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An updated review on phytopharmacological profile of *Euphorbia tithymaloides* (L.) Poit

Rajani Srivastava and Neetu Soni

Abstract
Euphorbia tithymaloides (L.) Poit or *Pedilanthus tithymaloides*, (Family: Euphorbiaceae), is a tropical and subtropical succulent plant. This plant is available in various parts of India: Assam, Bihar, Gujarat, Madhya Pradesh, Maharashtra, Odisha, and Uttar Pradesh. The stem of this plant has morphological resemblance with spinal column due to zigzag structure. The fleshy tubular stems of this plant are thin pencil like which produce thick, dark-green or variegated, fleshy, ovate leaves and peculiar beak shaped flowers. *Pedilanthus tithymaloides* is mostly used as an ornamental plant and for making fencing in garden. It is latex producing plant and its latex has been traditionally used to treat various pathological conditions apart from latex its leaves, stem and roots also used to treat ear ache, insect stings, ringworm, skin cancer, toothache, umbilical hernias, and warts. This plant is reported to possess various phytochemicals viz. steroids, tannins, triterpenes, coumarins and saponins which have been shown to possess anti-diabetic, antioxidant, analgesic, stomachic, hemostatic, anti-microbial, antifungal, anti-helminthic, antimutagenic, anti-tubercular, antimalarial, anti-inflammatory, abortifacient, antivenom, antibiotic, antiseptic, antihemorrhagic, antiviral and antitumor effect and useful for venereal diseases. The isolated phytochemicals reported in this plant were cycloartenone, dammaronol A, dotriacontan- 1-ol, friedelanol, hentriacontan-1-ol and sitosterol. Some of the antioxidant principles like Kaempferol, quercitrin, isoquercitrin, and scopoletin were isolated. The significant bioactive principles reported in *Pedilanthus tithymaloides* were diterpenoids, triterpene, flavonoids, carotenoids, pedilanthus coumarin A, pedilanthus coumarin B, 5,7-dihydroxy-8-(2-methylbutyryl)-4-phenylcournarin, theraphin C, isodispar B, isodisparinol B and isomesuol. Recently silver nanoparticles of plant latex have been synthesized for their potential use as antibacterial agents. The aim of present review is an effort to provide coherent literature survey of plant *Euphorbia tithymaloides or Pedilanthus tithymaloides* in relation to its phyto-pharmacological, ethnobotanical and therapeutical uses that would pave the way for development of phytopharmaceuticals.

Keywords: *Euphorbia tithymaloides*, *Pedilanthus tithymaloides*, pharmacological, phytochemical

1. Introduction
Euphorbia tithymaloides (L.) Poit (Family: Euphorbiaceae), also known by its old scientific name *Pedilanthus tithymaloides*, is one of the common succulent plant native to tropical and subtropical, North America and Central America and some areas of South Asia. The common vernacular names of *Pedilanthus tithymaloides* are *redbird flower, devil's-backbone, buck-thorn, cimora misha, christmas candle, fiddle flower, Jacob's ladder, Japanese poinsettia, Jew's slipper, Jewbush, milk-hedge, myrtle-leaved spurge, Padus-leaved clipper plant, red slipper spurge, redbird cactus, slipper flower, slipper plant, slipper spurge, timora misha, gin-ryu* (Japan); *pokok lipan and penawar lipan* (Indonesia); *airi, baire, and agia* (India); *aperejo* (Yoruba); *sapatinho do diabo* (Brazil); *itamo real* (Puerto Rico); *pantoufle* (France) and *zapatilla del diablo* (Mexico). *Euphorbia tithymaloides* distributed in various states of India; Assam, Bihar, Gujarat, Madhya Pradesh, Maharashtra, Odisha, Utter Pradesh. This plant is known as naagfani in Uttar Pradesh and naagdon in Madya Pradesh. *Euphorbia tithymaloides* is 0.4 to 3 m tall and 40-60 cm wide plant, that branch profusely from the base. It grows well in variety of soils, sandy, well-drained, and nutrient-rich, particularly with higher concentrations of boron, copper, iron, manganese, molybdenum, and zinc, relatively intolerant of high soil salinity levels, but exhibits saline tolerance if well fertilized. The fleshy tubular stems of this plant are thin pencil like which produce thick, dark-green fleshy, ovate leaves and peculiar beak shaped flowers. To some, the flower bracts resemble a slipper, hence one of its many common names. The stem of this plant has morphological resemblance with spinal column due to zigzag structure hence it is known as *devil's-backbone*.

The color of flowers varies from bright white to pink, leaves bright green in colour, sessile, about 1.4 to 3 inches (3.6 to 7.6 cm) in length, glabrous or smooth with acuminate apex and entire edges or margin. It possesses apical or axillary dichotomous congested cyme inflorescence near the tip of stem. Each cyathia (flower structures containing separate male and female parts) supported by a peduncle of 3-8 mm long, red, green below and enclosed in bright red involucre, bracts, ovate and irregularly acuminate in shape (e.g., like a slipper) 4-12 mm long, 2-5 mm wide. Fruits are capsule, cuboid with truncated ends, deeply 3- lobed which have 3-4.5 mm long ovoid seeds [1, 2].

Fig 1: Medicinally

Medicinally, this plant has powerful emetic, irritant and caustic properties. The extract of leaves used for treating asthma, mouth ulcers, venereal troubles, ringworms and insect stings. This plant is also known to possess anti protozoal, mitogenic, anti-inflammatory, anti-plasmodial, anti-mycobacterial, anthelminthic and antimicrobial activities. It is also reported to have activity to minimize nematode damage in mushrooms [3]. It is also used as an ornamental specimen in any garden with its extremely impressive variegated foliage. Based on folklore, leaves are brewed into tea to treat asthma, persistent coughing and mouth ulcers. Sap has been traditionally used to treat callouses, ear ache, insect stings, ringworm, skin cancer, toothache, umbilical hernias [4]. The aim of present review is an effort to provide coherent literature survey of plant *Euphorbia tithymaloides or Pedilanthus tithymaloides* in relation to its phyto-pharmacological, ethnobotanical and therapeutical uses that would pave the way for development of phytopharmaceuticals.

This updated review article is an attempt towards, compilation of scientific information obtained from the research papers published since last two decades, through various search engine facility provided by SHUATS e- journals like CeRA, Springer, CABI and also other reputed information sources like Science Direct, PubMed, etc. This review paper could be helpful for providing backbone in plant based researches and advanced plant based qualitative researches in herbal drug technology.

2. Pharmacological potentials of plant *E. tithymaloides*

2.1 Wound healing activity

The study aimed to investigate the potential of an ethanolic extract of *Pedilanthus tithymaloides* to stimulate excision wound healing. In this study samples of 42 female mice were divided into three groups: group I – methylcellulose (negative control); group II – 0.5% (w/w) crude extract; and group III – 1.5% (w/w) crude extract. The results were compared among treatments and a control group, in terms of wound appearance, parameters of wound healing and a histopathological study. In the treatment groups, the parameters of wound healing were significantly higher in comparison with the control group. The histopathological study also showed increased fibroblast, collagen fiber and blood vessel formation. However, the wounds treated by 0.5% crude extract healed faster when compared to the group with 1.5% crude extract. In conclusion, 0.5% crude extract of *P. tithymaloides* was more suitable for the stimulation of wound healing than 1.5% crude extract because the latter was too concentrated that caused irritation and inflammation, leading to delayed healing [5].

2.2 Anti-inflammatory activity

In the present study, the anti-inflammatory activity performed on hexane, methylene chloride, chloroform, ethyl acetate and methanol extracts of *Pedilanthus tithymaloides* leaves. The male albino rats selected as model animal and carrageenin induced paw edema model used with the help of Plethysmometer. The different extracts at the dose of 200 mg/kg body weight suspended in Tween 80 in sodium chloride aqueous solution, were administered orally 30 minutes prior to the injection of carrageenan into sub-plantar region of the right hind paw. Inflammation was expressed in terms of paw edema volume displaced by the inflammed rat paw. The percentage inhibition of inflammation was measured. Among the different extracts, methanol extract at the dose of 200 mg/kg body weight showed significantly more anti-inflammatory activity in comparison with other extracts and in compared to the standard drug, Phenylbutazone. After that the anti-inflammatory activity of methanol extract was also observed using histamine-induced rat paw edema, and dextran-induced rat paw edema model. The methanol extracts exhibited anti-inflammatory activity in a dose dependent manner in these models as compared to the standard drug, phenylbutazone. It was concluded in present research paper that methanol extract of *Pedilanthus tithymaloides* showed a significant anti-inflammatory effect [6].

2.3 Antioxidant activity

In the present study, a tincture from *P. tithymaloides* collected in Cuba was evaluated for its in vitro scavenging effects on reactive oxygen species, nitrogen species and DPPH radical. In the scavenging assays the tincture showed to be effective against all the assayed reactive oxygen and nitrogen species especially but displayed weak activity in the DPPH Assay. Due to the role of reactive species in the inflammatory process and, the relation between periodontal disease/stomatitis and impaired antioxidant status, the scavenging effects of the tincture on reactive oxygen and nitrogen species could be considered for plant anti-inflammatory effect [7].

2.4 Anthelminthic activity

In the present investigation, the ethanolic leaf extract of *Euphorbia tithymaloides* was evaluated for its possible anthelminthic activity using albendazole as standard and adult earthworm (*Pheretima posthuma*) as a test organism. The function of the anthelmintic drugs like albendazole is to cause paralysis of worms so that they are expelled in the feces of man and animals. The extracts demonstrated anthelminthic property of *Euphorbia tithymaloides* leaves, the extract also showed a positive result in the form of death of the worms, as compared with the albendazole. The drug showed dose

dependent activity as compared to the standard drug albendazole [8].

2.5 Anti-diabetic and anti-inflammatory activity

In the present study, the Ethanolic extract of *E. tithymaloides* **(**ETE) was investigated for anti-diabetic anti-inflammatory activity by glucose uptake assay, Oil -Red -O staining, triglyceride assay, and by analyzing adipogenic markers expression. The anti-inflammatory and anti-diabetic activities were studied through the treatment of RAW 264.7 murine macrophages cells and 3T3-L1 adipocytes. To determine the glucose uptake in 3T3-L1 pre-adipocytes, 3T3-L1 cells were incubated with different concentration of ETE and insulin for 24hrs. Thereafter, addition 2-NBDG (N-(7-Nitrobemz-2-oxa-1,3-diazol-4-yl) Amino)-2- deoxy glucose), the cells were incubated for a further 30 min. Negative control and positive control were designed to identify the effect of ETE in 3T3-L1 preadipocytes cells. The addition of insulin was considered as positive control which helps to enhance glucose uptake to the cells. To measure the accumulation of triglycerides, adipocyte differentiation was induced at the end of the treatment period, which is a common measurement of PPARγ agonist activity. The differentiated adipocytes cells were fixed with formaldehyde and washed with distilled water. Oil-Red-O solution was used to stain the cells and incubated for 1h. After washing, the fat droplets in 3T3-L1 adipocytes were monitored under microscope. The amount of triglyceride was determined by isopropanol dissolution and quantified by spectrophotometric analysis at 490 nm. The adipogenic markers expression such as PPARγ, C/EBPα, GLUT4, and IRS1 was determined by western blotting. The results indicated that ETE significantly increased glucose uptake in a dose-dependent manner. 400µg/mL ETE caused a two-fold increase in glucose uptake in insulin-induced 3T3-L1 cells. Similarly, GLUT4 protein expression was also increased along with increasing the concentration of ETE. In contrast, 1µg/mL insulin increased GLUT4 expression of positive control and 400µg/mL ETE by 8 and 13- fold, respectively. ETE was also found to significantly enhance adipogenesis in a dose dependent manner in 3T3-L1 preadipocytes. The lipid accumulation by ETE in fully differentiated 3T3-L1 cells significantly increased as the concentration was increased to 400µg/ml. The expression of adipogenic markers, such as PPARγ, C/EBPα, and IRS-1 also significantly increased as the concentration of ETE increased. These findings suggested that ETE is herbal component with potential use in the development of new immunomodulatory and anti-diabetic agents for treating inflammation and diabetes mellitus, respectively [9].

2.6 Anti-viral activity (Inhibition of HSV-2 replication)

In the current study, the in vitro antiviral activity of a methanolic extract of the leaves and its isolated compounds against Herpes Simplex Virus type 2 (HSV-2) was evaluated. Bioactivity-guided studies revealed that the extract and one of its constituents, luteolin, had potent antiviral activity against wild-type and clinical isolates of HSV-2. The inhibitory effect was significant when the drug was added 2 hours prior to infection, and was effective up to 4 hours post infection. As viral replication requires NF- κB activation, it was examined whether the observed extract-induced inhibition of HSV-2 was related to NF-κB inhibition. It was observed that treatment of HSV-2-infected cells with extract or luteolin suppressed NF-κB activation. Although NF-κB, JNK and MAPK activation was compromised during HSV replication, neither the extract nor luteolin affected HSV-2-induced JNK1/2 and MAPK activation. The leaf extract and luteolin potently down-regulated the expression of tumor necrosis factor (TNF)-α, Interleukin (IL)- 1β, IL-6, NO and iNOS and the production of gamma interferon (IFN-γ), which are directly involved in controlling the NF-κB signaling pathway. Thus, the results indicate that both leaf extract and luteolin modulate the NF-κB signaling pathway, resulting in the inhibition of HSV-2 replication [10].

2.7 Alloxan induced antihyperlipidemic and antihyperglycemic activities

In the recent research *P. tithymaloides* ethanolic leaf extract was evaluated on serum lipid profile changes in normal and alloxan induced diabetic albino Wistar rats, rats were divided into five groups. Group I consist of normal rats that were given only normal saline solution and served as a control group. Group II consists of normal rats that were given alloxan monohydrate, Group III consists of alloxan induced diabetic rats that were given daily sterile solution, ethanolic leaf extract of *Pedilanthus tithymaloides* (500 mg/kg), Group IV consists of alloxan induced diabetic rats that were given daily sterile solution, ethanolic leaf extract of *Pedilanthus tithymaloides* (1000 mg/kg), Group V consists of alloxan induced diabetic rats that were given daily sterile solution and glibenclamide (5mg/kg) respectively for 21 days by an intragastric tube with free access of food and water. Several biochemical parameters were assessed. Oral administration of the extract resulted in significant reduction in mean values of blood glucose, cholesterol, triglycerides, LDL-C, VLDL accompanied by an increase in the mean values of the HDL in diabetic rats. The effects produced by this extract were closely similar to a standard anti diabetic drug, glibenclamide. In conclusion, the present study indicates that the ethanolic extract of *Pedilanthus tithymaloides* exhibited antihyperlipidemic and antihyperglycemic activities in alloxan induced diabetic rats [11].

2.8 Anti-microbial activity

In the recent investigation, the phytochemical prospection and a screening of the antimicrobial effects of *P. tithymaloides* was performed. Leaves samples were processed to obtain extracts using hexane, ethyl acetate and ethanol by maceration. Phytochemical prospection of relevant secondary metabolites and antimicrobial evaluation by microdilution method against one yeast and six pathogenic bacteria were performed. Triterpenes, steroids, saponins, tannin and coumarins were detected in the plant extracts. Hexane and ethyl acetate, both were effective against *Streptococcus sanguinis*, hexane inhibited *Enterococcus faecalis*. The extracts also inhibited *Candida albicans*. No inhibition was detected against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa or Salmonella enterica*. These findings were in support with the potential use of *P. tithymaloides* as antimicrobials against relevant pathogens [12].

2.9 Haemostatic activity

In the present study, various proteolytic activities namely protease, gelatinase, milk clotting and whole blood clotting assay of the enzyme fraction of latices of *Euphorbia nivulia*, *Pedilanthus tithymaloides* and *Synadenium grantii* were investigated along with the assessment of the inhibition profile of protease specific inhibitors. The effects of protein

fractions were also studied using bleeding/clotting time test of fresh experimentally-induced wounds in mice. The results obtained from this latest study showed that *Euphorbia nivulia* latex protease has got noticeable blood clotting activity followed by *Pedilanthus tithymaloides* and *Synadenium grantii*. Stem latex protease of *Pedilanthus tithymaloides* exhibits superior procoagulant activity in different mammal's blood samples viz., *Capra hircus, Bubalus bubalis, Ovibos moschatus* and *Bos indicus*. Blood sample of ox was the most sensitive to latex protease than other mammal's blood. Concomitantly, the plant latex protease could significantly reduce whole blood clotting time of human and mice blood samples. The finding of this study also showed that the protease enzyme of *Pedilanthus tithymaloides* has the most potent haemostatic agent [13].

2.10 Larvicidal activity

The crude ethanolic leaf extract of *Pedillanthus tithymaloides* was evaluated for larvicidal activity against the dengue vector, *Aedes aegypti.* Mortality was observed for 24 and 48 hours. The crude ethanolic leaf extract of *Pedilanthus tithymaloides* exhibited a moderate level of larvicidal property [14].

3. Phytochemical potentials of plant *E. tithymaloides*

3.1 The leaves of *Pedilanthus tithymaloides* Poit (L.). (Euphorbiaceae) were processed to obtain phytochemical composition of the crude extracts. Leaves were the main plant part used in the cited studies as well as registered by the folk medicine. The hexane (Hex), ethyl acetate (EA) and ethanol (EtOH) used for extraction. A rapid and useful colorimetric methodology was applied to determine the most relevant groups of secondary metabolites obtained within the extracts. Relevant phytochemical groups were identified as steroids in hexane and ethyl acetate, triterpenes in hexane, tannins in ethyl acetate, coumarins in ethyl acetate and saponins in hexane and ethyl acetate extracts [15].

3.2 A bioassay-guided isolation of powdered stems and leaves of *P. tithymaloides* performed to find out the main antioxidant principles. The principles were identified as kaempferol 3-O-b-D-glucopyranoside-600-(3-hydroxy-3-methylglutarate), quercitrin, isoquercitrin, and scopoletin. The contents of total phenolics and flavonoids were found to be 76.0 ± 4.8 mg of gallic acid equivalents/g extract and 9.8 ± 0.4 mg of rutin equivalents/g extract, respectively [7].

3.3 Bioactivity-guided isolation of the active component led to the identification of a series of coumarin derivates from extracts of *Pedilanthus tithymaloides*. In this research work, a series of 10 coumarin derivatives were isolated from *Pedilanthus tithymaloides* (Euphorbiaceae). Their structures were established on the basis of spectroscopic data and X-ray crystallography. Nine out of 10 coumarin derivatives were found to inhibit conidial germination in the phytopathogenic fungus at low concentrations. Compound pedilanthus coumarin A as a yellow oil, Compound 2 pedilanthus coumarin B, yellow oil, compound 3 was identified as 5,7-dihydroxy-6- (2-hydroxy-3-methylbut-3-enyl)-8-(2-methyl-1-oxopropyl)-4-phenyl- 2H-benzopyran-2-one. Compound 4–10 were found to be identical to 5, 7-dihydroxy-8-(2-methylbutyryl)-4-phenylcournarin, theraphin C, isodispar B, mammea E/BB, mammea E/BD, isodisparinol B and isomesuol [16].

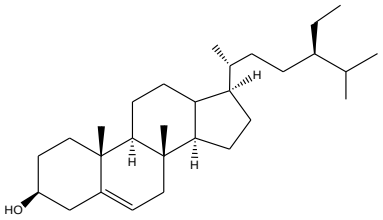


Fig 2: β-Sitosterol

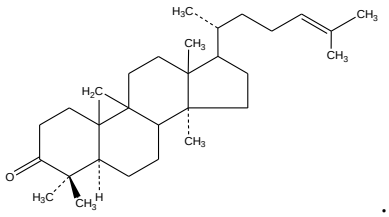


Fig 3: Cycloartenone

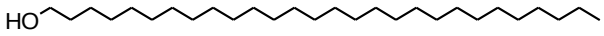


Fig 4: Octacosanol

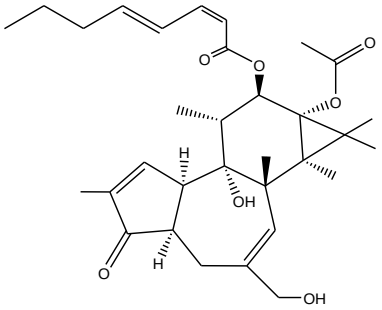


Fig 5: Pedilstatin [13-*O*-acetyl-12-*O*-[2‘*Z*,4‘*E*-octadienoyl]-4α-deoxyphorbol]

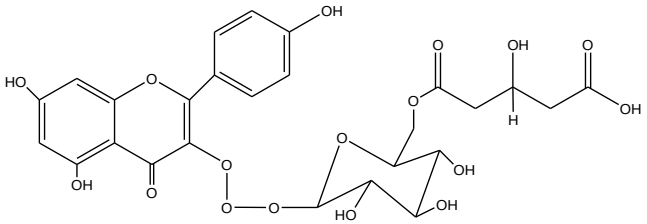


Fig 6: Pedilanthain

Fig 7: N-hentriacontanol

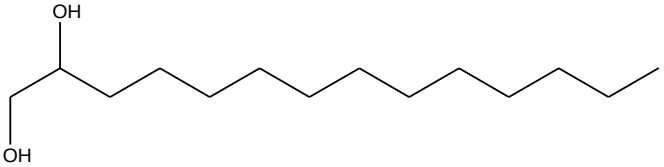


Fig 8: 1, 2-Tetradecanediol 1-(hydrogen sulfate) sodium salt

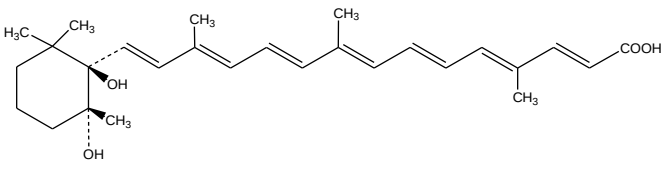


Fig 9: Azafrin

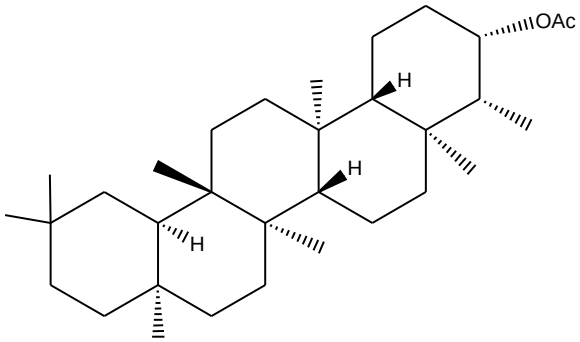


Fig 10: Epifriedelanyl acetate

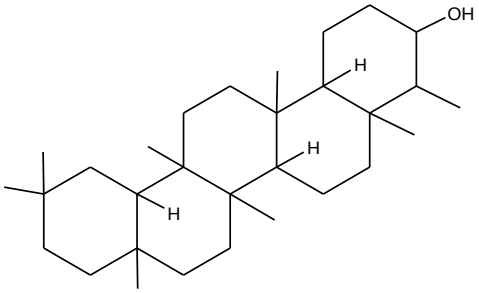


Fig 11: Friedelanol

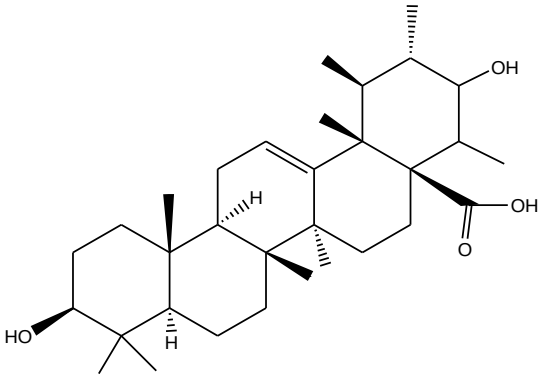


Fig 12: Ursolic acid

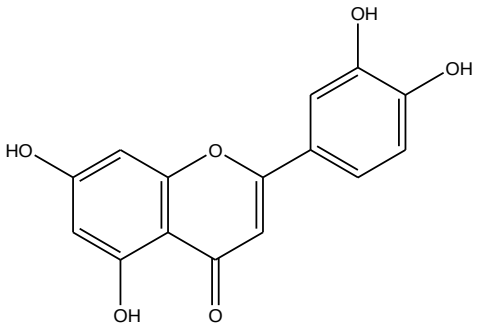
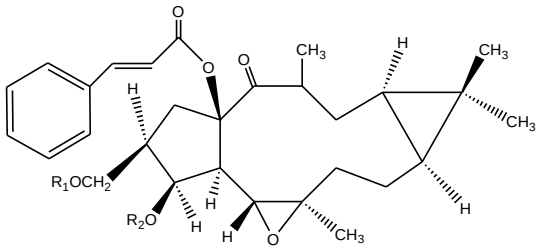
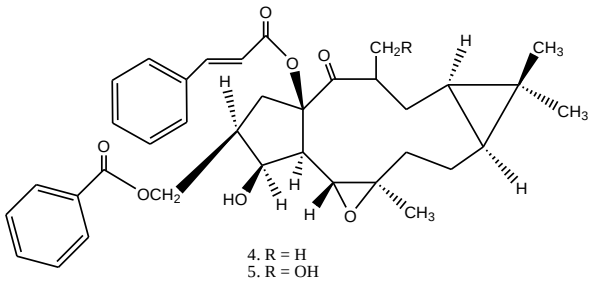


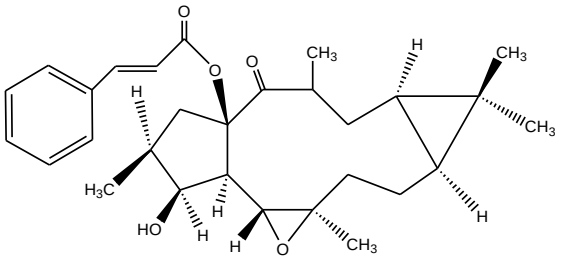
Fig 13: Luteolin



1. R_1= Ac; R_2= H
2. R_1= R_2 =H
3. R_1= R_2 =Ac



4. R = H
5. R = OH



6

Fig 14: Poly-o-acylated jatrophane diterpenes

3.4 The present research focused on phytochemical screening of medicinally important plants: *Acalypha ciliata* Forssk, *Croton bonplandianum* Baill., *Euphorbia geniculata* Orteg., *Euphorbia hirta* L., *Jatropha gossypifolia* L., *Pedilanthus tithymaloides* (L.) Poir., *Ricinnus communis* L. from family Euphorbiaceae. Plant extracts were prepared in various solvents and phytochemically tested. Phytochemical tests were carried out specially for screening secondary metabolites from the selected exotic medicinal plants from family Euphorbiaceae. Steroids, Unsaturated steroids, Cardenolides, Anthraquinone, Alkaloids, Phenolics, Leucoantho-cyanin etc reported in *Pedilanthus tithymaloides (L.) Poir* [17].

3.5 The methanolic extract of the leaves of *Pedilanthus tithymaloides* evaluated for total phenol, total flavonoid, total antioxidant activity and detection of phytoconstituents by using GC-MS. The constituents of methanolic extract of *Pedilanthus tithymaloides* analysed by GC-MS resulted in the detection of 5 different compounds, of which three esters, an amine and an alkaloid. Compound detected in GC-MS analysis were Pentadecanoic acid, 14-methyl-, methyl ester, 10-Octadecenoic acid, methyl ester, Cyclopropane butanoic acid, 2-[[2-[[2-[(2-pentylcyclopropyl)methyl] cyclopropyl] methyl]cyclopropyl]methyl]-, methyl ester, (4,4-Diphenyl-butyl)-(3-phenyl-piperidin-4-yl-)-amine, Rescinnamine [18].

3.6 In this study phytochemical evaluation performed on aqueous filtrate of leaf and stem of *Euphorbia tithymaloides or Pedilanthus tithymaloides.* The phytochemical screening revealed the presence of phytochemicals like alkaloids,

flavonoids, terpenoids, phenols, tannins, saponins, glycosides, sterols, amino acid, and reducing sugar in aqueous filtrate of tested plants. The results suggest that the presence of phytochemical constituents will be potential deliverable as active metabolites for the development of alternative bio control agent against the economically challenged crop insect pest and mosquito vectors [19].

3.7 Analyses were carried out on latex bearing twenty one plant species of Khandesh region of Maharashtra, India. The reported secondary metabolites in selected plant species were (including *E. tithymaloides*) alkaloids, flavonoids, terpenoids, cynogenic glycosides, phenolics, tannins and saponins. Phenolic compounds were found in all latex producing plants. The main finding of research was exploration of latex bearing plant for presence pharmaceutically important secondary metabolites [20].

3.8 Pedilstatin a new cancer cell growth inhibitor was isolated from *Pedilanthus tithymaloides* plants distributed in Maldives. Its structure was determined as 13-*O*-acetyl-12-*O*-[2‘*Z*, 4 ‘*E*-octadienoyl]-4α-deoxyphorbol on the basis of spectral analysis. Pedilstatin was found to significantly inhibit growth of the P388 lymphocytic leukemia cell line [21].

3.9 *Pedilanthus tithymaloides* L. whole plant extract contains octacosanol, cycloartenone, oxime and beta-sitosterol while, stem latex reported to contain the proteolytic enzyme, pedilanthain. It showed anti-inflammatory activity in carrageenan-induced rat paw oedema. The enzyme showed anthelmintic property. Its leaves contain *n*-hentriacontanol and dehydrodammaronol-A and root contain azafrin [22].

3.10 The chloroform and methanol Extract of *Pedilanthus tithymaloides* (PT) leaves yielded five known compounds, namely epifriedelanyl acetate (1), friedelanol (2), *β*-sitosterol (3), ursolic acid (4), and luteolin (5), along with the new compound 1,2-tetradecanediol 1-(hydrogen sulfate) sodium salt (6). This plant also tested for treatment of inflammation and pain. The results revealed significant antiinflammatory activity of chloroform and methanol extract in carrageenan-induced paw edema, vascular permeability and cotton pellet granuloma models [23].

3.11 This present study based on isolation of six new poly-O-acylated jatrophane diterpenes and five other known compounds from latex of *Pedilanthus tithymaloides*. The structural identification was achieved on the basis of 2D NMR and Mass Spectroscopy. Some of these poly-O-oxygenated jatrophane diterpenes possess a rare O-acetyl enol moiety. Compounds 1 and 3- 5 showed antiplasmodial activity and antimycobacterial activity against *Mycobacterium tuberculosis* [24].

3.12 An ethanolic extract of leaves of *Pedilanthus tithymaloides* L. was evaluated for biological activity against the eggs, larvae, and pupae of *Culex quinquefasciatus*. Significant mortality effects were observed in each life stage. Qualitative chemical analyses of the leaf extract revealed the presence of flavonoids, phenols, and steroids but the absence of alkaloids, glycosides, resins, saponins, and tannins [14].

4. Conclusion

The purpose of present literature review is to contribute to the knowledge about *Pedilanthus tithymaloides* L. or *E. tithymaloides* concerning its pharmacological and phytochemical evaluation and investigation. The various studies showed that some novel phytoconstituents of significant medicinal importance for example epifriedelanyl acetate, friedelanol, beta-sitosterol, ursolic acid, luteolin, 1, 2-tetradecanediol 1-(hydrogen sulfate) sodium salt, Among these, compounds ursolic acid and luteolin produced analgesic, anti-inflammatory, antinociceptive, and antipyretic drug response from leaves of *Pedilanthus tithymaloides* L. The latex obtained from the stem contains the proteolytic enzyme, pedilanthain which produces anti inflammatory and anthelmintica property. The leaves reported to contain *n*-hentriacontanol and dehydrodammaronol-A, the roots reported to have azafrin. The plant latex proteases exhibited wound healing as well as hemostasis. Plant latex from *Pedilanthus tithymaloides* L. reported to stop bleeding and to promote healing of wounds in various traditional medicines. So this plant latex popularly known for their behavior as plasmin for hemostasis and thrombin like in wound healing. A numbers of diterpenoids reported from latex of *Pedilanthus tithymaloides* for antimalarial, antituberculous, antiplasmodial, antimycobacterial response, mainly poly-O-acylated jatrophane diterpenoids. The recent development towards green synthesis of silver nano particle of *Pedilanthus tithymaloides* leaves contributes efficacy against dengue vector *Aedes aegypti* L. which could be helpful for developing bio insecticide for control of vector. In conclusion wide numbers of pharmacological responses and phyto-constituents were isolated from different parts of the *Pedilanthus tithymaloides* but there is still need for future evaluation in order to reveal concealed information and their formulation development as well as its clinical application.

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