

MODERN ANTIDEPRESSANTS BASED ON MEDICINAL PLANTS: RESEARCH IN A NATURAL DIRECTION

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Abstract

Depression is a prevalent psychiatric disorder worldwide, with limited efficacy and side effects of synthetic antidepressants. Therefore, medicinal preparations derived from plants are gaining great acceptance as a natural alternative. This article analyzes recent clinical studies on plants such as St. John's wort (*Hypericum perforatum*), saffron (*Crocus sativus*), lavender (*Lavandula angustifolia*), and curcuma (*Curcuma longa*). Mechanisms, efficacy, safety, and comparison of natural antidepressants with synthetic antidepressants are reviewed. In conclusion, it is emphasized that herbal antidepressants are promising as solitary and adjunctive therapy, but the need for large-scale, high-quality studies is highlighted.

Keywords: Herbal antidepressants, *Hypericum perforatum*, *Crocus sativus*, *Curcuma longa*, clinical trials, mechanism, side effects.

Introduction

Depression (major depressive disorder (MDD)) is a serious health problem as a result of factors such as globalization, pandemics, modern living conditions. Although synthetic antidepressants (e.g., SSRIs, SNRIs, tricyclic antidepressants) are effective, many patients suffer from side effects, do not respond to treatment, or may experience dangerous conditions as a result of an overdose. Therefore, there is a growing interest in natural products — extracts from plants, phenolic compounds, adaptogens. Recent articles have analyzed the efficacy and safety profile of herbal preparations in relieving depression [4],[7],[9].

Methodology

The data reviewed in this article are primarily obtained from clinical trials, systematic reviews, and meta-analyses over the past 5 years (2018–2025). Basic data were searched from PubMed, Scopus, Web of Science, MDPI, and other academic databases. Terms like "herbal antidepressant randomized controlled trial", "St. John's wort depression meta-analysis", "saffron clinical trial depression", "Curcuma longa depression humans" were used as key words. Selected studies: RCT (randomized controlled trials), systematic reviews, meta-analyses, as well as herbal use in post-stroke depression, mild-to-moderate depression.

Preclinical (animal, cellular) studies, studies that reveal only biological mechanisms, are also briefly reviewed, but the article center is on clinical data.

Results

Below are the most researched plants and their clinical effects and mechanisms:

O'simlik Preparat	/ Tadqiqot Formats	Samarasi (Clinic)	Mexanism(s)	Side Effects / Restrictions
St. John's wort (Hypericum perforatum)	RCT and meta-analyses, mild-to-moderate depression; Specific trials compared to SSRIs [3],[4]	Equal outcome with SSRIs in mild-medium depression; leads to remission [3]	inhibits serotonin, noradrenaline and dopamine reuptake; decreases monoamine oxidase activity; on GABA and NMDA receptors; inflammatory effects [4]	Phototoxicity; and pharmacokinetic interactions — induction of CYP450; Sometimes in the pathways of the central nervous system, feeling of heaviness, lethargy, indigestion [4]
Saffron (Crocus sativus L.)	Multiple RCTs, a meta-analysis; mild-moderate depression	It significantly reduced symptoms of depression, sometimes compared to placebo and sometimes SSRIs [7],[9]	antioxidant, anti-inflammatory effect; increases serotonin and dopamine levels; regulates stress hormones (e.g. cortisol) [7]	anti-effect; Price and quality vary; long-term data is less; Occasional gastrointestinal discomfort
Lavandula angustifolia (Lavender)	Clinical and meta-analyses, mainly on mild depression incidence component [7]	It improves mood, relieves sleep and anxiety states; Small-medium effects [7]	GABA or benzodiazepine substitution, NMDA receptor effect; sedative and anxiolytic effects; as well as potential antioxidant effects [7]	Sedation, dizziness; sometimes it is necessary to adjust the dosage; Sometimes allergic reactions
Curcuma longa (Qurkuma)	RCTs and clinical trials; Compound depression has also been considered adjunctive therapy [7]	reduces symptoms of depression; May improve mood and as cognitive function [7]	Curcumin — anti-inflammatory, antioxidant; NF-κB pathways, reducing pro-inflammatory cytokines (IL-6, TNF-α); Increase BDNF [7]	Absorption can be low; a higher dose can affect the internal organs; Methods to enhance the bioavailability of some drugs are required
Herbalic medication for post-stroke depression	RCTlar tarmog'i, meta-analiz (network + meta-analysis) [5]	Combinations such as Shugan Jieyu Capsule + SSRI, Jie-Yu Pills + SSRI, Wuling Capsule + SSRIs can significantly reduce the HAMD score; Improved response rate [5]	The herbal formulations used often involve various mechanisms — monoamine modulation, antioxidant and anti-inflammatory effects, alteration of neurotropic factor (e.g. BDNF) [5]	Often the drug formulations are diverse; — non-standardization; Since combinations are made up of different components, it requires precision to whom which component is suitable

Analysis and discussion

Current research on antidepressants made from medicinal plants indicates that they are widely studied in clinical practice as an alternative and complementary agent to traditional chemical antidepressants. The results obtained in the field of phytotherapy, on the one hand, confirm the

very effectiveness of natural drugs, and on the other hand, show a higher safety profile and the possibility of long-term use [1].

The main advantage of medicinal plants is their multi-component content. For example, the substances hypericin and hyperforin in the plant **Hypericum perforatum** (zveroboy) influence the metabolism of neurotransmitters is scientifically proven. In clinical studies, it has been observed that these extracts inhibit serotonin reuptake, resulting in reduced depression symptoms [2]. However, the rates of side effects associated with synthetic antidepressants, such as drowsiness, body weight gain, or sexual dysfunction, were found to be significantly lower [3].

Clinical efficacy of medicinal herbs

Foreign studies show that in clinical trials conducted among patients with moderate depression, zveroboy extract showed a higher efficacy than in the placebo group. Also, **Crocus sativus** (za'faron) extract has been found to have an antidepressant effect clinically, balancing the activity of the serotonin and dopamine systems [4].

The table below shows the main active substances of some medicinal plants and their mechanisms of antidepressant action:

Table 1. Mechanisms of antidepressant action of medicinal plants

O'simlik nomi	Active Ingredient	Ta'sir Mexanisms	Literature
Hypericum perforatum	Giperitsin, giperforin	Inhibits serotonin and dopamine reuptake	[2], [5]
Crocus sativus	Safranal, krosin	Stimulates serotonin metabolism	[4], [6]
Rhodiola rosea	Rozavin, salidrozyd	Increases stress resistance, bringing HPA axis back to normal	[7]
Withania somnifera	Vitanolids	Lowers cortisol levels, improves neuroplasticity	[8]

As can be seen, the mechanisms of action of plants are of various types, producing complementary interactions in the central nervous system in several directions.

Security and Side Effects

Another important aspect of medicinal herbs is their safety profile. For example, in clinical studies, saffron drugs have been well absorbed, only cases of mild dyspepsia or headache have been reported [6]. Rhodiola rosea, on the other hand, is characterized mainly by improving sleep quality, increasing energy, with a very low level of side effects [7]. However, cautions should be observed when using Hypericum perforatum regarding its use, as it may begin pharmacokinetic interactions with some drugs (e.g. anticoagulants, immunosuppressants) [9].

Analysis of Clinical Studies

The results of clinical studies in European and Asian countries showed that the effectiveness of natural antidepressants was significantly higher than in the placebo group. However, their



efficacy has been shown to be lower than that of chemical antidepressants in cases of severe depression [10].

Table 2. Clinical results of antidepressants based on medicinal plants

Vegetative	Number of participants in the Samaradorlik clinical trial	(%)	Placebo Versus Placebo	Literature
Hypericum perforatum	300	65	25% higher	[5], [10]
Crocus sativus	150	60	22% higher	[4], [6]
Rhodiola rosea	120	55	18% higher	[7], [11]
Withania somnifera	100	58	20% higher	[8], [12]

These results suggest that medicinal plant-based preparations may be effective in the treatment of mild to moderate depression, it is worthwhile to add them to complex therapy.

Discussion

The role of medicinal plants in the quality of modern antidepressants is increasing. Their multifunctional mechanisms of action are explained by the fact that they influence several biological pathways in the central nervous system. This suggests that they may also be useful in various clinical forms of depression, including depressive disorders related to anxiety (anxiety) [13].

However, according to the analysis of articles published in scientific journals, large-scale randomized clinical studies are not enough to fully prove the effectiveness of medicinal herbs. Most of the studies were based on small samples, with results limited to generalize. Therefore, more extensive international studies are needed in the future [14].

In addition, there is the problem of standardization of natural preparations. The amount of bioactive components in the plant may vary depending on the region of cultivation, harvesting and processing technology. This leads to disparities between clinical outcomes [15].

Conclusion

Herbal medicines are promising alternatives in the treatment of depression and appear to be good in terms of efficacy and safety, especially in mild-to-moderate cases. Clinical data on plants such as St. John's wort, saffron, lavender, and curcuma are reliable. Their mechanisms include pathways similar to synthetic antidepressants—monoamine reuptake inhibitions, receptor modulation, antioxidant, and anti-inflammatory effects. However, there are limitations, such as small samples, non-standardized drugs, pharmacokinetic interactions, and a lack of long-term safety data.

Future research will require:

- Placebo-controlled, double-bound RCTs in high-quality, large samples;
- Standardized extracts and active ingredient identification;
- long-term follow-up and monitoring of side effects;



- It is possible to use combinations with synthetic drugs; To whom which plant is more effective — analyses based on genetic, biochemical differences;
- A thorough study of drug and plant-drug interactions.

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