

Depression and the Healing Herbs: Exploring Herbal Medicine's Role in Mental Health

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ABSTRACT:

Depression is a prevalent psychiatric disorder with profound effects on both mental and physical health, significantly impacting societal well-being. It is a leading cause of disability worldwide, with a rising prevalence driven by socio-cultural factors, demographic changes, and increased chronic medical conditions. The disorder encompasses various types, including major depression, persistent depressive disorder, bipolar disorder, and seasonal affective disorder. Symptoms range from sadness and loss of interest in activities to severe signs such as suicidal thoughts. Depression's pathophysiology is linked to imbalances in neurotransmitters like serotonin, norepinephrine, and dopamine, as well as disruptions in the hypothalamic-pituitary-adrenal (HPA) axis and neurogenesis.

Despite the availability of antidepressants, treatment outcomes remain suboptimal due to side effects, delayed onset, and relapse. Common antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs), are frequently prescribed but are often limited by side effects like nausea, insomnia, and sexual dysfunction, as well as the risk of suicidal ideation. This has sparked interest in alternative therapies, particularly herbal medicine, which may offer effective solutions with fewer side effects. Traditional herbs like *Glycyrrhiza uralensis* (Mulethi), *Siphocampylus verticillatus*, *Curcuma longa* (turmeric), and *Bacopa monnieri* (Brahmi) have demonstrated antidepressant-like effects in animal models, suggesting their potential as viable treatment options. This article emphasizes the need for further research into these herbal therapies to offer safer, more effective alternatives to current pharmacological treatments.

Keywords: Depression, Pathophysiology of depression, Epidemiology of depression, Antidepressant drugs, Medicinal plants.

I. INTRODUCTION

Depression has been labelled the common cold of psychopathology. The comparison is surely, for it conveys the impression of frequent but mild complaint. In reality some depressions end fatally. Depression is responsible for the majority of suicide deaths, those most vulnerable to suicide are depressed and have lost hope (Minkoff, Kenneth; Bergman, Eric; Beck, Aaron T.; 1 Apr 2006) (Gilbert, 2017)¹⁻³.

In many developed countries suicide is in the top ten most frequent causes of death. Depression and anxiety disorders are most common illness in the community and in primary care. Patients with depression often have features of anxiety disorder, and those with anxiety disorder commonly also have depression. Moreover, depression may well reduce life expectancy in certain physical disorders, e.g., cancer (Whitlock & Siskind, 1979), (Kautu et al., 2017)².

In the World Health Organization (WHO) report on the collaborative study of the assessment of the depressive disorders, Sartorius and his colleagues, [Sartorius et al., 1983] maintain that there are probably 100 million depressives in the world and that the number may be increasing because of deleterious sociocultural effects, demographic changes, psychological factors, the increased number of patients with chronic medical disorders, and the widespread use of medications that have depressive side effects (Gilbert, 2017)¹.

According to the fifth edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, depression is classified as a mood disorder and causes problems with how a person feels, thinks, acts, and behaves. For a diagnosis of depression, symptoms must be present for at least two consecutive weeks (Gilbert, 2017). They can range from mild to severe and may include the following⁴:



- Feeling sad or having a depressed mood.
- Loss of interest or pleasure in activities once enjoyed.
- Changes in appetite-weight loss or gain unrelated to dieting.
- Trouble sleeping or sleeping too much.
- Loss of energy or increased fatigue.
- Increase in purposeless physical activity (such as hand-wringing or pacing) or slowed movements and speech (actions observable by others).
- Feeling worthless or guilty.
- Difficulty thinking, concentrating, or making decisions.
- Thoughts of death or suicide (Kendler, Kenneth S.; Heath, and Lewinsohn; Martin, Nicholas; 1987).

Depression is a universal phenomenon. There is a strong correlation between several medical diseases and disorders and mental health issues. For example, people with cardiac problems often have depression, and those who have depression often develop heart disease. It's therefore important that nurses are aware of the history, indications for use, adverse effects, and special considerations related to antidepressants⁵.

Between 5 to 13% of primary care patients convey a diagnosis of depression, contributing to morbidity and mortality. Numerous efficacious treatments exist, but nearly four in five depressed individuals worldwide fail to receive nominally adequate treatment. Depression is under-recognized in primary care, contributing to low treatment uptake. Yet, even when recognized half of referred patients fail to attend psychotherapy visits or fill their first prescribed antidepressant medication.

According to the World Health Organization (WHO), depression affects more than

300 million people worldwide. It is the leading cause of disability globally, knows no age limitation, tends to affect women more than men, and can lead to suicide. Although several treatments are available, the WHO reports that fewer than 50% of people receive treatment. According to the WHO, the number of people affected by depression rose by 18% from 2005 to 2015.

Adults, however, aren't the only people experiencing symptoms of depression. In 2015, the NIMH (National Institute of Mental Health) reported that an estimated 3 million U.S. adolescents 12 to 17 years of age had at least one major depressive episode in the past year, with that number representing 12.5% of children in this age group. Major depressive disorder, which is a chronic, recurring form of depression, is regarded as the most common mood disorder among Americans. Although treatment can help manage symptoms in some people, currently there is no cure for this devastating disease⁵⁻¹¹.

DEPRESSION

Depression can be defined as the most common of the affective disorders, it is defined as disorders of mood rather than disturbances of thoughts or cognition; it may range from a very mild condition, bordering on normality, to severe psychotic depression accompanied by hallucinations and delusions. In other words, depression is a major cause of disability and premature death. Major depression is a common disorder that continues to result in considerable morbidity and mortality despite major advances in treatment. We can say that mental depression can affect the individual's mood, physical health, behavior and thoughts¹²⁻¹⁶.

TYPE OF DEPRESSION

Major depression-

It is a state where a dark mood is all-consuming and one loses interest in activities, even ones that are usually pleasurable. Symptoms of this type of depression include trouble sleeping, changes in appetite or weight, loss of energy and feeling worthless. Thoughts of death or suicide may occur.

Persistent depressive disorder- formerly called "dysthymia", this type of depression refers to low mood that has lasted for at least two years but may not reach the intensity of major depression. Many people with this type of depression are able to function day to day, but feel low or joyless much of the time. Other depressive symptoms may include appetite and sleep changes, low energy, low self-

esteem, or hopelessness.

Bipolar disorder-: known as manic-depressive disease, have episodes of depression. Manic symptoms are opposite of depression symptoms: magnificent ideas, unrealistically high self-esteem, decreased need for sleep, thoughts and activity at higher speed. Being manic can feel great, but it doesn't last long and can lead to self-destructive behavior, and is followed by a period of depression.

Seasonal affective disorder (SAD)-: this type of depression emerges as days get shorter in the fall and winter. The mood change may result from alterations in the body's natural daily rhythms, in the eye's sensitivity to light, or in how chemical messengers like serotonin and melatonin function. The leading treatment is light therapy, which involves daily sessions sitting close to an especially intense light source.

Depression types unique to women-:

Perinatal depression-: this type of depression includes major and minor depressive episodes that occur during pregnancy or in the first 12 months after delivery (also known as postpartum depression). Perinatal depression affects up to one in seven women who give birth and can have devastating effects on the women, their infants, and their families. Treatment includes counseling and medication.

PMDD-: this type of depression is a severe form of premenstrual syndrome, or PMS. Symptoms of PMDD usually begin shortly after ovulation and end once menstruation starts. Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine and sertraline, may reduce symptoms¹⁷.

SYMPTOMS OF DEPRESSION

- Biological components retardation of thought and thinking
- Persistent sad, anxious, or empty feelings
- Feelings of hopelessness or pessimism
- Feelings of guilt, worthlessness, or helplessness
- Irritability, restlessness
- Loss of interest in activities or hobbies once pleasurable, including sex
- Fatigue and decreased energy

- Difficulty concentrating, remembering details, and making decisions
- Insomnia, early-morning wakefulness, or excessive sleeping
- Overeating, or appetite loss
- Thoughts of suicide, suicide attempts
- Aches, headaches, cramps or digestive problems that do not ease even with treatment¹⁸⁻²¹.

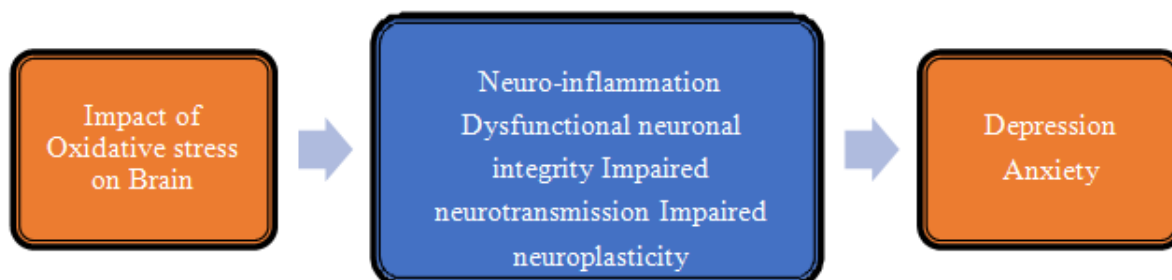
PATHOPHYSIOLOGY OF DEPRESSION

Major depression is a serious disorder of enormous sociological and clinical relevance. The discovery of antidepressant drugs in the 1950s led to the first biochemical hypothesis of depression, which suggested that impairment in central monoaminergic function was the major lesion underlying the disorder. Basic research in all fields of neuroscience (including genetics) and the discovery of new antidepressant drugs have revolutionized our understanding of the

mechanisms underlying depression and drug action. There is no doubt that the monoaminergic system is one of the cornerstones of these mechanisms, but multiple interactions with other brain systems and the regulation of central nervous system function must also be taken into account. Several factors appear to work together to cause or precipitate depressive disorders: symptoms reported by patients with major depression consistently reflect changes in brain monoamine neurotransmitter specifically, and other neurotransmitters are norepinephrine (NE), serotonin (5-HT), dopamine (DA)²²⁻²⁴.

MECHANISMS BELIEVED IN PATHOPHYSIOLOGY OF DEPRESSION

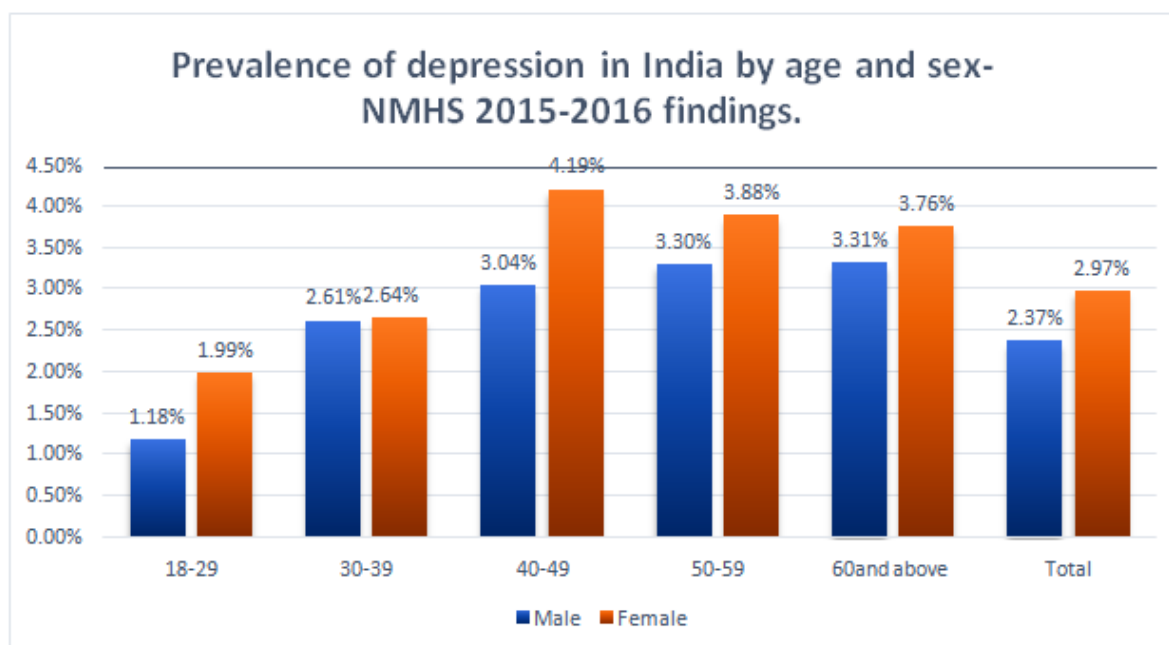
The main depressive axis involves the hypothalamic-pituitary-adrenal (HPA) axis, which is activated by stress and in turn enhances the excitotoxic action of glutamate, mediated by NMDA receptors and switches on the expression of genes that promote neuronal apoptosis in the hippocampus and prefrontal cortex. The anti-depressive pathways involved in the monoamines norepinephrine (NA) and 5-hydroxytryptamine (5-HT), which act on kinase-linked receptors, switching on the genes that protect neurons against apoptosis and also promote neurogenesis²⁵⁻²⁶.



EPIDEMIOLOGY OF DEPRESSION

The epidemiology of depression has been studied across the world. Depression is a major cause of morbidity worldwide, as the epidemiology has shown. According to the World Health Organization (WHO), depression affects more than 300 million people worldwide. It is the leading cause of disability globally, knows no age limitation, tends to affect women more than men, and can lead to suicide. Although several treatments are available, the WHO reports that fewer than 50% of people receive treatment. According to the WHO, the number of people affected by depression rose by

18% from 2005 to 2015. The total number of people with depression was estimated to exceed 300 million in 2015 worldwide, equivalent to 4.3% of the world's population. In India, the National Mental Health Survey 2015-16 revealed that nearly 15% Indian adults need active intervention for one or more mental health issues and one in 20 Indians suffers from depression. It is assessed that in 2012, India had over 258 000 suicides, with the age-group of 15-49 years being most affected²⁷⁻²⁸.



Women are increased risk of depression from early adolescence until their mid-50's with lifetime rate that is 1.7-2.7 times greater than for men. Although depression can occur at any age but adults 18-19 years of age experience highest rates of major depression during any given year. Estimated life time prevalence of

major depression in individuals aged 65-80 recently was reported to be 20.4% in women and 9.6% in men²⁹.

The prevalence of psychiatric disorders differs between countries and within countries across various cities. Lifetime prevalence estimates vary widely, from 3% in Japan to 17% in the

United States. Epidemiological data shows higher rates of depression in the middle East, North Africa, South Asia and America than in other countries. Among the 10 countries studied, the number of people who would suffer from depression during their lives falls within an 8-12% range in most of them. In North America, the probability of having a major depressive episode within any year-long period is 3-5% for males and 8-10% for females³⁰.

ANTIDEPRESSANTS

Antidepressants are those drugs which help in the reduction in symptoms of depressive disorders by altering chemical imbalances of neurotransmitters in the brain. The change in mood and behavior is due to chemical imbalance. Neurotransmitters are the communication link between neurons in the brain. Neurotransmitter

are relocated in vesicles found in nerve cells³¹.

The neurotransmitter such as serotonin, dopamine, and noradrenaline are released by the axon end of one nerve and received by the other, the phenomenon called as reuptake. The antidepressants inhibit reuptake of neurotransmitter through selective receptor thereby increasing the concentration of specific neurotransmitter around the nerves in the brain. One of such antidepressants is selective serotonin reuptake inhibitor (SSRI), which affects the brain serotonin level. Antidepressants may recover the signs of depression, but also exert some side effects³².

Antidepressants and their classification³³⁻³⁴:-

- Tricyclic antidepressants (TCAs),
- Selective serotonin-reuptake inhibitors (SSRIs),
- Monoamine oxidase inhibitors (MAOIs),
- Atypical antidepressant.

S.No.	Types of drug	Side effects
1	Reversible inhibitor of MAO-A:- Moclobemide, clorgyline	Cheese reaction, nausea, insomnia, agitation, weight gain, liver damage.
2	Tricyclic antidepressants:- a. NA+5-HT reuptake inhibitors- : imipramine, amitriptyline, clomipramine, doxepin. b. Predominantly NA reuptake inhibitors- : desipramine, nortriptyline, amoxapine.	Sedation, dry mouth, constipation, blurred vision, urinary retention, seizures, postural hypotension, impotence, interaction with CNS depressants.
3	Selective serotonin reuptake inhibitors:- fluoxetine, fluvoxamine, paroxetine, sertraline.	Nausea, diarrhea, agitation, insomnia, anorgasmia,
		inhibit metabolism of other drugs.
4	Atypical inhibitors:- Trazodone, duloxetine, bupropion.	Bradycardia, seizures, dry mouth, epigastric pain, tremor, bodyache.

DRAWBACKS WITH CURRENT THERAPEUTICS

Nowadays researchers facing many problems in the diagnostic classification and treatment strategies for depression because of lack of clear biological pathogenesis. The diagnostic criteria for depressive disorders in the International Statistical Classification of Diseases and Related Health

Problems 10th Revision (ICD-10) and the fifth edition of the Diagnostic and Statistical Manual of Mental Disorder (DSM-5), require individual to display at least five out of nine symptoms almost daily for at least two weeks and that these five symptoms must include either a depressive mood or a lack of interest or pleasure. The delayed onset of action of antidepressants becomes a critical factor in

the particular cases of depressions, in which the risks of suicide are strongly increased. The limited efficacy of antidepressants also a major limitation as they act by increasing monoamine levels, although individuals with depression do not suffer lower levels of these neurotransmitter³⁶.

Antidepressants produce common side effects like insomnia, skin rashes, headaches, joint, muscle pain, stomach upset, diarrhea or nausea. These problems are usually temporary or mild or both.

A more serious potential problem is reduced blood clotting capacity because of decreased concentrations of the neurotransmitter serotonin in platelets.

The serious side effects associated with the use of antidepressants may include serotonin syndrome, hyponatremia, allergic reactions, mania and seizures.

Researches also reported that antidepressant increase the risk of having suicidal thoughts and during pregnancy cause neonatal abstinence syndrome. However, high rates of relapse after discontinuing antidepressants are also affect the effectiveness of the treatment. As the currently available treatments associated with several limitations, there is need of further novel targets for the effective treatment of depression³⁷⁻³⁸.

2° COMPLICATIONS

- Bladder and bowel problems.
- Loss of appetite.
- Loss of libido.
- Irregular heart beat.
- Seizures.
- Hyponatremia.
- Psychosis.
- Long term use of SSRIs and TCAs increased risk of developing Type-2 Diabetes³⁹⁻⁴⁰.

NEEDS OF HERBAL DRUG FOR NEW THERAPEUTICS

The ultimate aim of antidepressant therapy is to stop or slow down the disease progression. But the allopathic treatments have limited efficacy and have been reported to be associated with undesirable side effects. The inability of antidepressant agents to provide an adequate explanation for the shortcomings such as high/low treatment resistance rate, treatment failure, slow onset of action, side effects. To overcome these limitations associated with synthetic antidepressants interest has been shifted to use of other alternative medicine. Herbal

medicines still remain the widespread choice in the developing countries due to their ease of availability, lesser side effects and lower cost. World Health Organization (WHO) has recommended the traditional plant for the treatment of various disease. Moreover, today it is necessary to provide scientific proof as to whether it is justified to use a plant or its active principle for treatment. Traditional medicine and extracts from medicinal plants have been extensively used as an alternative medicine for better control and management of depressive disorder⁴¹⁻⁴².

The mechanisms by which herbs generally act are not established, however, most of medicinal plants possess antioxidant activities. Antioxidant activities of herbal medicines are also effective in reducing the toxicities of toxic agents or other drugs. The aim of herbal drugs is to integrate and balance the body, mind and spirit to prevent disease and promote wellness. In the past 10 years, however, herbal drugs have seldom been approved for use alone in treating depression. According to current evidence, some of these herbal plants show promising results to overcome depression⁴³.

MEDICINAL PLANTS ANTI-DEPRESSANTS

Glycyrrhizauralensis (Mulethi): Many flavonoid extracted from nature plants have been reported to exert antidepressant-like effect in animal studies. The present study was designed to observe the effects of liquiritin, a flavonoid compound derived from *Glycyrrhizauralensis*, on the behavior of chronic variable stress induced depression model rats and to explore the possible association between its antidepressant-like effect and antioxidative activity by measuring erythrocyte superoxide dismutase (SOD) activity and plasma malondialdehyde (MDA) level of the experimental animals⁴⁴.

Siphocampylus verticillatus: The antidepressant-like effect of the hydroalcoholic extract obtained from aerial parts of *Siphocampylus verticillatus*, a Brazilian medicinal plant, was investigated in two models of depression in mice and against synaptosomal uptake of serotonin, noradrenaline and dopamine. The immobility times in the forced swimming test (FST) and in the tail suspension test (TST) were significantly reduced by the extract (dose range 100–1000 mg/kg, i.p.), without accompanying changes in ambulation when assessed in an open-field. Its action seems to involve an interaction with adrenergic,

dopaminergic, glutamatergic and serotonergic systems⁴⁵.

Allium macrostemon (Chinese garlic): The aim of this study was to identify the effects of water extracts of *Allium macrostemon* Bunge (AM-W), a traditional herb, in mice. The antidepressant-like activities of AM-W were evaluated through behavioral despair in forced swimming test and tail suspension test⁴⁶.

Curcuma longa: *Curcuma longa* (turmeric) is a well-known indigenous herbal medicine. The aqueous extracts, when administered orally to the mice from 140 to 560 mg/kg for 14 days, were able to elicit dose-dependent relation of immobility reduction in the tail suspension test and the forced swimming test in mice. The effects of the extracts at the dose of 560 mg/kg were more potent than that of reference antidepressant fluoxetine. The activity of *C. longa* in antidepressant may mediate in part through MAO A inhibition in mouse brain⁴⁷.

Piper tuberculatum (black pepper): In the present work, we studied the effects of piperazine (PIP), an amide alkaloid isolated from the root of *Piper tuberculatum* (Piperaceae), in the elevated plus maze, open field, rota rod, pentylenetetrazole (PTZ)-induced seizures, and forced swimming tests, in mice (Swiss, male, 25 g) to assess anxiolytic, sedative, muscle relaxant, anticonvulsant and antidepressant effects, respectively. Furthermore, a significant and dose-dependent decrease in the immobility time, as evaluated by the forced swimming test, was observed after PIP administration (41% and 75% decrease, at the doses of 50 and 100 mg/kg, respectively), suggesting an antidepressant effect, similar to that observed with mirtazapine, a classical antidepressant drug used as standard. In conclusion, we showed that PIP presents significant anxiolytic and antidepressant activities, making this drug potentially useful in anxiety and depression⁴⁸.

Emblica officinalis (amla): Depression is a widespread psychiatric disorder affecting around 5% of the population. Furthermore, it is difficult to predict which patient will respond to any given treatment. In the traditional systems of medicine, many plants and formulations have been used to treat depression for thousands of years. The present study was undertaken to evaluate the antidepressant potential of acute and chronic administration of EO in force

dswim test (FST) and tail suspension test (TST). The antidepressant activity of EO was comparable to that of standard drug mirtazapine. The results of the present study indicate the potential for use of EO as an adjuvant in the treatment of depression⁴⁹.

Bacopa monnieri (Brahmi): *Bacopa monnieri* Wettst. (Syn. *Herpestismonnieri* L.; Scrophulariaceae) is a commonly used Ayurvedic drug for mental disorders. The standardized extract was reported earlier to have significant anti-oxidant effect, anxiolytic activity and improve memory retention in Alzheimer's disease. Presently, the standardized methanolic extract of *Bacopa monnieri* (bacoside A - 38.0±0.9) was investigated for potential antidepressant activity in rodent models of depression. The effect was compared with the standard antidepressant drug mirtazapine (15 mg/kg, ip)⁵⁰. These are some few examples that showed herbal medicine used as therapeutic nowadays.

II. CONCLUSION

Depression is a widespread and debilitating mental health disorder that affects millions of people worldwide. It is a significant cause of disability, morbidity, and mortality, with increasing prevalence rates globally. Depression is not only associated with emotional distress but also with a range of physical symptoms and complications, including an increased risk of suicide. Despite the availability of several antidepressant treatments, a large number of individuals suffering from depression do not receive adequate care, and many treatments have limitations, such as delayed onset, side effects, and high relapse rates.

While conventional antidepressants, including SSRIs, TCAs, and MAOIs, are commonly used, they are not without drawbacks, including side effects like gastrointestinal disturbances, insomnia, and sexual dysfunction. Moreover, the limited efficacy and long onset time of these treatments highlight the need for alternative therapeutic options.

Herbal medicines have gained attention as potential antidepressant treatments, particularly due to their lower cost, fewer side effects, and long-standing use in traditional medicine. Several medicinal plants, such as *Glycyrrhiza uralensis*, *Siphocampylus verticillatus*, *Curcuma longa*, and *Bacopa monnieri*, have shown promising antidepressant-like effects in preclinical studies,

often through mechanisms involving neurotransmitter modulation and antioxidant activities.

Therefore, further research into the efficacy, safety, and mechanisms of action of these herbal remedies is essential. Integrating herbal therapies with conventional treatments could offer more effective, accessible, and holistic solutions for managing depression, particularly in resource-limited settings. The potential for herbal medicine to complement existing treatments holds promise for improving outcomes for those struggling with depression.

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