Chapter 39

Use of Peganum harmala in Veterinary Medicine

Shafique A¹, Shakoor MW², Khan JM³, Ismail A⁴, SA Baloch⁵, Islam AM⁶, Riaz M⁷, Majeed S⁸, Gulshan MZ⁹ and Ayesha Faiz¹⁰

¹Department of Clinical Medicine and Surgery, University of Agriculture Faisalabad, Pakistan

²University of Veterinary and Animal Sciences, Lahore, Pakistan

³Department of Chemistry, Abbottabad University of Science and Technology, Abbottabad, Pakistan

⁴ Department of Plant Breeding and Genetics, University of Agriculture Faisalabad, Pakistan

⁵Lasbela University of Agriculture Water and Marine Sciences, Balochistan, Pakistan

⁶Department of Livestock Services (DLS), Ministry of Fisheries and Livestock (MOFL), 1215, Bangladesh and Research Assistant (RA), Laboratory of Veterinary Laboratory Medicine, College of Veterinary Medicine, Chungbuk National

University (CBNU), Cheongju 28644, South Korea.

⁷Riphah International University Lahore, Pakistan

8Chungbuk National University, Korea

9Bahauddin Zakaria University Multan, Pakistan

10Department of Botany, University of Agriculture Faisalabad, Pakistan

*Corresponding author: drasyiashafique@gmail.com

ABSTRACT

Peganum harmala is known by different names such as Syrian rue. This plant has flowers and it is grown in many regions throughout the world. The seeds of this plant have essentially hallucinogenic and hypothermic properties. Functions of this plant's extract against the pain are very well understood. We can use the aqueous extract of *P. harmala* to increase the growth rate in rabbits. So, we isolate the *E. coli* bacteria from horses and use *P. harmaline* as an antibacterial drug. Different infectious diseases in wild-fish cause high number of deaths. *P. harmala* controls many bacterial diseases in aquaculture. It has been widely used against round worms of animals. This plant is used in almost all disorders of animals. *P. harmala* is a multipurpose, traditional medicinal plant that has very good impact on some viruses. The extract of this plant causes many reproductive changes such as: prolonged diestrus phase. The extract of this plant causes decrease in the number of litter size.

KEYWORDS	Received: 18-May-2024	CLENTIFIC ALE	A Publication of
Peganum harmala, Medicinal plant, Bacterial diseases,	Revised: 13-Jul-2024		Unique Scientific
Wild-fish, Veterinary medicine	Accepted: 09-Aug-2024		Publishers
	1 5		

Cite this Article as: Shafique A, Shakoor MW, Khan JM, Ismail A, SA Baloch, Islam AM, Riaz M, Majeed S, Gulshan MZ and Ayesha Faiz, 2024. Use of *Peganum harmala* in veterinary medicine. In: Abbas RZ, Khan AMA, Qamar W, Arshad J and Mehnaz S (eds), Complementary and Alternative Medicine: Botanicals/Homeopathy/Herbal Medicine. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 333-338. <u>https://doi.org/10.47278/book.CAM/2024.162</u>

INTRODUCTION

Peganum harmala is known by different names in all countries of the world. This plant has its different parts including flowers as it is present in different regions of the world. Abortion is common in animals that ingest this plant during dry year. The fruits of *P. harmala* are used as antiseptic in different types of medicine. *P. harmala* can be used against asthma, colic and jaundice. Its seeds are well known that possess essentially hallucinogenic and hypothermic properties. The root extract is effective against *Listeria* than other extracts such as seed extract (Asgarpanah and Ramezanloo, 2012).

This multi-purpose plant is widely used in the treatment of diseases at home. We can use the aqueous extract of *P. harmala* to increase the growth rate in rabbits (Ahmad et al., 2013). This plant is present in semi-arid areas of Pakistan (Mamadalieva et al., 2022). To relief from pain, *P. harmala* liquid extract from seeds is used to treat different animal diseases (Farouk et al., 2009).

Use of Peganum harmala against Various Infections

One of the most important diseases is *E. coli* infection that affects many animals and causes diarrhea, dysentery and urinary tract problems depending upon the type of *E. coli*. Most of the studies have been done about the factors responsible for *E. coli* problems and the process by which bacterial different forms cause diarrhea in humans and calves. Now a day, bacteria become resistant against many kinds of drugs. Alkaloids of *P. harmaline* are very effective than other antimicrobials. It is very effective in different diseases. *E. coli* has been isolated in horses and effects of that plant both in

lab and on live animals are effective (Hamzah, 2020).

WHO Reviews about Peganum harmala?

World Health Organization says that *P. harmala* is a source of medicine for human beings. By using plants or herbs we can reduce the cost of medicines. One of the most important factors related to chemical drugs problem is high cost. These factors can reduce the therapeutic effects of drugs containing chemicals. All that because there is resistance of drugs against the pathogens. There are different types of plants used for making medicines that are: the olive and *P. harmala* for the treatment of different diseases. *P. harmala* is used against inflammation, pain relieving agent and it has been used to treat many disorders including depression. It is used against drug-resistant bacteria and has antibacterial activity and in India it is used in treatment of prolapse, syphilis, fever, hysteria and neuralgia. It is effective against protozoa and stops abortions. The alkaloids that are active in the seeds of this plant are some inhibitory enzymes. The *P. harmala* extract is used against fungal infections and different microbes. Tree of olive or its shrub is green and the shaft is purple when ripe while this plant is green in color. It helps to relax blood vessels and it also has antioxidant properties (Bahmani et al., 2013).

Peganum harmala use against Bacterial and Fungal Infections

There are different bacterial infections caused by many drug resistant bacteria. It is very big problem now a day. So, we are discovering new compounds that have good and better activity. This plant helps in healing of wounds caused by bacteria and fungi. There are different pharmacological activities of this plant i.e., it is effective against insects, leishmanial infections, spasms, leukemia, hypoglycemia and has immune system modulation. This plant has many effects; against bacteria, fungi and viruses. Extract of seeds is very effective. It is effective against *E. coli* infections and *Acinetobacter baumannii* (Javadian et al., 2016). The methanol extract from different parts of *P. harmala* has been used against some most important human pathogenic bacteria (Darabpouretal, 2011).

Peganum harmala use in Fish

Different infectious diseases in wild-fish cause high number of deaths. However, due to continuous use of antibiotics, drug resistance has been developed that cause decrease in the efficiency of the drugs. *P. harmala* is a medicinal plant that plays important role in drug discovery. It has been used in some rainbow trout affected by pathogenic bacteria (Akbary et al., 2015).

Peganum harmala use in Different Regions of Pakistan

Microbiologists and phytochemists think that synthetic pharmaceutical products to control infectious diseases in animals are very beneficial. As this herbal remedy can be used in traditional medicine, it provides information regarding the discovery of new drugs that are helpful to decrease the resistance caused by antimicrobials. We can derive medicines from this plant. Traditional medicine recipes are important in providing health and care benefits to under-developed countries and also in rural areas of the world. This plant changes in form due to unfavorable circumstances during the time of reaching from a buyer to a consumer. Different medicinal plants are available in all areas and are also available in indigenous areas. This plant has different antimicrobial activities against bacterial pathogens showing antimicrobial resistance. Methanol extracts of this plant have antibacterial activity (Ali et al., 2011).

This plant has some bio-active compounds that can be used against various diseases. But its excess use can cause serious effects on liver, kidney and brain. So, it can be used for various symptoms of various diseases (Liu et al., 2022).

Peganum harmala use against Nematodes

P. harmala has been widely used against round worms of animals. As already discussed, its excessive use can affect different body systems. In chicks, it causes congestion and hemorrhage by its leaves. In result, it causes anemia and different changes in total protein and other serum constituents (Qazan, 2009).

Gastrointestinal nematodes, in small ruminants causes decrease in production. By using this plant by-products, the round worms can be treated. Use of this compound, is very beneficial for animals. Harmaline and piperine alkaloids anthelmintic activity is very well known. Within lab, the effect of alkaloids prepared by this plant extract against the nematodes is good. The cytotoxicity of these compounds has been checked by in Vero cells (da Silva, 2021).

Peganum harmala use against Viral Diseases

P. harmala is a multipurpose, traditional medicinal plant that has different effects on some viruses. As already discussed, those different parts of this plant contain an extract, effective against viruses if compared with other such compounds. If we perform the experiments by using such extracts of this plant then many animals and human diseases can be treated. *P. harmala* is used against many important viral infections (Dashti, 2020).

Peganum harmala use against Influenza

Influenza is an important respiratory disease caused by virus. Virus circulates through different parts of the world. In hospitals, many deaths occur due to high-risk in all age groups. The mechanism by which the virus completes process of multiplication, is inhibited through inhibition of its different genetic materials. Influenza virus source in humans and animals has the ability to change the pathogenic type within their new hosts. For viral

infections, annual vaccination is done to prevent influenza infections and many drugs against viral infections have multiple benefits in term of treatment and prevention. The influenza A type virus is treated by using seeds of this plant, which inactivate the enzymes important for further spread of viruses. Influenza A type virus has resistance against many medicines. To treat resistant forms, it is necessary to make the new and very effective medicines against influenza. Extract of this plant is used as an alternative of the antivirals. *P. harmala* is used as a remedy in herbal medicines. We can perform different actions by using extracts along with antiviral drugs. So, this herbal medicine has been used as therapeutic agent and has very good results (Moradi et al., 2017).

Peganum harmala Effects against Different Infections

P. harmala seeds can be used against fungi, parasites, bacteria and insects (Nenaah, 2010) This traditional medicine has very good effects on animal health. For example, in Middle East, *P. harmala* has been used against infections due to fungus (Mirzaiedehaghi, 2006). The extracts of *P. harmala* have good effects to cause inhibition of the growth in different types of fungus which causes serious problems in animals (Khaliq *et al.*, 2009). Different products prepared from *P. harmala* are used in homeopathic medicine in different countries for leishmanial infections (Samoylenko *et al.*, 2010).

Powder of seeds and different extracts are used for making medicines against cestodes infections in animals as well as humans (Branch, 2012). Different effects of *P. harmala* against different forms of leishmaniasis are authentic in labs and on live animals (Herraiz and Guillén, 2011). Even if harmaline is used against this infection, it shows strong toxicity for the developing forms of this parasite that resides inside the blood cells. The mechanism to stop the growth of enzymes in parasites by this plant is very effective. Activity of different enzymes this plant against leishmanial infections is good (Frison et al., 2008).

Extract of this plant is as effective as enzymes to treat parasitic infections. *P. harmala* extract cause reduction in the size of lesions and with the total number of the parasites in different forms of this disease (Pieroni *et al.*, 2005). *P. harmala* extract cause decrease in the size of lesions and with the total number of the parasites in different forms of this disease (El Gendy et al., 2009).

P. harmala stops the toxicity caused by different developmental forms of leishmanial. Visceral form leishmaniasis is treated by using this plant extract at a dose rate of 100 mg/kg body weight. *P. harmala* extract is much effective against blood parasites, e.g. with a dose of 5mg/kg body weight one time a day daily for 5 days on cattle and sheep theileria infection. Recovery rate is very good in both species of animals as cattle and sheep (Wanntorp et al., 2011). Beta-carbolines causes inhibition of respiratory chain of plasmodium (Mirzaei, 2007).

Seeds of *P. harmala* have such compounds that have strong activity against trypanosomes (Farouk et al., 2008). Alkaloids of this plant have many important bactericidal properties that can be compared with antibiotics (Farzin and Mansouri, 2006). Different species of bacteria are susceptible to these alkaloids. Harmine, (the methanolic extract) have greater potency against bacteria than other extracts (chloroform and petroleum) (Mahmoudian et al., 2002).

Different type compounds of *P. harmala* and mixture of these is used to treat different animals suffering from fungal infections (Arshad et al., 2008). This gives a synergistic effect of different alkaloids that are present in the total extract of this plant (Nasehi et al., 2010). The effect of this plant against insects is also due to beta-carbolines (Fortunato et al., 2009). This plant causes prevention of the larvae of this pest that are present in the stored food, also inhibits its different developmental stages (Herraiz et al., 2011). One of the most important effects of harmaline are: inhibition of severe toxicity of the epithelial cells in the midgut (Jimenez et al., 2008).

P. harmala extract is used against pest that eats grains as their food. The adult forms of the insects are susceptible to cause diseases in animals (Nafisi et al., 2010). Therefore, we use *P. harmala* as a good source to control the number of these harmful insects (Li et al., 2007). *P. harmala* is used as healers to make different treatment of all non- treatable diseases many countries of the world. For example, powder of its seed has been used to treat skin diseases and different types of tumors under skin (Monsef et al., 2004).

The extract of seed of *P. harmala* is used in much ethno botanical preparation (Tahraoui et al., 2007). *P. harmala* has different effects on tumor cell lines in labs and in live animals. The methanolic extract of *P. harmala* has decreased significantly the proliferation of tumor cell lines. The inhibitory effect produced on these cell lines is very good and long lasting. A cell undergo breakdown due to its effect can be seen in the 24 h and total cells are destroyed within 3 days (Shi et al., 2001).

P. harmala has different extracts in various parts of it, but seed extract is effective to stop the genetic material which is effective against all types of infections. This plant has the efficiency to treat colic that is due to its effects against spasms. It acts to block different types of channels responsible for maintenance of calcium in intestine. The content obtained from this plant is effective against nausea and vomiting. Harmful effects of this are: it increases osteoblast differentiation probably through the activation of bone genetic protein pathways that are responsible to change the shape organs. Harmal play an important role in the development processes and it is proven from experiments that it is useful for treatment of some diseases of bone. *P. harmala* contains some compounds to enhance immune system and has good impact on animal health (Berrougui et al., 2006).

Different compounds of this plant are important against inflammatory processes. *P. harmala* is used to treat diabetes in experimental medicine in different parts of the Universe. It acts to treat several hypoglycemic activities when used at

high dose rate (Abu-Irmaileh andAfifi, 2003). Harmine is the main component of *P. harmala* that has important antidiabetic effect. Harmine is responsible for the expression of gamma receptors (Leporatti and Ghedira, 2009). *P. harmala* extract if given in high-doses and causes liver damage, in the central nervous system cause sponge formation, paralysis and convulsions (Astulla et al., 2008). There are different therapeutic doses that are used in animal's models. There may be inhibition of action of *P. harmala* constituents (Hamsa and Kuttan, 2010).

Peganum harmala use in birds

When this plant is used along with vaccines in laying hens it causes toxicity and due to its effect birds go into stress condition (Dawood and Qubih, 2012). *E. coli* has been separated from hens and chicken along with typical lesions of this infection due to excessive antibiotic intake and lesions have been seen on lungs, liver, heart, and spleen (Tanweer et al., 2014). This plant is used for improving the respiratory disorders, dermatoses, and knee osteoarthritis (Sharifi-Rad et al., 2021). The compounds present in *P. harmala* have been used and showed good effect in the treatment of cutaneous leishmaniasis (Khoshzaban et al., 2014).

Peganum harmala use against Blood Parasites

P. harmala is effective against all type of microorganisms including blood parasite. When parasites enter into the blood, they cause different signs in animals such as lethargy, anemia and loss of function. We can use this plant if there is anemia and other signs of parasitic infections. We can check the activity to inhibit the ova by different compounds of *P. harmala* seeds to stop the growth of eggs of hepatic parasites (Moazeni et al., 2017). In adult male rats, this plant is used to treat different infectious agents (Hamden, 2007). *P. harmala* extract has decreased the use of drugs against babesiosis and other piroplasm. *Plasmodium* and *Babesia* have similar characteristics that's why this plant is used against these blood parasites (Eltaysh et al., 2022). This plant is best in clinical cases of many parasites including Giardiasis (Mbaya and Ogwiji, 2014).

Conclusion

Peganum harmala is known by different names such as Syrian rue. It can be used against asthma, colic and jaundice. Its seeds are well known that possess essentially hallucinogenic and hypothermic properties. It is an important plant used in medicines and distributed in semi-arid areas of Pakistan. World Health Organization says that plants are source of medicines for human beings. By using these plants or herbs, we can reduce the cost of medicines. There are many factors that can affect the access to many of the chemical drugs. Moreover, the cost of different drugs is also an issue. The alkaloids that are active in seeds are beneficial compounds. Many studies in different countries reveal that the *P. harmala* compounds have activity against fungi and all other microbes. It helps to relax blood vessels and it also has antioxidant properties. Microbiologists and phytochemists think that synthetic pharmaceutical products to control infectious diseases in animals are very beneficial. Gastrointestinal nematodes in small ruminants cause loss of production. The nematodes can be controlled by the drugs specific against these parasites.

REFERENCES

- Ahmad, M., Ashraf, M., Khan, M. S., Javeed, A., Durrani, A. Z., Altaf, I., and Malik, N. A. (2013). Toxic effects of chloroform and aqueous extracts of *Peganum Harmala* on hematological and growth parameters in rabbits. *Pakistan Journal of Zoolology*, *45*(4), 989-995.
- Abu-Irmaileh, B. E., and Afifi, F. U. (2003). Herbal medicine in Jordan with special emphasis on commonly used herbs. *Journal of Ethnopharmacology*, 89(2-3), 193-197.
- Akbary, P., Fereidouni, M. S., and Akhlaghi, M. (2015). In vitro antibacterial activity of *Peganum Harmala* (L) extracts to some fish pathogenic bacteria. *Sustainable Aquaculture and Health Management Journal*, 1(1), 7-16.
- Ali, N. H., Faizi, S., and Kazmi, S. U. (2011). Antibacterial activity in spices and local medicinal plants against clinical isolates of Karachi, Pakistan. *Pharmaceutical Biology*, 49(8), 833-839.
- Arshad, N., Zitterl-Eglseer, K., Hasnain, S., and Hess, M. (2008). Effect of Peganum harmala or its β-carboline alkaloids on certain antibiotic resistant strains of bacteria and protozoa from poultry. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, *22*(11), 1533-1538.
- Asgarpanah, J., and Ramezanloo, F. (2012). Chemistry, pharmacology and medicinal properties of *Peganum Harmala* L. Afr. Journal Pharmacy Pharmacology, 6(22), 1573-1580.
- Aslam, N., Wani, A. A., Nawchoo, I. A., and Bhat, M. A. (2014). Distribution and medicinal importance of *Peganum Harmala*. A review. *International Journal Advance Research*, *2*(2), 751-755.
- Astulla, A., Zaima, K., Matsuno, Y., Hirasawa, Y., Ekasari, W., Widyawaruyanti, A., and Morita, H. (2008). Alkaloids from the seeds of Peganum harmala showing antiplasmodial and vasorelaxant activities. *Journal of Natural Medicines*, *62*, 470-472.
- Bahmani, M., Rafieian-Kopaei, M., Eftekhari, Z., Banihabib, E. K., Hajigholizadeh, G. H., Bahmani, F., ... and Jelodari, M. (2013). Evaluating the anti-leech effects of methanolic extracts of *Peganum Harmala* L. and Olea europaea L. on Limnatis nilotica. *World's Veterinary Journal*, *3*(2), 33-37.

- Berrougui, H., Martín-Cordero, C., Khalil, A., Hmamouchi, M., Ettaib, A., Marhuenda, E., and Herrera, M. D. (2006). Vasorelaxant effects of harmine and harmaline extracted from Peganum harmala L. seed's in isolated rat aorta. *Pharmacological Research*, *54*(2), 150-157.
- Branch, S. (2012). Etymological review on chemical and pharmaceutical substances of the oriental origin. *Internationa Journal Animal Veterinary Advance*, *4*, 40-44.
- da Silva, G. D., de Lima, H. G., de Sousa, N. B., de Jesus Genipapeiro, I. L., Uzêda, R. S., Branco, A., and Botura, M. B. (2021). In vitro anthelmintic evaluation of three alkaloids against gastrointestinal nematodes of goats. *Veterinary Parasitology*, *296*, 109505.
- Darabpour, E., Bavi, A. P., Motamedi, H., and Nejad, S. M. S. (2011). Antibacterial activity of different parts of *Peganum Harmala* L. growing in Iran against multi-drug resistant bacteria. *EXCLI Journal*, *10*, 252.
- Dashti, S. (2020). Antiviral properties of *Peganum Harmala* (Espand) as a medicinal plant: A literature review. *Herbal Medicines Journal*, 5(3).
- Dawood, Z. A., and Qubih, T. S. (2012). Effect of *Peganum Harmala* on histological reactions after post Marek's disease vaccination in layer hens. *Iraqi Journal of Veterinary Sciences*, *26*, 339-346.
- El Gendy, M. A., and El-Kadi, A. O. (2009). Peganum harmala L. differentially modulates cytochrome P450 gene expression in human hepatoma HepG2 cells. *Drug Metabolism Letters*, *3*(4), 212-216.
- El Gendy, M. A., Somayaji, V., and El-Kadi, A. O. (2010). *Peganum Harmala* L. is a candidate herbal plant for preventing dioxin mediated effects. *Planta Medica*, *76*(07), 671-677.
- Eltaysh, R., Rizk, M. A., El-Sayed, S. A. E. S., Abouelnasr, K., Abdallah, A. A., and Igarashi, I. (2022). Evaluation of the in vitro and in vivo inhibitory effects of Artemisia herba-alba against the growth of piroplasm parasites. *Journal of Advanced Veterinary and Animal Research*, 9(2), 267.
- Farouk, L., Laroubi, A., Aboufatima, R., Benharref, A., and Chait, A. (2008). Evaluation of the analgesic effect of alkaloid extract of Peganum harmala L.: possible mechanisms involved. *Journal of Ethnopharmacology*, *115*(3), 449-454.
- Farouk, L., Laroubi, A., Ouachrif, A., Aboufatima, R., Benharref, A., and Chait, A. (2009). Antinociceptive activity of various extracts of *Peganum Harmala* L. and possible mechanism of action.
- Farzin, D., and Mansouri, N. (2006). Antidepressant-like effect of harmane and other β-carbolines in the mouse forced swim test. *European Neuropsychopharmacology*, *16*(5), 324-328.
- Fortunato, J. J., Réus, G. Z., Kirsch, T. R., Stringari, R. B., Stertz, L., Kapczinski, F., and Quevedo, J. (2009). Acute harmine administration induces antidepressive-like effects and increases BDNF levels in the rat hippocampus. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 33(8), 1425-1430.
- Frison, G., Favretto, D., Zancanaro, F., Fazzin, G., and Ferrara, S. D. (2008). A case of β-carboline alkaloid intoxication following ingestion of Peganum harmala seed extract. *Forensic Science International*, *179*(2-3), e37-e43.
- Hamden, K., Masmoudi, H., Ellouz, F., ElFeki, A., and Carreau, S. (2007). Protective effects of *Peganum Harmala* extracts on thiourea-induced diseases in adult male rat. *Journal of Environmental Biology*, 29(1), 73.
- Hamsa, T. P., and Kuttan, G. (2010). Harmine inhibits tumour specific neo-vessel formation by regulating VEGF, MMP, TIMP and pro-inflammatory mediators both in vivo and in vitro. *European Journal of Pharmacology*, 649(1-3), 64-73.
- Hamzah, A. M. (2020). Escherichia coli Isolated from Horses and Study the Effect of the Peganum harmaline Extract In Vitro and In Vivo and Antibiofilm Effect In Vitro. *European Journal of Molecular and Clinical Medicine*, 7(2).
- Herraiz, T., and Guillén, H. (2011). Inhibition of the bioactivation of the neurotoxin MPTP by antioxidants, redox agents and monoamine oxidase inhibitors. *Food and Chemical Toxicology*, 49(8), 1773-1781.
- Herraiz, T., González, D., Ancín-Azpilicueta, C., Arán, V. J., and Guillén, H. (2010). β-Carboline alkaloids in Peganum harmala and inhibition of human monoamine oxidase (MAO). *Food and Chemical Toxicology*, *48*(3), 839-845.
- Javadian, F., Saeidi, S., and Jahani, S. (2016). Antimicrobial activity of *Peganum Harmala* and Heracleum persicum against Acinetobacter baumannii. *International Journal of Infection*, 3(1).
- Jimenez, J., Riveron-Negrete, L., Abdullaev, F., Espinosa-Aguirre, J., and Rodríguez-Arnaiz, R. (2008). Cytotoxicity of the βcarboline alkaloids harmine and harmaline in human cell assays in vitro. *Experimental and Toxicologic Pathology*, 60(4-5), 381-389
- Khaliq, T., Misra, P., Gupta, S., Reddy, K. P., Kant, R., Maulik, P. R., and Narender, T. (2009). Peganine hydrochloride dihydrate an orally active antileishmanial agent. *Bioorganic and Medicinal Chemistry Letters*, 19(9), 2585-2586.
- Khoshzaban, F., Ghaffarifar, F., and Koohsari, H. R. J. (2014). *Peganum Harmala* aqueous and ethanol extracts effects on lesions caused by Leishmania major (MRHO/IR/75/ER) in BALB/c mice. *Jundishapur Journal of Microbiology*, 7(7).
- Leporatti, M. L., and Ghedira, K. (2009). Comparative analysis of medicinal plants used in traditional medicine in Italy and Tunisia. *Journal of Ethnobiology and Ethnomedicine*, 5, 1-8.
- Li, Y., Liang, F., Jiang, W., Yu, F., Cao, R., Ma, Q., and Si, S. (2007). DH334, a β-carboline anti-cancer drug, inhibits the CDK activity of budding yeast. *Cancer Biology and Therapy*, 6(8), 1204-1210.
- Liu, C., Gao, J., and Liang, Y. (2022). Phytochemistry, pharmacology and toxicology of *Peganum Harmala*. *Bangladesh Journal of Pharmacology*, 17(4), 124-140.
- Mahmoudian, M., Salehian, P., and Jalilpour, H. (2002). Toxicity of Peganum harmala: review and a case report.
- Mamadalieva, N. Z., Ashour, M. L., and Mamedov, N. A. (2022). Peganum Harmala: Phytochemistry, traditional uses, and biological activities. In Biodiversity, Conservation and Sustainability in Asia: Volume 2: Prospects and Challenges in

South and Middle Asia (pp. 721-744). Cham: Springer International Publishing.

- Mbaya, A. W., and Ogwiji, M. (2014). In-vivo and in-vitro activities of medicinal plants on ecto, endo and haemoparasitic infections: A review. *Current Clinical Pharmacology*, *9*(3), 271-282.
- Mirzaei, M. (2007). Treatment of natural tropical theileriosis with the extract of the plant Peganum harmala. *The Korean Journal of Parasitology*, 45(4), 267.
- Mirzaiedehaghi, M. (2006). Treatment of natural ovine malignant theileriosis with a chloroform extract of the plant Peganum harmala: research communication. *Onderstepoort Journal of Veterinary Research*, 73(2), 153-155.
- Moazeni, M., Saadaty Ardakani, Z. S., Saharkhiz, M. J., Jalaei, J., Khademolhoseini, A. A., Shams Esfand Abad, S., and Mootabi Alavi, A. (2017). In vitro ovicidal activity of *Peganum Harmala* seeds extract on the eggs of Fasciola hepatica. *Journal of Parasitic Diseases*, 41, 467-472.
- Moloudizargari, M., Mikaili, P., Aghajanshakeri, S., Asghari, M. H., and Shayegh, J. (2013). Pharmacological and therapeutic effects of *Peganum Harmala* and its main alkaloids. *Pharmacognosy Reviews*, 7(14), 199.
- Monsef, H. R., Ghobadi, A., Iranshahi, M., and Abdollahi, M. (2004). Antinociceptive effects of Peganum harmala L. alkaloid extract on mouse formalin test. *Journal Pharmacy Pharm Science*, 7(1), 65-9.
- Moradi, M. T., Karimi, A., Rafieian-Kopaei, M., and Fotouhi, F. (2017). In vitro antiviral effects of *Peganum Harmala* seed extract and its total alkaloids against Influenza virus. *Microbial Pathogenesis*, 110, 42-49.
- Nafisi, S., Malekabady, Z. M., and Khalilzadeh, M. A. (2010). Interaction of β-carboline alkaloids with RNA. *DNA and Cell Biology*, *29*(12), 753-761.
- Nasehi, M., Piri, M., Nouri, M., Farzin, D., Nayer-Nouri, T., and Zarrindast, M. R. (2010). Involvement of dopamine D1/D2 receptors on harmane-induced amnesia in the step-down passive avoidance test. *European Journal of Pharmacology*, 634(1-3), 77-83.
- Nenaah, G. (2010). Antibacterial and antifungal activities of (beta)-carboline alkaloids of Peganum harmala (L) seeds and their combination effects. *Fitoterapia*, *81*(7), 779-782.
- Pieroni, A., Muenz, H., Akbulut, M., Başer, K. H. C., and Durmuşkahya, C. (2005). Traditional phytotherapy and trans-cultural pharmacy among Turkish migrants living in Cologne, Germany. *Journal of Ethnopharmacology*, *102*(1), 69-88.
- Samoylenko, V., Rahman, M. M., Tekwani, B. L., Tripathi, L. M., Wang, Y. H., Khan, S. I., and Muhammad, I. (2010). Banisteriopsis caapi, a unique combination of MAO inhibitory and antioxidative constituents for the activities relevant to neurodegenerative disorders and Parkinson's disease. *Journal of Ethnopharmacology*, 127(2), 357-367.
- Sharifi-Rad, J., Quispe, C., Herrera-Bravo, J., Semwal, P., Painuli, S., Özçelik, B., and Cho, W. C. (2021). Peganum spp.: a comprehensive review on bioactivities and health-enhancing effects and their potential for the formulation of functional foods and pharmaceutical drugs. *Oxidative Medicine and Cellular Longevity*, 2021.
- Shi, C. C., Liao, J. F., and Chen, C. F. (2001). Comparative study on the vasorelaxant effects of three harmala alkaloids in vitro. *Japanese Journal of Pharmacology*, 85(3), 299-305.
- Tahraoui, A., El-Hilaly, J., Israili, Z. H., and Lyoussi, B. (2007). Ethnopharmacological survey of plants used in the traditional treatment of hypertension and diabetes in south-eastern Morocco (Errachidia province). *Journal of Ethnopharmacology*, *110*(1), 105-117.
- Tanweer, A. J., Chand, N., Saddique, U., Bailey, C. A., and Khan, R. U. (2014). Antiparasitic effect of wild rue (*Peganum Harmala* L.) against experimentally induced s in broiler chicks. *Parasitology Research*, *113*, 2951-2960.
- Wanntorp, L., and De Craene, L. P. R. (Eds.). (2011). Flowers on the tree of life (Vol. 80). Cambridge University Press.