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Review Article

Herbs Used to Treat Depression: An Updated Review

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Abstract

Depression is a prevalent mental illness. In addition to being a substantial contribution to the overall global disease burden, depression is one of the main causes of disability worldwide. Complementary therapies are necessary because of the drawbacks of standard antidepressant therapy, including side effects, even though the former can help reduce depression symptoms and avoid relapse of the illness. Because they have fewer side effects and are less expensive than other therapies for depression, herbal medications have drawn a lot of interest recently. Compared to synthetic medications, herbal plants have fewer adverse effects and exhibit antidepressant properties. As such, they may be able to help people who are depressed. Because herbs have fewer adverse effects than conventional drugs, many people prefer them for symptom treatment. If traditional medications aren't working for you because of side effects, poor efficacy, or accessibility issues, using phytomedicine can be a good alternative. This review will concentrate on herbs that are used to cure depression.

Keywords: Herbal medicines, Depression, Herb, Treatment, St. John's Wort

INTRODUCTION

Anhedonia, a diminished capacity for experiencing delight, sleeplessness or hypersomnia, psychomotor disturbances or retardation, exhaustion, emotions of guilt or worthlessness, trouble focusing, and recurrent thoughts of suicide or death are some of the symptoms of depression, a significant mood disorder.¹ Depression is a mental health condition that is recurring, ongoing, and debilitating and is associated with a high rate of death and morbidity.² Major depression is expected to rise from its current ranking of fourth among health concerns to become the second most burdensome factor globally by 2020, says the World Health Organization.³ Herbal medications are utilized as antidepressants since they are safer, natural, and don't have any negative effects.⁴ Women experience depression disorders at a higher rate than males do. Antidepressants, psychotherapy, and medication plus psychotherapy are the most widely used therapies for depression. The reuptake of neurotransmitters in the brain is suppressed by a variety of antidepressant medications, including herbal remedies.⁵

The use of natural therapies to treat a wide range of illnesses, including anxiety and depression, has significantly increased during the previous several decades. These goods are seen to be safer than medication as there is less chance of side effects or withdrawal.¹ Recurrent depression can have a serious negative impact on a patient's functioning and quality of life. Years of life with a handicap are a measure of the cost of various disorders. Depressive disorders can cause suicidal

thoughts and feelings, as well as melancholy, loss of interest or pleasure, guilt or low self-worth, difficulty sleeping or eating, and poor concentration. They are separated into dysthymia and major depressive disorder, also known as depressive episode. Depressed mood, diminished interest and enjoyment, and low energy are all signs of major depressive illness, which can range in severity from mild to severe. Similar symptoms that are less severe but persist longer are seen in dysthymia.⁶ Studies have demonstrated that the likelihood of acquiring this condition is markedly increased by psychological, genetic, and environmental variables. Viral infections, stress, and trauma all increase the risk of this illness.⁷ Brain-derived neurotrophic factor deficiency, glutamate-mediated toxicity, and aberrant hypothalamic-pituitary-adrenal axis function appear to be associated with both both functional and structural brain problems.⁸

Furthermore, the use of antidepressants may raise the risk of suicidal thoughts and actions in certain children and adolescents. Furthermore, when continuous therapy with antidepressants is either halted or ended, discontinuation disorder, which mostly consists of symptoms similar to the flu, sleep difficulties, nausea, balance disturbances, changes in mood, anxiety, and sadness, might happen. Consequently, herbal remedies have garnered growing attention globally as alternative and complementary medicine that can somewhat offset the shortcomings of synthetic substances.⁹

In these kinds of situations, herbal medication is chosen due to the following qualities,

- a. More affordable and sensible;
- b. Easily available;
- c. having fewer or no adverse effects
- d. Time-tested;
- e. seen as natural and safe⁴

Tricyclic antidepressants, second-generation antidepressants, and monoamine oxidase (MAO) inhibitors are the three main classes of traditional pharmacological medicines used to treat depression. Chemicals known as MAO inhibitors prevent the monoamine oxidase enzyme family from acting. First-line treatment frequently involves the use of MAO inhibitors, such as tranylcypromine, isocarboxazid, phenelzine, and moclobemide. Even with the advancement of those traditional medications, many cases of depression treatment still end in clinical remission.¹⁰ Herbal medicine is the most commonly utilized alternative therapy. Herbal remedies are well-suited for treating depression, and most patients with the illness also attempt complementary therapies. These antidepressant herbs include psychopharmacological actions that include neuroendocrine modulation, MAO inhibition, and control of 5-HT/dopamine/noradrenaline reuptake.¹⁰ Anxiety, diaphoresis, tachycardia, tremor, sedation, sleeplessness, serotonin syndrome, parkinsonism, postural hypotension, impaired vision, and other side effects are associated with antidepressant medications.^{11,12} Considerable progress has been made in the examination of some phytochemicals and medicinal plants for the treatment of depression.

PHYTOCHEMICALS FOR TREATING DEPRESSION

Herbal phytochemicals have been shown to reduce the risk of a number of serious illnesses, including as neurological and cardiovascular diseases as well as autoimmune disorders. In fact, a number of well-known polyphenols have demonstrated strong anti-inflammatory and antioxidant qualities, including resveratrol, curcumin, ferulic acid, proanthocyanidin, and quercetin. Numerous studies have shown these phytochemicals to have neuroprotective properties, which strongly implies that they may be able to lessen the symptoms of depression.

Berberine: A naturally occurring isoquinoline alkaloid has been extracted from a variety of herbal plants, such as *Xanthorhiza simplicissima*, *Eschscholzia California*, *Phellodendron aureum* (Amur cork tree), *Argemone mexicana* (prickly poppy), and *Berberis Hydrastiscanadensis* (golden seal). Berberine has a variety of effects on depression, including raising levels of DA, 5-HT, N.E., and inhibiting monoamine oxidase activity.

Carvacrol. A monoterpene phenol called carvacrol has been extracted from thyme and oregano among other fragrant plants. The neuroprotective, analgesic, anti-arthritis, antidiabetic, gastroprotective, hepatoprotective, and anti-inflammatory qualities of this aromatic phytochemical are well-documented. Carvacrol (12.5–50 mg/kg) given orally to mice has antidepressant properties that appear to be controlled through dopaminergic brain circuits.^{13,10}

Curcumin. Turmeric (*Curcuma longa* Linn) has a natural chemical component called curcumin. By affecting the molecular mechanisms underlying depression, such as the inflammatory process, oxidative and nitrate pathways, monoaminergic activity, and HPA axis activity, curcumin alleviates the symptoms of depression. Mice exposed to depression also exhibit increased neurogenesis in the hippocampus and frontal cortex when curcumin is administered.³ One of *Curcuma longa*'s main active ingredients

is curcumin. Oriental medicine has long utilized this yellow-colored natural phenol, and research is being done to see whether it has any therapeutic benefits.¹⁴ The antidepressant properties of curcumin supplements have been demonstrated in a number of mouse models. In a research, it was investigated if 5-HT receptors, more especially the 5-HT_{1A}/1B and 5-HT_{2C} subtypes, are involved in the antidepressant effect of curcumin (10 mg/kg, PO).¹⁵

Ferulic Acid. One phytochemical with a strong antioxidant activity is ferulic acid. This chemical has been demonstrated to exhibit a range of therapeutic effects, including anti-inflammatory, anticancer, antidiabetic, and neuroprotective characteristics. It is generated from phenylalanine, which is transformed to 4-hydroxycinnamic acid and subsequently caffeic acid. Yabe et colleagues. discovered that giving ferulic acid orally can lessen the aberrant behavior that stress causes in mice with depression.^{10,16}

L-Theanine. In 1949, the amino acid L-theanine was found to be present in *Camellia sinensis*, or green tea. Numerous therapeutic benefits of this amino acid have been shown, including enhanced learning and concentration, increased antitumor activity, prevention of vascular diseases, blood pressure reduction, anti-obesity effect, immune system improvement, and neuroprotection.¹⁰

Proanthocyanidins. Proanthocyanidins, also known as oligomeric and polymeric flavan-3-ols, are present in a variety of plants, such as tea, apples, cocoa beans, and grapes. These phytochemicals have been shown by researchers to have a wide range of pharmacological effects. According to the authors, proanthocyanidin's antidepressant effects might be related to the central monoaminergic neurotransmitter systems.¹⁷

Quercetin. A polyphenolic flavonoid, quercetin may be found in a wide variety of fruits, vegetables, and herbal remedies. Quercetin (20–40 mg/kg, PO) protected mice against depression-like behaviors brought on by hyperactivation of the hypothalamic–pituitary–adrenal (HPA) axis in preclinical experiments. The outcome was similar to that of fluoxetine.¹⁰

Resveratrol. Red wine and grapes are two natural sources of resveratrol, a kind of phenol. Numerous studies have demonstrated its neuroprotective and anti-inflammatory properties. This phytochemical can prevent depressive-like behaviors brought on by prolonged stress.^{18,10}

MEDICAL HERBS USEFUL FOR DEPRESSION

Hypericum perforatum (St John's Wort). The most well-known herb in the family Hypericaceae is *Hypericum perforatum*, also known as St. John's wort (SJW). It is a herbaceous perennial plant. Compared to conventional antidepressants, hypericum extracts show less adverse effects when used to treat depression. Comparing St. John's Wort to conventional antidepressants, the former has a better short-term safety profile. Hyperforin and hypericin are the primary active components of the herb; research indicates that hyperforin has more anti-depressant potential than hypericin. In the frontal brain, H. perforatum inhibits MAO-A and NAO-B, synaptosomal absorption of serotonin, dopamine, and norepinephrine, and up-regulates 5-HT₂ receptors while down-regulating beta receptors. Iran has seen the production and introduction of several medicinal medicines manufactured from this plant, such as Hypercaps, *Hypericum STADA*, *Hypericum 300*, and *Perforan* tablets.^{19,5,3} The whole plant or chopped blooming tops are the parts used medicinally.⁶ *Hypericum perforatum* has been shown in several clinical trials to be clinically effective in treating depression. In order to determine the remission rates, 426 responders to *Hypericum perforatum* extract (3 × 300 mg/day) were

included in a long-term follow-up research. The extract from *Hypericum perforatum* was found to have a positive impact in preventing relapses after acute depression recovery, but its long-term maintenance and tolerance were no different from placebo.¹⁰

Camellia sinensis (Green Tea). Green tea comes from the leaves of the *Camellia sinensis* plant. Anti-inflammatory, anti-fibrotic, anti-cancer, and anti-neurodegenerative effects have all been demonstrated by green tea. A recent preclinical study showed that polyphenols from *Camellia sinensis* (5, 10, and 20 mg/kg PO for 7 days) improved behavior resembling depression and lowered cortisol levels in the blood. These findings imply that the HPA axis, which is implicated in the pathophysiology of depression, can be regulated by green tea polyphenols.^{20,10}

Crocus sativus (Saffron). Saffron belonging to the Iridaceae family, scientific name: *Crocus sativus* L.³ It is a perennial plant that is extensively grown in Iran as well as other nations like Greece and India. Commercial saffron is a spice made from dried crimson stigma that has a tiny bit of yellowish style still adhering to the *Crocus sativus* flower.⁴ Persian traditional medicine uses it as a side-effect-free depression therapy. Treatment with saffron was sufficient to help cure mild to severe depression because it inhibited the release of serotonin by nerve cells, or neurons.⁵ On the Hamilton Rating Scale for Depression, patients showed a significant improvement in depression compared to a placebo in two randomized controlled studies utilizing saffron (30 mg/day). A small-scale meta-analysis found that supplementing with saffron can help people with depression by reducing symptoms. The authors suggest that the serotonergic, antioxidant, anti-inflammatory, neuroendocrine, and neuroprotective properties of saffron may be responsible for some of its antidepressant benefits. Mazidi et al. recently completed a double-blind, randomized, placebo-controlled experiment that demonstrated the considerable efficacy of saffron medication (100 mg/day PO for 12 weeks) in the treatment of depression, with few adverse effects.^{21,10}

Echium amoenum (Borage). *Echium amoenum* belongs to the family Borage. In complementary medicine, the blossom of *Echium amoenum* is utilized as an antidepressant, antifebrile, anti-inflammatory, and perhaps cancer-preventive agent.²² γ - and α -linolenic acids, $\delta 6$ -fatty acryloyl desaturase, $\delta 8$ -sphingolipid desaturase, pyrrolizidine alkaloids, mucilages, resin, potassium nitrate, calcium, and inorganic acids are among the active components of *E. amoenum*.⁹ Sayyah et al. carried out a preliminary randomized, double-blind clinical experiment to clarify the effects of *Echium amoenum* against depression. By week four of the trial, the aqueous extract of *Echium amoenum* (375 mg/day PO) outperformed a placebo in terms of improving the Hamilton Rating Scale for Depression; however, by week six, the difference was not statistically significant ($p = 0.07$).¹⁰ A recent clinical trial that compared the effectiveness of citalopram with *E. amoenum* syrup found that the latter was less problematic after eight weeks and less successful in treating depressed symptoms.⁹

Piper methysticum (Kava). The South Pacific area has traditionally employed the root of *Piper methysticum* to manufacture a hallucinogenic beverage. It reaches a height of two to three meters as a shrub.⁶ According to a research, taking 16 grams of *Piper methysticum* aqueous extract (which contains 250 mg of kavalactones daily) significantly reduces the symptoms of comorbid depression as measured by the Montgomery-Asberg Depression Rating Scale. Crucially, the extract did not exhibit any serious adverse effects or clinical hepatotoxicity, indicating that it is safe for use as a medication.^{23,10}

Rhodiola rosea (Rose Root) *Rhodiola rosea* is a biennial flowering plant that promotes physical vigor and boosts resilience to stress. It is sometimes referred to as an adaptogen plant or golden root.^{3,9} It has been utilized as a physical and mental enhancer in traditional medicine. Using behavioral tests on rats, Mattioli et al. demonstrated the antidepressant efficacy of *Rhodiola rosea* extract (10–20 mg/kg, PO for 3 weeks). Chronic moderate stress-induced behavioral and physiological changes were significantly suppressed by long-term treatment of *Rhodiola rosea* extract.^{24,10} By raising serotonin, dopamine, and norepinephrine levels in several brain regions, this plant's extract has antidepressant properties.³ In the depression-like behavior paradigm, the psychopharmacological mechanisms of RL were mostly associated with inhibition of monoamine oxidase A, modification of 5-HT content, and increased neuronal quantity and proliferation in depressed rats and mice.⁹ A notable recovery was shown in the *Rhodiola rosea*-treated group compared with the placebo group in a phase III clinical trial that was randomized, double-blind, placebo-controlled, and used *Rhodiola rosea* extract (340–680 mg/day) for mild to moderate depression.¹⁰

Lavandula angustifolia (Lavender). Native to the Mediterranean, *Lavender angustifolia* is a flowering plant in the Lamiaceae family.²⁵ It helps relieve nervous stomach irritation, nervous intestinal pain, and mood disorders including sleeplessness or restlessness. As a result, the nervous system becomes stronger and less depressed and nervous tiredness occurs.⁵ Lavender flowers are useful for making tinctures and essential oils by steam distillation, as well as for brewing tea. Chronic exposure to lavender oil, according to Hritcu et al., significantly reduced depression-like behaviors in rats as measured by elevated plus-maze tests and forced swimming. In high-risk postpartum women, four weeks of lavender aromatherapy improved the Edinburgh Postnatal Depression Scale. Forty-five individuals receiving imipramine and lavender oil complementary therapy for mild depression had better and quicker outcomes.^{26,10}

Nelumbo nucifera. Asian nations have traditionally utilized the fruit of *Nelumbo nucifera*, also known as *Nelumbinis* semen, as a natural sedative. Its mechanism of action on depression has been elucidated by our team and others. Reversing a reduction in 5-HT_{1A} receptor binding, *Nelumbinis* semen demonstrated antidepressant properties in a rat model of depression. Interestingly, its therapeutic impact outperformed that of *Hypericum perforatum*, the most widely used natural antidepressant now available.^{10,27}

Valeriana officinalis L.: Traditional medicine systems as well as pharmacopeias have suggested *V. officinalis* extract as a cure for symptoms including anxiety, depression, and moderate insomnia. Valerian extract has been shown to have antidepressant effects in the elevated plus maze and forced swimming tests by preclinical investigations conducted on animal models.⁹

CONCLUSION

Not only do these mental illnesses affect people's daily lives, but they also have a big financial impact on society. It is now well accepted that nature contains potent phytochemicals with neuroprotective properties. When used to treat individuals with serious depression as well as mild to moderate depression, several medicinal herbs have demonstrated antidepressant benefits comparable to those of conventional antidepressants. There are plenty of these items on the market, and they are utilized as dietary supplements in addition to being approved medicines. In conclusion, a plethora of preclinical and clinical research has demonstrated the medicinal herb and phytochemical potential for treating

depression. Additionally, research in vivo and in vitro is required to learn more about their antidepressant processes.

However, patients should exercise caution while using phytomedicines because not all natural products are safe to use.

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Conflicts of Interests

There are no conflicts of interest.

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Authors Contributions

All the authors have contributed equally.

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