

## A comprehensive review of phytochemical components as potential antidepressants

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### Abstract

Depression is a heterogeneous mood disorder that has been classified and treated in a variety of ways. Despite the fact that a variety of synthetic medications are utilized as conventional treatment for clinically depressed patients, these drugs have side effects that can jeopardize the therapeutic outcome. In recent decades, there has been a rise in research and interest in the psychopharmacology of natural treatments. Thus, it's worthwhile researching for antidepressants derived from plants that have a demonstrated effect and a favorable benefit-to-risk ratio. By virtue of their medicinal constituents, a variety of medicinal plants and medicines produced from these plants have exhibited antidepressant properties. As a result, major pharmaceutical companies are currently researching plant materials extensively for their possible medical benefit. Depression is caused by low levels of monoamines such as norepinephrine, dopamine, and serotonin in the brain. Therefore, treatments that restore lowered levels of these monoamines in the brain by blocking monoamine oxidase or decreasing reuptake of these neurotransmitters could be beneficial in the treatment of depression. The current review focuses on medicinal plants and plant-based formulations that have been shown to have antidepressant effect in both animal and human studies.

### Introduction

Depression is an etiologically heterogeneous group of brain disorders characterized by a wide range of symptoms that reflect alterations in cognitive, psychomotor and emotional processes.<sup>1</sup> The prevalence of depression is consistently high worldwide, and is associated with considerable morbidity and mortality. According to WHO estimation, 121 million people

worldwide suffer from clinical depression.<sup>2</sup> The high prevalence of suicide among depressed individuals (up to 15%), as well as other stress-related disorders and their impact on the cardiovascular system, imply that by 2020, it will be the second leading cause of mortality.<sup>3</sup> Depression is the leading cause of disease related disability among women in the world today. It is much more common among women than in men with female/male ratio roughly 2:1.<sup>4</sup>

Symptoms of depression include biological and emotional components. Biological symptoms include retardation of thought and action, loss of libido, sleep disturbance, and loss of appetite.<sup>5</sup> Emotional symptoms include misery, apathy and pessimism, low self-esteem consisting of feeling of guilt, inadequacy and ugliness, indecisiveness and loss of motivation.<sup>6</sup>

There are two distinct types of depressive syndrome, namely *unipolar depression*, in which the mood changes are always in the same direction, and *bipolar affective disorder*, in which depression alternates with mania.

Unipolar depression is commonly (about 75% of cases) non-familial, clearly associated with stressful life events, and usually accompanied by symptoms of anxiety and agitation; this type is sometimes termed reactive depression.<sup>7</sup>

Bipolar depression usually appears in early adult life, is less common and results in oscillating depression and mania over a period of a few weeks. It can be difficult to differentiate between mild bipolar depression and unipolar depression.<sup>8</sup> Bipolar manic episodes can be confused with episodes of psychosis.

A number of classes of medication are available in the treatment of depression. These drugs include Selective Serotonin Reuptake Inhibitors (SSRIs) like fluoxetine and fluvoxamine; Monoamine Oxidase Inhibitors (MAOIs) like phenelzine and moclobemide, tricyclic antidepressants like imipramine and desipramine, atypical antidepressants like mirtazapine, trazodone, and finally selective Serotonin and Norepinephrine Reuptake Inhibitors (SNRI) like venlafaxine, desvenlafaxine, and lithium salts<sup>9,10</sup>

The main drawback of using these drugs is that those drugs cannot arrest progression of the disease, they even though reduce its symptoms.<sup>11</sup> In addition those drugs are supplemented with an array of side effects. Tricyclic antidepressants produce dizziness, headache, sweating, tremor, palpitation, dry mouth, constipation, blurred vision, difficulty passing urine, and orthostatic hypotension. Other less-common adverse effects include seizure, liver

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dysfunction, ECG changes and abnormal blood count. SSRIs show nausea, vomiting, gastrointestinal discomfort, dry mouth, tremor, headache, sweating, sexual dysfunction and weight loss, etc. Occasionally, some patients may experience excitement, anxiety, insomnia, restlessness or seizure. SNRIs produce side effects similar to SSRIs. But these drugs may also cause hypertension at high dose. MAOIs show dizziness, headache, nervousness, gastrointestinal disturbance, etc. These drugs may also interact with tyramine rich food or drinks, as a consequence inducing sweating, vomiting and hypertensive crisis. Foods rich in tyramine are pigeon, alcoholic beverages, cheese, chicken and beef liver, chocolate, etc.<sup>12</sup> Lithium salts produce bit-

ter taste, dry mouth, tremor, polyuria, fatigue and weight gain. Other less-common side effects include hyperthyroidism, hypothyroidism, ECG changes, raised antidiuretic hormone concentrations, renal failure or leucocytosis.<sup>13</sup>

Along with these side effects the cost of these drugs is very high, and also it will take almost a decade to develop a new drug. These conditions create an opportunity for alternative treatment of depression.<sup>14</sup>

## Need for alternative or complementary medicine

Alternative to these synthetic agents, plants provide a potential source of antidepressant drugs and are widely used in several traditional systems of medicine to prevent depression. Ayurveda is the widely used medicine system because of rich heritage of various flora throughout the world. It is the Indian traditional medicine system, as it mentions a number of single and compound drug formulations of plant origin that are used in the treatment of psychiatric disorders.

Ayurveda is the first real scientific medical branch which evolved in India and was practiced since ancient times. It is a natural process of healing health and mind. It is the science of combating nature's problems with natural solutions and hence there are no side effects as such of this branch of medicine. The major treatment of Ayurveda is based on two factors: cause and symptoms. Ayurveda names three elemental substances, the *doshas* (called *Vata*, *Pitta* and *Kapha*), and states that a balance of the *doshas* results in health, while imbalance results in disease. Ayurveda has eight canonical components, which are derived from classical Sanskrit literature.

Many plants are explored for their antidepressant activity because of the presence of wide range of phytoconstituents.

## Antidepressant effects of various medicinal plants: Preclinical and clinical evidence

### *Hypericum perforatum*

Antidepressant effects of St. John's Wort (*Hypericum perforatum*, SJW) i.e., *Hypericin* (HY) was evaluated on Chronic Unpredictable Mild Stress (CUMS) model rats and identified the possible mechanisms. Changes in the classic behavioral tests and pharmacological biochemical indices reflected that HY alleviated the symptoms of depression. Metabolites analysis of urine

revealed that HY affected excitatory amino acids and monoamine neurotransmitter metabolites. These results provide important mechanistic insights into the protective effects of HY against CUMS-induced depression and metabolic dysfunction.<sup>14</sup>

### *Asparagus racemosus*

In the FST and TST, 200 mg/kg of methanolic extract of dried seeds of *Asparagus racemosus* resulted in a considerable reduction in the duration of immobility. In an *in vitro* study, *Asparagus racemosus* at doses of 100 mg/kg and 200 mg/kg *p.o.* elevated dopamine levels. Alkaloids, flavonoids, glycosides, tannins, and reducing sugars were identified in the methanolic extract of *Asparagus racemosus* seeds, which are responsible for its antidepressant effect.<sup>15</sup>

### *Foeniculum vulgare*

In a forced swim test, dosages of 250 mg/kg and 500 mg/kg of methanolic extract *Foeniculum vulgare* significantly reduced immobility times in rats. However, extract was found to be a poor adrenergic agent in the NE toxicity model. At a dose of 500 mg/kg of extract, the duration of haloperidol-induced catalepsy was significantly reduced. As a result, it was concluded that *Foeniculum vulgare*'s monoamine oxidase inhibitory and anti-oxidant effects may be contributing to its antidepressant-like effect. Flavonoids, saponins, tannins, and steroids were found in *Foeniculum vulgare*. Flavonoids are thought to be responsible for antidepressant action in experimental animal models.<sup>16</sup>

### *Cucurbita pepo*

In a forced swim test, the extracts reduced immobility time with increased swimming time (or better behavioral activity) and significantly raised enzymic and nonenzymic antioxidant status in the brain and serum, as well as HDL and LDL levels in serum. Thus, it was concluded that *C. pepo* seed extract has significant antioxidant and antidepressant properties. *Cucurbita pepo*'s antidepressant potential could be related to the presence of alkaloids, glycosides, and flavanoids.<sup>17</sup>

### Curcumin

Curcumin significantly reduced olfactory bulbectomy-induced behavioural abnormalities such as step-down passive avoidance deficits, increased open-area activity, and immobility time. Curcumin also restores dopamine, noradrenaline, and 5-hydroxy indole acetic acid levels in the frontal cortex of rats. Taking all of these findings into account, it was proposed that

curcumin could be an effective antidepressant in male albino rats.<sup>18</sup>

### *Basella alba*

Oral administration of methanolic extract of *Basella alba* at a dose of 25 and 50 mg/kg body weight produced a significant decrease in duration of immobility in FST (47.82% and 45.23%) and TST (38.59% and 48.43%) in comparison to the control group. Similarly, animals treated with Diazepam (5 mg/kg, i.p.) show a significant decrease in immobility time (84.48% and 81.81%). Based on the results of the study the study concluded that the methanolic extract of *Basella alba* possesses a significant antidepressant-like effect. The effect could be attributed to and the presence of saponins, flavonoids, glycosides, tannins, and phenolic compounds.<sup>19</sup>

### *Rosmarinus officinalis*

The consumption of *Rosmarinus officinalis* L. leaf infusion significantly reduced anxiety/fear and depression-like behavior in mice, but had no effect on memory/learning. The results demonstrated that the phenolic components and the inhibitors may share pharmacophores. The results imply that rosemary tea treatment has anxiolytic and depressive effects in mice, as well as inhibiting cholinesterase activity; its main phytochemicals like diterpenes, flavonoids and hydroxycinnamic derivatives may function in a similar way as inhibitors.<sup>20</sup>

### *Amaranthus spinosus*

Methanolic extract of *Amaranthus spinosus* (MEAS) at higher concentration (200 mg/kg, *p.o.*) showed significant ( $p < 0.01$ ) reduction in immobility in tail suspension and forced swim model of depression comparable to Escitalopram and Imipramine. The preliminary phytochemical analysis of MEAS showed the presence of flavonoids, saponins, glycosides, terpenoids amino acids, alkaloids, carbohydrates, phenolic compounds and proteins, which are responsible for its antidepressant activity.<sup>21</sup>

### *Spirulina platensis*

Spray dried powder of *Spirulina platensis* at different doses (100 mg/kg, 200 mg/kg and 400 mg/kg, *p.o.*) reduced immobility in both FST and TST and increased frequency of 5-HTP induced head twitches, Clonidine induced aggression and L-DOPA induced hyperactivity and aggressive behavior indicating its enhanced activity on serotonergic, noradrenergic and dopaminergic pathways respectively. From the results, it was observed that the *Spirulina platensis* possess the dose dependent antidepressant activity.<sup>22</sup>

### Hibiscus rosasinensis

In the Forced Swimming Test (FST) and Tail Suspension Test (TST), crude ethanolic extract of floral part of *Hibiscus rosasinensis* (HRS) at doses of 100 mg/kg, 250 mg/kg, and 500 mg/kg, *i.p.* showed significant dose dependent decline in immobility time, whereas none of the doses of HRS showed effect in the Open Field Test (OFT). *In vitro* results demonstrated that each dose of this plant had a significant inhibitory effect on MAO-A, whereas only 250 mg/kg, *i.p.* dose had a significant inhibitory effect on MAO-B.<sup>23</sup>

### Murraya koenigii

In the tail suspension test and despair

swimming test, the hydroalcoholic leaf extract of *Murraya koenigii* at dosages of 100 mg/kg, 250 mg/kg, and 500 mg/kg orally significantly reduced the duration of immobility of mice compared to the untreated group. The apomorphine gnawing behavior was also improved by extract. Its antidepressant effect may be due to the presence of phytosterols in petroleum ether extract, carbohydrates, glycosides, proteins, and amino acids in aqueous extract, and alkaloids and phenolic chemicals in hydroalcoholic and methanolic extracts.<sup>24</sup>

### Eclipta alba

At doses of 200 and 400 mg/kg administered for 7 and 14 days, *Eclipta alba* Leaf

Extract (EALE) showed a substantial antidepressant-like effect in rats, as evidenced by shorter immobility durations in the Tail Suspension Test (TST) and Forced Swim Test (FST). EALE's efficacy at 200 mg/kg was shown to be comparable to Fluoxetine and Imipramine at doses of 20 mg/kg and 15 mg/kg, respectively. Ecliptin alkaloid and culumbin, a flavonoid found in EALE, may facilitate monoaminergic transmission and therefore have antidepressant properties. The findings revealed that EALE had potent antidepressant properties.<sup>25</sup>

### Apium graveolens

In the Forced Swim Test (FST) and Tail

**Table 1. List of plants that have been reported to have antidepressant properties.**

Author	Name of plant	Part used	Doses tested	Models employed	References
Strik <i>et al.</i> , 2001	<i>Hypericum perforatum</i>	Leaf	100 & 200 mg/kg	Chronic unpredictable mild stress (CUMS)	14
Xue-Jia Zhai <i>et al.</i> , 2015	<i>Asparagus racemosus</i>	Seed	100 & 200 mg/kg	Forced Swimming Test (FST) & Tail Suspension Test (TST)	15
Jamwal Neetu Singh <i>et al.</i> , 2013	<i>Foeniculum vulgare</i>	Fruit	250 & 500 mg/kg	Force Swim Test, Potentiation of norepinephrine toxicity, Haloperidol induced catalepsy	16
Umadevi <i>et al.</i> , 2011	Cucurbita pepo	Seed	100 mg/kg	Forced Swim Test	17
Xue-run Chang <i>et al.</i> , 2016	<i>Curcumin</i>	-	10, 20 & 40 mg/kg	Passive Avoidance Test, Open Field Test & Forced Swim Test	18
Abhinayani <i>et al.</i> , 2016	<i>Basella alba</i> L	Leaf	25 & 50 mg/kg	Despair Swim Test & Tail Suspension Test	19
Anastasia-Varvara Ferlemi <i>et al.</i> , 2015	<i>Rosmarinus officinalis</i> L	Leaf	2% w/v/day	Forced swimming test	20
Ashok Kumar <i>et al.</i> , 2014	<i>Amaranthus spinosus</i>	Whole plant	100 and 200 mg/kg	Forced Swim Test & Tail Suspension Test	21
Suresh <i>et al.</i> , 2014	<i>Spirulina platensis</i>	Whole plant	100, 200 & 400 mg/kg	Forced swimming test, Tail suspension test, 5-HTP induced head twitches, Clonidine induced aggression, L-DOPA induced hyper activity and aggressive behavior	22
Leena Khalid <i>et al.</i> , 2014	<i>Hibiscus rosa sinensis</i>	Flowers	100, 250 & 500 mg/kg	Forced induced swimming test, tail suspension test & open field test	23
Krishna Prasad <i>et al.</i> , 2013	<i>Murraya koenigii</i>	Leaf	100, 250 & 500 mg/kg	Despair swimming test, Tail suspension test, Enhancement of amphetamine-induced excitation, Compulsive gnawing	24
Mishra Swati <i>et al.</i> , 2013	<i>Eclipta alba</i>	Leaf	100, 200 & 400 mg/kg	Forced swim test, Tail suspension test	25
Brahma Srinivasa Rao & Sivaramakrishna, 2012	<i>Apium graveolens</i>	Seeds	100, 200 mg/kg	Forced swim test, Tail suspension method	26
Singh Rudra Pratap <i>et al.</i> , 2012	<i>Zingiber officinale</i>	Rhizomes	150, 300 mg/kg	Forced swim test, Tail suspension test	27
Santosh <i>et al.</i> , 2011	<i>Passiflora foetida</i>	Leaf	100, 200, 300 mg/kg	Tail suspension test, Forced swim test	28
Vimal Kant Sharma <i>et al.</i> , 2009	<i>Zizyphus xylopyrus</i>	Leaf	50 & 10 mg/kg	Forced swimming stress, Tail suspension test	29
Ahsana Dar & Shaguftha Khatoon, 2000	<i>Areca catechu</i>	Nut	1, 4, 7, 10 & 13 mg/kg	Forced swim test, Tail-suspension test, Yohimbine potentiation test & Locomotor test	30
Sai ram <i>et al.</i> , 2002	<i>Bacopa monniera</i>	Whole plant	20, 40 mg/kg	Behavioral despair test, Learned helplessness test	31
Xiao-song Qin <i>et al.</i> , 2005	<i>Ginkgo biloba</i>	Leaf	100, 200 mg/kg	Chronic & comprehensive stress induced depression	32
Tapan Maity <i>et al.</i> , 2000	<i>Ocimum sanctum</i>	Root	100, 200, 400 mg/kg	Swimming performance in mice	33
Bhattacharya <i>et al.</i> , 2000	<i>Withania somnifera</i>	Root	20, 50 mg/kg	Forced swim-induced behavioral despair test, Learned helplessness test	34
Moonyky Kang <i>et al.</i> , 2005	<i>Nelumbinis semen</i>	Whole plant	2.1 g/kg	Forced swim test	35
Takahiro Nakazawa <i>et al.</i> , 2003	<i>Perilla frutescens</i>	Whole plant	6.25, 12.5, 25, 50 & 100 mg/kg	Forced swimming test	36
Ana Lucia Rodrigues <i>et al.</i> , 2002	<i>Siphocampylus verticillatus</i>	Stem and leaf	300 and 600 mg/kg	Tail suspension test, Forced swimming test, Open-field behavior	37
Ali <i>et al.</i> , 1998	<i>Rhazya stricta</i> Decne	Leaf	0.025, 0.05, 0.1, 0.2, 0.4, 0.8, 1.6, 6.4 g/kg	Forced swimming test	38
Amrita Chowdhury, Archana Juvekar, 2014	<i>Indigofera tinctoria</i>	Leaf	250, 500 mg/kg	Forced swim test, Tail suspension test, Tetrabenazine antagonism in mice	39
Charles Kwaku Benneh <i>et al.</i> , 2018	<i>Maerua angolensis</i>	Stem bark	100 – 1000 mg/kg	Forced swim test, Tail suspension test	40
Hafiz Muhammad Asif <i>et al.</i> , 2019	<i>Onosma bracteatum</i>	Whole plant	50, 100 & 200 mg/kg	Forced swim model, Tail suspension model	41
Sanat Udyavar <i>et al.</i> , 2020	<i>Mimosa pudica</i>	Leaves	100, 200 & 400 mg/kg	Tail suspension test, Forced swim test	42
Francis Ackah Armah <i>et al.</i> , 2021	<i>Psychotria ankasensis</i>	Aerial parts	30, 100 & 300 mg/kg	Forced swim test, Tail suspension test	43



Suspension Test, methanolic extract of *Apium graveolens* seeds (AGM) (100 and 200 mg/kg, *p.o.*) showed statistically significant reductions in duration of immobility that were comparable to Imipramine (20 mg/kg, *p.o.*). (TST). The effect of 200 mg/kg AGM was superior to Imipramine (20 mg/kg). In the ethanolic extract of *Apium graveolens* seeds, preliminary phytochemical investigation revealed the presence of flavonoids, alkaloids, steroids, and glycosides (AGM). In animal models, the presence of these phytoconstituents may be responsible for considerable antidepressant effect.<sup>26</sup>

### Zingiber officinale

Hydroalcoholic extract of dried rhizomes of *Zingiber officinale* (150 mg/kg and 300 mg/kg, *p.o.*) showed significant reduction of immobility time in forced swim test (FST) and tail suspension test (TST). The effect of the extract was comparable to that of standard drug imipramine (10 mg/kg, *p.o.*). The extract had a similar effect to the conventional medicine imipramine (10 mg/kg, *p.o.*). The antidepressant effects of *Zingiber officinale* extract appear to be mostly due to dopaminergic system activation, and it may have anxiolytic and depressive properties.<sup>27</sup>

### Passiflora foetida

Methanolic extract of leaves of *P. foetida* (PF) (100, 200 and 300 mg/kg) was able to decrease the immobility time of mice dose-dependently when subjected to both tail suspension and forced swim tests and the effects are comparable to that of standard drugs i.e., fluoxetine (20 mg/kg) and imipramine (15 mg/kg). Neither the extracts of PF nor fluoxetine, at the doses tested, produced significant effects on locomotor activity when subjected to open field behavioral test. These results demonstrated that PF had specifically antidepressant effects *in vivo*.<sup>28</sup>

### Zizyphus xylopyrus

Ethanolic extract of *Zizyphus xylopyrus* when administered at an acute dose of 50 mg/kg ( $P < 0.01$ ) reduced the immobility time by 10 and 15 seconds as compared to the immobility time of control in both Forced Swimming Test (FST) and Tail Suspension Test (TST) models. Similarly Ethyl Acetate (EA) fraction reduced latter by 30 and 35 secs. The precipitate fraction showed the best activity, reducing the immobility time by 50 and 60 secs. in both the tests. These results showed that after standard *i.e.* Imipramine HCl (30 mg/kg), the precipitate fraction is potent amongst all the studied drugs. It was clearly demonstrat-

ed that *Zizyphus xylopyrus* exerts an antidepressant effect, which might be due to the presence of flavonoids.<sup>29</sup>

### Areca Catechu

In a forced swim test and a tail-suspension test in rodents, it demonstrated strong antidepressant efficacy. Alkaloids contained in areca nuts, such as arecaidine and arecoline, as well as a few other compounds, were found to have no effect on monoamine oxidase (MAO). The dichloromethane fraction from areca nuts, on the other hand, was found to have antidepressant properties through inhibiting MAO-A.<sup>30</sup>

### Bacopa monnieri

In the forced swim test and learned helplessness models of depression, the standardized methanolic extract of *Bacopa monnieri* (20 and 40 mg/kg, *p.o.*) given once daily for 5 days demonstrated considerable antidepressant effect, which was comparable to that of conventional imipramine. Alkaloids, such as brahmine, herpestine, and a mixture of three additional alkaloids, as well as saponins, such as bacoside A and B, may be responsible for the activity.<sup>31</sup>

### Ginkgo biloba

*Ginkgo biloba* extract (14 mg/kg, *p.o.*) reversed the restraint stress-induced rise in catecholamines (norepinephrine, dopamine) and serotonin levels in the whole brain. In healthy older volunteers, the extract has a demonstrable effect in improving mood. The combination of *G. biloba* extract and venlafaxine improved neuron protection and reduced brain damage while alleviating the adverse effects of synthetic antidepressants.<sup>32</sup>

### Ocimum sanctum

In rats and mice, an ethanolic extract of *Ocimum sanctum* leaves reduced immobility in a behavioral experiment involving forced swimming. Haloperidol and sulpiride were found to block this activity, indicating that dopaminergic neurons may be involved. Methanol extract from roots (400 mg/kg, *i.p.*) increased swimming time, indicating that it has antidepressant properties.<sup>33</sup>

### Withania somnifera

In a mouse model of chronic fatigue syndrome, where mice were forced to swim for 6 minutes each day for 15 days and the immobility period was measured, a standardized extract of roots (100 mg/kg, *p.o.*) resulted in a substantial reduction in immobility period. Antioxidants combined with

*W. somnifera* dramatically reduced lipid peroxidation and restored glutathione levels in rats that had been depleted by continuous swimming. Bioactive glycowithanolides (20 and 50 mg/kg, *p.o.*), isolated from roots, were found to have an antidepressant effect comparable to imipramine (10 mg/kg, *i.p.*) in the forced-swimming produced behavior despair and learnt aid test.<sup>34</sup>

### Nelumbo nucifera

In both the chronic mild stress model and the FST, it had antidepressant-like effects. *Nelumbo nucifera* has a better antidepressant potential than *Hypericum perforatum*. It dramatically boosted 5-HT release in the hippocampus of rats exposed to chronic mild stress for 8 weeks and reversed stress-induced decreases in 5-HT release.<sup>35</sup>

### Perilla frutescens

*Perilla frutescens* leaves are primarily used in the treatment of affective disorders such as depression and anxiety. The aqueous extract of *P. frutescens*, as well as its 50 percent methanol fraction, shortened the duration of immobility in FST mice. The extract's active phytoconstituent, rosmarinic acid, has a significant anti-immobility effect in FST. A phytoconstituent from *P. frutescens*, apigenin, was found to have antidepressant-like action in FST via dopaminergic processes in the mouse brain.<sup>36</sup>

### Siphocampylus verticillatus

In the tail-suspension test and forced swimming test in mice, hydroalcoholic extract (100-1000 mg/kg, *i.p.*) elicited a significant antidepressant effect. This antidepressant effect is most likely to be mediated through an interaction with adrenergic, dopaminergic, glutamatergic and serotonergic systems. The active component responsible has yet to be identified, however the presence of the alkaloid cis-8,10-dinpropyllobelidiol hydrochloride dihydrate could account for much of the extract's effect. Also, other constituents such as flavonoids (3-methoxyluteolin), triterpenes (-amirin and -amirin), and steroids (campessterol, -sitosterol, stigmasterol, and stigmasterol glycoside) could possibly have a role in the antidepressant activities, at least in part.<sup>37</sup>

### Rhazya stricta

In a forced-swimming test in rats, an aqueous extract of *Rhazya stricta* leaves demonstrated antidepressant-like effect, which could be attributed to its ability to inhibit both MAO-A and MAO-B. Any one of the constituents present, such as alkaloids

with a -carboline nucleus (akuamidine, rhaziminine, and tetrahydro secamine), flavonoids, namely isorhamnetine, 3-(6-dirhamnosyl galactoside)-7-rhamnoside, and 3-(6-rhamnosyl galactoside)-7-rhamnoside, could be responsible for the plant extract's antidepressant effect.<sup>38</sup>

### Indigofera tinctoria

Aqueous extract of *Indigofera tinctoria* showed antidepressant-like effect in forced swim test, tail suspension test and tetra-benzazine induced catalepsy and ptosis models. The presence of flavonoids such as apigenin, quercetin and kaempferol and isatin precursors could be responsible for the antidepressant effect of the plant.<sup>39</sup>

### Maerua angolensis

In the forced swim test and tail suspension test, a petroleum ether/ethyl acetate (50:50) extract of *Maerua angolensis* stem bark demonstrated a significant reduction in immobility period. The extract's antidepressant-like activity could be due to an interaction with both the noradrenergic and serotonergic systems.<sup>40</sup>

### Onosma bracteatum

In forced swim and tail suspension models, hydroalcoholic extract of *Onosma bracteatum* had an antidepressant effect. It's possible that the inhibitory effect on monoamine oxidase is the mechanism of action. More research is needed to determine the chemical constituents responsible for the activity as well as the mechanism of action.<sup>41</sup>

### Mimosa pudica

In the Forced Swim Test (FST) and tail suspension test, an ethanolic extract of *Mimosa pudica* showed antidepressant effect (TST). The extract's antidepressant activity is likely to be similar to that of antidepressants like imipramine. The presence of alkaloids, flavonoids, and tannins in the extract could be responsible for its action.<sup>42</sup>

### Psychotria ankasensis

The forced swim test and the tail suspension test were used to examine the antidepressant effect of *Psychotria ankasensis* methanolic extract in mice. In both mice, extract dosages of 100 and 300 mg/kg significantly reduced the frequency and duration of immobility. The presence of alkaloids, triterpenoids, steroids, tannins, anthraquinone glycosides, and saponins in the extract is thought to be responsible for its antidepressant properties.<sup>43</sup>

### Few marketed polyherbal formulations

A few marketed polyherbal formulations are listed as below.

Chaihu-Shugan-San, EuMil, Mentat, Siotone, Catuama, Banxia-houpu, Kamishoyo-san and Sho-ju-sen. It has been observed that the main ingredients of these preparations include: *Withaniasomnifera*, *Ocimum sanctum*, *Asparagus racemosus* Willd., *Emblica officinalis* Gaertn., *Panax ginseng*, *Bacopa monnieri*, *Centellaasiatica*, *Nardostachysjatamansi* DC., *Evolvulusalsinoides* Linn., *Valerianajatamansi* Jones, *Acorus calamus* Linn., *Tinosporacordifolia* (Willd.) Miers. ex Hook. f. & Thoms., *Celastrus paniculatus* Willd., *Saussurealappa* C.B. Clarke, *Terminalia chebula* Retz., *Terminalia bellirica* Roxb., *Sasakurinensis* Makino et Sibata, *Pinus densiflora* Sieb. et Zucc. and *Tribulus terrestris* Linn.<sup>39,44-47</sup>

### Conclusions

Antidepressant medicines on the market can cause nausea, vomiting, irritability, sleeplessness, tremor, and other unpleasant side effects. Natural antidepressants, on the other hand, have a lot of potential for treating depression with minimal side effects. Medicinal herbs and preparations have antidepressant efficacy comparable to that of clinically effective synthetic antidepressants.

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