activities of *H. enneaspermus* discussed in this review could be useful to carry out further research work in this plant leading to active compounds isolation which can be used as potential drugs for life-threatening diseases after clinical trials.

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