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

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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 with the aim 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 disorder, bronchitis, and in 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 hydro-alcoholic 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 the 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 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. Latices of *E. ingens*, *E. tirucalli*, *E. mey*, and *E. triangularis* are possible sources of rubber [3].

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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 gastrointestinal disorders (Diarrhea, amoebic dysentery, intestinal parasitosis, peptic ulcers etc.), bronchial and respiratory diseases (Asthma, bronchitis, hay fever, laryngeal spasms, cough-colds), and in conjunctivitis [5, 6, 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, anti-

malarial, larvicidal, diuretic, and antidiabetic activity [8, 9, 10, 11, 12, 13, 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 a long time. A 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 the traditional medicinal system due to its wide range of biological and pharmacological properties.

Keeping in mind the effects of *E. hirta* in curing skin ulcers 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 a first composite review on this Kumaun Himalayan invasive plant, which provides 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 uses, phytoconstituents and pharmacological potential of *E. hirta* were collected by consulting a large number of literature. The scientific data are based on google scholar, web of science, pub med, 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 a number of times. Chemical structures were drawn using Chem Draw Professional 16.0 software.

Botanical Description: *E. hirta* Linn. as illustrated in **Fig. 1** (A & B) is a small annual, branched herb reaching up to 70 cm in height, purplish or reddish in colour with ample amount of latex and coated with shoot hairs. Leaves are opposite, distichous and simple; stipules are linear, leaf blade 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 monoecious, axillary or terminal cluster of flowers, known as cyathium with several cyathia arranged into a cyme. The male and female flowers are in one involucre and both apetalate. The flowers are unisexual, male flowers are sessile, bracteoles are linear, fringed, perianth is absent and possesses one stamen, female flowers have small pedicel, perianth is rimmed, the 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, 21, 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 consists 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, lowland, 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 a dry plant is used externally in burned and scald, whereas freshly crushed leaves are applied in the treatment of skin disease [18]. Decoction or tincture of this plant 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 in 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* are used in 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 in the treatment of sore, boils and it also has wound healing property [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, 32, 33, 34]. The extracts of the root 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 property [37].

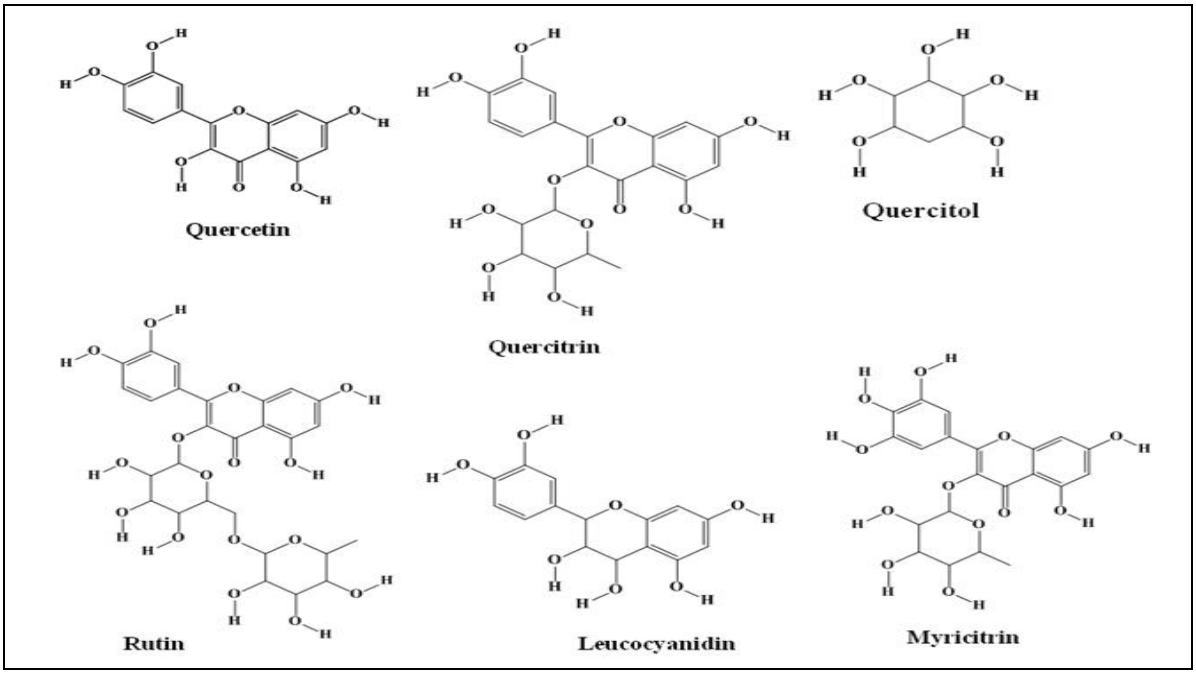
Phytochemistry: The main group of bioactive phytochemicals of *E. hirta*, which have been distinguished and identified as illustrated in **Fig. 2** includes, flavonoids, steroids, terpenoids, coumarins, tannins and polyphenols [38, 39, 40]. Phyto-chemical analysis of leaf extract revealed the presence of carbohydrates, terpenoids, alkaloids, reducing sugars, steroids, tannins, proteins, fats, oils, mucilages, glycoside, saponin, coumarin, anthraquinones, 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. β- 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]. The second group of compounds isolated from *E. hirta* is 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 pentadecanone, 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. These components of volatile oil may be responsible in 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 acid, and mineral. 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]. Two novel kinds of rhamnopyranosides (1 & 2) have been extracted from the various non-polar and polar extracts of Indian-born *E. hirta* plants recently. They were distinguished as- n- butyl-1-o-L-rhamno-pyranoside (1) and n- butyl -1-o-L-rhamnopyranoside [52].

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



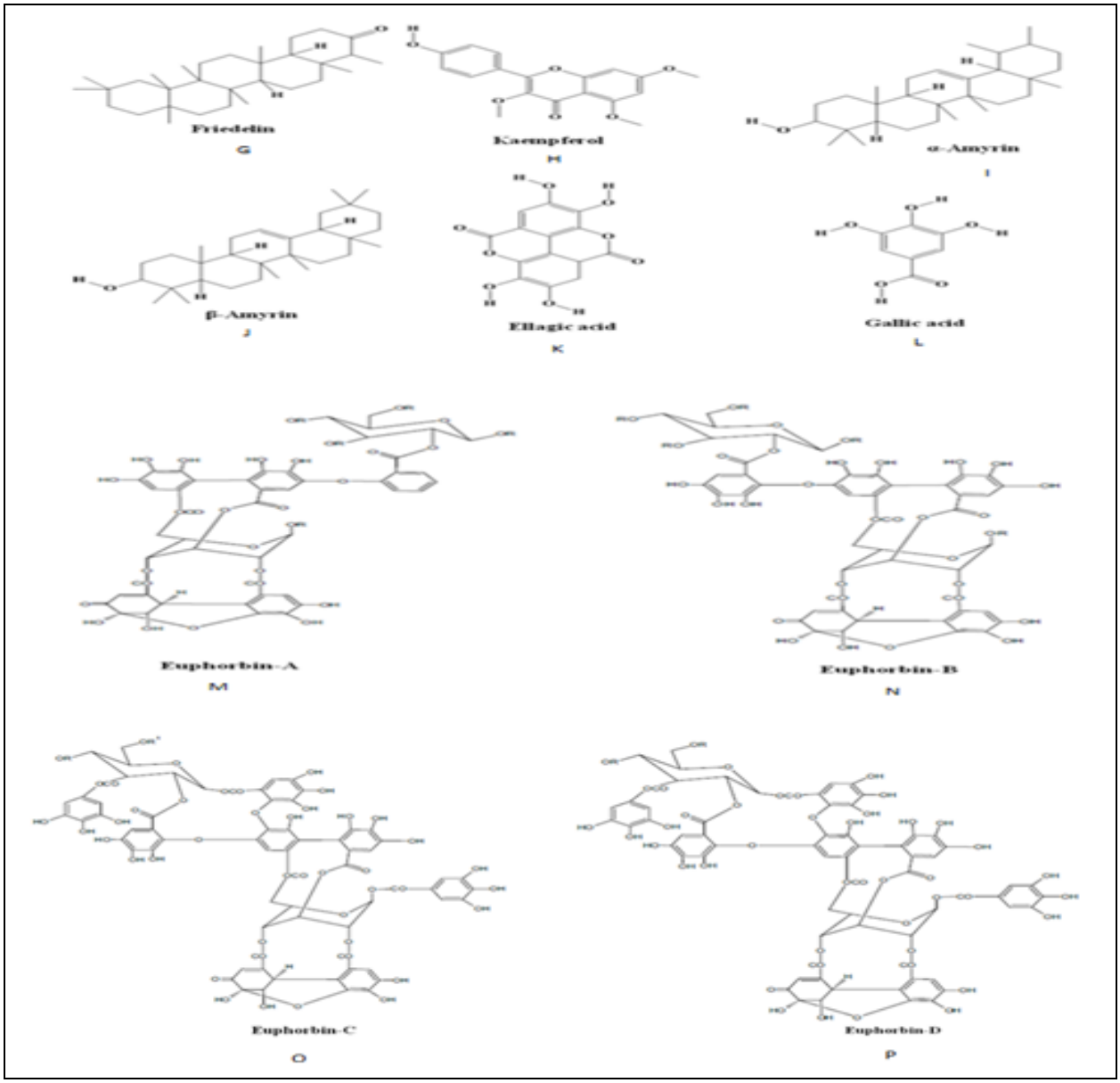


FIG. 2: THE CHEMICAL STRUCTURE OF MAIN COMPOUNDS FOUND IN *E. HIRTA*

Different parts of *E. hirta* plant were studied for total polyphenolic and flavonoid content. Leaves extract revealed the great amount of total phenolic content (26.17 ± 1.95) mg GAE /g dry weight. Leaves also showed the highest amount of 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-inflamatory, antidiarrheal, sedative and anxiolytic, anticancer, antipyretic, antioxidant, antiasthmatic, antitumar, antimalarial, diuretic and increases electrolytes, antidiabetic and antiviral activities [51-58].

Since 1980s the antibacterial activities of *E. hirta* has been investigated in-depth and proven by several studies. Vijay *et al.,* tested the antibacterial activity of methanolic extract of *E. hirta* against *Shigella spp*. using vero cell line. The decoction exhibit good antibacterial activity against dysentery-causing bacteria [59]. The antibacterial activity of the crude ethanolic extract of *E. hirta* have 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 m*irabilis) bacteria. The leaves decoction exhibited a large zone of inhibition to all the evaluated microorganisms followed by flowers [64]. The root extract also showed 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. aerogin*osa, *S. typhae* and *Shigella dysenteriae*) and Gram positive (*Staphylococcus aureus* and *Bascillus subtilis*) bacteria.

The hexane extract was found with least activity, against *Proteus vulgaris* while dichloromethane and ethyl acetate extracts proved moderate activities with MIC values rainging from 1 -0.5 mg/ ml should be attached in earlier paragraph. Gram positive (*Staphylococcus bacteria* and *Bacillus subtillis*) bacteria.

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* have 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 effects 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 pharmaco-logical model consisting of *in-vivo* studies are also needed to confirm potential toxicity and their therapeutic activities [70].

The phyto-constituents 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 carageenam induced edema tests with 100 mg /kg body weight of rat [25].

Aqueous extract of *E. hirta* showed 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 hydro-alcoholic 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 depend 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 mutagenicity 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 the free radical scavenging potential of these extract 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.* (2018) has examined the methanolic and aqueous extracts of *E. hirta* for antioxidant activity, which are 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 falciperum* at various concentrations [84]. Furthermore, Agenes *et al.,* evaluated 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 cell. They reported that 50% methanolic decoction displayed significant antiretroviral property 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, cholestrol, 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 decreased serum cholestrol level with a rise of HDL [55].

E. hirta Linn. has been used in conventional medicine in the remote past. However, the research findings of the toxicity and safety evaluations are lacking, and little information of 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 the 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 a 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 the 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 respiratory system disorders. Some compounds have also been isolated and identified as flavonoids, terpenoids, 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 phytochemistry and pharmacology of *E. hirta*, however, there is some drawback in the scientific literature which need to be further investigated for speed up the ongoing scientific and clinical research. The crude extracts of *E. hirta* have numerous biological activities, but 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 to understand 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 the flower had LC_{50} values of nearly 1 mg/ml [69]. Therefore, it is necessary to further explore the toxicity and side effects of the herb, biologically active crude extracts, and main active component of this plant.

CONCLUSION: The present study reviewed botanical description, medicinal uses, active phyto-chemicals, and pharmacological activities of an invasive plant *E. hirta* Linn. This plant shows a significant therapeutic potential, however, unfortunately, some of the pharmaco-logical studies were conducted *in-vitro*, whereas *in-vivo* studies also needed to explore their activities against animals to validate it *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 the *in-vivo* condition and clinical trials. In addition, the clinical test must also be conducted to determine the clinical efficacy of *E. hirta* for humans.

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