

**PARTHENIN: A SESQUITERPENE LACTONE FROM ANGIOSPERMIC PLANT PARTHENIUM HYSTEROPHORUS**

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**ABSTRACT**

Parthenium dermatitis is an immunologically mediated allergic contact dermatitis caused by plant extracts of *Parthenium hysterophorus* and related species. It is a chronic disease lasting for months to years and often lifetime with seasonal exacerbations and remissions. It is mainly caused by dried leaves and trichomes. Pollen play role, mainly in respiratory allergy. These may not pass beyond the nasal mucosa and hence more often causes allergic rhinitis rather than bronchial asthma. It is a noxious weed in America, Asia, Africa and Australia. This weed is considered to be a cause of allergic respiratory problems, contact dermatitis, mutagenicity in human and livestock. The pollen grains, airborne dried plant parts, and roots of parthenium cause various allergies like contact dermatitis, hay fever, asthma, and bronchitis in human beings. The common allergens found in this weed are parthenin, coronopilin, tetraeneuric, and ambrosin.

**KEYWORDS:** trichomes, pollen, sesquiolactone, angiosperm, parthenin, allergy, genotoxic, dermatitis, trichomes, allelopathic.

**Taxonomy**

Kingdom: Plantae; Branch: Angiosperms; Group: Asterids; Clade: Tracheophytes; Nature: Angiosperms; Order: Asterales; Family: Asteraceae; Subfamily:

Asteroidae; Tribe: Heliantheae; Subtribe: Ambrosiinae; Genus: *Parthenium*; Species: *Hysterophorus Parthenium hysterophorus* is a species of flowering plant in the family Asteraceae. It is native to the American tropics.



**Figure-1: Parthenium Plant.**

**Occurrence:** Common names include Santa-Maria, Santa Maria feverfew, whitetop weed, and famine weed. In India, it is locally known as carrot grass, congress grass or gajar ghas or dhanura. It is a common invasive species in India, Australia, and parts of Africa. Mexico, Central America, and parts of South America are the natural home of parthenium weed. Locations within

which *Parthenium hysterophorus* is naturalised include the Indian sub-continent, south-eastern Asia, tropical/subtropical Australia, eastern USA, southern and eastern Africa, Madagascar and many oceanic islands with warm climates. Two most important diseases associated with parthenium were a rust disease, caused by *Puccinia abrupta* var. *parthenicola*, and a phyllody

disease, caused by a phytoplasma of fababean phyllody (PBP) phytoplasma group. *Parthenium hysterophorus* invades disturbed land, including roadsides. It infests pastures and farmland, causing often disastrous loss of

yield, as reflected in common names such as famine weed. In some areas, heavy outbreaks have been ubiquitous, affecting livestock and crop production, and human health.<sup>[1-4]</sup>

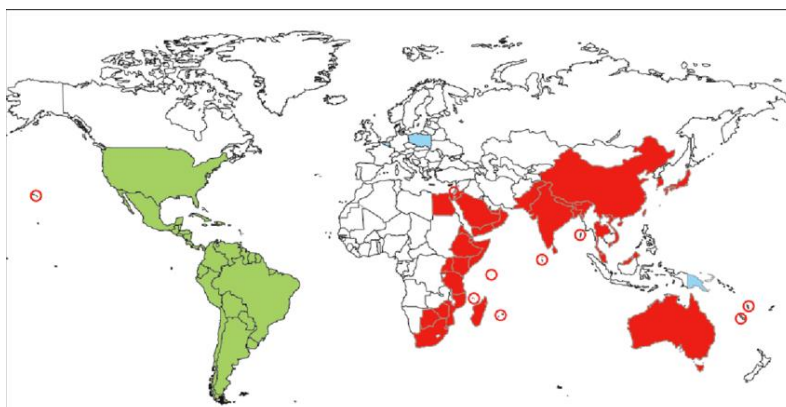


Figure-2: Geographical Occurrence.

The plant produces allelopathic chemicals that suppress crop and pasture plants, and allergens that affect humans and livestock. It also frequently causes pollen allergies. Allelopathy refers to a negative or positive effect on one type of plant, by a chemical produced by another type of plant. Various types of chemicals, including phenolics, hydroxamic acids, and short-chain fatty acids, have been identified as having allelopathic properties. A study published in 2021 further showed that the plant could promote malaria by supplying much appreciated food and shelter to mosquitoes in Eastern Africa. It is being investigated as a means of removing heavy metals and dyes from the environment, control of aquatic weeds, commercial enzyme production, an additive in manure for biogas production, as a biopesticide, and as green manure and compost. The species has been listed as an invasive alien species of Union Concern.<sup>[5-7]</sup>

This means it is illegal to import or sell this species in the whole of the European Union. Contact with the plant causes dermatitis and respiratory malfunction in humans, and dermatitis in cattle and domestic animals. The main substance responsible is parthenin, which is dangerously toxic. It also is responsible for bitter milk disease in livestock when their fodder is contaminated with *Parthenium* leaves. Side effects after ingestion of any

part of plants that encumber the trichomes and pollen are eczema skin inflammation, hay fever, asthma, burning and blisters, breathlessness and choking, allergic rhinitis, black spots, diarrhoea, severe erythematous eruptions.<sup>[8-10]</sup>

**Chemistry:** Parthenin is a chemical compound classified as a sesquiterpene lactone. It has been isolated from *Parthenium hysterophorus*. Except where otherwise noted, data are given for materials in their standard state (at 25°C [77°F], 100kPa). It is genotoxic, allergenic, and an irritant. Among other allelopathic effects of the species, the presence of *Parthenium* pollen grains inhibits fruit set in tomato, brinjal, beans, and a number of other crop plants. Light infestations of *Parthenium hysterophorus* in cultivated fields may be hoed or weeded by hand if labour is available at acceptable cost. Generally the application of herbicides is expensive and often harmful; Paraquat [IUPAC: N,N'-dimethyl-4,4'-bipyridinium dichloride; CAS: 1910-42-5; Formula: C<sub>12</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>2</sub>] sprays may be applied while the weeds are young. Glyphosate is not effective against this species. The most satisfactory and promising means of practical long-term control are biological. Several species that feed on the weed are variously in use or on trial in various countries.

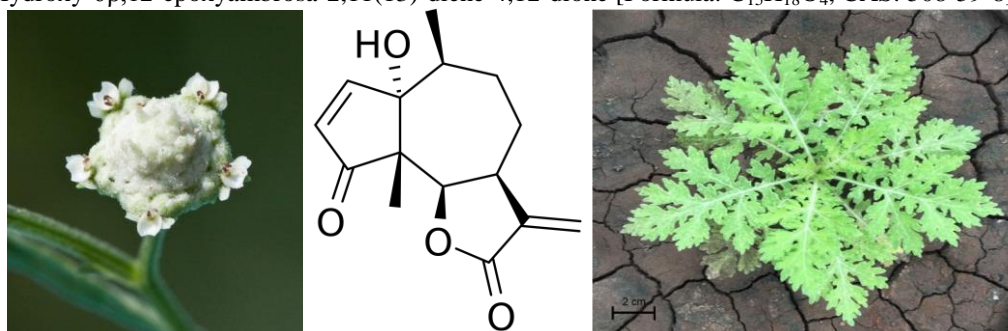


Figure-3: Allergy of Parthenin.

The best-established control organism so far is a beetle native to Mexico, *Zygogramma bicolorata* (Mexican beetle), which was first introduced to India in 1984. It since has become widespread and well-established on the subcontinent. It defoliates and often kills the weed, and its damage to the young flowering tops reduces seed production. In various countries, such as Australia and South Africa, several other biocontrol agents have been released or are under evaluation. These include at least two more species of beetles that have been released in South Africa, a stem boring weevil *Listronotus setosipennis*, and a seed weevil *Smicronyx lutulentus*. Also in South Africa, rust fungi have been of some use: the winter rust *Puccinia abrupta* var. *parthenicola* plus

the summer rust *Puccinia xanthii*. In Australia, apart from the foregoing, yet other biocontrol agents have been employed or evaluated on *Parthenium hysterophorus*, to a total of 11 species since 1980. Of those eleven, nine appear to have established in various regions. The two with the greatest effect seem to be the Parthenium beetle *Zygogramma bicolorata* and a stem-galling moth *Epiblema strenuana*. However, other species that appear to have established usefully include a leaf-mining moth, *Bucculatrix parthenica*; a stem-galling weevil, *Conotrachelus albocinereus*; and a root-boring moth *Carmenta ithacae*. Parthenin is a chemical compound classified as a sesquiterpene lactone. It has been isolated from *Parthenium hysterophorus*.<sup>[11-13]</sup>

IUPAC: 1-Hydroxy-6 $\beta$ ,12-epoxyambrosa-2,11(13)-diene-4,12-dione [Formula: C<sub>15</sub>H<sub>18</sub>O<sub>4</sub>, CAS: 508-59-8]



**Figure-4: Parthenium flower, Parthenin the sesquiterpene lactone and Parthenium leaf.**

It is genotoxic, allergenic, and an irritant. Parthenin is believed to be responsible for the dermatitis caused by *Parthenium hysterophorus*. It invades disturbed land, including roadsides. It infests pastures and farmland, causing often disastrous loss of yield, as reflected in common names such as famine weed. In some areas, heavy outbreaks have been ubiquitous, affecting livestock and crop production, and human health. The plant produces allelopathic chemicals [Allelopathy is the direct or indirect effects of chemicals produced by plants or microorganisms on the growth, development, and distribution of other plants and microorganisms in natural and agricultural ecosystems] that suppress crop and pasture plants, and allergens that affect humans and livestock. It also frequently causes pollen allergies. A study published in 2021 further showed that the plant could promote malaria by supplying much appreciated food and shelter to mosquitoes in Eastern Africa. It is being investigated as a means of removing heavy metals and dyes from the environment, control of aquatic weeds, commercial enzyme production, an additive in manure for biogas production, as a biopesticide, and as green manure and compost. The species has been listed as an invasive alien species of Union Concern. This means it is illegal to import or sell this species in the whole of the European Union. Two most important diseases associated with parthenium were a rust disease, caused by *Puccinia abrupta* var. *parthenicola*, and a phyllody disease, caused by a phytoplasma of fababean phyllody (PBP) phytoplasma group. *Parthenium hysterophorus* can produce a spectrum of clinical

patterns. The dermatitis usually presents as itchy, erythematous, papules and plaques on exposed areas of the body like the face, including upper eyelids, side of neck, the “V” of the upper chest, Parthenium dermatitis is mainly caused by dried leaves and trichomes. Pollen play role, mainly in respiratory allergy. These may not pass beyond the nasal mucosa and hence more often causes allergic rhinitis rather than bronchial asthma. Topical steroids, antihistamines, and avoidance of Parthenium are the mainstay of treatment for localized dermatitis. Systemic corticosteroids and azathioprine are frequently needed for severe or persistent dermatitis.<sup>[14-16]</sup>

**Toxicity:** Contact with the plant causes dermatitis and respiratory malfunction in humans, and dermatitis in cattle and domestic animals. It also is responsible for bitter milk disease in livestock when their fodder is polluted with Parthenium leaves. The main substance responsible is parthenin, which is dangerously toxic. Contact with this plant cause dermatitis and respiratory malfunction in humans, dermatitis in cattle and domestic animals due to the presence of toxin parthenin. It is a sesquiterpene lactone. It is a photodynamic substance causing primary photosensitization. Diarrhoea followed by cutaneous lesions characterised by itching etc.

**Mechanism:** The major sesquiterpene lactone of Parthenium weed Parthenin is a photodynamic substance. Hence as seen with other photodynamic agents ingestion of pathenium weed result in primary photosensitization causing liver pathology and skin reaction.

**Symptoms:** Erythematous eruptions over much of the body. Alopecia and depigmentation of neck and shoulders. Oedema around eyelids and facial muscles. Diarrhoea followed by cutaneous lesions characterised by itching, erythematous eruption on the tip and base of the ear, neck sides of thorax, abdomen, knee joint and briske.

**Weedicides:** Weedicides such as atrazine [It is a chlorinated herbicide of the triazine class. IUPAC: 1-Chloro-3-ethylamino-5-isopropylamino-2,4,6-triazine; CAS: 1912-24-9; Formula:  $C_8H_{14}ClN_5$ ], metribuzin [IUPAC: 4-amino-6-tert-butyl-3-(methylthio)-1,2,4-

triazin-5(4H)-one; CAS: 21087-64-9; Formula:  $C_8H_{14}N_4OS$ ] is a herbicide used both pre- and post-emergence in crops including soy bean, potatoes, tomatoes and sugar cane., monuron [IUPAC: 3-(p-Chlorophenyl)-1,1-dimethylurea; CAS: 150-68-5; Formula:  $C_9H_{11}ClN_2O$ ], simazine [It is an herbicide of the triazine class; IUPAC: 6-Chloro-N<sup>2</sup>,N<sup>4</sup>-diethyl-1,3,5-triazine-2,4-diamine; CAS: 122-34-9; Formula:  $C_7H_{12}ClN_5$ ], terbutryn [IUPAC: 2-t-Butylamino-4-ethylamino-6-methylthio-s-triazin; CAS: 886-50-0; Formula:  $C_{10}H_{19}N_5S$ ] have been found effective in controlling parthenium. Herbicides such as dicamba, glyphosate and picloram have also yielded good results.

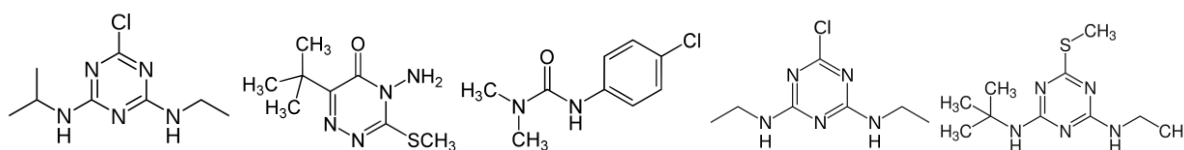


Figure-5: Weedicides.

The pollen grain of the parthenium plant causes allergies in humans. Parthenium is also known as carrot grass. It is invasive plant species and was imported along with wheat. Pollen play role, mainly in respiratory allergy. These may not pass beyond the nasal mucosa and hence more often causes allergic rhinitis rather than bronchial asthma. Parthenium dermatitis is caused by dry powder

of leaves and flowers and hair-like structures (trichomes). Sesquiterpene lactones (SQLs) are the most important allergens responsible for ACD to parthenium. Among other allelopathic effects of the species, the presence of Parthenium pollen grains inhibits fruit set in tomato, brinjal, beans, and a number of other crop plants.<sup>[17-20]</sup>

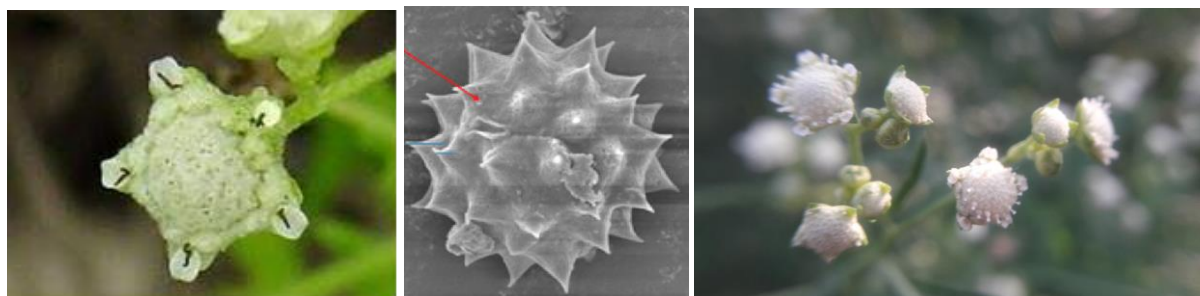


Figure-6: Allergy producing pollen grains.

## CONCLUSION

Parthenium hysterophorus is a noxious weed in America, Asia, Africa and Australia. This weed is considered to be a cause of allergic respiratory problems, contact dermatitis, mutagenicity in human and livestock. Crop production is drastically reduced owing to its allelopathy. Also aggressive dominance of this weed threatens biodiversity. Eradication of *P. hysterophorus* by burning, chemical herbicides, eucalyptus oil and biological control by leaf-feeding beetle, stem-galling moth, stem-boring weevil and fungi have been carried out with variable degrees of success. Recently many innovative uses of this hitherto notorious plant have been discovered. It confers many health benefits, viz remedy for skin inflammation, rheumatic pain, diarrhoea, urinary tract infections, dysentery, malaria and neuralgia. Its prospect as nano-medicine is being carried out with some preliminary success so far. Removal of heavy metals and dye from the environment, eradication of aquatic weeds, use as substrate for commercial enzyme production,

additives in cattle manure for biogas production, as biopesticide, as green manure and compost are to name a few of some other potentials. The active compounds responsible for hazardous properties have been summarized.

## REFERENCES

1. Hausen B M, Schulz K H. Chrysanthemen – Allergie (I. Mitteilung). *Dermatosen*, 1973; 21: 199–214.
2. Hausen B M, Schulz K H. Chrysanthemum allergy III. Identification of the allergens. *Archives for Dermatological Research*, 1976; 255: 111–121.
3. Bleumink E, Mitchell J C. Geissman T A, Towers G H N. Contact hypersensitivity to sesquiterpene lactones in *Chrysanthemum dermatitis*. *Contact Dermatitis*, 1976; 2: 81–88.
4. Mitchell J C, Schofield B. Singh B, Towers G H N. Allergy to *Frullania*. Allergic contact dermatitis occurring in forest workers caused by exposure to

- Frullania. Archives of Dermatology, 1969; 100: 46–49.
5. Storrs F J, Mitchell J C, Rasmussen J E. Contact hypersensitivity to liverwort and the Compositae family of plants. Cutis, 1979; 18: 681–686.
  6. Lonkar A, Nagasampagi B A, Narayanan C R, Landge A B, Sawaikar D. An antigen from Parthenium hysterophorus Linn. Contact Dermatitis, 1976; 2: 151–154.
  7. Towers G H N, Mitchell J C, Rodriguez E, Subba Rao P V, Bennett F D. Biology and chemistry of Parthenium hysterophorus L., a problem weed in India. Journal of Scientific and Industrial Research, 1977; 36: 672–684.
  8. Towers G H N, Mitchell J C. The current status of the weed Parthenium hysterophorus L as a cause of allergic contact dermatitis. Contact Dermatitis, 1983; 9: 465–469.
  9. Rodriguez E, Dillon M O, Mabry T J, Mitchell J C, Towers G H N. Dermatologically-active sesquiterpene lactones in trichomes of Parthenium hysterophorus L. Compositae. Experientia, 1976; 32: 236–237.
  10. Picman A K, Towers G H N, Subba Rao P V. Coronopilin – another major sesquiterpene lactone in Parthenium hysterophorus. Phytochemistry, 1980; 19: 2206–2207.
  11. Mitchell J N S. Plants. In: E Cronin, (ed.): Contact dermatitis. New York; Churchill Livingstone, 1980.
  12. Mitchell J C. Contact allergy from plants. In: V C Runeckles, (ed.): Recent advances in phytochemistry. New York: Plenum Press, 1975; 9: 199–138.
  13. Dupuis G, Mitchell J C, Towers G H N. Reaction of alantolactone, an allergenic sesquiterpene lactone, with some amino acids. Canadian Journal of Biochemistry, 1974; 5: 575–581.
  14. Pitman A K, Rodriguez E, Towers G H N. Formation of adducts of parthenin and related sesquiterpene lactones with cysteine and glutathione. Chemical-Biological Interactions, 1979; 28: 83–89.
  15. Dupuis G, Benezra C, Schlewer G, Stampf J-L. Allergic contact dermatitis to  $\alpha$ -methylene- $\gamma$ -butyrolactones. Molecular Immunology, 1980; 17: 1045–1051.
  16. Picman A K, Towers G H N. Sesquiterpene lactones in various populations of Parthenium hysterophorus. Biochemical Systematics and Ecology, 1982; 10: 145–153.
  17. Picman A K, Elliott R H, Towers G M N. Cardiac-inhibiting properties of the sesquiterpene lactone, parthenin, in the migratory grasshopper, Melanoplus sanguinipes, Canadian Journal of Zoology, 1981; 59: 285–292.
  18. Picman A K, Picman J, Towers G H N. Cross-reactivity between sesquiterpene lactones related to parthenin in parthenin-sensitized guinea pigs. Contact Dermatitis, 1982; 8: 294–301.
  19. Lonkar A, Mitchell J C, Calnan C D. Contact dermatitis from Parthenium hysterophorus. Transactions of the St. John's Hospital Dermatological Society, 1974; 60: 43–53.
  20. Fisher A A. Contact dermatitis due to American Parthenium weed in India. Cutis., 1979; 23: 20–36.