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A COMPREHENSIVE REVIEW OF MEDICINAL PLANTS WITH ANTI-DEPRESSANT ACTIVITY

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ABSTRACT

Depression is a major mental health disorder affecting millions globally. The increasing side effects and limitations of conventional antidepressant medications have prompted interest in alternative therapies, particularly those derived from medicinal plants. This review compiles findings from 32 plants, analyzing their antidepressant properties, plant parts used, extraction solvents, mechanisms of action, and experimental outcomes. Notable herbs such as *Crocus sativus*, *Curcuma longa*, *Hypericum perforatum*, and *Bacopa monniera* showed comparable or synergistic effects with standard antidepressants like fluoxetine. Extracts, often methanolic, ethanolic, or aqueous, targeted neurotransmitter systems (serotonin, dopamine, noradrenaline) and exhibited monoamine oxidase inhibition, antioxidative effects, and modulation of neurotrophic factors. These findings support the therapeutic potential of plant-based treatments for depressive disorders.

KEYWORDS: Medicinal plants, Antidepressant activity, Herbal therapy, Phytoconstituents, Neurotransmitters.

1. INTRODUCTION

Approximately 450 million individuals have a mental or behavioral disease, according to a world health report. 1. After heart disease, depression is predicted to be the second leading cause of illness burden worldwide by 2020. 2. Depression is a whole-body disease that affects not just the body and mind but also mood and emotion. The inability to enjoy routine activities, changes in eating and sleeping habits, low energy, suicidal thoughts, and extreme feelings of sadness, hopelessness, and despair are all signs of depression.3.

There are two varieties of mental depression: unipolar depression, which is frequent (approximately 75 percent of cases), non-familial, and obviously linked to stressful life events. It is characterized by mood swings that are constantly in the same direction and is accompanied by symptoms of worry and agitation. About 25% of cases are bipolar depression, also known as endogenous depression. It typically manifests in early adulthood, exhibits a recognizable pattern, is unrelated to outside stressors, and causes mania and despair to alternate over a few weeks 4. Decreases in monoamine neurotransmitters, particularly dopamine, serotonin, and norepinephrine, are reflected in the symptoms of depressed patients. Every year, 500,000 people are diagnosed with depression.

Even though many synthetic medications are used as the standard treatment for patients with clinical depression, they have side effects that can jeopardize the effectiveness of the therapeutic intervention. These side effects include fatigue, gastrointestinal or respiratory issues, anxiety, agitation, drowsiness, dry mouth, and cardiac arrhythmias. Several drug-drug interactions can also occur. These conditions create an opportunity for alternative treatment of depression by used of medicinal plant.^[1]



Fig: 1 Antidepressant.

2. Plant profile

2.1 piper betel

Betel leaves are commonly used as paan (a combination of betel leaf, slaked lime, and areca nut), which acts as a mouth freshener or is sometimes consumed with tobacco. We often eat betel leaves casually, without realizing their potential benefits for our bodies.

Betel leaf, also known as paan leaf, belongs to the Piper genus, with the scientific name Piper betel. It is a heart-shaped perennial creeper found in tropical and subtropical regions such as India, Sri Lanka, Malaysia, Indonesia, the Philippines, and East Africa. Betel leaves are used both for religious purposes and for chewing.



Fig. 2: Piper Betel.

Synonym: piper betle, paan, betel pepper, sireh, phlu

Biological source: The biological source of betel leaf is the plant piper betel.

Family: Piperaceae

2.1.1 TAXONOMICAL CLASSIFICATION

• **Kingdom:** Plantae

• Clade: Tracheophytes

• Clade: Angiosperms

• Clade: Magnoliids

• Order: Piperales

• Family: Piperaceae

• Genus: Piper

• **Species:** P. betle

2.1.2 MORPHOLOGY

• Shape: Broadly ovate, heart-shaped (cordate), and often unequal at the base.

• **Apex:** Acuminate (tapering to a point).

• Base: Cordate (heart-shaped) and often unequal.

• Margin: Entire (smooth) and narrowly recurved.

• Surface: Glabrous (smooth and hairless), shining, and coriaceous (leathery).

• **Venation:** Reticulate (net-like), with 7-9 veins arising from the base.

• Color: Bright green or yellowish-green, with a glossy appearance.

• **Texture:** Fleshy and leathery.

• **Petiole:** Stout, 2-5 cm long, and pubescent (hairy).

• **Size:** 10-20 cm long and 7-11 cm wide.

• **Stomata:** Cyclocytic stomata are present on the lower epidermis.

2.1.3 VERNACULAR NAME

• **Tamil**: Vettilai, Vetrilai

• English: Betel leaf

• Hindi: Paan

• **Telugu**: Thamalapaku

• Kannada: Veeleyada dele

• Sanskrit: Tambula, Nagavalli

• Malayalam: Vettila

• Arabic: Tanbol

• Gujarati: Nagarbel

2.1.4 CHEMICAL CONSTITUENTS

Essential Oils

• **Eugenol:** A major component, contributing to the leaf's aromatic and medicinal properties.

• Caryophyllene: Another significant component of the essential oil, contributing to the leaf's aroma and potential medicinal benefits.

- **Piperine:** An alkaloid that enhances the therapeutic effects of the leaf.
- Other volatile compounds: Contribute to the leaf's distinct aroma.

Other Compounds

- **Alkaloids:** Besides piperine, other alkaloids like piperlonguminine, piperdardine, and guineensine are also found.
- **Flavonoids:** Quercetin and kaempferol contribute to antioxidant and anti-inflammatory effects.
- **Phenolic Compounds:** Contribute to the leaf's medicinal properties and antioxidant activity.
- **Vitamins:** Vitamin C is present, along with B vitamins like thiamine and riboflavin.
- Minerals: Calcium, iron, phosphorus, and potassium are found in varying amounts.
- Other: Saponins and tannins are also present, contributing to astringency and antimicrobial properties.

Variations

The specific chemical composition can vary geographically and between different betel leaf varieties. For example, safrole is a major component in Sri Lankan betel leaves, while eugenol, isoeugenol, and germacrene D are dominant in other chemotypes.

Other Components

The leaves also contain enzymes like diastase and catalase, as well as amino acids, although some like lysine, histidine, and arginine are present in trace amounts. Sugars like maltose, fructose, glucose, and sucrose are also found.

Fig. 3: Chemical Structure.

2.1.5 MEDICINAL USES

- Adjuvant (anupana) It is used as anupana in kapha related diseases like cough, running nose, bloating etc
- Paan It is used as paan to relieve bad breath, toothache, tastelessness, cough, sore
 Chewing betel leaf after meal relieves indigestion, bloating, anorexia and cleanses the
 mouth.
- Leaves juice is used in asthma, laryngitis (swelling of vocal cords) and sore throat.
- Betel leaves applied with castor oil is warmed and tied over the chest relieves asthma and cough in children.
- In diphtheria juice of 4 betel leaves or 2 drops of betel leaf oil is mixed with warm water is used to gargle. Its steam can also be inhaled.
- Betel leaves are warmed and tied over arthritic joints to relieve pain, swelling and inflammation. To stop breast milk it is tied over the breast.
- Eye drops In netraabhishyanda (conjunctivitis) juice of betel leaf with honey is used as eye drops.
- Purgative Due to its sramsana effect it is used as mild purgative. For constipation cold infusion of betel leaves taken in empty stomach can be used.
- In children stalk of betel leaf dipped in castor oil is used as suppository to relieve constipation.

2.2 PHYLLANTHUS EMBLICA

- **Biological Source:** The biological source of an amla leaf is Phyllanthus emblica L.
- Family: Euphobiaceae



Fig. 4: Phyllanthus emblica L.

2.2.1 TAXONOMICAL CLASSIFICATION

• Kingdom: Plantae

• Clade: Tracheophytes

• Clade: Angiosperms

• Clade: Eudicots

• Clade: Rosids

• Order: Malpighiales

• Family: Phyllanthaceae

• Genus: Phyllanthus

• **Species**: P. emblica

2.2.2 MORPHOLOGY

- **Size and Shape:** Amla leaves are small, typically 10-13 mm long and 2-3 mm broad. They are oblong in shape.
- **Arrangement:** The leaves are arranged closely together along the branchlets, giving the branchlets a feathery appearance.
- Color: They are light green in color.
- **Attachment:** The leaves are subsessile, meaning they have a very short petiole (leaf stalk), and are attached directly to the branchlet.
- **Resemblance:** Amla leaves are described as resembling pinnate leaves, which are compound leaves with leaflets arranged on either side of a common axis.
- Other Features: They are described as finely pubescent (covered in fine hairs) and sometimes deciduous (falling off seasonally).

2.2.3 CHEMICAL CONSTITUENTS

- **Hydrolysable Tannins:** These include emblicanin A and B, which are known for their antioxidant properties. They also include punigluconin, pedunculagin, chebulinic acid, chebulagic acid, corilagin, and geraniin.
- **Alkaloids:** Phyllantine, phyllembein, and phyllantidine are found in Amla leaves.
- **Phenolic Compounds:** Gallic acid, methyl gallate, ellagic acid, and trigalloyl glucose are among the phenolic compounds.
- **Amino Acids:** The leaves contain glutamic acid, proline, aspartic acid, alanine, cystine, and lysine.

- Carbohydrates: Pectin is one of the carbohydrates found in Amla leaves.
- **Vitamins:** Ascorbic acid (Vitamin C) is a significant component.
- **Flavonoids:** Quercetin and kaempferol are examples of flavonoids present.
- **Organic Acids:** Citric acid is one of the organic acids found.

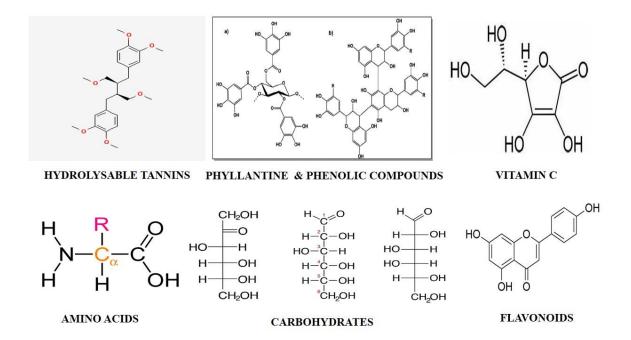


Fig: 5 Chemical Structures.

2.2.4 MEDICINAL USES

- Amla is best anti-ageing herb (vayastapna).
- It improves vision and good for overall health of eyes (chakshushya).
- This herb is useful to pacify all three dosha (sarvangdosha) in various disorders of body.
- It is very effective in various bleeding disorders (rakatpittaghna).
- Amla is anti-diabetic and reduces sugar level in urine (premaghna).
- The herb has aphrodisiac properties (virshya) and help to reduce burning sensation (dahahara).
- This herb is very effective for heart (hirya) and also useful in fever (jwarghna).
- It is used to improve voice, sore throat and various disorders related to throat (kanthya).
- Amlaki powder is also used in the preparation of salt i.e vida lavana.
- This herb protect us from various viral, fungal and bacterial infections.

3. LITERATURE REVIEW

Table: 1 Review Of Herbal Plant Used Anti – Depression.

S.NO	PLANT NAME	PART USED	SOLVENT	ACTIVITY	RESULT (CONCLUSION)	REFERENCES
1.	Crocus sativus	Petals	Aqueous And Ethanol	Antidepressant	It is found To Be Effective As Similar To Fluoxetine In the Treatment Of Mild-To- Moderate Depression	TALHA JAWAID, 2011 ^[11]
2.	Nardostachys jatamansi	Root, Rhizo me	Methanol	Antidepressant	Statistically Significant Result With Increasing Dose And Had Synergic Effect When Given Along With Fluoxetine	RADHIKA PANCHAK, 2017 ^[10]
3.	Hypericum perforatum	leaf	Methanol	Antidepressants	showed significant antidepressant effect compared to placebo	KASPER S,2006 ^[9]
4.	Glycyrrhiza uralensis	Root	Ethanol	Antidepressants, Anti- Inflammatory, Antithrombotic, Antiviral And Antiulcer	Antidepressant-Like Effect And Antioxidative Activity By Measuring Erythrocyte Superoxide Dismutase (SOD) Activity And Plasma Malondialdehyde (MDA) Level Of The Experimental	Zhao Z 2008 ^[2]
5.	Lafoensia pacari	Leaves	Ethanolic	Antidepressants, Antibacterial, Anti- Inflammatory, Analgesic, Antioedematous, Antinociceptive	(Lythraceae) Has Been Referred In Brazilian Traditional Medicine For The Treatment Of Different Diseases, Among Them Depression	Galdino PM 2009 ^[3]
6.	Siphocampyl us verticillatus	Aerial Parts	Hydro alcoholic Extract	Antidepressants, Arthritis	Its action seems to involve an interaction with adrenergic, dopaminergic, glutamatergic and serotonergic systems	Rodrigues AL, 2002 ^[4]
7.	Schinus molle L	Leaves	Ethanol	Antidepressants , Antioxidant, Anticancer Activity	These results provide evidence that the extract from S. molle shares with established antidepressants some pharmacological effects, at least at a preclinical	Machado DG 2008 ^[5]

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8.	Tabebuia Avellaneda	Bark	Ethanol	Antidepressants, Antitumor, Anti inflammatory, Anti-bacterial, Antifungal	The mechanisms involved in this antidepressant-like action and the effects of the association of the extract with the antidepressants fluoxetine, desipramine and bupropion in the TST were investigated	Freitas AE 2010 ^[6]
9.	Curcuma longa	Rhizo me	Aqueous Extract	Antidepressants ,Antiseptic, Alzheimer's Disease, Cancer, Arthritis	The activity of <i>C. longa</i> in antidepressant may mediate in part through MAO A inhibition in mouse brain	Kong LD 2002 ^[7]
10.	Bupleurum falcatum	Root	methanolic	Antidepressants , Anti- Inflammatory, Antitussive	In the present study, the antidepressant-like effect of methanolic extract of BFM and its neuropharma-cological mechanism were investigated in mice.	Kwon S 2010 ^[8]
11.	Zingiber officinale	Rhizo me	Hydro- alcoholic	Antidepressants	Showed antidepressant activity in FST test model and significant antinociceptive effect acetic acid.	Fatehi M 2003 [12]
12.	Tinospora cordifolia	Whole plant	Aqueous	Antidepressants	Increasing the levels of monoamines like noradrenalin, serotonin, and dopamine, and decreasing the levels of GABA.	Noorbala AA 2005 ^[13]
13.	Glycyrrhiza glabra	Root	Aqueous	Antidepressants	Increase of brain norepinephrine and dopamine, but not by increase of serotonin. Monoamine oxidase inhibiting effect of liquorice may be contributing favourably to the antidepressant-like activity	Hosseinzadeh H 2004 ^[14]

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14.	Cimicifuga racemosa	Root	Ethanolic	Antidepressants	Improvement of menopausal symptoms assessed by the total KIM score and its sub-item scores with an effect size.	Tranter R 2002 ^[15]
15.	Curcuma longa	Root (rhizo me)	Methanolic	Antidepressants	It increase monoamines and brain derived neurotrophic factor level may inhibit the production of proinflammatory cytokines and neuronal apoptosis in the brain.	Jain NN 2003 ^[16]
16.	Areca catechu	Areca nut	Dichlorome thane, Ethanolic	Antidepressants	These alkaloids showed significant antidepressant activity in Forced Swimming Test (FST) and Tail Immersion Test (TST).	Dar A 2000 ^[17]
17.	Apocynum venetum Linn	Leaves	Ethanolic	Antidepressants	The leave extract of the plant showed significant decrease in immobility time in FST at the dose 125mg/kg.	Butter V 2001 ^[18]
18.	Aniba riparia	Unripe fruit	Ethanolic	Antidepressants	which at the dose of 25 and 50 mg/kg, <i>i.p.</i> , showed antidepressantlike activity in mice when tested in Tail Suspension Test (TST) and FST	Sousa FCF 2004 ^[19]
19.	Aloysia polystachya	Aerial part	Hydroalcoh olic	Antidepressants	Thujone and carvone was the main phytoconstituent responsible for antidepressant-like action. The efficacy of the extract was comparable to fluoxetine (10 mg/kg, <i>i.p</i>) and imipramine (12.5 mg/kg, <i>i.p.</i>)	Diaz-Veliz SMG 2005 ^[20]

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20.	Bacopa monniera	Aerial part	Methanolic	Antidepressants	At the dose of 20 and 40mg/kg: p.o possesses significant antidepressant activity in FST and Learned helpless Test (LTH)	Sairam K 2002 ^[21]
21.	Clitoria ternatea	Plant powder	Methanolic	Antidepressants	This herb is mainly found in tropics. The methanolic extract of the plant showed significant decrease in immobility time in TST	Jain NN 2003 ^[22]
22.	Canavalia brasiliensis	Seed	Ethanolic	Antidepressants	The lectins isolated from plant significantly reduced immobility time of male Swiss albino mice in FST.	Barauna SC 2006 ^[23]
23.	Curcuma longa	Root (rhizo me)	Aqueous	Antidepressants	The aqueous extract of the plant was found to reduce immobility time in dose dependent manner in a 14 days chronic treatment. Its mode of action is due to inhibition of MAO-A enzyme	Yu ZF 2002 ^[24]
24.	Cecropia glazioui	Leaves	Aqueous	Antidepressants	The butanolic fractions (Catechin and epicatechin) significantly increased hippocampal monoamines levels and inhibited the uptake of serotonin, dopamine and noradrenaline by synaptosomes of different brain regions	Rocha FF 2007 ^[25]
25.	Cimicifuga racemosa	Root (rhizo me)	Ethanolic- aqueous	Antidepressants	The ethanol-aqueous extract of the plant found to reduce time period of immobility in TST. Hence it has a good	Winterhoff H 2002 ^[26]

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					antidannassant manantra	
					antidepressant property	
26.	Gentiana kochiana	Aerial parts	Diethylethe r	Antidepressants	Gentiacaulein, the active component of the extract strongly inhibited rat microsomal MAO-A	Tomic M 2005 ^[27]
27.	Hypericum reflexum L	Aerial part	Methanolic	Antidepressants	The methanol extract obtained from the aerial part of <i>Hypericum reflexum</i> L. fill. was found to decrease in immobility time in forced swimming test	Sánchez-Mateo CC 2007 ^[28]
28.	Lepidium meyenii	Hypoc otyls	Aqueous	Antidepressants	Aqueous extract of hypocotyls of <i>Lepidium meyenii</i> Walp. at the dose of 1g/kg/day, <i>p.o.</i> to Swiss female ovariectomized mice for 21 consecutive days, showed significant anti-depressant like activity.	Rubio J 2006 ^[29]
29.	Magnolia officinalis	Bark	Aqueous	Antidepressants	The active phytoconstituent such as magnolol and dihydroxydihydromagn olol obtained from the aqueous extract of <i>Magnolia officinalis</i> bark, at dose of 50-100 mg/kg, <i>i.p.</i> to mice, showed anti-depression like activity	Yi LT 2009 ^[30]
30.	Morinda officinalis F.C	Root	Ethanolic	Antidepressants	The aqueous extract (50 mg/kg) of the roots showed antidepressant-like activity in male mice in FST model	Zhang ZQ 2001 ^[31]
31.	Piper laetispicum	Stem And Root	Ethanolic	Antidepressants, Anti- Inflammatory, Immunomodulato ry, Antitumor	In conclusion, we showed that laetispicine possessed significant antidepressant and antinociceptive properties, making this drug potentially useful in depression and pain	Yao CY 2009 ^[32]

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32.	Clitoria ternatea	Plant powder	Methanolic	Antidepressants	Clitoria ternatea may be served as a potential resource for natural psychotherapeutic agent against depression	Sairam K 2002 ^[33]
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4. CONCLUSION

The compiled data underscore the efficacy of various medicinal plants in exhibiting antidepressant-like effects in preclinical studies. Many herbs act through modulation of monoamines, antioxidant mechanisms, and anti-inflammatory pathways. This review validates the traditional use of such plants and suggests their potential in developing novel, safer, and cost-effective antidepressant therapies. Further clinical trials are essential to confirm efficacy, safety, and dosage in human subjects.

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