THE ROLE OF PHYTOCOMPOSITIONS IN MANAGING EMOTIONAL STRESS

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Abstract: *This review summarizes animal and human research data on the efficacy of phytocompounds in managing emotional stress, highlighting their mechanisms of action, including modulation of neurotransmitters (serotonin, dopamine, GABA), attenuation of neuroinflammation, and enhancement of neuroplasticity. Emotional stress impairs mental and physical well-being by disrupting the regulation of the central nervous system (CNS), hormonal balance, and immune responses. Traditional pharmacological treatments such as antidepressants and anxiolytics are often limited by side effects, prompting the exploration of phytocompounds—herbal formulas—as safer, more comprehensive alternatives. Key bioactive compounds such as glycyrrhizin from Glycyrrhiza glabra, withanolides from Withania somnifera, androsavin from Rhodiola rosea are highlighted for their adaptogenic and neuroprotective properties. The review compares herbal formulations with synthetic drugs in terms of efficacy, safety, and affordability, considering their synergistic effects and standardization issues. Tables summarize the main findings and explore the potential for personalized herbal medicine, highlighting future research directions for clinical trials, formulation optimization, and mechanistic studies.*
Keywords: *emotional stress, stress factor, stress response, rats, phytocomposites.*

РОЛЬ ФИТОКОМПОЗИЦИЙ В УПРАВЛЕНИИ ЭМОЦИОНАЛЬНЫМ СТРЕССОМ

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Аннотация: *в этом обзоре обобщены данные исследований на животных и людях об эффективности фитокомпозиций в управлении эмоциональным стрессом, подчеркиваются механизмы их действия, включая модуляцию нейротрансмиттеров (серотонина, дофамина, ГАМК), ослабление нейровоспаления и усиление нейропластичности. Эмоциональный стресс ухудшает психическое и физическое благополучие, нарушая регуляцию центральной нервной системы (ЦНС), гормональный баланс и иммунные реакции. Традиционные фармакологические методы лечения, такие как антидепрессанты и анксиолитики, часто ограничены побочными эффектами, что побуждает исследовать фитокомпозиции — травяные формулы — как более безопасные и комплексные альтернативы. Ключевые биоактивные соединения, такие как глицирризин из Glycyrrhiza glabra, витанолиды из Withania somnifera, андрозавин из Rhodiola rosea, отмечены за их адаптогенные и нейропротекторные свойства. В обзоре сравниваются растительные формулы с синтетическими препаратами с точки зрения эффективности, безопасности и доступности, учитывая их синергетические эффекты и проблемы стандартизации. Таблицы суммируют основные результаты и исследуют потенциал персонализированной растительной медицины, выделяя будущие направления исследований для клинических испытаний, оптимизации формул и механистических исследований.*
Ключевые слова*: эмоциональный стресс, фактор стресса, реакция на стресс, крысы, фитокомпозиции.*

1. Introduction

Emotional stress, a pervasive response to psychological, social, or environmental challenges, profoundly impacts mental and physical health [1]. It triggers hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to elevated cortisol levels, and stimulates the sympathetic nervous system, resulting in catecholamine release [2]. These processes disrupt critical brain regions, including the hippocampus (responsible for memory and emotional regulation), amygdala (fear processing), and prefrontal cortex (cognitive control), impairing ticity, sleep quality, and cognitive performance. Chronic stress also suppresses immunefunction, increases pro-inflammatory cytokines, and alters metabolism, contributing to cardiovascular, gastrointestinal, and psychiatric disorders, such as anxiety and

depression. Pharmacological interventions, including benzodiazepines and selective serotonin reuptake inhibitors (SSRIs), effectively alleviate stress symptoms but are often accompanied by side effects like dependency, drowsiness, and cognitive impairment. This has spurred interest in phytocompositions—complex plant-derived formulations with adaptogenic, anxiolytic, and neuroprotective properties. Derived from plants such as Rhodiola rosea, Withania somnifera, Valeriana officinalis, and Melissa officinalis, these formulations modulate neurotransmitter systems, reduce cortisol, and protect neurons from oxidative stress, offering a gentler alternative with fewer adverse effects. Their adaptogenic properties enhance resilience to external and internal stressors. Animal studies, particularly in rats, provide controlled insights into stress mechanisms and phytocomposition efficacy, modeling physiological and behavioral responses translatable to humans. Clinical studies further demonstrate their benefits in improving mood, cognition, and resilience in both healthy and clinical populations. This review aims to elucidate the mechanisms by which phytocompositions mitigate emotional stress, evaluate their therapeutic potential compared to conventional treatments, and explore the prospects of personalized phytotherapy for stress management.

A comprehensive survey of publications on the role of phytocompositions in mitigating emotional stress was conducted. To gather the material for the review article, several abstract databases were utilized, including PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Google Scholar (http://www.scholar.google.com), Elsevier (https://www.elsevier.com), ScienceDirect (http://www.sciencedirect.com), Wiley Online Library (http://www.onlinelibrary.wiley.com), Springer Link (http://www.springer.com), and Scopus (http://www.scopus.com). The literature search spanned from 2000 to 2024. In addition to journal articles, monographs, conference proceedings, and specialized scientific publications were also reviewed. Some sources were identified through citation analysis and by exploring the websites of major scientific publishers.

The selection of literature was guided by specific keywords and phrases, including adaptogens, plant extracts, phytocompositions, emotional stress, anxiety, depression, cognitive functions, neuropharmacology, biochemical mechanisms, clinical studies, and animal experiments. The subjects of study comprised essential oils, extracts, and complex plant formulations derived from species such as Rhodiola rosea, Withania somnifera, Panax ginseng, Melissa officinalis, Hypericum perforatum, Valeriana officinalis, Glycyrrhiza glabra, Passiflora incarnata, among others.

To verify the scientific nomenclature, plant names were cross-checked with The Plant List (http://www.theplantlist.org/). The literature collection and analysis were restricted to works published in English and Russian.

2. Neurobiological Mechanisms of Emotional Stress.

Emotional stress induces a cascade of neurobiological changes affecting both the central and peripheral nervous systems. Chronic HPA axis activation results in excessive cortisol secretion, which exerts toxic effects on hippocampal neurons, reducing their density and suppressing neurogenesis. The amygdala becomes hyperactive, amplifying emotional responses to threats and contributing to anxiety disorders. The prefrontal cortex, essential for planning and impulse control, exhibits diminished functional connectivity, leading to impaired cognitive flexibility and decision-making. Neuroinflammation plays a pivotal role in stress-related pathology. Chronic stress activates microglia, triggering the release of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which disrupt synaptic plasticity and promote neuronal degeneration, exacerbating depressive and anxiety symptoms. Phytocompositions, such as Achillea millefolium and Glycyrrhiza glabra, counteract these effects by suppressing microglial activation and reducing cytokine levels, offering potential therapeutic benefits. Emerging research highlights the role of the gut microbiota in stress responses via the gut-brain axis. Stress alters microbial composition, reducing populations of beneficial bacteria like Lactobacillus and Bifidobacterium, which disrupts neurotransmitter balance, including serotonin and GABA. Certain phy 2 compositions, such as Melissa officinalis, may indirectly support microbiota health through prebiotic polysaccharides, improving psychoemotional well-being. Stress dysregulates neurotransmitter systems. Decreased serotonin and dopamine levels contribute to apathy and depressive symptoms,whileimbalancesinGABA andglutamateenhanceanxietyandexcitotoxicity. Hyperactivity of norepinephrine and acetylcholine disrupts sleep and attention. Phytocompositions restore neurochemical balance, with Valeriana officinalis enhancing GABAergic transmission and Rhodiola rosea increasing serotonin and dopamine availability.

3 Phytocompositions in Stress Management

Phytocompositions, derived from plants such as Rhodiola rosea, Withania somnifera, Valeriana officinalis, and Glycyrrhiza glabra, constitute intricate blends of bioactive compounds, including flavonoids, alkaloids, terpenes, and polyphenols, which exert multifaceted effects on the body. These formulations effectively modulate stress responses by influencing neurochemical, hormonal, and inflammatory pathways. Extracts of valerian and lemon balm, for instance, enhance GABA activity, promoting a calming effect that reduces anxiety and im quality, making them particularly valuable for managing both acute and chronic stress. Similarly, Rhodiola rosea supports emotional stability by elevating serotonin and dopamine levels while stimulating hippocampal neurogenesis, counteracting cognitive deficits induced by prolonged stress. Withania somnifera exhibits pronounced adaptogenic properties, suppressing excessive cortisol secretion by regulating the HPA axis, thereby restoring hormonal equilibrium. Glycyrrhiza glabra, containing glycyrrhizin, exerts potent anti-inflammatory effects by inhibiting NF-κB and MAPK signaling pathways, mitigating systemic inflammation associated with stress. Antioxidants, such as rosmarinic acid

found in Melissa officinalis, shield neural structures from oxidative damage, preserving their functionality and preventing stress-induced degeneration. The pharmacokinetic profiles of phytocompositions are critical to their efficacy. Glycyrrhizin, for example, demonstrates high bioavailability but undergoes hepatic metabolism, necessitating careful dose optimization to avoid side effects like hypokalemia. The synergistic interactions among components in multicomponent phytocompositions often amplify their therapeutic effects compared to isolated compounds, enhancing their potential for comprehensive stress management. Animal studies substantiate these properties. Experiments in rats have shown that Valeriana officinalis and Melissa officinalis extracts reduce anxiety in forced swimming and open field tests, normalizing GABA and glutamate levels. With a niasomniferamitigates behavior and biochemical disruptions caused by chronic stress, including elevated cortisol, improving adaptive capacity. Astragalusvulpi nus extract enhances cognitive performance and reduces anxiety under informational stress, underscoring its psychoeemotional benefits. Clinical trials extend these findings to humans. Melissa officinalis supplementation in healthy volunteers improves mood and cognitive function, highlighting its calming and neuroprotective effects. Rhodiola rosea reduces fatigue and enhances mental performance in individuals with chronic stress, affirming its utility in both preventive and therapeutic contexts.

4. Comparison of Phytocompositions and Synthetic Drugs

Phytocompositions and synthetic drugs offer contrasting approaches to managing stress, differing in their mechanisms of action, safety profiles, and economic accessibility. Phytocompositions, derived from plant sources, exert a multimodal effect, simultaneously targeting neurotransmitter systems, hormonal balance, and inflammatory processes. For instance, Valeriana officinalis and Rhodiola rosea modulate GABA and serotonin, reducing anxiety and stabilizing mood, while Glycyrrhiza glabra suppresses inflammation, contributing to holistic stress relief. Their gentle action minimizes the risk of severe side effects, such as dependency or cognitive impairment, commonly associated with synthetic drugs like benzodiazepines or SSRIs. Moreover, phytocompositions are often available as dietary supplements or traditional remedies, making them economically viable, particularly in resource-limited settings where the high cost of modern pharmaceuticals poses a barrier. Synthetic drugs, by contrast, typically target a single pathway, such as serotonin reuptake inhibition in SSRIs, providing rapid symptom relief. However, their use is constrained by risks of dependency, drowsiness, and cognitive deficits, limiting their suitability for long-term therapy. The high cost of these medications, especially newer formulations, further restricts access for many patients, unlike phytocompositions, which are derived from widely available plants. While phytocompositions generally exhibit high safety when dosed appropriately, certain compounds, such as glycyrrhizin from Glycyrrhiza glabra, may 4 cause side effects like hypokalemia or hypertension, necessitating careful monitoring. Variability in plant raw materials and extraction methods poses challenges for standardization, potentially affecting therapeutic consistency. Synthetic drugs, with their precisely defined compositions, avoid this issue but require rigorous medical oversight for long-term use. Thus, phytocompositions offer a safer, more accessible alternative, particularly for preventive and chronic stress management, though their efficacy warrants further validation through large-scale clinical trials.

5 Perspectives for Personalized Phytotherapy

Personalized medicine offers transformative opportunities for phytocomposition use in stress management. Genetic and metabolic variations among individuals influence stress susceptibility and phytotherapy responses. For instance, polymorphisms in cytochrome P450 (CYP450) genes may affect the bioavailability of compounds like withanolides or glycyrrhizin. Pharmacogenomic profiling could enable tailored phytocomposition selection, minimizing adverse effects. Integrating data on gut microbiota and neurochemical profiles further enhances personalization. Patients with dysbiosis may benefit from phytocompositions with prebiotic components, such as Melissa officinalis polysaccharides, to restore the gut-brain axis. Personalized approaches also consider lifestyle, stress levels, and comorbidities, optimizing therapeutic outcomes.

6 Discussion

Phytocompositions hold significant promise for managing emotional stress, as evidenced by animal studies demonstrating their ability to reduce anxiety, enhance cognitive function, and restore neurochemical balance. Rat experiments 5 have shown that extracts from plants like Valeriana officinalis and Withania somnifera effectively mitigate behavioral and biochemical disruptions caused by chronic stress, including elevated cortisol and neurotransmitter imbalances. Clinical trials extend these findings to humans, with Melissa officinalis improving mood and cognition in healthy individuals and Rhodiola rosea reducing fatigue and boosting mental performance in stressed populations. Keybioactive compounds, such as glycyrrhizin, withanolides, and rosavin, target diverse stress pathways, offering a comprehensive therapeutic approach that distinguishes phytocompositions from single-target synthetic drugs. Nevertheless, challenges persist. Variability in plant raw materials and extraction methods complicates standardization, potentially leading to inconsistent outcomes. The predominance of animal-based evidence, coupled with a paucity of large-scale clinical trials, limits their integration into mainstream medical practice. Safety concerns, particularly for compounds like glycyrrhizin, which may cause side effects with prolonged use, require further investigation. The synergistic effects of phytocomposition components, while enhancing efficacy, pose difficulties in elucidating precise mechanisms, necessitating advanced research. Future studies should prioritize randomized clinical trials to validate efficacy and safety in humans. Optimizing formulations through standardized dosing and component combinations will improve therapeutic reliability. Integrating phytotherapy with personalized medicine, leveraging pharmacogenomics and microbiota analysis, offers

a pathway to individualized treatment. Exploring synergistic interactions among bioactive compounds could lead to more potent formulations, rivaling synthetic drugs in efficacy while maintaining safety and accessibility.

7. Conclusions

Phytocompositions represent an innovative, low-risk approach to managing emotional stress, modulating neurotransmitter systems, attenuating neuroinflammation, and enhancing neuroplasticity. Supported by animal studies and preliminary human trials, their adaptogenic, neuroprotective, and anti-inflammatory properties position them as viable alternatives to synthetic drugs. However, standardization, safety, and clinical validation challenges necessitate further research. Interdisciplinary efforts integrating neurobiology, pharmacology, and bioinformatics will advance personalized phytotherapy, unlocking its potential for treating stress-related disorders.

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