MEDICINAL PLANTS USED IN PERSIAN MEDICINE TO TREAT DEPRESSION

Azadeh Kiani1,2, Ali Firoozabadi3*, Hossein Rezaeizadeh4, Hamed Fatemi Abhari5
1Department of Traditional Persian Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
2Research center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
3Research Center for Psychiatry and Behavioral Sciences, Department of Psychiatry, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
4Department of Traditional Medicine, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
5Department of Mechanical Engineering, Islamic Azad University, Abhar Branch, Abhar, Iran

Abstract: Depression is a common psychiatric disorder and a major worldwide health problem. Many herbs can play an important role in the treatment of psychiatric disorders with fewer side effects. Various herbal remedies have been used in traditional Persian medicine (TPM) for depression. Nowadays some of these herbs are used for the treatment of depressed patients. In the current study, known sources of TPM were searched and the writings of prominent scholars and physicians about medicinal herbs that have been used for treatment of depression were collected. PubMed and Google Scholar were then searched and eight medical herbs having the ability to alleviate depression were found. The aim of current study is to summarize the biological activity of some natural antidepressant drugs to further understand the beneficial effects of these herbs against depression. It is hoped that further investigation of medical plants will be conducted for the treatment of depression.

Key words: Herbal medicine; Depression; Medicinal plants; Traditional Persian Medicine

Corresponding author: Azadeh Kiani,
Department of Traditional Persian Medicine,
Shiraz University of Medical Sciences, Shiraz, Iran
Research center for Traditional Medicine and History of Medicine,
Shiraz University of Medical Sciences,
Shiraz, Iran
Email address: Kianiazade@yahoo.com Tel:+987132305887

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INTRODUCTION:
Depression is a chronic, recurring and debilitating illness that has a significant effect on quality of life, including on the health, work, overall functioning, social and family life of the depressed person[1-3]. It is the fourth highest cause of disability globally, with over 150 million people estimated to be suffering from depression. The World Health Organization (WHO) predicts that, by 2020, major depression will be the second most common risk for morbidity after cardiovascular disease [4]. Depression is a multifactorial and complex disease, the etiology of which is not well understood. The pathophysiology of MDD includes at least three main categories: peripheral hormone-type factors, pro-inflammatory cytokines and dysregulation of the hypothalamic-pituitary-adrenal axis. Recently, it has been suggested that an imbalance between the oxidative-antioxidative system and a decrease antioxidant status, plays important roles in the pathophysiology of MDD [5-7].

In traditional Persian medicine (TPM), the symptoms of “malikhulia” or “melancholy” seem to be identical to those of depression. Various herbal medicines have been used in TPM to treat depression. These herbs have been used for years by Persian physicians such as Rhazes and Avicenna for the treatment of depression in humans.

The mechanisms of action for herbal medicines used for treatment of psychiatric disorders involve modulation of neuronal communication by specific plant metabolites that bind to the neurotransmitter/neuromodulator receptors and stimulate or sedate CNS activity, regulating or supporting the healthy function of the expression of antioxidant system [8].

METHODS:
In the current study, known sources of TPM were searched and the impressions of prominent scholars and physicians about herbal medicine that could be used for the treatment of depression were collected. MEDLINE (PubMed) and Google Scholar were then searched and herbal medicines having the ability to treat depression were found. Current knowledge about these herbs and how they act to improve the symptoms of depression are summarized. Their mechanisms of action are also provided.

1. Medical Herbs Used to Treat Depression
Herbal medicines have been preferred since ancient times when treating depression due to their efficacy and their comparative lack of side effects when treating mental disorders (Table 1).

1.1. Melissa officinalis
Melissa officinalis L., known as lemon balm, is a perennial herb belonging to the Lamiaceae family. It is native to southern Europe and northern Africa, the Caucasus and northern Iran. It was commonly used for its antidepressant, antimicrobial, anticancer, anti-stress and anti-anxiolytic, antidepressant, memory improving, anti-inflammatory effects [9]. M. officinalis is an important medicinal plant in the TPM. Avicenna recommended this plant as a medication for all diseases caused by phlegm and black bile, including depression, anxiety, obsession and psychosis [10]. The main active components of M. officinalis are volatile compounds, triterpenes and phenolics [11].

1.2. Echium amoenum
Echium amoenum (Borage) is a wild annual herb that belongs to Boraginaceae family which grows in parts of Europe, Mediterranean region and it is native to Iran. The flowers of borage are known as a traditional remedy and possesses antioxidant, antibacterial, anxiolytic, antidepressant, and immunomodulatory capacities [12]. E. amoenum have been distinguished as an important source of phenolic compounds like rosmarinic acid, cyanidin, and delphinidin [13]. It is a traditional remedy for depression and possesses antioxidant activity because of the presence of anthocyanin [14]. The antidepressant effect of E. amoenum has been demonstrated in several experimental studies in mice and humans [15].

1.3. Lavandula angustifolia
Lavender (Lavandula angustifolia) is a common herb with a long history in folk medicine and continues to be therapeutically used. L. angustifolia is a flowering plant in the family Lamiaceae and is native to the Mediterranean. Lavender oil possesses antibacterial, antifungal, carminative, sedative and antidepressant effects [16]. The antidepressant effects of L. officinalis have been confirmed in human subjects and it is available to treat depression. The antidepressive properties of linalool, the main compound in L. angustifolia essential oil and extract have been demonstrated [17].

1.4. Matricaria recutita Chamomila
Chamomile (Matricaria recutita) belongs to the Asteraceae family and is one of the most popular and widely used medicinal plants in the world. It has been applied as a traditional herbal medicine for its calming effect [18]. The main components of the plant include phenolic compounds, the flavonoids apigenin,
quercetin, patuletin, luteolin and their glucosides Coumarins [19]. Extracts prepared from M. recutita have been reported for a diverse range of pharmacological actions, including antipruritic, anti-inflammatory, antimicrobial and antioxidant activity [20]. The results suggest an antidepressive effect of the chamomile extract. However, at the present stage of study, its antidepressive effect has not been proven [21].

1.5. Crocus sativus L. (Saffron)
Crocus sativus L., commonly known as saffron, belongs to the family Iridaceae. Saffron and its active constituent (crocin) are effective as an antidepressant, memory enhancer and sedative in the treatment of central nervous system disorders [22]. The efficacy of C. sativus for the treatment of mild to moderate depression also has been reported in clinical trials [23,24].

1.6. Terminalia chebula
Terminalia chebula commonly called as black myrobalan, ink tree, or chebulic myrobalan. It belongs to the family Combretaceae [25]. TPM sources report that myrobalan useful for confusion, melancholy (depression), obsession and insomnia [26, 27]. T. chebula has recently garnered the attention of researchers globally because of its reported medicinal anti-oxidant, antibacterial, antifungal, anti-neoplastic, antiviral, anti-diabetic, cardio-protective and immunomodulatory activity [28]. The significant component in this fruit is the tannin, which includes Gallic acid and chebulic acid [29].

1.7. Valeriana officinalis
Valeriana officinalis (Valerianaceae family) is a perennial herb found in North America, Europe, and Asia. V. officinalis is a medicinal plant used in complementary and alternative medicine. It is said to offer sedative and anxiolytic properties. The active components of the plant are the essential oils, valerenic acid and valenol, and a few alkaloids [13].

1.8. Cuscuta chinensis Lam.
Cuscuta chinensis Lam. (Convolvulaceae family) is an important herb in traditional medicine. In ancient Persian medical manuscripts, C. chinensis has been recommended by scholars such as Avicenna (980-1037 CE) and Rhazes (865-925 CE) for the treatment of psychiatric disorders, including depression [30, 31]. Modern pharmacological experiments have demonstrated the different biological activities of this plant. These include hepatoprotective, anti-cancer, anti-oxidation, anti-inflammatory and anti-aging effects. The active constituents in C. chinensis include flavonoids, lignans, cinnamic acid and polysaccharides. Polyphenols and flavonoids have shown multiple pharmacological activities, including antioxidant, antineoplastic and antidepressant effects [32,33].
Table 1: Herbal medicines used in Traditional Persian Medicine to treat depression.

<table>
<thead>
<tr>
<th>Herbal medicine</th>
<th>Common name</th>
<th>Part used</th>
<th>Mechanisms of action</th>
<th>Major active component</th>
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| Melissa officinalis      | Lemon balm  | Leaves    | MAO-A inhibition (in vitro study)  
GABA Transaminase inhibition in self-rated calmness on a human stress tests  
Enhance norepinephrine neurotransmission  
High phenolics content and antioxidant properties [8,11,14] | Citranellal, geraniol                       |
| Echium amoenum           | Borage      | Flowers   | Increase serotonin and dopamine? (in vitro study) [8]  
Inhibition of 5HT reuptake  
Immunomodulation? (not enough data) [21] | Rosaminic acid, cyanidin, delphinidin       |
| Lavandula angustifolia   | Lavender    | Flowers   | GABA modulation [34] | Linalool, linayl acetate |
| Matricaria recutita      | Chamomile   | Flowers   | GABA modulation  
Modulation of monoamine transmission Neuroendocrine modulation [21] | Apigenin | |
| Crocus sativus L.        | Saffron     | Stigma    | Dopamine, norepinephrine, serotonin reuptake inhibition  
GABA agonist  
NMDA receptor antagonism [34,35] | Crocin, safranal |
| Terminalia chebula       | Myrobalan   | Fruits    | Unknown mechanism | Chebulic acid, chebulinic acid |
| Valeriana officinalis    | Valerian    | Roots     | Unknown mechanism | Valerenic acid, valenol |
| C. chinensis Lam.        | Dodder      | Whole plant especially seeds | Unknown mechanism | Quercetin, kaempferol, rutin |
CONCLUSION:
Over the last century, scientific knowledge about psychoactive herbs has progressed remarkably. The natural products which have been considered show promise in acting as antidepressants. This knowledge can produce better antidepressant drugs with fewer side effects.

Saffron therapy is now the second-best documented herbal therapy for symptoms of depression after H. perforatum (St. John’s wort). Herbal remedies, such as M. officinalis, E. amoenum, L. angustifolia and M. Chamomila appear to offer an antidepressive effects, but it must be emphasized that these effects have not been proven thus far. For other herbal products used in TPM, such as T. chebula, V. officinalis and C. chinensis, there have been no or insufficient investigation confirming their benefits as they relate to depression. It has been suggested that an evaluation of the effects of these plants on different aspects of depression should be performed.

We hope that further research on herbal medicine will have benefit for the treatment of depression. Detailed and planned researches in this area provide a new line in the request for effective treatment.

Conflict of interest:
Authors of this manuscript have no conflicts of interest.

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