

Phytochemical and Pharmacological Evaluation of *Parthenium hysterophorus*: A Comprehensive Review.

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ABSTRACT

Parthenium hysterophorus (Linn.) is violent everywhere annual, herbivorous weed. It is commonly known as congress grass or gajar ghas. *P. hysterophorus* shown several hazardous effects on human health and livestock. It reduces the crop production due to its allelopathic effect. In spite of these drawbacks *P. hysterophorus* is traditionally recognized for its use in the treatment of wounds, fever, ulcerated sores and malaria. It is a weed of global importance. Pharmacological investigation revealed that it possess several therapeutic applications such as antibacterial, antifungal, anti-feedant, antiinflammatory, antinociceptive, nematicidal, hypoglycaemic, pesticidal, antiamebic, antioxidant and antiparasitic activities. The aim of this review is to summarise the pharmacological benefits of *P. hysterophorus*.

Keywords: *Parthenium hysterophorus* Linn., traditional medicine, antimicrobial potential phytochemistry and pharmacology.

INTRODUCTION

Parthenium hysterophorus Linn. belongs to family Asteraceae. It is an obnoxious invasive weed. It is a biological pollutant because of its adverse effects on human health. Owing to its invasive nature, the weed is included in the Global Invasive Species database of IUCN. The weed spreads very rapidly over large areas and quickly forms its own monoculture. It occurs widely in different habitats varying from hot and arid, semi-arid to humid and from low- to middle- to high-altitude regions¹.

P. hysterophorus contains a large number of important bioactive compounds, mainly sesquiterpene lactones, flavonoid glycosides and pinenes. It has multiple pharmacological properties, such as anticancer, antiinflammatory, cardiotoxic, antispasmodic and as an enema for worms².

The chemical constituents of the weed have also been used as an insecticide and for curing skin diseases such as psoriasis³. Furthermore, the properties of the weed in stimulating menstrual function and reducing fever and neuralgic pain have also been described. Zutshi *et al.*, (1975) explored the antibacterial activity of essential oils from *P. hysterophorus* against *E. coli*, *V. cholerae* and *Klebsiella aerogenes*⁴. Its antiamebic activity against axenic and polyxenic cultures of *E. histolytica* was reported⁵. Its anti-malarial activity has been found effective against *Plasmodium falciparum*⁶, and it also possesses herbicidal and pesticidal properties^{7,8}. Aqueous extracts of pollen grains of *P. hysterophorus* exhibited antifungal activity by inhibiting sporangial germination and zoospore motility in *Sclerospora graminicola* infesting *Pennisetum typhoides*⁹.

Taxonomy

Kingdom- Plantae
Division-Tracheophyta Class-Mangnoliopsida
Order-Asterales
Family-Asteraceae

Genus- *Parthenium* Species- *hysterophorus* Vernacular name

It is known by several common and vernacular names such as parthenium weed, ragweed parthenium, starweed, bastard feverfew, gajar ghas, safed topi, chatak chandni, white top weed and congress grass.

Geographical Distribution

The exact area of origin of *Parthenium* is difficult to pinpoint because of its very wide distribution. However, it is presumed to be a native of central Argentina, the West Indies and the Gulf of Mexico. The weed has been reported from China, Taiwan, Nepal, Pakistan, Sri Lanka, Bangladesh, Vietnam, Pacific islands and African countries including Ethiopia, Kenya, Madagascar, South Africa, Somalia, Mozambique and Zimbabwe and also USA and several countries of South and Central America. In India it is known to be one of the most serious weeds in terms of its potential to replace other plant species^{3,10}.

Plant description

It is an annual, erect herb with a tendency to be perennial, normally attaining a height of 1 m (sometimes reaching up to 2 m under favourable conditions). It possesses deeply penetrating root system and an angular, grooved, profusely branched stem bearing. The leaves are pale green in colour. Leaves are pinnately, irregularly, dissected and pubescent on both sides. The stem is pubescent and covered by hairy structures known as trichomes. Four different kinds of trichomes observed on the upper and lower leaf surfaces. Trichomes are considered as storehouses for toxic chemicals found in the weed such as parthenin. The flowers are creamy-whitish and are arranged in capitula. Pollen grains are produced in clusters and are anemophilous^{11,12}.

Traditional uses

P. hysterophorus is used in the treatment of ulcerated sores, wounds, fever, migraine headaches, rheumatoid arthritis, stomach aches, toothaches, insect bites, infertility, and problems with menstruation, labour during childbirth anaemia and heart troubles. A decoction of the

root finds use in treatment of dysentery and the lower concentrations of extracts might find use as antifungal agent. It is applied externally on skin disorders and decoction of the plant is often taken internally as a remedy for a wide variety of ailments. It is also reported as promising remedy against hepatic amoebiasis². Decoction prepared from its roots has been used by American and Indians in traditional medicine to treat amoebotic dysentery¹³. Ramos *et al.* (2001) reported its applications in treating neurologic disorders, fever, urinary infections, dysentery and malaria and as emmenagogue¹⁴.

Pharmacological uses Antibacterial activity

Different extracts of *P. hysterothorus* were reported antibacterial potential Dichloromethane extract of leaves was found as the most effective against *E. coli* and methanolic extract of leaves was found highest for *S. aureus*¹⁵. All types of organic extracts and aqueous extract of inflorescence were highly effective against *P. aeruginosa* and *C. freundii*¹⁶. Antibacterial efficacy of *P. hysterothorus* has also been reported by several researchers against *E. coli*¹⁷, *B. subtilis*, *Enterococcus* spp.¹⁸, *S. aureus*¹⁹, *S. typhimurium*, *S. epidermidis*, *V. cholerae*, *S. flexneri*²⁰, *P. aeruginosa*¹⁷, *Micrococcus luteus*²¹, *B. cereus*²², *K. pneumoniae*, *E. aerogenes*²³, *Xanthomonas vesicatoria* and *Ralstonia solanacearum*²⁴.

Antifungal activity

Antifungal potential of different extracts of *P. hysterothorus* against human pathogenic fungi were reported by Rai and Upadhyay (1990)²⁵ and Rai (1993, 1994, 1995)²⁶⁻²⁸. The dermatophytes and other fungal pathogens have been found to be sensitive to sesquiterpene lactones which are present as active agent in *P. hysterothorus*²⁹. *Fusarium solani* was significantly inhibited by aqueous, methanol and n-hexane extracts³⁰. Aqueous extract of inflorescence of *P. hysterothorus* was found effective at higher concentrations of 1000 µg/ml and 500µg/ml against *Penicillium*

chrysogenum, *Microsporum gypseum* and *Rhizopus stolonifer* but different organic extracts showed no activity¹⁶. Aqueous leaves extract of *P. hysterothorus* also showed antifungal activity against *Alternaria alternata*³¹. Antifungal property of *P. hysterothorus* has been reported by several researchers and plant and human pathogenic fungi viz., *F. solani*^{32,33}, *A. alternata*³⁴⁻³⁵, *C. albicans*³⁶, *F. oxysporium*, *A. niger*^{17,19,37}, *Candida kefyr*³⁶, *A. flavus*²², *Drechslera tetramera*, *Phoma glomerata*³⁷, *A. fumigatus*²³, *Drechslera hawaiiensis*, *A. alternata* keissl, *F. moniliforme*³⁸, *A. brassicae*, *A. brassicicola*³⁹, *S. cerevisiae*²², *Bipolaris oryzae*⁴⁰.

Antifeedant activity

Parthenin has been shown to act as a feeding deterrent to the adult of *Dysdercus koenigii*, *Tribolium castaneum*, *Phthorimaea operculella*, *Callosobruchus chinensis* L. and sixth instar larvae of *Spodoptera litura*⁴¹⁻⁴².

Anti-inflammatory activity

Oral administration 10, 20, 40 mg/kg of body weight of *P. hysterothorus* extract led to significant antiinflammatory effects against carrageenan induced paw edema in rats. 200mg/kg of body weight of fresh leaves ethanolic extract

exhibited high degree anti-inflammatory in carrageenan induced paw edema rats. 1, 2 mg/kg of body weight parthenolide administration also produced antiinflammatory effects⁴³⁻⁴⁴.

Antinociceptive activity

Oral administration 10, 20, 40 mg/kg of body weight of *P. hysterothorus* extract led to significant antinociceptive effects against acetic acid induced writhing in mice⁴⁴.

Nematicidal potential

P. hysterothorus extract reported nematicidal activity against *Meloidogyne incognita*, *Helicotylenus dihyslera*. Crushed leaves admixed into the soil are used to reduced root galling in papaya caused by *M. incognita*⁴⁵⁻⁴⁶.

Hypoglycemic activity

Aaqueous extract of *P. hysterothorus* flower (100 mg/kg of body weight) shown significantly decreased the serum glucose level in normal and alloxan induced diabetic rats. Slightly decreased blood glucose level was found in rats after oral administration of fresh leaves extract of *P. hysterothorus*⁴⁷⁻⁴⁸.

Thrombolytic activity

Crude methanol extract of *P. hysterothorus* has been shown thrombolytic effect comparable to standard thrombolytic agent, streptokinase. Parthenolide and some other metabolites were determined as the inhibitor of human blood platelet function⁴⁹⁻⁵⁰.

Pesticidal activity

Antifeedant 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*⁸. Petroleum ether extracts of leaves, stem and inflorescence of *P. hysterothorus* at 500, 1000, 2000 and 5000 ppm concentrations significantly decreased the life span and progeny production of mustard aphid, *Lipaphis erysimi*⁵¹.

Herbicidal activity

Pure parthenin as well as extract of different parts of *P. hysterothorus* shown phytotoxic effects on many aquatic as well as terrestrial weeds⁵²⁻⁵⁴. The sesquiterpene lactone parthenin has received most attention regarding allelopathy or potential herbicidal properties of *P. hysterothorus*⁵⁵.

Antiamoebic activity

Antiamoebic activity of parthenin has been evaluated *in vitro* against axenic and polyxenic cultures of *Entamoeba histolytica*. Parthenin has *in vitro* activity comparable to that of metronidazole. *P. hysterothorus* demonstrated antiamoebic activity comparable to the standard drug metronidazole against axenic and polygenic cultures of *E. histolytica*^{5,56}.

Anti-malarial activity

Parthenin and some of its derivatives were evaluated for antimalarial activity against a multi drug resistant strain of *Plasmodium falciparum*. Parthenin and related compounds have significant antimalarial action. Hydroalcoholic extract of *P. hysterothorus* was *in vitro* effective against *P. falciparum*⁵⁷⁻⁵⁸.

Insecticidal activity

Parthenin is known to shown activity against termites, cockroaches as well as migratory grasshoppers,

*Melanoplus sanguinipes*⁵⁹⁻⁶¹. Whole plant extract of *P. hysterothorus* showed insect growth regulatory activity against the *Dysdercus angulatus*⁶², fifth instar larvae of *S. litura*⁶³⁻⁶⁴ and toxic effect on *Crociodomia binolalis* (cabbage leaf webber), and *Callosobruchus maculatus* (pulse beetle) infesting cowpea seeds⁶⁵ and mites⁶⁶. The natural occurring resin material of *Parthenium* spp. has been demonstrated to protect wood against termite, molluscan borer and fungal attacks⁶⁷. Petroleum ether extract of leaves, stem and inflorescence of *P. hysterothorus* shown toxic effect on mean life span and progeny production of adults of the mustard aphid, *Lipaphis erysimi*⁵¹.

Trypanocidal activity or antiparasitic activity

50% crude ethanolic extract of *P. hysterothorus* shown *in vitro* activities against *Trypanosoma evansi*. The extract exerts antitrypanosomal effect at intraperitoneal doses of 100 and 300 mg/kg body weight when used for treatment of infected rats⁶⁸.

Wound healing activity

Externally leaf paste application of *P. hysterothorus* showed wound healing activity⁶⁹.

Antioxidant activity

DPPH (2, 2-diphenyl-1-picrylhydrazyl radical) scavenging assay revealed that methanolic and ethanolic extract of *P. hysterothorus* showed antioxidant activity 78.25561% and 66.28858% respectively. The acetone extract was found to have higher anti-oxidant activity than methanol and chloroform extracts. 200mg/kg of body weight of fresh leaves ethanolic extract has been showed significant antioxidant activity in rats^{43,70}.

Antiviral activity

Parthenium extract exhibits significant antiviral action against potato virus Y. This virus extensively damages the chilli crops. Parthenin might find use as an effective agent against potato virus Y⁵⁷.

Cytotoxic activity

Pseudoguaianolides and their analogues possess cytotoxic effect. Parthenin exhibits cytotoxicity with chromosomal aberrations in peripheral blood lymphocytes when administered to mice. A single intra-peritoneal dose of 4-31 mg/kg body weight of animal of parthenin increases the frequency of micro nucleated reticulocytes in mice^{70,72}.

Anticancer activity

The methanolic extract of *P. hysterothorus* has been found to have anti-tumour effect in host mice bearing transplantable lymphocytic leukemia. The active compound leads to slow development of tumour and increases the survival of mice bearing lymphocytic leukemia⁷³. Studies conducted *in vitro* cytotoxicity against human cancer cells have shown that *P. hysterothorus* possess anti-cancerous properties⁷⁴⁻⁷⁵.

Analgesic activity

Methanolic extract of *P. hysterothorus* 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 system⁷⁶.

Anti-rheumatoid arthritis activity

P. hysterothorus was reported to inhibit granule secretion in blood neutrophils, which is related with the etiology of rheumatoid arthritis⁷⁷.

Mutagenic activity

Column chromatography fraction of *P. hysterothorus* crude extract was mutagenic in strain TA 98 of *Salmonella*. Next investigation showed that 0.19 to 1.22µmole of parthenin per plate was weakly mutagenic in *S. 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^{14,72}.

Phytochemistry

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 constituents⁷⁸⁻⁷⁹. Twenty-three compounds, representing 90.1% or more of the volatile oils, have been identified from *P. hysterothorus*⁸⁰.

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, epoxyartemorin⁸⁰⁻⁸¹. **Volatile oils** 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, chrysanthone, pinocarvone, borneol, terpinen-4-ol, p-cymen-8-ol, α-terpineol, myrtenal, carvacrol, eugenol, trans-myrtenol acetate, isobornyl 2-methyl butanoate, caryophyllene oxide, germacrene, farnesene and their esters)^{80,83}.

Amino acids

Rich in Glycine and proline and moderate amount with alanine and lysine⁸⁴.

Amino sugars

N-acetylgalactosamine and N-acetylglucosamine⁸⁴.

Phenolic derivatives

Caffeic, vanillic, ferulic, chlorogenic and anisic acids⁸¹.

Flavonoids

Luteolin, apigenin, 6-hydroxykaempferol 3,6-dimethyl ether, 6-hydroxykaempferol 3,6,4'-trimethyl ether (tanetin), quercetagenin 3,6-dimethyl ether, quercetagenin 3,6,3'-trimethyl ether (accompanied by isomeric 3,6,4'-trimethyl ether), quercetin, chrysoeriol, santin, jaceidin and centaureidin⁸⁰.

CONCLUSION

P. hysterothorus can be listed among various medicinal plants with potent pharmacological and ethno medicinal properties. *P. hysterothorus* shown several hazardous effects on human health and livestock. It reduces the crop production due to its allelopathic effect. In spite of these drawbacks *P. hysterothorus* is traditionally recognized for its use in the treatment of wounds, fever, ulcerated sores and malaria. *Parthenium* is a weed of global importance. Pharmacological investigation revealed that it possess

several therapeutic applications such as antibacterial, antifungal, anti-feedant, anti-inflammatory, antinociceptive, nematocidal, hypoglycaemic, pesticidal, antiamoebic, antioxidant and antiparasitic activities.

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