Persian Herbal Medicines with Anxiolytic Properties

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Receive: 20 June 2011 **Acceptance:** 6 Aug. 2011

Abstract

Anxiety disorders are amongst the most popular diseases which interfere with normal life. Benzodiazepines are used as a first line of treatment, but difficulties with pharmacotherapy of anxiety disorders such as dependence and low response rate, encourage researchers to find new approaches.

From the past, the role of medicinal plants have been a subject of intense interest. In this respect, *Citrus aurantium, Coriandrum sativum, Crocus sativus, Echium amoenum, Nepeta persica Boiss, Stachys lavandulifolia and Salix aegyptiaca* are widely used by Iranian population. This review summarized the information on Iranian plant species that have been explored for their potential anti-anxiety profile using validated animal models, doses and possible mechanism.

Keywords: **Anxiety disorders, Iranian native plants, Stress**

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Introduction

Anxiety disorders are among the most prevalent disorders in the world that are characterized by symptoms of overriding apprehension or mental tension which could easily disrupt normal daily activity. Most anxiety disorders tend to run a long course and thus require long-term treatment [1]. Wide range of drugs, from over the counter-, prescriptions and herbal-anti-anxiety medicines has been used in the past to treat various forms of anxiety disorders. Although synthetic drugs such as benzodiazepines have the advantage of rapid onset of action, they have the potential to interfere with patient's normal activity and often difficult to stop once started the therapy. These Problems and the host of other side effects that exist with synthetic anxiolytic drugs have enforced more people to seek natural and herbal therapies [2-6]. Some of the best examples of anxiolytic herbs and their clinical effectiveness have been reviewed elsewhere by Gilhotra [7]. Iran's varied topography and climate have given rise to a remarkable diversity of plant species that have not been fully explored for their pharmacological properties. During the last decade, several studies have examined the effectiveness of local plants that are traditionally known to cause anxiolytic effects [8]. As some articles have emphasized on other Iranian herbal medicines which are used in other diseases like diabetes [9], the aim of present paper is to collect the available information on Iranian plant species that have been explored for their potential anti-anxiety profile using validated animal models, dose and possible mechanisms.

Citrus aurantium

Citrus aurantium is indigenous to tropical regions of Iran and commonly known as sour orange. The flower extract has been reported to show anxiolytic effect in elevated plus mase model of anxiety in rats at doses of 62.5 and 125 mg/kg [10], which exploration of open arms by animals showed anxiolytic effect. The extract has been found to contain flavonoids include neohespiridine, as they have affinity to bind to benzodiazepine receptors [10].

Coriandrum sativum

Coriandrum sativum L. (Umbelliferae) is widely cultivated in Isfahan, center part of Iran, and has been indicated for some of medical conditions such as dyspeptic complaints, loss of appetite, convulsion, insomnia and anxiety in folk medicine [11]. The aqueous extract of coriander seed at doses of 50, 100 and 500 mg/kg showed anxiolytic effects on EPM model in mice, and also produced reduction of the locomotor activity of the animals in a dose-dependent manner. In addition administration of coriander extract had influence on motor coordination in a dose-dependent manner, suggesting possible muscle-relaxant effects [12].

Crocus sativus

Iranian *Crocus sativus* L. (Iridaceae) which is called Saffron is native to Khorasan (north east of Iran) and is known to be used for insomnia and anxiety in traditional medicine [13]. The aqueous extract reduced locomotor activity dose dependently and showed a significant increase in the time on the open arms. At the hypnotic test induced by Phenobarbital 300 mg/kg, only a dose of 0.56 g/kg of saffron increased the total sleep. The plants constituent, Crocin, showed no anxiolytic, hypnotic or myorelaxation effects. Safranal, another constituent, in higher doses (0.15 and 0.35 ml/kg) showed anxiolytic effects. It increased the total sleep time dose

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dependently. This constituent at lower doses (0.05 and 0.15 ml/kg) decreased some locomotion activity parameters and suggested that had no effects on motor coordination. Finally it is believed that saffron aqueous extract and Safranal have anxiolytic and hypnotic effects [14].

Echium amoenum

Echium amoenum Fisch. Is a biennial herb which belongs to the northern part of Iran and to Boraginaceae family .Its decocts of dried violet-blue petal has long been used as a tranquillizer among the Iranian people [15, 16]. In mice model of anxiety (EPM) 50 mg/kg of the plant extract produced anxiolytic effect in compare to diazepam, beside that in the locomotor study, plant extract at 50 mg/kg produced a significant reduction in locomotor activity, that showed sedative effect of extract but less than diazepam. Interestingly the extract of *E. amoenum*, did not significantly affect the duration of sleep induced by ketamine, so it showed certainly different sedative effect than diazepam [17].

***Nepeta persica* Boiss.**

Nepeta is a genus of perennial or annual herbs that belongs to lamiaceae family. 67 species are available in Iran [18]. *Nepeta* species, which grow extensively in different parts of the country, are used in folk medicine as antispasmodic, expectorant, diuretic, antiseptic, antitussive, antiasthmatic and febrifuge activities [19 - 21]. In the EPM model of anxiety in mice the hydro alcoholic extract of *N. persica* at a dose of 50 mg/kg significantly showed anxiolytic effects, but unlike many plants with sedative effects, with increasing doses of *N.persica* extract showed simulative property in locomotor activity test [22].

Salvia reuterana

Salvia reuterana Which is called Mariam Goli in Farsi is a perennial herb, grows in the center of Iran. [21]. In a study, which provides a support to use of *Salvia reuterana,* the hydro alcoholic extract at dose of 100 mg/kg markedly reduced anxiety in EPM model test in mice [23]. In the locomotor activity test the extracts had sedative effect much lower than diazepam. The sedative property of the plant extract was further demonstrated by its effects on locomotor activity producing sedation at the dose of 100 mg/kg. Lower doses than 100 mg/kg did neither change the locomotor activity nor had a significant anxiolytic effects. In this study, the sedative effect of the *Salvia reuterana* extract at 100 mg/kg was much lower than those produced by diazepam, thus showing a better profile as an anxiolytic medicine. With increase in dose sedative properties increased but not anxiolytic effects. It anxiolytic mechanism might believed to affect GABA receptors [23].

Salix aegyptiaca

Salix aegyptiaca (Bidmeshk or musk willow) is native plant of Urmia (north-west part of Iran) .The extract of the flowers of *Salix aegyptiaca* on EPM model of anxiety in mice at the doses of 100 or 200 mg/kg i.p or oral produced anxiolytic effects, and reduced locomotor activity. These doses did not affect ketamine induced-sleep intervals [24].

Stachys lavandulifolia

The genus *Stachys*, is belong to the Lamiaceae family. 34 species of this genus are present in Iran and 13 are endemic [8]. *Stachys lavanduifolia,* grows in north east of Iran. It has been used as an anxiolytic in Iranian folk medicine [21]. The hydro alcoholic plant extract at a dose of 100 mg/kg in mice

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exhibited anxiolytic effect in EPM model which was accompanied by a decrease in locomotor activity that suggests its sedative activity. Administration of the extract of *Stachys lavandulifolia* prolonged the duration of sleep and shortened the latency to sleep induced by ketamin which was similar to diazepam [25].

Conclusion

In conclusion, this review has focused on some of native existing anxiolytic plants in Iran (Table 1). However very few of them have been approved to be used clinically. Because studies on these plants are still in such a state of infancy, it is difficult to determine which of them has the best potential to effectively manage the worldwide epidemic of anxiety. Many other trials are needed before these agents are employed as anxiolytics. It is required to determine their effective substances and their mechanisms of action or possible toxicities in the future.

Table 1- Major Persian herbal medicines with anxiolytic activity and their possible pharmacological effects

Herb name	Effect on locomotor activity	Effect on sleep	Dose (in mice)	Possible mechanism
Citrus aurantium	?	?	62.2, 125 mg/kg	Benzodiazepine receptors
Coriandrum sativum	?	Muscle relaxant	50, 100, 500 mg/kg	?
Crocus sativus	reduced	Increased	0.15, 0.35 ml/kg	?
Echium amoenum	Reduced but less than diazepam	No effects	50 mg/kg	?
Nepeta persica	Increased	?	50 mg/kg	?
Salvia reuterana	reduced	Increased	100 mg/kg	GABA
Salix aegyptiaca	reduced	No effect	100, 200 mg/kg	?
Stachy lavandulifolia	Decreased	Increased	100 mg/kg	?

?=unknown

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