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MEDICINAL AND BIOLOGICAL ASPECTS OF *EUPHORBIA HIRTA* PLANT: A REVIEW

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Abstract: The common medicinal plant of *Euphorbia hirta* (Family: Euphorbiaceae) has potent molluscicidal and piscicidal activity against freshwater snails and fishes. The toxicological actions of the diterpenoids, rutin, β-sitosterol, botulin, and ellagic acid present in the *Euphorbia hirta* plant. *Euphorbia hirta* is an important medicinal herb, it is a widely used local and traditional medicine in clinical practice. The whole plant is commonly applied to cure various diseases especially gastrointestinal disorders including intestinal parasites, diarrhea, peptic ulcers, heartburn, vomiting, amoebic dysentery, afflictions of the skin, asthma, bronchitis, fever, coughs, and colds. The freshwater harmful snails *Lymnaea acuminata* and *Indoplanorbis exustus* are very common in the Northern part of India. Both snails are vectors of *Fasciola hepatica*, which causes endemic fascioliasis in cattle and livestock in the Northern part of India. Fishing with the aid of plant toxins was formerly very common. Today this easy method of fishing is still practiced in remote areas. The method is simple the poisonous ingredients are pounded and thrown into a pool or dammed-up sections of a small river. After a short time, the fish begin to raise the surface and can then readily be taken by hand. The present work is an extensive review of published literature concerning medicinal and biological aspects of the *Euphorbia hirta* plant to give comprehensive information in an attempt to provide direction for further research. It is commonly known as Dudhi.

***Index Terms*:** Molluscicides, Piscicides, Snails, Fishes, Plant

I. INTRODUCTION

The plant *Euphorbia hirta* is an important medicinal herb, it is widely used in local and traditional medicine in clinical practice. The whole plant is commonly applied to cure various diseases especially gastrointestinal disorders including intestinal parasites, diarrhea, peptic ulcers, heartburn, vomiting, amoebic dysentery, afflictions of the skin, asthma, bronchitis, fever, coughs, and colds (Chopra *et al.*, 1969; Nadkarni, 1976; Zhong, 1986; Zhong, 1999; Bhatnagar *et el.*, 2000; Patil *et al.*, 2009; Huang *et al.*, 2012; Tripathi *et al.*, 2021). In East, Central, and West Africa, a decoction of the herb is used to treat asthma, oral thrust, boils, sores, skin, and wound infections, in addition to its being used as an antispasmodic, antipruritic, carminative, depurative,

diuretic, febrifuge, purgative and vermifuge (Alabashi *et al.,* 1999; Palombo and Semple, 2001; Darwish *et al.,* 2002; Ogbolie *et al.,* 2007).

India has one of the richest herbal medical traditions in the world. Ayurveda is the system of traditional medicine prevalent in India since 2000 B.C. Ayurveda meaning the "science of life" is the oldest existing medical system recognized by WHO which is widely practiced. India is a land of immense biodiversity in which two (the Eastern Himalayas and the Western Ghats of India) out of twenty-five hot spots of the world are located. This country is perhaps the largest producer of medicinal herbs and is rightly called the botanical garden of the world. It is generally estimated that in India over 6000 plants are used in traditional, folk, and herbal medicine, representing about 75% of the medicinal needs of the Third World Countries (Rajshekharan, 2002 and Bigoniya and Rana, 2008). Medicinal herbs as a potential source of therapeutic aids have attained a significant role in the health system all over the world for both human's animals not only in diseased conditions but also as potential material for maintaining proper health.

Interest in traditional drugs is not new but has been spurred in recent years due to an upsurge of interest in renewable resources in traditional medicine by methodological advances in pharmacology and phytochemistry. Medicinal plants are important for pharmacological research and drug development, not only when plant constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds (Mukherjee *et al.,* 2003). A significant number of modern pharmaceutical drugs are thus based on or derived from medicinal plants. Traditional medicine is a powerful source of biologically active compounds. Ethno-pharmacology has become a scientific backbone in the development of active therapeutics based on the traditional medicine of various ethnic groups.

The above-mentioned properties of plant products have opened a new vista. About India, our country possesses a rich biodiversity of medicinal plants that are used for many purposes. The plant products (extracts also) have been used from immemorial. The Vrikshayurveda is the branch of Ayurveda that deals with plant health and recommends drugs possessing specific qualities of treatment of insect attack. During the co-evolution of plants and insects, the plant has bio-synthesized several secondary metabolites to serve as defense chemicals against pest attacks. Although only 10,000 secondary metabolites have been chemically identified so, the total number may exceed 400,000 (Swain, 1977, Cooper and Johnson, 1984). A list of various plant products has been tested during the past decade and has been shown to possess molluscicidal and piscicidal activity. The present review deals with botanical products, which have demonstrated their efficacy in the management of disease vectors as alterations of synthetic pesticides.

The freshwater harmful snails *Lymnaea acuminata* and *Indoplanorbis exustus* are very common in the Northern part of India. Both the snails are vectors of *Fasciola hepatica*, which cause endemic fascioliasis in cattle and live-stock in the Northern part of India (Singh and Agarwal, 1981; Singh and Agarwal, 1990; Singh, 2000; Singh *et al.,* 2000; Yadav and Singh, 2001; 2002; Yadav *et al.,* 2002; Singh and Singh, 2003; 2003; 2003; Singh *et al.,* 2004; 2004; Singh and Singh, 2004; Singh and Singh, 2005; Singh *et al.,* 2005; Yadav *et al.,* 2005; 2006; Yadav and Singh, 2006; 2007; Singh *et al.,* 2009; Yadav *et al.,* 2099; Singh *et al.,* 2010). Fascioliasis, a devastating disease, is associated with significant economic loss in the livestock industry and has public health importance. This disease is caused by *Fasciola hepatica* in Europe, America, and Oceania (Torgerson and Claxton, 1999; Terasaki *et al.,* 2001; 2003). Snail control is a somewhat neglected aspect of the control of fascioliasis. However, it is an essential element of an integrated approach to preventing the infection caused by this parasite, which remains one of the most important diseases in this region. The use of synthetic or petroleum-based molluscicides for controlling vector snails causes serious environmental pollution (Redinger, 1976; Mian and Mulla, 1992; Dua *et al.,* 1998; Susan *et al.,* 1999; Waliszewski *et al.,* 1999). To overcome the problem and to search for eco-friendly molluscicides, several extracts and essential oils and their isolates have been evaluated for use as molluscicides due to their high toxicity, easy availability, low mammalian toxicity, low cost, and easy bio-degradability (Kinghorn and Evans, 1975; Marston and Hostettmann, 1985; Singh *et al.,* 1996). These materials have shown encouraging results for vector-controlling properties with various snail species.

Fishing with the aid of plant toxins was formerly very common. Today this easy method of fishing is still practiced in remote areas. The method is simple the poisonous ingredients are pounded and thrown into a pool or dammed-up sections of a small river. After a short time, the fish begin to raise the surface and can then readily be taken by hand. The fish can be eaten without health problems (Singh, 2001). Several biocidal plants have been in use for fish-catching practices by the tribal communities in large numbers including Tharu, Bhotia, Kol,

Gond, Kharwar, and Korwas that inhabit remote villages and forest areas of the States Uttar Pradesh and Bihar (Prakash and Singh, 2000). Different species of plants employed as piscicides have different effects, depending on the species of fish targeted (Van Andel, 2000). The active principles in the plant part used (leaves, seeds, kernals, and bark) have varying potencies and modes of action depending on whether it is applied directly and the forms of extracts (aqueous and solvent extracts) used (Sambasivan *et al.,* 2003; Neuwinger, 2004; Singh and Singh, 2010; Singh *et al.*, 2010; Singh *et al.*, 2013).

Recently *Euphorbia hirta* is one of the medicinal plants currently being investigated in the Philippines for its potential against coronavirus (CoV) disease 2019 (COVID-19). The goal is to develop a formulation utilizing the plant as an adjuvant treatment for mild to moderate COVID-19. A recently published review article identified *E. hirta* as one of the Philippine medicinal plants with immunomodulatory effects and potential against severe acute respiratory syndrome-CoV-2 (SARS-CoV-2) (Dayrit *et al.,* 2021), the virus responsible for COVID-19. In this connection, a parallel and complementary in silico study was conducted to investigate the potential of its phytochemicals against a specific COVID-19 drug target, SARS-CoV-2 main protease (Mpro). Mpro is seen as an important COVID-19 drug target because of the role it plays in the regulation of viral replication (Di Micco *et al.,* 2021; Cayona and Creencia, 2022).

II. MEDICINAL PROPERTIES

Euphorbia hirta is a small annual, branched herb prostrate to ascending with branches reaching 70 cm in height, reddish or purplish in color, with abundant latex, and is covered with short hairs (Figure 01). Its leaves are opposite, distichously and simple; its obvious stipules are linear. The leaf blades of *E. hirta* are lanceolate-oblong, long elliptic, or ovate-lanceolate; its base is very unequal; one side is cuneate, the other side is round; the apex is almost acute and its margins are finely toothed, often with a purple blotch near the midvein. The toxicological actions of the diterpenoids, rutin, β-sitosterol, botulin, and ellagic acid present in the *Euphorbia hirta* plant. *Euphorbia hirta* is an important medicinal herb, it is a widely used local and traditional medicine in clinical practice. The whole plant is commonly applied to cure various diseases especially gastrointestinal disorders including intestinal parasites, diarrhea, peptic ulcers, heartburn, vomiting, amoebic dysentery, afflictions of the skin, asthma, bronchitis, fever, coughs, and colds (Zhong, 1999; Bhatnagar *et el.,* 2000; Patil *et al.,* 2009; Huang *et al.,* 2012; Tripathi *et al.,* 2021 and Di Micco *et al.,* 2021; Cayona and Creencia, 2022).

Euphorbia hirta mainly contains flavonoids, terpenoids, rutin, β-sitosterol, botulin, ellagic acid phenols, essential oil, and other compounds. The major chemical structures of these compounds are shown in Figure 1. One type of the important constituents of *Euphorbia hirta* is flavonoids including quercetin, quercitrin, quercetin, and derivatives containing rhamnose, quercetin-rhamnose, a chlorophenol acid, rutin, leucocyanidin, leucocyanidol, myricitrin, cyanidin 3,5-diglucoside, pelargonium 3,5-glucoside, and, camphol. The flavonol glycoside xanthorhamnin was also isolated from *Euphorbia hirta*. The stems contain hydrocarbon hentriacontane and myricyl alcohol. The latex contains inositol, taraxerol, friedelin, β-sitosterol, ellagic acid, kaempferol, quercitol and quercitrin. Another type of constituent of the aerial parts of *E. hirta* is terpenoids, including triterpenes: α-amyrin, β-amyrin, friedelin, taraxerol, and its esterst: Taraxerone, 11α, 12α-oxidotaraxerol, cycloartenol, 24-methylene cycloartenol, and euphorbol hexacosoate. The aerial parts and roots of *Euphorbia hirta* also contain diterpene esters of the phorbol type and ingenious type, including 12-deoxyphorbol-13-dodecanoate-20-acetate, 12-deoxy horbol-13-phenylacetate-20-acetate, ingenol triacetate, as well as the highly toxic tiny toxin, a resiniferous derivative. Some new ent-kaurane diterpenoids were isolated from the ethanol extract of *Euphorbia hirta* and identified as 2-beta, 16-alpha, 19-trihydroxy-ent-kaurane, 2-beta, 16-alpha-dihydroxy-ent-kaurane, and 16-alpha, 19-dihydroxy ent-karate (Yan et al., 2011). The other terpenoids isolated are sterols, including β-sitosterol, campesterol, cholesterol, and stigmasterol (Hazimi et al., 2008; Baslas and Agarwal, 1980).

Figure 01: *Euphorbia hirta* plant

Tannins isolated from *Euphorbia hirta* include the dimeric hydrolyzable de-hydro ellagitannins euphorbias A, B, C, E, and terchebin, the monomeric hydrolyzable tannins geraniin, 2,4,6-tri-O-galloyl-β-D-glucose and 1,2,3,4,6-penta-O-galloyl-β-D-glucose and the esters 5-Ocaffeoylquinic acid (neochlorogenic acid), and 3,4-di-Ogalloylquinic acid, and benzyl gallate. Acids isolated from *Euphorbia hirta* include ellagic, gallic, tannic, malic, and tartaric acids.

The major components of the essential oil include 3,7,11,15-tetramethyl-2hexadecen-1-ol, 6,10,14-trimethyl-2-pentadecanone, hexadecanal, phytol, and n-hexadecanoic acid adding up to 61.01%. The minor constituents of *Euphorbia hirta* include 2-butoxyethanol, tetradecane, phthalic acid, butyl tetradecyl ester, oleic acid, 13-heptadecyn-1-ol, 2-methyl-1-hexadecanol, and 1,2-benzene dicarboxylic acid diisooctylester. The component in essential oil may be responsible for the treatment of asthma and function as a repellent against Anopheles species, and thus, is useful for the treatment of malaria (Ogunlesi et al., 2009). The other compounds found in *Euphorbia hirta* are alkaloids, saponins, amino acids, and minerals. The mineral content of a sample of the dried leaves was: Ca 1.1%, P 0.3%, Fe 0.03%, Mg 0.5%, Mn 0.01%, Zn 0.01%, and Cu 0.002%. Fresh leaves from *Euphorbia hirta* plants of Nigerian origin were found to contain high levels of Mn (189 ppm), Cu (30.5 ppm), Zn (152 ppm), and NO_3 (4600 ppm). Varying proportions of Fe, Mg, K, Ca, and Na were also found. More recently, two novel butanol rhamnopyranosides (1 and 2), have been isolated from various non-polar and polar extracts of an Indian traditional herb, *Euphorbia hirta*. The structures of the new compounds were elucidated as n-butyl-1-O-L-rhamnopyranoside (1) and n-butyl-1-O-L-rhamnopyranoside (Mallavadhani and Narasimhan, 2009).

III. BIOLOGICAL PROPERTIES

Molluscicidal properties

Earlier observations indicate that the aqueous extracts of the leaf and bark of *Euphorbia hirta* plant (Family: Euphorbiaceae) have potent molluscicidal activity against freshwater vector snails *Lymnaea acuminata* and *Indoplanorbis exustus* (Singh *et al.*, 2003; Singh *et al.*, 2004; Singh *et al.*, 2005; Singh *et al.*, 2010; Singh and Singh, 2010), Both the snails are the intermediate host of liver-flukes *Fasciola hepatica* and *Fasciola gigantica*, which cause endemic fascioliasis in the cattle and livestock of Northern part of India (Hyman, 1970; Singh and Agarwal, 1981). The use of plant products as molluscicide is a simple, easily biodegradable, inexpensive, and appropriate technology for focal snail vectors (Kinghorn and Evans, 1975; Kloos and Mccullough, 1987; Marston and Hostettmann, 1985; Singh *et al.*, 1996; Yadav and Singh, 2001; Singh *et al.*, 2004; Singh *et al.*, 2005; Azare *et al.*, 2007; Plan *et al.*, 2008; El-Sherbini *et al.*, 2009; El-Kamali *et al.*, 2010). Furthermore, investigation of plants used in traditional medicine or recorded in ethnopharmacological literature provides a ready means of increasing the diversity of available molluscicides and simplifying the choice of selective, ecologically safe snail-killing compounds (Fransworth *et al.*, 1987). The plant-origin pesticides to control the vector snails for the best methods in comparison to synthetic pesticides (Table 1).

Table 1. Comparison of LC_{50} to plant origin pesticides and synthetic pesticides against snails.

Plants	Plant parts	Active moiety	LC_{50} mg/L	Snail species	References
Plant origin pesticides					
Euphorbia hirta	Latex	Unknown	1.29 (24h)	*L. acuminata*	Singh *et al.*, 2004a
Euphorbia hirta	Latex (Diethyl ether)	Unknown	0.69 (24h)	*L. acuminata*	Singh *et al.*, 2004c
Synthetic pesticides					
Mexacarbate	-	-	3.5 (24h)	*L. acuminata*	Singh and Agarwal, 1981
Aldicarb	-	-	30 (24h)	*L. acuminata*	Singh and Agarwal, 1981
Carbaryl	-	-	14.4 (96h)	*L. acuminata*	Singh and Agarwal, 1981
Formothion	-	-	27 (24h)	*L. acuminata*	Singh and Agarwal, 1981
Phorate	-	-	15 (96h)	*L. acuminata*	Singh and Agarwal, 1981
Trichlorofon	-	-	14.4 (96h)	*L. acuminata*	Singh and Agarwal, 1981
Niclosamide	-	-	11.8 (24h)	*L. acuminata*	Singh and Agarwal, 1986
Cypermethrin	-	-	0.80 (24h)	*L. acuminata*	Singh and Agarwal, 1986
Permethrin	-	-	0.73 (24h)	*L. acuminata*	Singh and Agarwal, 1986
Fenvalerate	-	-	2.5 (24h)	*L. acuminata*	Sahay *et al.*, 1991

Piscicidal properties

Several biocidal plants have been in use for fish-catching practices by the tribal communities in large numbers including Tharu, Bhotia, Kol, Gond, Kharwar, and Korwas that inhabit remote villages and forest areas of the States Uttar Pradesh and Bihar (Prakash and Singh, 2000). Different species of plants employed as piscicides have different effects, depending on the species of fish targeted (Van Andel, 2000). The active principles in the plant part used (leaves, seeds, kernels, and bark) have varying potencies and modes of action depending on whether it is applied directly and the forms of extracts (aqueous and solvent extracts) used (Sambasivan *et al.*, 2003; Neuwinger, 2004; Singh and Singh, 2010; Singh *et al.*, 2010; Singh *et al.*, 2013).

Plant extracts are referred to as botanicals and when poisonous to fish are called piscicides (Burkill, 1985). Such piscicidal plants contain different active ingredients known as resin, tannins, saponins, nicotine, and diosgenin. However, these alkaloids are toxic to fish at high concentrations and wear off within a short time. Several plant materials are toxic to zooplankton (Kreutzweiser *et al.*, 2004), shrimps commercial fish species both in the laboratory and field studies (Singh and Singh, 2002). The Indian major carp *Labeo rohita* (Hamilton) was used as the test animal because it is present in almost all freshwater reservoirs in India and is suitable for toxicity monitoring (Table 2). Recently the freshwater fish *Channa punctatus* was used as the test animal in almost all freshwater reservoirs in India and is suitable for toxicity monitoring (Singh *et al.*, 2013).

Table 2. Comparison of LC_{50} to plant-origin pesticides and synthetic pesticides against fishes.

Plants	Plant parts	Active moiety	LC_{50} mg/L	Fish species	References
Plant origin pesticides					
Euphorbia hirta	Latex	Aqueous extract	4.23 (24h)	*Channa punctatus*	Yadav and Singh, 2013
Euphorbia hirta	Stem Bark	Aqueous extract	3.82 (24h)	*Channa punctatus*	Yadav and Singh, 2013
Euphorbia hirta	Latex	Aqueous extract	6.37 (24h)	*Labeo rohita*	Singh *et al.*, 2014
Synthetic pesticides					
Methyl parathion		-	8.48 ppm (24h)	*Poecilia reticulate*	Sharbidre *et al.*, 2011
Dimecron 100 SCW		-	22.95 ppm (96h)	*Channa panctatus*	Hossain *et al.*, 2002
Dimecron 100 SCW		-	375.26 ppm (96h)	*Barbodes gonionotus*	Hossain *et al.*, 2002

IV. CONCLUSION

In the present review, we have congregated information about the medicinal and biological aspects of molluscicidal and piscicidal claims and scientific studies. The above plant is immense potential and has a broad spectrum of activity for several ailments. *Euphorbia hirta* is an important medicinal herb, it is a widely used local and traditional medicine in clinical practice. The whole plant is commonly applied to cure various diseases especially gastrointestinal disorders including intestinal parasites, diarrhea, peptic ulcers, heartburn, vomiting, amoebic dysentery, afflictions of the skin, asthma, bronchitis, fever, coughs, and colds (Zhong, 1999; Bhatnagar *et el.,* 2000; Patil *et al.,* 2009; Huang *et al.,* 2012; Tripathi *et al.,* 2021). There are a very large number of plants, which contain compounds lethal to target as well as non-target organisms at doses, which are much below those for synthetic pyrethroids. The use of such products has the additional advantage that these contain biodegradable compounds, which are less likely to cause environmental contamination. After all such compounds are not only confined to the plants in which they are found but also possibly get distributed in the environment. We strongly feel that if these herbaceous products are used as molluscicides they would not only control the vector snail, predatory fish, and mosquitoes but would also have the advantage of easy availability, low-cost biodegradability, and greater acceptance amongst the users. Further, we feel that with further progress in biotechnology, such products could be raised from, sources other than those plants in which they are currently found. Production of plant pesticides could, in the long run also become an important industry using biotechnological methods.

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