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Phytotherapies for Dementia

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Abstract

Dementia is a disorder that, without changing the level of consciousness, causes various cognitive impairments in the affected people. Currently, dementia is considered a health problem due to high prevalence in the elderly, high medical expenses, and the resulting psychological and physical stress. Dementia is a psychiatric disorder that can be treated in traditional medicine using medicinal plants. The use of medicinal plants is definitely effective to improve brain function and promising drugs are produced from the plants. Therefore, in this review, we reported the most important medicinal plants that are effective on dementia. For this purpose, first, the keywords *medicinal plants*, *herbal remedies*, *herbal medicine*, *traditional medicine*, and *dementia* were used to retrieve relevant articles indexed in the databases such as *Scopus*, *PubMed*, *ISI*, *Google Scholar*, *SID*, and *Megiran*. Here, some useful herbal remedies useful and effective to treat Alzheimer's disease or dementia, including *Lavandula angustifolia*, *Ginko biloba*, *Melissa officinalis*, *Saliva officinalis* and *Huperzia serrate* are reported. Besides, chemical compounds and vitamin E, L-carnitine, phosphatidyl serine, vinpocetine, choline alphasicrite, vitamin B1, and inositol are among the compounds that have positive effects on dementia. These herbal remedies can be used for preparation of new drugs.

Keywords: Psychiatric Disorders, Dementia, Herbal Medicine, Medicinal Plants.

Introduction

The composition of the population in different countries is changing and moving towards aging, and now a large number of elderly people are seen in different countries across the world (Kessler and et al., 2005). With increasing number of elderly, neurological examination of this age population is increasing in importance. Dementia is one of the major diseases affecting the elderly (Erickson and et al., 2009; Schaffer and et al., 2012). Dementia is a disorder that, without changing the level of consciousness, causes various cognitive problems in a person (Nepon and et al., 2010). Currently, dementia is considered a health problem due to high prevalence in the elderly, high medical expenses, and the resulting psychological and physical stress (American Psychiatric Association, 1980; Dohrenwend, 1928; Leon and et al., 1995). Dementia complications include memory impairment, speech impairment, psychological and psychiatric changes, and memory loss (Weissman, 1988; Greenberg and et al., 2001; Kessler and et al., 2001; Weissman, 1988; Dhawan and Kumar, 2001). The etiology of dementia can be related to a general medical condition, permanent effects and substance abuse, or a combination of these factors. The disease generally starts to develop at the end of life, usually in the seventh decade of life and beyond (Samani and et al., 2018; Moradi and et al., 2018; Bahmani and et al., 2018; Dadkhah and et al., 2016). Plants have properties that are able to treat many diseases (Setork and et a., 2011; Asgary and et al., 2011; Asgari and et al., 2012; Fallah and et al., 2018; Bahmani and et al., 2014; Rabiei and et al., 2014). Human beings have always used plants as drugs (Jalaly and et al., 2015). Today, the use of medicinal plants has a very important role in the health system, and many of the chemical drugs of modern medicine are plant-derived (Karimi and et al., 2016; Holmes and et al., 2002). These plants mostly have long been used by humans to treat diseases (Jamshidi-Kia and et al., 2018). The use of medicinal plants is definitely effective to improve brain function, with the best drugs for the brain obtained from plants. Various psychiatric disorders including dementia can be treated in traditional medicine using medicinal plants (Rabiei and et al., 2016; Beheshti & Shahmoradi, 2018; Sarrafchi and et al., 2016; Bahmani and et al., 2016; Rahimi-Madiseh and et al., 2017; Rabiei and et al., 2015). Therefore, in this review, we will report the most important medicinal plants that are effective on dementia.

Method

To conduct this review article, first, the keywords medicinal plants, herbal remedies, herbal medicine, traditional medicine, and dementia

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were used to retrieve relevant articles indexed in the databases Scopus, PubMed, ISI, Google Scholar, SID, and Megiran.

Results

Based on the results, medicinal herbs and anti-dementia compounds included *Lavandula angustifolia*, *Ginko biloba*, *Melissa officinalis*, *Saliva officinalis* and *Huperzia serrate* and vitamin E, L-carnitine, phosphatidyl serine, vinpocetine, choline alphasicrite, vitamin B1, and inositol . (Table 1 and Table 2).

Table 1. The most important anti-dementia plants

Scientific name	Herbal family	Persian name	Efrrects
Lavandula angustifolia	Lamiaceae	Lavender	Lavender essential oil destroys the distress caused by acute dementia (Schulz and et al., 1998).
Ginko biloba	Ginkgoaceae	Ginkgo	Ginkgo biloba has had a positive therapeutic effect on various types of dementia (Kleijnen & Knipschild, 1992; Kanowski and et al., 1996; Hofferberth, 1994).
Melissa officinalis	Lamiaceae	Lemongrass	Lemongrass produces cholinergic effects and anti-dementia effects, and eliminates dementia-induced distress (Ballard and et al., 2002). It is also effective to improve perceptual activities in mild to moderate Alzheimer's disease (Hudson & Tabet, 2003; Akhondzadeh and et al., 2003).
Saliva officinalis	Lamiaceae	Sage	Sage produces cholinergic effects and anti-dementia effects (Akhondzadeh and et sl., 2003).
Huperzia serrata	Huperzia serrata	Huperzia serrate	Huperzin A is a booster of memory impairment that is extracted from Huperzia serrate moss (Xu and et al., 1995; Zhang and et al., 1991; Zhang and et al., 2002).

Table 2. The most important anti-dementia drugs

Compound	Effects
Vitamin E	Daily intake of 2000 units of vitamin E prevents Alzheimer's disease progression (Sano and et al., 1997).
Acetyl-L-carnitine	The effect of Acetyl-L-carnitine for the treatment of dementia has been widely studied (Vecchi and et al., 1991).
Phosphatidylcholine	Choline-containing supplements or phosphatidylcholine-related substance are recommended for the treatment of Alzheimer's disease (Thal and et al., 1996).
N-acetylcystein	N-acetylcysteine reduces the progression of Alzheimer's disease (Sano and et al., 1992).
Vinpocetine	Vinpocetine is used to treat memory impairment (Balestreri and et al., 1987; Fenzl and et al., 1986)
Phosphatidylserine	Phosphatidylserine is a treatment for Alzheimer's disease and other types of dementia (Cenacchi and et al., 1993).
Vitamin B1	Vitamin B1 is suggested for the treatment of Alzheimer's disease
Inositol	Inositol is suggested for the treatment of Alzheimer's disease

Discussion

Ethnobotanical preparations are the promising remedies for memory and cognition deficits which recently are widely investigared. The proved psychological and clinical efficacy and safety of these remedies have caused high focuses on these plants. In this regards Lavandula angustifolia, Ginko biloba, Melissa officinalis, Saliva officinalis and Huperzia serrate are reported. Besides, chemical compounds and vitamin E, L-carnitine, phosphatidyl serine, vinpocetine, choline alphasicrite, vitamin B1, and inositol are among remedies which have promising effects against dementia and cognitive problems. Cholinesterase inhibitors such as galantamine are among the present drugs which are frequently prescribed for dementia problem. Therefore, cholinergic inhibition is possible mechanism involved in the mechanism action of these plants. In this regard, various medicinal plants have also been shown to be effective against amnesia through cholinergic inhibition (Baradaran and et al., 2012).

However, free radicals which induce oxidative stress have been shown to be involved in aging process and aging process is one of the main causes of aging. In fact telomeres at the end of chromosomes are shortened during each replication which is a mitotic counting mechanism. The rate of telomere shortening has been shown to get modulated through oxidative stress, especially the differences in the capacity of antioxidant defense between various cell strains. There is a correlation between the rate of short telomeres in lymphocytes and the rate of vascular dementia. Hence, antioxidants which have potential to act in this process may delay the aging process and dementia (Saretzki & Von Zglinicki, 2002). The antioxidant properties of the medicinal plants presented in this article have previously determined. Therefore, they may have acted, in part, through this mechanism. There are a lot of other herbs containing components with

antioxidant activities (Shahrahmani and et al., 2018; Nejad and et al., 2018; Ghaderi and et al., 2018; Torki and et al., 2018; Rahimi-Madiseh and et al., 2017; Heidarian & Rafieian-Kopaei, 2013; Torki and et al., 2018; Lorigooini and et al., 2017; Bahmani and et al., 2017). These plants may also have these effects.

Chronic inflammation also has been considered as an important factor not only in pathogenesis of dementia, but also in pathogenesis of a wide range of other diseases such as major depression, cardiovascular disease, diabetes, cancer and multiple sclerosis (Leonard, 2007; Shayganni and et al., 2016; Kazemi and et al., 2018; Asgary and et al., 2014). It should be noted that chronic inflammatory can also predispose depressed and other patients to neurodegenerative diseases, too. Indeed inflammation and depression are early manifestations of dementia. It has been hypothesized that progress from depression and inflammation which will promote to dementia can result from macrophages activation in human blood, as well as microglia in the brain which usually release pro-inflammatory cytokines (Leonard, 2007). These cytokines can stimulate inflammatory process by enhancement of nitric oxide, prostaglandin E2, cortisol and pro-inflammatory cytokines. Corticosteroids can inhibit protein synthesis and reduction in synthesis of neurotrophic factors which in turn prevent repair in neuronal damages (Leonard, 2007). Hence, antioxidant and anti-inflammatory plants may be effective in delaying dementia. In this regard, there are a lot of other plants which have antioxidant and anti-inflammatory activities (Asgharzade and et al., 2015; Rouhi-Boroujeni and et al., 2017; Asadi-Samani and et al., 2017; Hosseini and et al., 2017; Rahimi-Madiseh and et al., 2017; Karami and et al., 2017) which might be effective in this problem. This hypothesis and the effects of these plants on dementia should be examined. Furthermore, elderly patients usually have several other diseases and these plants which have a wide range of activities on various diseases (Nazarian-Samani and et al., 2018; Shabanian, and et al., 2017; Karami and et al., 2017; Sepahvand and et al., 2017; Talei and et al., 2017) are usually more beneficial for these patients.

References

Akhondzadeh, S., Noroozian, M., Mohammadi, M., Ohadinia, S., Jamshidi, A. H., & Khani, M. (2003). Melissa officinalis extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomised, placebo controlled trial. *Journal of Neurology, Neurosurgery & Psychiatry*, *74*(7), 863-866.

Akhondzadeh, S., Noroozian, M., Mohammadi, M., Ohadinia, S., Jamshidi, A. H., & Khani, M. (2003). Salvia officinalis extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomized and placebo-controlled trial. *Journal of clinical pharmacy and therapeutics*, *28*(1), 53-59.

American Psychiatric Association. (1980). Diagnostic and statistical manual of mental disorders; DSM-III. *Washington DC*

Asadi-Samani, M., Bagheri, N., Rafieian-Kopaei, M., & Shirzad, H. (2017). Inhibition of Th1 and Th17 cells by medicinal plants and their derivatives: A systematic review. *Phytotherapy Research*, *31*(8), 1128-1139.

Asgari, S., Setorki, M., Rafieian-Kopaei, M., Heidarian, E., Fard, S., Ansari Samani, R., & Foroozandeh, Z. (2012). Postprandial hypolipidemic and hypoglycemic effects of Allium hertifolium and Sesamum indicum on hypercholesterolemic rabbits. *African Journal of Pharmacy and Pharmacology*, *6*(15), 1131-1135.

Asgary, S., Moshtaghian, S. J., Setorki, M., Kazemi, S., Rafieian-Kopaei, M., Adelnia, A., & Shamsi, F. (2011). Hypoglycaemic and hypolipidemic effects of pumpkin (Cucurbita pepo L.) on alloxan-induced diabetic rats. *African Journal of Pharmacy and Pharmacology*, *5*(23), 2620-2626.

Asgary, S., Sahebkar, A., Afshani, M. R., Keshvari, M., Haghjooyjavanmard, S., & Rafieian-Kopaei, M. (2014). Clinical evaluation of blood pressure lowering, endothelial function improving, hypolipidemic and anti-inflammatory effects of pomegranate juice in hypertensive subjects. *Phytotherapy Research*, *28*(2), 193-199.

Asgharzade, S., Rafieian-Kopaei, M., Mirzaeian, A., Reiisi, S., & Salimzadeh, L. (2015). Aloe vera toxic effects: expression of inducible nitric oxide synthase (iNOS) in testis of Wistar rat. *Iranian journal of basic medical sciences*, *18*(10), 967.

Bahmani, M., Khaksarian, M., Rafieian-Kopaei, M., & Abbasi, N. (2018). Overview of the therapeutic effects of Origanum vulgare and Hypericum perforatum based on Iran's ethnopharmacological documents. *Journal of Clinical and Diagnostic Research*, *12*(7).

Bahmani, M., Sarrafchi, A., Shirzad, H., & Rafieian-Kopaei, M. (2016). Autism: Pathophysiology and promising herbal remedies. *Current pharmaceutical design*, *22*(3), 277-285.

Bahmani, M., Sarrafchi, A., Shirzad, H., Asgari, S., & Rafieian-Kopaei, M. (2017). Cardiovascular Toxicity of Cyclooxygenase Inhibitors and Promising Natur al Substitutes. *Current pharmaceutical design*, *23*(6), 952-960.

Bahmani, M., Zargaran, A., & Rafieian-Kopaei, M. (2014). Identification of medicinal plants of Urmia for treatment of gastrointestinal disorders. *Revista Brasileira de Farmacognosia*, *24*(4), 468-480.

Balestreri, R., Fontana, L., & Astengo, F. (1987). A double-blind placebo controlled evaluation of the safety and efficacy of vinpocetine in the treatment of patients with chronic vascular senile cerebral dysfunction. *Journal of the American Geriatrics Society*, *35*(5), 425-430.

Ballard, C. G., O'Brien, J. T., Reichelt, K., & Perry, E. K. (2002). Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: The results of a double-blind. placebo-controlled trial with Melissa. *The Journal of clinical psychiatry*.

Baradaran, A., Rabiei, Z., & Rafieian, M. (2012). A review study on medicinal plants affecting amnesia through cholinergic system. *Journal of HerbMed Pharmacology*, *1*.

Beheshti, S., & Shahmoradi, B. (2018). Therapeutic effect of Melissa officinalis in an amyloid-β rat model of alzheimer's disease. *Journal of Herbmed Pharmacology*, *7*(3).

Cenacchi, T., Bertoldin, T., Farina, C., Fiori, M. G., Crepaldi, G., Azzini, C. F., ... & Belloni, G. (1993). Cognitive decline in the elderly: a double-blind, placebo-controlled multicenter study on efficacy of phosphatidylserine administration. *Aging Clinical and Experimental Research*, *5*(2), 123-133.

Dadkhah, N., Eskandarian, R., & Rahimi-Madiseh, M. (2016). The medicinal plants and plant-based products of Iran effective on dysmenorrheal. *Int J PharmTech Res*, *9*, 392-406.

Dhawan, K., Kumar, S., & Sharma, A. (2001). Anti-anxiety studies on extracts of Passiflora incarnata Linneaus. *Journal of ethnopharmacology*, *78*(2-3), 165-170.

Dohrenwend, B. P., & Dohrenwend, B. S. (1982). Perspectives on the past and future of psychiatric epidemiology. The 1981 Rema Lapouse Lecture. *American Journal of Public Health*, *72*(11), 1271-1279.

Erickson, S. R., Guthrie, S., VanEtten-Lee, M., Himle, J., Hoffman, J., Santos, S. F., ... & Abelson, J. L. (2009). Severity of anxiety and work-related outcomes of patients with anxiety disorders. *Depression and Anxiety*, *26*(12), 1165-1171.

Fallah, S., Rostaei, M., Lorigooini, Z., & Surki, A. A. (2018). Chemical compositions of essential oil and antioxidant activity of dragonhead (Dracocephalum moldavica) in sole crop and dragonhead-soybean (Glycine max) intercropping system under organic manure and chemical fertilizers. *Industrial Crops and Products*, *115*, 158-165.

Fenzl, E., Apecechea, M., & Schaltenbrand, R. (1986, July). Efficacy and tolerance of vinpocetine administered intravenously, in addition of standard therapy, to patients suffering from an apoplectic insult. In *Pharmacology of Cerebral Ischemia: Proceedings of the International Symposium on Pharmacology of Cerebral Ischemia. New York, NY: Elsevier Science Publishers* (pp. 430-434).

Ghaderi, H., Rafieian, M., & Nezhad, H. (2018). Effect Of Hydroalcoholic Cinnamomum Zeylanicum Extract On Reserpine-Induced Depression Symptoms In Mice. *Pharmacophore*, *9*(2), 35-44.

Greenberg, P. E., Sisitsky, T., & Kessler, R. C. (2001). The economic burden of anxiety disorders in the 1990s. *Year Book of Psychiatry and Applied Mental Health*, *2001*(1), 186-187.

Heidarian, E., & Rafieian-Kopaei, M. (2013). Protective effect of artichoke (Cynara scolymus) leaf extract against lead toxicity in rat. *Pharmaceutical biology*, *51*(9), 1104-1109.

Hofferberth, B. (1994). The efficacy of EGb 761 in patients with senile dementia of the Alzheimer type, a double-blind, placebo-controlled study on different levels of investigation. *Human Psychopharmacology: Clinical and Experimental*, *9*(3), 215-222.

Holmes, C., Hopkins, V., Hensford, C., MacLaughlin, V., Wilkinson, D., & Rosenvinge, H. (2002). Lavender oil as a treatment for agitated behaviour in severe dementia: a placebo controlled study. *International journal of geriatric psychiatry*, *17*(4), 305-308.

Hosseini, Z., Lorigooini, Z., Rafieian-Kopaei, M., Shirmardi, H. A., & Solati, K. (2017). A review of botany and pharmacological effect and chemical composition of Echinophora species growing in Iran. *Pharmacognosy research*, *9*(4), 305.

Hudson, S. A., & Tabet, N. (2003). Acetyl-l-carnitine for dementia. *Cochrane Database of Systematic Reviews*, (2).

Jalaly, L., Sharifi, G., Faramarzi, M., Nematollahi, A., Rafieian-Kopaei, M., Amiri, M., & Moattar, F. (2015). 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 Journal of Pharmaceutical Sciences*, *23*(1), 54.

Jamshidi-Kia, F., Lorigooini, Z., & Amini-Khoei, H. (2018). Medicinal plants: past history and future perspective. *Journal of herbmed pharmacology*, *1*, 1-7.

Kanowski, S., Herrmann, W. M., Stephan, K., Wierich, W., & Hörr, R. (1996). Proof of efficacy of the ginkgo biloba special extract EGb 761 in outpatients suffering from mild to moderate primary degenerative dementia of the Alzheimer type or multi-infarct dementia. *Pharmacopsychiatry*, *29*(02), 47-56.

Karami, S., Roayaei, M., Hamzavi, H., Bahmani, M., Hassanzad-Azar, H., Leila, M., & Rafieian-Kopaei, M. (2017). Isolation and identification of probiotic Lactobacillus from local dairy and evaluating their antagonistic effect on pathogens. *International journal of pharmaceutical investigation*, *7*(3), 137.

Karami, S., Roayaei, M., Zahedi, E., Bahmani, M., Mahmoodnia, L., Hamzavi, H., & Rafieian-Kopaei, M. (2017). Antifungal effects of Lactobacillus species isolated from local dairy products. *International journal of pharmaceutical investigation*, *7*(2), 77.

Karimi, A., Mohammadi-Kamalabadi, M., Rafieian-Kopaei, M., & Amjad, L. (2016). Determination of antioxidant activity, phenolic contents and antiviral potential of methanol extract of Euphorbia spinidens Bornm (Euphorbiaceae). *Tropical Journal of Pharmaceutical Research*, *15*(4), 759-764.

Kazemi, S., Shirzad, H., & Rafieian-Kopaei, M. (2018). Recent findings in molecular basis of inflammation and anti-inflammatory plants. *Current pharmaceutical design*, *24*(14), 1551-1562.

Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of general psychiatry*, *62*(6), 617-627.

Kessler, R. C., Keller, M. B., & Wittchen, H. U. (2001). The epidemiology of generalized anxiety disorder. *Psychiatric Clinics of North America*, *24*(1), 19-39.

Kleijnen, J., & Knipschild, P. (1992). Ginkgo biloba. *The Lancet*, *340*(8828), 1136-1139.

Leon, A. C., Portera, L., & Weissman, M. M. (1995). The social costs of anxiety disorders. *The British journal of psychiatry*, *166*(S27), 19-22.

Leonard, B. E. (2007). Inflammation, depression and dementia: are they connected?. *Neurochemical research*, *32*(10), 1749-1756.

Lorigooini, Z., Koravand, M., Haddadi, H., Rafieian-Kopaei, M., Shirmardi, H. A., & Hosseini, Z. (2017). A review of botany, phytochemical and pharmacological properties of Ferulago angulata. *Toxin Reviews*, 1-8.

Moradi, F., Sewell, R. D., Lorigooini, Z., & Rafieian-Kopaei, M. (2018). Immunosuppression-lipid metabolism interplay and medicinal plants in atherosclerosis: a review. *Current pharmaceutical design*, *24*(24), 2789-2793.

Nazarian-Samani, Z., Sewell, R. D., Lorigooini, Z., & Rafieian-Kopaei, M. (2018). Medicinal plants with multiple effects on diabetes mellitus and its complications: A Systematic review. *Current diabetes reports*, *18*(10), 72.

Nejad, A. S. M., Bahmani, M., Shah, N. A., Shah, S. A., & Rafieian-Kopaei, M. (2018). Beliefs of herbal therapies of the community of the Ilam city of Ilam province, Iran. *Journal of Pharmacy & Pharmacognosy Research*, *6*(4), 299-317.

Nepon, J., Belik, S. L., Bolton, J., & Sareen, J. (2010). The relationship between anxiety disorders and suicide attempts: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Depression and anxiety*, *27*(9), 791-798.

Rabiei, Z., Gholami, M., & Rafieian-Kopaei, M. (2016). Antidepressant effects of Mentha pulegium in mice. *Bangladesh Journal of Pharmacology*, *11*(3), 711-715.

Rabiei, Z., Lorigooini, Z., & Rafieian-Kopaei, M. (2016). Effects of hydroalcoholic extract of Borago officinalis on naloxone-precipitated withdrawal syndrome in morphine-dependent mice. *Bangladesh Journal of Pharmacology*, *11*(4), 824-829.

Rabiei, Z., Rafieian-Kopaei, M., Mokhtari, S., & Shahrani, M. (2014). Effect of dietary ethanolic extract of Lavandula officinalis on serum lipids profile in rats. *Iranian journal of pharmaceutical research: IJPR*, *13*(4), 1295.

Rahimi-Madiseh, M., Heidarian, E., Kheiri, S., & Rafieian-Kopaei, M. (2017). Effect of hydroalcoholic Allium ampeloprasum extract on oxidative stress, diabetes mellitus and dyslipidemia in alloxan-induced diabetic rats. *Biomedicine & Pharmacotherapy*, *86*, 363-367.

Rahimi-Madiseh, M., Karimian, P., Kafeshani, M., & Rafieian-Kopaei, M. (2017). The effects of ethanol extract of Berberis vulgaris fruit on histopathological changes and biochemical markers of the liver damage in diabetic rats. *Iranian journal of basic medical sciences*, *20*(5), 552.

Rahimi-Madiseh, M., Lorigoini, Z., Zamani-Gharaghoshi, H., & Rafieian-Kopaei, M. (2017). Berberis vulgaris: specifications and traditional uses. *Iranian journal of basic medical sciences*, *20*(5), 569.

Rouhi-Boroujeni, H., Heidarian, E., Rouhi-Boroujeni, H., Deris, F., & Rafieian-Kopaei, M. (2017). Medicinal plants with multiple effects on cardiovascular diseases: A systematic review. *Current pharmaceutical design*, *23*(7), 999-1015.

Samani, B. H., Gudarzi, H., Rostami, S., Lorigooini, Z., Esmaeili, Z., & Jamshidi-kia, F. (2018). Development and optimization of the new ultrasonic-infrared-vacuum dryer in drying Kelussia odoratissima and its comparison with conventional methods. *Industrial Crops and Products*, *123*, 46-54.

Sano, M., Bell, K., Cote, L., Dooneief, G., Lawton, A., Legler, L., ... & Mayeux, R. (1992). Double-blind parallel design pilot study of acetyl levocarnitine in patients with Alzheimer's disease. *Archives of neurology*, *49*(11), 1137-1141.

Sano, M., Ernesto, C., Thomas, R. G., Klauber, M. R., Schafer, K., Grundman, M., ... & Schneider, L. S. (1997). A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. *New England Journal of Medicine*, *336*(17), 1216-1222.

Saretzki, G., & Von Zglinicki, T. (2002). Replicative aging, telomeres, and oxidative stress. *Annals of the New York Academy of Sciences*, *959*(1), 24-29.

Sarrafchi, A., Bahmani, M., Shirzad, H., & Rafieian-Kopaei, M. (2016). Oxidative stress and Parkinson's disease: new hopes in treatment with herbal antioxidants. *Current pharmaceutical design*, *22*(2), 238-246.

Schaffer, A., McIntosh, D., Goldstein, B. I., Rector, N. A., McIntyre, R. S., Beaulieu, S., ... & Yatham, L. N. (2012). The CANMAT task force recommendations for the management of patients with mood disorders and comorbid anxiety disorders. *Annals of clinical psychiatry: official journal of the American Academy of Clinical Psychiatrists*, *24*(1), 6-22.

Schulz, V., Hansel, R., & Tyler, V. E. (1998). A Physician's Guide to Herbal Medicine. 168-173.

Sepahvand, A., Ezatpour, B., Tarkhan, F., Bahmani, M., Khonsari, A., & Rafieian-Kopaei, M. (2017). Phytotherapy In Fungi And Fungal Disease: A Review Of Effective Medicinal Plants On Important Fungal Strains And Diseases. *International Journal of Pharmaceutical Sciences and Research*, *8*(11), 4473-4495.

Setorki, M., Nazari, B., Asgary, S., Azadbakht, L., & Rafieian-Kopaei, M. (2011). Anti atherosclerotic effects of verjuice on hypocholesterolemic rabbits. *African Journal of Pharmacy and Pharmacology*, *5*(8), 1038-1045.

Shabanian, S., Farahbod, F., Rafieian, M., Ganji, F., & Adib, A. (2017). The effects of Vitamin C on sperm quality parameters in laboratory rats following long-term exposure to cyclophosphamide. *Journal of advanced pharmaceutical technology & research*, *8*(2), 73.

Shahrahmani, H., Kariman, N., Jannesari, S., Rafieian-Kopaei, M., Mirzaei, M., Ghalandari, S., ... & Mardani, G. (2018). The effect of green tea ointment on episiotomy pain and wound healing in primiparous women: A randomized, double-blind, placebo-controlled clinical trial. *Phytotherapy Research*, *32*(3), 522-530.

Shayganni, E., Bahmani, M., Asgary, S., & Rafieian-Kopaei, M. (2016). Inflammaging and cardiovascular disease: Management by medicinal plants. *Phytomedicine*, *23*(11), 1119-1126.

Talei, G. R., Mohammadi, M., Bahmani, M., & Kopaei, M. R. (2017). Synergistic effect of Carum copticum and Mentha piperita essential oils with ciprofloxacin, vancomycin, and gentamicin on Gram-negative and Gram-positive bacteria. *International journal of pharmaceutical investigation*, *7*(2), 82.

Thal, L. J., Carta, A., Clarke, W. R., Ferris, S. H., Friedland, R. P., Petersen, R. C., ... & Tuszynski, M. H. (1996). A 1-year multicenter placebo-controlled study of acetyl-L-carnitine in patients with Alzheimer's disease. *Neurology*, *47*(3), 705-711.

Torki, A., Khalaji-Pirbalouty, V., Lorigooini, Z., Rafieian-Kopaei, M., Sadeghimanesh, A., & Rabiei, Z. (2018). Anchusa italica extract: phytochemical and neuroprotective evaluation on global cerebral ischemia and reperfusion. *Brazilian Journal of Pharmaceutical Sciences*, *54*(1).

Torki, A., Khalaji-Pirbalouty, V., Lorigooini, Z., Rafieian-Kopaei, M., Sadeghimanesh, A., & Rabiei, Z. (2018). Anchusa italica extract: phytochemical and neuroprotective evaluation on global cerebral ischemia and reperfusion. *Brazilian Journal of Pharmaceutical Sciences*, *54*(1).

Vecchi, G. P., Chiari, G., Cipolli, C., & Cortelloni, C. (1991). Acetyl-l-carnitine treatment of mental impairment in the elderly: Evidence from a multicentre study. *Archives of gerontology and geriatrics*.

Weissman, M. M. (1988). The epidemiology of anxiety disorders: rates, risks and familial patterns. *Journal of Psychiatric Research*, *22*, 99-114.

Weissman, M. M. (1988). The epidemiology of anxiety disorders: rates, risks and familial patterns. *Journal of Psychiatric Research*, *22*, 99-114.

Xu, S. S., Gao, Z. X., Weng, Z., Du, Z. M., Xu, W. A., Yang, J. S., ... & Chai, X. S. (1995). Efficacy of tablet huperzine-A on memory, cognition, and behavior in Alzheimer's disease. *Zhongguo yao li xue bao= Acta pharmacologica Sinica*, *16*(5), 391-395.

Zhang, R. W., Tang, X. C., Han, Y. Y., Sang, G. W., Zhang, Y. D., Ma, Y. X., ... & Yang, R. M. (1991). Drug evaluation of huperzine A in the treatment of senile memory disorders. *Zhongguo yao li xue bao= Acta pharmacologica Sinica*, *12*(3), 250-252.

Zhang, Z., Wang, X., Chen, Q., Shu, L., Wang, J., & Shan, G. (2002). Clinical efficacy and safety of huperzine Alpha in treatment of mild to moderate Alzheimer disease, a placebo-controlled, double-blind, randomized trial. *Zhonghua yi xue za zhi*, *82*(14), 941-944.