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REVIEW ARTICLE

THE BOON AND BANE OF *PARTHENIUM HYSTEROPHORUS* FOR HUMAN HEALTH

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Summary

The annual or ephemeral plant *Parthenium hysterophorus L.* is an upright and heavily branched member of the *Asteraceae* family. The herb is used to treat heart issues, fever, anemia, wounds, and ulcerated sores. It is applied topically to treat skin issues, while the plant's decoction is frequently taken orally to address a wide range of ailments. Psoriasis, rheumatoid arthritis, diarrhea, urinary tract infections, dysentery, malaria, psoriasis, allergies, asthma, tinnitus, nausea, vomiting, and neuralgia are just a few of the health benefits that *P. hysterophorus L.* can provide. Asthma, bronchitis, dermatitis, and hay fever are some of the major problems caused by this weed, which is harmful to all living things because it also depletes nutrient levels and competes with the cultivation of major crops and vegetation. This review discusses the potential health benefits as well as the origin, distribution, morphology, and harmful effects of the plant on human health.

Key words: Pharmacological activities; Health benefits; Harmful effects; Weed; Asteraceae

1. INTRODUCTION

Since the advent of written history, plants have been utilized as medicines. Herbs are commonly employed to treat illnesses in non-industrialized nations, and they are often more cost-effective than modern pharmaceuticals (1). The advantages of herbal medications include safety, effectiveness, and fewer side effects. Herbal medications and their bioactive components have various uses, such as antibacterial, anti-dermatophytes, anti-inflammatory, anti-proliferative, and chemoprotective properties (2, 3).

The invasive *Parthenium hysterophorus L.* is a weed plant in the *Asteraceae* family (Figure 1). The classification of this plant is listed in Table 1. This upright, slender plant is well-known for its abundant growth, particularly in warmer climates. Originally endemic to north-eastern Mexico, it was previously exclusive to America, but now it is widely distributed throughout Asia and Europe (4). It is believed to have originated in tropical Americas. Other common names for this plant include altamisa, bitter weed, carrot grass, congress grass, gajar ghas, santa maria, star weed, white top, and wild feverfew (5). Its presence was first observed in Ethiopia in the 1980s in the Dire-Dawa

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region, and the initial reports of its occurrence in Ethiopia were from Dire-Dawa and Harerge in 1988. Since then, it has rapidly spread to other regions of the nation through vehicle traffic, wind, water, and urban trash (6). Due to its disruptive nature, ability to spread, and its impact on the economy, human health, and environmental, it is considered one of the most noxious weeds. It significantly affects the beef pasture industry; resulting in an annual cost of approximately $100 million. Decreased production leads to increased control costs (7). Extensive research on nanoparticles in antibacterial advancements is gaining momentum as they can be used as an alternative to antibiotics (8).

Figure 1. *Parthenium hysterophorus L.* plant.

Table 1. Classification of *Parthenium hysterophorus L.* according to taxonomy.

Kingdom	*Plantae*
Subkingdom	*Viridiplantae*
Superdivision	*Embryophyte*
Division	*Tracheophyte*
Subdivision	*Spermatophytina*
Class	*Magnoliopsida*
Superorder	*Asteranae*
Order	*Asterales*
Family	*Asteraceae*
Genus	*Parthenium*

People who encounter the plant or its pollen often experience severe allergies, which can have various negative consequences. *Parthenium* has certain advantages when taken in large doses (9). Although sesquiterpene lactones (SLs) isolated from *P. hysterophorus L.* plants possess therapeutic, germicidal, and pesticidal properties, the plant is still considered hazardous. Parthenin, a SLs found in the flower, leaf, root, and stem extracts of *P. hysterophorus L.*, has reportedly been shown to inhibit seedling development and germination (root and shoot length) in a various crop, including linseed and chickpea (10).

In traditional medicine, the decoction of this plant is used as an emmenagogue and to treat fever, diarrhea, neurological diseases, urinary tract infections, dysentery, and malaria. It is an ethnobotanical remedy used for the treatment of eczema, gynecological disorders, herpes, inflammation, rheumatic pain, and skin rashes. *P. hysterophorus L.* has been found to have pharmacological activity as a vermifuge, an analgesic for neuralgia, and a treatment for muscular rheumatism. This weed is also considered as a potential remedy for liver amoebiasis. The primary plant constituent, Parthenin, possesses important therapeutic qualities, including an anticancer property (11).

Numerous secondary metabolites, including phenolic acids found in *P. hysterophorus L.*, have been utilized as antitumor, antispasmodic, antiviral, antibacterial, antiamoebic, enzyme inhibitors, neuroprotective, and oxidative stress (OS) agents (12). Asthma, bronchitis, dermatitis, and hay fever are among the health issues that *P. hysterophorus L.* can induce on in individuals. This weed contaminates animal milk and flesh, which reduces the value of animal products (13).

2. ORIGIN AND DISTRIBUTION

Only 44 of the 91 nations where *Parthenium* weed is currently found appear to be within its native range. In various regions of Africa, Asia, and Australia where it has been introduced, it is considered as one of the most problematic weeds. The *Parthenium* weed, originally discovered in India in 1956 and may have arrived there as a contamination of wheat brought in from the United States (14). It adapts to different agroclimatic circumstances and easily spread to various environmental settings. Bangladesh, China, Ethiopia, India, Kenya, Madagascar, Mozambique, Nepal, Pakistan, Somalia, South Africa, Sri Lanka, Taiwan, Vietnam, Zimbabwe, the Pacific Islands, and several South and Central American nations are among the nations where this plant is distributed (15). Asia, Australia, and Africa are now all heavily affected by it (16).

2.1. Distribution in India

All states in India have reported varying degrees of *P. hysterophorus L.* spread (Figure 2). Generally, the states with highest density and distribution levels of *Parthenium* are Andhra Pradesh, Tamil Nadu, Bihar, Madhya Pradesh, Chhattisgarh, Karnataka, Delhi, Uttar Pradesh, Punjab, Maharashtra, and Haryana; the next highest states are Jharkhand, Jammu and Kashmir, Gujarat, Rajasthan, Assam, West Bengal, Himachal Pradesh, Uttarakhand, and Orissa. The states with the lowest levels of *Parthenium* infestation are Andaman. However, the extent of invasion varies between states and even within states (17, 18). While it was initially discovered in Pantnagar, U.P., near the train station, this weed has now spread to several agricultural fields, the Rae-Bareilly district, and the Jhansi districts (19).

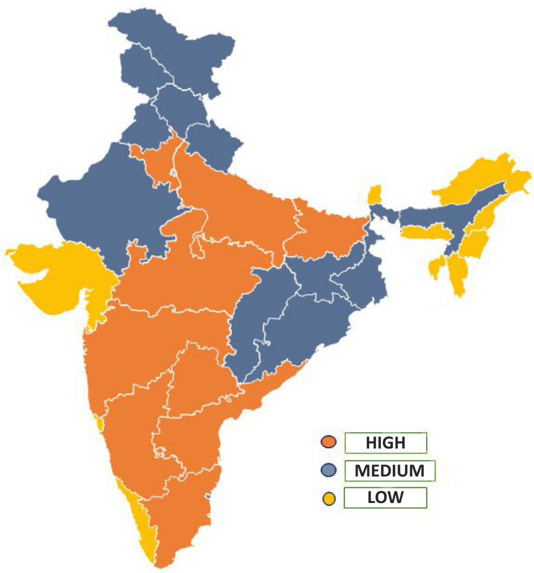


Figure 2. Spread level of *Parthenium hysterophorus L.* in several Indian states.

3. MORPHOLOGY

P. hysterophorus L. is an annual or ephemeral herb that grows rapidly, has an upright habit, and numerous branches. The plant goes through different stages, including the juvenile, rosette, or vegetative stage, as well as the adult, mature, or reproductive stage. In the juvenile stage, a cluster of wide, deep greenish, simple, radicle, and small sharp leaves without flowers is observed (Figure 3) (20).

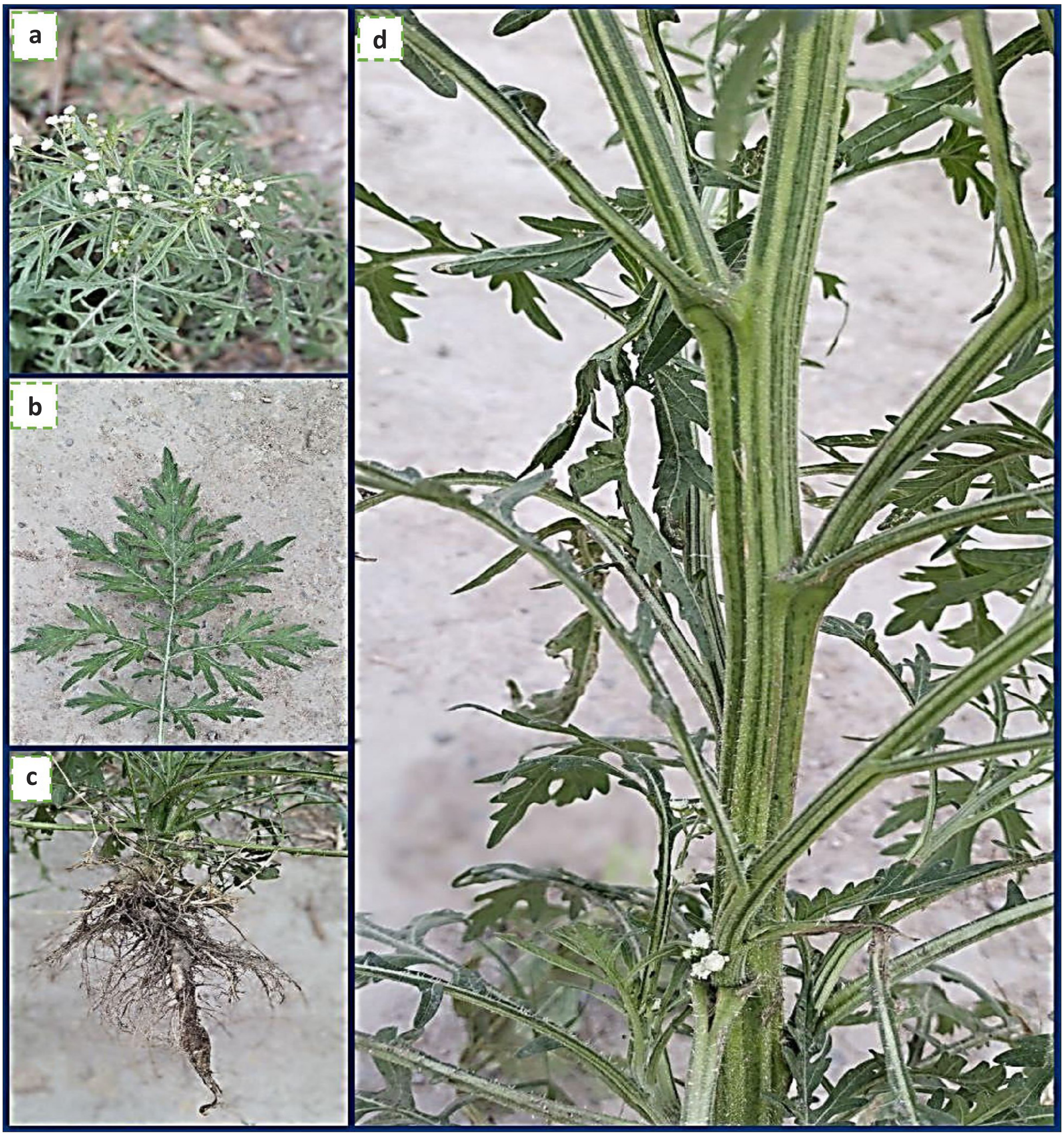


Figure 3. Different parts of *Parthenium hysterophorus L*. A-fruit, B-leave, C-root, D-stem.

In the mature stage, the plant grows upright, becomes heavily branched, and develops a deep taproot system that can reach up to 2 meters in height. As the weed matures, the hairy, octagonal, longitudinally grooved stem becomes stiff and woody. The leaves are simple, alternate, pinnately, or bipinnately divided, measuring 20–30×12–25 cm, and they gradually decrease in size towards the branch tips. The stem and leaf surfaces are covered with four different types of multicellular, white trichomes, both glandular and non-glandular. The flowers, which are creamy white and approximately 4 mm in diameter, emerge from the leaf forks. Each plant produces 624 million anemophilous or wind-pollinated pollen grains. The flowers give rise to four to five 2 mm long, black, wedge-shaped seeds that are difficult to detect with the naked eye. A single plant can generate up to 25,000 seedlings, resulting in a vast underground seed bank (21).

4. CHEMICAL COMPOSITION

Most *Parthenium* weed plants contain primary SLs, namely Parthenin or Hymenin, along with lower quantities of ambrosin, coronopilin, tetraneurin A, and hysterophorin. The main SL found in *Parthenium* weed is Hymenin, which also includes hysterin and dihydroisoparthenin. Parthenin, identified as the primary allergen of *Parthenium* weed, belongs to the class of SLs known as pseudoguinolides. It possesses an α-methylene, γ-lactone structure, which is believed to be primarily responsible for immune responses such as dermatitis (22). The main chemical constituents are classified in Table 2.

Table 2. Chemical Constituents of *Parthenium hysterophorus L.*

Chemical Class	Constituents
Terpenoids	Germacranolides (parthenolide, artemorin, and chrysanthemonin), guaianolides (chrysartemin A, partho-lide, and chrysanthemolide), and eudesmanolides (santamarin, reynosin, and magnolialide) are examples of sesquiterpene lactones. Other examples are parthenin, cornopolin, artecanin, and balchan.
Volatile oils	Numerous monoterpenes and sesquiterpene components (e.g., camphor, camphene, ρ-cymene, bornyl acetate, tricylene, α-thujene, α-pinene, β-pinene, γ-terpinene, their esters) are present.
Amino acids	Proline and Glycine are abundant, and alanine and Lysine are present in moderate amounts.
Amino sugars	Together with acetylglucosamine, N-acetylgalactosamine.
Flavonoids	Luteolin, apigenin, quercetin, chrysoeriol, santin, jaceidin, and centaureidin are some of the compounds found in luteol. Other compounds include 6-hydroxy kaempferol 3,6-dimethyl ether, 3,6,4′-trimethyl ether (tanetin), quercetagetin 3,6-dimethyl ether, 3,6,3′-trimethyl ether, and centaure.
Others	Charminarone, 8-acetoxyhysterone C, 8-acetoxymethylacrylyloxyambrosin, 8-acetoxymethylacrylyloxy-11, 13-dihydroparthenin, 8-acetoxymethylacrylyloxyparthenin, 2-acetoxycoronopilin, Hysterone (A, B, C, D), 1, 2, 4, and 12-olide, Pyrethrin, tannins (of an unknown type), melatonin, potassium chloride, protein.

5. RELATED SPECIES

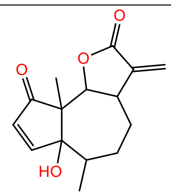
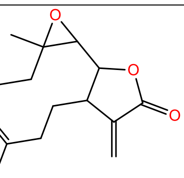
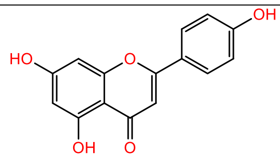
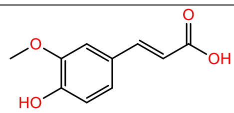
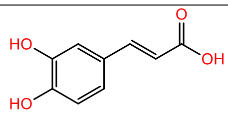
Common flavonoids are present in many *Parthenium* species. *P. hysterophorus L.*, *Philodendron bipinnatifidum*, and *Pythium glomeratum* were discovered with kaempferol and quercetin 3-0-glycosides, whereas the North and South American species pair indicate that they are closely related *P. Bipinnatifidum* (Mexico) and *P. Glomeratum* (Argentina) produced. The primary aglycone is the 3,7,3′-trimethyl ether of quercetin. This genus's members are popular for triggering hypersensitivity in both humans and animals. Rubber is frequently produced using an interconnected species called *P. argentatum* (23). Table 3 enlists the common compounds isolated from *Parthenium hysterophorus L.* and their main activity.

6. INDIVIDUAL BIOACTIVITIES OF COMMON COMPOUNDS ISOLATED FROM *PARTHENIUM HYSTEROPHORUS*

6.1. Parthenin

Parthenin, the main component of the invasive tropical weed *P. hysterophorus L.* is a pseudoguaianolide STL (Asteraceae) (24). Most of it is stored in the capitate-sessile trichomes that are found in various parts of *P. hysterophorus L.*, mostly within the leaves (25). Parthenin production is about 49% higher at 400 ppm CO_2 than at 350 ppm, which has recently been related to higher CO_2 levels (26). Like other STLs, parthenin is produced by the mevalonic acid route from farnesyl pyrophosphate. However, the precise mechanism that sets parthenin's formation from that of the other STLs is still not entirely understood. Parthenin is continuously produced by plants, with reproductive stages showing the highest levels. It is either released by degraded tissues or is naturally leached from the plant through ruptured trichomes and root exudates. Parthenin has a wide range of biological functions, and its multi-step production has also been noticed (25).

Table 3. Isolated compounds, their structures, and the widely used activity they exhibit.

COMPOUNDS	STRUCTURE	WIDELY USED ACTIVITY
Parthenin		Antimalarial
Parthenolide		Anticancer
Apigenin		Antiviral
Ferulic acid		Antioxidant
Caffeic acid		Antioxidant

6.1.1. Antimalarial Activity of Parthenin

Additionally, parthenin demonstrated considerable antimalarial action against a *Plasmodium falciparum* strain that was drug-resistant to multiple medications and shared no structural similarities with the newly developed antimalarial drug qinghaosu (25). When treating parasites that are resistant to artemisinin, parthenin's action against *P. falciparum* was strong enough to potentially take the place of artemisinin-related medications (27). Some ligands with excellent binding affinities against *P. Vivax* and *P. Falciparum* were identified using a docking study of parthenin analogs against lactate dehydrogenase proteins. As a result, these compounds may be used as medications for the treatment of malaria (28).

6.2. Parthenolide

Parthenolide is a major SLs that naturally exists in medicinal plants, especially in feverfew. The nucleophilic nature of the epoxide group and methylene lactone ring allows for quick interactions with biological sites. It has been discovered that these interactions are linked to its capacity to cause OS and that it possesses a variety of anticancer and pro-apoptotic properties (29, 30).

6.2.1. Anticancer Activity of Parthenolide

Parthenolide is expected to have a pro-apoptotic effect, leading to the activation of p53 and increased generation of ROS. It is worth noting that normal cells do not display pro-apoptotic activity, as this is primarily observed in cancerous cells with elevated ROS levels. The intracellular redox status of cells has been found to profoundly influence both cell survival and cell death. Two primary effects of Parthenolide that have been identified are the inhibition of NF-κB and OS (31).

6.3. Apigenin

Apigenin, also known chemically as 4′, 5, 7-trihydroxy flavone, is a naturally occurring substance that belongs to the flavone class. Numerous biological activities, and a variety of substances, such as anti-inflammatory, anticancer, anti-genotoxic, anti-allergic, neuroprotective, cardioprotective, and antibacterial, have been discovered to be linked to flavones and some of their synthetic counterparts. A yellow crystalline substance called apigenin has been used to color wool. The metabolic precursor phenylalanine and tyrosine, which are both derived from the shikimate, can be used to make apigenin, a by-product of the phenylpropanoid pathway. While p-coumaric acid is produced from tyrosine instantly by deamination, cinnamic acid is produced from phenylalanine by non-oxidative deamination followed by oxidation at C-4. Three malonyl-CoA residues are added to p-coumarate after CoA activation, which is subsequently aromatized by chalcone synthase to create chalcone. Chalcone is then isomerized by chalcone isomerase to create naringenin, which is a flavanone synthase and then oxidizes to apigenin (32, 33).

6.3.1 Antiviral Activity of Apigenin

Apigenin 7-O-D-glucopyranoside and Apigenin 7-O-D- (4′ caffeoyl) glucuronide has been reported to boost anti-HIV activity in T-cell line (H9) transfected with HIV-I and HIV-1 (IIIB) infected MT-4 cells, respectively, by providing significant integrase inhibitory activity. By blocking viral internal ribosome translational activity mediated by the entry site (IRES) and altering the c-Jun N-terminal kinase (JNK) pathway in cells, most viral infections can be prevented. In independent research, it was discovered that apigenin inhibits the cellular JNK pathway and prevents viral access to IRES, which is differently necessary for viral replication, limiting HFM disease caused by enterovirus or the Hand, Foot, and Mouth (HFM) virus (HFMD). On TNF-induced OM-10.1 cells, the anti-HIV effects of apigenin, along with associated flavonoids, are investigated. The chemical's ability to decrease HIV expression has resulted in a variety of treatment indices. Additionally, they concluded that flavonoid therapy did not prevent virus replication since the NF-κB pathway was not downregulated (32).

6.4. Ferulic acid

The family of phenolic acids, which contains ferulic acid ([E]-3-[4-hydroxy-3-methoxy-phenyl] Prop-2-enoic acid), is widely found in the plant (34). Secondary metabolites, known as phenolic acids, come in a variety of chemical and biological forms. Organic compounds with the additive can be separated into phenolic acids of unique nature and benzoic acid and cinnamic acid derivatives, depending on the amount of replacement of the hydroxyl and methoxy groups. The depside, which is made up of two or more phenolic acids, is an extra group. Ferulic acid is the most prevalent derivative of cinnamic acid, as well as vanillin, caffeic, p-coumaric, synapse, and syryte acids. Whole parsley, grapes, grains, spinach, rhubarb, and cereal seeds, primarily those foods that contain ferulic acid, most frequently include those made from wheat, oats, rye, and barley. The antioxidant activity of phenolic acids, particularly those derived from cinnamic acid, is one of the most significant functions. The amount of hydroxyl and methoxy groups connected to the phenyl ring has the biggest impact on this action (35–37). Ferulic acid is more easily absorbed by the body and stays in circulation for a longer period than other phenolic acids. Ferulic acid is thought to be a powerful antioxidant (37).

6.4.1 Antioxidant Activity of Ferulic acid

Ferulic acid shows high antioxidant qualities. It has good resonance stability due to the phenolic ring and can more readily receive the electron from a free radical. As a result, it directly scavenges free radicals. Additionally, ferulic acid effectively scavenges free radicals produced by hydrogen peroxide, superoxide, hydroxyl radicals, and nitrogen dioxide. Ferulic acid has significantly greater anti-nitric oxide than caffeic acid. In a Fenton reaction system, ferulic acid at a concentration of 250 mg/L also scavenged hydroxyl radicals almost entirely. Ferulic acid promotes the activity and functionality of the antioxidant enzymes that scavenge free radicals. Additionally, it prevents tissue enzymes from creating free radicals. Previous studies have revealed that cardiac superoxide dismutase, glutathione peroxidase (GPx), catalase (CAT), and mRNA expression were improved by ferulic acid and p-coumaric acid. Both diabetic rats and mice on a high-fat diet have increased antioxidant enzyme activity (38).

6.5. Caffeic acid

A significant phenolic molecule called numerous plant products, such as fruits, wine, olive oil, and coffee, contain caffeic acid (3,4-dihydroxy cinnamic acid), legumes, wine, and coffee. Numerous variations of caffeic acid have been discovered, including derivatives of sugar esters, organic esters, glycosides, and amides that are monomeric, dimeric, trimeric, and oligomeric. Caffeic acid is widely used as an antioxidant since it is mostly physiologically active. Its extra therapeutic benefits for treating microbial infections have also been the subject of several kinds of research and are widely known for its antithrombotic, antihypertensive, antidiabetic, anticancer, and anti-inflammatory effects. There are many applications of caffeine. However, some of them are limited by their drawbacks, including their insolubility in water. It is known that caffeic acid inhibits enzyme activity, alters membrane permeability, damages protein structure, and damages DNA as its principal antibacterial action against bacterial and fungal infections. Additionally, caffeine acts as a potential antiviral agent against several viruses, such as influenza, thrombocytopenia syndrome, and herpes simplex viruses. By concentrating on certain stages of the virus life cycle and blocking the virus from growing inside the host, most of the antiviral action has been uncovered (39).

7. PHARMACOLOGICAL ACTIVITIES

7.1. Traditional Uses

The plant is used to treat ulcers, wounds, fever, anemia, and heart problems. The decoction made from the root is used to treat diarrhea, and smaller amounts of extracts may be utilized as an antifungal agent. It is applied topically to treat skin issues, while the plant's decoction is orally taken to treat a wide range of maladies. Furthermore, it is believed to show potential as a therapy for hepatic amebiasis (40). This plant has conventionally utilized to treat high fever, stomach pains, rheumatoid arthritis, migraine headaches, insect bites, infertility, toothaches, and menstrual and labor difficulties during birth. The plant includes several beneficial chemicals, primarily SLs, flavonoid glycosides, and pinenes. It has several pharmacologic effects; additionally, it is thought to have anticancer, anti-inflammatory, cardiotonic, antispasmodic, emmenagogue, and worm enema properties (41).

7.2. Anti-inflammatory Activity

The biological reaction to potentially dangerous stimuli, such as bacteria, allergens, or an immune reaction, is referred to as inflammation (42). According to studies, giving mice carrageenan-induced paw edema through oral administration of *Parthenium* treated with acetic acid prevents them from writing (43). The following investigation on some parthenolide dosages revealed that these behaviors and reactions were consistent with doses (10, 20, 30, and 40 mg/kg) and had no impact on the mice's inducible sleep time or locomotor activity. Additionally, it did not affect the rats' body temperatures and did not alter the mice's regular life cycle (44).

7.3. Antifungal Activity

Different fungi are susceptible to the antifungal actions of *Parthenium*. *Parthenium* has a property that can be utilized to treat fungus-related illnesses in both people and animals. The SLs discovered in *P. hysterophorus L.* were found to be sensitive to dermatitis-related fungi and can be used to treat skin conditions. Different extracts of *P. hysterophorus L.* were investigated for their antifungal potential against human pathogenic fungi (45).

7.4. Antimicrobial Activity

A hydroalcoholic extract of *P. hysterophorus L.* effectively inhibited *Plasmodium falciparum in vitro* (46). *In vitro*, this plant showed Antiamoebic action against polygenic cultures and axenic cultures of *Entamoeba histolytica*, the causative agent of amoebiasis, comparable to the common medication metronidazole (47). Aqueous, methanol, and n-hexane extract strongly work against *Fusarium wilt*, a significant potato fungal disease that is caused by *Fusarium solani* (48). Hepatic amoebiasis is another potential application (49). Concerning it exhibits antibacterial, antifungal, and antiviral activities against *P. aeruginosa*, *E. coli*, and *Candida albicans*, respectively (50).

7.5. Antiamoebic Activity

Entamoeba histolytica axenic and polygenic cultures have been examined *in vitro* for the antiamoebic activities of parthenin from *P. hysterophorus L*. The cultivated organisms have been discovered to be acutely poisonous to Parthenin. Like metronidazole, Parthenin exhibits activity (51).

7.6. Thrombolytic Activity

P. hysterophorus L. extracts' ability to prevent H_2O_2-induced erythrocyte membrane damage in rat blood was tested. The antihemolytic function of several plant parts like leaf, stem, flower, and root extract ranged from 30% to 45%. The remaining test extract did not offer any shield against H_2O_2-induced erythrocyte membrane damage (52).

Streptokinase parthenolide and a few other metabolites were shown to be the inhibitors of human blood platelet function, and the crude *P. hysterophorus L.* methanolic extract shows strong thrombolytic activity in comparison to the standard thrombolytic medicines (53).

7.7. Anti-HIV Activity

P. hysterophorus L. leaf extract has antiviral action that targets the enzyme HIV reverse transcriptase. Reverse transcriptase for HIV inhibition kit was used in the experiment to determine the efficacy at 0.6 and 6.0 g/ml, two different concentrations. The extracts showed low to moderate inhibitory potential, indicating that the active chemical inhibiting reverse transcriptase may be found with further research and purification (54).

7.8. Anticancer Activity

According to a study, *P. hysterophorus L.* has anticancer properties. It was discovered that *P. hysterophorus L.* methanolic extract exhibits anticancer activity in host mice having transplantable lymphocytic leukemia. After injecting *Parthenium* extra in mice having cancer cells, the extract either totally cured them or prolonged their survival time (55). A SLs called Parthenolide is obtained from the Feverfew herb's leaves. It has an epoxide group and a ring of β-methylene-lactone that can interact with biological molecules' nucleophilic sites. As extensively reviewed, Parthenolide has been utilized as a natural remedy for numerous years due to its ability to reduce inflammation and prevent migraines. The anticancer potential of Parthenolide has received a lot of attention nowadays. Several preclinical in-vivo and in-vitro studies employing cancer cells have been conducted from solid tumors and hematological malignancies were conducted on Parthenolide and dimethylamino-parthenolide (DMAPT), a synthetic derivative of Parthenolide that is 1000 times more soluble in water (56).

7.9. Skeletal Muscle Relaxant Activity

The Rota-Rod method and traction test were used to determine the methanolic extract's activity from *P. hysterophorus L*. having the ability to relax skeletal muscle. Swiss Albino mice received oral doses of *P. hysterophorus L.* methanolic extract at 3 mg/kg and 6 mg/kg. At 30 minutes, the methanolic extract becomes highly significant in reducing the fall-off time (motor coordination). The traction test also has a notable muscular relaxant effect. Because of the existence of several chemical components in the extract, the results indicated that *P. hysterophorus L.* methanolic extract possesses skeletal muscle-relaxing properties (57).

7.10. Larvicidal Effect

Synthetic pesticides utilized to manage insects and their larvae are not an environmentally beneficial source of food method, of doing so because they are unsafe for human use, adversely impact the environment, are not biodegradable, and can be harmful to animals. It may result in biomagnification, which reduces biodiversity (58). Extracts from the roots and stems of *P. hysterophorus L.* are excellent at killing mosquito larvae, especially Aedes *aegyptib* (59). Chemical components separated from leaves have a significant impact on the lifespan and reproduction of adult *Lipaphis erysimi*. If *Parthenium* leaf extract was employed instead of anticholinesterase drugs like neostigmine, a novel depolarization neuromuscular junctional block was seen in rats (60).

7.11. Antioxidant Activity

ROS (Reactive Oxygen Species) are thought to affect three major biological macromolecules: proteins, DNA, and lipids. Polyunsaturated fatty acids may peroxide due to intermediates that are reactively created by OS. This, in turn, alters the lipid bilayer's flexibility and permeability in the membrane, which has a significant impact on the integrity of the cell. Numerous antioxidant enzymes and compounds are present in cells, preventing ROS from causing harm. Powerful antioxidants can stop the advancement of carcinogenesis because it is widely known that OS can lead to the initiation of cancer (52). After determining the active antioxidant components in *Parthenium*, a novel, strong natural antioxidant may be made commercially (61).

7.12. Antidiabetic Activity

When *Parthenium* was given to rat models of alloxan-induced diabetes, many animals lived without experiencing any adverse reaction or dying. The concentration of blood glucose comparatively decreased. In contrast, glibenclamide treatment in another group of rats demonstrated that the blood glucose level decreased by 30% or more on average rats over the same period, while it only decreased by 7% in *P. hysterophorus L.*-injected rats. Compared to the group who took glibenclamide treatment, the reduction is, however, less (62).

8. HARMFUL EFFECTS OF PARTHENIUM ON HUMAN HEALTH

Parthenium weed has a harmful influence on humans, both directly or indirectly, by affecting agriculture and livestock productivity. *Parthenium* weed is believed to affect up to 73% of individuals, with females being twice as susceptible as males (63). Asthma, hay fever, skin rashes, excessive water loss, skin peeling, edoema, photodermatitis, and irritation of the mouth and nose can all be caused by *Parthenium* roots (64). Anisic, chlorogenic, p-anisic, caffeic, and benzoic acids are some examples of some of the primary components found in the *Parthenium* and are extremely toxic to people (65). Hand weeding in *Parthenium*-infested areas can lead to skin disorders, and allergies to *Parthenium* may contribute to fever associated with malaria. Long-term contact with this plant can cause allergies, allergic rhinitis, dermatitis, dark patches, eyes burning and swelling, fever, and skin infections. *P. hysterophorus L.* produces severe papular erythematous, diarrhea, rashes, and shortness of breath (66). Respiratory symptoms typically begin with elevated temperature and breathing difficulties and develop into allergic bronchitis and asthma after 3-5 years of cumulative exposures (67). According to a survey conducted in Queensland, Australia, 10% of employees in *Parthenium*-infested regions experienced visible allergic reactions to the plant. Karim *et al*. have observed allergy reactions on the hands of farmers in *Parthenium* weed-infested districts of Malaysia. These are due to the presence of chemical allergens in the plant, such as ambrosin, coronopilin, parthenin, and tetraneurin-A (68). *P. hysterophorus L.* has several negative consequences, many of which are listed below:

8.1. Effect on the Environment: The aggressive invasion of *P. hysterophorus L.* can quickly dominate damaged habitats, agricultural fields, and ecological systems (69). It outcompetes native plant species, leading to decreased biodiversity and disrupting the environmental balance. The dense clumps it forms hinder the growth of other vegetation, resulting in the loss of ecosystems and wildlife habitat (70).

8.2. Harm to Agriculture: *P. hysterophorus L.* poses a threat to agricultural productivity. It competes with crops for water, nutrients, and sunlight, leading to reduced yields (5). Growers incur higher management costs due to the plant's rapid growth and abundant seed production. Additionally, allelopathic chemicals are released, which further inhibit the growth of neighbouring plants, reducing agricultural output (9, 71).

8.3. Health Hazards: *P. hysterophorus L.* has been linked to several health issues in both people and animals. The pollen of this plant can cause severe allergic reactions, such as asthma, hay fever, and skin rashes, in sensitive individuals (72). Continuous exposure to *Parthenium* pollen can lead to chronic respiratory disorders. Contact with the plant's sap can cause skin itching and contact dermatitis (73, 74).

8.4. Livestock and Wildlife Concerns: *P. hysterophorus L.* is harmful to both livestock and wildlife. Animals such as, cattle, and goats that consume the plant may experience various health issues, including rashes, respiratory troubles, issues with digestion, and possible mortality (75). The presence of *Parthenium* in grazing pastures reduces fodder availability, affecting the nutrition and productivity of animals (76, 77).

8.5. Economic Burden: The presence of *P. hysterophorus L.* has significant economic implications. Reduced crop yields and increased weed management costs lower agricultural productivity (78). Farmers, landowners, and governmental organizations may be burdened by the cost of the management and eradication activities for this invasive species (79).

P. hysterophorus L. is being managed and controlled using a variety of techniques, involving as physical elimination, topical herbicides, biological agents for control, and educational programs. To save the surroundings, agriculture, and human health, it is essential to halt the growth of this invasive weed and lessen its negative impacts.

9. CONCLUSION

During this period of rapid population growth in India, it is critical to utilize land wisely for agriculture and forestry. It is essential that we can make the most of every natural resource for improvement. Despite having several pharmacological activities, the *Parthenium* weed (*Parthenium hysterophorus L.*) is one of the most destructive invasive weeds, posing a threat to agroecosystems and natural ecosystems worldwide. *Parthenium* spreads quickly in India due to its fast growth and high seed production. The goal of regulating *Parthenium* should be to ensure that no hazardous substances are released into the environment. Several experts are searching for ways to regulate it by exploiting it for the sake of humankind and the environment. In India, an integrated management system for the control and eradication of *Parthenium* is being developed. We can effectively manage this plant if we have a thorough understanding of both its positive and detrimental effects.

10. DECLARATIONS

Ethics approval and consent to participate

Not Applicable.

Consent for publication

Not Applicable.

Availability of data and material

The review work has been carried out by us, and we assure you that it can be provided to you whenever required.

Competing interests

Not applicable.

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Authors' contributions

We have assured that all the authors have read and approved the manuscript. The authors confirm their contribution to the paper as follows:

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Analysis and interpretation of results: Sadique Hussain, Mudita Mishra, Swati Tyagi
Draft manuscript preparation: Sadique Hussain.
All the authors reviewed the results and approved the final version of the manuscript.

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