A Review on Antidepressant Activity of Various Plants

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Abstract

Depressive disorder, or depression, is a common mental health condition and is characterized by a low mood or loss of pleasure or interest in activities for long periods of time. It is a complex neuropsychiatric disorder, that affects the life style and has been classified and treated in a variety of ways. Now a days, number of synthetic antidepressant drugs are available, these drugs have limited effect and associated with more side effects as well as chronic toxicity. To obtain better therapeutic benefits and minor adverse reactions, search for alternative antidepressant from natural source i.e., herbal remedies, which were used traditionally, and are safe on human health, is gaining global attention. Recently, it has been reported that the use of polyherbal formulation exhibit synergistic activity to achievement of maximum beneficial potency as compared to single herb. Therefore, the objective of this review is to enlist medicinal herbs &plants which have antidepressant action using the various rodent models of depression. The multiple causing factors of depression are decreased levels of neurotransmitter in brain including noradrenalin, dopamine and serotonin. Therefore, these medicinal herbs restore the reduced levels of neurotransmitter in the brain either by inhibiting reuptake of neurotransmitters or by inhibiting monoamine oxidase and treat mild to moderate depression. Antidepressants decrease the duration of immobility in the forced swim test in the rat and the mouse and in the tail suspension test in the mouse.

Keywords

Antidepressant activity, Depression, Forced Swim test, Medicinal Plants, Rodents, Tail Suspension Test.

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INTRODUCTION

Depression

Sadness and grief are normal human emotions. Everyone have such feelings from time to time, but it goes away within a few days but major depression is something more. It's a period of overwhelming sadness. Depression is a common mental disorder that is accompanied with decreased energy, loss of pleasure or interest, guilt feeling, disturbed sleep, unable to concentrate, disturbed sleep, low self-worth and depressed mood. It is an etiologically heterogeneous group of brain disorders characterized by a wide range of symptoms that reflect alterations in cognitive, psychomotor and emotional processes. Moreover, depression often accompanied with symptoms of anxiety. These problems can become chronic or recurrent which can also lead to substantial impairments where an individual's cannot take care of his or her day-to-day responsibilities. Depression is more common in

women than men. At its worst, it can lead to suicide. Today,
350 million people is estimated to be affected by depression.[1]

According to the World Health report, approximately 450 million people suffer from a mental or behavioral disorder. This amounts to 12.3% of the global burden of disease, and will rise to 15% by 2020. It has suggested that it will be the second leading cause of death by the year 2020 because of its high prevalence of suicide in depressed patients coupled with complication arising from stress and its effects on the cardiovascular system. Depression is associated with a serious impairment of marital, occupational functioning and social as well as prominent personal and interpersonal distress. Depression can be treated by antidepressants, Transcranial magnetic stimulation (TMS) and Light therapy may relieve depression symptoms in the winter time and Talk therapy called psychotherapy and other treatments for depression are Electroconvulsive therapy (ECT) [1]

The World Health Organization (WHO) has provided guidelines for managing depression during clinical practice. The antidepressants medications significantly cure the disease. The most popular medications used to treat acute and major depressive disorder are selective serotonin reuptake inhibitors (SSRIs), selective serotonin-norepinephrine reuptake inhibitors (SNRIs), Noradrenaline and specific serotonergic antidepressants(NASSAs), Tricyclic antidepressants(TCAs), Serotonin antagonists and reuptake inhibitors(SARIs), Monoamine oxidase inhibitors(MAOIs).According to the report, about 63

percent of patients taking SSRIs and SNRIs antidepressant drugs experience more side effects . Because of this, most physicians prefer non-pharmacological therapy also.

Medicinal plants are an important source of natural active compounds that can helps to discover new molecules for the treatment of different types of diseases. Herbal medicines are used to treat mental illnesses, which are becoming more common as natural remedies for the management of depression and anxiety. The World Health Organization and the European Medicine Agency have proved some herbal medicines, such as Lavandula angustifolia Mill., Crocus sativus L., Passiflora incarnata L., and Valeriana officinalis L., for the treatment of anxiety and depression because of its lower side effects and withdrawal symptoms. Various pharmacological methods have been developed in recent decades to assess the neuropharmacological activities of medicinal plants .People are generally not aware of the selection and use of these medicinal plants for curing various diseases. Therefore, present study was carried out to elucidate the in-vitro anti-depressant activity through in-vivo study of aqueous extract of plants in experimental animals.[2]

DISCUSSION:
This review includes detailed description of antidepressant activity of 15 medicinal plants whose roots, leaves, fruits extracts were used to evaluate the activity from various research articles. The tests employed for antidepressant activity includes FST, TST using rotarod and THB. These tests are employed with slight modification from original method, keeping basic concept same. [3]

PARAMETER	SYNTHETIC ANTIDEPRRESSANTS	HERBAL ANTIDEPRASSANTS
Mechanism of Action	Inhibit serotonin/norepinephrine reuptake	Multi-targeted: Mao inhibition, neurotransmitter modulation, anti-inflammatory effects.
Onset of action	Takes 2-4 weeks	Some herbal extracts show faster onset
Side effects	Weight gain, sexual-dysfunction, withdrawal symptoms.	Fewer side effects, but long-term safety needs more study.
Dependency Risk	Moderate to high	Low to negligible
Regulatory approval	FDA approved but needs prescription	Used traditionally but requires more clinical trials for FDA/WHO approval.

Table 1: Parameters

MODELS TO EVALUATE ANTIDEPRESSANT ACTIVITY
Acute stress models – Predictive models of antidepressant activity
 Forced swimming test
The forced swimming test (FST) was developed by Porsolt so as to examine the antidepressant activity

of drugs. FTS is one of the most widely used tests of antidepressant action. Although it works in a subacute condition (30 minutes after drug administration), this test has strong reliability in predicting the therapeutic potential of investigated compounds. In FST, mice or rats are placed into an

inescapable cylinder filled with water (Figure 1). In this situation, animals try to leave the cylinder but they cannot escape, so they are eventually induced to displaying a characteristic behaviour of immobility. The test is based on the observation of an immobile posture that is common to rodents. The duration of this immobility in rodents that have been tested after administration of a drug with antidepressant activity is shorter than that seen in a control group. In this test, both groups of drugs, classical as well as atypical antidepressants, are active. The Porsolt test has a lot of advantages. Among these are relative simplicity, low costs and the fact that it is a fast and reliable tool for researching potential antidepressant activity (as it has strong predictive validity). This test has a wide range of applications, it is even used as a quick pre-screening test. Unfortunately, the test has poor face and construct validities. Moreover, FST may give false positive results for compounds which increase the general activity (psychostimulants such as caffeine and amphetamine). To verify this, the locomotor activity test is usually employed to control the impact of the investigated compounds on locomotion. [4]
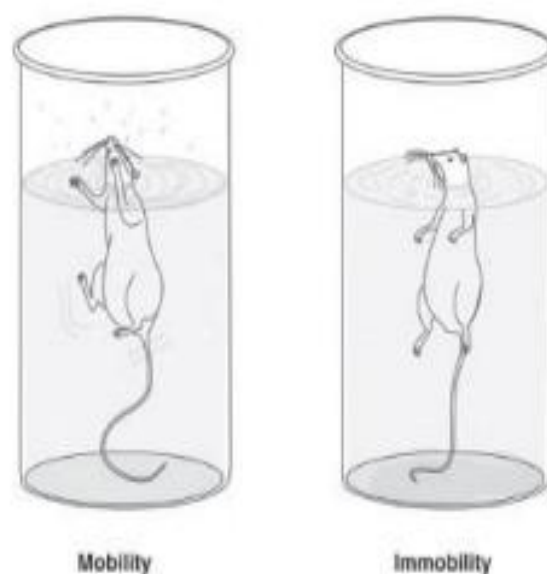

Mobility   Immobility

Figure 1. Schematic representation of mobility and immobility in the forced swimming test . [4]

TAIL SUSPENSION TEST

The Tail Suspension Test is a mouse behavioural paradigm measuring behavioural despair or "depression-like" behaviour and learned helplessness. It is useful in the screening of potential antidepressant drugs and in assessing other manipulations that are expected to affect depression-related behaviours. It is conducted in a small 3-sided chamber in which the mice are suspended by the tail from a hook extending from the ceiling of the chamber, in such a position that they cannot escape or hold on to nearby surfaces; its primary measure is immobility.

Procedure Steps:
- Equipment set-ups may vary.
- The mouse must be suspended using a piece of adhesive tape.
- The tape should be strong enough to prevent the mouse from falling and should not damage the skin of the tail.
- Tape length may vary with specific systems) and should only be applied to the very end of the tail (with 2-3 millimetres of tail remaining outside of the tape).[5]

Advantages:
1. Highly sensitive for detecting antidepressant like effects.
2. Quick and easy to perform compared to other behavioural tests.
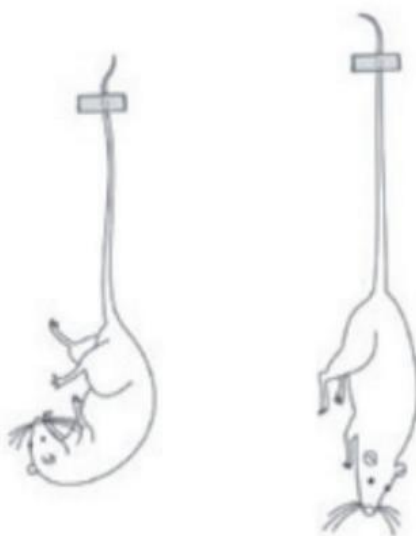3. Does not require pre training of animals.

Figure 2 Depicts a system in which the tape is about 15 cm long and is attached to the bar.[5]

ANTI-DEPRESSANT PLANTS:

 The Indian landmass is enriched by a range of flora each aromatic and medicative plants. This is often due to the wide diversity of weather conditions in Asian country starting from deserts to swamplands. Varied kinds of herbs are well recognized and listed by life scientist from the high ranges of the chain tract up to the sea-shores of Kanyakumari. In recent years, specialize in plants analysis has inflated everywhere the globe and an oversized body of proof has been collected to indicate vast potential of medicative plants utilized in varied ancient systems.[6] The history of flavouring medicines is as recent as human civilization. The documents disclosed that plants were used medicinally in China, India, Egypt and Greece long before the start of the Christian era. The human being seems to be afflicted with a lot of diseases than the other animal's species. They wanted to alleviate their sufferings from injury and illness by taking advantage of plant growing around them. Depression is such a standard disturbance that affects the personal and social relations of someone. There are style of neuro chemical theories proposed and range of artificial medication antidepressant are obtainable currently a days, but their effectiveness doesn't return up the whole vary of population tormented by this disorder. What are more the facet effects and also the drug interactions are major restrictions in their clinical applications. Unlike, artificial medications, seasoning medicines are wide used across the world because of their wide relevancy and therapeutic effectualness related to least facet effects that successively has initiated the research project concerning the medication activity. The aim of this review is to enlist those plants which have antidepressant activity and therefore the used to experimental models accustomed screen their numerous activities.[6]

1. Ashwagandha (Withania somnifera):

 W. somnifera also known as Indian ginseng is widely used as a rasayana (rejuvenator) to promote physical and mental health and healthy ageing and also possess as an anti-cancer, neuroprotective, anti-epileptic, spermatogenic, hepatoprotective, anti-microbial, anti-oxidant, anti-inflammatory, and anti-arthritic activities. Recently, it has demonstrated as anti-depressant, anxiolytic, and adaptogenic properties in a range of rodent behavioural tests such as the open field test, forced swim test, tail suspension test and learned helplessness test etc. It contains multiple bioactive constituents and is likely to exert its pharmacological effects via multiple targets which also include the serotonergic system and other. [7]

2. Curcuma longa (Haridra):

 Traditionally, Curcuma longa, known as Haridra or Haldi or turmeric in India, belongs to the family Zingiberaceae. It contains the active phytochemical such as alkaloid – curcumin which possesses a range of pharmacological properties-anti-inflammatory, anti-oxidant, antimicrobial, anti-carcinogenic, anti-diabetic, and neuroprotective activities. Recent studies have also demonstrated the anti-depressant activity in mice using the TST and FST which was of greater potency than fluoxetine. [7]

3. Allium macrostemon:

 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 test.[8]

4. Rosmarinus officinalis L.:

Rosemary, Rosmarinus officinalis L. (Labiatae) has several therapeutic applications in folk medicine in curing or managing a wide range of diseases, including depression. In this study, the effect of the hydroalcoholic extract of the stems and leaves of this plant was investigated in two behavioral models, the forced swimming test (FST) and tail suspension test (TST) in mice. The results suggest that the antidepressant action of the extract of R. officinalis is mediated by an interaction with the monoaminergic system and that this plant should be further investigated as an alternative therapeutic approach for the treatment of depression. [8]

5.Emblica officinalis:

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 forced swim test (FST) and tail suspension test (TST). The antidepressant activity of EO was comparable to that of standard drug imipramine. The results of the present study indicate the potential for use of EO as an adjuvant in the treatment of depression. [8]

6. Asparagus racemosus (Shatavari):

Family: Asparagaceae Chemical composition: Steroidal saponins, vit-A, B1 , B2, C, E, Mg, P, Ca, Fe and folic acid, essential oils, asparagine, arginine, tyrosine, flavonoids, resins, tannins glycosides etc., Uses: The roots are bitter, sweet oleaginous, cooling and indigestible, appetizer, useful in dysentery, tumours, inflammation, biliousness, leprosy, epilepsy, night blindness, as laxative, tonics etc ., It is also known as shatavari, is made up of dried roots and plant leaves it is a popular home remedy used as a rejuvenator, power booster. The prevailing investigation evaluates the antidepressant impact of methanolic extract of Asparagus racemosus standardized to saponins (62.2% w/w). A doses of 100, 200 and 400 mg/kg of A.racemosus were given daily basis for 7days and then subjected to Forced swim test (FST) and discovered helplessness check or learned helplessness (LH). The outcomes showed that methanolic extract of A.racemosus decreased immobility in FST and expanded avoidance response in LH indicating antidepressant pastime. In behavioral experiments, it improved the number of head twitches and expanded clonidinecaused competitive behavior indicating facilitatory impact on every serotonergic and adrenergic systems respectively. However, methanolic extract had insignificant effect on lDOPA-prompted competitive conduct indicating absence of activity on dopaminergic system. A.racemosus additionally reversed changes to the endogenous antioxidant system brought on through way of FST. Thus, A racemosus has massive antidepressant interest and this impact might be mediated through the serotonergic, noradrenergic structures and augmentation of antioxidant defenses. [9]

7. Glycyrrhiza glabra:

Family: Leguminosae Chemical composition: Triterpenoidal saponis, flavonoids, tannins, alkaloids, and phenolic compounds etc., Uses: Prophylaxix for gastric, duodenal ulcers, antiinflammatory, laxatives, anti-asthmatic, demulcent, expectorant, anemia, gout, sexual disabilities, fever, cough, skin diseases etc. It is a perennial herb native to the Mediterranean region. It is now widely cultivated throughout Europe also known as liquorice. The ethanolic and aqueous extract of Glycyrrhiza glabra showed a major decrease in immobility time in albino rats using the antidepressant model Forced swim (FST) and Tail suspension test (TST) compared to the standard drug Imipramine 15 mg / kg. Ethanol extract in rats decreased brain MAO-A and MAO-B activity compared to control. The percentage inhibition of MAO-A was higher compared to MAO-B activity. Liquorice extracts reversed reserpine-induced extension of immobility period of mice in FST and TST. Sulpiride (50 mg/kg) and prazosin (62.5 microg/kg) significantly attenuated the extract-induced antidepressant-like effect in TST. On the other hand, p-chlorophenylalanine (100 mg/kg) did not reverse antidepressant-like impact of liquorice extract. This implies that antidepressant-like effect of liquorice extract seems to be mediated by increase of brain norepinephrine and dopamine, however not by increase of serotonin. Monoamine oxidase inhibiting effect of liquorice could also be contributive favorably to the antidepressantlike activity. Thus, it is all over that liquorice extract could possess associate degree antidepressant-like effect. [9]

8. FOENICULUM VULGARE:

Foeniculum Vulgare (Fennel) Fruit is known as "Saunf" in hindi and "Madhurika" in Sanskrit.

Foeniculum vulgare has been scientifically proved to possess various pharmacological activities, which include antidiabetic, antioxidant, hepatoprotective, antifungal, antimicrobial, antithrombotic, antispasmodic, antiosteoporotic and toxicology. Foeniculum vulgare is monoamine inhibitor and the previous evidences indicate that monoamine inhibitors increase the level of norepinephrine, serotonin and dopamine in brain. The present study was undertaken to investigate the effects of methanolic extract of Foeniculum vulgare fruit on depression using force swim test in rats, potentiation of norepinephrine toxicity in mice and haloperidol induce catalepsy in mice and proves that the methanolic extract of Foeniculum vulgare possess significant antidepressant activity due to its reduction in the immobility period in FST and reduction in the duration of catalepsy in haloperidol induce catalepsy. [10]

9. JASMINUM SAMBAC:

Jasminum sambac (JS), an evergreen plant belongs to the family of Oleaceae, extensively used in traditional Malay medicine for the treatment of depressive disorders. It possesses immense therapeutic applications like curing mouth infections, weakness of sight, insanity, ulcers, leprosy and skin diseases, as analgesic, anti-inflammatory, antidepressant, antiseptic, aphrodisiac, sedative, antimicrobial, cytotoxic and expectorant. The present study investigates the antidepressant activity of JS and also to evaluate possible mechanisms involved in its antidepressant action. The study concluded that JS produces antidepressant activity and the mechanism involves serotonergic and dopaminergic systems thereby causing generalized increase in the monoamine turnover. [10]

10. Magnolia officinalis:

Magnolia officinalis, M. dealbata, M. obovata, and M. grandiflora are the plants from family Magnoliacea which are used to treat neurological diseases such as convulsion, seizure, depression, and anxiety and as sedative and painkiller. These plants are the main constituents of the herbal drugs used in Japan and China such as Banxiahoupu and Saiboku-to. Magnolol and honokiol are two main compounds identified in these plants. These compounds have been reported to cause antidepressant effects through affecting serotonergic system Xu et al (2008) investigated the effect of the oral use of these two compounds on mild chronic stressinduced depression. Mild chronic stress caused decrease in 5-HT and its metabolite, 5-HIAA, in different regions of the brain and suppressed the activity of platelets

adenylyl cyclase. Serum corticosterone decreased due to chronic stress-induced depression, as well. Oral use of magnolol and honokiol (20 and 40 mg/kg) caused a decrease in duration of immobility in forced swim test and increased sucrose preference. These two compounds caused the changed amounts of 5-HT, 5-HIAA, corticosterone, and adenylyl cyclase to return to baseline levels. The antidepressant effects of magnolol and honokiol in this study were attributed to the repair of the induced disturbance in serotonergic system, HPA axis, and AC-cAMP pathway. [11]

11. Hypericum perforatum:

H. perforatum, St John's wort in English language, is native to Europe but exhibits spontaneous distribution across the world particularly in temperate and subtropical regions including China, Turkey, Ukraine, Russia, India, Canada and the USA (Butterweck and Schmidt, To date, several studies have been conducted on antidepressant effects of H. perforatum in mice and humans that confirmed the potential therapeutic effects of this plant; H. perforatum extract contributes to not only treating depression but also preventing its recurrence. H. perforatum has a longer duration of response than citalopram. In the recent years, H. perforatum has been competing for being commercially available as an antidepressant and for this reason several studies have been conducted to detect the chemical compounds responsible for this effect and their action mechanisms. Biochemical investigations have demonstrated that H. perforatum is a weak inhibitor of monoamine oxidase but inhibits synaptosomal resorption of serotonin, dopamine, and norepinephrine. H. perforatum extract exerts down-regulatory effect on beta-adrenergic receptors and up-regulatory effect on serotonin receptors, and changes the neurotransmitters concentrations in certain regions of the brain. Moreover, methanolic H. perforatum extract causes expression of HPA axis-controlling genes.[12] A study showed that 150-75 mg/kg of H. perforatum extract improved chronic stress-induced depression symptoms and decreased the escalated levels of serum ACTH and corticosterone. This extract also caused reinforcement of antioxidant defence system and decline in two inflammatory factors, IL-6 and TNF-‡. H. perforatum antidepressant effect was attributed to antioxidant, anti-inflammatory, and endocrine system regulatory effects of this plant. The antidepressant effects of H. perforatum certain compounds such as hypericin, hyperforin, and isoquercetin have been demonstrated. Injection with hypericin caused CRH and expression of its related

mRNA to decrease in mice with depression. The aboveground parts (leaves, flowers and stem) were dried before extraction with 80% ethanol (vol/vol). The herb-to-extract ratio is 12:1 for a 100% native extract.[11]

12. Evening Prime Rose:

Evening Primerose Oil is the fixed oil obtained from the seeds of Oenothera species. The principal species cultivated in the UK is O. Biennis linn. Evening primerose oil showed significant antidepressant effect on all days of treatment in mouse model of chronic fatigue syndrome {CFS} in which mice were forced to swim every day for 7days for 6mins session.[12]

13. Ginkgo Biloba:

It is native of China and occasionally cultivated in Indian gardens., particularly on Hills. A few trees are found in Himachal Pradesh. Its extract restored restraint stress induced elevation in whole brain levels of catecholamines and serotonin. The extract has a demonstrable effect in improving mood in healthy older volunteers. The combination of G.biloba extract with venlafaxine enhanced the protection of neurons and decreased damage to the brain, while relieving the side effects of synthetic antidepressants.[12]

14. Panax ginseng:

Family: Araliaceous, Parts used: Root and leaves. Ginseng is used as a general tonic affecting the whole body. It promotes appetite and is useful in digestive disturbances. The tea taken hot is effective for colds, chest troubles and coughs. It is used to normalize blood pressure, tone the heart, increase circulation and reduce cholesterol. It reduces blood sugar which makes it useful for diabetics. As a nutritive tonic it has been used to treat anaemia.[13] Yamada et al reported the antidepressant effects of this plant16. Study: Dang et al reported antidepressant components from this plant. Ginseng total saponins (GTS) are found in this plant and are used as brain tonic, Ginseng total saponins were investigated for their antidepressant activity in two classic animal models: the forced swimming test (FST) and the chronic mild stress (CMS) model. Ginseng total saponins were given at doses of 50 and 100 mg/kg that was able to reduce the immobility time in the forced swimming times in mice after 7-day treatment. Ginseng total saponins exhibited antidepressant in both models of depression. This activity may be due to enhancing the monoamine neurotransmitter concentration. [13]

15. Mimosa pudica:

Family: Mimosaseae, Parts used: Roots and leaves. Chemical constituents: Tannin, minosine, turqorins, phytohormoe, tubulin, glycosyl flavone, rhamnosylorientin, and rhamnosyliso-orientin. It is carminative, aphrodisiac, antiseptic, alterative and blood purifier. It is prescribed in itching, scabic patches, diarrhea, fever, headache, hemorrhage and vomiting. Study: Molina et al. has reported that Mimosa pudica may possess antidepressant actions in the rat. This study was conducted in Mexico. Aqueous extracts of this plant were used for activity [13]. Various concentrations of extracts of this plant were used to alleviate depression. This study was 30-day duration. Saline, various concentrations of extracts, desipramine and clomipramine were administered to rats. Extract was administered at four levels 2, 4, 6 and 8mg/kg. Parameters for assessment were forced swimming test and rate of reinforcers in the DRL72s test. Anti-anxiety effect of extract at different concentrations was noted in comparison with diazepam at a dose of 1.3 mg/kg intra-peritoneal in the elevated plus-maze test. Reduction in immobility in the forced swimming test was observed by use of M. pudica at dose of 6 and 8 mg/kg. Same activity was observed by use of clomipramine and desipramine at dose of 1.25 mg/kg and 2.14 mg/kg respectively. These all drugs were administered intraperitoneally. This study showed that this plant has antidepressant activity in the rat. Furthermore, it was concluded that activity of this plant is just like tricyclic antidepressants.[13]

CONCLUSION:

The above review mentions the antidepressant activity of various medicinal plants collected from the
various journals and can be concluded that there are still many plants which needs to explore to study their therapeutic value. The Herbal plants mentioned in the review are the best research areas of exploring various antidepressant activities with promising results, without side-effects. As, we can see from the review that India has rich assortment of medicinal plants distributed in different geographical and ecological conditions widespread in the country and the mentioned plants have been used from prehistoric times to treat various ailments and depression is one of them. Hence this review gives a note on the treatment of depression using herbal plants. The mentioned plants not only work as an herbal medicine for antidepressant activity but also for other ailments as well.

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