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The use of selected medicinal plants in the regulation of the autonomic nervous system through the neurotransmitter system during stress

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Abstract

Stress is an inherent component of human life that cannot be entirely eliminated; however, effective coping strategies can mitigate its impact and improve problem-solving capabilities. Alongside pharmacotherapy, interventions such as psychotherapy, physical exercise, and herbal medicine are widely employed to support mental health. Herbal therapy utilizes plants with bioactive properties to complement conventional treatments, often providing benefits without the adverse effects commonly associated with synthetic drugs. Herbal interventions should be used under professional supervision, as inappropriate combinations with conventional medications, incorrect dosages, or use in contraindicated conditions may lead to unpredictable and potentially harmful outcomes. Medicinal plants used in the management of depression can be categorized according to their effects: mood-enhancing (e.g., *Hypericum perforatum*, saffron), anxiolytic and calming, and sleep-promoting. Such interventions may also alleviate neurovegetative symptoms, including gastrointestinal disturbances, tachycardia, hot flashes, and panic attacks. When appropriately integrated with psychotherapy, pharmacotherapy, and structured physical activity, herbal remedies can significantly enhance both psychological and physiological functioning. *Hypericum perforatum* (St. John's wort) is among the most extensively studied herbs for depression, acting through modulation of neurotransmitter systems, particularly serotonin, which influences mood, sleep, appetite, blood pressure, and body temperature. The aim of this study is to present the fundamental mechanisms of action of selected medicinal plants on the human body, with particular emphasis on their use in alleviating stress and associated disorders, including depression and sleep disturbances

Keywords: depression; herbal medicine; adaptogens; St. John's wort

Introduction

Depression is one of the most significant challenges in contemporary psychiatry and public health, both due to its high prevalence and its multidimensional social, economic, and health-related consequences. In the cognitive framework developed by Aaron T. Beck, depression is understood as a disorder resulting from persistent maladaptive cognitive schemas and dysfunctional beliefs concerning the self, the surrounding world, and the future. These schemas influence the interpretation of stimuli and life experiences, leading to systematic cognitive distortions and the reinforcement of a negative view of reality. Individuals suffering from depression tend to exhibit excessive self-criticism, reduced self-esteem, and beliefs about their own incompetence and worthlessness. At the same time, they are prone to perceiving the world as threatening, unjust, or lacking in support, as well as maintaining pessimistic beliefs regarding the future and the possibility of improving their life situation (Golonka et al., 2024). These cognitive mechanisms form the so-called Beck cognitive triad, considered one of the key elements in the pathogenesis of depression.

From the perspective of medical classifications, depression is defined in the International Classification of Diseases (ICD-11), developed by the World Health Organization, as a mood disorder, while in the DSM-5-TR classification it is included among major depressive disorders. However, it should be emphasized that referring to depression solely as a “disease” may be an oversimplification, as it is a complex and multifactorial condition. Its pathogenesis involves biological, genetic, and neurochemical factors, as well as psychological, environmental, and social influences. Unlike many somatic diseases, depression does not have a single specific diagnostic biomarker, and its clinical presentation is highly heterogeneous and variable in symptom severity. Functional disturbances affecting emotional, cognitive, behavioral, and somatic domains are also characteristic, and in many cases may be reversible with appropriately selected treatment and therapeutic support.

Depression is currently one of the most frequently diagnosed mental disorders worldwide, affecting individuals regardless of age, gender, social status, or level of education. According to the World Health Organization, at least 350 million people worldwide suffer from depression, with prevalence being nearly twice as high in women as in men (WHO, 2017; Salk, Hyde, & Abramson, 2017). These differences are explained, among other factors, by hormonal influences, psychosocial determinants, and differing coping strategies for stress. In 2002, depression ranked fourth among the leading causes of disability worldwide, while epidemiological projections suggest that by 2030 it may become the second most common cause of disease burden, particularly in low- and middle-income countries (Mathers et al., 2006). This rapid increase in the significance of depression is linked, among other factors, to ongoing urbanization, chronic stress, socioeconomic changes, and limited access to specialized psychiatric care in many regions of the world.

The consequences of depression are multifaceted and include both a decline in individual quality of life and a substantial burden on healthcare systems and the economy. The disorder leads to significant psychological distress, loss of motivation, reduced occupational and social functioning, as well as impaired interpersonal relationships and family functioning. Individuals with depression often experience reduced concentration, memory impairment, chronic fatigue, sleep disturbances, and an increased risk of self-harm and suicidal behavior. In many cases, patients require long-term

pharmacological treatment, psychotherapy, hospitalization, rehabilitation, and various social services, all of which generate considerable economic and social costs (Pużyński, 2002).

In recent years, there has been growing interest in complementary approaches to the treatment of depression, including phytotherapy (herbal medicine). Phytotherapy is based on the use of bioactive compounds present in medicinal plants, which may influence central nervous system function, neurotransmitter regulation, and the body's stress response. Numerous studies indicate that plant-based preparations may exhibit antidepressant, anxiolytic, anti-inflammatory, and neuroprotective effects, particularly in mild to moderate depressive disorders (Chrzanowska, 2013; Linde, Berner, & Kriston, 2008). Plant-based therapies have been used since ancient civilizations in Egypt, Greece, China, and India, making phytotherapy one of the oldest therapeutic systems in the history of medicine (Petrovska, 2012; Klimuszko, 2020).

Modern pharmacological and clinical research confirms the effectiveness of certain medicinal plants in alleviating symptoms of depression and stress-related disorders. Among the best studied are saffron (*Crocus sativus* L.), lavender (*Lavandula angustifolia*), and St John's wort (*Hypericum perforatum* L.), which are attributed antidepressant, anxiolytic, anti-inflammatory, and mood-stabilizing properties (Picheta et al., 2024). The mechanisms of action of these plants include modulation of serotonergic, dopaminergic, and GABAergic systems, effects on the hypothalamic–pituitary–adrenal axis, and reduction of oxidative stress and inflammatory processes. Herbal preparations are generally characterized by relatively good tolerability and a lower risk of adverse effects compared to some synthetic antidepressants, which allows for their long-term use (Możdżeń et al., 2021).

However, despite the natural origin of their active compounds, phytotherapy is not entirely risk-free. Of particular importance are potential interactions between herbal preparations and conventional medications used in the treatment of chronic diseases; therefore, their combined use should be supervised by a physician or pharmacist (Rogowska & Giermaziak, 2018).

The aim of this study is to analyze and discuss the mechanisms of action of selected medicinal plants used in the reduction of stress and the alleviation of disorders associated with chronic psychological tension, with particular emphasis on depression and sleep disturbances. The paper also focuses on presenting current data regarding the efficacy and safety of phytotherapy as a complementary approach in the treatment of mental disorders.

Materials and Methods

This study has a descriptive and narrative review character. The analysis included available scientific publications concerning the use of selected medicinal plants in the alleviation of stress, depression, associated psychological disorders, and sleep disturbances. The objective of the study was to present the principal mechanisms of action of selected medicinal plants on the human organism, with particular emphasis on their potential application in reducing stress and accompanying disorders, including depression and sleep-related disturbances. The literature review was conducted using scientific articles, reports, and academic papers published between 2000 and 2025. Sources were identified through searches of international scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar, as well as printed scientific materials and professional medical and pharmaceutical websites. The inclusion criteria comprised peer-reviewed scientific publications addressing phytotherapy, adaptogens, medicinal plants used in stress reduction, depression, anxiety disorders, and sleep disturbances, with particular consideration given to studies describing mechanisms of action, clinical efficacy, and safety of use. Both experimental and clinical studies, systematic reviews, and meta-analyses were included in the analysis. Studies unavailable in full-text form, popular science publications, non-verified internet sources, and materials lacking scientific credibility were excluded from the review. Particular attention was paid to publications discussing the safety of herbal medicine use, including potential herb–drug interactions and contraindications

associated with the concomitant use of herbal preparations and conventional pharmacotherapy. The methodological approach adopted in this study was based on a critical analysis and synthesis of current scientific evidence regarding the role of medicinal plants in supportive treatment of stress-related disorders. Special emphasis was placed on herbal agents affecting mood regulation, reduction of anxiety symptoms, improvement of sleep quality, and alleviation of neurovegetative symptoms accompanying depressive disorders.

Results

The conducted analysis of the scientific literature indicates that selected medicinal plants may play a significant supportive role in the prevention and treatment of depressive disorders, chronic stress, anxiety disorders, and problems related to impaired sleep quality. Data derived from experimental studies, clinical trials, and systematic reviews suggest that the pharmacological activity of plant-derived substances is multifaceted and involves simultaneous effects on numerous biological mechanisms involved in the pathophysiology of depression. Among the most important mechanisms of action are the modulation of neurotransmitter systems, regulation of the hypothalamic–pituitary–adrenal (HPA) axis, antioxidant and anti-inflammatory effects, influence on neuroplasticity, and the ability to improve sleep quality and architecture. The analyzed publications emphasize that particularly high therapeutic potential is exhibited by preparations containing St John's wort (*Hypericum perforatum*), saffron (*Crocus sativus*), ashwagandha (*Withania somnifera*), *Rhodiola rosea*, and turmeric (*Curcuma longa*). These plants are attributed with the ability to alleviate depressive symptoms, reduce psychological tension, and improve the organism's resistance to chronic stress. Clinical studies have shown that some of these herbal substances may positively influence mental well-being, cognitive functioning, normalization of circadian rhythm, and reduction of somatic symptoms associated with depression, such as chronic fatigue, irritability, and concentration difficulties. Particular importance is also attributed to the adaptogenic and neuroprotective properties of these plants, which enhance the body's ability to adapt to long-term stress exposure and may reduce the negative effects of chronic activation of stress-response systems. The obtained results indicate that phytotherapeutic agents exert a more complex influence on the body than many conventional synthetic drugs used in psychiatry. While some pharmaceuticals primarily target a single neurotransmitter system, plant-derived substances exhibit pleiotropic activity, involving simultaneous modulation of neurochemical, immune, hormonal, and oxidative processes. Such a multifactorial mechanism of action may be particularly relevant in the treatment of depressive disorders, whose etiology is complex and multifactorial. Many of the analyzed studies also highlight the potential use of herbal preparations as adjunctive therapy alongside pharmacological and psychotherapeutic treatment, particularly in patients with mild to moderate depressive symptoms and comorbid anxiety disorders and insomnia.

1. Mechanisms of Action of Herbal Medicines in the Prevention and Treatment of Depression

Medicinal plant materials used in the prevention and treatment of depressive disorders can be classified according to their dominant pharmacological mechanisms and their effects on specific neurobiological systems. One of the most important groups includes plants with well-documented antidepressant and mood-modulating effects, primarily St John's wort (*Hypericum perforatum* L.) and saffron (*Crocus sativus* L.). The therapeutic efficacy of these herbs has been confirmed in both randomized clinical trials and numerous meta-analyses involving patients with mild to moderate depressive disorders (Lopresti & Drummond, 2014). The mechanism of action of St John's wort is primarily associated with the inhibition of the reuptake of serotonin, dopamine, and norepinephrine in central nervous system synapses. This leads to increased availability of these neurotransmitters, which play a key role in regulating mood, motivation, and emotional processes. Particular importance is attributed to biologically active compounds present in St John's wort, such as hyperforin and hypericin,

which exhibit anti-inflammatory, antioxidant, and neuroprotective properties. Studies also suggest that these compounds may influence the expression of neurotrophic factors, including BDNF (brain-derived neurotrophic factor), which is responsible for neuroplasticity and neuronal regeneration. Saffron, on the other hand, modulates serotonergic system activity and reduces oxidative stress due to the presence of crocin, picrocrocin, and safranal. These compounds may improve mood, reduce anxiety symptoms, and protect nerve cells from damage induced by chronic stress. Another important group consists of plants that influence neurotransmitter systems responsible for regulating emotional tension, sleep, and stress responses. This group includes hops (*Humulus lupulus* L.), valerian (*Valeriana officinalis* L.), ginseng (*Panax ginseng* C.A. Meyer), basil (*Ocimum basilicum* L.), and lemon balm (*Melissa officinalis* L.). Their biological activity is primarily associated with effects on the GABAergic and monoaminergic systems, leading to reduced psychomotor agitation, decreased emotional tension, and improved sleep quality (Awad et al., 2007; Spinella, 2001; Sarris et al., 2011). The effects of valerian and lemon balm are particularly well understood; they increase the activity of gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the central nervous system. As a result, sedative, anxiolytic, and sleep-promoting effects are observed. Additionally, lemon balm exhibits antioxidant properties and may reduce HPA axis activity, contributing to the alleviation of chronic stress symptoms. Ginseng, classified as an adaptogen, enhances the body's resistance to physical and psychological stress by modulating neurotransmitter activity and influencing immune and endocrine system function.

2. Effects of Medicinal Plants on Neurotransmitter Systems

Dysfunction of neurotransmitter systems in the central nervous system is one of the most important elements in the pathophysiology of depression and stress-related disorders. Neurotransmitters regulate mood, cognitive processes, emotional responses, sleep, motivation, and the organism's adaptation to stressors. Chronic psychological stress leads to neurochemical imbalance affecting dopaminergic, serotonergic, noradrenergic, GABAergic, glutamatergic, and cholinergic systems. These alterations may result in depression, anxiety disorders, insomnia, chronic fatigue, and cognitive impairment. Increasing attention is being given to medicinal plants that, through their multifaceted actions, may modulate neurotransmitter activity and help restore neurochemical homeostasis.

2.1. Dopamine and the Dopaminergic System

Dopamine (DA) is a key neurotransmitter responsible for reward processing, motivation, the experience of pleasure, psychomotor activity, and cognitive functions. It plays an important role in regulating attention, decision-making, energy levels, and motivational drive. Proper dopaminergic function is essential for maintaining psychological activity, adaptive capacity, and stress resilience. Chronic stress may disrupt dopaminergic function through prolonged activation of the hypothalamic–pituitary–adrenal (HPA) axis and increased glucocorticoid secretion. Sustained elevation of cortisol may reduce dopamine synthesis and release, leading to anhedonia, reduced motivation, chronic fatigue, and psychomotor slowing, which are characteristic symptoms of depression (Dunlop et al., 2007). St John's wort (*Hypericum perforatum*) inhibits the reuptake of neurotransmitters and monoamine oxidase A (MAO-A) activity, thereby increasing dopamine availability and stabilizing mood (Gilani et al., 2005). *Bacopa monnieri* enhances neuronal communication and increases dopamine and serotonin levels, supporting cognitive function and stress resilience. A significant dopaminergic effect is also exhibited by *Mucuna pruriens*, a natural source of L-DOPA—the direct precursor of dopamine. This plant is used in conditions associated with dopaminergic deficiency, including depression characterized by low motivation and energy levels (Katzenschlager et al., 2004). *Rhodiola rosea* increases dopamine and norepinephrine levels while reducing symptoms of mental fatigue and depression (Panossian et al., 2004). Its adaptogenic properties enhance the body's ability to cope with chronic stress and reduce the negative impact of HPA axis overactivation on the nervous system.

Green tea, due to the presence of L-theanine and caffeine, indirectly supports dopaminergic neurotransmission, improving concentration, alertness, and psychophysical performance.

2.2. Serotonin and the Serotonergic System

Serotonin (5-HT) is a neurotransmitter that plays a fundamental role in regulating mood, emotions, appetite, sleep–wake cycles, and impulse control. It is also responsible for psychological well-being, emotional stability, and the ability to adapt to stressful situations. Dysfunction of the serotonergic system is one of the most commonly reported biological mechanisms associated with depression. Chronic stress leads to increased cortisol secretion and activation of inflammatory processes that may reduce serotonin synthesis by shifting tryptophan metabolism toward the kynurenine pathway. Serotonin deficiency is associated with increased depressive symptoms, anxiety, sleep disturbances, and heightened stress vulnerability (Cowen et al., 2015; Krishnan et al., 2008). *Bacopa monnieri* increases serotonin availability and modulates 5-HT_{1A} receptor expression due to bacosides A and B (Stough et al., 2008; Bhattacharya et al., 2000). St John's wort acts similarly to selective serotonin reuptake inhibitors (SSRIs), inhibiting the reuptake of serotonin, dopamine, and norepinephrine (Butterweck, 2003). Saffron (*Crocus sativus*) also exerts significant effects on the serotonergic system by inhibiting serotonin reuptake and enhancing its synthesis. Studies suggest that its antidepressant efficacy may be comparable to fluoxetine in the treatment of depressive disorders (Hausenblas et al., 2013). Additionally, saffron exhibits antioxidant and neuroprotective properties, further supporting nervous system function under chronic stress conditions.

2.3. Gamma-aminobutyric acid (GABA) and the GABAergic system

Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the central nervous system. It is responsible for reducing excessive neuronal excitability, regulating emotional tension, and maintaining the balance between excitatory and inhibitory processes in the brain. Proper functioning of the GABAergic system ensures the organism's ability to downregulate the stress response and maintain emotional stability. Reduced GABA levels are particularly observed in patients suffering from depression with a predominant anxiety component, chronic stress, and sleep disturbances (Dobros, 2017). A deficiency in GABAergic activity leads to increased neuronal excitability, heightened anxiety, psychological tension, and difficulties in falling asleep. Prolonged stress may further impair GABA-A receptor function and disrupt neurochemical balance in the brain. Lavender (*Lavandula angustifolia*) increases GABA-A receptor activity, exerting anxiolytic and sedative effects (Woelk et al., 2010). As a result, it may reduce psychological tension, improve sleep quality, and support emotional regulation. Valerian (*Valeriana officinalis*) increases GABA release and reduces its degradation, producing a sedative effect and decreasing excessive neural excitability (Khom et al., 2007). This plant is particularly used in sleep disorders and conditions of chronic nervous tension.

2.4. Noradrenaline and the noradrenergic system

Noradrenaline (NA) is involved in the regulation of mood, arousal, motivation, stress response, and energy metabolism. This neurotransmitter is responsible for mobilizing the organism for action, maintaining attention, and enabling responses to environmental stimuli. Proper functioning of the noradrenergic system is essential for adequate mental and physical performance. Chronic stress leads to overactivation of the sympathetic nervous system and the HPA axis, initially increasing noradrenaline secretion; however, prolonged overload may result in regulatory exhaustion and reduced noradrenergic activity. Noradrenaline deficiency manifests as apathy, reduced energy, decreased

motivation, and impaired concentration (Ressler et al., 2000). Ashwagandha (*Withania somnifera*) modulates noradrenaline and cortisol activity, demonstrating adaptogenic and antidepressant effects (Chandrasekhar et al., 2012). This plant supports the organism's ability to adapt to chronic stress and reduces the negative effects of prolonged HPA axis activation. St John's wort and green tea also influence noradrenergic neurotransmission, supporting concentration, emotional stability, and psychophysical performance (Nobre et al., 2008).

2.5. Acetylcholine and the cholinergic system

Acetylcholine (ACh) plays an important role in the regulation of cognitive processes, memory, learning, and attention. This neurotransmitter is responsible for proper communication between neurons and is involved in mechanisms of brain neuroplasticity. Alterations in cholinergic activity may contribute both to cognitive impairment and mood regulation disturbances. Excessive cholinergic activity has been associated with lowered mood, particularly in melancholic depression (Matławska, 2008). Chronic stress may disrupt the balance between the cholinergic and monoaminergic systems, leading to impaired memory, difficulties in concentration, and increased psychological burden. *Bacopa monnieri* supports cholinergic neurotransmission and neuroplasticity processes, contributing to improved memory and learning capacity (Stough et al., 2001). *Ginkgo biloba* enhances acetylcholine release and improves cerebral blood flow, thereby supporting cognitive function and protecting neurons against oxidative stress (Kennedy et al., 2001).

2.6. Glutamate and the glutamatergic system

Glutamate is the main excitatory neurotransmitter in the central nervous system and plays a key role in neuroplasticity, learning, and synaptic adaptation. Its action is mediated, among others, through NMDA receptors, which are involved in memory processes and emotional regulation. Proper functioning of the glutamatergic system is essential for brain function; however, chronic stress may lead to excessive NMDA receptor activation and excitotoxicity. Several medicinal plants have been shown to modulate glutamatergic neurotransmission. Ashwagandha, kava (*Piper methysticum*), turmeric (*Curcuma longa*), *Ginkgo biloba*, *Rhodiola rosea*, and green tea protect neurons against glutamate-induced excitotoxicity, modulate oxidative stress, and increase the expression of brain-derived neurotrophic factor (BDNF) (Dar et al., 2010; Singh et al., 2002; Kulkarni et al., 2006; Ahlemeyer et al., 2003; Panossian et al., 2009; Levites et al., 2002). Through these mechanisms, they support the balance between glutamatergic and GABAergic neurotransmission, thereby reducing the negative effects of chronic stress on nervous system functioning.

Discussion

Current scientific data suggest that selected medicinal plants may constitute a valuable adjunct to the treatment of depression, particularly in cases of mild to moderate severity. The mechanisms of action of plant-derived substances include, among others, the modulation of neurotransmitter systems—serotonergic, dopaminergic, and GABAergic—the regulation of the hypothalamic–pituitary–adrenal (HPA) axis activity, the reduction of oxidative stress, and anti-inflammatory effects. Contemporary concepts of the pathogenesis of depression increasingly highlight the importance of chronic inflammation, impaired neuroplasticity, and dysregulation of stress response mechanisms, which justifies the growing interest in the potential use of phytotherapy in the treatment of affective disorders (Miller i Raison, 2016). The best-documented clinical efficacy among plants used in depression is observed for St. John's wort (*Hypericum perforatum*). Results from numerous clinical trials and meta-analyses confirm its antidepressant effects in the treatment of mild to moderate depression. Linde et al. (2008) showed that St. John's wort preparations were superior to placebo and achieved therapeutic

effects comparable to standard antidepressant medications, with better patient tolerance. The mechanism of action of this plant is primarily associated with the inhibition of serotonin, dopamine, and noradrenaline reuptake, leading to increased availability of these neurotransmitters in the synaptic cleft. Additionally, St. John's wort exhibits anti-inflammatory and neuroprotective properties that may reduce the negative impact of chronic stress on the central nervous system. Significant therapeutic potential is also attributed to saffron (*Crocus sativus*). Studies indicate that this plant may reduce the severity of depressive symptoms through modulation of the serotonergic system, achieving efficacy comparable to fluoxetine and imipramine (Hausenblas *et al.*, 2013). The biological activity of saffron is mainly attributed to crocin and safranal, which increase serotonin availability and exhibit antioxidant and neuroprotective properties. As a result, saffron may positively influence not only mood improvement but also anxiety reduction, sleep quality, and overall psychological functioning. Increasing research attention is also directed toward curcumin—the main active compound of turmeric (*Curcuma longa*). It demonstrates strong anti-inflammatory and antioxidant properties that may reduce neuroinflammation and oxidative damage associated with depression (Lopresti *et al.*, 2014). The mechanism of curcumin action includes inhibition of the NF- κ B transcription factor, reduction of pro-inflammatory cytokine levels, and increased expression of brain-derived neurotrophic factor (BDNF). These effects may support neurogenesis, improve neuroplasticity, and protect neurons from the consequences of chronic stress and inflammatory disturbances. Another important area of research is the analysis of adaptogenic properties of plants such as ashwagandha (*Withania somnifera*) and rhodiola (*Rhodiola rosea*). These plants have been shown to regulate HPA axis activity, contribute to reduced cortisol levels, and enhance the body's ability to adapt to chronic stress (Chandrasekhar *et al.*, 2012; Panossian *et al.*, 2010). This effect may be particularly important in depression co-occurring with anxiety disorders, chronic psychological tension, and insomnia. Furthermore, adaptogens may support improvements in cognitive function, sleep quality, and overall mental well-being through neuroprotective effects against oxidative stress and modulation of monoaminergic neurotransmission. Despite promising research results, phytotherapy should not be considered an alternative to standard psychiatric treatment but rather as a complementary approach to pharmacological and psychotherapeutic interventions. One of the main limitations remains the lack of full standardization of herbal preparations, variability in active compound content, and the potential for interactions between herbal substances and synthetic drugs. Of particular clinical importance are interactions associated with the use of St. John's wort, which, through the induction of cytochrome P450 enzymes, may affect the metabolism of many medications and reduce their therapeutic efficacy (Izzo *et al.*, 2009). Further randomized clinical trials involving larger patient groups are necessary to more accurately assess the efficacy and safety of long-term use of herbal preparations in the treatment of depression. In particular, it is important to determine optimal therapeutic dosages, treatment duration, potential interactions with antidepressant medications, and the effects of individual plant compounds on different forms of depressive disorders and stress-related conditions.

Conclusions

Medicinal plants demonstrate multi-target pharmacological activity that may contribute to the alleviation of depressive symptoms through modulation of monoaminergic neurotransmission, attenuation of neuroinflammatory processes, reduction of oxidative stress, and regulation of the hypothalamic–pituitary–adrenal (HPA) axis. The available evidence suggests that phytotherapy may act as a clinically relevant adjunct to conventional antidepressant and psychotherapeutic interventions, particularly in mild to moderate forms of depression. Among the investigated herbal preparations, the strongest clinical evidence supports the efficacy of *Hypericum perforatum* (St. John's wort) and *Crocus sativus* (saffron), which demonstrate antidepressant effects comparable to standard pharmacotherapy in selected patient populations. Adaptogenic plants, including *Withania somnifera* (ashwagandha) and *Rhodiola rosea*, additionally appear to play a significant role in stress modulation

and HPA axis regulation, which may indirectly contribute to improvement of depressive symptoms and associated sleep disturbances. Phytotherapeutic agents may also support neurobiological mechanisms underlying resilience, including enhancement of neuroplasticity and reduction of allostatic load, suggesting their broader neuroprotective potential. However, despite promising clinical and experimental data, herbal medicine should not be considered a substitute for evidence-based psychiatric treatment. A key limitation of phytotherapy remains the variability in phytochemical composition, insufficient standardization of preparations, and the risk of clinically significant herb–drug interactions, particularly in patients receiving antidepressants or other psychotropic medications. Therefore, the use of medicinal plants should always be supervised by qualified healthcare professionals. In conclusion, phytotherapy represents a promising complementary approach in the management of depressive disorders, although further high-quality randomized controlled trials are required to fully establish its efficacy, safety profile, and standardized clinical applications.

Summary

Depression is currently one of the most prevalent mental disorders, with significant consequences for affected individuals as well as their family and professional environments. It leads to psychological suffering, loss of interest or pleasure in life, and reduced quality of functioning in everyday activities. In addition, depression generates considerable economic burden resulting from medication and therapy costs, reduced workplace productivity, increased sickness-related absenteeism, and more frequent medical consultations and hospitalizations, sometimes associated with co-occurring somatic symptoms such as syncope, cardiac rhythm disturbances, or pain disorders affecting internal organs and the musculoskeletal system. Raising public awareness of depression may significantly improve the quality of life of affected individuals and their surroundings. As part of supportive therapeutic approaches, phytotherapy plays an important role and may serve as an adjunct to pharmacotherapy and psychotherapy. However, the use of herbal preparations should only take place following consultation with a physician or pharmacist, as improper use, like any therapeutic intervention, may lead to adverse health effects.

Disclosure

Author Contribution Statement

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