The Bioscan
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
20(3): 771-776, 2025 www.thebioscan.com

Impact Assessment of *Parthenium hysterophorus* L Induced Changes in Biological Parameters of Mammals

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DOI: 10.63001/tbs.2025.v20.i03.pp771-776

KEYWORDS
Invasive Alien Plant Species, Parthenium hysterophorus, Toxic effects, Endocrine and reproductive system, Mus musculus
Received on:

04-08-2025

Accepted on:

08-09-2025

Published on:

13-10-2025

ABSTRACT

The present assessment study has been undertaken to review the toxic effects of exposure of one of the most important plant of Invasive Alien Plant Species (IAPS) group i.e. *Parthenium hysterophorus*. It endangers human health and livestock by disrupting the important glands function. The scientific studies have revealed that pollens, trichomes and other parts of *Parthenium hysterophorus* exhibit a wide spectrum of biological activities such as allergic, cytotoxic and phytotoxic. It contains certain chemical like sesquiterpene lactone, polyphenols and flavonoids which are harmful to human and other livestocks health. Our FTIR study of functional groups present in different parts of *Parthenium* plant has validated the presence of harmful toxic chemicals.Its toxic symptoms creates problem in the gastrointestinal tract, hametological parameters and degenerative changes in liver and kidneys. It has also been observed that *P. hysterophorus* can also disrupt endocrine function in mice. A valiant attempt has been made in this paper to consolidate and compile the research work carried out so far for the quick assessment of deleterious impact of *Parthenium* exposure on mice and rats on their respective reproductive and endocrine systems. This present work would pave the way for its vast pharmacologic applications for the development of a potential multipurpose medicinal agent.

INTRODUCTION

Invasive Alien Plants Species (IAPS) considered to be one of the major drivers of biodiversity loss and altering the ecosystem. Therefore, loss of native plant diversity through invasive plant pathogens may indirectly affect human health through perturbations in the environmental quality. Spread of the IAPS can profoundly affect human health through their pollen and toxins resulting in cardiovascular/ pulmonary problems in human beings. The human health impacts of invasive plants are further deteriorated by the rapid spread of vector-borne pathogens.

Health hazards to humans and livestock

Human health is negatively impacted by the dispersion of vector-borne diseases, pollens, and toxins from IAPs. (Plaza et al. 2018). The common allergens found in this weed are parthenin, coronopilin, tetraneuris, and ambrosin which cause various allergies like contact dermatitis, hay fever, asthma, and bronchitis in human beings (Wiesner *et.al,*. 2007). The roots of parthenium can cause allergy-type responses like hay fever, photodermatitis, asthma, skin rashes, peeling skin, puffy eyes, excessive water loss, swelling and itching of mouth and nose, constant cough, running nose and eczema. It contains allergenic sesquiterpene lactones (SQLs). The SQLs are found in the leaves, stems, flowers, and some pollen. The highest concentrations are found in trichomes which are present on stems, the underside of leaves and in the flowering heads.

The deleterious effects of *Parthenium hysterophorus*toxicity have been reviewed (Ahmed *et al.*, 1988;Mahadevappa, 1999). *P. hysterophorus*can cause acuteallergic contact dermatitis and respiratory, gastrointestinal tract, liver and kidneys problems inhumans, which under continued exposure becomechronic (Lonkar*et al.*, 1974; Mahadevappa, 1999). Cattle and buffalo feeding on *P. hysterophorus* develop loss of skin pigmentation and severe facial and bodydermatitis (Narasimhan *et al.*, 1977).The milk of cattle, buffalo and also the meat of sheep may be tainted by parthenin (Towers and Subba Rao, 1992; Tudor *et al.*, 1982, Kandhane et al. 1992). It has also recently been shown that *P. hysterophorus*can also disrupt endocrine function in mice (Vijayalakshmi, et al., 1999; Verma 2005, 2007; Veena, 2012). Some of the common diseases and with their symptoms caused by Parthenium exposure on human beings and livestocks are listed in Table-1.

So *Parthenium hysterophorus* has been focussed immensely for the research work by a number of the investigators for last so many years.

Table 1 : Diseases and symptoms of Mammalians after exposure of *Parthenium hysterophorus*.

CAUSED DISEASES	SYMPTOMS
Disorder	Reaction
Contact dermatitis	Seasonal eruption of the exposed skin surface
Eczema	Chronic lichensified eczema of the exposed skin surface

Eczematoid dermatitis	Skin eruptions and etching
Dermatitis	-do-
Allergic reaction	Cracks all over the sole
Allergic papules	Sore throat, bubbles in the mouth
Fatigue	General weakness, skin eruptions.
Severe dermatitis	Loss of scalp, body hair, ridging on nails
Fever in cows	Inflamed udder and rashes
Hypersensitivity in rabbit	Restlessness, natural falling of hairs from the dorsal region of the neck and back, small boils and oozing of boils.
Ulcerations in buffaloes horses donkeys, sheep, and goats.	Acute and chronic toxicity, ulcers both in the mouth and digestive tract, oesophagus and abnormal folds, necrosis of kidney and liver

Chemical analysis of *Parthenium hysterophorus*

The chemical analysis of Parthenium was essentially carried out by isolation and structural elucidation. 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). Parthenin, hymenin, coronopilindihydroisoparthenin, hysterin, hysterophorin and tetraneurin are the principal constituents of the sesquiterpene lactones along with phytotoxic compounds like hysterin and ambrosin. 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- 2. Parthenin, hymenin and ambrosin are reported to be responsible for the menacing role of this weed in provoking health hazards (Lata *et al.,* 2008).

Table 2 : Chemical Constituents of *Parthenium hystrophorus*

Main group	Constituents	References
Terpenoids	*Sesquiterpene lactones* (SLQ) : 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; Pareek *etal.*,2011
	α-unsaturated γ-lactones : 3-ß-hydroxy- parthenolide, costunolide, 3-ß hydroxycostunolide, 8-α-hydroxyestafiatin, artecanin, two chlorine containing sesquiterpene lactones, 1-ß-hydroxyarbusculin and 5-ß- hydroxyreynosin.	Barnes *et al.,* 2007
Volatile oils (0.02 to 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, ß-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-*ß*-Acetoxyhysterone C, Charminarone, 8*α*-Epoxymethylacrylyloxyambrosin, 8*α* Epoxymethylacrylyloxy-11, 13-dihydroparthenin, 8*α* Epoxymethylacrylyloxyparthenin, 2*ß*-Hydroxycoronopilin, Hysterone (A, B, C, D), 1*α*, 2*ß*, 4*ß*-Trihydroxypseudoguaian-6*ß*, 12-olide, Pyrethrin, tannins (type unspecified), melatonin, potassium chloride, protein.	Parsons and Cuthbertson, 2001; Barnes *et al.,* 2007; Zhou *et al.,* 2011a,

Source :Rajesh K. Meena et al, 2017

FTIR analysis :

To analyze the Functional group of different parts (Flower, Leaf, Stem and Root) of the *Parthenium* plant, the Instrument (Burker- Alpha-II Platinum ATR Germany) was used in the frequency range of 4000-400 cm^{-1}.

As observed in Fig.1, IR spectra of the aqueous extracts of plant parts have peaks mostly around at 1020 cm^{-1}, 1595 cm^{-1}, 2365 cm^{-1}, 2926 cm^{-1}. These peaks are attributed to broad C= N, C= O, C-N and C-O stretching bands characterized by phytochemicals, phenols flavonoids, alkaloids and polysaccharides, amine metabolites in the aqueous extract. Most intense peak at 1020 cm^{-1} found in stem and root may correspond to sesquiterpene lactones (SQLs) termed as parthenin. It is also prevalent in the IR spectra (Fig. 2) of aqueous extract of whole parthenium plant. These results conforms the finding of similar work as described elsewhere (Dennis Nzilu et al 2024).

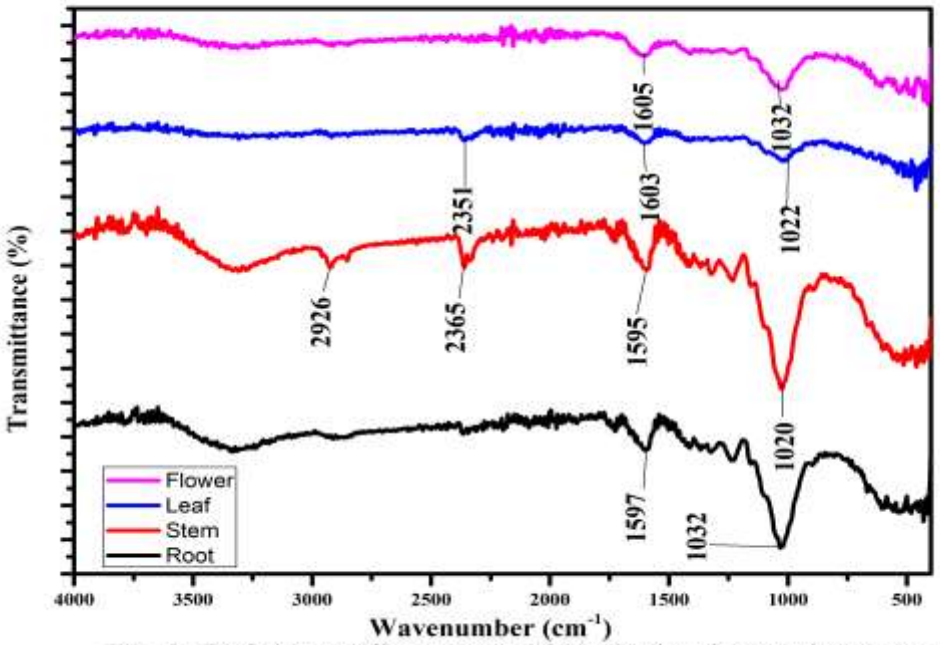

Fig . 1 : IR Spectra different parts of *Parthenium hysterophorus* plant

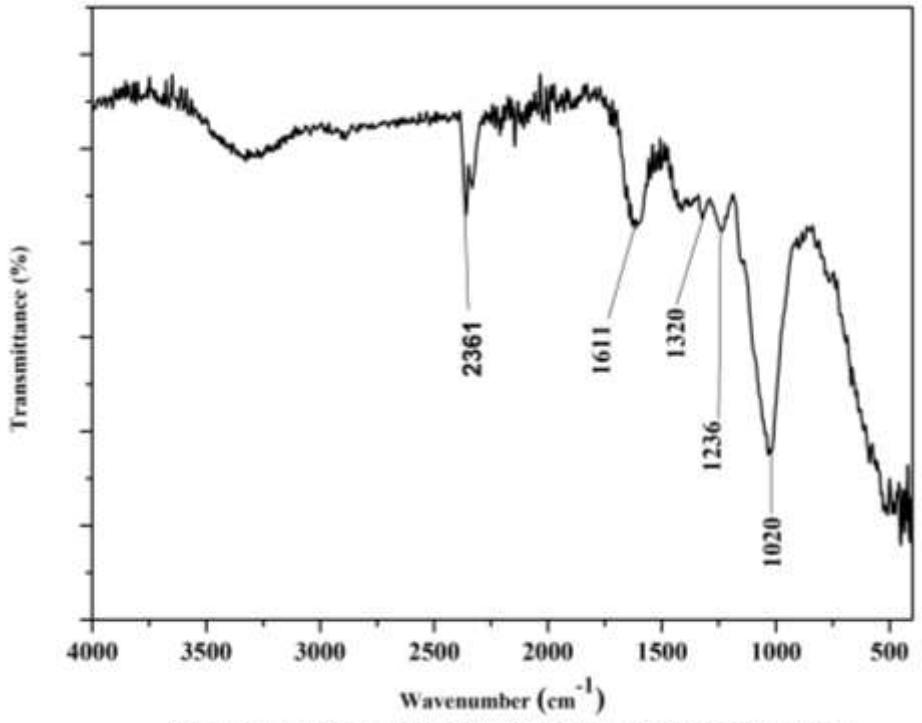

Fig. 2 : IR Spectra of whole *Parthenium hysterophorus* plant

DISCUSSION

It is evident by experimental results of many investigators that administration of *P. hysterophorus* either in alcoholic (methnol/ethanol) or in aqueous extract form to mice or rat at some fixed dosage and duration, disrupts the function of different endocrine and reproductive glands which negatively impacts on their life behaviour. The results of toxicological effects of *Parthenium hysterophorus* on the reproductive and endocrine systems of male mice Mus Musculus and rats has been compiled and shown in Table-3.

Table 3 : Toxicological effects of *Parthenium hysterophorus* on the reproductive and endocrine systems of mice Mus Musculus and rats.

Extract type	Test animal/ Dose / Duration	Symptoms / Effects / Changes	Reference
Ethanolic	Rats 200 and 400 mg/kg body weight	Significant decrease in erythrocyte count (RBC), Haemoglobin concentration Hb), Lymphocyte percentage (LYM) and Increase in neutrophil percentage (NEUT) and leukocyte count (WBC) with respect to time and dose.	Maurya and Kushwaha (2010)
Ethanolic	Rats 676.65 mg/kg body weight	Convulsion, Tremor, Laboured breathing, Food avoidance, Reduced food consumption, Increase in relative liver weight, decrease in body weight, Impairment in the functioning of digestive system.	Kushwaha and Maurya (2010) Patel V et al. 2008
Leaf extract	Rats	Depolarizing neuromuscular junctional blocking action	Kushwaha and Maurya (2012)
Dry leaf powder extract	Rats 100 mg/100 g body weight	Electromyographic (EMG) and electrodiagnostic studies revealed depolarizing neuromuscular junctional (NMJ) blocking effects .	Vijayalakshmi et al (1999)
Methanolic extract	Wistar Albino rats 20 mg/100g body wt	Haematological parameters analyzed : Total RBC count significantly decreased, Haemoglobin dropped. Overall significant reduction in WBC count signified that rat immune system becomes weak after oral treatment of Parthenium extract.	Neha Yadav et al (2010) Shivani et al. 2010
Methanolic extract	Swiss Albino Mice; 2.5 and 5 mg/kg body wt.	The results altogether indicates that the extract shows CNS depressant activity.	Jha et al (2011)
Leaves crude extract	Rabbits 10, 20, 40 and 80 mg kg–1	P. hysterophorus leaves extract had toxic effects on the hematological and biochemical parameters in rabbits which caused abnormal blood profile.	Adil et al (2022)
White flowering tops Aqueous extract	Male mice 10 mg/0.1 ml/kg body weight on alternate days for 30 & 60 days	Decreased the levels of (5-hydroxytryptamine (5-HT), Noradrenaline (NA) and Dopamine (DA) in total brain which is suspected in turn affects the physiology of the peripheral endocrine glands.	Verma et al., (2007)
Do	- do-	Thyroid stimulating hormone (TSH) levels significantly decreased after 60 days of exposures.	Verma et al., (2008)
Do	-do-	Decline in serum Gonadotropic hormones (Luteinizing Hormone, LH and Follicle-Stimulating Hormone, FSH) and Testosterone levels in later parts of the experiment.	Verma et al., (2005, 2025)

Daily administration of P. *hysterophorus*(10 mg/0.1 ml/kg body weight) dose to 20 adult male Mus musculus gradually lowered significantly the levels of 5-hydroxytrypamine (5HT), noradrenaline (NA) and dopamine DA) in whole mouse brain in all the treated groups after both 30 and 60 days of treatment when compared with the control group. It is suspected in turn to affect the physiology of the peripheral endocrine glands (Verma et al., 2007). *Parthenium hysterophorus* induced changes in gonadotropic hormones (Luteinizing Hormone, LH and Follicle-Stimulating Hormone, FSH)and testosterone levels in male *Mus musculus* and the effects were duration dependent (Verma et al., 2005, 2007, 2008, 2025). All neurotransmitter levels were decreased significantly, with the effects more prominent in the later part of the experiment. It was concluded that *P. hysterophorus* modulates the brain functions by altering the levels of biogenic amines. Alteration in biogenic amines may be responsible for general development.

The haematological parameters, such as erythrocyte and leukocyte count, hemoglobin concentration (Hb), lymphocyte (WBC) and neutrophil (NEUT) percentage of blood has been considered as bio indicators of toxicosis in animals exposed to xenobiotics. Ethanolic extract of the plant of Parthenium *hysterophorus* at sub lethal dose, 200 and 400 mg/kg body weight dose when tested against rats in the laboratory reveals a significant decrease in erythrocyte count, haemoglobin concentration, lymphocyte percentage and increase in neutrophil percentage and leukocyte count with respect to time and dose (Maurya and Kushwaha, 2010). Similar results were observed about *Parthenium hysterophorus* called ``*parthenium* poisoning." A substantial decrease in rat WBC count indicates that Parthenium extract weakens the immune system (Yadav, 2010).

The labored breathing on exposure to ethanolic extract of P. *hysterophorus* may lead to oxygen insufficiency which in turn disturbs the neuromuscular function that results in weakness of leg leading to abnormal gait in treated rats as observed in case of exposure to various pesticides by Fisher and Metcalf, 1983. The findings of present investigations are in accordance with Shull and Cheeke, 1983; Kononen, et al., 1992; and Ceron, et al., 1995. The abnormal gait in rats may also be attributed to the impaired neuromuscular physiology (Verma, et al., 2007, Vijayalakshmi, et al. 1999, Boyd, et al. 1990).

LD_{50} of ethanolic extract of Parthenium hysterophorus L. after oral administration was found to be 676.65 mg/kg body weight against rats. Tremor, convulsion, diarrhea, labored breathing, abnormal gait, food avoidance, reduced food consumption, increase in relative liver weight and decrease in body weight was observed in rats on exposure to sub lethal dosage of ethanolic extract of Parthenium *hysterophorus*. All the observations were found to be time and dose dependent in both male and female rats (Kushwaha and Maurya, 2010).

P. hysterophorus L. whole plant is used as allergen (Dwivedi *et al*., 2008). It also shows hypoglycemic effect in normal and diabetic rats (Patel *et al*., 2008). The flower extract has apasmogenic action in isolated rabbit duodenum (The wealth of India, 2003). The flower extract possess cardiac depressant

effect as concluded from experiments on perfused frog heart. Aqueous extract of flowers and leaves exert lethal effect on frog tadpoles. Phyto constituents particularly phytotoxins present in extracts have been reported to be responsible for this action (The wealth of India, 2003).

The possible CNS activity of methanolic extract of Parthenium hysterophorus L was investigated by common psycho pharmacological tests. The reduction in exploratory behavior in animals is similar with the action of other CNS depressant agents. The results altogether indicates that the extract shows CNS depressant activity.

CONCLUSION

Parthenium is known for its allergic effect on humans and alleged to have allelopathy on plants. The harmful effects of this weed on human health, animals, agriculture and environmental have been reported . It is a curse for bio-diversity. In our country 4-7 per cent of human population suffers from recognizable clinical symptoms associated with *Parthenium*, while 42-50 per cent are sensitized without showing symptoms.

Parthenium hysterophorus plant contains a large number of natural products, but the active principles probably include one or more of the sesquiterpene lactones known to be present, including parthenolide. It has multiple pharmacologic properties, such as anticancer, anti-inflammatory, cardiotonic, antispasmodic and as an enema for worms. We have compiled the various toxic effects of the *Parthenium* plant on the endocrine and reproductive systems of male mice Mus musculus which would pave the way for its vast pharmacologic applications as a potential multipurpose medicinal agent.

Parthenium exposure also creates a lot of problem and abnormalities in the human body, for example; Mind, Head, Ears, Eyes, Nose, Face, Mouth, Stomach, Abdomen, Stool and anus, Urinary organs, Male genetalia, Female genetalia, Respiratory organs, Heart, Extremities, Skin and Kidney and Liver. Besides this, it was observed that parthenin has the properties of breaking human leucocyte chromosomes.

It was observed from the studies that *Parthenium hysterophorus* lowered the brain 5HT, NA and DA levels after 30 and 60 days when compared with control group. Lowering of 5HT, NA and DA levels may suggest that *Parthenium hysterophorus* modulate the brain functions which alters the biogenic amines levels. TSH, FSH, LH and testostoren levels were lowered in blood of male Mus musculus after *Parthenium hysterophorus* exposures. This suggests that *Parthenium hysterophorus* alters the TSH, FSH, LH and testostoren levels by altering the neurotransmitters levels. Ateration in trophic hormone may cause histopathological changes in endocrine gland. The toxicological effects were more severe and prominent in a duration dependent manner.

In connection to this, an attempt has been made in this research paper to evaluate and summarize the impacts of *Parthenium* exposures on reproductive and endocrine systems of Mus Musculus which may be helpful for vast pharmacological applications.

DECLARATIONS

Funding : It is declared that No Financial Support was provided from any Government or Private agency for the present research work.

Conflict of interests :The authors declare that they do not have any conflict of interests.

Data availability : The data used to support the findings of this study are included within the article.

ACKNOWLEDGEMENT

Authors are grateful to Dr Murari Prasad, Senior Scientist (Retd.), CSIR-AMPRI, Bhopal, India, Prof Vinoy K Shrivastava, ex Head, Dept of Bioscience, Barkatullah University, Bhopal and Prof. P.K. Prasad, ex Principal, C.M. Science College, Darbhanga for his valuable inputs during present research work and while preparing the manuscript.

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