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Proceeding Paper

Wild Rue (*Peganum harmala*), an Extraordinary Source of Natural Products and Pharmacological Benefits †

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Abstract: *Peganum harmala* is a perennial herbaceous, glabrous plant mainly found in North Africa, the Middle East, and Central Asia. Its seeds showed that alkaloids belonging to the β-carboline family such as harmaline, harmine, harman, harmalol, and harmol which are responsible for a wide range of pharmacological impacts. The main components from its seeds are tetradecane, dodecane, hexadecane, methyl dodecanoate, heptadecane, 2-octanol benzoate, methyl tetradecanoate, octadecane, 2,6,10,14-tetramethyl pentadecane, 2,6,10,14-tetramethyl hexadecane, methyl hexadecanoate, nonadecane, eicosane, dibutyl phthalate, henicosane, methyl oleate, harmine, docosane, and tricosane. The current searching was done by the keywords in main indexing systems including Scopus, Pub/Med/MEDLINE, and Institute for Scientific Information Web of Science as well as the search engine of Google Scholar. The most important pharmacological benefits of *Peganum harmala* are anti-tumor, anti-cholinesterase, antiparasitic effects, angiogenesis, cytotoxicity and anti-inflammatory effects, anti-cancer, anti-tumor, antioxidant, cerebroprotective, antibacterial, hypoglycemis and pesticide effects. Due to its wonderful pharmacological characteristics, it is a high potential medicinal herb, and it can be suggested to other parts of the world.

Keywords: natural products; medicinal plant; *Peganum harmala*; wild rue; African rue; Syrian rue; harman

1. Introduction

Medicinal plants and herbs are potential source of natural products which play a significant function in preventing and treatment of different human diseases [1–10]. Medicinal and aromatic plants as an important source of alternative and complementary medicine have been recently bring many hopes in reducing of symptomatology and curing associated with many diseases [16–21]. *Peganum harmala* is used traditionally as emmenagogue and abortifacient agent in West of Asia and North of Africa, which belongs to the family of Zygophyllaceae, and it is a wild growing flowering plant; moreover, its seeds are the major medicinal part of the plant. It is a traditional medicinal plant which is used various purposes, and it is considered as one of the most notable medicinal plant in Iranian traditional medicine [21–34]

This review article emphasizes on the need of widespread studies and researches for covering the supplementary knowledge and information on the importance of this wonderful medicinal plant, and also it suggests more evidences for other researches to utilize *Peganum harmala* as an ancient effective natural drug in an organic life.

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2. Chemical Components, Nutritional Composition, and Pharmaceutical Benefits of *Peganum harmala*

Peganum harmala's seeds and fruits are digestive, diuretic, antipyretic, emetic, hallucinogenic, antispasmodic, narcotic, nauseant, and a uterine stimulant [35,36], and its leaves used in the treatment of colic, asthma, neuralgia, dysmenorrhea, hiccups, rheumatism, and hysteria [37]. Massoud et al. [38] expressed that the main alkaloids present are harmine, harmaline, harmalol, and peganine; and Lamchouri et al. [39] also showed that harmaline which is the active principle of its seeds and its derivatives cause agitation, visual troubles, delirium, loss of coordination and it can produce paralysis at high dose. Faridi et al. [40] revealed that the major constituents of *Peganum harmala* smoke were α-pinen, styrene, limonene, and those of the volatile oil were trans-verbenole, α-pinene, and sabinene. Phytochemical screening in the leaves showed the presence of alkaloids, flavonoids, tannins, saponins, terpenoids, glycosides, and steroids [41,42]. Major metabolites in Peganum harmala extracts according to H-NMR analysis were valine, isoleucine, alanine, threonine, acetic acid, lysine, proline, succinic acid, 4-hydroxyisoleucine, asparagines, malic acid, phosphorylcholine, choline, sucrose, β-glucose, betaine, harmaline, harmine, formic acid, and vasicinone [43,44]. *Peganum harmala* alkaloids extract may be helpful in providing of new cytotoxic agents against chem-resistant cancer cell, and its extracts significantly decreased the growth rate and cell survival of cancer cell lines, and the extract may induce cell death regarding natural cell growth; moreover, the seed extract induced cell death and decreased the cell growth in the breast cancer cell lines, and they have anti-proliferative effects against tumor cells via induction of apoptosis and inhibition of cell migration [45–47]. Harmine was identified as antiviral active compound, its aerial parts are an effective traditional folk medicine for the treatment of cough with potent antitussive, expectorant and bronchodilating activities, furthermore, antiviral activity of extract against influenza virus is most probably associated with inhibiting viral RNA transcription [48–50]. Harmine reduced inflammatory cytokines and averted inflammatory damage in the lung of LPS (lipopolysaccharides)-challenged mouse; methanol extracts of *Peganum harmala* has also the highest anti-inflammatory activity [51,52]. Treatment with 4-HPS (4-hydroxypipecolic acid) stimulated both glucose uptake and glucose transporter-4 (GLUT4) translocation from intracellular to cell surface in skeletal muscle cells in a concentration-dependent manner, which might be leading to antihyperglycemic effect [53]. The ethanolic extracts of *Peganum harmala* has anti-tuberculosis effects comparable to isoniazid and rifampin and can be good candidates for novel and safe natural products against tuberculosis [54,55]. Leishmaniasis is a major public health problem worldwide, and *Peganum harmala* has natural components with anti-Leishmania activity (108,109). The alkaloid may be valuable source for lead components discovery and drugs development for treatment of memory impairment such as Alzheimer's disease [56–58].

3. Conclusions

The main reason of antioxidant activity of *Peganum harmala* are phenolic compounds. The most important applications of *Peganum harmala* in traditional pharmaceutical sciences are in gasterointestinal, cardiovascular, endocrine, nervous, tumors and neoplasm, pain relieving, organisms, respiratory, diabetes, anti-pyretic, hair and skin, disinfectant, arthritis, rheumatism, ulcers and inflammation. The most notable pharmacological impacts of *Peganum harmala* are in nervous system, cardiovasuclar system, antineoplasm, antimicrobial effects, endocrine, nervous system, osteocytes, gastrointestinal effects, and respiratory system. On the basis of its tremendous benefits, *Peganum harmala* can be considered as a high potential herb, which can be suggested for applications, however, more researches are needed about its efficacy and safety.

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