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Toxicology, Phytochemistry, Bioactive compounds and Pharmacology of *Parthenium hysterophorus*

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Parthenium hysterophorus, members of the Asteraceae family is a noxious weed in America, Asia, Africa and Australia. This weed is considered to be a cause of a spectrum of clinical patterns: allergic respiratory problems, contact dermatitis, mutagenicity in human and livestock. Its allelophathic nature can drastically reduced the crop production and aggressive dominance of this weed threatens biodiversity. Attempts to control spread of the plant have so far not been successful. On the other hand, *P. hysterophorus* confers many health benefits, viz remedy for skin inflammation, rheumatic pain, diarrhoea, urinary tract infections, dysentery, malaria, psoriasis, allergies, asthma, tinnitus, dizziness, nausea, vomiting, neuralgia. This plant traditionally used for the treatment of fevers, migraine headaches, rheumatoid arthritis, stomachaches, toothaches, insect bites, infertility, and problems with menstruation and labor during childbirth. The plant contains a large number of important bioactive compounds, mainly sesquiterpene lactones, flavonoid glycosides and pinenes. It has multiple pharmacologic properties, such as anticancer, anti-inflammatory, cardiotonic, antispasmodic, an emmenagogue, and as an enema for worms. The aim of this review article is to explore the toxicological reports of *P. hysterophorus,* summarized the active compounds responsible for different pharmacological properties, the effective control measures that can be implemented as well as to unravel the latent beneficial prospects of this weed.

Keyword: *Parthenium hysterophorus*, Sesquiterpene lactone, Dermatitis, Phytochemistry, Pharmacological activity, Toxicity.

1. Introduction

Parthenium hysterophorus L. is an aromatic annual and obnoxious invasive herb under Asteraceae family, now commonly known as feverfew, *Tanacetum parthenium, Chrysanthemum parthenium* (Parsons and Cuthbertson, 2001; Bhatt *et al.,* 2012). The normal height of this erect plant is up to 1 m but under favorable conditions the height may reach up to 2 m having deeply penetrating taproot with many finely branched feeding roots and an angular, longitudinally grooved and profusely branched hairy stem (Parsons and Cuthbertson, 2001; Bhatt *et al.,* 2012). Allergen containing 8-20 cm long and 4-5 cm wide shortly hairy pale green leaves are alternate and rosette that are resemble to carrot leaves during initial growth (Parsons and Cuthbertson, 2001; Bhatt *et al.,* 2012). Rising from the stem nodes and terminating at about the same height, each head (4-10 mm diameter) of clustered flowers bears about 40 tubular male and 5 ligulate female white florets and produces 2 mm long flattened black seeds (Parsons and

Cuthbertson, 2001). Seeds germinate any time of the year under wide range of environmental condition. High humidity, high moisture content and temperature around 25°C are the standard factors for seed germination (Bhatt *et al.,* 2012). A native of tropical America *P. hysterophorus* was introduced during the 1950s into Africa, Asia and Oceania (Labrada *et al.,* 1994). Now this species is frequently found on roadsides, railway reserves, stock yards, cultivated fields, rundown pastures and vacant lots in China, Taiwan, Pakistan, Nepal, Sri Lanka, Bangladesh, Vietnam, Pacific islands, Ethiopia, Kenya, Madagascar, South Africa, Somalia, Mozambique, Zimbabwe and several countries of South and Central America (Parsons and Cuthbertson, 2001; Bhatt *et al.,* 2012). It is included in the Global Invasive Species database of IUCN due to the invasive nature (Bhatt *et al.,* 2012). Not only this weed is well thought-out to be a factor of allergic respiratory problems, contact dermatitis and mutagenicity in human and livestock but also considered as a severely crop production reducing agent due the allopathic nature (Patel, 2011). Thus P. hysterophorus is a threat for the biodiversity. Besides the harmful effects, *P. hysterophorus* shows anti-inflammatory, antimicrobial, anti-cancerous, pesticidal, thrombolytic activities.

1.1 Phytochemistry

The chemistry of feverfew is now well defined. Chemotype and geographical distribution of seeds are the varying factors for the constituents of *P. hysterophorus* (Blumenthal *et al.,* 2003). More than 45 sesquiterpene lactones were identified from leaves and flower among them the major is sesquiterpene lactone parthenolide, which is up to 0.9% of total constituents (Anonymous, 2003; Fugh-Berman, 2003). Twenty-three compounds, representing 90.1% or more of the volatile oils, have been identified from *P. hysterophorus* (Pareek *et al.,* 2011). The toxic and inhibitory constituents contained by all parts (stem, leaves, leaf hair, flower, pollen grain) of *P. hysterophorus* are summarized in table 1.

Table 1: Chemical constituents of *P. hysterophorus*

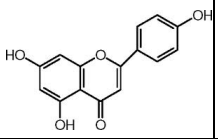
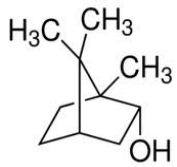
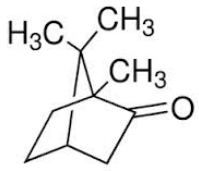
Main groups	Constituents	References
Terpenoids	*Sesquiterpene lactones:* germacranolides (including parthenolide, artemorin and chrysanthemonin) guaianolides (including chrysartemin A, partholide and chrysanthemolide) and eudesmanolides (including santamarin, reynosin and magnolialide), parthenin, cornopolin, artecanin, balchanin, costunolide, epoxyartemorin.	(Parsons and Cuthbertson, 2001; Boon and Smith, 2004; Pareek *et al.,* 2011)
	α-unsaturated γ-lactones: 3-β-hydroxy- parthenolide, costunolide, 3-β-hydroxycostunolide, 8-α-hydroxyestafiatin, artecanin, two chlorine-containing sesquiterpene lactones, 1-β-hydroxyarbusculin and 5-β-hydroxyreynosin.	(Barnes *et al.,* 2007)
Volatile oils (0.02–0.07%)	Various monoterpene and sesquiterpene components (e.g. camphor (56.9%), camphene (12.7%), p-cymene (5.2%), bornyl acetate (4.6%), tricylene, α-thujene, α-pinene, β-pinene, α-phellandrene, α-terpinene, γ-terpinene, chrysantheone, pinocarvone, borneol, terpinen-4-ol, ρ-cymen-8-ol, α-terpineol, myrtenal, carvacrol, eugenol, trans-myrtenol acetate, isobornyl 2-methyl butanoate, caryophyllene oxide, germacrene, farnesene and their esters).	(Barnes *et al.,* 2007; Pareek *et al.,* 2011)
Amino acids	Rich in Glycine and proline and moderate amount with alanine and lysine	(Gupta *et al.,* 1996)

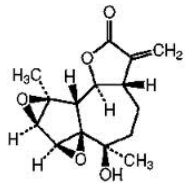
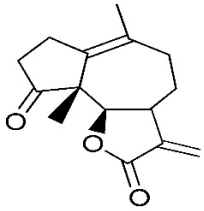
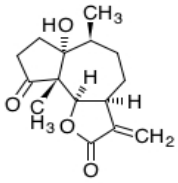
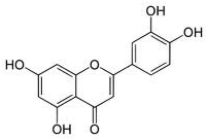
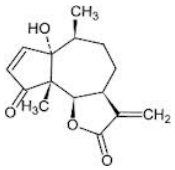
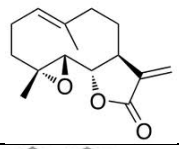
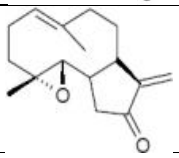
Amino sugars	N-acetylgalactosamine and N-acetylglucosamine.	(Gupta *et al.,* 1996)
Phenolic derivatives	Caffeic, vanllic, ferfulic, chlorogenic and anisic acids.	(Parsons and Cuthbertson, 2001)
Flavonoids	Luteolin, apigenin, 6-hydroxykaempferol 3,6-dimethyl ether, 6-hydroxykaempferol 3,6,4′-trimethyl ether (tanetin), quercetagetin 3,6-dimethyl ether, quercetagetin 3,6,3′-trimethyl ether (accompanied by isomeric 3,6,4′-trimethyl ether), quercetin, chrysoeriol, santin, jaceidin and centaureidin.	(Pareek *et al.,* 2011)
Others	8-*β*-Acetoxyhysterone C, Charminarone, 8*α*-Epoxymethylacrylyloxyambrosin, 8*α*-Epoxymethylacrylyloxy-11, 13-dihydroparthenin, 8*α*-Epoxymethylacrylyloxyparthenin, 2*β*-Hydroxycoronopilin, Hysterone (A, B, C, D), 1*α*, 2*β*, 4*β*-Trihydroxypseudoguaian-6*β*, 12-olide, Pyrethrin, tannins (type unspecified), melatonin, potassium chloride, protein.	(Parsons and Cuthbertson, 2001; Barnes *et al.,* 2007; Zhou *et al.,* 2011b, 2011c, 2011d, 2011e, 2011f)

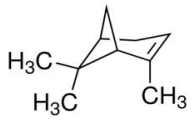
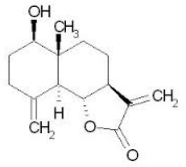
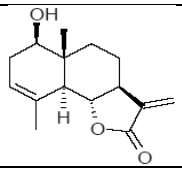
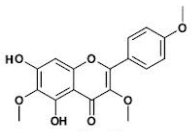
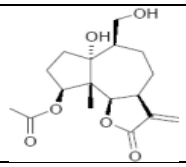
1.2 Bioactive Compounds

Plants produce a diverse range of bioactive molecules, making them rich source for different types of medicines. The main isolated bioactive compounds from *P. hysterophorus* are parthenolide, parthenin, coronopilin, canin. Identified bioactive compounds from *P. hysterophorus* with their activity are summarized in table 2.

Table 2: Individual bioactivities of some bioactive compounds isolated from *P. hysterophorus*

Name of the compounds	Structure	Biological activity	References
Apigenin ($C_{15}H_{10}O_5$; mw = 270.24)		Antibacterial, antiulcerative, antispasmodic, diuretic, aldose reductase inhibitor, antihypertensive, nodulation signal for metabiosis of pea and *Rhizobium leguminosarum*, binding activity to benzodiazepine receptor, anti-inflammatory, platelet aggregation inhibitor, antioxidant, cytotoxic	(Kuhn and Winston, 2007; Zhou *et al.,* 2011a)
Borneol ($C_{10}H_{18}O$; mw = 154.25)		Antibacterial, anthelmintic, antispasmodic, stimulant, analgesic, induces sweatiness	(Barnes *et al.,* 2007; Zhou *et al.,* 2011f)▪
Camphor ($C_{10}H_{16}O$; mw = 152.24)		Cardiotonic, irritant, antifungal	(Barnes *et al.,* 2007; Zhou *et al.,* 2011b)▪

Canin ($C_{15}H_{18}O_5$; mw = 278.31)		Antineoplastic, cytotoxic, insect antifeedant, plant growth regulator	(Zhou *et al.,* 2011b)▪
Charminarone ($C_{15}H_{18}O_5$; mw = 278.31)		Anticancer property	(Venkataiah *et al.,* 2003)
Coronopilin ($C_{15}H_{20}O_4$; mw = 264.32)		Dermatitic (causes contact dermatitis), insect antifeedant	(Zhou *et al.,* 2011b)
Luteolin ($C_{15}H_{10}O_6$; mw = 286.24)		Antiallergic, antibacterial, antifungal, cytotoxic, anti-inflammatory, antispasmodic, antitussive, dispels phlegm, enhances arterial tension and lowers intravenous tension, enhances blood capillary permeability, immunoenhancer; increases coronary flow, dihydrocoenzyme I (NADH) oxidase inhibitor, iodine-induced thyronine deiodinase inhibitor; aldose reductase inhibitor, protein kinase C inhibitor, succinic oxidase inhibitor; antihypercholesterolemic	(Kumar and Soodan, 2006; Zhou *et al.,* 2011c)
Parthenin ($C_{15}H_{18}O_4$; mw = 262.31)		Antifungal, dermatitic (causes contact dermatitis), cytotoxic, inhibits heart (dog), insect antifeedant, molluscacide	(Zhou *et al.,* 2011d)
Parthenolide ($C_{15}H_{20}O_3$; mw = 248.32)		Antineoplastic, cytotoxic, antibacterial, antifungal, anti-inflammatory, lower serotonin level, antileishmanial	(Kuhn and Winston, 2007; Zhou *et al.,* 2011d)
Pathenolide ($C_{16}H_{22}O_2$; mw = 246.35)		Anti-inflammatory, antitumor, antiangiogenic	(Kuhn and Winston, 2007; Zhou *et al.,* 2011d)

α-Pinene ($C_{10}H_{16}$; mw = 136.24)		Antifungal, antitussive (dispels phlegm), irritant	(Barnes *et al.,* 2007; Zhou *et al.,* 2011d)
Reynosin ($C_{15}H_{20}O_3$; mw = 248.32)		Anti-inflammatory, cytotoxic	(Boon and Smith, 2004; Zhou *et al.,* 2011d)
Santamarin ($C_{15}H_{20}O_3$; mw = 248.33)		Anti-inflammatory, antineoplastic, cytotoxic	(Boon and Smith, 2004; Zhou *et al.,* 2011d)▪
Santin ($C_{18}H_{16}O_7$; mw = 344.32)		Cyclo-oxygenase inhibitor, 5-lipoxygenase inhibitor, NO production inhibitor, PGE2 production inhibitor, antitubercular	(Zhou *et al.,* 2011d)▪
Tetraneurin E ($C_{17}H_{24}O_6$; mw = 324.38)		larvacide (insect larva growth inhibitor)	(De la Fuente *et al.,* 2000; Zhou *et al.,* 2011e)
Caffeic, vanllic, ferfulic, chlorogenic and anisic acids.	-	Autotoxic, inhibitory effect to other plant.	(Parsons and Cuthbertson, 2001)▪

1.2 Toxicity and Adverse Effect

Clinical safety and toxicity data for *P. hysterophorus* is limited, and further investigation of these aspects is required. Several randomized, double-blind, placebo-controlled trials have been reported the adverse effects during *P. hysterophorus* administration.

1.2.1 Allergy: Patch testing report of acetone extract (better than aqueous extract) elicited that sesquiterpene lactones (Parthenin, the major allergen) of *P. hysterophorus* present in the oleoresin fraction of the leaf, the stem, and the flower and also in pollen were responsible for contact dermatitis (Lonkar *et al.,* 1976; Sharma and Sethuraman, 2007). Study in 331 patients revealed that *P. hysterophorus* pollen were responsible for the occurrence of high percentage (30.21%) of allergy related symptoms (Lal *et al.,* 2011). 12 patients among 14 suffering from parthenium dermatitis showed increased level of IgE, so *P. hysterophorus* induced Type-I and Type-IV hypersensitivity (Srinivas and Lakshmi, 2007b). Patch test and Skin prick test to *P. hysterophorus*

respectively revealed 52% (the leading) allergen sensitization to the patients (26 of 50) suffering from plant dermatitis and 35.7% to the patients (25 of 70) suffering from atopic dermatitis (Davis *et al.,* 2011; Kumar *et al.,* 2012).

1.2.2 Allelopathic effect: *P. hysterophorus* produced and released allelochemicals to the soil by leaching or decomposition, exhibit powerful toxic effects on the growth of other plant species by altering the physico-chemical properties of soil. *P. hysterophorus* residues mixing in soil adversely affected the germination and subsequent seedling growth of *Acacia catechu, Achyranthes aspera and Cassia tora* (Dogra and Sood, 2012). Emergence percentage and rate and radicle and plumule lengths of lettuce were repressed by fresh parthenium than composting (Wakjira *et al.,* 2009). Different concentration of rhizospheric soil diffusates and germinating seed diffusates of *P. hysterophorus* retarded and minimized the germination of *Raphanus sativus* seeds (Paudel *et al.,* 2010). Above 2% aqueous leaf extract completely inhibited the seed germination of *Raphanus sativus, Brassica campestris* and *Brassica oleracea* but *Triticum aestivum* and *Ageratina adenophora* were of complete failure of seed germination at above 6% and *Oryza sativa* and *Artemisia dubia* at 10% (Maharjan *et al.,* 2007). Exploiting this allelopathic nature, *P. hysterophorus* can be a potential source of bio herbicide in future.

1.2.3 Central Nervous System (CNS) Depressant: Methanolic extract of *P. hysterophorus* at dose 2.5 and 5 mg/kg of body weight caused significant analgesic activity similar to pathidine in Swiss albino mice may be due to the action on central nervous system (Jha *et al.,* 2011).

1.2.4 Loss of Immunity: Oral treatment with methanol extract at dose 20mg/100g of body weight reduced the immunity in rat by significantly decreasing the WBC (Neha *et al.,* 2010). *In vitro*, parthenium extract inhibited phagocytosis of *Candida guilliermondii* and its overall killing by neutrophils (Williamson *et al.,* 1988). Ulceration also revealed in the alimentary tract of cattle and buffaloes autopsy (Narasimhan *et al.,* 1977).

1.2.5 Against Mosquitos: *P. hysterophorus* feeding reduced the survival time and fecundity of *Anopheles gambiae*, the primary vector for *Plasmodium falciparum*, due to the presence of low sugar content (Manda *et al.,* 2007). 1,000 ppm diethyl ether extract from the leaves of *P. hysterophorus* was found to be the most effective in *Aedes aegypti* mosquitos in maximum effective repellency (99.7%) leading to the highest levels of reduced fecundity and 100% egg mortality followed by 1,000 ppm benzene extracts causing 93.8% reduced oviposition and 100% ovicidal effect (Kumar *et al.,* 2011). The ethanolic extract of leaves showed 83-90% larvaecidal activity against *Anopheles stephensi* larvae (Ahmad *et al.,* 2011).

1.3 Mutagenic: Column chromatography fraction 1 of *P. hysterophorus* crude extract was mutagenic in strain TA 98 of *Salmonella* (Ramos *et al.,* 2001). Next investigation showed that 0.19 to 1.22µmole of parthenin per plate was weakly mutagenic in *Salmonella typhimurium* TA 102 strain but 7.62µmole per plate or higher was toxic and 10–60µM during 20h induced chromosomal aberrations in mouse blood lymphocytes (Ramos *et al.,* 2002).

1.4 Others: Parthenin was suspected to its interference with oxidative phosphorylation by inhibiting 'state 3' respiration and stimulated 'state 4' respiration in rat liver and kidney mitochondria as well as ATPase activity in the presence of Mg^{2+} ions (Narasimhan *et al.,* 1985). Daily administration of *P. hysterophorus* (10 mg/0.1 ml/kg body weight) to 20 adult male mice significantly decreased the levels of 5-hydroxytryptamine, noradrenaline and dopamine in total brain which is suspected in turn affect the physiology of the peripheral endocrine glands (Verma *et al.,* 2007). Two saponins isolated from *P. hysterophorus* were found to be potent inhibitors of TNF-alpha (Shah *et al.,* 2009).

1.5 Pharmacological Actions

Animal and *in vivo* studies

1.5.1.Anti-Inflammatory Activity*:* Oral administration 10, 20, 40 mg/kg of body weight of *P. hysterophorus* extract led to significant antinociceptive and anti-inflammatory effects against acetic acid-induced writhing in mice and carrageenan-induced paw edema in rats, respectively (Jain and Kulkarni, 1999). 200mg/kg of body weight of fresh leaves ethanolic extract exhibited high degree anti-inflammatory in carrageenan induced paw edema rats (Pandey *et al.,* 2012). 1, 2 mg/kg of body weight parthenolide administration also produced antinociceptive and anti-inflammatory effects (Jain and Kulkarni, 1999). The anti-inflammatory property may be due to an inhibitor of cellular phospholipases, which prevents release of arachidonic acid in response to appropriate physiological stimuli (Makheja and Bailey, 1982).

1.5.2 Antioxidant Activity: The anti-oxidant phytochemicals protect the cells from oxidative damage caused by free radicals. DPPH (2, 2-diphenyl-1-picrylhydrazyl radical) scavenging assay revealed that Methanolic and ethanolic extract of *Parthenium hysterophorus* showed antioxidant activity 78.25561% and 66.28858% respectively (N. *et al.,* 2010). But next time acetone extract was found to have higher anti-oxidant activity than methanol and chloroform extracts (Priya *et al.,* 2011). 200mg/kg of body weight of fresh leaves ethanolic extract showed significant antioxidant activity in rats (Pandey *et al.,* 2012).

1.5.3 Anticancer and Cytotoxic Activity: Anticancer and cytotoxic properties of *P. hysterophorus* are the bright potential in oncology as anticancer therapeutics. The methanolic flower extract exhibited antitumor effects in host mice bearing transplantable lymphocytic leukemia (Mukherjee and Chatterjee, 1993). Crude methanolic extract showed cytotoxic activity against brine shrimp nauplii (Al-mamun *et al.,* 2010). Methanol, Ethanol, Chloroform & Aqueous were found that all extracts were significantly cytotoxic to the investigated human cancerous cell lines Ovary (IGROV-I), lung (A-549), prostate (PC-3), breast (MCF-7) and CNS (SF-295) except Lung cancerous cell line (HOP-62) (Haq *et al.,* 2011). Parthenolide, in the presence of α-methylene-glactone moiety, has been reported to have cytotoxic activity in Eagle's 9KB carcinoma of the nasopharynx cell culture system (Berry MI, 1984). *In vitro*, parthenolide functioned as growth inhibitor of mouse fibrosarcoma (MN-11), human lymphoma (TK6), human lung carcinoma (A549), human medulloblastoma (TE671), human colon adenocarcinoma (HT-29) and human umbilical vein endothelial cells

(HUVEC) (Ross *et al.,* 1999; Parada-Turska *et al.,* 2007).

1.5.4 Antimicrobial Activity: Different extracts of *P. hysterophorus* tested for antimicrobial potential showed varying degree of antimicrobial activities. Dichloro-methane extract of leaves was found as the most effective against *E. coli* and methanolic extract of leaves was found nil for *K. pneumoniae* and highest for *S. aureus* (Fazal *et al.,* 2011). All types of organic extracts and aqueous extract of inflorescence were highly effective against *P. aeruginosa* and *C. freundii* (Sharma and Gupta, 2012). Hydroalcoholic extract of *P. hysterophorus* was *in vitro* effective against *Plasmodium falciparum* (Valdés *et al.,* 2010). Crude 50% ethanolic extract of *P. hysterophorus* flowers exhibited trypanocidal *activity against* a flagellate protozoa *Trypanosoma evansi* both *in vitro and in vivo* (Talakal *et al.,* 1995). *In vitro*, this plant demonstrated antiamoebic activity comparable to the standard drug Metronidazole against axenic and polygenic cultures of *Entamoeba histolytica,* responsible for amoebiasis (Khare, 2008). Fusarium wilt, an economically important fungal disease in potato caused by *Fusarium solani* was significantly inhibited by aqueous, methanol and n-hexane extracts (Zaheer *et al.,* 2012). Aqueous extract of inflorescence of this plant was found effective at higher concentrations of 1000 µg/ml and 500µg/ml against *Penicilliusm chrysogenum, Microsporum gypseum and Rhizopus stolonifer* but different organic extracts showed no activity (Sharma and Gupta, 2012). Leaves aqueous extract also showed antifungal activity against *Alternaria alternate* (Ramanujam *et al.,* 2011).

1.5.5 Pesticidal Activity: Antifeedent bioassay revealed that lactone was found to be about 2.25 times more active than parthenin against sixth-instar larvae of *Spodoptera litura* and pyrazoline adduct was found to be the most effective as an insecticide against the adults of store grain pest *Callosobruchus maculatus* (Datta and Saxena, 2001). Petroleum ether extracts of leaves, stem and inflorescence of *P. hysterophorus* at 500, 1000, 2000 and 5000 ppm concentrations significantly decreased the life span and progeny production of mustard aphid, *Lipaphis erysimi* (Sohal *et al.,* 2002).

1.5.6 Wound healing activity: Externally leaf paste application of *P. hysterophorus* showed wound healing activity (Kumar *et al.,* 2012).

1.5.7 Hypoglycemic Activity: Administration of aqueous extract of *P. hysterophorus* flower (100 mg/kg of body weight) significantly decreased the serum glucose level in normal and alloxan induced diabetic rats (Patel *et al.,* 2008). Slightly decreased blood glucose level was found in rats after oral administration of fresh leaves extract (Arya *et al.,* 2012).

1.5.8 Thrombolytic Activity: Crude methanolic extract of *P. hysterophorus* showed significant thrombolytic effect comparable to standard thrombolytic agent, streptokinase (Al-mamun *et al.,* 2010). Parthenolide and some other metabolites were determined as the inhibitor of human blood platelet function (Hewlett *et al.,* 1996). The Thrombolytic activity is a possible relevant effect to migraine prophylaxis through the inhibition of serotonin releasing from platelet by platelet aggregating agents: adenosine diphosphate, adrenaline, sodium arachidonate, collagen, and U46619 (Heptinstall *et al.,* 1985; Hewlett *et al.,* 1996).

1.6 Clinical studies

1.6.1 Prevention and Treatment of Migraine: Prevention and treatment of migraine by *P. hysterophorus* is now a matter of debate. However, based on pharmacological studies of the herb and parthenolide, three possible mechanisms are involved: Anti-inflammatory activity, an effect on platelets and inhibition of serotonin binding (Anonymous, 2003).

P. hysterophorus was reported to inhibit granule secretion in blood platelets, which is related with the etiology of migraine (Heptinstall *et al.,* 1985). A randomised, double-blind, placebo-controlled trial for three months successfully controlled migraine in 17 patients by eating raw feverfew leaves (Johnson *et al.,* 1985). Another randomised, double–blind, placebo–controlled trial demonstrated lowering the migraine pain intensity significantly during powdered leaves (parthenolide 0.2%) 100 mg daily for 60 days administration in 57 patients (Palevitch *et al.,* 1997). 24% reduction of migraine attack in 72 patients was observed after *P. hysterophorus* treatment (70–114 mg *P. hysterophorus* equivalent to 2.19 µg parthenolide; one capsule daily) in another randomised double–blind, placebo–controlled, crossover trial (Murphy *et al.,* 1988). The above studies suggest that the preparations are admirable in preventing migraine but further well–designed clinical trials are required to establish the beneficial effects of *P. hysterophorus* for migraine prophylaxis.

1.6.2 Rheumatoid Arthritis: *P. hysterophorus* was reported to inhibit granule secretion in blood neutrophils, which is related with the etiology of Rheumatoid arthritis (Heptinstall *et al.,* 1985). But a double-blind, placebo-controlled study demonstrated no beneficial effect when forty-one female patients with inflammatory joint symptoms were given daily either one placebo capsule or one *P. hysterophorus* capsule (70–86 mg equivalent to 2–3 µmol parthenolide), for six weeks (Pattrick *et al.,* 1989).

1.7 Economic Importance

Though *P. hysterophorus* is an obnoxious herb, when exploited by proper means and technology, it can prove to be a valuable asset. In West Indies this weed is used as a remedy against ulcerated sores, certain skin disease, facial neuralgia, fever and anemia (Bhatt *et al.,* 2012). Inflammations, eczema, skin rashes, herpes, rheumatic pain, cold heart trouble, menstrual disorders, difficulty during labour, stomach ache, toothache, diarrhoea, neurologic disorders, urinary infections, dysentery, malaria and insect bites are also treated (Barnes *et al.,* 2007; Patel, 2011). Chemical constituents are useful as insecticide and for curing psoriasis (Kohli and Rani, 1994). A preparation with and ginger is effective for treating migraines during the early pain phase (Kuhn and Winston, 2007). Its broad-spectrum ovicidal, antimicrobial, lervicidal, nematocidal, herbicidal activities designate the improvement of public health and crop production (Bhatt *et al.,* 2012). Greenish yellow dye mordant with chrome produced from stems and leaves is used in wool processing (Kowalchik *et al.,* 1998). It is useable as an additive with cattle manure in biogas production (Patel, 2011).

1.8 Contradictions

P. hysterophorus should not be taken by individuals who develop various kinds of allergic reactions. Though clinical study showed that the *P. hysterophorus* reduces migraine attack, self-medication should not be undertaken without consulting with doctor. It shows abortifacient activity and affects menstrual cycle (Barnes *et al.,* 2007).

This plant is not applicable for the children under two years old (Awang, 1993).

1.9 Control Strategy

As *P. hysterophorus* is a fast spreading plant, all control strategies (physical, chemical and biological) should be integrated. Deep ploughing, uprooting by hand or burning in the infested areas can reduce the spreading of this plant. The *P. hysterophorus* infested areas can be replaced by highly invasive plants: *Hyptis suaveolens and Senna uniflora* (Kumari *et al.,* 2010). *Listronotus setosipennis* (a stem-boring weevil), *Zygogramma bicolorata* (a leaf-feeding chrysomelid) and *Epiblema strenuana* (a stem-galling moth) can be used against the spreading of this plant (McFadyen, 1984). Aqueous shoot and root extract of *Cenchrus pennisetiformis* completely suppress the seed germination (Javaid and Anjum, 2006) and aqueous and methanolic extracts of *Datura metel* and *Withania somnifera*, can control the germination and growth of *P. hysterophorus* (Javaid *et al.,* 2010, 2011). Herbicides: norflurazon, clomazone, fluometuron, flumioxazin, halosulfuron, chlorimuron and trifloxysulfuron are very effective to pre- and post-emergence control *P. hysterophorus* (Reddy *et al.,* 2007). Some fungal species: *Alternaria* spp., *Fusarium* spp., *Rhizoctonia solani*, *Colletotrichum capsici* also control this plant spreading (Srinivas and Lakshmi, 2007a).

2. Conclussion

P. hysterophorus is a rich source of terpenoids, volatile oils and flavonoids as well as amino acid, sugars and phenolic derivatives. Parthenolide (the major sesquiterpene lactone), parthenin and different solvent extracts showed significant analgesic, anti-inflammatory and antipyretic activities, which confirmed the use for treatment of migraine headache, fever, common cold, and arthritis. Solvent extracts and constituents also showed both beneficial and harmful effects such as anticancer, pesticidal, antimicrobial, allelopathic, allergic, lervicidal, ovicidal, herbicidal etc. However, as *P. hysterophorus* is a toxic plant, further clinical researches and investigations are essential to establish it as a standard medicinal plant.

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