International Journal of Science and Research Archive

eISSN: 2582-8185

Cross Ref DOI: 10.30574/ijsra

Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

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Treatment of Cestoda tapeworms using *Peganum harmala:* Review article

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International Journal of Science and Research Archive, 2025, 14(01), 1663-1670

Publication history: Received on 03 December 2024; revised on 12 January 2025; accepted on 14 January 2025

Article DOI: https://doi.org/10.30574/ijsra.2025.14.1.0126

Abstract

The human intestine is home to parasites called tapeworms. The term "tapeworm infection" describes this ailment. A larval cyst is the term for the young, dormant tapeworm. It is not limited to the intestine; it can also reside in other body areas. This illness is called cysticercosis or larval cyst infection. The symptoms of intestinal tapeworms are typically modest. Moderate to severe symptoms include diarrhea and stomach pain. Larval cysts can cause serious illness if they form in the brain, liver, lungs, heart, or eyes. Tapeworm infections can be treated with anti-parasitic medications, and larval cyst infections can be treated with anti-parasitic medications or surgically removing the cyst. Herbs and medicinal plants, such as *Peganum harmala*, which has safe and effective therapeutic capabilities without causing severe adverse effects to the human body and intestines, can be used as an alternative to chemical pharmaceuticals and to treat symptoms. Traditional medicines have been made from this well-known plant's seeds, bark, and root. *P. harmala* and its active alkaloids, harmine and harmaline, in particular, have shown a number of pharmacological and therapeutic benefits in recent years. According to analytical analyses of its chemical makeup, the most significant components of the plant are beta-carboline alkaloids, which include harmalol, harmaline, and harmine. Among these naturally occurring alkaloids, harmine has been investigated the most. These beta-carbolines are found in various other plants outside P. harmala, including Banisteria caapi, and are used to treat various illnesses.

Keywords: *Peganum harmala*; Tapeworm infection; Antiparasitic; Treatments; Medical plants.

1. Introduction

Worm infection is a common health condition, as it is highly contagious and easily transmitted, especially among members of the same family. Despite the inconvenience and pain caused by worm infection, it is easy to treat when adhering to the prescribed doses prescribed by the doctor and adhering to general and personal hygiene measures. Many worms infect humans, and there are many different ways to treat worms, which depend on the type of worms and the age group that needs treatment, including medicinal, herbal and natural [1].

The scarcity of anthelmintic medications, along with their continued use, will undoubtedly result in anthelmintic drug resistance [2]. One example of how anthelmintic resistance may spread in people is the resistance to anthelmintic drugs in veterinary species [3]. Eggs from human faeces have been found to contain mutations linked to benzimidazole resistance [4]. New anthelmintic medications are thus required, and plants used in traditional medicine to treat parasitic helminths may offer intriguing candidates. The WHO's designation of 2011–2020 as the Second Decade of Traditional Medicine and the creation of the WHO Traditional Medicine Strategy 2014–2023 further reinforced the importance of traditional medicine in health systems. In order to diagnose, prevent, or eradicate physical, mental, and social disorders, traditional medicine is crucial. The use of traditional medicine has been and continues to be a major factor in the provision of primary healthcare throughout Africa and the Diaspora. [5,6].

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One of traditional medicine's most commonly used herbal remedies is P. harmala. Many African, European, Central, East, and North Asian nations use it as a medical herb, particularly those in the Arabian Gulf region, including Saudi Arabia, and the neighbouring nations, including Iran, Pakistan, and India. [1]. *P. harmala* belongs to the *Zygophyllaceae* family, which includes approximately 25 genera. There are more than 250 species, and because of the bitter taste of *P. harmala* and its pungent smell that repels most grazing animals, this plant is not used for grazing, as all grazing animals are sensitive to the toxicity of *P. harmala* [7].

P. harmala has long been used to eliminate worms and treat stomach and intestinal pain. In Yemen, it is used as a drink to treat chronic malaria after being mixed with tamarind. In Turkey, it is a dry capsule that treats colic and expels intestinal worms. *P. harmala* is also burned after mixing with some substances for inhalation to induce sneezing or to purify the air and numb the nerves [8]. This article determined the anthelminthic biological activity of medicinal plants, including P. harmala. It also documented the traditional medical knowledge related to widespread helminth diseases.

2. Main Text

2.1. Tapeworms

Tapeworms resemble ribbons or lace and are long, flatworms. The types of tapeworms are numerous. They range from 15 feet (4.5 m) to over 30 feet (9 m). Fish and other animals' flesh is home to several tapeworm species. Humans can contract the disease when they consume raw food from animals with tapeworms in their meat. In the intestines, the tapeworms subsequently develop. Physicians look for tapeworm eggs in stool. The majority of the time, tapeworms are killed by medications. [9]

3. Diagnosis of tapeworms

3.1. Stool Microscopy

Stool sample analysis. A specialist often diagnoses tapeworm infection by examining stool samples for tapeworm eggs or fragments [9].

3.2. Blood tests

Blood tests can sometimes reveal antibodies to tapeworms, indicating infection [9].

3.3. Imaging

Imaging tests. In severe cases, imaging tests such as X-rays, CT scans or MRI may be used to identify cysts or other complications [9].

4. Symptoms of tapeworm infection

Symptoms depend primarily on where in the body the infection occursThere may be no symptoms associated with intestinal tapeworms. The quantity of tapeworms affects how severe the symptoms are, and each case has a different set of symptoms. Some symptoms are more likely to occur with certain types of tapeworms. Symptoms may include stomach upset or nausea, stomach cramps or pain, lack of desire to eat, weight loss, diarrhea, loose stools, gas, hunger pains, and cravings for salty foods [10].

5. Ways to treat worms for adults and children

5.1. Medications

Anti-parasitic drugs, such as praziquantel or albendazole, are usually prescribed to eliminate tapeworms. These drugs work either by killing the tapeworm or by causing it to separate from the intestinal wall so that it can be expelled from the body. [10].

6. Biological Characteristics of P. harmal

Often referred to as the "smelly ancient flower," *P. harmala* is a glabrous perennial herb that grows to a height of 30 to 70 cm. It features upright or spreading stems with many branches branching from the base and multiple roots up to 2 cm thick. It has oval, alternating leaves with three to five lanceolate-striate lobes that are 1.5 to 3 mm broad and 1 to 3.5 cm long [11]. Figure 1 depicts the morphology of P. harmala.

Figure 1 *P. harmala* (A) plant; (B) flower; (C) ripe fruits; (D) seeds [7]

The *P.harmala* plant, a staple of herbal medicine in many countries, is renowned for its medicinal properties. It contains alkaloids of the beta-carboline type (B-Carbolines), the active medicinal substances in the plant, which make up (2-7)% of the dry seeds. The biological and medical effectiveness of the *P. harmala* plant is primarily attributed to these alkaloids, especially the indolic alkaloids of Harmal such as harmaline, harmine, harmalol, and peganine. Indolic compounds, which include more than (1400) different compounds, have functional functions used in various medical fields [12].

7. Main Components of *P. harmala*

The inhibitory effects of *P. harmala's* total alkaloids were investigated as early as 1900. Researchers have examined *P. harmala's* pharmacological, chemical, and biological properties for almost a century. *P. harmala* has many chemicals [6,13], some thoroughly documented in 2017 [5]. Ninety-seven alkaloids, 24 flavonoids, ten triterpenoids, three anthraquinones, two phenylpropanoids, 18 carbohydrates, 17 amino acids, 99 volatile oils, 26 fatty acids, three sterols, one vitamin, one protein, one carotene, and six other trace elements are among the more than 308 chemicals that have been identified from *P. harmala*. The most abundant of these substances are β-carboline alkaloids (βCs). Up to 10% of seeds contain alkaloids, followed by roots, while leaves have the least amount. A few novel compounds have been discovered recently, but the primary ones include harmine, harmaline, harmalol, harmane, and harmol[7].

An investigation on the chemical makeup of *P. harmala* seeds was carried out in 2017 by Wang et al. [12]. Nine chemicals were obtained by extracting the *P. harmala* seeds using ethanol reflux, concentrating the extract, adjusting the pH, and separating it using a silica gel column. Among these, the uncommon carboline-vasicinone hybrid alkaloid enantiomers (−)-peharmaline A (1) (Figure 2) and (+)-peharmaline A (2) (Figure 2) have an unidentified hybrid dimer system.

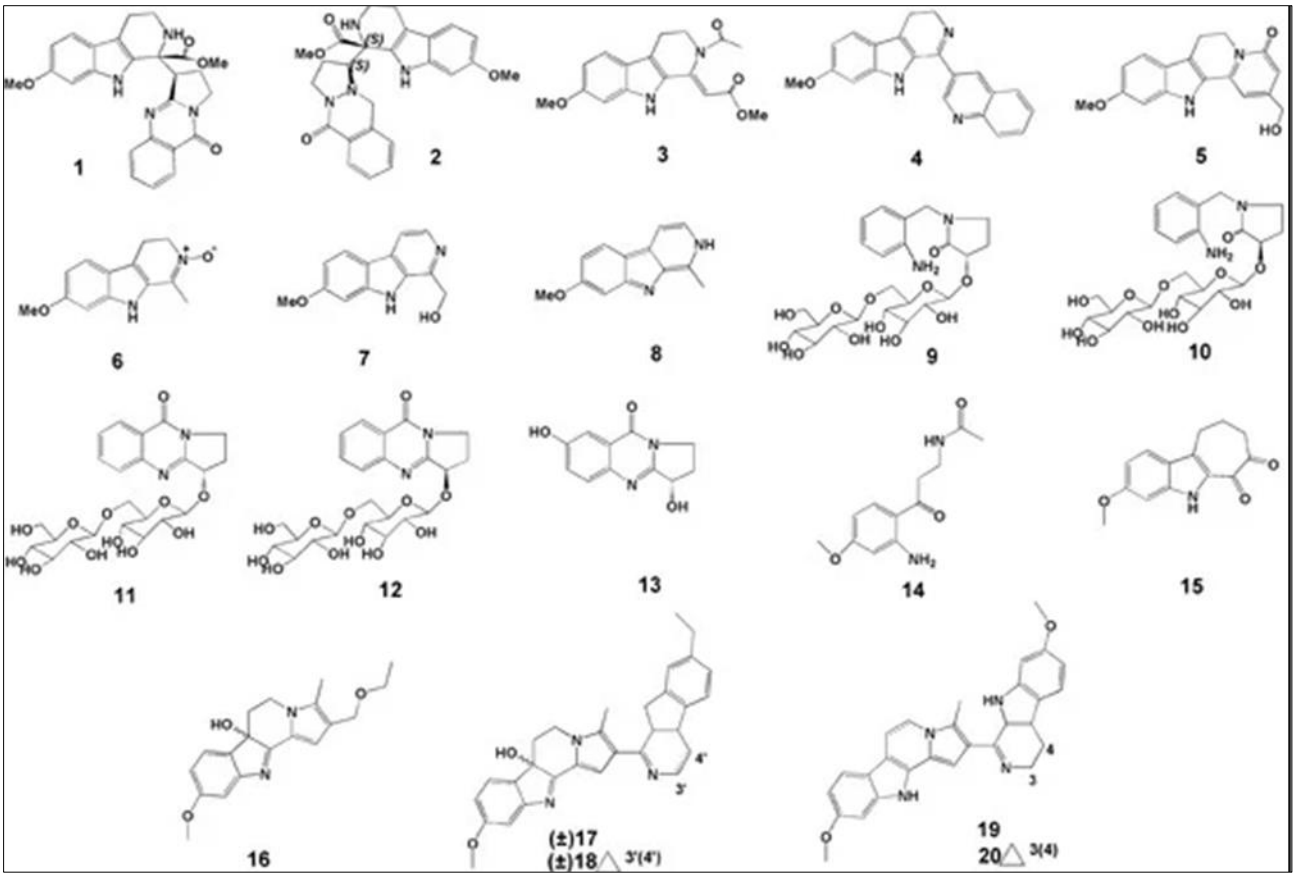

Figure 2 Structures of the twenty new compounds from *P. harmala* [7]

8. Antiparasitic Activity

It has been demonstrated that *P. harmala* possesses strong anti-parasitic properties. Using a hamster model, Lasa et al. [14], investigated the antileishmanial properties of several *harmala* varieties. Free liposome, vesicle, and nano-articular *harmala* decreased the splenic parasite load by approximately 40%, 60%, 70%, and 80%, respectively. Harmine disrupted the cell division stage, according to a cell cycle analysis study employing flow cytometry and confocal microscopy, which demonstrated that non-specific membrane damage was the cause of cell death.

Mirzaei et al. [15] administered an extract of *P. harmala's* aerial parts at a rate of 5 mg/kg for five days to 50 cattle naturally infected with Theileria annulata. Thirty-nine cattle's symptoms and parasites vanished after roughly 15 ± 3 days. The rate of recovery was 78%. T. annulata schizonts were not seen in lymph node biopsy smears.

Four alkaloids (harmine, harmaline, vasicinone, and deoxyvasicinone) from *P. harmala* seed extract were tested for their anti-P. falciparum properties by Astulla et al. [16]. They discovered that harmine (IC50 value of 8.0 µg/mL) and harmaline (IC50 value of 25.1 µg/mL) moderately inhibited P. falciparumin vitro. The protozoa were not inhibited by vasicinone or deoxyvasicinone (IC50 > 10 µg/mL). Tetrahydroharman and harman were observed to decrease THP1 cells in the S phase of the cell cycle in human monocyte toxicity experiments, likely due to their inhibition of total protein synthesis [16].

After infecting 5- to 6-month-old lambs with T. hirci, Derakhshanfar et al. [17] administered 5 mg/kg of *P. harmala* aerial component extracts to the infected animals. Microscopic analysis revealed that the parasites vanished after nine days, and the lambs in the treatment group's lymph nodes and peripheral blood smears exhibited an average rectal temperature. These findings demonstrated the effectiveness of *P. harmala* extracts in repairing T. hirci-induced tissue damage in sheep [18].

Tanweer et al. employed *P. harmala* seed methanol extract [19], which was demonstrated to have strong anticoccidial qualities.

Shafiq et al. [20] examined the acaricidal effects of methanol extracts of three plants (Curcuma longa rhizome, Citrullus colocynthis fruit, and *P. harmala* seed) against R. microplus using a modified larval immersion method (syringe method). After six days, at a dose of 50 mg/mL, it was found that the activity of all three extracts peaked. After 3.125 mg/mL, *P. harmala* by itself had the lowest acaricidal efficacy after 24 hours. Based on these results, it was proposed that farms may utilise this readily available and affordable plant combination composition.

Tabari et al. [21] used the wet mounting method to collect Trichomonas gallinae from pigeons. They then cultured the organism in trypsin/yeast extract/maltose (TYM) medium on multiwell plates containing *P. harmala* alkaloid extract, metronidazole, harmine, and harmaline at different concentrations. A pigeon experimentally infected with T. gallinae was given metronidazole, harmine, harmaline, and the alkaloid extract. After receiving the alkaloids for three days, the infected pigeons recovered utterly; however, metronidazole did not lead to complete recovery.

The seed extract from *P. harmala* has demonstrated sound inhibitory effects on infections and suppression of some protozoa (T. pigeon), sometimes outperforming a positive control medication. Its action method has yet to be well studied, and it is unclear what makes it effective. Thus, more research utilizing contemporary molecular biology and other techniques is required [7].

9. Use of *Peganum harmala* in medicine

P. harmala has been used in ancient Arab medicine recipes to treat joint and colon pain, asthma, chest diseases, epilepsy, headaches and other diseases. Seeds have many medicinal activities and are used as antispasmodic and vasodilator substances. *P. harmala* seed powder is used as an anti-helminthic treatment and to kill protozoa. The seeds contain red gum that is used as an anesthetic and a vermifuge for tapeworms. seeds also treat asthma, jaundice, chronic malaria and chest crises. They are a diuretic and antipyretic. Oil is extracted from the seeds to treat eyes and skin diseases such as visceral leishmaniasis. *P. harmala* is an abortifacient and antibacterial agent with bactericidal activity that acts on the cell wall and is fungicidal. It is used to treat mental illnesses [22]. It also has anti-inflammatory effects, is anti-tumor, anti-cough, anti-allergic, and analgesic for eczema. The seeds can remarkably activate phagocytic cells and stimulate the ovaries. It is used to lower blood pressure, hypotensive, and as an emetic agent. In addition, the smoke of *P. harmala* seeds is used as incense to eliminate epidemics and as a narcotic sedative [23,24]. In many studies that addressed the harmful effects of *P. harmala*, it was found that excessive use causes the appearance of disorders in the nervous system, such as symptoms of tremors and shaking resulting from the effect of the alkaloids present in the plant, especially harmaline, whose effects are similar to the effects of other alkaloids such as morphine and cocaine, as consuming (3) grams of seeds inhibits the enzymes acetylcholine esterase and monoamine oxidase, which play an essential role in transmitting nerve impulses. In Tunisia, about 56 medical cases were recorded on patients to know the toxic effects of *P. harmala* from 1983 to 1998, where the ratio of men to women aged 26 years was 1/2, in addition to the occurrence of neurological effects of *P. harmala* at a rate of 91% and intestinal and gastric effects at 73%, while the percentage of its effect on the heart and vessels was 18% [25]. As for the toxic effect of *P. harmala* on rabbits, young camels, monkeys, sheep and horses leads to poisoning and congestion in the heart, lungs, kidneys, stomach and intestines, and bleeding in the liver [26]. Today, *harmal* is considered one of the most promising plants and the most attractive to scientists in the field of pharmaceutical manufacturing, as the importance of the plant began to appear in 1920 in the United States of America, especially after more in-depth studies were conducted, to know the pharmacological and toxic effects of many extracts and components of this plant [27].

To prepare *P. harmala* seed powder, crush the seeds until they become powder and mix them with olive oil, a spoonful of apple cider vinegar, and white vinegar. Take a spoonful of the mixture every morning before eating daily. You will notice the worms being expelled in the stool at the beginning of treatment. [28]. This demonstrates the effectiveness of these extracts as a treatment and follows more research on all plant active substances [29].

10. Conclusion

Intestinal tapeworm infection and the severe damage it causes to the intestines, such as ulcers, erosion, intestinal inflammation, and a malfunction in the digestive enzymes that affect the physiology of the digestive system, which reduces the digestion and absorption of nutrients and a deficiency in nutrients and vitamins, which causes anemia, body thinness, and other side effects in humans of all ages. Intestinal tapeworm infection may treat the infected person with medical drugs or alternative treatment, including good herbs, such as the plant. This is an excellent example of this and has many uses in alternative medicine to cure many human diseases.

P. harmala is found all over the world and is abundant in resources. It has about 2,000 years of therapeutic history. Its successful use in treating and preventing human, animal, and plant diseases can be attributed to its historical use in disinfectants and mosquito control. In recent years, epidemics have emerged as the most significant danger to plant quality and human health. Humans are seriously threatened by drug resistance and the introduction and variety of novel diseases. Effective medications are, therefore, desperately needed to reverse this circumstance. *P. harmala* extract, harmine, and other βCs inhibit a wide range of bacteria. Effective medications are, therefore, desperately needed to reverse this circumstance. *P. harmala* extract, harmine, and other βCs inhibit a wide range of bacteria. Therefore, *P. harmala* is a possible source of natural and safe antiparasitic medications, mainly when viruses threaten human safety.

Numerous compounds underlie its broad-spectrum antiparasitic action. At least 308 chemical compounds, including alkaloids, flavonoids, triterpenoids, anthraquinones, phenylpropanoids, carbohydrates, amino acids, volatile oils, sterols, vitamins, proteins, carotenoids, and trace elements, have been extracted and identified from *P. harmala*. Alkaloids have demonstrated superior antiparasitic activity in tests. However, novel compounds have been found in *P. harmala* extracts because of the variety of secondary metabolites found in plants and technological advancements. More research is required to determine these novel chemicals' antiparasitic properties. Using the chemicals in *P. harmala* as antiparasitic scaffolding to create effective broad-spectrum antiparasitic medications would be a worthwhile research target. According to recent research, it possesses a wide range of biological actions and hundreds of different chemicals. These findings indicate that *P. harmala* has a promising future as a natural source of next-generation medications. They also set the stage for additional research into its therapeutic mechanisms to uncover the connections between *P.harmala's* chemical constituents, biological activities, and clinical applications

Compliance with ethical standards

Acknowledgments

The authors would like to express their great appreciation and gratitude to Department of Biology, College of Education for Pure Sciences, University of Kirkuk, Iraq.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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