Future Integrative Medicine **2024** vol. 3(3) | 183–191
DOI: 10.14218/FIM.2024.00024

Review Article

Herbal Plants for Mental Disorders in Sri Lanka

Ruwini Nishadini Senarathne[1], Banukie Nirosha Jayasuriya[2] and Shehara Lakchani Abeysinghe Gunawardana[1*]

[1]*Department of Pharmacy and Pharmaceutical Sciences, Faculty of Health Sciences, CINEC Campus, Malabe, Sri Lanka;* [2]*Department of Pharmacy and Pharmaceutical Sciences, Faculty of Allied Health Sciences, University of Sri Jayewardenepura, Nugegoda, Sri Lanka*

Received: April 26, 2024 | **Revised:** July 12, 2024 | **Accepted:** July 26, 2024 | **Published online:** September 03, 2024

Abstract

A mental disorder, also referred to as a psychiatric disorder or mental illness, is characterized by significant disturbances in an individual's thinking, emotions, or behavior. In Ayurveda, herbal plants are used as alternative therapies for various ailments, including mental disorders. This review aims to provide a comprehensive overview of herbal medicines used in treating mental disorders in Sri Lanka. It relies on foundational books as primary sources to systematically identify and analyze the therapeutic potential of 24 traditional medicinal plants for treating mental disorders. Each plant was evaluated based on its scientific name, plant parts used, distribution in Sri Lanka, mechanisms of action, and identified phytochemicals. Furthermore, additional research was conducted using keywords such as mental disorders, herbal plants, plant distribution, phytochemicals, side effects, and mechanism of action through scientific databases. The phytochemicals present in these herbal plants possess antioxidant, anti-inflammatory, and neuroprotective properties, contributing to their potential antipsychotic activities. Trigonelline (from *Abrus precatorius*), bacosides (from *Bacopa monnieri*), asiaticoside and asiatic acid (from *Centella asiatica*), quercetin (from *Ginkgo biloba)*, alliin and allicin (from *Allium sativum*), luteolin-7-O-glucoside (from *Eclipta alba*), and shogaol (from *Zingiber officinale*) demonstrate significant potential in modulating neurotransmitter levels, reducing oxidative stress, and alleviating symptoms associated with mental disorders such as depression, anxiety, and neurodegenerative diseases. The suggested therapeutic value of these identified herbal plants and their bioactive phytochemicals indicates the need for preserving and extensively investigating these remedies to establish their clinical effectiveness.

Introduction

A mental disorder, also known as a psychiatric disorder or mental illness, is characterized by a clinically significant disturbance in an individual's cognition, emotional regulation, or behavior.[1] Genetic, environmental, and psychological factors can cause these disorders, and their symptoms and severity can vary. Millions of people worldwide are affected by mental disorders today, including anxiety disorders, depression, bipolar disorder, post-traumatic stress disorder, schizophrenia, eating disorders, disruptive behavior disorders, and various neurodevelopmental conditions. According to a survey conducted by the Institute of Health Metrics and Evaluation in 2019, approximately 970 million people worldwide, or one in every eight individuals, were living with a mental disorder.[2] Anxiety and depressive disorders were found to be the most prevalent, significantly impacting global health.[3] This highlights the urgent need for effective interventions and targeted strategies to address and manage mental health issues.

Despite advancements in modern medicine, herbal medicines have maintained their relevance for thousands of years, offering numerous benefits such as easy accessibility, cultural significance, personal preference, and a growing demand for natural and organic products.[4] Herbal remedies and medicines are currently in high demand due to their perceived lower incidence of side effects. Additionally, herbal medicine is often used in conjunction with conventional treatments because they are believed to possess synergistic effects, enhancing the therapeutic activity of conventional drugs. Therefore, herbal therapy is commonly sought as an adjunct to conventional treatment for mental disorders.[5] This review aimed to provide a comprehensive overview of herbal medicines used in treating mental disorders in Sri Lanka.

Sri Lanka is recognized as one of the world's biodiversity hotspots, abundant with diverse medicinal plants and traditional healing systems that have long been relied upon for mental and physical well-being. According to the Department of Ayurveda

Keywords: Herbal plants; Mental disorders; Ayurveda; Phytochemicals; Sri Lanka; Neuroprotection; Depression; Anxiety disorders.

***Correspondence to:** Shehara Lakchani Abeysinghe Gunawardana, Department of Pharmacy and Pharmaceutical Sciences, Faculty of Health Sciences, CINEC Campus, Malabe 10115, Sri Lanka. ORCID: https://orcid.org/0000-0001-7415-8992. Tel: +94-713950131, E-mail: shehara.gunawardana@cinec.edu

How to cite this article: Senarathne RN, Jayasuriya BN, Gunawardana SLA. Herbal Plants for Mental Disorders in Sri Lanka. *Future Integr Med* 2024;3(3):183–191. doi: 10.14218/FIM.2024.00024.

in Sri Lanka, there are over 1,200 plant species with documented medicinal properties, and 174 of these plants (12%) are unique to Sri Lanka.[6] Ayurvedic plants and herbs serve as alternative therapies for various diseases, including mental disorders. In Sri Lanka, mental health has become a growing concern due to the increasing number of patients with mental illnesses. In the first quarter of 2017, the following percentages of patients with mental disorders were reported in Sri Lanka: anxiety disorder (4.53%), depression (30.44%), bipolar disorder (5.2%), schizophrenia (7.72%), and disruptive behavior and dissocial disorders (1.73%).[7] In traditional Ayurveda, *Bacopa monnieri*, *Centella asiatica*, *Withania somnifera*, *Valeriana wallichii*, and *Aloe barbadensis* have been primarily employed for treating mental disorders, particularly anxiety and depression, to reduce stress and mental fatigue. Additionally, *Hypericum perforatum*, *Ginkgo biloba*, and *Rhodiola rosea* have been used to treat bipolar disorder, disruptive behavior, and dissociative disorders. *Valeriana wallichii*, *Curcuma longa*, *Centella asiatica*, and *Withania somnifera* have also been reportedly used in traditional Ayurveda for treating mental disorders such as schizophrenia.[7]

No studies have primarily focused on reviewing the herbal plants used for treating mental disorders in Sri Lanka. Comprehensive data on plant species, the parts used, cultural practices, pharmacological action, and methods of incorporation are needed. Furthermore, most herbal plants' therapeutic potential, central nervous system properties, and safety profile remain largely unknown. The primary objective of this study was to address the existing knowledge gap by reviewing the herbal plants traditionally used in Sri Lanka for treating mental disorders. The specific objectives include evaluating the selected medicinal plants based on their distribution within Sri Lanka, their pharmacological uses and mechanisms of action, and the phytochemicals discovered in these plants to date.

Data collection for the analysis

In this comprehensive review, data were gathered from the Library of the Faculty of Indigenous Medicine, University Colombo at Rajagiriya, Sri Lanka, and the Pallekale Provincial Ayurvedic Hospital in Kandy, Sri Lanka. A variety of books were consulted, including "Medicinal Plants Used in Ceylon" Parts I to V, "Atlas of Ayurvedic Medicinal Plants," and "Sinhala Waidya Widya." These texts served as foundational resources for systematically identifying and analyzing the therapeutic potential of 24 traditional medicinal plants for mental disorders. Each selected plant underwent meticulous examination, focusing on its scientific name, mechanisms of action, distribution in Sri Lanka, and discovered phytochemicals. Additionally, further research was conducted using keywords such as mental disorders, herbal plants, plant distribution, phytochemicals, side effects, and mechanism of action. This supplementary investigation utilized research articles published in scientific databases such as PubMed, Google Scholar, and Web of Science spanning from 2001 to 2023 to enhance understanding and insights into the subject matter. The flow chart below visualizes the selection process of sources used to conduct this comprehensive review (Fig. 1).

Exploring herbal plants as biocompatible therapeutics for mental disorders

A variety of herbal plants have traditionally been utilized in the Sri Lankan Ayurvedic system to treat mental disorders, with a particular focus on managing anxiety and depression (Table 1).[8–40] These remedies often combine different plant parts due to the biochemical diversity inherent in each part, whether used individually or in polyherbal blends. For example, leaves from plants such as *Abrus precatorius*, *Asparagus falcatus*, *Eclipta prostrata*, *Sesbania grandiflora*, and *Foeniculum vulgare* are combined to prepare mixtures prescribed for mental conditions like 'Olmada sanni'.[41] Different plant parts (leaves, roots, stems, flowers, seeds) typically contain varying concentrations and types of active compounds (phytochemicals), contributing to a wider range of therapeutic effects.[41] In Sri Lanka, and herbal plants are predominantly found in dry, wet, and intermediate zones, as well as along coastal areas. While there's been considerable research into the pharmacological mechanisms of herbal plants for managing conditions like anxiety and depression, the scientific investigation into their effects on more complex mental health disorders, such as schizophrenia, anorexia, and obsessive-compulsive disorder (OCD), is less extensive. Some herbal plants exhibit multiple antipsychotic activities, including *Ginkgo biloba*, *Zingiber officinale*, *Glycyrrhiza glabra*, *Curcuma longa*, and *Centella asiatica.*

Mechanisms of phytochemicals and their impact on mental disorders

According to the literature, the mechanism of action of herbal plants has demonstrated effectiveness against mental disorders due to the antioxidant activity of phytochemicals and their potential impact on cellular metabolism.[42] Phytochemicals in medicinal plants have been found to regulate neurotransmitter synthesis and distribution or modulate immunological functions.[43] For instance, the antidepressant activity of herbal compounds is associated with their ability to counteract diverse stressors, normalize monoamine receptors, and enhance monoamine neurotransmitter levels in specific cortex regions.[44] The statement from Fajemiroye *et al*.[45] highlights that several polyphenols found in herbal plants, including curcumin, ferulic acid, proanthocyanidin, quercetin, and resveratrol, are noted for their strong anti-inflammatory and antioxidant properties. These properties are important because they contribute to the polyphenols' effectiveness in addressing neuropathic conditions. These properties are effective in treating mental stress and mood disorders. Figure 2 represents some of the phytochemicals used in the treatment of mental disorders.

Abrine and trigonelline are natural alkaloids found in the seeds of *Abrus precatorius*. Trigonelline has been studied for its antioxidant properties, which may aid in combating chronic diseases by reducing oxidative stress.[46] It has also shown promise in improving cognitive function and alleviating mental disorders such as depression. Research suggests trigonelline may have neuroprotective effects, potentially preventing neurodegenerative disorders like Alzheimer's disease.[47] In contrast, abrine is toxic and serves as a defense mechanism for the plant. Due to its toxicity, abrine is not utilized for medicinal purposes.[46] Alliin and allicin, found in garlic (*Allium sativum*), have demonstrated antioxidant, anti-inflammatory, and neuroprotective activities, which are claimed to exhibit potential antipsychotic effects. However, more research is needed to fully understand the mechanisms involved.[47] Bacoside-A and B are primarily found in the leaves of *Bacopa monnieri*, with Bacoside-A being more pharmacologically active than Bacoside-B.[48] Some studies suggest that bacosides may modulate neurotransmitter levels in brain, which are involved in mood and behavior regulation. Additionally, bacosides have been found to exhibit antioxidant and anti-inflammatory effects, which could help mitigate oxidative stress and inflammation in brain. These

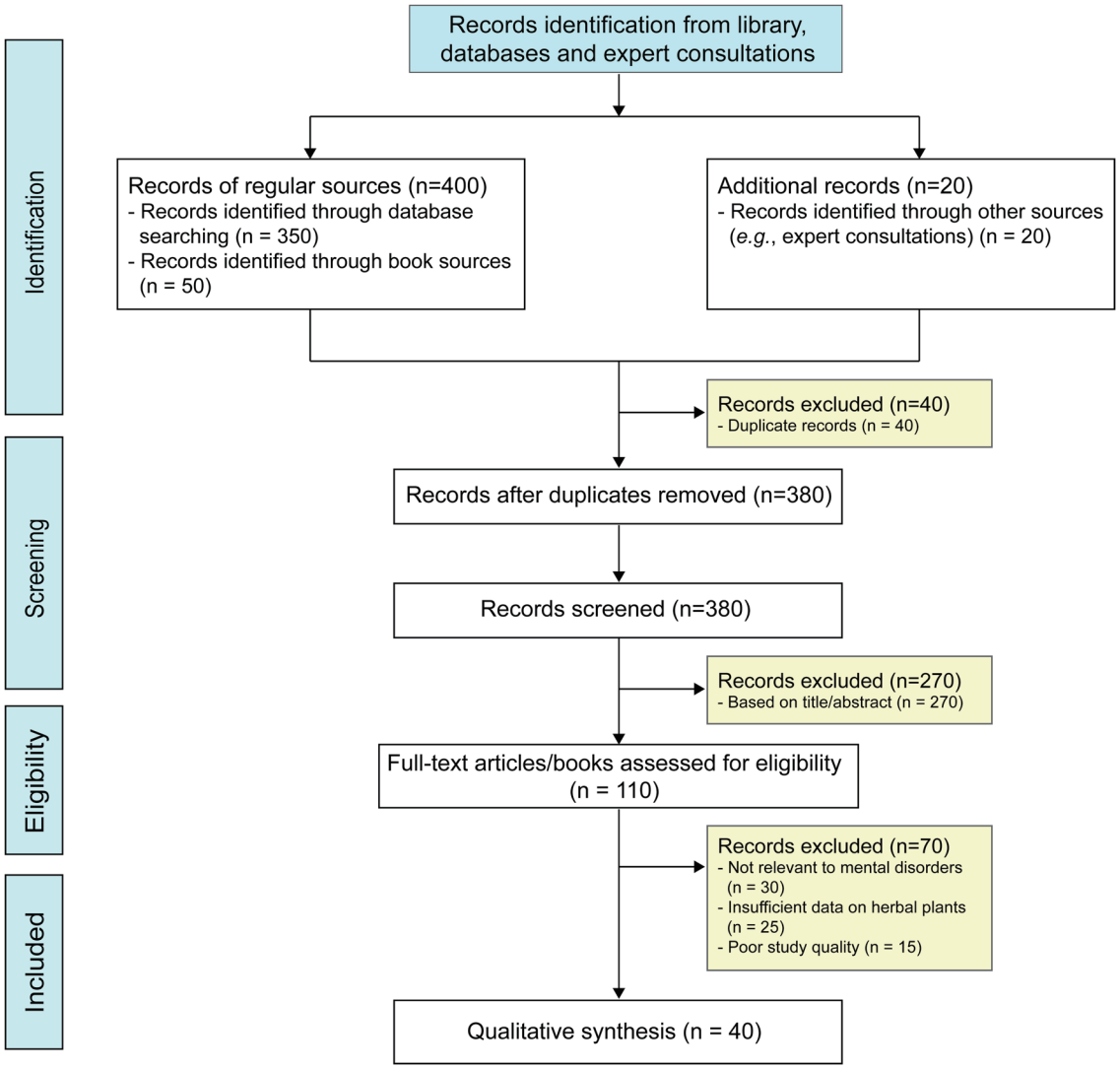

Fig. 1. Flow chart for the selection process of sources.

processes are implicated in certain mental disorders, including anxiety and depression.[49]

Asiaticoside and asiatic acid, primarily found in *Centella asiatica*, have exhibited antidepressant, anxiolytic, antioxidative, and neuroprotective activities. These compounds may regulate mood by influencing neurotransmitter activity and neuroplasticity in brain. Furthermore, they aid in reducing inflammation and oxidative stress in brain. These processes are implicated in various mental disorders, including depression and anxiety.[50] Luteolin-7-O-glucoside, a flavonoid primarily found in the leaves of *Eclipta alba*, has shown antioxidant, neuroprotective, and anti-inflammatory activities, similar to the mechanism of asiaticoside and asiatic acid against mental disorders.[51] Quercetin, a flavonoid found in the leaves of *Ginkgo biloba,* influences the levels of neurotransmitters in the brain, including serotonin, dopamine, and norepinephrine. This regulation of neurotransmitters can impact mood and emotional well-being, potentially leading to mood-stabilizing effects and relief from the symptoms of mental disorders.[52] Shogaol, a phenolic ketone found in the rhizome of ginger (*Zingiber officinale*), has been found to exhibit antioxidant, neuroprotective, and anti-inflammatory activities, as well as stress reduction properties. Shogaol protects brain cells from oxidative damage and promotes relaxation, which may help individuals cope with stressors more effectively.[53] However, the mechanisms of herbal plants against mental disorders have not been sufficiently evaluated by scientific methods. More research and findings are needed to fully understand their working principles.

Ayurvedic poly herbal formulations for mental disorders: Benefits and challenges

Moreover, in traditional Ayurvedic prescriptions, treatments often come in the form of poly herbal formulations, contributing to their widespread use and popularity.[54] Poly herbal formulations offer distinct advantages not typically found in conventional drugs. They are known for their broad therapeutic range and effectiveness even at low doses, while still being safe at higher doses.[55] This characteristic provides a superior risk-to-benefit ratio com-

Table 1. Herbal plants used in Sri Lankan Ayurveda to treat mental disorders

Plant name	Part of the plant	Distribution of Sri Lanka	Ayurveda use	Pharmacology action/MOA	Discovered phytochemicals
Abrus precatorius	Roots, leaves, and seeds	Wet zone (throughout plains)	Depression	Not known yet	Abrine, trigonelline, abrol, abrasine, precasine and precool, and amino acids.[8]
Acacia arabica	Bark, leaves, flower, gum, roots	Along the coast	Anxiety	The potent antioxidant activity of the plant controls the oxidative stress markers in brain tissues.[9]	Tannins, terpenoids, alkaloids, saponins, glycosides, polysaccharides, and anthraquinone.[10]
Allium sativum	Bulb	Dry and intermediate zones	Anxiety and depression	Treatment with a dose of 0.5 g/kg attenuated malondialdehyde levels and enhanced superoxide dismutase and glutathione peroxidase activities in the brain. Alleviates anxiety and depression related behaviors in diabetic rats possibly by attenuation of brain oxidative stress.[11]	Alliin, allicin, ajoenes, vinyldithiins, and flavonoids such as quercetin.[12]
Azadirachta indica	Bark	Commonly found in forest edges of the wet zone	Anxiety	Production of free radicals in the brain is increased in conditions like anxiety and depression, leading to a reduction in glutathione, a tripeptide crucial for maintaining oxidative balance and detoxifying reactive oxygen species in brain cells. The phenolic compounds in this plant have shown antioxidant properties and thereby act as antidepressants and anxiolytics.[13]	Phenol, flavonoids, alkanes, aldehydes, ether.[13]
Bacopa monniera	Entire plant	Low counties of Sri Lanka	Depression, anxiety	Reduce stress and anxiety by elevating mood and reducing cortisol levels.[14]	Alkaloids (brahmine, nicotinine, herpestine, bacosides A and B), saponins A, B, and C, triterpenoid saponins, stigmastanol, β-sitosterol.[14]
Cannabis Sativa	Leaves	Dry zone (under strict restriction on cultivation)	Schizophrenia	Not known	Flavonoids, terpenoids, cannabinoids, alkaloids, glycoproteins and phytosteroids.[15]
Cassia auriculata	Entire plant	Dry zone	Depression	The ethanolic seed extract may decrease the release of cortisol or CRF or ACTH from the HPA axis and increase the level of GABA that has an inhibitory effect on HPA axis. Hence increased GABA activity leads to hindrance to the stimulation of the hypothalamus for CRF release. In turn, it decreases the release of ACTH and cortisol from the pituitary and adrenal gland respectively which helps respond to stress.[16]	Flavonoids, tannins, lipids, polyphenols, triterpenoids and steroids.[16]
Centella asiatica	Entire plant	Very common weed growing in waste grassy places from sea level to highest elevation.[17]	Antidepressive, and Anxiolytic effects Bipolar diorder, and OCD	Inhibition of acetylcholinesterase activity, reduction of phospholipase A2 activity, and protection against ß-amyloid formation.[18]	Asiaticoside and Asiatic acid.[18]

(continued)

DOI: 10.14218/FIM.2024.00024 | Volume 3 Issue 3, September 2024

Table 1. *(continued)*

Plant name	Part of the plant	Distribution of Sri Lanka	Ayurveda use	Pharmacology action/MOA	Discovered phytochemicals
Cinnamomum zeylanicum	Bark	Coastal area of Sri Lanka	Depression	Eugenol increased the expression of neurotrophic factors in the hippocampus, leading to brain cell regeneration.[19]	Cinnamaldehyde and Eugenol.[19]
Curcuma longa	Rhizome	Wet and intermediate zones of Sri Lanka	Depression, bipolar and OCD	Reduces the negative effects of swim stress on levels of serotonin, 5-hydroxyindoleacetic acid, noradrenaline, and dopamine in the body. It also decreases the increase in serotonin turnover caused by the stress.[20]	Curcuminoids curcumin, demethoxycurcumin, and bis-demethoxycurcumin.[20]
Datura metel	Leaves and seeds	Dry zone	Schizophrenia	Not known	Hyoscyamine, scopolamine and atropine, withanolides, daturanolone, fastusic acid, and some tropane alkaloids.[21]
Eclipta alba	Leaves	Wet zone	Anxiety	Not known	Luteolin, apigenin, diosmetin, buddleoside and luteolin-7-o-glucoside etc.[22]
Foeniculum vulgare	Aerial parts and seeds	Only under cultivation	Depression, anxiety symptoms in postmenopausal women	Causes protective effects against stress and stress-related conditions by increasing the total neurotransmitter content and its antioxidant properties.[23]	Trans anethole, fenchone, estragol, p-anisaldehyde, among others.[23]
Ginkgo biloba	Leaves	Not widely spread/ Usually imported for use.	Depression, acute mania, bipolar disorder, and acute or chronic schizophrenia	The antioxidant and anti-inflammatory properties contribute to reestablishing the brain homeostasis in persons with mental illnesses.[24]	Di-trans-poly-cis-octadecaprenol, Quercetin (c), kaempferol (d), isorhamnetin (e), rutin, luteolin, delphidenon, myricetin, benzoic acid derivatives (ginkgolic acid), N-containing acids, sciadopitysin, ginkgetin, isoginkgetin, amentoflavone, bilobetin, and 5′-methoxybilobeti.[25]
Glycyrrhiza glabra	Root	Dry zone	Depression, anxiety	Glycyrrhizin acts as an inhibitor of 11β-hydroxysteroid-dehydrogenase type-2, which is responsible for converting cortisol to cortisone and antagonist of toll-like receptor 4.[26]	Glycyrrhizin, glycyrrhetic acid, isoliquiritin, isoflavones, among others.[27]
Hamidesmus indicus	Leaves	Western, central, and southern areas of Sri Lanka	Anxiety	The leaf extract showed facilitation of cholinergic transmission and inhibition of dopaminergic transmission.[28]	Flavonoids, phenols, glycosides[28].
Hibiscus tiliaceus	Flower	Very common in low counties	Postpartum depression	Phytosterols potentially help manage or prevent postpartum depression by establishing a balance between pregnancy-related hormone levels.[29]	Stigmasterol, stigmastadienol, and stigmastadienon.[29]

(continued)

Table 1. *(continued)*

Plant name	Part of the plant	Distribution of Sri Lanka	Ayurveda use	Pharmacology action/MOA	Discovered phytochemicals
Passiflora incarnate	Aerial parts of the flower	Mainly in the south coast	Anxiety and Bipolar disorder	Alkaloids and phenolic compounds of the flower are reportedly responsible for its anti-anxiety and sedative activity and it is mediated via its affinity to GABA - A and GABA - B receptors, and the effect on GABA uptake.[30]	Flavonoids (apigenin, luteolin, quercetin, kaempferol); Indole alkaloids (harman, harmine, harmalol, and harmaline); Cyanogenic glycoside (yanocardin).[30]
Piper methysticum	Root	Often found in dry zone	Generalized anxiety disorder, bipolar disorder, and schizophrenia.	Modulation of GABA receptors via blockage of voltage-gated sodium ion channels, leading to a reduction in excitatory neurotransmitter release.[31]	Lipophilic kavalactones.[32]
Piper retrofractum	Leaves	Often found in dry zone	Schizophrenia	Not known	Retrofractamide A, retrofractamide B, piperine, methyl piperate, dihydropiperlonguminine and piperoside.[32]
Rhodiola rosea	Root	Costal/mountain ranges	fatigue and cognitive dullness	Act as an agonist for serotonin and dopamine, due to its ability to inhibit enzyme monoamine oxidase.[33]	Flavonoids, glycosides, phenolic compounds, and organic acids.[34]
Sesbania grandiflora	Leaves	Only under cultivation	Depression, anxiety	The triterpene exhibits a wide spectrum of anticonvulsant profile and anxiolytic activity which also affects the action of GABA and serotonin, thus responding to bodily stress.[35]	Alkaloids, flavonoids, glycosides, triterpenoids, and saponins, among others.[35]
Vetiveria zizanioides	*Root*	Dry zone in Sri Lanka	Anxiety	Enhances the cholinergic transmission in the brain by increasing the onset of sodium nitrite, which further could support the nootropic activity.[36]	Phenolic compounds, flavonoids, sterols, saponins, tannins, glycosides, and carbohydrates.[37]
Zingiber officinale	Rhizome	Dry and wet zones	Anorexia, depression	It is a potent stimulator of pancreatic amylase and intestinal lipase activity, decreases intestinal transit time, and increases the appetite.[38] MAO-A enzyme catalyzes the deamination of the neurotransmitters (chiefly dopamine, serotonin, and noradrenaline) in the antidepressant activity of *Zingiber officinale* extract.[39]	Shogaol, gingerol, trans-1,8-cineole-3,6-dihydroxy-3-O-β-d-glucopyranoside, and trans-1,8-cineole-3,6-dihydroxy-3-O-β-d-glucopyranoside, gingerenone-A, and paradols.[40]

ACTH, adrenocorticotropic hormone; CRF, corticotropin releasing factor; GABA, gamma-aminobutyric acid; HPA, hypothalamic-pituitary-adrenal; MOA, mechanism of action; MAO-A, monoamine oxidase; OCD, obsessive-compulsive disorder.

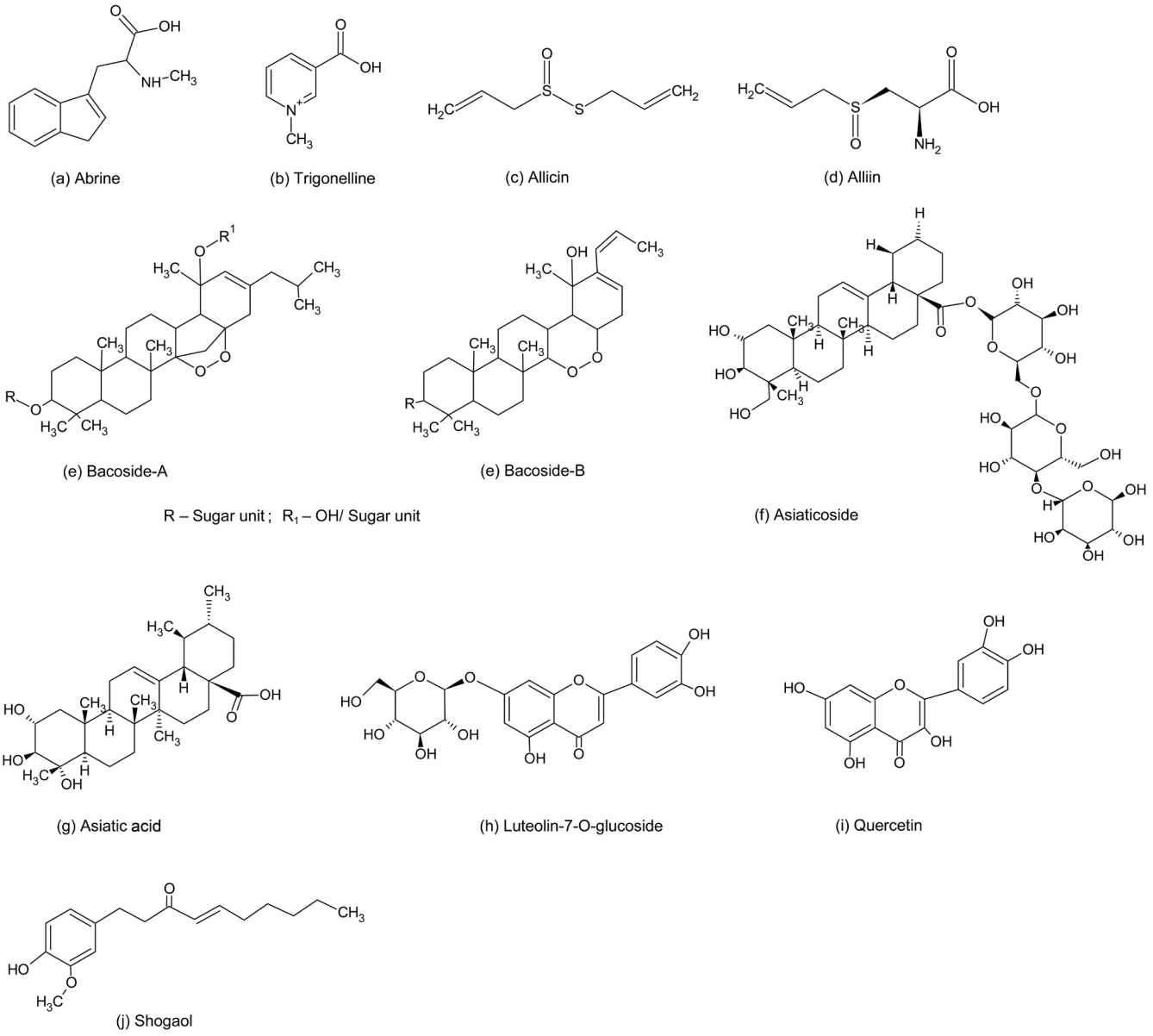

Fig. 2. Discovered phytochemicals from herbal plants used to treat mental disorders.

pared to conventional medications. While herbal plants have been effectively utilized in Ayurvedic practice for treating mental disorders, there are drawbacks alongside their beneficial effects. These include a lack of scientific evaluations, the potential for contamination during storage (such as fungal infection), the presence of metals that are difficult to remove (lead, cadmium, among others), and the possibility that certain plants may induce toxicity in various organs of the body.[56]

The therapeutic effectiveness of various natural compounds in treating mental disorders is promising, especially given their antioxidant, anti-inflammatory, and neuroprotective properties. Compounds like trigonelline, bacosides, asiaticoside, asiatic acid, and quercetin show significant potential in modulating neurotransmitter levels, reducing oxidative stress, and alleviating symptoms of mental disorders such as depression, anxiety, and neurodegenerative diseases. However, while these compounds offer substantial therapeutic potential, there are notable challenges and limitations. The lack of comprehensive scientific evaluation, risks of contamination, and potential toxicity are significant concerns that need to be addressed through further investigations.

Conclusions

In Sri Lankan Ayurvedic practice, a range of plant species is used for the treatment of mental health disorders. The growing dependence on and purported therapeutic benefits of various herbal plants and their bioactive compounds highlight the necessity for both their preservation and thorough research. To establish their clinical effectiveness, it's essential to investigate these remedies extensively. Such studies may help in isolating and purifying the bioactive

compounds, confirming the safety and tolerability of these products, and supporting the incorporation of herbal plants currently used in Ayurvedic medicine into clinical practice. Despite promising findings, the current review is limited to just 24 herbal plants, necessitating further investigation into a broader range of species. Additionally, more in-depth scientific research is needed to clarify the mechanisms of action of these plants and validate their clinical effectiveness. These efforts could offer potential solutions to the increasing prevalence of mental disorders.

Acknowledgments

We extend our gratitude to the Library of the Faculty of Indigenous Medicine at the University of Colombo, Rajagiriya, Sri Lanka, and the Pallekale Provincial Ayurvedic Hospital in Kandy, Sri Lanka for generously providing their resources to facilitate the data collection for this review.

Funding

This research received no specific grant from any funding agency.

Conflict of interest

The authors declare that there are no conflicts of interest in the publication of this manuscript.

Author contributions

Conceptualization (BJ, SG), acquisition of data (RS), analysis and interpretation of data (RS, SG), drafting the manuscript (RS), critical revision of the manuscript (SG, BJ), and study supervision (SG, BJ). All authors have made a significant contribution to this study and have approved the final manuscript.

References

[1] Stein DJ, Palk AC, Kendler KS. What is a mental disorder? An exemplar-focused approach. Psychological Medicine 2021;51(6):894–901. doi:10.1017/S0033291721001185, PMID:33843505.

[2] GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry 2022;9(2):137–150. doi:10.1016/S2215-0366(21)00395-3, PMID:35026139.

[3] Javaid SF, Hashim IJ, Hashim MJ, Stip E, Samad MA, Ahbabi AA. Epidemiology of anxiety disorders: global burden and sociodemographic associations. Middle East Curr Psychiatry 2023;30(1):44. doi:10.1186/s43045-023-00315-3.

[4] Ahmad Khan MS, Ahmad I. Herbal Medicine: Current Trends and Future Prospects. In: Ahmad Khan MS, Ahmad I, Chattopadhyay D (eds). New Look to Phytomedicine. Cambridge: Academic Press; 2019:3–13. doi:10.1016/B978-0-12-814619-4.00001-X.

[5] Sharma A, Gerbarg PL, Brown RP. Non-Pharmacological Treatments for ADHD in Youth. Adolesc Psychiatry (Hilversum) 2015;5(2):84–95. doi:10.2174/2210676605021504301549 37, PMID:27489754.

[6] Waisundara VY, Watawana MI. The classification of sri lankan medicinal herbs: an extensive comparison of the antioxidant activities. J Tradit Complement Med 2014;4(3):196–202. doi:10.4103/2225-4110.126175, PMID:25161925.

[7] Dharmadasa RM, Akalanka GC, Muthukumarana PR, Wijesekara RG. Ethnopharmacological survey on medicinal plants used in snakebite treatments in Western and Sabaragamuwa provinces in Sri Lanka. J Ethnopharmacol 2016;179:110–127. doi:10.1016/j.jep.2015.12.041, PMID:26724891.

[8] Farzana MUZN, Tharique IA, Sultana A. A review of ethnomedicine, phytochemical and pharmacological activities of *Acacia nilotica* (Linn) wild. J Pharmacogn Phytochem 2014;3(1):84–90.

[9] Afsar T, Razak S, Khan MR, Almajwal A. Anti-depressant and anxiolytic potential of *Acacia hydaspica* R. Parker aerial parts extract: Modulation of brain antioxidant enzyme status. BMC Complement Altern Med 2017;17(1):228. doi:10.1186/s12906-017-1671-x, PMID:28438149.

[10] Batiha GE, Akhtar N, Alsayegh AA, Abusudah WF, Almohmadi NH, Shaheen HM, *et al*. Bioactive Compounds, Pharmacological Actions, and Pharmacokinetics of Genus *Acacia*. Molecules 2022;27(21):7340. doi:10.3390/molecules27217340, PMID:36364163.

[11] Rahmani G, Farajdokht F, Mohaddes G, Babri S, Ebrahimi V, Ebrahimi H. Garlic (*Allium sativum*) improves anxiety- and depressive-related behaviors and brain oxidative stress in diabetic rats. Arch Physiol Biochem 2020;126(2):95–100. doi:10.1080/13813455.2018.1494746, PMID:30169970.

[12] El-Saber Batiha G, Magdy Beshbishy A, Wasef LG, Elewa YHA, Al-Sagan AA, Abd El-Hack ME, *et al*. Chemical Constituents and Pharmacological Activities of Garlic (*Allium sativum* L.): A Review. Nutrients 2020;12(3):872. doi:10.3390/nu12030872, PMID:32213941.

[13] de Souza AB, Pinheiro JCA, Soares JB, de Araújo JIF, de Araújo SMB, Batista FLA, *et al*. Antibacterial activity and anxiolytic-like effect of *Ziziphus joazeiro* Mart. leaves in adult zebrafish (*Danio rerio*). Fish Shellfish Immunol Rep 2023;5:100108. doi:10.1016/j.fsirep.2023.100108, PMID:37409181.

[14] Calabrese C, Gregory WL, Leo M, Kraemer D, Bone K, Oken B. Effects of a standardized *Bacopa monnieri* extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial. J Altern Complement Med 2008;14(6):707–713. doi:10.1089/acm.2008.0018, PMID:18611150.

[15] Patil N, Chandel V, Rana A, Jain M, Kaushik P. Investigation of *Cannabis sativa* Phytochemicals as Anti-Alzheimer's Agents: An In Silico Study. Plants (Basel) 2023;12(3):510. doi:10.3390/plants12030510, PMID:36771595.

[16] Bandawane DD, Beautikumari S, Gate SS, Patel AN. Evaluation of anti-arthritic activity of ethyl acetate fraction of *Cassia auriculata* Linn. leaves. Biomedicine & Aging Pathology 2014;4(2):105–115. doi:10.1016/j.biomag.2013.10.009.

[17] Jayaweera DMA. Medicinal Plants (indigenous and Exotic) Used in Ceylon: *Acanthaceae-Burseraceae*. Colombo: National Science Council of Sri Lanka; 1981.

[18] Puttarak P, Dilokthornsakul P, Saokaew S, Dhippayom T, Kongkaew C, Sruamsiri R, *et al*. Effects of *Centella asiatica* (L.) Urb. on cognitive function and mood related outcomes: A Systematic Review and Meta-analysis. Sci Rep 2017;7(1):10646. doi:10.1038/s41598-017-09823-9, PMID:28878245.

[19] Aryanezhad M, Abdi M, Amini S, Hassanzadeh K, Valadbeigi E, Rahimi K, *et al*. *Cinnamomum zeylanicum* extract has antidepressant-like effects by increasing brain-derived neurotrophic factor (BDNF) and its receptor in prefrontal cortex of rats. Avicenna J Phytomed 2021;11(3):302–313. PMID:34046326.

[20] Xia X, Cheng G, Pan Y, Xia ZH, Kong LD. Behavioral, neurochemical and neuroendocrine effects of the ethanolic extract from *Curcuma longa* L. in the mouse forced swimming test. J Ethnopharmacol 2007;110(2):356–363. doi:10.1016/j.jep.2006.09.042, PMID:17134862.

[21] Islam T, Ara I, Islam T, Sah PK, Almeida RS, Matias EFF, *et al*. Ethnobotanical uses and phytochemical, biological, and toxicological profiles of *Datura metel* L.: A review. Curr Res Toxicol 2023;4:100106. doi:10.1016/j.crtox.2023.100106, PMID:37228329.

[22] Jahan R, Al-Nahain A, Majumder S, Rahmatullah M. Ethnopharmacological Significance of *Eclipta alba* (L.) Hassk. (Asteraceae). Int Sch Res Notices 2014;2014:385969. doi:10.1155/2014/385969, PMID:27355071.

[23] Rather MA, Dar BA, Sofi SN, Bhat BA, Qurishi MA. Foeniculum vulgare: A comprehensive review of its traditional use, phytochemistry, pharmacology, and safety. Arab J Chem 2016;9(Suppl 2):S1574–S1583. doi:10.1016/j.arabjc.2012.04.011.

[24] Nazarinasab M, Behrouzian F, Negahban S, Sadegh AM, Zeynali E. Investigating the efficacy of *Ginkgo biloba* on the cognitive function

of patients undergoing treatment with electric shock: a double-blind clinical trial. J Med Life 2022;15(12):1540–1547. doi:10.25122/jml-2021-0262, PMID:36762332.
[25] Noor-E-Tabassum, Das R, Lami MS, Chakraborty AJ, Mitra S, Tallei TE, *et al*. *Ginkgo biloba*: A Treasure of Functional Phytochemicals with Multimedicinal Applications. Evid Based Complement Alternat Med 2022;2022:8288818. doi:10.1155/2022/8288818, PMID:35265150.
[26] Chakravarthi KK, Avadhani R. Beneficial effect of aqueous root extract of *Glycyrrhiza glabra* on learning and memory using different behavioral models: An experimental study. J Nat Sci Biol Med 2013;4(2):420–425. doi:10.4103/0976-9668.117025, PMID:24082744.
[27] Sharma V, Katiyar A, Agrawal RC. *Glycyrrhiza glabra*: Chemistry and Pharmacological Activity. Sweeteners. 2017:87–100. doi:10.1007/978-3-319-27027-2_21.
[28] Dautan D, Souza AS, Huerta-Ocampo I, Valencia M, Assous M, Witten IB, *et al*. Segregated cholinergic transmission modulates dopamine neurons integrated in distinct functional circuits. Nat Neurosci 2016;19(8):1025–1033. doi:10.1038/nn.4335, PMID:27348215.
[29] Shewale PB, Patil RA, Hiray YA. Antidepressant-like activity of anthocyanidins from *Hibiscus rosa-sinensis* flowers in tail suspension test and forced swim test. Indian J Pharmacol 2012;44(4):454–457. doi:10.4103/0253-7613.99303, PMID:23087504.
[30] Dhawan K, Kumar S, Sharma A. Anti-anxiety studies on extracts of *Passiflora incarnata* Linneaus. J Ethnopharmacol 2001;78(2-3):165–170. doi:10.1016/s0378-8741(01)00339-7, PMID:11694362.
[31] Sarris J, Kavanagh DJ, Byrne G, Bone KM, Adams J, Deed G. The Kava Anxiety Depression Spectrum Study (KADSS): a randomized, placebo-controlled crossover trial using an aqueous extract of *Piper methysticum*. Psychopharmacology (Berl) 2009;205(3):399–407. doi:10.1007/s00213-009-1549-9, PMID:19430766.
[32] Salleh WMNHW, Farediah A. Phytopharmacological investigations of *Piper retrofractum* Vahl. - a review. Agric Conspec Sci 2020;85(3):193–202.
[33] Ivanova Stojcheva E, Quintela JC. The Effectiveness of *Rhodiola rosea* L. Preparations in Alleviating Various Aspects of Life-Stress Symptoms and Stress-Induced Conditions-Encouraging Clinical Evidence. Molecules 2022;27(12):3902. doi:10.3390/molecules27123902, PMID: 35745023.
[34] Zhang S, Jiang S, Deng N, Zheng B, Li T, Liu RH. Phytochemical Profiles, Antioxidant Activity and Antiproliferative Mechanism of *Rhodiola rosea* L. Phenolic Extract. Nutrients 2022;14(17):3602. doi:10.3390/nu14173602, PMID:36079857.
[35] Choudhury NF, Sutradhar KB. Analgesic and CNS depressant activity of the crude extract of *Sesbania grandiflora*. Int Curr Pharm J 2012;1(3):56–61. doi:10.3329/icpj.v1i3.9663.
[36] Nirwane AM, Gupta PV, Shet JH, Patil SB. Anxiolytic and nootropic activity of *Vetiveria zizanioides* roots in mice. J Ayurveda Integr Med 2015;6(3):158–164. doi:10.4103/0975-9476.146548, PMID:26604550.
[37] Cheaha D, Issuriya A, Manor R, Kwangjai J, Rujiralai T, Kumarnsit E. Modification of sleep-waking and electroencephalogram induced by vetiver essential oil inhalation. J Intercult Ethnopharmacol 2016;5(1):72–78. doi:10.5455/jice.20160208050736, PMID:27069728.
[38] Nimrouzi M, Zarshenas MM. Anorexia: Highlights in Traditional Persian medicine and conventional medicine. Avicenna J Phytomed 2018;8(1):1–13. PMID:29387569.
[39] Olanrewaju JA, Owolabi JO, Awodein IP, Enya JI, Adelodun ST, Olatunji SY, *et al*. *Zingiber officinale* Ethanolic Extract Attenuated Reserpine-Induced Depression-Like Condition and Associated Hippocampal Aberrations in Experimental Wistar Rats. J Exp Pharmacol 2020;12:439–446. doi:10.2147/JEP.S275260, PMID:33173355.
[40] Rampogu S, Baek A, Gajula RG, Zeb A, Bavi RS, Kumar R, *et al*. Ginger (*Zingiber officinale*) phytochemicals-gingerenone-A and shogaol inhibit SaHPPK: molecular docking, molecular dynamics simulations and in vitro approaches. Ann Clin Microbiol Antimicrob 2018;17(1):16. doi:10.1186/s12941-018-0266-9, PMID:29609660.
[41] Ambathalawa SP. Sinahala Waidya Widyawa. 1st ed. Colombo: Samayawardana Pothhala; 2001.
[42] Lee G, Bae H. Therapeutic Effects of Phytochemicals and Medicinal Herbs on Depression. Biomed Res Int 2017;2017:6596241. doi:10.1155/2017/6596241, PMID:28503571.
[43] Plotsky PM, Owens MJ, Nemeroff CB. Psychoneuroendocrinology of depression. Hypothalamic-pituitary-adrenal axis. Psychiatr Clin North Am 1998;21(2):293–307. doi:10.1016/s0193-953x(05)70006-x, PMID:9670227.
[44] Liu B, Xu C, Wu X, Liu F, Du Y, Sun J, *et al*. Icariin exerts an antidepressant effect in an unpredictable chronic mild stress model of depression in rats and is associated with the regulation of hippocampal neuroinflammation. Neuroscience 2015;294:193–205. doi:10.1016/j.neuroscience.2015.02.053, PMID:25791226.
[45] Fajemiroye JO, da Silva DM, de Oliveira DR, Costa EA. Treatment of anxiety and depression: medicinal plants in retrospect. Fundam Clin Pharmacol 2016;30(3):198–215. doi:10.1111/fcp.12186, PMID:26851117.
[46] Nassir ZS, Khadem EJ. Phytochemical investigations of Iraqi *Abrus precatorius* Linn. Plant. Iraqi J Pharm Sci 2018;27(1):30–38. doi:10.31351/vol27iss1pp30-38.
[47] Țigu AB, Moldovan CS, Toma VA, Farcaș AD, Moț AC, Jurj A, *et al*. Phytochemical Analysis and In Vitro Effects of *Allium fistulosum* L. and *Allium sativum* L. Extracts on Human Normal and Tumor Cell Lines: A Comparative Study. Molecules 2021;26(3):574. doi:10.3390/molecules26030574, PMID:33499159.
[48] Majumdar S, Basu A, Paul P, Halder M, Jha S. Bacosides and Neuroprotection. In: Ramawat KG, Mérillon JM (eds). Natural Products: Phytochemistry, Botany and Metabolism of Alkaloids, Phenolics and Terpenes. Berlin: Springer; 2013:3639–3660. doi:10.1007/978-3-642-22144-6_157.
[49] Sekhar VC, Viswanathan G, Baby S. Insights Into the Molecular Aspects of Neuroprotective Bacoside A and Bacopaside I. Curr Neuropharmacol 2019;17(5):438–446. doi:10.2174/1570159X16666180419123022, PMID:29676230.
[50] Wong JH, Barron AM, Abdullah JM. Mitoprotective Effects of *Centella asiatica* (L.) Urb.: Anti-Inflammatory and Neuroprotective Opportunities in Neurodegenerative Disease. Front Pharmacol 2021;12:687935. doi:10.3389/fphar.2021.687935, PMID:34267660.
[51] Rehfeldt SCH, Silva J, Alves C, Pinteus S, Pedrosa R, Laufer S, *et al*. Neuroprotective Effect of Luteolin-7-O-Glucoside against 6-OHDA-Induced Damage in Undifferentiated and RA-Differentiated SH-SY5Y Cells. Int J Mol Sci 2022;23(6):2914. doi:10.3390/ijms23062914, PMID:35328335.
[52] Silvestro S, Bramanti P, Mazzon E. Role of Quercetin in Depressive-Like Behaviors: Findings from Animal Models. Appl Sci 2021;11(15):7116. doi:10.3390/app11157116.
[53] Mao QQ, Xu XY, Cao SY, Gan RY, Corke H, Beta T, *et al*. Bioactive Compounds and Bioactivities of Ginger (*Zingiber officinale* Roscoe). Foods 2019;8(6):185. doi:10.3390/foods8060185, PMID:31151279.
[54] Lavretsky H. Complementary and alternative medicine use for treatment and prevention of late-life mood and cognitive disorders. Aging Health 2009;5(1):61–78. doi:10.2217/1745509X.5.1.61, PMID:19956796.
[55] Fathinezhad Z, Sewell RDE, Lorigooini Z, Rafieian-Kopaei M. Depression and Treatment with Effective Herbs. Curr Pharm Des 2019;25(6):738–745. doi:10.2174/1381612825666190402105803, PMID:30947651.
[56] Schmidt M, Betti G, Hensel A. Saffron in phytotherapy: pharmacology and clinical uses. Wien Med Wochenschr 2007;157(13-14):315–319. doi:10.1007/s10354-007-0428-4, PMID:17704979.