International Journal of Secondary Metabolite

Journal homepage: http://ijate.net/index.php/ijsm
http://dergipark.gov.tr/ijsm

ISSN: 2148-6905

Pharmacological studies of Syrian rue (*Peganum harmala* L., *Zygophyllaceae*)

Nazim A. Mamedov, Ardalan Pasdaran, Nilufar Z. Mamadalieva

To cite this article: Mamedov, N.A. Pasdaran, A., Mamadalieva, N.Z. (2018). Pharmacological studies of Syrian rue (*Peganum harmala* L., *Zygophyllaceae*), *International Journal of Secondary Metabolite*, 5(1), 1-6. DOI: 10.21448/ijsm.335539

To link to this article: http://ijate.net/index.php/ijsm
http://dergipark.gov.tr/ijsm

IJSM International Journal of Secondary Metabolite

Int. J. Sec. Metabolite, Vol. 5, Issue 1 (2018) pp. 1-6

Research Article

ISSN: 2148-6905 online Journal homepage: http://www.ijate.net/index.php/ijsm

Pharmacological studies of Syrian rue (*Peganum harmala* L., *Zygophyllaceae*)

Nazim A. Mamedov[1,*], Ardalan Pasdaran[2], Nilufar Z. Mamadalieva[3]

[1]Medicinal Plants Program, Stockbridge School of Agriculture, University of Massachusetts, Amherst MA 01003, USA
[2]Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Institute of the Chemistry of Plant Substances, Uzbekistan Academy of Sciences, Mirzo Ulugbek str. 77, Tashkent 100170, Uzbekistan

Abstract: Syrian rue (*Peganum harmala* L., *Zygophyllaceae*) has been used in traditional medicine of Central Asia, the Middle East, and Caucasus areas (Azerbaijan) for centuries, mainly as ritual and psychedelic plant. At full growth, this erect, dichotomously branched shrub is about 1 m in height with a dense foliage consisting of narrow, linear, pinnate leaves with acute spreading lobes, and small solitary, axillary, white flowers and globe capsules enclosing numerous angular seeds. All parts of the plant (including roots) contain alkaloids. The seeds contain β-carbolineses (harmine, harmalol and harman) with the active hallucinogen being the alkaloid harmine. The seeds contain a red pigment used for coloring wool and carpets and for use as a spice and, in traditional medicine, as valuable aphrodisiac.

ARTICLE HISTORY

Received: 3 June 2017

Revised: 10 August 2017

Accepted: 19 August 2017

KEYWORDS

pharmacological studies, Syrian rue, *Peganum harmala* L., *Zygophyllaceae*

1. Introduction

Syrian rue (*Peganum harmala* L., Zygophyllaceae) is a native plant of the Middle East that has become widely distributed in dry places throughout Central Asia and the Caucasus (Azerbaijan) (as a wild plant and as a weed in grain plantations). For many centuries, Syrian rue was used in traditional medicines of the Middle East, Central Asia, Azerbaijan, and India as ritual, psychedelic plant, for coloring wool in carpets, and as a spice [1, 2, 3, 4, 5, 6]. Traditional uses of the plant include treatment of stomach pain, external wounds and rashes.

The plant, which is hallucinogenic and toxic, is used for antispasmodic and painkilling effects, particularly in treatment of Parkinson's disease, eye afflictions, rheumatism, nervous disorders, and impotence. Smoke from burning pods with seeds is a traditional intoxicant, relaxant, and sexual stimulant in countries of Central Asia. The smoke from burning seed pods

*Corresponding Author E-mail: mamedov@cas.umass.edu

ISSN: 2148-6905 online /© 2018 DOI: 10.21448/ijsm.335539

which commonly named "Esphand" is also believed to have antiseptic properties and used for treatment of palsy and lumbago [7]. Seeds in the form of powder are given as anthelmintic against tapeworms [5]. A decoction of the seeds is considered useful in the treatment of fevers and malaria [8]. Among the many benefits claimed for *P. harmala*, are use as a vasorelaxant [9], as a treatment for hypertension and diabetes [3], as a, analgesic and insecticide, and of behavior modifier of pests [10].

The chemical composition of *P. harmala* has been investigated since the 1970s [2, 11]. Macro- and microelements content which can have a direct impact on pharmacological activities of medicinal plants [12], are also a key to understand many diseases [3]. Among the important phytochemicals of *P. harmala* β- carboline alkaloids constitute the most important constitutions of this plant. This class of alkaloids is well known for several pharmacological activity include neuropsychological effects, that as an major investigated mechanism these compounds can facilities dopaminergic effects and intract with D_1 and D_2 dopamine receptors in brain also observed some cross interaction between these chemicals and benzodiazepine receptors [13, 14, 15]. *P. harmala* main alkaloids (harmine and harmaline in seeds and roots) can be played role in antinociceptive and antidepressant effects of this plant [16, 17, 18].

Medicinal plants used in herbal medicine for treatment of depression accumulated K and Mg most among other macro-elements and Se, Sr, and Ba among microelements. Mg and K are known as supplements used to reduce anxiety, depression, and effects of stress on central nervous system and cardiovascular system [3, 12, 19]. This study investigated both the macro and microelements in aboveground parts of *P. harmala*.

2. Material and Methods

The study was performed in Spring 1994 in Biological Center of National Academy of Sciences (Baku, Azerbaijan) by Dr.Mamedov with assistance of graduate students [20]. Plant material was collected from Zagulba (Apsheron peninsula, near Baku). Voucher specimen was identified by Dr.Mamedov and kept in Herbarium of Komarov Botanical Institute of National Academy of Sciences.

Analysis of macro- and microelements of *Peganum harmala* showed that aboveground parts of the plant accumulated K and Ca most among other macro-elements and Zn, Sr, Mo, Se, and Ba among microelements (Table 1.)

Treatment of Hypertension and Diabetes: A. Tahroui and colleagues did an ethnopharmacological survey in south-eastern Morocco which showed *P. harmala* along with five other plants are used in folk medicine for the treatment of hypertension and diabetes. Their survey shows that the alcoholic extract of *P. harmala* is taken orally and this treatment is considered effective in the region [21].

Vasorelaxant: H. Berrougui and colleagues show the vasorelaxant effects of harmine and harmaline [9]. These two alkaloids abundantly present in *P. harmala*, and are readily extractable via alcoholic extraction. Both alkaloids are not effective as a contact poison but active in vapor form [5].

Analgesic Effects: L. Farouk and colleagues [22] injected experimental mice with formaline, which causes acute pain, then they treated the mice with alkaloid extract of *P. harmala*. Animals treated with alkaloid extract of *P.harmala* showed ~35 to 69% pain inhibition.

Insecticidal Effects: In 2008 R. Jbilou and colleagues have studied the effects several plant extracts (including *P. harmala* extract) on α-amylase activity and off-spring production of the red flour beetle, *Tribolium castaneum* (Herbst). Their study shows that treatment with *P.*

harmala methanolic extract causes a 58±5.7 percent larval mortality. This is quite significant in the experimental group; however, the authors do not clarify whether they had controlled for the possible effects of methanol or not (10). A paste of the seeds made with mustard oil is used to kill head lice [3].

Anti-cancer properties: F. Jahaniani and colleagues report xanthomicrol present in *P. harmala* to be cytotoxic but also a possible anti-cancer agent [23].The authors have tested extracts of *P. harmala* on different human cell lines and the extract shows obvious cytotoxic properties. F. Jahaniani also claim in vivo tumor suppressing effects for *P. harmala* alcoholic extract administration in mice.

Table 1. Macro- and micro-element content of *Peganum harmala* L. (above ground parts).

Chemical element	Concentration	References
Ash	10.55	Mamedov et al., 1994
macro-elements (mg/g)		
Ca	16.55	Mamedov et al., 1994
K	32.95	Mamedov et al., 1994
Mg	5.9	Mamedov et al., 1994
Fe	0.15	Mamedov et al., 1994
micro-elements (μg/g)		
Mn	13	Mamedov et al., 1994
Cu	37	Mamedov et al., 1994
Zn	78.5	Mamedov et al., 1994
Mo	64.8	Mamedov et al., 1994
Cr	0.45	Mamedov et al., 1994
Al	10.2	Mamedov et al., 1994
Ba	69.76	Mamedov et al., 1994
Se	0.19	Mamedov et al., 1994
Ni	2.06	Mamedov et al., 1994
Sr	190	Mamedov et al., 1994
Pb	0.98	Mamedov et al., 1994
B	59	Mamedov et al., 1994

Depression and sleep-loss treatment: According to traditional herbal medicine of Azerbaijan Syrian rue is useful for treatment of insomnia and depression [2]. In Spring 1994 Dr.Mamedov studied possibility of use *Peganum harmala* for treatment of mild to moderate depression, anxiety and insomnia in Baku (Azerbaijan). Plant material for the study collected from Zagulba (Apsheron peninsula, near Baku), Voucher specimen was identified by Dr.Mamedov and kept in Herbarium of Komarov Botanical Institute National Academy of Sciences. Result of this study was reported in May 1994 at the seminar in National Institute of Post-graduate Training for Medical Doctors in Baku. The group of ten young veterans of war in Karabakh (Azerbaijan) suffering from medically recognized mild to moderate depression, anxiety and sleeping disorder was selected for the study. The men aged from 19 to 25 years old and were outpatients of City Psychiatric Clinic. Patients were required to be free of all psychotropic medications for at least 4 weeks before study entry. *P.harmala* was administered in traditional way. The whole herb were used, 50g of dried pods used each time. Every day bedrooms were heavily fumigated with burning dried pods of *P.harmala* before sleep time. As

a result of studies 8 men (19-25) reported to their primary physicians overall improvement and better sleep after six weeks (80 percent), one man (23 years old) asked for one more week and reported improvement after 7 weeks (10 percent), and one man (25 years old) reported no improvement after 6 weeks and discontinued use of *P.harmala* (10 percent) (Table 2.). There were no side effects reported after using plant. Studies have shown that Syrian rue is safe and might be used as an alternative to conventional drugs for treatment of mild to moderate depression, anxiety and insomnia. *P.harmala* chemical compounds offered various effects on central nervous system (CNS). Among of these compounds, alkaloids have unique position in CNS neurotransmitters receptors regulation changes. Harmine, harmaline and tetrahydroharmine that known as harmala alkaloids, belong to β-carbolines. These alkaloids are found mostly in the seeds and the roots (2–7% by dry weight). β-carbolines chemical compounds could change CNS neurotransmitters and caused some behavioral changes such as hallucinogenic effects (23, 24, 25). Psychoactivity of these alkaloids due to direct activation of the 5-HT2A or 5- HT2C receptors (26). Harmala alkaloids also interact with benzodiazepine receptors that caused a mild sedative effect [27]. Competitive and reversible inhibition of monoamine oxidase type-A (MAO-A) enzymes have been determined for haramine and harmaline, similar serotonin uptake inhibition also detected for tetrahydroharmine [28].

Table 2. Using of *Peganum harmala* L. for treatment of mild to moderate anxiety and depression

Number of people	Age	Days	Result	Percent
8	19-25	42	Improvement	80
1	23	49	Improvement	10
1	25	42	No improvement	10
10				100

Note: Study participants were required to not take any psychotropic medication for at least four weeks prior to the study.

3. Results and Discussion

We used whole plant for our trial. Meanwhile, we didn't determine which biologically active compounds were responsible for observed pharmacological actions. Syrian rue has a big potential as medicinal plant. Although, plant contains toxic alkaloids and was never used internally, its use as psychedelic and ritual plant is widely spread in Middle East and Central Asia for centuries. Future studies are needed to identify biologically active compounds responsible for healing abilities of Syrian rue.

4. Conclusion

Syrian rue (*Peganum harmala* L., Zygophyllaceae) used for centuries in traditional medicine. Our study shows that *Peganum harmala* has a potential for treatment of anxiety and depression. More clinical studies are needed in order to confirm activity of *Peganum harmala* for treatment of anxiety and depression.

5. References

[1]. Shultes, E. (1976). *Hallucinogenic plants*, Golden Press, New York

[2]. Damirov, I.A., Prilipko L.I., Shukurov J.Z., and J.B.Kerimov. (1983). *Medicinal plants of Azerbaijan*, Maarif, Baku (in Russian)

[3]. Muravyova, D.A. (1991). *Pharmacognosy*, Medicina, Moscow (in Russian)

[4]. Khalmatov, H.H., Kharlamov I.A., and Z.I. Mavlankulova, (1998). *Medicinal plants of Central Asia,* Ibn Sina Press, Tashkent (in Russian)

[5]. Kapoor, L.D. (2001). *Handbook of Ayurvedic Medicinal Plants*, CRC Press

[6]. Daniel, M. (2006). *Medicinal Plants:Chemistry and Properties*, Science Publishers, Enfield, NH, USA

[7]. Shahverdi, A. R., H.R.Monsef-Esfahani, B.Nikavar, L. Bitarafan, S. Khodaee, N.Khoshakhlagh (2005). Antimicrobial activity and main chemical composition of two smoke condensates from Peganum harmala seeds. *Zeitschrift für Naturforschung*, 60(9-10): 707-710.

[8]. Alakbarli, F. (2006). *Medical Manuscripts of Azerbaijan*, Heydar Aliyev Foundation, Baku

[9]. Berrougui, H.; Martín-Cordero, C.; Khalil, A.; Hmamouchi, M.; Ettaib, A.; Marhuenda, E.; Herrera, M. D.(2006). Vasorelaxant effects of harmine and harmaline extracted from Peganum harmala L. seeds in isolated rat aorta. *Pharmacological Research, 54*, 150-157.

[10]. Jbilou, R.; Amri, H.; Bouayad, N.; Ghailani, N.; Ennabili, A.; Sayah, F.(2008). Insecticidal effects of extracts of seven plant species on larval development, alpha-amylase activity and offspring production of Tribolium castaneum (Herbst) (Insecta: Coleoptera: Tenebrionidae). *Bioresour. Technology, 99*, 959-964.

[11]. Agedilova, M. T.; Turmukhambetov, A. Z.,; Schultz, E. E.; Shakirov, M. M.; Adekenov, S. M. (2006). Components of the aerial part of Peganum harmala. *Chemistry of Natural Compounds, 42*, 226-227.

[12]. Somer E., (1992). *The essential Guide to Vitamins and Minerals*, NY: Harper Collins Publishers, New York

[13]. Bourke, C.A., M.J.Carrigan, R.J. Dixon (1990). Upper motor neurone effects in sheep of some beta-carboline alkaloids identified in zygophyllaceous plants. *Australian veterinary journal*, 67(7): 248-251.

[14]. Herraiz T., González D., Ancin-Azpilicueta C., Arán V.J., Guillén H. (2010). β-Carboline alkaloids in *Peganum harmala* and inhibition of human monoamine oxidase (MAO). *Food and Chemical Toxicology*, 48 (3): 839-845.

[15]. Farzin, D., et al. (2011). Effects of harmane and other β-carbolines on apomorphine-induced licking behavior in rat. *Pharmacology Biochemistry and Behavior,* 98(2): 215-219.

[16]. Youdim, M. B. and M. Weinstock (2004). Therapeutic applications of selective and non-selective inhibitors of monoamine oxidase A and B that do not cause significant tyramine potentiation. *Neurotoxicology,* 25(1): 243-250.

[17]. Herraiz, T. and C. Chaparro (2005). Human monoamine oxidase is inhibited by tobacco smoke: β-carboline alkaloids act as potent and reversible inhibitors. *Biochemical and biophysical research communications,* 326(2): 378-386.

[18]. Youdim, M. B., D, Edmondson, K.F. Tipton (2006). The therapeutic potential of monoamine oxidase inhibitors. *Nature Reviews Neuroscience,* 7 (4): 295-309.

[19]. Murray, M. (1996). *Encyclopedia of Nutritional Supplements*. Prima Publishing

[20]. Mamedov N., Aliyeva S., and T Musayeva, (1994). Syrian rue in traditional herbal medicine of Azerbaijan (independent study project), National Academy of Sciences, Institute of Botany, Baku (in Russian)

[21]. Tahraoui, A.; El-Hilaly, J.; Israili, Z. H.; Lyoussi, B. (2007). Ethnopharmacological survey of plants used in the traditional treatment of hypertension and diabetes in south-eastern Morocco (Errachidia province). *J. Ethnopharmacol., 110*, 105-117.

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

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

[24]. Baum, S. S., R.Hill, H. Rommelspacher (1996). Harman-induced changes of extracellular concentrations of neurotransmitters in the nucleus accumbens of rats. *European journal of pharmacology,* 314(1): 75-82.

[25]. Grella, B., M. Dukat, R. Younga, M. Teitlerb, K. Henrick-Davisb, C.B. Gauthierb, R.A. Glennon (1998). Investigation of hallucinogenic and related β-carbolines. *Drug and Alcohol dependence,* 50(2): 99-107.

[26]. Glennon, R. A., M. Dukat, B. Grella, Seoung-Soo Hong, L. Constantino, M. Teitler, C. Smith, C. Egan, K. Davis, M. Mattson (2000). Binding of β-carbolines and related agents at serotonin (5-HT 2 and 5-HT 1A), dopamine (D 2) and benzodiazepine receptors. *Drug and Alcohol dependence,* 60(2): 121-132.

[27]. Stephens, D., H.H. Schneider, W. Kehr, Jensen L.N., Petersen E., Honore T. (1987). Modulation of anxiety by β-carbolines and other benzodiazepine receptor ligands: relationship of pharmacological to biochemical measures of efficacy. *Brain research bulletin,* 19(3): 309-318.

[28]. Brush, D. E., S.B. Bird, E.W.Boyer (2004). Monoamine oxidase inhibitor poisoning resulting from Internet misinformation on illicit substances. *Journal of Toxicology: Clinical Toxicology,* 42(2): 191-195.