Peganam harmala Indian traditional plant: A Scientific Update

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Peganam harmala Indian traditional plant: A Scientific Update

Ravindra Kumar Pandey[1], Shiv Shankar Shukla[1], Rajkumar Tiwari[1], Nagendra Singh Chauhan [2]

[1]Columbia Institute of Pharmacy, Tekari, Raipur (493111), Chhattisgarh, India.
[2] Drugs testing laboratory Avam Anusandhan Kendra, Raipur, Chhattisgarh, India.

ABSTRACT

P. harmala Linn (*P. harmala*) is an indigenous plant of India .It is a highly branched and bushy perennial herb. Parts of the plant are known to possess therapeutic benefits. The plant is used locally in Indian medicine to cure various diseases. It is used in stomach complaints, urinary and sexual disorders, epilepsy, menstrual problems, mental and nervous illnesses etc. the chemical study of the plant reveals that the plant contains important alkaloids(harmine, harmaline, harmalol and peganine), steroid(lanosterol and kryptogenin)and Fatty acids/volatile acids/fixed oil(palmitic, stearic, arachidic, behenic, oleic, linoleic acids, β-sitosterol) etc. Based on the comprehensive literature survey phytochemistry, pharmacognosy, toxicity data and medicinal uses were discussed. Scientific information of the plant was collected from various sources like electronic (Google scholar, pub med) and some old classical text books of ayurveda and ethnopharmacology, In addition the paper covers the literature, primarily pharmacological, and important findings of the drug since last 25 years. This paper will be emerging tool for young researchers who want to start the meticulous research on *P. harm*ala

Keywords: *P*eganam *harmala,* phytochemistry, pharmacognosy, ethnopharmacology, medicinal uses

Corresponding Author:
Dr. Ravindra Kumar Pandey
Columbia Institute of Pharmacy,
Tekari, Raipur (C.G.)
E. mail: ravindraiop@gmail.com

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INTRODUCTION

Alterations in geographical regions and biodiversities in the Indian subcontinent have helped to develop the use of a variety of plant species and other natural resources for health care. These natural resources contributed to the traditional Indian system of medicine[1]. India has an ancient heritage of traditional medicine[1]. Ayurveda is accepted to be oldest exposition on medical system. The Ayurveda is believed to be an upaveda (part) of Atharavaveda (1000 B.C), an old holy transcript of hindus. Ayurvedic literature is enormous and enriched with profiles of plants and their medicinal uses [1].

The most ancient used plant in global folk medicine is the Soma plant, the original Rue, called Assyrian Rue. It has been widely used in the Ayurvedic medicine of the Rig Veda, as the Soma plant, and mixed with gold and metorite and special elements.

It is considered as the plant of life of the great Zoroaster (Zurathustra), and was called Haoma, in the Avesta Veda, and was specified to him by the "god" Masda, the Wise God of Light, just as Soma was specified by Brahma-Manu in the Rig Veda [2-5]. The plant is a middle eastern shrub, found in North Africa, Middle-east, Pakistan and India.

The local tribals of india and Pakistan used powdered seed for the remedyof piles and measales.The decoction of root is used as a anti-lice shampoo by tribal community.

The plant is reported to have abortificant, aphrodisiac, sedative, vermifuge and soporific, prolapse of the womb, analgesic, antibacterial, antidiabetic, uterine contraction, anticancer,

antioxidant antiviral, CNS depressant, antineoseptic, anti imflamatory, genoprotective, muscle stimulant, Antileishmanial , Anti-helminthic etc which is discussed under table no. 6 [6-11]. The plant is reported to have mainly alkaloids as a chemical constituent in the seed and root, which is mainly responsible for their pharmacological activity [12].

Plant Profile:

Figure 1 Picture of the plant *Peganam harmala*

Table 1.The scientific classification of *P. harmala*

Botanical Name	Pegnum harmala
Family	Nitrariaceae
Kingdom	Plantae
Division	Magnoliophyta
Class:	Magnoliopsida
Order:	Sapindales
Family	Nitrariaceae
Genus	Peganum

Table 2. Vernacular names of *P. harmala*:

Hindi	Harmal, Isband, Isband Lahouri
Kannada	Eeme goranti
Marathi	Harmala
Sanaskrit	Haramala, soma
Tamil	Simaiyalavinai, Smaiyaravandi, Cimai alavanam
Telgu	Shima-goranti-Vittulu
Urdu	Ispand, Aspand, Tukhm kunch hi maing

Description:

Leaves are alternate, not glandular, entire or irregularly multifold, stipules setaceous. Flowers are solitary on subterminal leaf-opposed pedicles, white. Sepals are 4-5, narrow, often foliceous and pinnatifid, open in aestivation, persistent. Petals are 4-5, subequal, imbricate. Disk annular or cup-shaped. Stamens are 12-15, inserted at the base of the disk, some without anthers; filaments dilated below; anthers linear. Ovary is globose, deeply 2-3 lobed, 2-3 celled; ovules many in each cell, suspended by short funicles from the central angle; basal style, twisted, 2-3 keeled over the middle, the keels stigmatose. Fruit are globose, 3-4 celled, dry and dehiscing with 3 valves, or baccate and indehiscent; cells multi-seeded. Seeds are angled; testa soft, scrobiculate; albumen fleshy; embryo curved [6].

Table 3. Chemical constituent of *P. harmala* [7, 8]

Class	Chemical Constituent
Alkaloids	harmine, harmaline, harmalol and peganine
Steroid	lanosterol and kryptogenin
Fatty acids/volatile acids/fixed oil	palmitic, stearic, arachidic, behenic, oleic, linoleic acids, β-sitosterol
Protein & Amino acids	Protein & Amino acids
Phenolic/glycosides/triterpenoids/steroids	β-sitosterol,

Medicinal importance of *P. harmala*:

P. harmala is of various medicinal uses. It is used in treatment of stomach complaints, menstrual problems, mental, urinary and sexual disorders, epilepsy, and nervous illnesses. The oil obtainedis said to have aphrodisiac activity. The oil is also said to have soporific, galactogogue, soporific, ophthalmic, and vermifuge properties. A decoction of the leaves is used in the management of rheumatism. The root part has shown parasiticide action in order to kill body lice. It is also used internally in the treatment of nervous conditions and rheumatism [9].

Phytochemestry:

The preliminary phytochemical screening conceded out on ethanolic, diethyl ether and aqueous extracts of *P. harmala* showed the occurrence of phytoconstituents such as flavonoids,

alkaloids, tannins, triterpenes, sterol, anthroquinones, coumarines and volatile oils. Diverse pharmacological properties and structurally novel compounds have been found for the alkaloids. The detailed phytochemestry is given in table no 8.

Table 4. Preliminary microscopical characters of *P.harmala* [10]

P. harmala		**Characters**
Stem	Length	30- 90 cm
	Branching	Highly branched and bushy
	Internodes	9 to 10 cm
	Taste	Tasteless
Leaves	Dimension	5 – 7.5 cm long
	Attachment	Leaf stalk absent
	Leaf lamina shape	Linear
	Venation	Alternate
	Edges	Smooth
	Apex	Accute
Flower	Petals	Petals 4-5, subequal, imbricate. Disk annular or cup-shaped
	Sepals	Sepals 4-5, narrow, often foliceous and pinnatifid, open in aestivation, persistent.
	Seed	Seed pod is a small (less than 0.5 in. diameter), round capsule with 2-4 chambers; can be green orange or brown
Root		Woody, branched taproot with short creeping roots

Table 5. Preliminary macroscopical characters of *P. harmala*[10]

P. harmala	**Characters**	
Roots	Epidermis	Outer surface
	Cortex	The cortex covers a very small area, and underneath the ring-shaped scleranchyma and this encompasses the entire Transporter bunch to the scleranchyma.
	Parenchyma	5- 6 cell form and fill the cortex
	Sclerenchyma	ring-shaped schlerancymatic cells are situated in patches after cortex
	Pith	Cell pithed in older stem
	xylem	To different rings
	Phloem	Vaguely picked and scattered

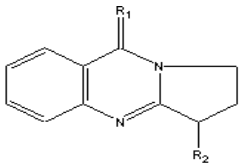
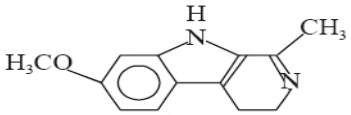
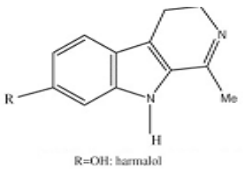
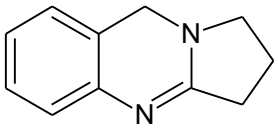
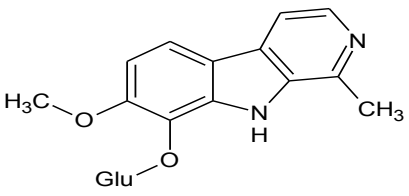
Table 6. : Preliminary pharmacological activities of *P. harmala*

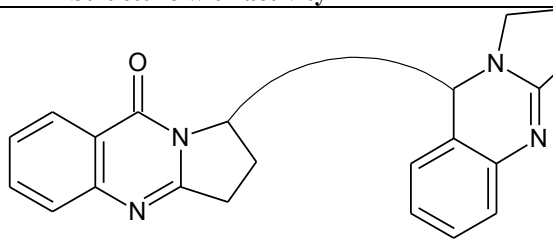
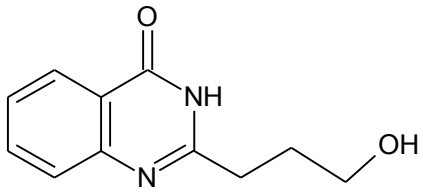
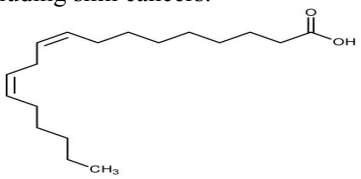
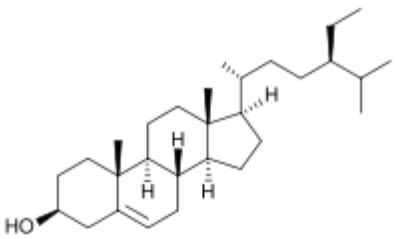
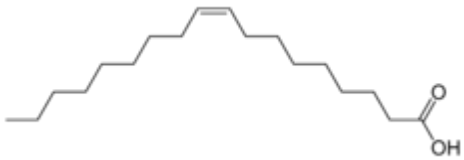
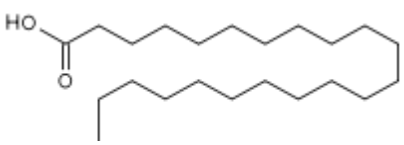
EXTRACT	ACTIVITY	ANIMAL TEST	DOSE	REFERENCE
PLANT PART: Seed				
Alkaloidal	Antinociceptive	Formalin	12 mg/kg	[11]
Ethanol	Antileishmanial activity	in vitro	100mg/kg	[12]
Aqueous	Antinociceptive	Hot plate and formalin	25mg/kg	[13]
Aquous	Antibacterial	Invitro	-	[14]
Methenol	Uterine contraction	-	0.1mg/kg	[15]
Harmane & harmine	CNS depressant	Forced swim test	5-15mg/kg i.p.	[16]
aqueous	Hypothermic effect	Serotonergic mechanism	100mg/kg	[17]
aqueous	Antitumour	Invitro	25mg/kg	[18]
aqueous	Anti microbial effects	Lactobacilli and Candida albicans	50%	[19]
alcholic	Anti fungal activity	*C. albicans*	1.25 mg/ml	[20]
Alkaloidal	Antifungal	MIC	3.2mg/ml	[21]
Hydroalcoholic	antileishmanial activities	***Leishmania major***	200 mg/kg body wt	[22]
Ethanol	Antidiabetic	Streptozotocin induced diabetes	150-250 mg/kg body wt.	[23]
Ethanol	Anticancer	DNA topoisomerase inhibition	1ug/ml -	[24]
Harmaline	Anti anxiety	+ maze test	5-10 mg/kg	[25]
Ethanol	Psycho active	MAO inhibition	27 µg/lt	[26]
Alcoholic extract	Wound healing	30 male Sprague-		[27]
Aqueous extract	activity	Dawley rats		
	Antiparkinsion activity	Rats	10 mg/kg	[46]
PLANT PART: Root				
Aquous	Antibacterial	Invitro	-	[28]
Aqueous	Nematicidal	Invitro	-	[29]
PLANT PART: Leaf				
Methanol	Antioxidant	lipid peroxidation inhibition by ammonium thiocyanate	-	[30]
Methanol	Antiviral	HCMV	25-100mg	[31]
PLANT PART: Arial part				
Alcoholic	Animicrobial	E. coli – 0157 inhibition (in-vitro)	0.15-0.4 mg/ml	[32]

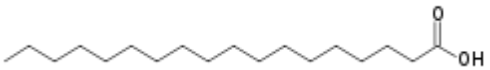
Table 7. Physical analysis of *P.harmala* [33]

Parameters	**Values**
Ash Value (%)	6.40
Essential Oils (%)	0.1
Extractive values	
a. Chloroform%	12.3
b. Water%	19.0
c. Ethanol%	7.1
d. Hexane%	6.8

Table 8. Phytochemical Structures present in *P. harmala* [34,35]

Chemical constituents	Structure with activity
Harmine	 vasicine(peganine) R1=H2 ,R2=OH vasicinone R1=O,R2=OH desoxyvasicinone R1=O,R2=H Harmine has been found to increase EAAT2 glutamate pump expression in central nervous system, therefore reducing glutamate toxicity
Harmaline	 Harmaline Harmaline is a central nervous system stimulant and a reversible inhibitor of MAO-A
Harmalol	 R=OH: harmalol Harmalol, a harmala (β-carboline) alkaloid, is a monoamine oxidase inhibitor (MAOi) useful for studies involving melanogenesis.
Ruine	 ***Used*** in medicine for treating damage to the peripheral nervous system
Dipegine	 used as an emmenagogue and abortifacient agent.

Chemical constituents	Structure with activity
Pegamine	 are used in neurasthenia and nervous and epileptic attacks
Pegamine	 Used to treat pain and skin inflammations, including skin cancers.
LInoleic acid	 Linoleic Acid is used to show antioxidant activity of natural phenols
B- sitosterol	 β-Sitosterol inhibits cholesterol absorption in the intestine
Oleic acid	 Oleic acid may be responsible for the hypotensive (blood pressure reducing) effects of olive oil.
Behenoic acid	

Chemical constituents	Structure with activity
	Commercially, behenic acid is often used to give hair conditioners and moisturizers their smoothing properties
Stearic acid	 showed alterations in central nervous system control of insulin secretion.Stearic acid is used to produce dietary supplements

HUMAN TOXICITY [36-37]

*P*eganam *harmala* has been traditionally used in Bedouin medicine as an emmenagogue. It is also used as abortifacient agent. Few reports had been reveled on its human toxic effects and syndrome. A case of overdose was reported with *P. harmala* with a young lady (aged 27 years) who has taken 50 g of seeds of this plant for the management of amenorrhea. Few minutes after intake of seeds in a cup of coffee, signs of intoxication were seen and the patient was taken to hospital. The signs of *P. harmala* overdose comprised of neurosensorial syndromes, bradycardia and GI disorder such as nausea and vomiting.

Drug Interaction & Doses

P. harmala has major interaction of drug metabolizing enzymes cytochrome P450S (cyp), harmine and harmaline increases the activity of CYP182, 2C19, 3A4 and decreases the activity of CYP2B6, 2D6, and 2E1. It clearly reflects that precautions should be taken while administering *P harmala* with other drugs.

ANIMAL TOXICITY [38,39]

Plant parts of *P. harmala* are said to be toxic, but it is not in all the cases. Since the toxicity is dose dependent in animals. Few studies on cattle's reported toxicity by administering intravenous injections (9 mg/kg) of harmine and harmaline which leaded accelerated breathing and colonic muscular spasm. Climatic changes are responsible for succesibility to poisoning in camels especially young camels are most affected in dry climate. There are reports of severe intoxification in cattle's like donkeys, sheep and horses. Overdosing and sub lethal dose of *P. harmala* reported to have digestive and nervous syndromes in animals. The symptoms of toxicity in animals are weakness, anorexia, hyper salivation, vomiting and diarrohea, followed by muscular excitability, crumbling and stiffness. Hastened breathing is a sign of nervous syndrome. The toxicity in animals emerges in a narcotic stage followed by dyspenia and mydriasis. Diuresis and abnormally low temperature have also been reported in cattle's. Overdosing in animal's causes the limbs of the corpse to stiffen, as a consequence animal died. The smooth muscles organs like heart, pulmonary are reported to be congested.

Table 9. Toxic doses of various alkaloids of *P. harmala.*

Alkaloid	Response	Animal	Dose (mg/kg)
Harmaline	LD_{50}-sc	rats	20
Harman	LD_{50}-sc	rabbits	00
Harmine	LD_{50}-iv	mice	08
Harmine	MLD-sc	rats	00

Table 10. Reported finger print analysis of *peganum harmala*

Plant part	Extract	Solvant used	Compound	Method	Reference
SEED	alkaloidal	methyl *tert*-butyl ether/THF /water (2:2:3)	harmine	HPTLC	[40]
SEED	alcoholic	methanol-water-acetic acid	harmine	HPLC	[41]
SEED	alcoholic	acetonitrile-ammonium formate (13:87, v/v)	harmine	Capillary liquid chromatography	[42]
SEED	hydroalcoholic	55 ml double distilled water, 45 ml ethyl acetate and 100 ml 95% ethanol	harmine harmane, harmalol harmaline	HPLC	[43]
SEED	Aqueous extract	—	harmine, harmaline, harmol, harmalol, harmane, and norharmane γ-tocopherol and	Capillary electrophoresis and UV	[44]
SEED	Oil	mixture of 0.5% (vol/vol) propan-2-ol in n-hexane In HPLC	linoleic acid	HPLC And GC	[45]

Conclusion:

The present review confers the plant profile, pharmacognosy, pharmacology, phytochemistry of the herb *P. harmala*. The Chemical Constituent i.e. Glycosides, flavonoids, alkaloids, carbohydrates, steroids and proteins compounds are commonly present in this species. Pharmacological studies carried out on crude extracts and pure metabolites provided realistic credentials for its traditional uses, and have disclosed this herb to be a precious source for medicinally important compounds.

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