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Potential Applications of *Euphorbia hirta* in Pharmacology

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1. Introduction

Euphorbia is a genus of plants belonging to the family Euphorbiaceae. Botanist and taxonomist Carl Linnaeus assigned the name *Euphorbia* to the entire genus in the physician's honor. *Euphorbia hirta* is a very popular herb amongst practitioners of traditional herb medicine, 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. In this chapter we explore those investigations related to their pharmacological activities (see the section 2.2).

2. *Euphorbia hirta*

2.1 Chemical Composition of *Euphorbia hirta*

Phytochemical analysis of *Euphorbia hirta* (*E. hirta*) revealed the presence of reducing sugar, alkaloids, flavonoids, sterols, tannins and triterpenoids in the whole plant. Some of them are well known to possess biological activities (as shown in table 1).

2.1.1 Flavonoids

Epidemiological studies have revealed that polyphenols, including flavonoids, provide a significant protection against development of several chronic diseases such as cardiovascular diseases, cancer, diabetes, infections, aging, and asthma. Two flavonoids have been isolated from *E. hirta*, namely quercitrin and myricitrin (Johnson et al, 1999; Chen, 1991). In general, flavonoids have been reported to possess several proven medicinal properties including antioxidant (Kandaswami & Middleton, 1994), anti-allergic (Singh et al, 2006), antiinflammatory component of asthma (Miller, 2001) and antidiarrheal activity (Galvez et al, 1993; Mallavadhani et al, 2002). Many of the biological actions of flavonoids have been shown to attribute to their antioxidant properties, either through their reducing capacities or as a result of their possible influence on intracellular redox status (Williams et al, 2004). Flavonoids can also interact selectively within the mitogen-activated protein

(MAP) kinase signalling pathway, thereby existing antiinflammation (Lee, 2011) and anti-cancer activity (Ding et al, 2010).

2.1.2 Sterols

Sterols were isolated from *E. hirta* and chemically characterized as cycloarternol, 24-methylene-cycloarternol, β-sitosterol, euphorbol hexacozonate, 1-hexacosanol, tinyaloxin, campesterol and stigmasterol (Atallah and Nicholas, 1972; Galvez et al, 1993; Johnson et al, 1999). The compounds 24-methylene-cycloartenol and β-sitosterol have also been found to exert significant and dose-dependent anti-inflammatory effects, when treating acetate-induced ear inflammation (Martinez-Vazquez et al, 1999).

2.1.3 Tannins

Tannins are not widely known for their anti-inflammatory potential. *E. hirta* possesses a few such chemicals. Phytochemicals work synergistically, however, and therefore these tannins may assist in the anti-inflammatory action of the plant. *E. hirta* presents three hydrolysable tannins, namely, dimeric hydrolysable tannin, euphorbin E and the dimeric dehydroellagitannins, euphorbin A and euphorbin B (Yoshida et al, 1990). The following tannins from the leaves of *E. hirta* were also isolated by using physicochemical and spectroscopic methods: gallic acid, 2,4, 6-tri-O-galloyl-D-glucose and 1,2,3,4, 6-penta-O-galloyl-β-D-glucose as well as the quinic acid ester, 3,4-di-O-galloylquinic acid (Chen 1991).

2.1.4 Triterpenoids

Research has shown that triterpenoids possess anti-inflammatory properties. The triterpenes α-amyrin, β-amyrin, taraxerone (EH-1), taxerol as well as β-amyrin acetate have been identified from *E. hirta* (Martinez-Vazquez et al, 1999; Pinn, 2001; Mukherjee et al, 2004). Extracts of the plant were found to contain β-amyrin, which displayed a significant and dose dependent anti-inflammatory activity against acetate-induced ear inflammation (Martinez-Vazquez et al, 1999) or LPS-induced inflammatory model (Shih et al, 2010). Two additional triterpenoids, namely, taraxerone and 11α, 12α-oxidotaraxerol, have also been found in *E. hirta*. These compounds induce both antibacterial and antifungal effects, as tested against fourteen pathogenic bacteria (Abu-Sayeed et al, 2005).

2.2 Pharmacological effects of *Euphorbia hirta*

2.2.1 Effects of *E. hirta* on GI system

Protective effect of *E. hirta* against antitubercular drug-induced cytotoxicity was observed in freshly isolated hepatocytes. Antitubercular drug intoxication alters liver function by affecting aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase, triacylglycerol, cholesterol, total protein, albumin, total and direct bilirubin. A dose-dependent increase in percent viability was obtained when antitubercular drug exposed HepG2 cells were treated with different concentrations of alcoholic extract of *E. hirta* (125, 250, 500 and 1000 mg/mL). The effectiveness of liver protection was comparable to a standard hepatoprotective drug silymarin (Brindha et al, 2010). The antihepatotoxic

effect of *E. hirta* extracts were also evaluated in experimental models of liver injury in rats induced by CCL4 or paracetamol (Tiwari et al, 2011). Carbon tetrachloride and paracetamol are known to cause liver damage (Recknagel, 1983; James et al., 2003). When administered to rats, they act by inducing oxidative damages to liver cells which leads to cellular necrosis. *E. hirta* exhibited a 70 and 80% hepatoprotection compared to the 80 and 90% one exhibited by silymarin in CCL4 or paracetamol-injured rats, respectively. The extract *E. hirta* was demonstrated effectively in protecting the liver from toxic hepatitis.

Components	Chemicals	Possible biological function	References
Flavonoids	Quercitrin; Myricitrin	Antioxidation; Anti-allergy; Antibacterial activity; Molluscicidal activity; anti-diarrheal activity	Galvez et al, 1993; Kandaswami & Middleton, 1994; Mallavadhani et al, 2002; Singh et al, 2005; Singh et al, 2006; Park & Lee, 2006; Sudhakar et al, 2006; Rajeh et al, 2010; Ding et al, 2010; Lee, 2011
Sterols	Cycloarternol; 24-methylene-cycloarternol; β-sitosterol; euphorbol hexacozonate; 1-hexacosanol; tinyaloxin; campesterol; stigmasterol	anti-inflammatory effects	Martinez-Vazquez et al, 1999
Tannin	euphorbin E; euphorbin A; euphorbin B; gallic acid; 2,4, 6-tri-O-galloyl-D-glucose; 1,2,3,4, 6-penta-O-galloyl-β-D-glucose; 3,4-di-O-galloylquinic acid	anti-inflammatory activity	Yoshida et al, 1990; Chen 1991
Triterpenoids	α-amyrin; β-amyrin; taraxerone; taxerol; β-amyrin acetate; taraxerone; 11α, 12α-oxidotaraxerol	anti-inflammatory activity; anti-pruritic activity; antidiabetic activity; antimicrobial activity	Martinez-Vazquez et al, 1999; Pinn, 2001; Mukherjee et al, 2004; Abu-Sayeed et al, 2005; Park & Lee, 2006; Shih et al, 2010

Table 1. Chemical compounds isolated from *Euphorbia hirta.*

Aqueous leaf extract of *E. hirta* was shown to decrease the gastrointestinal motility in normal rats and decreased the effect of castor oil-induced diarrhoea in mice (Hore et al, 2006; Galvez et al, 1993). The anti-diarrheal activity of *E. hirta* was also effective in arachidonic acid- and prostaglandin E2-induced diarrhoea (Galvez et al, 1993). Quercetin-3-O-β-D-rhamnoside, a flavonoid, was found to be the active component with anti-diarrheal activity (Galvez et al, 1993; Mallavadhani et al, 2002).

2.2.2 Effects of *E. hirta* on analgesic, antipyretic and anti-inflammatory actions

E. hirta exists a dose-dependent analgesic action against chemical (writhing test) and thermic (hot plate test) stimuli from the doses of 20 and 25 mg/kg. This analgesic action was inhibited by pretreatment of naloxone, a specific morphinic antagonist compound. Therefore, it exerts central analgesic properties. In addition, *E. hirta* was effectively against acute pain in carrageenan-induced edema model (Lanhers et al, 1991). An antipyretic activity was obtained at the sedative doses of 100 and 400 mg/kg, on the yeast-induced hyperthermia (Lanhers et al, 1991).

Antiinflammatory effects of *E. hirta* were shown in 12-o-tetradecanoyl phorbol acetate-induced ear edema (Martinez-Vazquez et al, 1999; Lanhers et al, 1991). Although *E. hirta* was ineffective in Freund's adjuvant-induced rheumatoid arthritis model, it reduced the inflammatory hyperalgia of rheumatoid arthritis (Lanhers et al, 1991). The molecular pharmacology basis of this anti-inflammatory effect is revealed in an established inflammation model in lipopolysaccharide (LPS)-activated macrophages (fig 1). In the concentration range without showing cytotoxicity, *E. hirta* produced a remarkable anti-inflammatory effect via its active component of beta-amyrin and showed a dose-related inhibition against LPS-induced NO production (Camuesco et al, 2004; Comalada et al, 2005; Shih et al, 2010). The extract of *E. hirta* and beta-amyrin are able to block most of the iNOS protein functions and NO induction (fig 2). The extract of *E. hirta* and beta-amyrin were not as potent as Indomethacin in preventing LPS-induced PGE2 production (Shih et al, 2010). This indicated that the extract of *E. hirta* and its active component, beta-amyrin, may have less gastrointestinal adverse effect than indomethacin does. The extract of *E. hirta* and its component beta-amyrin could therefore be new selective NO inhibitors with great potential in treating endotoxin-induced inflammation.

2.2.3 Inhibition of allergic reactions and asthma by *E. hirta*

E. hirta has been used to treated asthma as a folk medicine (Watanabe et al, 2005). *E. hirta* functions for the treatment of asthma is probably through synergistic anti-inflammatory and antioxidant activities of especially the flavonoids, sterols and triterpenoids (Park & Lee, 2006). Asthma has long been associated with chronic inflammation and an overall increase in reactive groups and oxidative stress (Nadeem et al, 2003). *E. hirta* also existed significant activity to prevent early and late phase allergic reactions and thereby asthma. *E. hirta* reduced asthma attack has been shown as effective as corticosteroid did in the BALB/c asthmatic mouse mode (Ekpo & Pretorius, 2008). The possible active component of *E. hirta* is thought to be Quercitrin. *E. hirta* ethanol extract significantly prevented eosinophil accumulation and eosinophil peroxidase activity and reduced the protein

content in bronchoalveolar lavage fluid in a 'mild' model of asthma (Singh et al, 2006). Taken together, *E. hirta* is a very potent herb medicine in treatment of asthma. Ethanol extract of *E. hirta* has also been shown to inhibit polysorbate 80-induced degranulation of isolated peritoneal mast cells *in vitro*. Thus anti-inflammatory activity of *E. hirta* could be attributed to mast cell membrane stabilization, thereby inhibiting the release of inflammatory mediators (Ramesh & Padmavathi, 2010). *E. hirta* ethanol extract also significantly inhibited dextran-induced rat paw edema, attenuated the release of interleukin-4 (IL-4) and augmented IFN-gamma in ovalbumin-sensitized mouse splenocytes (Singh et al, 2006). Anaphylactic allergic reaction is a life-threatening syndrome induced by the sudden systemic release of inflammatory mediators such as histamine and pro-inflammatory cytokines and can be elicited by various stimulators including compound 48/80 (N-methyl-p-methoxy-phenethylamine) and anti-IgE (Paul et al, 1993). Compound 48/80-induced mortality could also be reduced by *E. hirta* ethanol extract administration in Wistar rats (Youssouf et al, 2007).

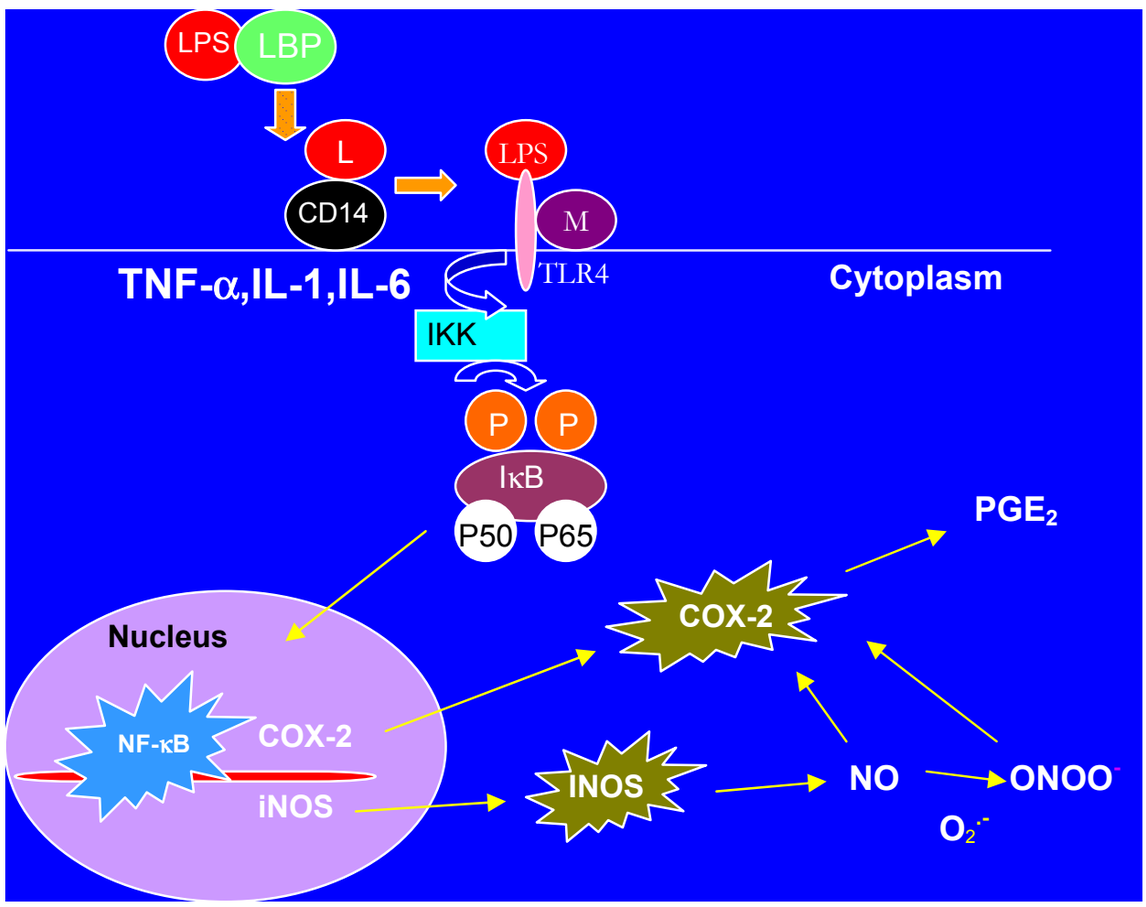


Fig. 1. Inflammatory model in LPS-activated Macrophage.

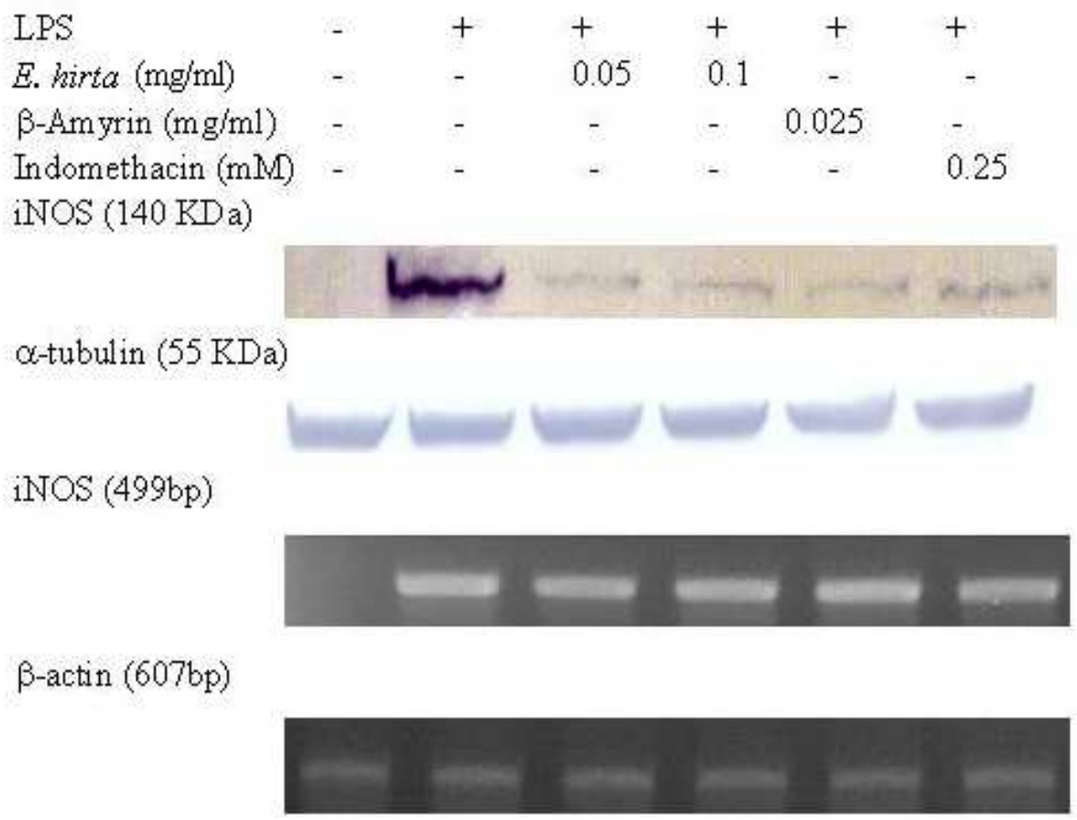


Fig. 2. Inhibition of *E. hirta* and β-amyrin on LPS-induced iNOS gene and protein expression.

2.2.4 Burn wound healing of *E. hirta*

Tissue damage from excessive heat, electricity, radioactivity or corrosive chemicals that destroy (denature) protein in the exposed cells is called a burn. Burns disrupt haemostasis because they destroy the protection afforded by the skin. They permit microbial invasion and infection, loss of body fluid and loss of thermoregulation. Various extracts of *E. hirta* exhibited antimicrobial activity against various microbes including those causing burn and wound infections like Pseudomonas aeruginosa and Staphylococcus aureus (Sudhakar et al, 2006; Rajeh et al, 2010). Hence, *E. hirta* could be beneficial in the management of burn wounds. The ethanol extract of whole plant of *E. hirta* was screened for burn wound healing activity in rats as 2% W/W cream. The study was carried out based on the assessment of percentage reduction in original wound. *E. hirta* was showed significant burn wound healing activity (Jaiprakash et al, 2006).

2.2.5 Effects of *E. hirta* on anti-oxidation

Free radicals have been claimed to play an important role in affecting human health by causing several chronic diseases, such as cancer, diabetes, aging, atherosclerosis, hypertension, heart attack and other degenerative diseases (Raghuveer et al, 2009). These free radicals are generated during body metabolism. Exogenous intake of antioxidants can

help the body scavenge free radicals effectively. There is a noticeable interest in antioxidants, especially in those which can prevent the presumed deleterious effects of free radicals in the human body, and to prevent the deterioration of fats and other constituents of foodstuffs. In both cases, there is a preference for antioxidants from natural rather than from synthetic sources (Molyneux et al, 2004). At present, most of the antioxidants are manufactured synthetically. The main disadvantage with the synthetic antioxidants is the side effects *in vivo* (Ramamoorthy et al, 2007). Previous studies reported that butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) accumulate in the body and result in liver damage and carcinogenesis (Jiangning et al, 2005). Phytochemical screening of *E. hirta* revealed the presence of several chemicals, including flavanoids, which may be responsible for its strong anti-oxidative activity (Basma et al, 2011). The anti-oxidant activity of *E. hirta* was comparable with that of ascorbic acid and found to be dose dependent (Basma et al, 2011).

2.2.6 Antidiabetic and free radicals scavenging potential of *E. hirta*

Diabetes mellitus is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It is well documented that chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and eventually the failure of organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Daily treatment of ethanol and petroleum ether flower extracts of *E. hirta* for three weeks significantly reduced alloxan-induced hyperglycemia, triglycerides and cholesterol (Kumar et al, 2010). Other biochemical parameters such as serum creatinine, urea and alkaline phosphatase levels were also found to be decreased whereas total proteins were found to be increased after treatments. Both extracts of *E. hirta* have significant antioxidant activity compared to other well characterized, standard antioxidant systems. Free radical scavenging potential was assessed against DPPH. The reductive capabilities of extract were compared with ascorbic acid and BHA. The extract showed dose dependent reducing power. This additional antioxidative effect of *E. hirta* may provide extract benefit in preventing oxidative-induced complications in diabetic patients.

2.2.7 Effects of *E. hirta* on anti-infection

The antimicrobial activities of the methanol extracts of *E. hirta* leaves, flowers, stems and roots were evaluated against some medically important bacteria and yeast using the agar disc diffusion method (Sudhakar et al, 2006; Rajeh et al, 2010; Singh et al, 2011). Four Gram positive (*Staphylococcus aureus*, *Micrococcus sp., Bacillus subtilis* and *Bacillus thuringensis*), four Gram negative (*Escherichia coli, Klebsiella pneumonia, Salmonella typhi* and *P. mirabilis*) and one yeast (*Candida albicans*) species were screened. Inhibition zones ranged between 16-29 mm. Leaves extract inhibited the growth of all tested microorganisms with large zones of inhibition, followed by that of flowers, which also inhibited all the bacteria except *C. albicans*. The most susceptible microbes to all extracts were *S. aureus* and *Micrococcus* sp. Root extract displayed larger inhibition zones against Gram positive bacteria than Gram negative bacteria and had larger inhibition zones compared to stem extract. The lowest MIC values were obtained with *E. coli* and *C. albicans*, followed by *S. aureus* and *P. mirabilis*. All the other bacteria had MIC values of

100.00 mg/mL. Scanning Electron Microscopic (SEM) studies revealed that the cells exposed to leaf extract displayed a rough surface with multiple blends and invaginations which increased with increasing time of treatment, and cells exposed to leaf extract for 36 h showed the most damage, with abundant surface cracks which may be related to final cell collapse and loss of function. Time-kill assay of *C. albicans* indicated a primarily fungicidal effect at 1- and 2-fold MIC. Therefore, methanol extract of *E. hirta* possessed a broad spectrum of antimicrobial activity against studied bacterial strains. However, its inhibitory effect on *H. pylori* effects was weak (Ndip et al, 2007). Interestingly, *E. hirta* was not found to be very effective for anti-fungal activity by others (Abu-Sayeed et al, 2005; Singh et al, 2011). Taken together, *E. hirta* can be used to discover new bioactive natural products that may serve as leads in the development of new pharmaceuticals.

The antiretroviral activities of extracts of *E. hirta* were investigated *in vitro* on the MT4 human T lymphocyte cell line. A dose-dependent inhibition activity was observed for HIV-1, HIV-2 and SIV (mac251) all three viruses. Methanol extract was found to exert a higher antiretroviral effect than that of the aqueous extract (Gyuris et al, 2009).

2.2.8 Effects of *E. hirta* on molluscicidal activity and Larvicidal activity

Mosquito-transmitted diseases remain a major cause of the loss of human life worldwide with more than 700 million people suffering from these diseases annually (Taubes 1997). Mosquito-borne diseases have an economic impact, including loss in commercial and labor outputs, particularly in countries with tropical and subtropical climates; however, no part of the world is free from vector-borne diseases (Fradin and Day 2002). Larvicidal activity of *E. hirta* has been found in petroleum ether extract with LC50 value 272.36 ppm (Abdul Rahuman et al, 2008).

Many aquatic snails act as vectors for the larvae of trematodes and thereby, cause a number of diseases (Bali et al., 1986). Two diseases carried by aquatic snails, schistosomiasis and fascioliasis, cause immense harm to man and his domestic animals. The freshwater vector snail *Lymnaea acuminata* is the intermediate hosts of *Fasciola hepatica* and *Fasciola gigantica* (Hyman, 1970). Which caused endemic fascioliasis in sheep, cattle, goat and others herbivorous animal. Aqueous stem bark and leaf extracts of plant *E. hirta* have potent molluscicidal activity. Sub-lethal doses (40% and 80% of LC50) of aqueous stem bark and leaf extracts of this plant also significantly alter the levels of total protein, total free amino acid, nucleic acids (DNA and RNA) and the activity of enzyme protease and acid and alkaline phosphatase in various tissues of the vector snail *Lymnaea acuminata* in time and dose dependent manners (Singh et al, 2005).

2.2.9 Immunostimulant effect of *E. hirta* in aquaculture

E. hirta leaves have been used in aquaculture to protect fish from bacterial infection. Aquaculture is one of the fastest growing food-producing fields in the world, with an annual average growth rate of 6.9% per year since 1970 and this sector contributed about 36% of the total global fisheries production in the year 2006 (FAO, 2009; Mohanty & Sahoo, 2010). Infectious diseases are a major problem in aquaculture, causing heavy loss to fish farmers. Immunostimulants increase resistance to infectious diseases by enhancing both

specific and nonspecific defence mechanisms. The use of immunostimulants in fish culture is a promising new development in the field (Logambal et al., 2000; Dügenci et al., 2003; Rairakhwada et al., 2007). *Pseudomonas fluorescens* Flügge (Pseudomonadaceae) is an opportunistic bacterial fish pathogen of the freshwater ecosystem, associated with septic and ulcerative condition, necrosis of internal organs, external lesions, loss of pigmentation, and so on (Saharia & Prasad, 2001). The leaf extracts of *E. hirta* administered through the diet enhanced the nonspecific defence mechanism in terms of increased number of activated neutrophils and enhanced the serum lysozyme activity (secreted from active macrophages) in *Cyprinus carpio* Linn. The immunological competence was developed earlier on the plant leaf extract fed fish (on 5th day) than the control fish (on 10th day) after infection with the pathogen. In addition, the extract also exhibited potent antibacterial activity (Pratheepa1 and Sukumaran, 2011). Immunostimulatory activity of *E. hirta* was also found to enhance *in vitro* phagocytosis of neutrophils and macrophages (Ramesh and Padmavathi, 2010).

2.2.10 Effects of *E. hirta* on anti-anxiety

Stress is increasingly recognized as the precipitant of several psychiatric illnesses including anxiety and depression (McEwen, 2000). When rats subjected to chronic immobilization stress (CIS) or forced swim stress (FSS) showed anxiety in the elevated plus maze (EPM) and the open field test (OFT) (Anuradha et al., 2008; Govindarajan et al., 2006; Vyas et al., 2002). In addition to anxiety, stress is also known to produce learning and memory deficits. For example, chronic stress impaired learning in the T-maze and radial arm maze (Ramkumar et al., 2008; Srikumar et al., 2006, 2007) or in other paradigms such as the Barnes maze and Morris water maze (Bodnoff et al., 1995; McLay et al., 1998). The dopaminergic and cholinergic neurotransmitter systems have been shown to be involved in mediating the stress induced deficits (Srikumar et al., 2006, 2007). CIS increased the acetylcholinesterase (AChE) activity in the frontal cortex, hippocampus, and septum, while *E. hirta* treatment brought it to normal levels. FSS increased the AChE activity only in the septum, and *E. hirta* treatment marginally normalized this change. Chronic stress not only induces impairment of learning and memory but also precipitates several affective disorders including depression and anxiety. Sedative properties of aqueous extract of *E. hirta* have been confirmed at high dose (100 mg of dried plant/kg) by showing a decrease of behavioral parameters measured in non-familiar environment tests (activitest and staircase test). For anti-conflict effects appeared at lower doses (12.5 and 25 mg of dried plant/kg) by revealing an enhancement of behavioral parameters measured in the staircase test and in the light/dark choice situation test (Lanhers et al, 1990). Anxiolytic property of *E. hirta* was also demonstrated in chronically stressed rats subjected to EPM and OFT (Anuradha et al, 2008). *E. hirta* treatment showed marked anti-anxiety activity in CIS rats. Co-treatment of rats with flumazenil, bicuculline or picrotoxin resulted in a significant reduction of anxiolytic effect of *E. hirta* indicating that its actions are mediated through $GABA_A$ receptor-benzodiazepine receptor-Cl channel complex. Acetylcholine and the cholinergic system are also known to involve in anxiety. Further study showed that anxiolytic effects of *E. hirta* in rats subjected to CIS was due to suppression of CIS-induced AChE activity in the frontal cortex, hippocampus, and septum brain regions (Anuradha et al, 2010). Together with GABA-mimic effect and AChE reducing effect may explain the anxiolytic activity of *E. hirta*.

2.2.11 Effects of *E. hirta* on renal system

Dickshit (1934) first reported the presence of a toxic principle in *E. hirta* that depressed the cardiovascular system with a resulting fall in blood pressure. The alcoholic and aqueous extracts of this plant have also been shown to depress the blood pressure of the dog (Hazleton and Hellerman, 1954). *E. hirta* is locally used to treat numerous diseases, including hypertension and edema in Africa (Khan et al., 1980). Diuretic effect of the *E. hirta* leaf extracts were assessed in rats using acetazolamide and furosemide as standard diuretic drugs. The water and ethanol extracts (50 and 100 mg/kg) of the plant produced time-dependent increase in urine output. Regarding the secretion of electrolytes, the ethanol extract of *E. hirta* increased the excretion of HCO_3^-, decreased the loss of K^+ and had little effect on renal removal of Na^+. Whereas, the water extract increased the urine excretion of Na^+, K^+ and HCO_3^- that was similar to acetazolamide (Johnson et al, 1999).

The renin–angiotensin system plays a vital role in the maintenance of vascular tone and peripheral resistance. Renin produced from the juxtaglomerular apparatus of the kidney splits angiotensinogen to produce the inactive decapeptide angiotensin I. The latter is then converted to the powerful octapeptide vasoconstrictor, angiotensin II by the action of angiotensin converting enzyme (ACE). ACE inhibitors are important agents for treating hypertension and congestive heart failure (Opie, 1992). *E. hirta* extract possessed compounds with potent ACE inhibitory activities. A dose of 500 mg crude extract expressed about 90% inhibition of the enzyme action. The study also revealed that the most active ACE inhibitory compounds were present in the medium polar (chloroform extract) and very polar (methanol and water) fractions. Extract of *E. hirta* (10 mg/100 mg body weight) also possessed anti-dipsogenic activities (Williams et al, 1997). Both diuresis and ACE inhibition effects of *E. hirta* may explain its antihypertensive effects.

3. Conclusion

Although *E. hirta* has been used wildly to treat various diseases in many countries, most of the involved molecular mechanisms have not been fully explored. However, the pharmacological mechanisms of *E. hirta* in asthma attacks and hypertension were relatively clear. The former can be due to its potent anti-inflammatory and anti-oxidative activities. The later may work through its actions of diuretic activity and ACE inhibition. For anxiolytic effects of *E. hirta* is thought to be mediated through $GABA_A$-mediated Cl channel as well as AChE reduction. The anti-infection of *E. hirta* is due to its direct bactericidal activity. Antiinflammatory and antioxidative activities of *E. hirta* can also be expected to use in treating scald, preventing sepsis or other chronic inflammatory diseases. In overall, there are still many clinical applications of *E. hirta* remained to be investigated for their molecular mechanisms.

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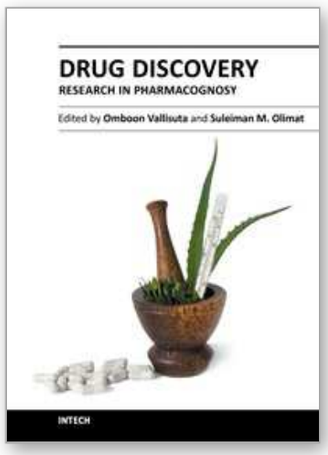
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This book, Drug Discovery Research in Pharmacognosy provides a full picture of research in the area of pharmacognosy with the goal of drug discovery from natural products based on the traditional knowledge or practices. Several plants that have been used as food show their potential as chemopreventive agents and the claims of many medicinal plants used in traditional medicine are now supported by scientific studies. Drug Discovery Research in Pharmacognosy is a promising road map which will help us find medicine for all!

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