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The distribution, status and mitigation methods of *Parthenium hysterophorus* L. in Ethiopia: A review

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Abstract
Parthenium, an aggressive invasive weed, is believed to be a native to North and South America. Due to its allelopathic effect and adaptability to different environmental conditions, it is now distributed throughout the world including Ethiopia, where it was reported first in 1988, in the eastern and later in the north-eastern parts of the country. Some scholars believe that Parthenium came to Ethiopia together with the donated grain when the country was hit by famine. Othersopine that entered into the country during the Ethiopia and Somalia war in 1976/77 through military vehicles from Somalia. Still others also presume it has slipped into Ethiopia from the neighboring countries like Kenya. The weed aggressively invaded several rangelands in the country due to its allelopathic effect, capacity to produce copious amount of seeds and its ability to compete for resources to survive. Parthenium can affect the biodiversity, agriculture, human and animal health and the economic activities of society. Although several mitigation methods, mechanical, chemical, biological and utilization methods are used to control it, there is no single effective method, as each method suffers from limitations. Therefore, combination approach is suggested for an effective management.

Keywords: parthenium, allelopathy, invasive species, mitigation method, rangeland

Introduction
Invasive alien species are those introduced to a region outside their natural range of distribution by an intentional or unintentional human activity [1]. Invasive species could be plants, animals or microorganisms that are not native to the given specific ecosystem [2]. In areas where they spread, invasive species can destroy the natural pasture, displace the native trees, and reduce the grazing potential of rangelands [3] since they compete for the nutrients and hence reduce the productivity of croplands) [4]. Invasion is considered as the second largest threat to biodiversity, next to the habitat destruction [2]. *Parthenium hysterophorus* (henceforth referred to as Parthenium) is among the major invasive species worldwide including Ethiopia [5]. Parthenium, an aggressive invasive weed, is believed to be a native to Southern and Northern America [6]. It is now broadly spread to Asia, Australia and Africa [7]. It has spread through trade as a contaminant of grain and other crop products and via farm machineries [8].
Currently, Partenium is widely distributed and has become a problem in countries such as Australia, India, China, Kenya, West Indies and Ethiopia [9]. Parthenium was first reported from Ethiopia in 1988 at Dire dawa and Harerge of the eastern Ethiopia and subsequently near Desse, the north-eastern Ethiopia [10]. Both these are the major food-aid distribution centers and there is a strong evidence that Parthenium seeds were imported from the subtropical North America as a contaminant of food aid during the 1980s famine and got distributed with the grain [8]. Since its introduction, Parthenium has been spreading persistently in the agricultural lands, forests, poorly managed arable crop lands and rangelands, almost throughout Ethiopia [11]. In Alamataalone, about 10,000 hectares of land has been invaded by Parthenium [12]. It is also a health hazard to human and livestock [1].
Parthenium has caused adverse effects on food security and biodiversity in the eastern and southern Africa [6]. Its light seeds can travel long distances via wind, water and other agents [5]. The Parthenium infestation causes the yield loss up to 40% in several crops and reduces the forage production up to 90% in India [13]. Sorghum grain yield losses of 40-97% were also reported in Ethiopia inareas left unmanaged throughout the season [7]. Parthenium does not directly compete with crops; rather it releases allelopathic chemicals to the soil that affect various crops and other plants [14].

Parthenium is already posing a threat to crop production in Ethiopia [3] and its rapid spread would further aggravate the risk to the expansion and sustainable production of many crops [7]. Therefore, managing this aggressive invasive weed in Ethiopia is crucial to boost the agricultural productivity and prevent the ecosystem from being destroyed. This review aims to assess the current status of the weed in Ethiopia and discuss the appropriate methods for its control.

Biology of *Parthenium*

Parthenium, a member of the plant family Asteraceae, is an annual herb growing to a height of 1 to 1.5 meter [15]. It is popularly known as Santa-Maria, broom bush, carrot weed, congress weed, star weed and white top [16]. This pioneer species can invade the neglected as well as cultivated areas, grazing lands, roadsides, recreation areas, river banks and floodplains [17]. Parthenium can produce copious flowers throughout the year since it is insensitive to photoperiod and thermal regimes [18]. The weed is drought-tolerant and can grow in almost all soil types but prefers heavy clays [19]. It can also grow over a wide range of moisture and temperature conditions [6] but requires high soil moisture for its seed germination. Furthermore, it has the ability to utilize the opportunity of drought-prone period when the indigenous plants deteriorate and leave a bare ground cover [11].

Reasons for rapid spread of *Parthenium*

The successful world-wide spread of Parthenium is due mainly to its allelopathic effect, which enables it to compete effectively with the native species [20, 21]. Apart from this, the lightness of its seed, adaptability to a wide range of habitats, drought tolerance, and its ability to release toxic chemicals against other plants, allow it to colonize new areas quickly and extensively [5]. Furthermore, it can produce seeds too enormously, up to 25,000 per plant and more than 340 million seeds per hectare in comparison to nearly 120,000 native grass seeds [22]. Besides to that, it is capable of establishing three successive generations at the same site in a year under favorable temperature and moisture conditions [19]. Parthenium seeds have the ability to undergo dormancy and retain more than 50% seed viability after remaining in the soil for more than two years [15].

Distribution and status in Ethiopia

In Ethiopia, *Parthenium* was first observed around Dire Dawa area in 1980s. Since then it has spread to several parts of the country in alarming proportion, through vehicular traffic, wind, water and urban waste. From non-agricultural areas, it has now entered into agricultural fields [23]. As to the introduction of *Parthenium* to Ethiopia. some believe that it has entered the country with imported or donated grain [10, 24, 25], othersclaim that it came in duringthe Ethio-Somalia warin 1976-77 through military vehicles [26, 5], while still others held that it stepped into Ethiopia from the neighbor countries like Kenya and Somalia through wind, water, and other means in a normal way .However, a study conducted in Hararge, Jigjiga and Dire Dawa shows that it was introduced into the area during the Ethiopia and Somalia war by means of the army vehicles [8].

It is estimated that about 37,105 hectares of land in Amhara region is infested with *Parthenium* [3]. In much of the lowlands of Wello, it has become the most dominant weed and is abundantly found in Gojjam and Gondar with a potential to spread to agricultural districts of Metama and Humera [23]. The weed is also common in many districts of South, north, and central Tigray. It has invaded about 10,000 hectares of the land in the district Alamataof Tigray region alone [12].

Even though there is no actual survey report on the total area of land infested in the region, the weed is also a serious problem in Oromia region. Currently, it is spreading at an alarming rate in East Shewa, Arsi, Ziway and Bale [27]. Parthenium is thus the most abundant and troublesome weed species in small scale farms inthe eastern Ethiopia [8]. The significance of the Awash National Park as a tourism spot isalso being lost due to Parthenium [11]. The same document also reveals that it has caused a decline in stand density of herbaceous species by an average of 69% within a few years since its introduction into the Park. The weed is also spreading in a series of small to large jumps to Jimma, Awasaand Gambella [23]. According to [8], Parthenium was ranked as the most abundant and troublesome weed species in small-scale farms in the eastern Ethiopia. Generally, the distribution of Parthenium in Ethiopia is concentrated to the rift valley between Arba Minch and Dire Dawa, stretching up along the road from Addis Ababa to the Eritrean border [15].

Farmers' perception

Eighty percent of the farmers in Bharatpur of Rajasthan (India) selected for a survey noticed the presence of this weed nearby their farms [9]. Similarly, pastoralists in Jigjiga rangelands of Ethiopia have revealed that *Parthenium* affected the quality of animal products and their marketability [3]. Furthermore, a study conducted in Gedeo of Ethiopia showed that73% of the respondents heard about Parthenium weed and had some information about its impact [30]. According to [8], 90% of the farmers interviewed in the lowlands of eastern Ethiopia ranked *Parthenium*as the most important weed. Another study conducted in India brought out that around 80% of the farmers covered by their survey could recognize the morphology of *Parthenium* [16]. However, a survey conducted around Ambo of Ethiopia revealed that the awareness level of the farmers towards *Parthenium* was low [27].

Allelopathic properties

The allelo-chemicals released from Parthenium, viz. sesquiterpene lactones and phenolics, affect many plant species [19]. Leaves and inflorescence have a higher level of allelochemicals than the stem and roots [9]. These allelochemicals affect other plants either directly by leaching, root exudation and residue decay or indirectly, leading ultimately to the loss of native flora [23], as they inhibit the growth of pasture grasses, legumes, cereals, vegetables, other weeds and even trees [22].

Impact on agriculture

Parthenium can cause yield decline up to 40% in agricultural crops [31] and 90% in forage production [28], possibly through inhibitory effects on nitrogen-fixing bacteria, seed germination and seedling growth. With the increasing concentration of *Parthenium* extracts, the seed germination and growth of *Eragrostis* decreased significantly [29]. Another indirect effect of *Parthenium* is that it has a potential role as an alternative host for crop pests and may act as the secondary host of plant diseases [23].

Impact on biodiversity

Due to its allelopathic potential, replaces the dominant flora by suppressing the natural vegetation in a wide range of

habitats, and becomes a big threat to biodiversity [30]. Infestation of *Parthenium* weed can degrade the natural ecosystem because it has a very high invasive capacity and allelopathic properties, which can disrupt the natural ecosystem [31]. Furthermore, *Parthenium* adversely affects the composition and diversity of species, thereby resulting in the displacement and imbalance of the natural and agricultural systems [9]. Because of its ability to release the plant growth-inhibiting toxic chemicals, it has become a threat to Eastern Africa, one of the world's richest regions of biodiversity [32]. Very little or sometimes no other vegetation is seen in the *Parthenium*-dominated areas [33]. Generally, areas with a long history of grazing the cattle usually present a low resistance to invasion by the invasive species like Parthenium [34].

Impact on the soil seed bank

Parthenium decreases water-holding capacity of soil and water-infiltration rate and enhances the surface runoff [35]. According to [36], the cover percentage of grasses was decreased from 62.7% (at the sites without *Parthenium*) to 16.6% (at the most infested sites). Similarly, the dry biomass of Poaceae was significantly declined from 428.1 g m^{-2} to 30.0 g m^{-2}at these sites respectively. In a correlation analysis, [34] observed the Parthenium frequency to be negatively associated with the Shannon index as well as with the dry matter of the remaining species. A similar trend was found within the soil seed bank, with the species diversity being lower when the frequency of *Parthenium* was higher.

Impact on livestock and human health

According to [37], direct contact with Parthenium or its parts, living or dead, results in dermatitis in mankind and the presence of its pollen in the air causes diseases such as air-borne contact dermatitis. The weed could also cause itching eruptions on exposed parts of body, particularly the upper eyelids, neck, face, fronts of elbows and back of knees [23]. Furthermore, Parthenium spoils the milk and meat of animals on being consumed by animals as fodder, thereby reducing the value of animal product, a significant amount (10-50%) of the weed in the feed can even kill cattle and buffalo.

Fig 1: Types of symptoms commonly known Parthenium dermatitis; (a & b) air born dermatitis (c) chronic actinic dermatitis in female and (d) lesions over hand *source:* [22]

Mitigation methods

Manual method

Manual method is labor intensive and uneconomical [38], because Parthenium produces seeds throughout the year [18] and requires repeated removal [14]. It may be effective only in agro-ecosystems with space weed cover [38]. However, it is not economical for infested pastures and wastelands of wider areas [3]. Moreover, direct contact with the weed could cause dermatitis to susceptible individuals. However, Parthenium removal in Ethiopia heavily depends on hand weeding, mainly done by women and children [32].

Chemical method

Chemical control of Parthenium is preferred to eradicate the weed in time and at a proper time [22]. The plants should be treated before flowering and seed setting. However, a large-scale chemical control proves too expensive [39] and the continuous use of the same chemicals gives rise to pollution hazards in the ecosystem [13]. Thus, farmers find it difficult to afford the purchase of herbicides and their use is also unsafe for the health of living beings and the environment [7]. Therefore, weed management strategy needs to be shifted towards non-chemical methods.

Biological method

Managing the weed via biological means is relatively less expensive and pollution-risk free [15]. Besides, it is long lasting too [40]. Several insects and pathogens have been tried from time to time to control the *Parthenium* weed. Of these, the leaf-feeding beetle *Zygogramma bicolorata* and the stem-galling *Listronotus setosipennis* are believed to be suitable for being used in Ethiopia [15]. The host range testing performed on 24 non-target species in Ethiopia and 41 species in South Africa established that *Z. bicolorata* is safe for release against *Parthenium* [6]. Host testing also showed that *Z. bicolorata* is unlikely to move to a non-target host plant in Ethiopia [32]. This document further elaborates that, IPM CRSP (Integrated Pest Management Collaborative Research Support Program) in collaboration with its Ethiopian partner institutions seeks to rear, release and assess the impact of *Z. bicolorata* in relation to the control of the spreading population of *Parthenium* in Ethiopia. The planned release site is Wollenchitti in the Oromiya regional state.

Table 1: The options available for *Parthenium* management methods and their effectiveness in different countries.

Control options	Inputs	Effectiveness	Country
Mechanized control	1 to 2 additional sprays per cropping season	95%	Australia
Hand-weeding and deep ploughing	40-140 dayslabor	Effective in small, isolated areas, combine within integrated approach	India, Ethiopia, South Africa
Biological control	*Zygogramma bicolorata* and *Epiblema Strenuana*	Highly effective but influenced by weather (rainfall)	Australia
Preventing long-distance dispersal	Wash down facilities for vehicles, mandatory inspections, adoptions of codes of practice by agribusiness	Highly effective but costly	Australia

***Source*:** [40]

Generally, there is no single effective method used to control the spread of parthenium, as each method suffers from one or the other limitation such as high cost, inefficiency, impracticability, environmental safety and temporary relief [39]. Therefore, integrated Parthenium management approach, involving several methods, is necessary [33].

Fig 2: The leaf-feeding beetle *Zygogramma bicolorata* (left) and the stem boring weevil *Listronotus setosipennis* (right)

Utility of *Parthenium*

Allelo-chemicals or plant-derived chemicals offer a great promise for acting as effective pesticides as they are comparatively safer for the environment [1]. Over the past two decades, much work has been done on plant-derived compounds as they are environmentally safe alternatives to herbicides for weed control [41]. Several researchers have documented the importance of *Parthenium* as a potential source of herbicide [29, 42]. Pre-emergence as well as post-emergence applications of *Parthenium* extracts at higher concentrations proved more effective in decreasing the fresh biomass of other weeds [43]. However, extensive studies are required to explore its real potential against different summer and winter weeds [1]. On the other hand, parthenium can be used on a large scale for various applications [38]. Using the weed as an organic fertilizer is one of the applications suggested. According to [44], vermin-compost prepared from parthenium leaf encouraged the germination, growth and yield of ladies finger at all levels of the vermin-compost application and it also affects positively with concentration.

Conclusion

Parthenium, which often displaces the native plant species of the ecosystem and dominates the area alone, has become a global problem. The allelopathic chemicals released from this weed are the main factors responsible for its rigorous invasion. Since its introduction, Parthenium is adversely affecting the food security, and the human and animal health in Ethiopia, but the method of its control is confined to hand weeding involves a direct health risk. Different methods are being performed to control the weed in Ethiopia. Although not yet practiced in the country, biological control method is believed to be effective as it is environmentally friendly and comparatively cost-effective method. Tested in Ethiopia under quarantine, it has given promising results, which is good news to the Ethiopian agricultural sector in general and to the poor farmers in particular. However, since every single control method has its own limitations, combination approach is recommended to control *Parthenium*.

Reference

1. Masum S, Hasanuzzaman M, Ali M. Threats of *Parthenium hysterophorus* on agroecosystems and its management: a review. IJACS. 2013; 6(11):684-697.
2. Habtamu K. Invasive Alien Weed Species Impacts on Biodiversity and Socio-Economic Aspect in Ethiopia: A Review. IJSR, 2014; 4:1-7.
3. Shashie A. The impact of parthenium (*Parthenium hysterophorus*) on the range ecosystem dynamics of the Jijiga rangeland, Ethiopia. M.Sc. Thesis, Haramaya University, 2007.
4. Dubale A. Invasive Plants and Food Security: the case of *Prosopis Juliflora* in the Afar region of Ethiopia. FARM-Africa, 2008.
5. Taye T, Einhorn G, Gossmann M, Buttner C, Metz R. The potential of rust as a biological control of parthenium in Ethiopia, 2004.
6. Wondi M, Lorraine S, Andrew M, Kassahun Z, Lisanework N, Ibrahim F *et al*. Managing the weed, parthenium (*Parthenium hysterophorus* L.) in eastern and southern Africa, 2006.
7. Mulatu W, Berecha G, Tulu S. Allelopathic effects of an

invasive alien weed *Parthenium hysterophorus* L. compost on lettuce germination and growth, Jimma University, Ethiopia, 2009.
8. Tamado T, Milberg P. Weed flora in arable fields of eastern Ethiopia with emphasis on the occurrence of *Parthenium hysterophorus*. Weed Research. 2000; 40:507-521.
9. Karki D. Ecological and socio- economic impacts of *Parthenium hysterophorus* L. invasion in two urban areas in Nepal, PhD thesis, Tribhuvan University, Kathmandu, Nepal, 2009.
10. Seifu W. *Parthen Parthenium hysterophorus iumhysterophorus* L., a recently introduced noxious weed to Ethiopia. A preliminary reconnaissance survey report on Eastern Ethiopia. East Harerge, Ministry of Agriculture, Ethiopia, 1990.
11. Ayana E, Ensermu K, Teshome S. Impact of *Partheniumhystero Parthenium hysterophorus phorus* L. (Asteraceae) on Herbaceous Plant Biodiversity of Awash National Park (ANP), Ethiopia. J Soil Sci. Environ. Manage. 2011; 6(5):117-124.
12. Bezabih F, Araya T. Spread and statusof partheinium in Tigray Regional State at Woreda level. Tigray Bureau of Agriculture and Natural Resources, 2002.
13. Gnanavel I. *Par Parthenium hysterophorus thenium hysterophorus* L.: A major threat for natural and agro eco-systems in India, 2013.
14. Zelalem B, Temam H, Taye T. Distribution, incidence, severity and effect of the rust on *Parthenium hysterophorus* L. in Western Hararghe Zone, Ethiopia. Afr. J Plant Sci. 2012; 6:337-345.
15. Robert D. Composting of an invasive weed species *Parthenium hysterophorus* L. An agroecological perspective in the case of *Alamataworeda* in Tigray, Ethiopia, 2014.
16. Kapoor R. Awareness related survey of an invasive alien weed, *Parthenium hysterophorus* L. in Gautam Budh Nagar district, Uttar Pradesh, India. Journal of Agricultural Technology. 2012; 8:2-8.
17. Wiesner M, Taye T, Hoffmann A, Wilfried P, Buettner C, Mewis I *et al*. Impact of the Pan-Tropical weed *Parthenium hysterophorus* L. on human health inEthiopia. Utilisation of diversity in land use systems: Sustainable and organic approaches to meet human needs, Tropentag, Witzenhausen, 2007.
18. Rao R. Parthenium. A new for India. J Bom Na History Soc. 1956; 54:218-226.
19. Lalitha P, Shivani K, Rama R. Parthenium an economical tool to increase the agricultural productivity. Int. J LifeSc. Bt & Pharm. Res. 2012; 1:114-122.
20. Batish D, Singh H, Pandher J, Kohli R. Allelopathic interference of *Parthenium hysterophorus* residues in soil. Allelo. J. 2005; 15:267-273.
21. Rashid H, Khan M, Amin A, Nawab K, Hussain N, Bhowmik P. Effect of *Parthenium hysterophorus* L., root extracts on seed germination and growth of maize and barley. The Americas J Plant Sci. Biotech. 2008; 2(2):51-55.
22. Manpreet K, Neeraj K, Vikas K, Romika D. Effects and Management of *Parthenium hysterophorus*: A Weed of Global Significance. International Scholarly Research Notices, Review article, 2014.
23. Rezene F, MekashaCh, Mengistu H. Spread and Ecological Consequences of *Parthenium hysterophorus* in Ethiopia. Ethiopian Weed Science Society. 2005; 6:11-21.
24. Fasil R. The Biology and control of parthenium. pp. 1-6. In Rezene Fessehaie (ed) Proceeding of the 9th Annual Conference of the Ethiopian Weed Science Committee. Addis Ababa, Ethiopia, 1994.
25. Frew M, Solomon K, Mashilla D. Prevalence and distribution of *Parthenium hysterophorus* L. In Eastern Ethiopia. Arem. 1996; 1:19-26.
26. Kifle B, Taye T. Assessment of Weed Flora Composition in parthenium (*Parthenium hysterophorus* L.) Infested Area of East Shewa Zone, Ethiopia. MJMBR, 2015; 2:63-70.
27. Muhammad I, Teklu Gand Salma H. Potential threat of alien invasive species: *Parthenium hysterophorus* L. to subsistence agriculture in Ethiopia. Sarhad J Agric. 2014; 30:118-123.
28. Haroon K, Khan B, Gul H, Muhammad A. Socio-economic impacts of parthenium in peshawar valley, Pakistan. Pak. J Weed Sci. Res. 201; 19(3):275-293.
29. Tefera T. Allelopathic effects of *Parthenium hysterophorus* extracts on seed germination and seedling growth of *Eragrostistef*. J Agron. Crop Sci. 2002; 188:306-310
30. Talemos S, Abreham A, Fisseha M, Alemayehu B. Distribution status and the impact of parthenium weed at Gedeo Zone (Southern Ethiopia). Afr. J Agric. Res. 2013; 8(4): 386-397.
31. Anil K. *v* L. and its impact on living world. Indian J Sci. Res. 2014; 4(1):8-14.
32. EPA. (Ethiopian Environmental Protection Authority) Environmental Evaluation for the Release of the Biological Agent Zygogramma (*Zygogramma bicolorata* L.) to Control the invasive weed Parthenium (*Parthenium hysterophorus* L.) in Ethiopia, 2011.
33. Kifle, Taye. Assessment of Weed Flora Composition in Parthenium (*Parthenium hysterophorus* L.) Infested Area of East Shewa Zone, Ethiopia. Malysian journal of medical and biological research. 2015; 2(1):1-10.
34. Amalia B, Sheldon C, Steve W. Effect of parthenium weed on grazed plant communities during a period of concerted management. Pak. J Weed Sci. Res. 2012; 18:39-48.
35. Kasahun K, Tesfaye G. Evaluation of parthinium composting using vermi at Adami Tulu agricultural research center, Ethiopia. WJ Agri Rese. 2014; 3(7):144-149.
36. Shashie A, Lisanework N, Tamado T, Steve W. Impact of parthenium weed on the above-ground and soil seed bank communities of rangelands in Southeast Ethiopia. Int Res J Agri Sci and Soil Science. 2013; 3(7):262-274.
37. Veena B, Shivani M. Biological utilities of *Parthenium hysterophorus*. Journal of Applied and Natural Science. 2012; 4:137-143.
38. Anita S, Neeraj K, Anuja Sh, Manpreet K, Anita Y. Utility Potential of *Parthenium hysterophorus* for its Strategic Management. Advances in Agriculture. 2014, 2-16.
39. Mulugeta K. Biological assessment and farmers' perception on socioeconomic impact of *Parthenium hysterophorus* on native biodiversity in Kobo, Amhara Region. MSc. thesis, Addis Ababa University, 2006.
40. Wise R, Wilgen W, Hill M, Schulthess F, Tweddle D, Chabi O *et al*. The Economic Impact and Appropriate Management of Selected Invasive Alien Species on the African Continent. Report for Global Invasive Species

Programme, 2007.
41. Duke S, Dayan F, Aliota G, Rongani I. Chemicals form nature for weed management. Weed Sci. 2002; 50:138-151.
42. Stephen W, Sowerby M. Allelopathic potential of the weed, *Parthenium hysterophorus* L., in Australia. Plant Protection. 1996; 11:20-23.
43. Marwat K, Khan M, Nawaz A, Amin A. *Parthenium hysterophorus* L. a potential source of bioherbicide. Pak. J Bot. 2008; 40(5):1933-1942.
44. Naseer H, Tasneem A, Shahid A. Detoxification of parthenium (*Parthenium hysterophorus*) and its metamorphosis into an organic fertilizer and bio-pesticide. *Bioresour*. Bioprocess. 2017; 4:26.