



REVIEW: The Importance of Using Medicinal Plants and Natural Products in Order to Treat Depression, Regarding Iranian Traditional and Islamic Medicine and Laboratory Studies

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ABSTRACT

Introduction: Depression is a chronic and common disease and is currently used to treat antidepressants such as tricyclics, which sometimes lead to the activity of certain brain chemicals called neurotransmitters. The use of chemical and industrial drugs by their patients can be due to the lack of treatment for depression. Therefore, in order to promote health, the use of natural products and herbs, and clinical trials and studies with traditional medicine approaches to the treatment of depression is important. In the past, natural products have also been used. The Qur'an and Islam, while analyzing the causes and phenomena of depression, have addressed the ways of its treatment. In particular, this study has been conducted in line with the on the revival of traditional Iranian and Islamic medicine, and it seems necessary.

Material and Methods: In this paper, materials based on electronic library resources, including scientific articles and relevant books from foreign and domestic authoritative journals and websites, have been conducted with proper keyword searches. The medicinal herbs used in depression in traditional medicine and modern medicine, the teachings of the Islamic religion, the reports presented in this regard in English and Persian, and the experiences of the several years of research on various indigenous herbs seeking research You know, it was a benchmark for study and was studied after collection.

Results: In traditional medicine, for the treatment of many diseases, such as depression and anxiety, some herbs such as *Citrus aurantium* L. and *Ocimum basilicum* have been known and used for many years. Studies on *Echium amoenum* L. and *Feijoa sellowiana* have also been carried out today. It is also used to treat acupuncture. In traditional medicine, and of course, Islam and the Quran, depression has been discussed and appropriate solutions have been presented. So that natural products derived from medicinal plants are known and recommended. Meanwhile, in Islam and the Qur'an, healthy, halal and herbal remedies have also been addressed. In ancient Traditional Iranian medicine, it has been given great importance to the theme of sport, heroism and its moral outcomes. Also, Islamic scholars believed in the benefits of spiritual education and its role in physical strengthening. Relaxing exercises also significantly reduced depression.

Conclusion: Given that patients with depression may be susceptible to suicide due to frustration. The use of medicinal herbs and traditional medicine and Iranian medicine, in view of their desirable, natural and safe effects, is necessary. According to Islamic texts, practical commitment to Islamic beliefs can be a deterrent to many psychological disorders. Reading the Qur'an, believing in God, practicing the teachings of the Qur'an and prayer, and other divine duties are also effective in creating calm and promoting the health and treatment of diseases such as depression.

Introduction

Depression is a serious, common and chronic disease which is the second cause of death in the world, according to WHO (1). All around the world, even in modern communities, depression affects most groups of people, both with high and low income (2), so the prevalence is around 21 percent (3).

Some of the non-hospitalized patient suffer from major depression. Chronic diseases can also lead to depression. This disorder can cause not feeling joy and also a decrease in function of patients in family, society and social levels. This disorder is reported by signs in psychological, behavioral and physiological levels (4,5). It can begin in childhood and adolescence and increases with aging. Despite the advanced improvement in health science the considerable amount of people don't benefit from the current drug. Depression can affect people of all ages and genders (7,8).

Using chemical and industrial drugs alone, can lead to incomplete treatment. Anti-depression drug groups are TCAs (Tricyclics), MAOI (Monoamine oxidase inhibitor), SSRI (Selective serotonin reuptake inhibitors) and SNRI (Serotonin-norepinephrine reuptake inhibitor). In some cases these drugs can activate some chemicals in brain called neurotransmitters.

In 50s and 60s, the first anti-depressant drugs called Mono Amin Oxidase (MAOs) and TCA which was a great leap in treatment of depression (9). These drugs include Nortriptyline (Pamelor), Amitriptyline (Elavil), Desipramine (Novopramine), Imipramine (Janimine / Tofranil) and citalopram from SSRI group (10).

Common side effects of these drugs are: dry mouth, amaraousis, constipation, problems with urinating, glaucoma, problems with thinking and fatigue. Also it can cause blood pressure and heart problems, it also affects heart beats. In depression, neurotransmitters including serotonin and noradrenalin are affected and because the duration of treatment is long, the side effects are

disturbing.

Other anti-depressant drug in SSRI group are Sertraline (Zoloft), Fluoxetine (Prozac), Paroxetine (Paxil) (11). Side effects are less than TCAs and include headache, sexual dysfunction, anger, loss of appetite, nausea and sleeping disorder. Also in people who are consuming Fluoxetine other side effects are suffering from fatigue and may not be able to stand up and treatments are time-consuming and expensive (12), so finding treatments which is more economic and have higher efficacy but lower side effects is an active research base in psychiatry (13)

Generally, chemical drugs are not accepted by patients due to their different side effects including bad taste. However, natural plant-based products are safer (14), edible and native so they are more accepted (15).

In Islam, health, like other aspects of life, is well-considered and given ways for improvement. Moreover, body, soul, self-esteem and faith are been talked about. Mental health has always been a challenging issue in all religions so working on it is of high importance (16). Therefore, the importance of using medicinal plants and natural products regarding related experiments is clear. Despite the incomplete treatments of modern medicine, which is the result of lack of solid basis, traditional medicine gives certain solution due to its solid basis. Therefore, this research intends to rectify modern treatments and finding appropriate solutions in traditional medicine and classical medicine and utilizing the results of their reliable therapies.

Methods

This descriptive review article is based on electronic and non-electronic resources, text books, articles from valid websites including ISI (Web of Science), PubMed, Scopus and Google Scholar. Searching keywords are studying medicinal plants and natural products, importance and function of medicinal plants, traditional and Islamic

medicine, depression, side effects of chemical drugs, medicinal plants which is used in depression in novel medicine and also traditional and Islamic one. Over 100 articles between years 1977 and 2019 were reviewed and over half of them were used. Non-electronic resources include reports, books and years of experiment by our research group on different native species, which have been published in Iranian and international articles

Discussion

Traditional medicine and chemical anti-depressants

Every year, all around the world, people suffer from adverse effects caused by chemical drugs which in some occasion lead to some diseases and also death. Some survive and some undergo more side effects and pass (17). Chemical drug have short effects but long uncommendable side effects which cause organ dysfunction and depression (18). Also long time treatment causes intoxication, which leads to acute chemical pancreatitis. Pancreatitis which is a rare side effect of these drugs may cause enteroparasia, long time bed rest and sometimes death (19).

In Traditional medicine of different countries and cultures

Human have been faced depression and searched for the cure since long in the past. In different cultures people used traditional medicine and natural products to cure depression (20). Researches have also been done on animals and reached conclusion (21). As an example, Chinese people have highly used *Ginseng rhizome* (Ginseng Radix et Rhizoma) *Polygalae Radix*, *Acori Tatarinowii* Rhizome *Poria* for treating major depression. Nowadays, it has been proved that some of this herbs can change enzymes that regulate neurotransmitters. So they can be effective in this field (22)

In the research done by Yu et al. (2017) the anti-depressant effect of *Paeonia lactifera Pall* was evaluated on rat. The effect of this

plant in the highest dose (600mg/Kg) was more effective than Fluoxetine (23).

In the research done by Chandrasekhar et al (2017), the anti-depressant effects of hydrolysable tannins of *Terminalia catappa* of the family Combretaceae was evaluated. The results show that this plant can decrease depression caused by stress by nerve regulators of monoamines, CREB, BDNF (Brain-derived neurotrophic factor) and cortisol. It also enhanced oxidative stress. So this plant can be used a supplement for treating depression (24).

Moreover, acupuncture has been used in treating depression. In the research done by Jiang et al (2017) it has been referred to and the anti-depressant mechanisms have been explained by PKA / CREB signaling way. It has been reported that acupuncture can improve this signaling way mostly by regulating phosphorylating levels of CREB (25).

Iranian traditional medicine and medicinal plants

Natural products

In Iranian traditional medicine, some of the herbs and Natural products (26) were used as medicine and food in order to tackle neuronal and behavioral disorder (27). For example, flower of *Citrus aurantium* L. was used to treat neural disorders, hysteria and epilepsy (28). In a research by Sarkolzaei et al (2004), the effect of orange drop on major depression was compared to Fluoxetine. The research was carried out on 150 patients over 15 years old who suffered from major depression. They have reported that the effectiveness of orange drop especially in low doses was more than the classic drug, Fluoxetine, in treatment duration of at least 6 weeks. So it was suggested as a treatment for this disorder (11).

One of the effects of *Ocimum basilicum* is its anti-depressant property. According to Ali et al (2017) the effectiveness of essence of this drug was evaluated mechanistically on changes of behavior, biochemistry and histology caused by Chronic Unpredictable Mild Stress due to depression. They reported

that, this plant can improve CUMS (chronic unpredictable mild stress) condition and decrease the levels of corticosterone and transcription of gene BDNF and GR (Glucocorticoid receptors). *Ocimum* can cause atrophy and apoptosis due to CUMS in hippocampus neurons and increase the number of astrocytes and neural cells. It also increased GFAP (Glial fibrillary acidic protein) cells and also the transcription of BDNF and GR immune-expression in hippocampus (29). These effects were proven by the forced swimming test in animals (30). Extract of basil has enough eugenol which has the anti-depressant effect. The mechanism is probably deamination inhibition of catechol amines in mitochondrial oxidation which leads to higher levels of norepinephrine, epinephrine and serotonin and a lower rate of depression conclusively.

In another study by Ayuob et al (2017), the reduction of stress-induced depression was investigated by the basil plant in mice. It was reported that basil has reduced apoptosis in both neurons and glia. It has also increased neurogenesis. Comparing fluoxetine -like work, it seems that the increased BDNF and GR genes and protein expression are due to the antidepressant effects of this plant (31).

Barberry (*Berberis* L) is one of the most used herbs in traditional medicine of Iran. Most of the properties of this plant is related to berbamine, brolicine, ascorbic acid, berberin, oxiacantine and clombamine which exist in different parts of the plant. They are useful in disease like Alzheimer, hypertension, kidney stone, gout, rheumatism, skin problems and also depression. On photochemical evaluations it is proven that barberry has antioxidant property and the fruit contains vitamin C and malic acid. Barberries extract inhibits MAO-A, which increases levels of monoamines like epinephrine and dopamine in mice brains which causes antidepressant property (32).

In traditional medicine of Iran, saffron (*Crocus sativus* L) of saffron tea was used to treat mild depression and some researches have been done (33). In a research done by Akhoonzadeh et al (2003), in a clinical trial,

extraction, formulation and effectiveness of saffron was done and the effect was compared to Imipramine, an anti-depressant drug. The results show that both of them had the same effect on mild to moderate depression. Side effects were not significant except anti-cholinergic effect of Imipramine. According to previous research and preclinical studies, saffron with dose of 30 mg per day have significant anti-depressant effect on patients with mild to moderate depression (34). This results have been proven in researches of Noorbala et al (2004) (35).

Clinical trial and Laboratory studies

Depression and anxiety is common in some diseases like Alzheimer. The anti-depressant effect of *Lavandula officinalis* was evaluated on mice which were under treatment of scopolamine by Rahmati et al (2017). The results show that lavender extracts improved memory disorder, anxiety and depression behavior due to scopolamine (36).

In a research by Nikfarjam et al (2009), the effect of lavender plant on depression in patients which are under treatment with citalopram was investigated. The results show that lavender had positive effect in these patients and can possibly be used alone or in combination with other anti-depressant drugs (37).

Some other herbs used in traditional medicine that are effective in treating depression are *Rose Consenstrate*, or *Citrus aurantium* L (38), *Hypericum perforatum* L (39), *Echium amoenum* L (40), Primrose Oil. On a research done by Saki et al (2007) it was shown that there is a relationship between low levels of Omega 3 and depression mood. Considering significant amount of Omega 3 in evening primrose oil and its effect on depression regarding its low side effect, it is suggested to be used as a first line treatment in patients with non-psychotic depression (41).

Oil extraction from dried root of valeriana officinalis is used to treat muscle cramps, epilepsy, sleep disorders, stress, panic disorder and also depression. Active substances including isovalerate, valpotriate

and dydrovalerate are very useful in pharmaceutical industries. These substances are used as hypnotics, seductive, anti-epileptic and also as a treatment for depression (42). Anti-depressant property of valerian is due to activation of serotonergic neurons of network system. On the other hand, valerian extraction increases the size of the neurons and the connection of these cells with surrounding astrocyte is very close.

In the research done by Hatami Jooni et al (2014), the effect of hydroalcoholic extraction of valerian on magnus Rafe astrocytes in the brain stem of rat was evaluated. The extraction increased number of the magnus rafe nuclei and decreased their size. The multiplication effect of the extraction was shown (43).

Sadeghi et al (2010) evaluated the effect of hydro alcoholic extraction of valerian on size and number of nuclei of magnus Rafe astrocytes in rats. The results show that the effect was not on number but on size of nuclei which show the hyperactivity of these neurons and therefore, an increase in levels of serotonin excretion (44).

Islamic medicine

In Islamic traditional medicine, depression is highly valued. "Hozn" or sadness means hard and uneven land, hardness and harshness of the soul. It also means deep sadness that is caused by unpleasant event or loss of pleasant thing (45,46). Sadness of heart for something which is lost or something which is impossible to gain (Surah al-Imran, verse 2; Surah Hadid, verse 2) (47,48) and leads human being to different reactions. Also a positive sadness could be recognized: when someone misses a perfection which leads to his sadness and tries to regain it by repentance and compensation for his wrong doing (45,46). Teaching and exerting social programs and treating this disorder is necessary (49).

Feeling loss is one of the reasons of sadness. Sorrow is a feeling that appears after losing an ability or after feeling loss which is usually accompanied by tear, loss of energy and loneliness. An increase in these feelings

accompanied by stressful agents can lead to depression which brings social and educational problems. God promises believers to keep their heart away from sadness and sorrow in this life and future life. In Quran some signs have been related to sad people which are, depending on the intensity, death (Surah Yusuf / 1,2 Surah Shoara / 1 in Quran), revealing their secrets (Surah al-Qasas/10), changes on their faces and behavior (Sura Nal/58), crying, erosion of body and blindness (Surah Yusuf /84-86) (45). According to Islamic articles, practicing Islamic believes can stop psychological disorders (50).

Treating depression with mind therapy and self-knowledge tries (Surah Hadid/22,23) (48) to change people's ideas about condition of the world and disasters that happen in human body, society and the world. It implies that god leads everything to perfection and losses and gains are means to this perfection. Creation of human is due to god's complex knowledge. Quran has insisted on begging for forgiveness to bring serenity. This is a way to avoid depression caused by guilt (45).

In Islam, natural products, medicinal plants and also healthy food were recognized and used. Also there is an emphasis on consuming Halal food. Examples are: fig, grape, date, pomegranate, olive, honey and fish, they have medicinal properties and are used for freshness, health (51) and also as treatment for depression (52). Potassium is an essential element for the body and should be obtained from food. It can also be connected to cancer and prevention from it. Sufficient amount of potassium is found in fig. It is also an effective treatment for osteoporosis, cardiovascular disorders, hypertension, schizophrenia and depression (53). In "Tin" Surah from Quran, god says: "swear to fig and olive, we created human in the best form" (52)

Fish suggested in Quran in Surah Kahf /61, Araaf /163, Safat /142, 144, Ghalam /48. Fish and cod liver oil have medicinal properties and are used in depression. Researches and examination around this matter have been done and prove (54), such as in Margiotta-

Casaluci et al.' article (2014) (55).

Moreover, most of the Islamic and traditional scientists Believing in training the soul in strengthening the body (Such as Abu Ali Sina), insisted on exercise in order to maintain normal psychological health (56). Exercise is useful and prevent diseases (57). It is also proven that exercise is effective in improving depression and decreasing of its signs (58).

As an example, result of the research by McCann et al (1984) on 43 depressed women indicated that the group which were participating in aerobic exercises illustrated obvious decrease in depression rate, compared to the group which participated in relaxation exercises without intervention (59). In another study by Sadeghi et al. (2013), which examined the effect of eight weeks of aerobic training on depression and cognitive components of students, it was found that this period of aerobic exercise was effective in reducing depression in students (60). Many researches have been done in recent years and traditional medicine and natural products are safe replacements of chemical drugs (61-63).

Conclusion

In the recent years many researches have been carry out on depression and plants which have the anti-depressant property. Some drugs also have been sent to markets but because of chemical substances, cost and side effects and the possibility of suicide in patients with this problem, using natural plants is essential because the side effects are low. Some useful studies also been carried out on this matter. Considering the amount of chemical drug in recent era and the tendency to use natural products in industry, nourishment and treatment of diseases like depression indicates the importance of using natural products in traditional medicine. Recent studies have proved and completed the treatment and orders for tackling this problem with traditional medicine to reach better results.

Studies have shown that people who follows

Islamic orders suffers less than people who don't. The more exact people follow the orders the less they reach depression. According to Islamic articles, following Islamic orders can prevent psychological disorders. These article shows that patience and religion decrease depression and anger. They also can increase social support. Reading Quran, believing in God, following Quran orders and say prayer to god cause calmness, health and decreases depression so it is important to use medicinal plants.

Suggestions

According to this research and the conclusions, it is suggested to carry out more scientific and professional researches in this field in order to receive more health and serenity.

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Conflicts of interest

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Authors' contributions

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Ethical considerations

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