

Potential uses and Analysis of Bioactive Natural Compounds of *Peganum harmala*

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Received: 21st Apr, 18; Revised: 5th May, 18, Accepted: 25th May, 18; Available Online: 25th Jun, 2018

ABSTRACT

Peganum harmala is of Asian Origin and grows in the Middle East and in part of South Asia mainly in India and Pakistan. In Iran, and some countries in the Arab world such as, Syria, Iraq, Saudi Arabia and Jordan, dried capsules mixed with other ingredients are placed onto red hot charcoal, where they explode with little popping noises in a way similar to American popcorn. *Peganum harmala* has been used to treat pain and to treat skin inflammations, including skin cancers. Some of these alkaloids such as harmaline, harmine, and norharmine are also endogenous compounds present in the body and since they have been found in high plasma concentrations in alcoholics, drug addicts, smokers, and patients with Parkinson's disease, they are thought to be crucially involved in various central nervous system (CNS) problems. All of these effects represent an idea that *P. harmala* and its derivatives could be used for treatment of mood disorders and are potent alternatives for current anti-depression drugs.

Keyword: *Peganum harmala*, Bioactive compounds, Applications, Review.

INTRODUCTION

The plant's seeds are especially noteworthy because they have seen continual use for thousands of years in the rites of many cultures. *Peganum harmala* has been used as an emmenagogue and abortifacient agent¹⁻⁴. It is a perennial plant which can grow to about 0.8 m tall, but normally it is about 0.3 m tall. The roots of the plant can reach a depth of up to 6.1 m, if the soil where it is growing is very dry⁵. The round seed capsules measure about 1–1.5 cm in diameter, have three chambers and carry more than 50 seeds. Another alkaloid, harmine, found in *P. harmala*, has appreciable efficacy in destroying intracellular parasites in the vesicular forms⁶. The endogenous harmala alkaloids have been proven to be involved in Parkinson's disease. One study on both endogenous and exogenous beta-carbolines showed that they all have general DAT-mediated (Dopamine active transporter-mediated) dopaminergic toxicity and therefore, are involved in the pathogenesis of Parkinson's disease. It has also been used widely as an anti-fungal and antiparasidal agent in traditional medicine of some parts of the world. For instance, in Saudi Arabia it has been so common to use *P. harmala* against fungal infections. One study on the effect of *P. harmala* extract on *Leishmania infantum* revealed that harmine and harmaline have weak anti-leishmanial activity against both promastigote and amastigote form of the parasite. There have been several studies indicating effectiveness of *P. harmala* extract against theileriosis. Larvae growth was significantly inhibited with the incorporation of the extract into their

diet. The adult form of the insect was also susceptible⁷⁻²². The antitumor activity of *P. harmala* and its active alkaloids (mainly beta-carbolines) have also drawn attentions of many researchers worldwide that has led to various pharmacological studies regarding this important effect of *P. harmala*. *P. harmala* has been used traditionally as an effective emmenagogue and abortifacient agent in the Middle East, India, and North Africa.

Potential uses of *Peganum harmala*

Several scientific laboratories have studied possible uses for *Peganum harmala* through studies in laboratory animals (in vivo) and in cells (in vitro)²³.

Fertility

In very large quantities (dosages exceeding those commonly used for medicinal, therapeutic, or spiritual purposes), it can reduce spermatogenesis and male fertility in rats.

Antiprotozoal

Peganum harmala has been shown to have antibacterial and anti-protozoal activity, including antibacterial activity against drug-resistant bacteria²⁴⁻²⁷. One of the compounds found in *P. harmala*, vasicine (peganine), has been found to kill *Leishmania donovani*, a protozoan parasite that can cause potentially fatal visceral leishmaniasis.

Anticancer

The beta-carboline alkaloids present in medicinal plants, such as *Peganum harmala* and *Eurycoma longifolia*, have

recently drawn attention due to their antitumor activities²⁶.

Cardiovascular effects

P. harmala is one of the most frequently used medicinal plants to treat hypertension and cardiac disease

worldwide. It has also been shown in various pharmacological studies that *P. harmala* extract or its main active alkaloids, harmine, harmaline, Harman and harmalol, have different cardiovascular effects such as

Table 1: Major phytochemical compounds identified in *Peganum harmala*.

No	Part of plant	System	Effects	Preparation	Ref.
1.	Seed		Antihypertensive in cardiac diseases	Not determined	8
		Cardiovascular	Antihypertensive	Infusion/powder	9
			Hypotensive	-----	7
			Antihypertensive	-----	8
			Blood purifier	-----	2
		Gastrointestinal	Diarrhea	Powder, decoction, maceration or infusion	11
			Intestinal pain	Powder /various extracts	7
			Antispasmodic in colic	Infusion/powder	9
			Antidiarrheal	-----	19
			Antispasmodic astringent	-----	20
			Antiparkinsonian	-----	7
		Nervous	Against nervosity	Powder /various extracts	4
			Psychiatric conditions	-----	9
			Narcotic	-----	
			Analgesic	Seed ground with ginger	
		Endocrine	Depression	Powder, decoction, maceration or infusion	6
			Hallucinogenic	Powder /infusion	21
			Sciatica	Extracts	17
		Neoplasm and tumours	Abortion		4
			Emmenagogue	Powder, decoction, maceration or infusion	21
		Pain relieving	Emmenagogue and an abortifacient agent	Powder, decoction, maceration or infusion	21
			Subcutaneous tumors	Powder, decoction, maceration or infusion	16
			Neoplasms	Powder, decoction, maceration or infusion	21
			Rheumatic pain	Powder seed and various extracts	4
			Painful joint	-----	20
		Organisms	Intestinal pain	Eaten	29
			Lumbago analgesic	Ground with ginger hony and some water for external massage	26
			Against tape worm infection in man and animals	Powderd seeds and various extracts	4
			Anthelmintic/ antimicrobial, antibacterial	Powder /infusion	27
		Diabetes	Leishmaniasis	Ground with ginger hony and some water for external massage	16
			Antifungal	-----	22
			Antiparacidal	-----	46
		Respiratory	Anthelmintic	Extract	43
			Antidiabetic	Infusion powderd	9
		Disinfectant	Asthma	Powder, dedication, maceration or infusion	21
			Bronchitis	Ethanol extract	35
			Expectorant		

			dermatologic	Ground with ginger hony and some water for external massage	18
	Skin and hair				
			Arthritis	Powder /infusion	20
	Ulcers		Cicatrizing		33
			Healing ulcers	External use only	20
2.	Fruit	Disinfectant	Air purifier	Smoke dried capsules	9
			Antiseptic		8
			disinfectant		2
3.	Full plant	Organism	Leishmaniasis	External use only	28
		Skin and hair	dermatologic	External use only	28
		Ulcers	Vulnerary	External use only	2
4.	leaves	Antineoplasm	Antibacterial	Methanol extracts	33
5.	Root	Nervous system	Inhepition of m.o.	Extract	7

bradycardia, decreasing systemic arterial blood pressure and total peripheral vascular resistance, increasing pulse pressure, peak aortic flow and cardiac contractile force, Vasorelaxant and angiogenic inhibitory effects²⁷⁻³¹.

Effects on the heart

There have been a few studies conducted regarding the direct effects of *P. harmala* extract and its alkaloids on heart muscle. For example, in one study it was shown that three *P. harmala* isolated alkaloids (Harmine, Harmaline and Harmalol) have ionotropic effect and also decrease heart rate in normal anesthetized dogs. In another in vivo study, harman dose-dependently produced transient hypotension and long-lasting bradycardia in anesthetized rats³².

Inhibitory effect on platelet aggregation

The alkaloids of *P. harmala* are also shown to have anti-platelet aggregation effects. However, there is not so much evidence on this effect of the plant so far.

Effect on nervous system

In traditional medicine, *P. harmala* has been used among societies to treat some nervous system disorders such as Parkinson's disease, in psychiatric conditions such as nervousity, and to relieve rigorous pain³³. The alkaloid content of *P. harmala* is shown to be psychoactive and various in vitro and in vivo studies indicate a wide range of effects produced by *P. harmala* and its active alkaloids on both central and peripheral nervous system including, analgesia, hallucination, excitation, and anti-depressant effect.

Analgesic and antinociceptive effects

The analgesic effect of different forms of *P. harmala* extract (ethyl acetate [EAE], butanolic [BE], and AqE) have been investigated in various parallel studies. In case of the AqE, the nociceptive effect was only observed in the second phase of the formalin test.

Antimicrobial Effects

Various studies have shown different antiparasidal, antifungal, antibacterial and insecticidal effects of the alkaloids derived from *P. harmala* seeds. In one study, the methanolic, AqE and chloroform extracts of *P. harmala* were shown to have respectively strong, moderate, and slight inhibitory effects on the growth of *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger* and *Candida albicans*³⁴⁻³⁹.

Antiprotozoal effect

Various studies have been carried out investigating in vitro and in vivo effects of different *P. harmala* extracts on forms of leishmania parasites. At the same time, harmaline showed strong toxicity against the amastigote forms inside the macrophages. Furthermore, there have been reports of antiplasmodial activity of different *P. harmala* alkaloids such as vasicinone, deoxyvasicinone, and beta-carbolines.

Antibacterial activity

One of other important features of *P. harmala* alkaloids is their bactericidal activity that is comparable with that of common antibiotics, which have many adverse effects. The activity of these alkaloids depended on the microorganism and the application method. It is concluded that *P. harmala* and its alkaloids could probably be used for the control of antibiotic resistant isolates of bacteria.

Insecticidal and antifungal activity

In vitro treatment with individual alkaloids of *P. harmala* or a mixture of them was so efficient against *A. niger* and *C. albicans*. Furthermore, there have been some reports about insecticidal activity of *P. harmala*-derived beta-carbolines indicating their inhibitory effects on the development and growth of the larval stages of some insects. Another study showed the insecticidal activity of methanolic *P. harmala* extract against *Tribolium castaneum*, the stored grain pest⁴⁰⁻⁴⁶.

Antidiabetic Effects

P. harmala has been traditionally used to treat diabetes in folk medicine of some parts of the world. This effect of *P. harmala* has been pharmacologically confirmed in several studies one of which showed that the plant would lose its hypoglycemic activity at high doses instead of increasing it.

ACKNOWLEDGEMENT

I thank Dr. Ali Al-Marzoki, College of Science for Women, for valuable suggestions and encouragement.

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