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Distribution, Status, Pharmacological, and Traditional importance of *Peganum harmala* L.

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ABSTRACT

Peganum harmala L. Commonly known as Syrian rue, Wild rue or Harmal is native to arid and semi-arid regions of Northern African and Asian deserts that have spread to parts of the southwestern United States and Northern Mexico. It is a multipurpose medicinal plant with antimicrobial, antifungal, anti-inflammatory, antidiabetic, anti cancerous, hypothermic and hallucinogenic activities. Phytochemical investigations has revealed the presences of a number of active alkaloids especially beta-carbolines such as harmalol, harmaline, and harmine. Seeds and roots contain the highest levels of alkaloids with low level in stem and leaves and absent in flowers. This emphasizes on the need of widespread study for covering the supplementary information on the medicinal importance of other species of genus peganum.

Keywords: Beta- carbolines, distribution, Peganum harmula, pharmalogy, Toxicity.

I. INTRODUCTION

Peganum is a genus of five to six species distributed in the old world from the Mediterranean to Mongolia and in the new world from Texas to Mexico [1] (Table 1). The genus contains perennial herbs which are dispersed in the central Asia, Mexico and the Southern United States. It is a member of Zygophyllaceae, consisting of six species in China out of which three species, *P. harmala* Linn. *P. nigellastrum* Bunge. and *P. multisectum* (Maxim.) Bobr. are found mainly in arid and semi-arid areas in northwest China and are vital components of the desert vegetation. Although it belongs to the family Zygophyllaceae but its taxonomic position is still debatable and a separate family Nitrariaceae has been proposed for this genus [2]. *Peganum harmala* L. (2n=24) is a perennial flowering herb growing in Africa, the Middle East, India, Pakistan, Mexico, South America and several other countries [3]. It is native to arid and semi-arid regions of Northern African and Asian deserts that have spread to parts of the South Western United States and Northern Mexico [4]. It is a drought tolerant plant in arid parts of Central Asia, North Africa and Middle East and has been introduced in America and Australia [5]. According to [6] *Peganum harmala* is native to eastern Mediterranean region and widely distributed in Middle East, India, Mongolia and China. *Peganum harmala* can grow in areas receiving as little as 100 mm annual precipitation [7, 8] and is considered drought tolerant [9]. The species grows with an altitudinal gradient of 1590-3400 m as

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indicating that the species can tolerate a broad range of environmental conditions. In India it is usually found in drier parts of Jammu and Kashmir, Punjab, Haryana, Rajasthan, Utter Pradesh and Delhi [10].

II. BOTANICAL DESCRIPTION

Peganum harmala L. is a perennial herbaceous, branched into 5-13 stems, glabrous plant which grows upto 30-100cms in height. The leaves are palmatisected into 3-5 linear lobes which are 3-6 cms long and 1.5-3.0 mm wide. Flowers arise by 1-3 on apexes of branches which bear whitish-yellow petals in color. The fruits are globular capsule with 3 chambers, 0.9-1.3 cm in diameter and containing 35-45 angular blackish seeds [11]. The plant is not usually grazed by animals due to its bitter taste.

III. PHARMACOLOGICAL USES

Peganum harmala is a well-known and effective medicinal plant in Turkey, Iran and China, especially in Xinjiang and Mongolia [3,12, 13]. Carboline alkaloids obtained from different parts of the plant are used against number of diseases [14]. The seeds and the whole plant possess medicinal properties (Uighur Drug Standard of the Ministry of Public Health) and various reports suggest that the plant can be used to treat ailments such as rheumatism, hypertension, diabetes, asthma and jaundice. The seeds also possess hallucinogenic and hypothermic properties and are used as a medical remedy, incense, condiment with necrotic, sedative, aphrodisiac, stimulant and emetic properties. The Seeds are used for the treatment of fever, malaria, hysteria, neuralgia, rheumatism, asthma, syphilis an eye. [15, 16, 17, 18, 19, 20,] In addition, *P. harmala* is also an anti-parasitic agent. Moreover, the alkaloids identified in *P. harmala* exhibit some pharmacological action, such as antitumor and analgesic effects [18, 21, 22], vasorelaxant activity [23], antimicrobial properties [24, 25] and are strong inhibitors of monoamine oxidase. [26]. The seeds and whole plants of *P. nigellastrum* and *P. multisectum* are sometimes used as substitutes for *P. harmala* in medicinal market. Carboline alkaloids obtained from various parts of the plant are used against number of diseases [13]. The alkaloid extract of seeds from *Peganum harmala* is considered to have anti cancerous activity which could prove as a novel anticancer therapy [27].The extract of *Peganum harmala* containing the alkaloids harmaline and harmine was topically used to treat certain (human) dermatoses of inflammatory nature (impetigo, pityriases alba, cutaneous and leishmaniasis) [28]. Results were encouraging and proved the antibacterial, antifungal, antipruritic and probably antiprotozoal effects of the extract.

IV.TOXICITY

The overdose ingestion of *Peganum harmala* for medicinal use is toxic and several cases of toxicity have been already reported. It causes headache, dizziness, nausea, convulsions, hallucinations, paralysis, euphoria, digestive problems, bronchodilator, hypothermia and bradycardia [5, 6, 17]. *Peganum harmala* is one of the most frequently used medicinal plants to treat hypertension and cardiac disease worldwide [29]. Many pharmacological studies suggest an antioxidant and free radical scavenging effect of *Peganum harmala* [30]. During in vivo study, intrapretoneal administration of *P. harmala* dose results in abnormal writhing, body tremors and slight reduction in locomotor activity. These reports have been also been ascertained in human cases wherein seed extract infusion of *P. harmala* depicted neuro;sensorial symptoms, visual hallucination, eleviation of body temperature, cardiovascular disorder, ataxia, diffuse tremors and vomiting. Elavated doses of *P. harmala* extract may lead to

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liver degeneration, spongiform alteration in CNS, hypothermia, convulsions and brady cardia. Besides, intercalation of *P. harmala* into DNA leads to mutagenic activity and results in genotoxic effects. The beta-carbolines of *P. harmla* interacts with various signalling pathways such as dopamine, benzodiazepine, imidazoline, and 5- hydroxytryptamine.

V. TRADITIONAL USES:

Peganum harmala has been traditionally used for the treatment of diabetes in folklore medicine in some parts of the world [31]. [32] reported the burning of seed of *Peganum harmala* after child birth in Northwestern India and West Pakistan. The seeds are placed on burning charcoal and the fumes are allowed to permeate the rooms for several days where a baby has been born. The seeds are also burnt during marriage ceremony and plant is proverbial in traditional medicine since earliest times as a remedy for a wide range of complaints [33]. A red dye extracted from seeds of *peganum* is used in Turkey and Iran for coloring carpets [34]. In traditional medicine, the species has been used to cure some nervous system disorders such as Parkinson's disease [35] in psychiatric conditions [36].

VI. PHYTOCHEMISTRY

The common known phytochemical compounds from *P. harmala* are alkaloids, flavonoids and anthraquinones [37, 38, 39]. The total alkaloid content of *P. harmala* varies between 2 to 5%. Seeds and roots are the richest sources of alkaloids with low levels in stems and leaves and absent in flowers. The above ground parts of *Peganum harmala* produce four new flavonoids acacetin 7-0-rhamnoside, 7-0-[6-0-glucosyl-2-0-(3- acelyl rhamnosyl) glucoside and the glycoflavone 2-0-rhamnosyl-2-o-glucosylcytisoside. Various alkaloids have found especially in seeds and roots of *P. harmala* such as harmine, harmaline, harman and quinazoline derivates; vasicine and vasicinone [3, 5, 40]. Roots contain harmine and harmol with 2.0 and 1.4% (w/w) respectively [41]. Harmaline was first isolated from the seeds and roots of p. harmala and is the major alkaloid of the plant [5]. Harmine is also present in the roots of *P.harmala* and pharmacologically resembles harmaline in its action, but is less toxic. Vasicine and Vasicinone the potential quinazoline alkaloids and were first discovered in flowers and stems of *P. harmala* [5]. [37] reported that in *Peganum harmala* the alkaloids harmine and harmaline are restricted in the roots and stem. The authors reported that these alkaloids were mainly investigated in seeds by using different methods (% yield, Rf values, melting points, UV and IR spectra) for their identification and isolation. [41] confirmed harmaline, harmine, harmalol, harmol and tetrahydroharmine and quantified as the main b-carboline alkaloids in *P. harmala* extracts. Harmine and harmaline accumulated in dry seeds at 4.3% and 5.6% (w/w), respectively, harmalol at 0.6%, and tetrahydroharmine at 0.1% (w/w). Roots contained harmine and harmol with 2.0% and 1.4% (w/w), respectively. The chemical analysis of various parts of *Peganum harmala* is given in Table 2.

VII. DISCUSSION

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The objective of this paper has been to show the recent advances in the exploration of Species *Peganum harmula* as distribution, traditional usage, pharmacological usage, toxic effects and to illustrate its potential to be used in various novel drugs based on the most recent findings. There are about 6 species of genus *peganum* but only *peganum harmala* have been studied for chemical analysis. Simultaneously rest of the species have not been confirmed to chemical characterization and other biological studies as evident from perusal of the review of literature during the present study. Different plant parts of *Peganum harmala* contain several phenolic compounds and other alkaloids such as harmine, harmaline, harmalol, vasicine, vasicinone etc. with antimicrobial, antifungal, anti-inflammatory, anti-cancerous hypothermic and hallucinogenic activities besides being medicinally important, also possess strong inhibitory activity on growth and germination of other plants [5, 42, 43,]. *Peganum harmala* widely distributed in North Africa, Mediterranean, the Middle East, Pakistan, India and Iran and has also been introduced in America and Australia [44, 45, 56].

Table 1: **World distribution of different species of the genus *Peganum*.**

Species	Continent	Country
Peganum harmala	Asia	India, China, Afghanistan, Pakistan, Mongolia, Kazakhstan, Uzbekistan, Iran, Iraq, turkey, Syria, Jordan, Israel, Greece, Arabia.
	Europe	Russia, south Europe
	North America	USA, north Mexico
	Australia	Australia
	Africa	North Africa
Peganum multisectum	Asia	China
Peganum nigellestrum	Europe	Russia
	Asia	China, Mongolia
Peganum mexicanum	North America	United states

Table 2: Chemical profile of *Peganum harmala* (Chopra *et al.*, 1949 and anonymous 1966).

Alkaloids	Root	Stem	Leaves	Flowers	Seeds	Percentage
Harmine	+	+	_	_	+	2.5-3%
Harmaline Dehydroharmine	+	+	_		+	2.5-3%
Quinzoline derivative de vasicine (Peganine)	_	+	_	+	+	2.5-3%
2,3 trimethylene 4 quinazolone	_	_	_	_		2.5-3%

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1,2,3 hydroxymethylene quinqzolone (Harmalol)	_	+	_	_	+	2.5-3%
Harmalidine β caroline	_	_	_	_	_	2.5-3%
Harmaline	_	_	_	_	+	2.5-3%
Pegamine	+	+	+	_	+	_
Vascinones	+	+	+	_	+	_

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REFERENCES

REFERENCES

[1.] L. P. R. Decreane, J. Delact, and E. F. Smets. Morphological studies of Zygophyllaceae II. The floral development and vascular anatomy of Peganum harmala. *Amer. J. Bot*, *83*, 1996, 201 – 215.

[2.] M.C. Sheahan, and W. M. Chase. A phylogenetic analysis of Zygophyllaceae R.Br. based on morphologica l, anatomical and rbcL DNA sequence data. *Bot. J. Linn. Soc*, 112, 1996, 279-300.

[3.] M. Kartal, M. L. Altun, and S. Kurucu. HPLC method for the analysis of harmol, harmalol, harmine and harmaline in the seeds of *Peganum harmala* L. *J. Pharmaceut. Biomed. Anal*, 31, 2003, 263–269.

[4.] L. B. Abbott, D. Lepak, and L. D. David. Vegetative and Reproductive Phenology of African Rue (*Peganum harmala*) in the Northern Chihuahuan Desert. *The South Western Naturalist*, *52*, 2007, 209–218.

[5.] M. Mahmoudian, H. Jalilpour, and P. Salehian. Toxicity of *Peganum harmala*: Review and a case report. *Iran J Pharmacol Ther*, *1*, 2002, 1–4.

[6.] G. Frison, D. Favretto, F. Zancanaro, G. Fazzin, and S.D. Ferrara. A case of β-carboline alkaloid intoxication following ingestion of Peganum harmala seed extract. *Forens Sci Int*, *179*, 2008, 37–43.

[7.] A. Mahmoud, A. M. El Sheikh, and S. Abdul-Basit. Germination of six desert species from Riyadh Distri ctSaudi Arabia. Journal of the College of Science of King Saud University, 14, 1983, 5-22.

[8.] H. Walter, and E.O. Box. Caspian lowland biome. Pages 9-41 In N.E. West, ed. Ecosystems of the World 5: Temperate Deserts and Semi-Deserts. Amsterdam: Elsevier. 1983.

[9.] J. Levitt. Responses of Plants to Environmental Stresses. Volume 2: Water, Radiation, Salt, and Other Stresses. New York: Academic Press. 1980. 607pp.

[10.] P. K. Hajra, V. J. Nair, and P. Daniel. Flora of India.Vol. 4, Botanical Survey of India,Calcutta, 1997.

[11.] K. H. Rechinger. Flora Iranica, Akademische Druck Verlagsanstalt: 1982, 18-20.

IJARSE
ISSN (O) 2319 - 8354
ISSN (P) 2319 - 8346

[12.] B. Hemmateenejad, A. Abbaspour, H. Maghami, R. Miri, and M.R. Panjehshahin. Partial least squares based multivariate spectral calibration method for simultaneous determination of beta-carboline derivative s in *Peganum harmala*. seed extracts. *Anal. Chim. Acta*, *575*, 2006, 290–299.

[13.] A.M. Sobhani, S.A. Ebrahimi, M. Mahmoudian. An in vitro evaluation of human DNA topoisomerase I inhibition by *Peganum harmala* L. Seeds extract and its b-carboline alkaloids. *J. Pharm. Pharm. Sci. 5*, 2002, 19–23**.**

[14.] A. F. M. Abdelfattah, K. Matsumoto, V. Gammaz, and H. Watanabe. Hypothermic effect of *harmala* alkaloid in rats. Involvement of serotonergic mechanism. *Pharmacol. Biochem. Behav*, *52*, 1995, 421–426.

[15.] A. Astulla, K. Zaima, Y. Matsuno, Y. Hirasawa, W. Ekasari, A. Widyawaruyanti, N.C. Zaini, and H. Morit aAlkaloids from the seeds of *Peganum harmala* showing antiplasmodial and vasorelaxant activities. *J. Nat. Med. 62*, 2008, 470–472.

[16.] H. Berrougui, M. Isabelle, M. Cloutier, M. Hmamouchi, and A. Khalil. Protective effects of *Peganum harmala* L. extract, harmine and harmaline against human low density lipoprotein oxidation. *J.Pharm. Pharmacol*, *58*, 2006, 967–974.

[17.] L. Elbahri, and R. Chemli. *Peganum harmala* L.: a poisonous plant of North Africa. *Vet. Human Toxicol. 33*, 1991, 276–277.

[18.] L. Farouk, A. Laroubi, R. Aboufatima, A. Benharref, and A. Chait . Evaluation of the analgesic effect of alkaloid extract of *Peganum harmala* L.: possible mechanisms involved. *J. Ethnopharmacol. 115*, 2008, 449–454.

[19.] H. Monsef, G. Ali, I. Mehrdad, and A. Mohamed. Antinociceptive effects of *P. Harmala* L. Alkaloids extract on mouse formaline test. *J. of pharmacy and pharmaceutical Sci., 7*, 2004, 65 – 69.

[20.] A. R. Shahverdi, S.N.Ostad, S. Khodaee, L. Bitarafan, H. R. Monsef Esfahani,H.Jamalifar, B.Nikavar,M. Mohseni. Antimicrobial and cytotoxicity potential of *Peganum harmala* smoke. *Pharmacogn. Mag, 4*, 2008, 236–240.

[21.] C.H.Wang, J. Liu, and L.M. Zheng."Analysis of harmine and harmaline of *Peganum harmala* in different parts and different localities." *Chinese Pharmaceutical Journal-Beijing*, *37*, 2002, 211-214.

[22.] F. Jahaniani, S.A. Ebrahimi, N. Rahbar-Roshandel, M. Mahmoudian (). Xanthomicrol is the main cytotoxic component of Dracocephalum kotschyii and a potential anti-cancer agent. *Phytochemistry, 66*, 2005, 1581-1592**.**

[23.] A. Astulla, K. Zaima, Y. Matsuno, Y. Hirasawa, W. Ekasari, A. Widyawaruyanti, N. C. Zaini,. and H. Morita. Alkaloids from the seeds of Peganum harmala showing antiplasmodial and vasorelaxant activities. *J. Nat. Med, 62*, 2008, 470–472.

[24.] D. Prashanth S. John .Antibacterial activity of *Peganum harmala*. Fitoterapia 70, 1999, 438–439.

[25.] N. Arshad, K. Zitterl-Eglseer, S. Hasnain, and M. Hess. Effect of *Peganum harmala* or its beta-carboline alkaloids on certain antibiotic resistant strains of bacteria and protozoa from poultry. *Phytother Res*, *22*, 2008, 1533-1538.

[26.] H. Kim, S.O. Sablin, R. R. Ramsay. Inhibition of monoamine oxidase A by beta-carboline derivatives. Arch. *Biochem. Biophys*, *337*, 1997, 137–142.

IJARSE
ISSN (O) 2319 - 8354
ISSN (P) 2319 - 8346

[27.] F. Lamchouri, A. Settaf, Y. Cherrah,M. Zemzami,B. Lyoussi,A. Zaid,N. Atif,and M. Hassar, Antitumor principles from Peganum harmala seeds. *Therapie, 54*, 1999, 753-758.

[28.] El-Rifaie. and M. E. Saad. Uses of Peganum harmala in certain dermatoses. *Int. J. Dermatol, 19*, 1981, 221-222.

[29.] A.Tahraoui, J. El. Hilaly, Z. H. Israili, and B. Lyoussi. Ethnopharmacological survey of plants used in the Traditional treatment of hypertension and diabetes in south eastern Morocco (Errachidia province). *J. Ethnopharmacol*, 110, 2007, 105–17.

[30.] K. Hamden, D. Silandre, C. Delalande, A. Elfeki, S. Carreau. Protective effects of estrogens and caloric restriction during aging on various rat testis parameters. *Asian J Androl,10*, 2008, 837–45.

[31.] M. Bnouham, H. Mekhfi, A. Legssyer, and A. Ziyyat. Medicinal plants used in the treatment of diabetes in Morocco. *Int J Diabetes Metab,10*, 2002, 33–50.

[32.] I. Hussain. Some folk uses of Peganum harmala in India and Pakistan. *Economic Botany, 21*, 1966, 284.

[33.] C. C. Shi, S. Y. Chen, G. J. Wang, J. F. Liao, and C. F. Chen .Vasorelaxant effect of harman. *Eur. J. Pharmacol, 390*, 2000, 319–325.

[34.] T. Baytop. Herbal treatments in Turkey, (Past and Present) 2. Baski, [Tükiye'de Bitkilerle Tedavi (Gecmiste ve Bugün)] Nobel Tip Kitapevleri Ltd. Sti., Istanbul Turkey, (In Turkish). 1999, 35-90

[35.] M.L Leporatti, and K. Ghedira. Comparative analysis of medicinal plants used in traditional medicine in Italy and Tunisia. *J Ethnobiol Ethnomed, 5*, 2009, 31.

[36.] D. González, C. Ancín-Azpilicueta, V.J. Arán, and H. Guillén. Beta-Carboline alkaloids in *Peganum harmala* and inhibition of human monoamine oxidase (MAO). *Food Chem Toxicol, 48*, 2010, 839–45.

[37.] N. Bukhari, J. H. Choi, C.W. Jeon, H. W. Park, W. H. Kim, and M. A. Khan. Phytochemical studies of the alkaloids from Peganum harmala. *Applied Chemistr, 12*, 2008, 101–104.

[38.] M. Sharaf, M.A. El-Ansari, S.A. Matlin, and N.A .Saleh. Four flavonoid glycosides from *Peganum harmala*. *Phytochem, 44*, 1997, 533-536.

[39.] S. Pitre, S.K. Srivastava. Two new anthraquinonsfrom the seeds of *Peganum harmala*. *Planta Medica, 53*, 1987, 106-107.

[40.] R. Zayed, and M. Wink, (). Beta-carboline and quinoline alkaloids in root cultures and intact plants of *Peganum harmala*. *Z Naturforsch*, 60, 2005, 451-458.

[41.] T. Herraiz, D. González, , C. Ancín-Azpilicueta, V. J. Arán, and H. Guillén. Beta Carboline alkaloids in *Peganum harmala* and inhibition of human monoamine oxidase (MAO). *Food Chem Toxicol, 48*, 2010, 839-45.

[42.] H. Sodaeizadeh, M. Rafieiolhossaini, J. Havlik, and P.Van Damme. Allelopathic activity of different plant parts of *Peganum harmala* L. and identification of their growth inhibitors substances. *Plant Growth Regulation*, 59, 2009, 227-236.

[43.] A.Q. Panhwar, and H. Abro. Ethnobotanical studies of Mahal Kohistan (Khirthar National Park). *Pak. J.Bot, 39*, 2007, 2301-2315.

[44.] G. Asghari, and B. G. Lockwood. Stereospecific biotransformation of (±) phenylethyl propionate by cell cultures of *Peganum harmala* L. *Iran Biomed J, 6*, 2002, 43–46.

IJARSE
ISSN (O) 2319 - 8354
ISSN (P) 2319 - 8346

[45.] A. A. Ehsanpour, and E. Saadat, 2002. Plant regeneration from hypocotyl culture of *Peganum harmala*. *Pak. J. Bot, 34*, 2002, 253-256.

[46.] R. Yousefi, F. Ghaffarifar, and A. Dalimi. The effect of Alkanna tincturia and *Peganum harmala* extracts on Leishmania major in vitro. *Iran J. Parasitol, 4*, 2009, 40-47.