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Mechanistic Insights into Medicinal Plants Used in Iranian Traditional Medicine for Depression

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ABSTRACT

Depression is a widespread mental disorder that significantly impairs physical and psychological health. Iranian traditional medicine, grounded in centuries of herbal knowledge, offers natural and low-risk options to alleviate depressive symptoms and improve emotional well-being. This review aims to identify key medicinal plants used in Iranian traditional medicine for depression and explore their mechanisms of action. For this purpose, a thorough review of authoritative Iranian traditional medicine texts, herbal pharmacopeias, and scientific literature was conducted. Data on plants with reported antidepressant properties were systematically gathered and analyzed. Results showed that numerous plants, including *Melissa officinalis* L., *Curcuma longa* L., *Valeriana officinalis* L., *Hypericum perforatum* L., *Borago officinalis* L., *Lavandula angustifolia* Mill. , *Ocimum basilicum* L., *Coriandrum sativum* L., *Malus domestica Borkh.*, *Crocus sativus* L., *Matricaria chamomilla* L., *Citrus aurantium* L., *Valeriana montana* L., *Rosa damascena Mill.*, *Viola odorata* L., *Cichorium intybus* L., *Boswellia serrata* Roxb., *Elettaria cardamomum* (L.) Maton, *Elaeagnus angustifolia* L., *Tanacetum vulgare* L., *Glycyrrhiza glabra* L., *Alcea rosea* L., *Thymus vulgaris* L., *Rosmarinus officinalis* L., *Camellia sinensis*, have shown antidepressant effects. Their efficacy is attributed to multiple mechanisms: enhancing GABA activity, modulating central nervous system function, reducing inflammation and oxidative stress, and regulating neurotransmitters such as serotonin, dopamine, and norepinephrine. These plants also exert anxiolytic effects by balancing hormonal activity and mitigating neuroinflammation. Beyond their therapeutic relevance, many of these species are recognized as medicinal and aromatic crops with considerable industrial value due to their use in phytopharmaceuticals, nutraceuticals, essential oils, and functional health products, highlighting their importance for the medicinal plant industry. In conclusion, medicinal plants used in Iranian traditional medicine demonstrate promising complementary potential for depression management through diverse biochemical pathways. However, more rigorous clinical and experimental studies are needed to validate their therapeutic efficacy and determine optimal dosages.

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1. Introduction

Depression is among the most prevalent psychiatric disorders worldwide, profoundly impacting individuals' quality of life, social functioning, and overall well-being (Khaksarian *et al*., 2019; Hosseinzadeh *et al*., 2018; Nazari *et al*., 2022). Characterized by persistent low mood, reduced motivation, sleep disturbances, fatigue, and impaired concentration, severe depression may lead to suicidal behavior (Khaksarian *et al*., 2021; Rashidipour *et al*., 2023; Ghorbanzadeh *et al*., 2022). According to the latest World Health Organization reports, depression affects roughly 300 million people globally and ranks as a leading cause of disability (Hammen, 2005; Paykel, 2008). The etiology of depression is complex and multifactorial, involving genetic, biological, psychological, and environmental influences. At the biological level, dysregulation of neurotransmitters—particularly serotonin, dopamine, and norepinephrine plays a crucial role, though the classic monoamine

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hypothesis is now understood to be incomplete (Saveanu and Nemeroff, 2012; Durisko *et al*., 2015). Emerging research highlights the importance of neurotrophic factors such as BDNF and the gut-brain axis in the pathophysiology of depression (Spalletta *et al*., 2006). Chronic inflammation and prolonged stress further contribute to structural and functional changes in brain regions responsible for mood regulation, including the prefrontal cortex, hippocampus, and amygdala. Psychosocial stressors, such as adverse life events and insufficient social support, also significantly influence the onset and persistence of depressive symptoms (Saveanu and Nemeroff, 2012; Durisko *et al*., 2015; Spalletta *et al*., 2006; Belzung *et al*., 2015; Dunlop and Nemeroff, 2007; Spellman and Liston, 2020).

Pharmacological treatments commonly include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and tricyclic antidepressants (TCAs), all targeting neurotransmitter systems to restore neural function (Brigitta, 2002; Beck and Alford, 2009). Despite their effectiveness, these medications frequently cause side effects—ranging from nausea and sexual dysfunction to weight gain—and carry an increased risk of suicidal ideation in vulnerable populations, especially children and adolescents, which limits their long-term use (Wong and Licinio, 2001; Johnson, 1981).

In contrast, Iranian traditional medicine offers a rich repository of herbal remedies that may provide safer, natural alternatives or complementary options for managing depression. Botanicals such as saffron, lemon balm, and valerian have garnered attention for their mood-stabilizing and anxiolytic effects (Zhang and Cheng, 2019; Guzmán Gutiérrez *et al*., 2014). However, despite promising safety profiles, the lack of rigorous clinical trials and standardized herbal preparations hampers definitive conclusions regarding their therapeutic value (Ding *et al*., 2024).

In addition to their medicinal importance, many of these species are cultivated as medicinal and aromatic plants and constitute valuable raw materials for the pharmaceutical, nutraceutical, food, and cosmetic industries. The growing global demand for plant-derived bioactive compounds, essential oils, and botanical extracts has increased the economic and industrial significance of medicinal and aromatic plants, particularly those rich in neuroactive secondary metabolites (Salamon, 2024; Mansinhos *et al*., 2024).

This review systematically identifies and evaluates medicinal plants used in Iranian traditional medicine for depression, emphasizing their pharmacological mechanisms of action. Additionally, it highlights the critical need for well-designed clinical studies to validate these treatments scientifically, aiming to expand their potential role in contemporary mental health care.

2. Materials and methods

This study employs a structured narrative review designed to identify medicinal plants reputed for their antidepressant properties within the framework of Iranian traditional medicine. Unlike a systematic review, this approach facilitates an integrative analysis of both classical herbal texts and contemporary pharmacological evidence, thereby offering a comprehensive perspective on the topic. Extensive searches were conducted across multiple electronic databases including PubMed, Scopus, EMBASE, Cochrane Library, as well as Iranian-specific databases such as Sid.ir and Magiran. The search strategy incorporated relevant keywords in both English and Persian to capture a broad spectrum of pertinent literature.

Inclusion criteria encompassed sources that provided documented evidence of medicinal plants traditionally used to alleviate depressive symptoms or enhance mental well-being according to Iranian traditional medical knowledge. Both classical manuscripts such as Avicenna's *Canon of Medicine* (Al-Qanun fi al-Tibb) and various *Qarabadins* (pharmacopoeias) and modern pharmacological studies demonstrating antidepressant effects were considered. Exclusion criteria involved studies lacking empirical data, those focused exclusively on non-herbal or unrelated psychiatric interventions, and reports not written in English or Persian. To ensure reliability, the credibility of both traditional and contemporary sources was critically appraised based on authorship, publication venue, and methodological rigor.

Data extraction was systematically organized into detailed tables summarizing each plant's botanical identification, traditional applications, and documented pharmacological mechanisms. The antidepressant potential of the selected plants was then evaluated by

synthesizing traditional claims with modern scientific evidence, enabling a nuanced understanding of their therapeutic roles in managing depression.

3. Results and discussion

The literature review highlighted a range of medicinal plants traditionally used in Iran for the management of depression. Notable examples include *Melissa officinalis* L., *Curcuma longa* L., *Valeriana officinalis* L., *Hypericum perforatum* L., *Borago officinalis* L., *Lavandula angustifolia* Mill., and *Crocus sativus* L. Additional medicinal plants and detailed information are presented in Table 1. These plants have been traditionally attributed with significant efficacy in alleviating depressive symptoms. A detailed summary of their therapeutic properties, traditional applications, and proposed mechanisms of action is provided in Table 1. The excerpted mechanisms of action of medicinal plants on depression are illustrated in Fig. 1. The general mechanisms of medicinal plants acting on factors influencing depression are illustrated in Fig. 2.

The findings indicate that medicinal plants exert their antidepressant effects primarily through three key mechanisms. First, they regulate neurotransmitter systems by increasing the levels of serotonin, dopamine, and norepinephrine, which play central roles in mood and motivation control. Plants such as *Crocus sativus* improve depressive symptoms by inhibiting serotonin reuptake, while enhancing GABA receptor activity reduces anxiety and stress, both crucial factors in mitigating depression severity. The second mechanism involves reducing inflammation and oxidative stress; plants like *Boswellia serrata* and *Rosmarinus officinalis* possess potent anti-inflammatory and antioxidant properties that decrease chronic inflammatory processes and neutralize free radical damage, thereby supporting neural health. This mechanism is particularly important for managing the structural and functional brain changes observed in depression. Lastly, modulation of the hypothalamic-pituitary-adrenal (HPA) axis represents the third significant mechanism. Certain plants, such as *Glycyrrhiza glabra*, regulate this axis by lowering cortisol levels, thereby balancing stress responses and exerting protective effects against mood disorders. Together, these integrated mechanisms underlie the comprehensive biological impact of medicinal plants on depression, highlighting their potential as complementary or alternative therapeutic options.

From an industrial perspective, several of the reviewed species, including *Crocus sativus*, *Melissa officinalis*, *L. angustifolia* Mill., *Thymus vulgaris*, *Rosmarinus officinalis*, and *Rosa damascena*, are commercially important medicinal and aromatic crops. Their bioactive metabolites and essential oils are extensively utilized in phytopharmaceutical, nutraceutical, cosmetic, and wellness industries, creating opportunities for value-added product development based on scientifically validated antidepressant properties (Mansinhos *et al*., 2024; Olivero-Verbel *et al*., 2024; Câmara *et al*., 2024).

This table introduces the biological characteristics and bioactive compounds of diverse medicinal plants. The information includes life cycle, plant type, habitat, environmental adaptability, and active compounds such as flavonoids, acids, and essential oils. These data can be useful for scientific research and medicinal plant applications, as mentioned in Table 2.

Depression is a complex psychiatric disorder with significant impact on quality of life. Conventional pharmacological and psychotherapeutic treatments often face challenges such as side effects, delayed onset of action, and patient non-compliance. These limitations highlight the need for complementary and safer therapeutic options. Traditional Iranian medicine, rooted in extensive botanical knowledge, provides a range of plant-based remedies that act through multiple physiological and psychological mechanisms, offering promising alternatives with fewer adverse effects.

A comprehensive review of the literature reveals over forty medicinal plant species with documented antidepressant properties, many of which have longstanding applications within traditional medicinal systems. Notable among these are *Albizia zygia*, *Calculus bovis sativus*, *Celastrus paniculatus*, various *Cinnamomum* species, *Erythrina velutina*, *Ficus platyphylla*, *Garcinia mangostana*, *Hyptis martiusii*, and *Polygonum multiflorum*. The antidepressant mechanisms attributed to these plants encompass antioxidant and anti-inflammatory activities, modulation of neurotransmitter systems, neuroprotective effects, and regulation of the hypothalamic-pituitary-adrenal (HPA) axis (Remali and Aizat, 2024).

Table 1. Characteristics and mechanisms of medicinal plants with anti-depressing properties

Scientific name	Family	Plant part	Traditional use	Mechanism of action	References
Melissa officinalis L.	Lamiaceae	Leaf	Sedative, antidepressant	Increases GABA activity, regulates CNS	Ghazizadeh et al. (2020)
Curcuma longa L.	Zingiberaceae	Root	Anti-inflammatory, antidepressant	Reduces inflammation, antioxidant effects, serotonin regulation	Oh et al. (2025)
Valeriana officinalis L.	Valerianaceae	Root	Sedative, improves sleep	Enhances GABA receptors, reduces anxiety and stress	Neamati et al. (2014)
Hypericum perforatum L.	Hypericaceae	Flower Leaf	Antidepressant, mood enhancer	Increases serotonin, dopamine, norepinephrine levels	Whiskey et al. (2001)
Borago officinalis L.	Boraginaceae	Flower Leaf	Antidepressant, sedative	Reduces neuroinflammation, modulates neurotransmitters	Ibrahim and Alshammaa (2023)
Lavandula angustifolia Mill.	Lamiaceae	Flower	Sedative, anxiolytic	Increases GABA, reduces stress	Nikfarjam et al. (2013)
Ocimum basilicum L.	Lamiaceae	Leaf	Antidepressant, anti-stress	Regulates neurotransmitter activity	Ayuob et al. (2017)
Coriandrum sativum L.	Apiaceae	Leaf	Sedative, anxiolytic	Anti-inflammatory effects, stress reduction	Kharade et al. (2011)
Malus domestica Borkh.	Rosaceae	Fruit	Mood enhancer, sedative	Antioxidant properties, improves brain health. Apple's antioxidant properties help improve mood and reduce depression.	Lim (2012)
Crocus sativus L.	Iridaceae	Stigma	Antidepressant, mood enhancer	*C. sativus* exerts antidepressant effects via serotonin reuptake inhibition, NMDA receptor antagonism, and antioxidant actions.	Lopresti and Drummond (2014)
Matricaria chamomilla L.	Asteraceae	Flower	Sedative, anti-inflammatory	Reduces inflammation, sedative effects	Amsterdam et al. (2020)
Citrus aurantium L.	Rutaceae	Flower	Sedative, anxiolytic	Regulates CNS	Li et al. (2024)
Valeriana montana L.	Valerianaceae	Root	Sedative, improves sleep	Enhances GABA receptor activity	Jung et al. (2014)
Rosa damascena Mill.	Rosaceae	Flower	Sedative, antidepressant	Hormone regulation, increases serotonin	Rasooli et al. (2021)
Viola odorata L.	Violaceae	Flower Leaf	Sedative, anti-inflammatory	Anti-inflammatory and anxiolytic effects	Shayesteh et al. (2020)
Cichorium intybus L.	Asteraceae	Root	Blood purifier, sedative	Anti-inflammatory and sedative effects	Luo et al. (2025)
Boswellia serrata Roxb.	Burseraceae	Resin	Anti-inflammatory, sedative	*B. serrata* reduces neuroinflammation linked to depression by inhibiting inflammatory pathways via boswellic acids.	Adake et al. (2015)
Elettaria cardamomum (L.) Maton	Zingiberaceae	Seed	Sedative, antidepressant	*E. cardamomum* may alleviate depression by antioxidant activity and HPA axis modulation, beyond just improving blood circulation.	Masoumi-Ardakani et al. (2017)
Elaeagnus angustifolia L.	Elaeagnaceae	Fruit	Sedative, analgesic	Anti-inflammatory and analgesic effects	Zeinalzadeh et al. (2016)
Tanacetum vulgare L.	Asteraceae	Flower Leaf	Sedative, antidepressant	Anti-inflammatory and sedative effects	Lechkova et al. (2024)
Glycyrrhiza glabra L.	Fabaceae	Root	Anti-stress, anti-inflammatory	Regulates cortisol, anti-inflammatory effects. *G. glabra* regulates HPA axis activity and cortisol metabolism by inhibiting 11β-HSD.	Zhao et al. (2008)
Alcea rosea L.	Malvaceae	Flower Leaf	Anti-inflammatory, sedative	Anti-inflammatory and analgesic effects	Mombeini et al. (2017)
Thymus vulgaris L.	Lamiaceae	Leaf, flower	Antidepressant, anxiolytic	Thymol from *T. vulgaris* demonstrates antidepressant and anxiolytic effects in the CUMS model, likely via reducing inflammatory markers and modulating the HPA axis.	Deng et al. (2015)
Rosmarinus officinalis L.	Lamiaceae	Leaf	Enhances concentration, antidepressant	Rosemary exhibits antidepressant effects through AChE inhibition and anti-inflammatory actions, beyond its antioxidant and blood flow benefits.	Zhang and Lu (2025)
Camellia sinensis	Theaceae	Leaf	Antidepressant	Green tea primarily exerts antidepressant effects through inhibition of MAO-A, the isoform more relevant to depression.	Rothenberg and Zhang (2019); Shastry et al. (2016)

Ethnographic research conducted in 2017 involving interviews with 29 traditional healers in the city of Shahrekord identified several plants prevalent in the treatment of anxiety and depression in that region. These include *Fritillaria imperialis*, *Ducrosia anethifolia*, *Stachys lavandulifolia*, *Thymus vulgaris*, *Valeriana officinalis*, and *Melissa officinalis*. These species are recognized in local traditional knowledge as

effective anxiolytic and antidepressant agents (Teimouri *et al*., 2019). Similarly, plants such as St. John's wort, lavender, ginseng, chamomile, saffron, and lemon balm have garnered widespread popular use due to their calming properties and antidepressant effects, offering natural, low-risk options for managing depression and associated conditions such as anxiety and insomnia (Ding *et al*., 2024).

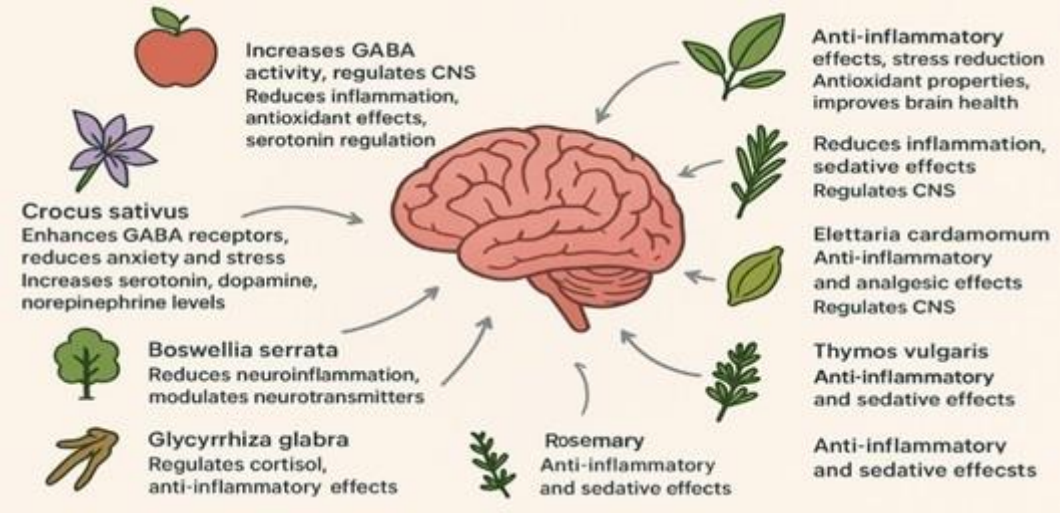


Figure 1. Excerpted mechanisms of action of medicinal plants on depression

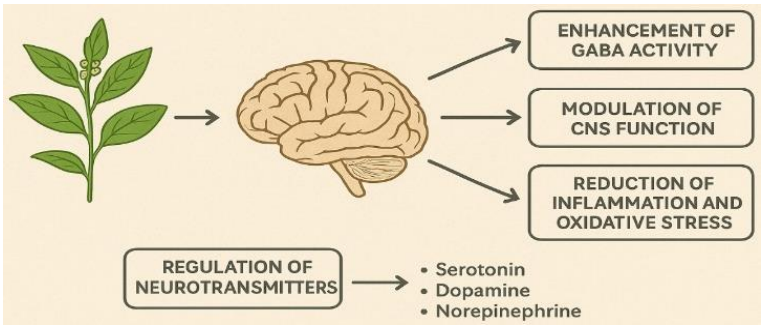


Figure 2. General mechanisms of medicinal plants on factors influencing depression

Table 2. Characteristics and bioactive compounds of various medicinal plants

Scientific name	Bioactive compounds
Melissa officinalis L.	Rosmarinic acid, flavonoids, terpenes
Curcuma longa L.	Curcumin, demethoxycurcumin, bisdemethoxycurcumin
Valeriana officinalis L.	Valerenic acid, valerenal, flavonoids
Hypericum perforatum L.	Hyperforin, Hypericin, pseudohypericin, flavonoids
Borago officinalis L.	Borage oil, gamma-linolenic acid (GLA)
Lavandula angustifolia Mill.	Linalool, linalyl acetate, flavonoids
Ocimum basilicum L.	Eugenol, flavonoids, rosmarinic acid
Coriandrum sativum L.	Linalool, decanal, coriandrin
Malus domestica Borkh.	Quercetin, phloridzin, flavonoids
Crocus sativus L.	Crocin, safranal, picrocrocin
Matricaria chamomilla L.	Chamazulene, apigenin, bisabolol
Citrus aurantium L.	Hesperidin, synephrine, flavonoids
Valeriana montana L.	Valerenic acid, iridoids
Rosa damascena Mill.	Rosmarinic acid, anthocyanins, essential oils
Viola odorata L.	Violanol, rutin, flavonoids
Cichorium intybus L.	Inulin, sesquiterpene lactones, flavonoids
Boswellia serrata Roxb.	Boswellic acids, essential oils
Elettaria cardamomum (L.) Maton	Cardamom oil, 1,8-cineole, flavonoids
Elaeagnus angustifolia L.	Ellagic acid, flavonoids
Tanacetum vulgare L.	Thujone, flavonoids, tannins
Glycyrrhiza glabra L.	Glycyrrhizin, flavonoids, saponins
Alcea rosea L.	Flavonoids, anthocyanins
Thymus vulgaris L.	Thymol and carvacrol
Rosmarinus officinalis L.	Rosmarinic acid, flavonoids, terpenes
Camellia sinensis	Catechins, flavonoids

Globally, various traditional medical systems acknowledge the antidepressant efficacy of certain botanicals, notably saffron and lavender. While promising, these findings highlight the imperative for further rigorous research to precisely delineate their efficacy and underlying mechanisms before such herbal remedies can be confidently positioned as alternatives to synthetic antidepressants (Remali and Aizat, 2024). Despite the proven efficacy of conventional antidepressants, including SSRIs, SNRIs, and tricyclic antidepressants (TCAs), their use is often accompanied by adverse effects, slow onset of action, and treatment resistance in some patients. Such challenges fuel patient interest in complementary therapies with better safety profiles (Grego *et al*., 2025). Traditional Iranian medicine, grounded in the principles of temperament modification and systemic balance, utilizes a diverse array of herbs with anxiolytic, antidepressant, and mood-enhancing effects that may complement or substitute standard pharmacotherapy (Manteghi *et al*., 2025).

These plants' multifactorial modes of action—encompassing antioxidant and anti-inflammatory properties, regulation of key neurotransmitters such as serotonin, dopamine, and norepinephrine, neuroprotection, and HPA axis modulation—endow them with a broader therapeutic scope than many conventional drugs (Nguyen *et al*., 2025). However, the absence of high-quality, controlled clinical trials, lack of standardized dosing, and variability in chemical composition and formulation presently impede their integration into mainstream clinical practice. This gap calls for intensified scientific inquiry and development of standardized protocols to ensure safety and efficacy (Nguyen *et al*., 2025).

Standardization is also essential for industrial utilization, as consistent phytochemical profiles are required for large-scale production of herbal medicines, botanical supplements, and plant-derived health products. Advances in cultivation, processing technologies, and metabolite characterization may facilitate the commercialization of these medicinal plant resources (Chen *et al*., 2024; Newman and Cragg, 2020).

Integrating the profound wisdom of Iranian traditional medicine with cutting-edge scientific research promises the development of holistic, safe, and effective treatments that can address patient needs more comprehensively and gain wider acceptance within the medical community.

Despite promising evidence supporting the antidepressant potential of medicinal plants, significant limitations hinder their widespread clinical application. Foremost among these is the scarcity of well-designed, controlled clinical trials that rigorously evaluate their efficacy and safety. Moreover, the lack of standardized dosing protocols and variations in plant composition affected by environmental factors and preparation methods pose considerable challenges to reproducibility and generalizability. Another critical gap lies in insufficient research on potential herb-drug interactions, which may impact patient safety when combined with conventional pharmaceuticals. Future studies should prioritize robust clinical investigations, the development of standardized formulations, and comprehensive safety assessments. Additionally, a deeper understanding of the precise biochemical mechanisms and consideration of individual patient differences are essential to optimize therapeutic outcomes. Ultimately, integrating traditional botanical wisdom with modern scientific approaches offers a promising pathway toward safe, effective, and accessible herbal treatments for depression.

4. Conclusion

While historical and preliminary scientific evidence provides promising support for the use of medicinal plants in managing depression, the lack of rigorous clinical trials and standardized herbal formulations remains a critical obstacle to their widespread clinical adoption. Furthermore, variability among plant species, influenced by environmental factors and preparation methods, poses significant challenges for both research consistency and practical application. Consequently, well-designed scientific studies and controlled clinical trials are essential to establish optimal dosages, confirm safety profiles, and clarify the precise mechanisms of action. Given the growing interest among patients and healthcare practitioners in natural and complementary therapies, addressing these gaps is both timely and necessary. Ultimately, integrating Iran's extensive traditional botanical knowledge with contemporary scientific methodologies could pave the way for safe, effective, and accessible herbal treatments for depression, thereby contributing meaningfully to public mental health care.

Conflict of interests

The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. No humans or animals were used in the present research. The authors have adhered to ethical standards, including avoiding plagiarism, data fabrication, and double publication.

Consent for publications

All authors read and approved the final manuscript for publication.

Availability of data and material

All the data are embedded in the manuscript.

Authors' contributions

Informed consent was obtained from all individual participants included in the study.

Informed consent

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Generative AI statement

The author declares that generative AI (artificial intelligence) tools, including Grammarly & QuillBot, were used to enhance the language & clarity of this work. The author takes full responsibility for the accuracy & integrity of the content.

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