IJPSR (2021), Volume 12, Issue 12 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 25 November 2020; received in revised form, 27 May 2021; accepted, 09 November 2021; published 01 December 2021

EUPHORBIA HIRTA LINN - AN INVASIVE PLANT: A REVIEW OF ITS TRADITIONAL USES, PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES

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Keywords:

E. hirta, Invasive plant, Traditional, Phytochemistry, Bioactivity

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ABSTRACT: *Euphorbia hirta* Linn. (Euphorbiaceae), commonly known as 'Dudhy' is an annual medicinal herb of Kumaun Himalaya Uttarakhand. It is an invasive plant used in conventional medicine to treat various diseases such as gastrointestinal disorders, respiratory system disorders, and asthma. The present review is designed to compile updated information on *E. hirta,* including its medicinal uses, phytochemicals, as well as biological activities. Qualitative and quantitative phytochemical studies on *E. hirta* revealed the presence of various chemical compounds in which flavonoids, terpenoids, and phenols are the major constituents. These monomeric compounds and crude extracts from *E. hirta* have also been screened for pharmacological activities *in-vivo* and *in-vitro*. Different parts of the plant have interesting antimicrobial, antioxidant, antidiabetic, and antitumor properties. Some traditional uses of this plant, such as in gastrointestinal disorders, bronchitis, and asthma, also indicated its high medicinal potentiality. *E. hirta* has been proved a valuable medicinal plant for the tribal people living in the rural region of Kumaun Himalaya. The crude hydroalcoholic extract of *E. hirta* has more pharmacological activities. It is used as an important medicinal and nutritional source for curing many severe illnesses in different parts of the world. Therefore, it is the need of modern time to isolate and identify more bioactive constituents and elucidate their structure, activity, and relationship of this plant. It is also emphasized for more detailed research and clinical trials to explore its pharmacological activity and clinical efficacy.

INTRODUCTION: *Euphorbia hirta* Linn. is commonly known as milkweed (Dudhy) and an asthma plant. It is known by the different names in different parts of the world [1, 2]. The plant is characterized by the presence of milky white latex, which is more or less toxic.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(12).6189-01

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(2).6189-01

Latices of *E. ingens, E. tirucalli, E. mey, and E. triangularis* are possible sources of rubber [3]. The plants of this family have been a subject of intense phytochemical examination such as flavonoids, triterpenoids, alkanes, amino acids and alkaloids [4]. *E. hirta* is used as folklore medicine in the treatment of the gastrointestinal disorder (Diarrhea, amoebic dysentery, intestinal parasitosis, peptic ulcers, *etc.*),

Bronchial and respiratory diseases (Asthma, bronchitis, hay fever, laryngeal spasms, cough-colds) and conjunctivitis [5-7]. Moreover, modern pharmacological investigations revealed that *E.*

hirta and its active constituents possess wide array of pharmacological potential *viz*, antibacterial, antifungal, antioxidant, anti-inflammatory, antiasthmatic, antitumor, antimalarial, larvicidal, diuretic and antidiabetic activity [8-14]. It is also noteworthy that *E. hirta* is used as antidiabetic, anti-inflammatory, antispasmodic and as anticancer curative agent [15]. *E. hirta* has been used as a medicinal herb in China for long time. Different composition such as crude drug, infusion, lotion, decoction, and powders are also used [16, 17].

The plant of *E. hirta* plays a major role in traditional medicinal system due to its wide range of biological and pharmacological properties. Keeping in minds the effects of *E. hirta* in curing skin ulcer and body swelling, the plant was first recorded in 'Ling Nan Cai Yao Lu'. More than 10 books regarding the folk medicinal uses of this plant have also been recorded in China [18, 19]. A comprehensive and updated review is desirable to advance research on *E. hirta*. Hence we reviewed different studies on this plant in recent years. Thus besides taxonomic detail and ethnobotany, the chemical constituents and pharmacological potential is discussed. As per information available, it is the first composite review on this Kumaun Himalayan invasive plant, which provides a piece of comprehensive knowledge about *E. hirta* with its pharmacological potential and chemical compositions.

Methodology: All relevant details provided in this review article on the botanical description, ethnomedicinal use phytoconstituents, and pharmacological potential of *E. hirta* were collected by consulting a large number of literatures. The scientific data are based on Google Scholar, Web of Science, PubMed, scopus sci finder, springer link, authentic books, thesis, and various research papers. The key words *E. hirta*, asthma plant, phytoconstituents, ethnopharmacology, Euphorbiaceae, ethnobotanical, antibacterial, antifungal, antidiabetic, and clinical were searched with the number of times. Chemical structures were drawn using Chem Draw Professional 16.0 software.

Botanical Description: *E. hirta* Linn. as illustrated in **Fig. 1A** & **B,** is a small annual, branched herb reaching up to 70 cm in height, purplish or reddish in colour with an ample amount of latex, and coated with shoot hairs. Leaves are opposite, distichous, and simple, stipules are linear, leaf blades are lanceolate, oblong serrated, long elliptic, acute apex, 3-4 cm in length and 1-1.4 cm in width, and its margin are smooth toothed. The inflorescence monoceious, an axillary or terminal cluster of flowers, is known as cyathium with several cyathia arranged into a cyme. The male and female flowers are in one involucre and both appellate. The flowers are unisexual, male flowers are sessile, bracteoles are linear, fringed, perianth is absent and possesses one stamen, female flowers have small pedicel, the perianth is rimmed, ovary is superior covered with minute hairs, 3- celled, possesses 3- styles, small and the apex is two-fold. The flowering period is usually the whole of the year. The fruit is allomorphic, pistillate, exerted, 3-lobed, truncate base covered with shoot hairs.

The seeds are oblong, 4- sided prismatic, wrinkled, and brownish pink in color, capsule 3- seeded, green, and covered with fleshy prickles, seed smooth, hard mottle crustaceous testa with a white caruncle at the top enclosing oily endosperm. The root is distinct and developed primary root (tap root system) [17, 20, 22].

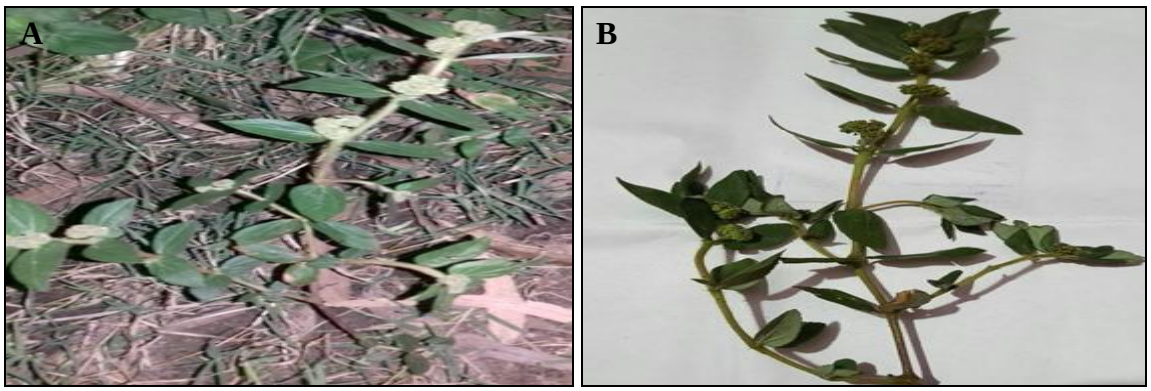


FIG. 1: A - PLANT OF *EUPHORBIA HIRTA* LINN. IN FLOWERING STATE IN NATURE, B- IN HERBARIUM

E. hirta Linn. belongs to the family Euphorbiaceae, known as the spurge family of flowering plants. It is the largest family consisting of nearly 300 genera and 5000 species [22]. Euphorbia is the largest genus of the Euphorbiaceae family, comprises about 1600 species [23].

Classification:

Kingdom	:	Plantae
Division	:	Spermatomatophyta
Class	:	Dicotyledonae
Order	:	Euphorbiales
Family	:	Euphorbiaceae
Genus	:	Euphorbia
Species	:	Hirta

Vernacular Names of *E. hirta*: *E. hirta* has diverse synonyms, and vernacular names vary from region to region. In India it is known as Dudhy (In Hindi), Asthma plant (In English), Amampatchairaisi, dugadhika (In Sanskrit), Dudeli (In Gujrat), Dudnali, govardhan (In Marathi), Jhotikhuntian (In Orissa), Daun bijii kacang (In Indonesia), Ambin Janyan, Keremak susu (In Malaysia), Boro kerui (In Bangladesh) [24].

Nativity and Distribution: The plant species *E. hirta* Linn. is native to Central America. It is cosmopolitan in distribution, widely distributed Throughout tropical or temperate regions of India, Asia, Africa, and Australia. It prefers dry and humid conditions, from sea level up to 2200 meters altitude. It commonly grows in paddy fields, gardens, lowlands, waste places near roadside [21, 23].

Medicinal Uses: The plant of *E. hirta* has a widespread traditional use in China and was recorded in Chinese pharmacopeia in the year 1977. The Yao people of China use the whole plant in the treatment of bronchitis. The decoction of dry plant is used externally in burned and scald, whereas freshly crushed leaves are applied to treat skin disease [18]. This plant's decoction or tincture is used to cure asthma, chronic bronchial disorders, and emphysema diseases by the Zhuang people of China [25]. Dai people of China applied *E. hirta* in the stimulation of milk secretion and also in cessation of cough [5]. It is extensively used in cough, kidney stones abscesses, and bronchial asthma [26]. It is also used traditionally to cure and prevent gastrointestinal disorders, afflictions of mucous membranes, and respiratory system disorders [27]. The cold extract of the leaves of *E. hirta* is used on a large scale to bathe small babies with skin infections in Nigeria. The literature of ethnomedicinal plant also indicates that it is commonly known for increasing milk flow in females and different disorders [17, 28]. The decoctions of this plant are also applicable in ear disease and the treatment of sore, boils, and it also has wound healing properties [19, 29, 30]. Different parts of this plant are traditionally used to cure the babies from worm infestations and also prove helpful in dysentery, jaundice, gonorrhea, acne, pimples, digestive orders, diabetes, several types of tumors, and in cancers in India [31-34]. The extracts of *E. hirta* are used against vomiting, diarrhea and as anti-venum against snakebite [35]. It is also used in the treatment of asthma in South Africa [36]. The leaves of *E. hirta* are mixed with leaves and petals of *Datura metal* to prepare asthma cigarettes in the Philippines [22]. *E. hirta* possesses antispasmodic, antidiabetic, anti-inflammatory and anticancer curative properties [37].

Phytochemistry: The main group of bioactive phytochemicals of *E. hirta* which have been distinguished and identified as illustrated in fig. 2 includes, flavonoids, steroids, terpenoids, coumarins, tannins and polyphenols [38-40]. Phytochemical analysis of leaf extract revealed the presence of carbohydrates, terpenoids, alkaloids, reducing sugars, steroids, tannins, proteins, fats, oils, mucilages, glycoside, saponin, coumarin, anthroquinones, chlorophyll, and carotenoids [41]. Flavonoids compound present in this plant includes quercetin, quercitrin, quercitol, and its by-products like rhamnose, quercetin, rhamnoside, chlorophenolic acid, rutin, leucocyanidin, myricitrin, cyaniding 3,5- diglucoside, camphol, flavonol, inositol, tetraxerol. B- sitosterol and Kaemferol.

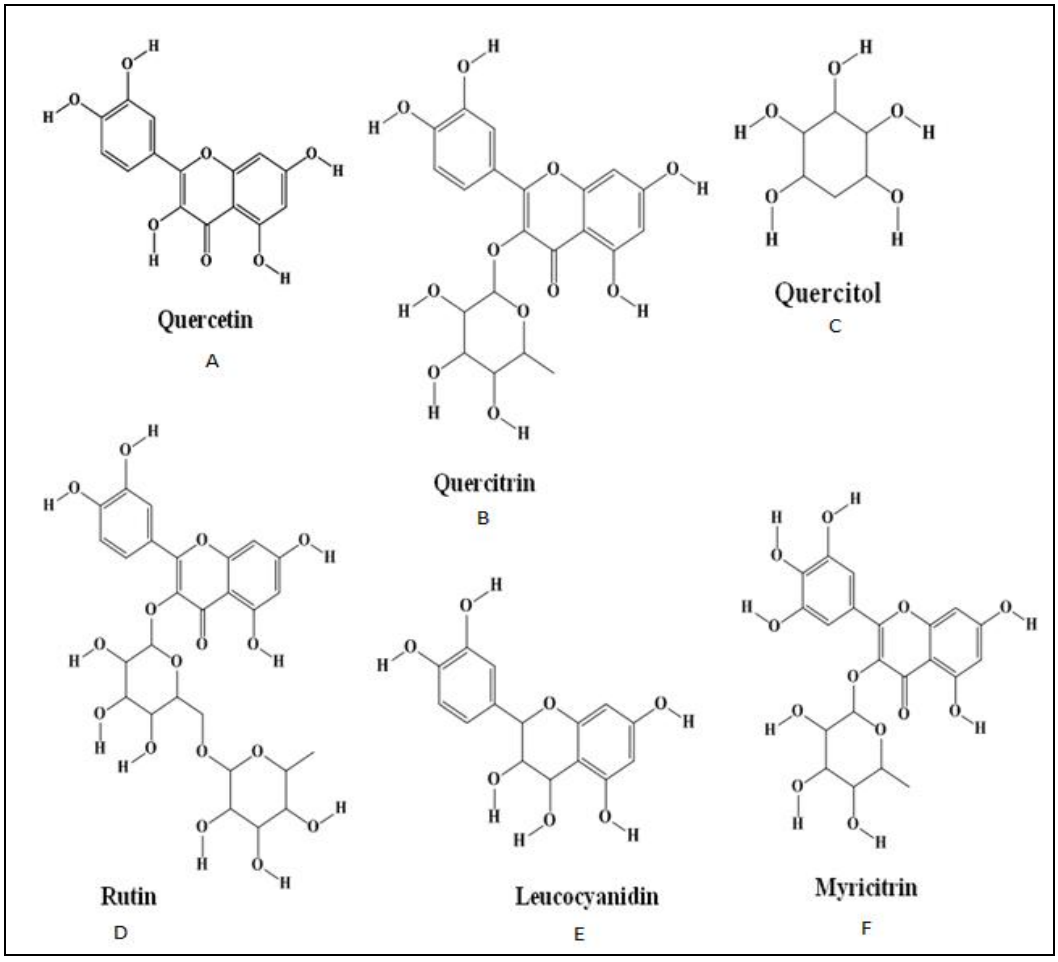
The aerial parts of *E. hirta* revealed the presence of Euphorbin-A, Euphorbin-B, Euphorbin-C, Euphorbin-D, gallic acid, and protocatechuic acid [42, 43]. Tannins which include the dimeric hydrolisable dehydro ellagi tannins Euphorbin-A, Euphorbin-B, Euphorbin-C, Euphorbin-D, and terchebin, the monomeric hydrolisable tannins geranin, 2,4,6 tri-o- galloyl-β-D-g hhhc2wlucose and 1,2,3,4,6- penta-o-galloyl-β-D-glucose and the

esters 5-o- caffeoylquinic acid, 3,4-di-o-galloylquinic acid and Benzyl gallate [44].Second group of compounds isolated from *E. hirta* are terpenoids *viz.*, triterpenes α- amyrin, β- amyrin, fridelin, tara xerol, taraxerone, 11α, 12α-oxidotaraxerol, cycloartenol, 24- methylene-cycloartenol and euphorbol hexacosoate. The aerial parts and roots of this plant also revealed the presence of diterpene esters of the phorbol type and igenbol type *viz*, 12- deoxyphorbol- 13-dodecanoate- 20 acetate, ingenol triacetate, in addition the highly toxic tinyatoxin, a resiniferonol by products. From the ethanol extract of this plant few new ent -kurane diterpinoid were isolated and identified as-2 β, 16-α, 19 trihydroxy ent kurane, 2β- 16α dihydroxy ent kurane and 16 α 19-dyhydroxy ent kurane [45].

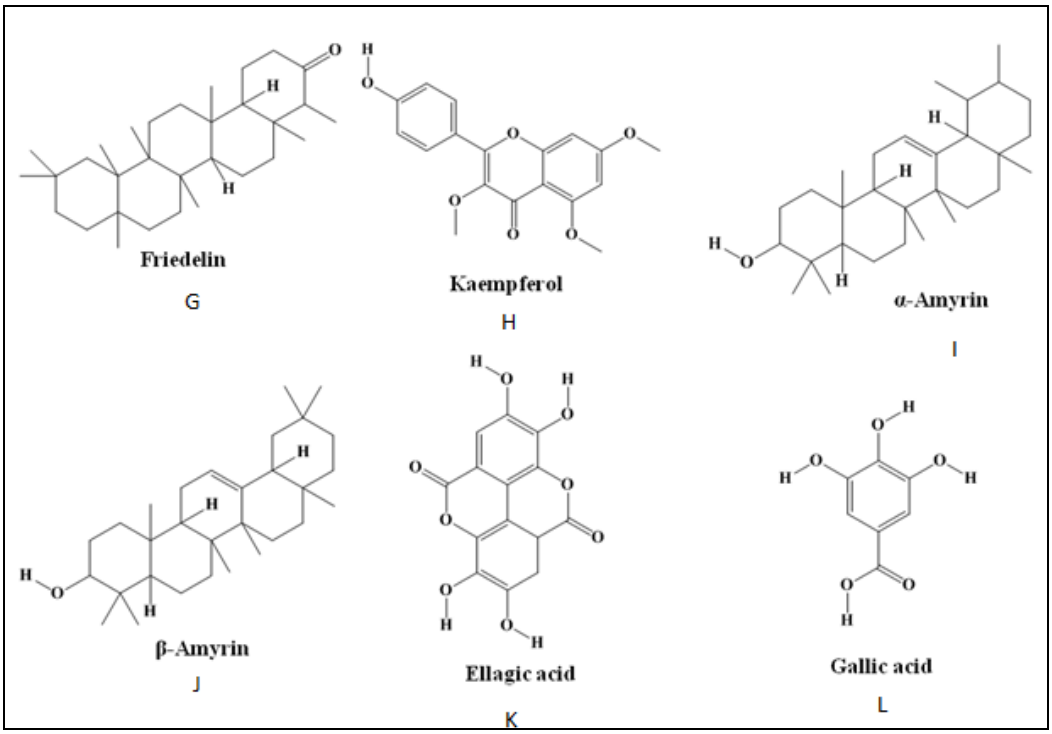
The other terpenoids screened from *E. hirta* are sterols, such as sitosterol, campesterol, cholesterol and stigmasterol [40, 41, 46]. The volatile oil of *E. hirta* consists of two main components, major components such as [3, 7, 11, 15], tetramethyl - 2 hexadecen-1-ol, 6, 10, 14- trimethyl - 2 penta-decanone, hexadecanol, Phytol and n-hexadecanoid acid. The minor elements include- 2 butoxyethanol, tetradecane, pthalic acid, butyl tetradecyl ester, oleic acid, 13 heptadecyn- 1ol, 2 methyl -1 -hexadecanol and 1, 2- benzene dicarboxylic acid, diiso octylester.

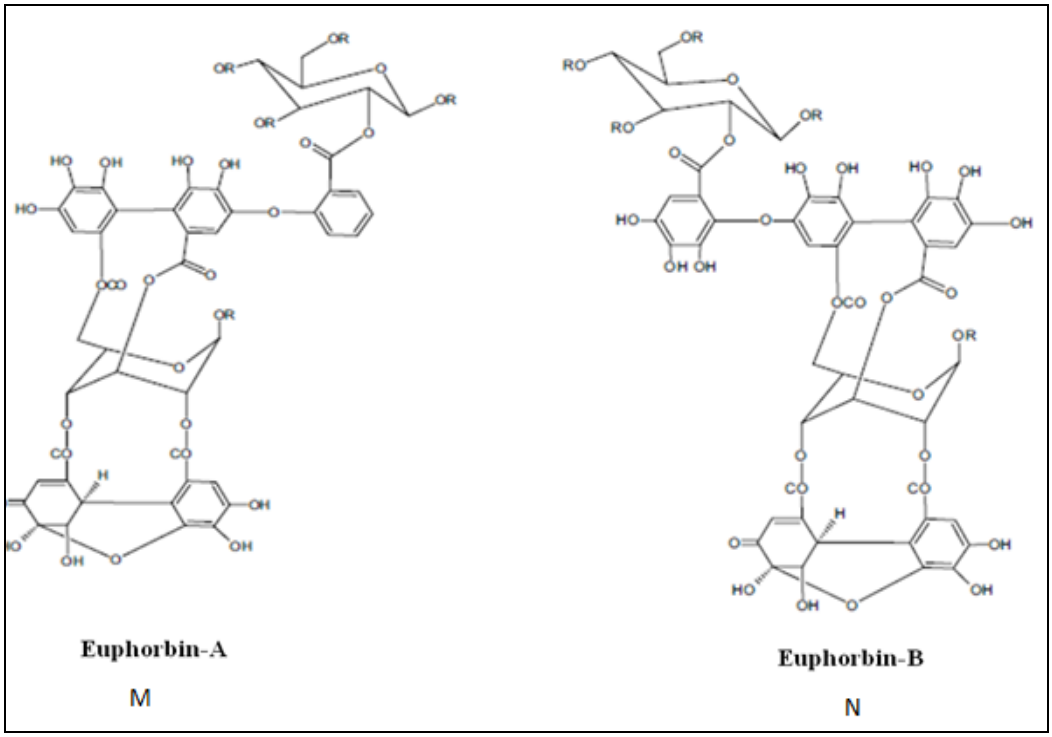
TABLE 1: CHEMICAL COMPOUND STUDIED IN *E. HIRTA* LINN.

S. no.	Name of compounds	Fig. No.
1	Querecetin	A
2	Querecitrin	B
3	Quercitol	C
4	Rutin	D
5	Leucocyanidin	E
6	Myricitrin	F
7	Fridelin	G
8	Kaempferol	H
9	α- Amyrin	I
10	β- Amyrin	J
11	Ellagic acid	K
12	Gallic acid	L
13	Euphorbin- A (Basic structure)	M
14	Euphorbin –B (Basic structure)	N
15	Euphorbin – C (Basic structure)	O
16	Euphorbin – D (Basic structure)	P



These components of volatile oil may be responsible in the curing of asthma and also useful in the therapy of malaria [47]. In another study, the volatile oils of *E. hirta* aerial parts revealed the presence of 11 compounds. The major compound was (Z) -9- octadecanamide (60-71 %) whereas the minor components present included- methyl hexadecanote (7.02 %), β elemene (2.54 %), phytol (4.80 %) and p- menth- 3-en-9-ol (3.64%) [48]. In other components of *E. hirta* plants are alkaloids, saponins, amino acids, and minerals. The dried leaves mineral content of this plant were ; Ca 1.1%, P 0.3 %, Fe 0.3%, Mg 0.5%, Mn 0.1% and Cu 0.02% [49]. Recently, two novel kinds of rhamnopyranosides (1 & 2) have been extracted from the various non-polar and polar extracts of Indian-born *E. hirta* plants. They were distinguished as n- butyl-1-o-L-rhamno-pyranoside (1) and n- butyl -1-o-L- rhamnopyranoside [52].





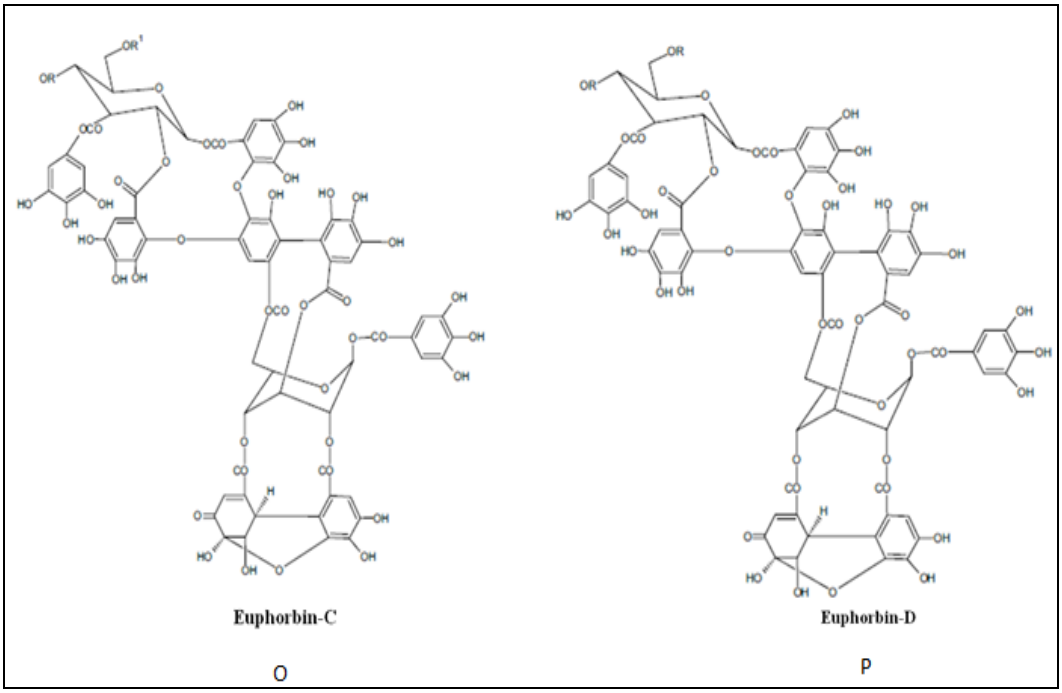


FIG. 2: THE CHEMICAL STRUCTURE OF MAIN COMPOUNDS FOUND IN *E. HIRTA*

Different parts of *E. hirta* plant were studied for total polyphenolic and flavonoid content. Leaves extract a great amount of total phenolic content 26.17 ± 1.95 mg GAE /g dry weight. Leaves also showed the highest total flavonoid content (37.90 ± 0.003) mg CE /g dry weight. The mineral constitution of *E. hirta* dried leaves has also been examined. The result showed different constituents composition such as- Ca: 1.1%, P: 0.3%, Fe: 0.03%, Mg: 0.5%, Zn: 0.01% and Cu: 0.002% [50].

Pharmacological Profile: *E. hirta* Linn. possesses numerous pharmacological potential with wide pharmacological activities such as antibacterial, antifungal, anti-inflammatory, antidiarrheal, sedative and anxiolytic, anticancer, antipyretic, antioxidant, antiasthmatic, antitumor, antimalarial, diuretic and increases electrolytes, antidiabetic and antiviral activities [51-58]. Since, the 1980s, the antibacterial activities of *E. hirta* have been investigated in depth and proven by several studies. Vijay *et al.*, tested the antibacterial activity of methanolic extract of *E. hirta* against *Shigella dysentriae* using vero cell line. The decoction exhibits good antibacterial activity against dysentery-causing bacteria [59]. The antibacterial activity of the crude ethanolic extract of *E. hirta* has been investigated against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Bacillus subtilis*.

The result showed remarkable antibacterial activity against tested bacterial strains [60]. The ethanolic extracts of *E. hirta* have been tested against Gram-positive and Gram-negative bacteria. The results exhibit more activity against Gram-positive bacteria as compared to Gram-negative bacteria [61]. The antibacterial potential of ethanolic extract of aerial parts of *E. hirta* has been examined against *E. coli, Proteus vulgaris, P. aeruginosa*, and *Staphylococcus aureus*. The results revealed a significant antibacterial potential [62]. The ethanolic extract of leaves of *E. hirta* was investigated for antibacterial activity against *S. aureus*, *B. cereus*, *Salmonella typhae, Klebsiella pneumonae*, and *P. aeruginosa.*

The result showed antibacterial activity which might be due to the presence of tannins, flavonoids, alkaloids, glycosides, proteins, sterols, and saponins [60, 63]. The antibacterial activity of methanolic extract of *E. hirta*, leaves, stems, flowers, and roots were tested against 4 Gram-positive (*S. aureus, Mycobacterium species, B. subtilis*, and *B. thuringensis*) and 4 Gram-negative (*E. coli, K. pneumonae, S. typhae*, and *Proteus mirabilis*) bacteria. The leaves' decoction exhibited a large zone of inhibition to all the evaluated microorganisms followed by flowers [64]. The root extract also showed a good zone of inhibition against Gram-positive bacteria as compared to

Gram-negative bacteria [59]. The antibacterial activity of different solvent (Hexane, dichloromethane, ethyl acetate, and ethanol) extract of aerial parts of *E. hirta* was evaluated against Gram-negative (*Enterobacterium aerogenes, E. coli, K. pneumonae, P. mirabilis, P. vulgaris, P. aeroginosa, S. typhae* and *Shigella dysenteriae*) and Gram-positive (*Staphylococcus aureus* and *Bascillus subtilis*) bacteria. The hexane extract was found to have the most minor activity against *Proteus vulgaris* while dichloromethane and ethyl acetate extracts proved moderate activities with MIC values ranging from 1-0.5 mg /ml [65]. Crude extracts in different solvents (Methanol, hexane, and distilled water) of *E. hirta* were evaluated against *E. coli, K. pneumonae, S. dysentery, S. typhae* and *P. mirabilis* bacteria by the agar well diffusion method. The highest zone of inhibition was shown by aqueous extract against *E. coli, K. pneumonae, P. mirabilis, S. dysentery,* and *S. typhae* followed by methanol and hexane extract [66]. The different solvents (Petroleum ether, methanol, and aqueous) extracts of *E. hirta* leaves were investigated against *B. subtilis, E. coli S. aureus,* and *Saccharomyces cereviseae* bacteria. All the extracts showed moderate to significant antibacterial activity [67].

In addition to its activity against various Gram-negative and Gram-positive bacteria, *E. hirta* demonstrated its inhibitory potential against some strains of fungi. Suresh *et al.,* evaluated the ethanolic extract of the leaves of *E. hirta* for antifungal activity against *Aspergillus niger, Aspergillus fumigatus, Aspergillus flavus,* and *Rhizopus oryzae*. A remarkable activity was observed against all the tested fungi [63].

The methanolic extract of leaf of *E. hirta* has been evaluated for antifungal activity against *Candida albicans* by checkerboard method. The result showed that some combination of the extract with antifungal drug (Nystatin) could be synergistic in activity [68]. Mohammad *et al.,* tested the ethanolic extract of *E. hirta* against *Colletotrichum capsici, Fusarium pallidoroseum, Botryodiplodia theobromae, Phomopsis caricae- papayae,* and *Aspergillus niger* fungal pathogens by paper disk diffusion technique. The results showed that the extract is active against all the pathogenic fungi tested [69]. The essential oil of the aerial parts of this plant was tested against 4 fungi *viz, C. albicans, A. niger, Rhizopus stolonifer,* and *Pencillium notatum* by Pour plate and surface plate method, and a significant antifungal activity were found against *Candida albicans* [48]. Jackson *et al.* evaluated the methanolic extract of leaves against Candida albicans. The results showed primarily fungicidal effect at 1 and 2 fold MIC [68]. Petroleum ether, methanolic and aqueous extract of *E. hirta* leaves were tested against the fungus *Saccharomyces cerevisae* by agar well diffusion method. The results revealed that among the three solvent extracts, methanolic extract was found more active, and it shows maximum inhibition [67]. Altogether the antibacterial and antifungal potentialities reported exhibiting a good approach applied however, a proper and comprehensive pharmacological model consisting of *in-vivo* studies is also needed to confirm potential toxicity and their therapeutic activities [70].

The phytoconstituents of *E. hirta* viz, flavonoids, quercitrin, miricitrin and sterols 24- methylene-cycloartenol, as well as sitosterol, triterpenes and β amyrin, are known for anti-inflammatory activity. All the phytoconstituents displayed remarkable and dose-dependent anti-inflammatory activity [37]. The ethanol extract of *E. hirta* and its active components were studied in lipopolysaccharide-induced macrophage cells (RAW 264.7) as an established inflammation model. The ethanolic extract and its components exhibited a significant ant-inflammatory potential [71]. In another study, Xia *et al.* reported that the distilled water extract of *E. hirta* exhibits conspicuous and dose-dependent anti-inflammatory potential in carrageenan induced edema tests with 100 mg /kg body weight of rat [25].

Aqueous extract of *E. hirta* showed a protuberant and dose-dependent decrease of the gastrointestinal motility in rats and also lowered the castor oil-induced diarrhea in mice [72]. The aqueous extract of this plant also showed antiamoebic, antitetanic and antidiarrheal activities. Total polyphenolic extract of *E. hirta* exhibited inhibitory growth of Entamoeba histolytica at a concentration of less than 10 mg /ml [73]. In another study, Kamgung *et al*, argued about the contractile activity of the aqueous extracts of *E. hirta* in rats. They reported that the aqueous extract possesses spasmogenic activity *in-vitro* and antidiarrheal activities *in-vivo* [74].

The aqueous extract of *E. hirta* was subjected to sedative and anxiolytic activity in mice. The results showed that the extract has positive effects on the sedative and anxiolytic potential [9]. The hydroalcoholic extract of this plant was also screened for anxiolytic activity in chronically stressed mice in two different stressors *viz,* chronic immobilization stress and forced swim stress. The results revealed that the extract showed anxiolytic potential in chronically immobilization stress and in others does not [75].

Ethyl acetate and acetone extract of *E. hirta* were tested for the determination of cytotoxicity effect in Brine Shrimp lethality test [76]. In a study, Envera *et al.,* reported that the extract of *E. hirta* leaves displayed a toxicity effect depending on the viability of cells by *in-vitro* analysis on the lymphocytes [77]. Sandeep and Chandrakant examined the antitumor potential of aerial part of *E. hirta* against EL-4 cell line in the swiss albino rat. The results revealed remarkable enrichment of mean survival time and depletion in solid tumor mass of EF-treated tumor affected mice [78, 79]. The aqueous, methanolic extracts and one of its phytoconstituents i.e., quercetin, were evaluated for mutagenic and antimutagenic activities in the ratio of 100 g/ml (aqueous extract) and 10 & 100 g/ml (methanolic extract). The aqueous and methanolic extract showed mutagencity of 2- aminoanthracene in *S. typhimurium* TA 98 in the presence of S-9 metabolic activation. The aqueous and methanolic decoctions of *E. hirta* were found potential as anticarcinogenic agents. The phytoconstituent quercetin did not display antimutagenic activity [80].

The petroleum ether and ethanolic extract of *E. hirta* flowers were tested to know these extracts' free radical scavenging potential by various *in-vitro* antioxidant assays *viz,* DPPH (2,2-Diphenyl-1 picrylhydrazyl) free radical scavenging method, nitric oxide scavenging and reducing power method, and superoxide radical scavenging assay. The standard antioxidant compound such as ascorbic acid and butylated hydroxyl anisole was used for comparison in the experiment. The result revealed that all the extracts displayed remarkable antioxidant potential [81]. Different parts (leaves, stems, flowers, and roots) of *E. hirta* were evaluated for antioxidant potential and flavonoid and polyphenolic content by DPPH radical scavenging assay. The results showed that the leaves' decoction displayed the highest DPPH scavenging potential up to 72% followed by other parts. Leaves extracts also had maximum total flavonoids and polyphenolic contents followed by flower root and stem decoctions [82]. Teeli *et al.* examined the methanolic and aqueous extracts of *E. hirta* for antioxidant activity comparable to black and green tea.

The study revealed that the phenolic acids showed remarkable antioxidant potential and also displayed synergistic interaction with BSA (Bovine serum albumin). It was also found that their antioxidant potential increased up to 20% after incubation with BSA [57]. The Aqueous decoction at 0.25 mg/ml concentration exhibits maximum antioxidant and free radical scavenging activities in various *in-vitro* models *viz,* DPPH (2,2- Diphenyl-1 picrylhydrazyl), ABTS [2,2- Azinobis (3-ethylbenzothiazoline-6- sulphonic acid)], FRAP (Ferric-reducing antioxidant power) and hydroxyl radical scavenging assays [83]. In a study, Salehi *et al.* reported that *E. hirta* possesses antiasthmatic activity because of the relaxation effect on the bronchial tubes and sedative action on respiration [53]. In addition, the ethanolic and aqueous extracts of *E. hirta* leaves could remarkably provoke diuresis in mice. It increased urine output and electrolytes as well. This study revealed that the functional constituents in the aqueous extract of the *E. hirta* leaf have similar diuretic effects that of acetazolamide [15].

Ajayi *et al.* studied the antimalarial activity of isolated flavonol glycosides afzelin, quercitrin, and myricitrin from *E. hirta*. The results revealed that these isolated compounds showed inhibition of proliferation of *Plasmodium falciparum* at various concentrations [84]. Furthermore, Agenes *et al.* evaluated the antiretroviral potential of aqueous and methanolic extracts of *E. hirta* by comparing against SIVmac2s1, HIV-1, and HIV-2 viruses on MT4 human T lymphocyte cells. They reported that 50% methanolic decoction displayed significant antiretroviral properties compared to the aqueous extract [85]. Ansari *et al.,* evaluated the ethanolic and petroleum ether decoctions of *E. hirta* flowers for antidiabetic potential in alloxan diabetic rats. The results showed a remarkable decrease in serum, cholesterol, triglycerides, creatinine, urea and

alkaline phosphatase levels after incorporation of the extract [3]. In another study, the ethanolic extracts of the different parts (Leaf, stem and flowers) of *E. hirta* were examined in streptozotocin-induced diabetic mice. The results revealed a remarkable reduction in blood glucose level and decrease in serum cholesterol level with a rise of HDL [55]. *E. hirta* Linn has been used in conventional medicine since the remote past. However, the research findings of the toxicity and safety evaluations are lacking, and little information on target organ toxicity or side effects is reported in the literature. Adedapo *et al.* evaluated the crude aqueous extract of this plant to ascertain the effects of the extracts on the male reproductive organs of rat. The extract was taken orally to a 38-week old rat at the dose of 400 mg/ kg. The result showed that the extract causes a different level of testicular degeneration and decrease in mean somniferous tubule diameter in male rats [86]. In another study, the effort was made to determine the toxicity of the plant extracts. This indicated that all the parts of *E. hirta* plant except flower had LC_{50} values of nearly 1 mg /ml [69]. Sunil *et al.* reported that the sub-lethal doses of extracts change the levels of protein, free amino acid, nucleic acids, and the property of protease enzyme, acid, and alkaline phosphatases in various tissues of the vector snail Lymnae accuminata in time and dose-dependent manners [87].

Future Prospects: It was noticed that the plant has wide applications as antiasthmatic, anti-inflammatory, antidiabetic, antimicrobial, and for respiratory system disorders. Some compounds have also been isolated and identified as flavonoids, terpinoids and phenols. In addition, 11 bioactive constituents have also been distinguished and identified from the essential oil of *E. hirta* among which (Z)- 9- Octadecenamide was found the most abundant. It exhibited antimicrobial and anti-inflammatory activities [88]. Besides it, fatty acid esters identified in the essential oil have been reported to show antibacterial and antifungal activities, and these constituents might have proven to be helpful for the antimicrobial activities of *E. hirta* [81]. These bioactive constituents and crude extracts of *E. hirta* have been examined for pharmacological potential *in-vitro,* and *in-vivo* tests indicate that it is pharmaceutically very important. The data presented in this review support the methods applied by traditional healers.

It is evident from the data that aqueous extract of *E. hirta* has shown remarkable antibacterial activity, suggesting that the active components are more soluble in dis. H_2O. Hence aqueous solvent is most appropriate for the extraction of bioactive components present in *E. hirta* [89]. Awesome work has been done in the phytochemistry and pharmacology of E. hirta however, there is some draw back in the scientific literature that needs to be further investigated to speed up the ongoing scientific and clinical research. The crude extracts of *E. hirta* have numerous biological activities. Still, their active chemical constituents need to be further elucidated by bioassay-guided isolation, and their action mechanism remains unclear and should be further investigated. Some bioactivities of *E. hirta* have been performed *in-vitro* but *in-vivo* studies following animal models to investigate their therapeutic are meager. Additionally, *E. hirta* have been authenticated to possess various kinds of pharmacological potentialities, but investigation on the action mechanism is lacking and should be further investigated. Toxicological studies are another important aspect of understanding the safety profile of herbal medicine. The toxicity effects include different levels of testicular degeneration and a decrease in mean somniferous tubule diameter in male rats.

Sub-lethal doses of extracts change the level of protein, free amino acid, nucleic acids, and the property of protease enzyme, acid, and alkaline phosphatases in various tissues of the vector snail *Lymnae accuminata* are less understandable and should be further assessed. Some previous studies demonstrate that all the parts of *E. hirta* plant except flower had LC_{50} values of nearly 1mg /ml [69]. Therefore, it is necessary to further explore the toxicity and side effects of the herb, biologically active crude extracts, and the main active component of this plant.

CONCLUSION: The present study reviewed botanical description, medicinal uses, active phytochemicals and pharmacological activities of an invasive plant *E. hirta* Linn. This plant shows a significant therapeutic potential, however, unfortunately, not all but some of the

pharmacological studies were conducted *in-vitro*, whereas *in-vivo* studies also needed to explore their activities against animals to validate its *in-vitro* activities. It is interesting to note that this plant reveals good therapeutic potential as an anticancer agent too. Further studies are desirable to evaluate *E. hirta* anticancer activity through *in-vivo* conditions and clinical trials. In addition, the clinical test must also be conducted to determine the clinical efficacy of *E. hirta* for humans.

ACKNOWLEDGEMENT: The authors convey sincere gratitude to the Head Department of Botany for providing necessary lab facilities for the study. The first author (A N T) is also thankful to UGC (SRF fellowship) for providing financial assistance. Thanks are also due to local people and knowledgeable persons who provided useful information about the traditional usage of *E. hirta* plants in the folk medicinal system.

CONFLICTS OF INTEREST: The author declares no potential conflict of interest.

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How to cite this article:
Tripathi AN, Sati SC and Kumar P: E*uphorbia hirta* Linn - an invasive plant: a review of its traditional uses, phytochemistry and pharmacological properties. Int J Pharm Sci & Res 2021; 12(12): 6189-01. doi: 10.13040/IJPSR.0975-8232.12(12).6189-01.