Treatment of anxiety disorders with plants and herbs

Kourosh Saki

Department of Psychiatry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Anxiety is a natural feeling in people and every person experiences in certain conditions in his/her life. Anxiety refers to an unpleasant and vague feeling accompanied by worry about known and unknown origin. Symptoms of anxiety include heart palpitations, restlessness, fatigue, insomnia, dyspnea, and disturbance in concentration and memory. Fortunately, in these days, there are many ways such as yoga, relaxation, and massage to overcome stress and mental pressures. In addition, there is a completely different, nature-based way to control adverse emotions and anxiety, which is phytotherapy. In this article, the use of medicinal plants in pharmaceutical industry and treatment of anxiety was investigated. To achieve this purpose, the keywords such as medicinal plants, herbal drugs, traditional medicine, and anxiety were used to search for related articles. The databases Scopus, PubMed, ISI, Google Scholar, SID, and Magiran were searched for relevant articles. Based on the results, plants such as *Valeriana officinalis*, *Passiflora incarnata*, *Rosmarinus officinalis*, *Lavandula angustifolia*, *Hypericum perforatum*, *Mentha piperita*, *Matricaria chamomilla*, *Glycyrrhiza glabra*, *Melissa officinalis*, *Crataegus aronia*, *Humulus lupulus*, *Echium amoenum*, *Prunus dulcis*, and *Foeniculum vulgare* are some of the flora that, in the references, are recommended to control anxiety.

Key words: Anxiety, medicinal plants, mental illness and disorder, treatment

INTRODUCTION

nxiety is a natural feeling in people that every person experiences certain conditions in his/her life. Anxiety refers to an unpleasant and vague feeling accompanied by horror and anxiety with unknown origin that comes to the individual.[1,2] In anxiety, the individual is not confident and has a feeling of helplessness and being physiologically aroused; the recurrence of situations that have been stressful in the past or in which the person experiences trauma can lead to anxiety and stress.[3-5] Everyone experiences anxiety in his/her life, which is normal, but severe and chronic anxiety is considered unusual. According to research, anxiety in women, lowincome groups, and older people is higher than other people. Anxiety has certain symptoms including heart palpitations, restlessness, fatigue, insomnia, shortness of breath, and concentration and memory problems. In severe and chronic anxiety, the person feels tightness in the chest. Other symptoms of severe and chronic anxiety can be severe heart palpitations, sweating, tremor, dizziness, and loss of balance.

Today, due to living a busy and competitive life, stress and anxiety are unavoidable. In

addition, some people are more prone to anger and anxiety than others. [6-10] Some causes of stress and anxiety include depression, sleep disorders, nutritional deficiencies, smoking, adrenal gland disorders, thyroid disorders, and some medications. [11] However, it seems that, in today's world, due to these tense lives, especially in the big cities, anxiety and stress are an integral part of everyday life and should be coped with in some ways.

Stress and anxiety are of the serious illnesses of our time. Fortunately, many ways are currently available to overcome stress and mental stress, such as yoga, relaxation, and massage. In addition, there is a completely different natural way of controlling adverse emotions and anxiety, i.e., phytotherapy.^[12,13] Medicinal plants include certain plants that are cultivated and sold in shops and supermarkets for therapeutic purposes after drying.^[14,15] Some plants are found in the environment and nature, many of which play a significant role in the treatment of diseases^[16-18] Human has

Address for correspondence:

Kourosh Saki, Department of Psychiatry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. E-mail: kouroshsaki@gmail.com

Received: 09-09-2018 **Revised:** 16-09-2018 **Accepted:** 24-09-2018 been aware of some medicinal plant properties for thousands of years and used them to treat diseases. [19-21] Each medicinal plant contains one or more active ingredients according to which the application of the plant is determined. Chemical drugs lead to side effects, which is the reason for considering medicinal plants valuable even after centuries. [22-24] Medicinal plants also offer many health benefits, and their uses mostly have been confirmed recently. [25-28] In fact, herbal drugs have been used to treat many illnesses for many thousands of years and their uses cause beneficial effects. [27,29] These plants may act by their antioxidant activity or other mechanisms. [30-40] In this article, the use of medicinal plants in the pharmaceutical industry and for the treatment of anxiety has been addressed.

MATERIALS AND METHODS

In this study, the keywords such as medicinal plants, herbal drugs, traditional medicine, and anxiety were used to search for related articles. The databases Scopus, PubMed, ISI, Google Scholar, SID, and Magiran were searched for relevant articles.

RESULTS

One of the issues that many people today are struggling with is stress and anxiety. Meanwhile, Iran is among the countries where traditional medicine and the use of medicinal herbs have a very long history. There are many plants that have sedative and anti-stress properties.

Based on the results, plants such as Valeriana officinalis, Passiflora incarnata, Rosmarinus officinalis, Lavandula angustifolia, Hypericum perforatum, Mentha piperita, Matricaria chamomilla, Glycyrrhiza glabra, Melissa officinalis, Crataegus aronia, Humulus lupulus, Echium amoenum, Prunus dulcis, Foeniculum vulgare, etc., are some of the flora that, in the references, are recommended to control anxiety [Table 1].

DISCUSSION

Anxiety is a natural feeling in people that everyone experiences in his/her life. Stress, anxiety, mental pressure, worry and apprehension, and worry about being late, failure, the future, and misery, occupational and educational stress, as well as 1000 other reasons cause anxiety to keep all over the person trapped. To overcome the anxiety and other neuropsychological disorders, a number of herbal drugs are used. [41] Usually, these plants are used as tea and sometimes used in combination with one or more plants. Based on the results, plants such as *V. officinalis*, *P. incarnata*, *R. officinalis*, *L. angustifolia*, *H. perforatum*, *M. piperita*, *M. chamomilla*, *G. glabra*, *M. officinalis*, *C. aronia*, *H. lupulus*, *E. amoenum*, *P. dulcis*, *F. Vulgare*, and *C. sinensis* are some

of the flora that, in the references, are recommended to control anxiety.

The mechanisms by which herbal drugs are effective against anxiety are not fully clear. Actually, the explanations for the mechanism involved in various types of anxiety are inadequate. Dysregulation of some specific neurotransmitters including gamma-aminobutyric acid, dopamine, and serotonin has been suggested as the most important probable causes of anxiety disorders. [41,42] However, these suggestions are based mostly on the results of pharmacological examinations, and no clinical trial demonstrated these changes in neurotransmitters mentioned as the main factors of anxiety. This is the main factor why the mechanisms involved in medicinal plants in the treatment of anxiety are not clear, too. It also may explain why anxiety treatment is often ineffective. The prevalence of lifetime anxiety disorders reaches more than 16% worldwide. [43] Hence, great efforts have been made to distinguish the causes of anxiety. Benzodiazepines, serotonin-specific reuptake inhibitors, and other antidepressants are among the drugs that are usually prescribed to patients suffering from anxiety disorders.[44] Therefore, medicinal plants effective on anxiety disorders may have the same mechanism as these drugs.

It should be noted that there is a positive correlation between oxidative status and level of anxiety. There is a correlation between the level of anxiety and related genes expression in mice brain as well as glutathione reductase 1 and glyoxalase 1 which usually protect brain cells from oxidative damage. [45] The imbalance between free radicals and antioxidants is important in maintaining healthy biological activities.[46,47] This imbalance induces oxidative stress which, in turn, can cause many chronic and acute diseases including anxiety, neurodegenerative diseases, cancer, cardiovascular disorders, and inflammation.^[48-55] There is also a correlation between intracellular redox status and the level of anxiety in mice.^[56] Therefore, medicinal plants which have antioxidant activity may have antianxiety property. Most of the introduced plants in this article have antioxidant activities. There are also a lot of other plants with antioxidant activity which with this hypothesis they should have antianxiety, too. [57-59]

In spite of the numerous classes of drugs that are available for the treatment of anxiety and depression, full remission has remained elusive. The emerging clinical cases have shown increasing interests among health practitioners and patients in phytomedicine. The development of anxiolytic and antidepressant drugs of plant origin takes advantage of multidisciplinary approach including but not limited to ethnopharmacological survey (careful investigation of folkloric application of medicinal plant) and phytochemical and pharmacological studies. The selection of a suitable plant for a pharmacological study is a basic and very important step. Relevant clues to achieving this step include traditional use, chemical composition, toxicity, randomized selection, or a combination of several criteria. Medicinal plants have been

Table 1: Antianxiety plants			
Scientific name	Herbal family	Persian name	Main findings [26-34]
Valeriana officinalis	Caprifoliaceae	Sonboloteib	Valeriana officinalis is fragrant and its aroma is one of the best anti-stress and sedative herbal remedies. This effect ultimately reduces anxiety.
Passiflora incarnata	Passifloraceae	Gole saati	The fruit and flowers of <i>Passiflora incarnata</i> plant are one of the best anti-stress and sedative herbal medicines used to relieve insomnia.
Rosmarinus officinalis	Lamiaceae	Rozmari	This plant that is very fragrant is used, in aromatherapy, as an analgesic and antidepressant agent. This effect ultimately reduces anxiety.
Lavandula angustifolia	Lamiaceae	Ostokhodous	Lavandula angustifolia is one of the medicinal plants whose consumption reduces irritability and anxiety and is sedative. Lavender is used to relieve tiredom, is sedative, and is used to treat difficulties falling asleep.
Hypericum perforatum	Hypericaceae	Gole raei	Hypericum perforatum is one of the medicinal plants that are used to reduce anxiety and stress and to treat depression and is also sedative. This effect ultimately reduces anxiety.
Mentha piperita	Labiatae	Nana	Mentha piperita is one of the medicinal plants that are used to reduce and relieve stress and anxiety.
Matricaria chamomilla	Asteraceae	Babouneh	Chamomile is one of the medicinal plants that are used to reduce and relieve stress and anxiety.
Glycyrrhiza glabra	Fabaceae	Shirin bayan	Licorice is one of the medicinal plants that are used to reduce and relieve stress and anxiety.
Melissa officinalis	Lamiaceae	Badranjbouyeh	Lemon balm is one of the medicinal plants that are used to reduce and relieve stress and anxiety.
Crataegus aronia	Rosaceae	Zalzalak	Hawthorn has a sedative property. This plant and its active ingredients reduce heartbeat, nervous states, irritability, or extreme feelings and adjust heart rate, and the plant is, therefore, anxiolytic.
Humulus lupulus	Cannabaceae	Razak	This plant is a natural sedative and hypnotic agent. This effect ultimately reduces anxiety.
Echium amoenum	Boraginaceae	Gav zaban	This plant, when combined with <i>Valeriana officinalis</i> , is refreshing, eliminates stress, and is anxiolytic.
Prunus dulcis	Rosaceae	Badam	Prunus dulcis or Almond is rich in certain nutrients, including omega-3 fatty acids, which increases tolerance and helps to treat anxiety and depression.
Foeniculum vulgare	Apiaceae	Razianeh	Fennel is effective in anxiety due to phytoestrogens, which seem to work through neurobiological systems such as GABA A receptors. This effect ultimately reduces anxiety.
Camellia sinensis	Theaceae	Chaye sabz	Green tea contains L-theanine, which helps to reduce heart rate, lower blood pressure, and reduce anxiety.

GABA: Gamma-aminobutyric acid

continued to be a rich source of biomolecule with therapeutic values for the treatment of anxiety and depression.

REFERENCES

 Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of

- 12-month DSM-IV disorders in the national comorbidity survey replication. Arch Gen Psychiatry 2005;62:617-27.
- 2. Erickson SR, Guthrie S, Vanetten-Lee M, Himle J, Hoffman J, Santos SF, *et al.* Severity of anxiety and work-related outcomes of patients with anxiety disorders. Depress Anxiety 2009;26:1165-71.
- 3. Schaffer A, McIntosh D, Goldstein BI, Rector NA, McIntyre RS, Beaulieu S, *et al.* The CANMAT task

- force recommendations for the management of patients with mood disorders and comorbid anxiety disorders. Ann Clin Psychiatry 2012;24:6-22.
- 4. Nepon J, Belik SL, Bolton J, Sareen J. The relationship between anxiety disorders and suicide attempts: Findings from the national epidemiologic survey on alcohol and related conditions. Depress Anxiety 2010;27:791-8.
- 5. Valerie CR. Diagnosing the Diagnostic and Statistical Manual of Mental Disorders. London: Karnac; 2014.
- Dohrenwend BP, Dohrenwend BS. Perspectives on the past and future of psychiatric epidemiology. The 1981 Rema Lapouse lecture. Am J Public Health 1982;72:1271-9.
- 7. Leon AC, Portera L, Weissman MM. The social costs of anxiety disorders. Br J Psychiatry Suppl 1995;27:19-22.
- 8. Martin P. The epidemiology of anxiety disorders: A review. Dialogues Clin Neurosci 2003;5:281-98.
- 9. Greenberg PE, Sisitsky T, Kessler RC, Finkelstein SN, Berndt ER, Davidson JR, *et al.* The economic burden of anxiety disorders in the 1990s. J Clin Psychiatry 1999;60:427-35.
- Kessler RC, Keller MB, Wittchen HU. The epidemiology of generalized anxiety disorder. Psychiatr Clin North Am 2001;24:19-39.
- 11. Weissman MM. The epidemiology of anxiety disorders: Rates, risks and familial patterns. J Psychiatr Res 1988;22 Suppl 1:99-114.
- 12. Reis JS, Oliveira GB, Monteiro MC, Machado CS, Torres YR, Prediger RD, *et al.* Antidepressant-and anxiolytic-like activities of an oil extract of propolis in rats. Phytomedicine 2014;21:1466-72.
- 13. Alami-Rostami S, Rafieirad M. The effect of hydroalcoholic *Ferulago angulata* extract on locomotor activity and anxiety caused by hypoperfusion ischemia in adult male rats. J Herbmed Pharm 2018;7:51-5.
- Rahimi-Madiseh M, Lorigoini Z, Zamani-Gharaghoshi H, Rafieian-Kopaei M. *Berberis vulgaris*: Specifications and traditional uses. Iran J Basic Med Sci 2017;20:569-87.
- 15. Sarrafchi A, Bahmani M, Shirzad H, Rafieian-Kopaei M. Oxidative stress and parkinson's disease: New hopes in treatment with herbal antioxidants. Curr Pharm Des 2016;22:238-46.
- Karami S, Roayaei M, Zahedi E, Bahmani M, Mahmoodnia L, Hamzavi H, et al. Antifungal effects of Lactobacillus species isolated from local dairy products. Int J Pharm Investig 2017;7:77-81.
- 17. Chinedu E, Onah IA, Amaje PO, Jacob DL. Evaluation of the antiproliferative potential of *Cocos nucifera* juice. J Herbmed Pharm 2018;7:124-8.
- Rahimi-Madiseh M, Karimian P, Kafeshani M, Rafieian-Kopaei M. The effects of ethanol extract of *Berberis vulgaris* fruit on histopathological changes and biochemical markers of the liver damage in diabetic rats. Iran J Basic Med Sci 2017;20:552-6.
- 19. Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: Past history and future perspective. J Herbmed

- Pharm 2018;7:1-7.
- Abbasi N, Mohammadpour S, Karimi E, Aidy A, Karimi P, Azizi M, et al. Protective effects of Smyrnium cordifolium Boiss essential oil on pentylenetetrazolinduced seizures in mice: Involvement of benzodiazepine and opioid antagonists. J Biol Regul Homeost Agents 2017;31:683-9.
- 21. Shirzad H, Shahrani M, Rafieian-Kopaei M. Comparison of morphine and tramadol effects on phagocytic activity of mice peritoneal phagocytes *in vivo*. Int Immunopharmacol 2009;9:968-70.
- 22. Zumrutdal E, Bilecik T, Koluman B, Turan U, Daglioglu K, Gunduz M, *et al.* Protective effect of *Solanum tuberosum* against the breakdown of red blood cells: An experimental study in burn injury model. J Herbmed Pharm 2018;7:13-7.
- Tajbakhsh M, Karimi A, Tohidpour A, Abbasi N, Fallah F, Akhavan MM, et al. The antimicrobial potential of a new derivative of cathelicidin from Bungarus fasciatus against Methicillin-resistant Staphylococcus aureus. J Microbiol 2018;56:128-37.
- Setorki M, Nazari B, Asgary S, Azadbakht L, Rafieian-Kopaei M. Anti-atherosclerotic effects of verjuice on hypocholesterolemic rabbits. Afr J Pharm Pharm 2011;5:1038-45.
- Asgari S, Setorki M, Rafieian-Kopaei M, Heidarian E, Shahinfard N, Ansari R, et al. Postprandial hypolipidemic and hypoglycemic effects of *Allium hertifolium* and *Sesamum indicum* on hypercholesterolemic rabbits. Afr J Pharm Pharm 2012;6:1131-5.
- Bahmani M, Zargaran A, Rafieian-Kopaei M. Identification of medicinal plants of Urmia for treatment of gastrointestinal disorders. Rev Bras Farmacogn 2014;24:468-80.
- 27. Asgary S, Sahebkar A, Afshani MR, Keshvari M, Haghjooyjavanmard S, Rafieian-Kopaei M, et al. Clinical evaluation of blood pressure lowering, endothelial function improving, hypolipidemic and anti-inflammatory effects of pomegranate juice in hypertensive subjects. Phytother Res 2014;28:193-9.
- 28. Khalighi-Sigaroodi F, Jarvandi S, Taghizadeh M. Therapeutic Indications of Medicinal Plants. Tehran: Arjmand; 2010. p. 1-6.
- Rabiei Z, Rafieian-Kopaei M, Mokhtari S, Shahrani M. Effect of dietary ethanolic extract of *Lavandula* officinalis on serum lipids profile in rats. Iran J Pharm Res 2014;13:1295-301.
- 30. Rechinger KH. Academische Druch-u, Verlagsanstalt. Vol. 120. Graze-Austria: Flora Iranica; 1976. p. 15-6.
- 31. Kebriaee-Zadeh A. Overview of national drug policy of Iran. Iran J Pharm Res 2003;2:1-2.
- 32. Amin GH. Popular Medicinal Plants of Iran. Tehran: Tehran University of Medical Sciences; 2005. p. 38-162.
- 33. Mozaffarian VA. A Dictionary of Iranian Plant Names. Tehran: Farhang Moaser; 2006. p. 198-515.
- 34. Zargari A. Medicinal Plants. 6th ed., Vol. 3. Tehran: Tehran University Publication; 1996.

- 35. Rabiei Z, Gholami M, Rafieian-Kopaei M. Antidepressant effects of *Mentha pulegium* in mice. Bangl J Pharm 2016;11:711-5.
- 36. Bahmani M, Sarrafchi A, Shirzad H, Rafieian-Kopaei M. Autism: Pathophysiology and promising herbal remedies. Curr Pharm Des 2016;22:277-85.
- 37. Rabiei Z, Naderi S, Rafieian-Kopaei M. Study of antidepressant effects of grape seed oil in male mice using tail suspension and forced swim tests. Bangl J Pharm 2017;12:397-402.
- 38. Bahmani M, Sarrafchi A, Shirzad H, Asgari S, Rafieian-Kopaei M. Cardiovascular toxicity of cyclooxygenase inhibitors and promising natural substitutes. Curr Pharm Des 2017;23:952-60.
- 39. Karimi A, Mohammadi-Kamalabadi M, Rafieian-Kopaei M, Amjad L, Salimzadeh I. Determination of antioxidant activity, phenolic contents and antiviral potential of methanol extract of *Euphorbia spinidens* Bornm (*Euphorbiaceae*). Trop J Pharm Res 2016;15:759-64.
- Hosseini Z, Lorigooini Z, Rafieian-Kopaei M, Shirmardi HA, Solati K. A review of botany and pharmacological effect and chemical composition of *Echinophora* species growing in Iran. Pharmacognosy Res 2017;9:305-12.
- 41. Christmas D, Hood S, Nutt D. Potential novel anxiolytic drugs. Curr Pharm Des 2008;14:3534-46.
- 42. Furmark T. Neurobiological aspects of social anxiety disorder. Isr J Psychiatry Relat Sci 2009;46:5-12.
- 43. Somers JM, Goldner EM, Waraich P, Hsu L. Prevalence and incidence studies of anxiety disorders: A systematic review of the literature. Can J Psychiatry 2006;51:100-13.
- 44. Davidson JR. First-line pharmacotherapy approaches for generalized anxiety disorder. J Clin Psychiatry 2009;70 Suppl 2:25-31.
- 45. Hovatta I, Tennant RS, Helton R, Marr RA, Singer O, Redwine JM, *et al.* Glyoxalase 1 and glutathione reductase 1 regulate anxiety in mice. Nature 2005;438:662-6.
- 46. Asgharzade S, Rafieian-Kopaei M, Mirzaeian A, Reiisi S, Salimzadeh L. *Aloe vera* toxic effects: Expression of inducible nitric oxide synthase (iNOS) in testis of Wistar rat. Iran J Basic Med Sci 2015;18:967-73.
- 47. Rahimi-Madiseh M, Heidarian E, Kheiri S, Rafieian-Kopaei M. Effect of hydroalcoholic *Allium ampeloprasum* extract on oxidative stress, diabetes mellitus and dyslipidemia in alloxan-induced diabetic rats. Biomed Pharmacother 2017;86:363-7.
- 48. Nazarian-Samani Z, Sewell RDE, Lorigooini Z, Rafieian-Kopaei M. Medicinal plants with multiple effects on

- diabetes mellitus and its complications: A Systematic review. Curr Diab Rep 2018;18:72.
- 49. Kazemi S, Shirzad H, Rafieian-Kopaei M. Recent findings in molecular basis of inflammation and anti-inflammatory plants. Curr Pharm Des 2018;24:1551-62.
- Rouhi-Boroujeni H, Heidarian E, Rouhi-Boroujeni H, Deris F, Rafieian-Kopaei M. Medicinal plants with multiple effects on cardiovascular diseases: A Systematic review. Curr Pharm Des 2017;23:999-1015.
- 51. Shayganni E, Bahmani M, Asgary S, Rafieian-Kopaei M. Inflammaging and cardiovascular disease: Management by medicinal plants. Phytomedicine 2016;23:1119-26.
- 52. Asadi-Samani M, Bagheri N, Rafieian-Kopaei M, Shirzad H. Inhibition of th1 and th17 cells by medicinal plants and their derivatives: A Systematic review. Phytother Res 2017;31:1128-39.
- 53. Karami S, Roayaei M, Hamzavi H, Bahmani M, Hassanzad-Azar H, Leila M, *et al.* Isolation and identification of probiotic *Lactobacillus* from local dairy and evaluating their antagonistic effect on pathogens. Int J Pharm Investig 2017;7:137-41.
- 54. Jalaly L, Sharifi G, Faramarzi M, Nematollahi A, Rafieian-kopaei M, Amiri M, et al. Comparison of the effects of *Crataegus oxyacantha* extract, aerobic exercise and their combination on the serum levels of ICAM-1 and E-selectin in patients with stable angina pectoris. Daru 2015;23:54.
- 55. Heidarian E, Rafieian-Kopaei M. Protective effect of artichoke (*Cynara scolymus*) leaf extract against lead toxicity in rat. Pharm Biol 2013;51:1104-9.
- 56. Bouayed J, Rammal H, Younos C, Soulimani R. Positive correlation between peripheral blood granulocyte oxidative status and level of anxiety in mice. Eur J Pharmacol 2007;564:146-9.
- 57. Torki A, Khalaji-Pirbalouty V, Lorigooini Z, Rafieian-Kopaei M, Sadeghimanesh A, Rabiei Z. *Anchusa italica* extract: Phytochemical and neuroprotective evaluation on global cerebral ischemia and reperfusion. Braz J Pharm Sci 2018;54:e17251.
- 58. Lorigooini Z, Koravand M, Haddadi H, Rafieian-Kopaei M, Shirmardi HA, Hosseini Z. A review of botany, phytochemical and pharmacological properties of *Ferulago angulata*. Toxin Rev 2017;2017:1-8.
- 59. Sadraei H, Asghari G, Jamali H. Antidiarrheal action of *Zataria multiflora* hydroalcoholic and hexane extracts in mice. J Herbmed Pharm 2018;7:22-8.

Source of Support: Nil. Conflict of Interest: None declared.