

Review / Derleme

Üzerlik tohumun [*Peganum harmala*]'daki harmalinin SSRI's [Selectif serotonin geri alım inhibitör] etkisi
The SSRI [Selective serotonin reuptake inhibitor] effect of harmaline in Syrien Rue [*Peganum harmala*]

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ÖZET

Harmaline ve tetrahydroharmine gibi alkaloidlerin en iyi bilinen kaynaklarından ilki üzerlik veya Suriye sedef otu olarak bilinen bitkidir. Harmal alkaloidleri, farmakolojik olarak geniş bir kullanıma sahiptir. B-karbolin alkaloidlerinin [harmine, harmal, harmalin ve harmalol] çoğu üzerlik tohumlarında az bir kısmı ise bitkinin üst kısımlarında bulunmaktadır. *Peganum harmala*, merkezi sinir sistemini uyaran ve MAO-A inhibitörünü tersine çeviren bir bitkidir. Genellikle otların antidepresanlarla birlikte kullanılmasında dikkatli olunmasında ve hastaların bu kombine kullanımında dikkatle takip edilmesi gerektiği söylenir. Bitkiler ile antidepresan ilaçların birlikte kullanıldığı çalışmalar olduğu gibi yan etki görüldüğü çalışmalar da vardır. Önemli olan hangi ilaç ile hangi bitkinin ne oranda ve ne sıklıkta kullanılabilceğinin tespit edilmesidir.

Anahtar Kelimeler: Üzerlik tohumu, harmalin, SSRI.

ABSTRACT

Harmal [*Peganum harmala*] or Syrian Rue is a plant from which harmine was first isolated, as well as a source of alkaloids, i.e., harmaline and tetrahydroharmine. The alkaloids in harmal, has a wide spectrum of pharmacological actions in various scales. The β -carboline alkaloids [harmine, harmal, harmaline and harmalol] are found in the harmal seeds and a minor amounts in the aerial parts of plant. *Peganum harmala*, is a central nervous system stimulant and a reversible inhibitor of MAO-A. Generally speaking, herbs should be combined cautiously with antidepressants and patients should be monitored carefully after starting combination therapy. There are few studies on whether herbs and antidepressant drugs work together well or might cause adverse effects. What is important is the use of drugs with which the plant, that is to determined how much and how often.

Key Words: Syrien rue, harmaline, SSRI.

INTRODUCTION

Many species have been found to contain beta-carboline harmala alkaloids with anti-depressant properties. There are several reports in the literature indicating a great variety of pharmacological activities for *Peganum harmala* L such as anti-bacterial, antifungal and MAO-inhibition [1].

The passiflora family contains small amounts of harmala alkaloids, harmane [passaflorine], and possibly harmine [telepathine], harmaline, harmol, and harmalol. The presence of the last four in *P. incarnata* is disputed [2].

Wild rue [*Peganum harmala*] which contains significant amounts of these substances [and after which they were named] is used therapeutically as a stimulant rather than a sedative [U.S. Dispensatory, 1947]. The harmala alkaloids which is the active principle in passiflora might also be a cause for concern for kidney toxicity, as these substances are toxic to the kidneys [3].

THE MECHANISMS OF ACTION

In terms of its possible origins, Richard Spruce [1873] is reported to have observed natives chewing *B. caapi* stems, perhaps to obtain a mild serotonergic buzz from the harmala alkaloids contained therein, or, as is also likely, for basic hygienic purposes [4].

In the late 1950s, Udenfriend, Witkop, Redfield, & Weissbach [1958] reported that the harmala alkaloids were short-acting reversible inhibitors of monoamine oxidase [MAO], an enzyme found in various parts of the human body, including the gut and the brain. MAO in humans has two types, MAO-A and MAO-B, both of which are catalysts in the deamination of some biogenic amine neurotransmitters, such as dopamine and norepinephrine; however, MAO-A is the type that is involved in the metabolism of tryptamine molecules, such as serotonin [5-hydroxytryptamine] and DMT [dimethyltryptamine] [5].

Callaway and Grob [1998] reported that potential adverse reactions may result from ayahuasca drinking by individuals who are also taking selective serotonin reuptake inhibitor [SSRI] medications [6].

Harmaline has also been reported to induce spasmolytic effects on guinea-pig isolated trachea with interaction to muscarinic, histaminic and β -Adreno-receptors [7].

Peganum harmala [Syrian rue] seed and root is a less well-known stimulant. Syrian rue contains the indole alkaloids harmaline and harmine among others. These are classic inhibitors of monoamine oxidase [MAO] in vitro. Syrian rue will tend to slow and strengthen the pulse while lowering blood pressure. If blood pressure becomes excessively low [to the point of causing dizziness] or, if hallucinations occur, Syrian rue should be discontinued. The more famous harmine alkaloid-containing plant is *Banisteriopsis caapi* [ayahuasca]. This use suggests that native peoples were taking advantage of MAO inhibitors long before they were discovered by pharmaceutical science [8]. Interestingly, Syrian rue was traditionally used as a vermifuge and amebicidal agent long before it was brought to the New World. The plant has shown antimicrobial activity in vitro [9].

N,N-dimethyltryptamine [DMT], Orally ingested DMT presents a special case, as DMT on its own is not orally active. This is because the drug is rapidly metabolized by the enzyme monoamine oxidase [MAO], which breaks down endogenous monoamines [the neurotransmitters serotonin, dopamine, adrenaline, and noradrenaline]. MAO in general exists as two isozymes: MAO-A and MAO-B. It is MAO-A that exclusively metabolizes and thereby deactivates both serotonin and DMT; the aliphatic nitrogen atom [the "monoamine"] of both serotonin and DMT is vulnerable to oxidation by MAO-A, forming inactive, watersoluble metabolites that are eventually excreted in the urine [10].

CONCLUSION

In Yemen it was used to treat depression, [11] and it has been established in the laboratory that harmaline, an active ingredient in *Peganum harmala*, is a central nervous system stimulant and a "reversible inhibitor of MAO-A [RIMA]," a category of antidepressant [12].

Harmaline, like other harmala alkaloids, does not seem to possess classical psychedelic activity [that activity similar to LSD, psilocybin/psilocin or mescaline]. The problem this individual had was that Syrian rue, *Peganum harmala*, contains several alkaloids that can either inhibit the enzyme monoamine oxidase that is responsible for the metabolism of serotonin or bind to serotonin receptors in addition to a variety of other effects that include production of tremors.

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