



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Phytochemical Approaches to Bipolar Disorder: A Systematic Review of Herbal Remedies and Their Bioactive Constituents

Farhan Ahamad. N. Pinjari*, Gayatri. B. Rajput, Prachi. N. Pote, Neha. J. Pursnani, Dipali. R. Mali

J.E.S'S College of Pharmacy, Nandurbar 425412- India.

ARTICLE INFO

Published: 06 Feb. 2025

Keywords:

bipolar disorder, mood fluctuations, manic episodes, depressive episodes, herbs.

DOI:

10.5281/zenodo.14825911

ABSTRACT

Bipolar disorder is a multifaceted mental health condition marked by profound mood fluctuations, encompassing both manic and depressive episodes. This review delves into the epidemiological, etiological, and diagnostic aspects of bipolar disorder, while also examining the complexities that arise during treatment. The interplay between various factors contributes to the development of bipolar disorder, including genetic predispositions, neurological abnormalities, environmental stressors, chemical imbalances, and traumatic experience. Effective management of bipolar disorder is often hindered by factors such as treatment nonadherence, comorbid conditions, mixed manic episodes, and depressive episodes. This abstract reviews various herbal drugs studied for their potential benefits in managing bipolar disorder symptoms. Key herbs such as , Ginkgo biloba, and Rhodiola rosea have shown promise in alleviating depressive symptoms, while Omega-3 fatty acids and Saffron have garnered attention for their mood-stabilizing effects other drugs like Ashwagandha ,Bacopa Monnieri ,Levender ,Valerian Root . Despite some positive findings, the efficacy and safety of these herbal treatments remain under-researched, necessitating further clinical trials. This review underscores the importance of a comprehensive approach that includes both pharmacological and herbal interventions, highlighting the need for careful monitoring and professional guidance when integrating herbal therapies into treatment plans for bipolar disorder.


INTRODUCTION

"Bipolar disorder is a persistent and recurrent mental health condition characterized by alternating episodes of mania or hypomania, often

interspersed with periods of depressive symptoms, and frequently misdiagnosed in its initial stages." Kraeplin in 1896 outlined the circumscribed disease entity manic-depressive psychoses. Manic

*Corresponding Author: Farhan Ahamad. N. Pinjari

Address: J.E.S'S College of Pharmacy, Nandurbar 425412- India.

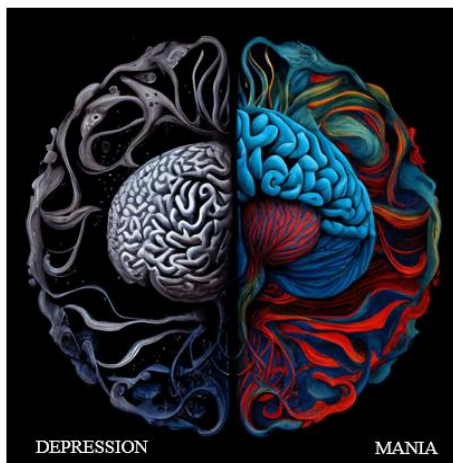
Email : farhanpinjari84@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



depressive psychosis, now commonly referred to as bipolar mood disorders, has been a subject of investigation in our country for several years. Bipolar disorder is a complex condition marked by recurring cycles of elevated mood, or hypomania,

alternating with depressive episodes, which can be challenging to diagnose accurately in the initial stages ⁽¹⁾.



Types of Bipolar Disorder: -

Bipolar disorder encompasses a range of conditions characterized by fluctuations in mood, energy, and activity levels. The primary types of bipolar disorder are:-

1. Bipolar Disorder type 1 :- Marked by the occurrence of at least one manic episode, which may be followed by depressive episodes. Manic episodes are characterized by abnormally elevated or irritable mood, accompanied by increased energy, talkativeness, and reckless behavior.
2. Bipolar Disorder type 2 :- Involves a pattern of depressive episodes alternating with hypomanic episodes. Hypomanic episodes are less severe than manic episodes but still involve abnormally elevated or irritable mood.
3. Bipolar Disorder Not Otherwise Specified (BP-NOS) :- A findings given when symptoms do not meet the criteria for bipolar I or II disorder. This may include individuals who experience symptoms that are not severe enough or do not last long enough to meet the diagnostic criteria.
4. Cyclothymic Disorder:- It is characterized by periods of hypomania alternating with periods of mild depression.

Overview

Bipolar disorder is a multifaceted psychiatric condition marked by recurrent fluctuations in mood, encompassing depressive, manic, and mixed states. Approximately 1-2% of the global population is affected by this condition, with bipolar I disorder exhibiting equal prevalence among both genders, whereas bipolar II disorder appears to be more prevalent among women.

The classification of bipolar disorder subtypes is based on the severity and frequency of episodes, encompassing bipolar I, II, rapid cycling, and cyclothymia. Rapid cycling is characterized by four or more episodes within a year, whereas cyclothymia is marked by hypomanic and subdepressive symptoms over a two-year period. Accurate diagnosis necessitates a comprehensive psychiatric and neurological evaluation, supplemented by clinical tests to rule out differential diagnoses. The illness is often complicated by psychiatric and somatic comorbidities, which can negatively impact prognosis. Ultimately, prognosis depends on individual factors, including comorbidities and psychotic symptoms ⁽²⁾.

Bipolar Disorder: -

Mania: -

Manic episodes are a key feature of bipolar I disorder. To be diagnosed with this condition, an individual must have experienced at least one manic episode lasting for at least one week, regardless of whether a depressive episode occurs. During a manic episode, individuals experience extreme mood shifts, which can include heightened energy, excessive talkativeness, and changes in emotions and thought processes. This state represents a significant departure from their usual behavior, marked by an intense level of activity both mentally and physically, which others may notice. People in a manic state may also partake in risky behaviors that can jeopardize their health, relationships, or finances, such as making

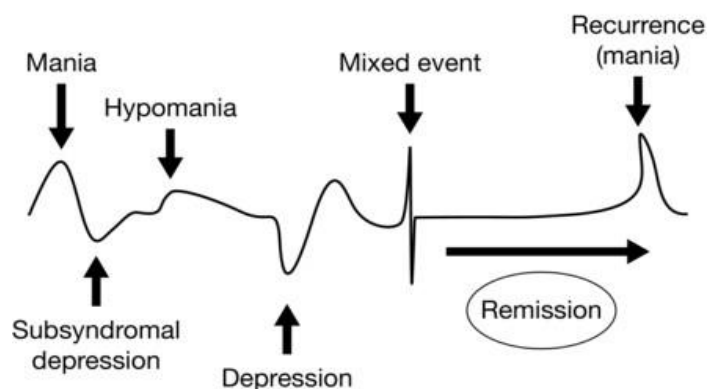
impulsive purchases, gambling significant amounts of money, or engaging in reckless actions like unsafe driving ⁽³⁾.

Depression: -

Periods of low mood are known as depressive episodes. They can linger for months at a time, although they usually do so for at least two weeks. Similar to episodes of manic or hypomania, they can seriously interfere with daily activities. Medicines or hospital stays may be necessary for severe depression.

For some people, manic or hypomanic periods are easier to handle than depressed ones. The disparity between your elevated and depressed states could exacerbate the appearance of your depression ⁽³⁾.

Bipolar disorder is multidimensional



Etiology of Bipolar Disorder :-

The precise cause of bipolar disorder remains unclear, as is typical with many psychiatric conditions. However, it is believed to arise from a complex interplay between genetic predispositions and various environmental risk factors that influence its development over time

Genetic epidemiology :-

Studies on families, twins, and adoptions have shown that a person's genetic makeup significantly influences their likelihood of developing bipolar disorder. Heritability estimates for psychiatric disorders are among the highest, with values close to 90% ⁽⁴⁾.

The twin study of bipolar disorder has been shown hereditary variables; this study witnessed that monozygotic concordance between 41% to 70% . and first-degree lifetime risk 5-7 times higher than those of relatives (5–10%) compared to the risk to the overall populace. However, family members of bipolar individuals are additional prone to practice unipolar depression rather than bipolar disorder, indicating that the hereditary risk extends beyond classifications for diagnosis. Additionally, there is proof of schizophrenia, autism, and bipolar disorder all have a hereditary risk.

Environmental factors :-

Risk factors include present physical sickness, exposure to illicit drugs (such as cocaine, amphetamine, and cannabis), and recent negative life events; nonetheless, Events in life are linked to manic episodes in considerably less stable than in cases of severe depression. Additionally, it is true that environmental danger in childhood Obstetric problems are likely among the variables that key factors that influence the likelihood of sickness (and are hence more similar to inherited weaknesses); nonetheless, subsequent risk Things frequently only function as adequate stressors in people who are already inclined.

During clinical visits, clients, and their frequently, families mistakenly identify these latter risk factors as having a strong causal relationship. Risk factors include present physical sickness, exposure to illicit drugs (such as cocaine, amphetamine, and cannabis), and recent negative life events; nonetheless, Events in life are linked to manic episodes in considerably less stable than in cases of severe depression. Additionally, it is true that environmental danger in childhood Obstetric problems are likely among the variables that key factors that influence the likelihood of sickness (and are hence more similar to inherited weaknesses); nonetheless, subsequent risk Things frequently only function as adequate stressors in people who are already inclined. During clinical visits, clients, and their frequently, families mistakenly identify these latter risk factors as having a strong causal relationship⁽⁴⁾.

Neurological factor:-

Bipolar disorder is associated with distinct changes in intracellular signaling pathways. Specifically, postmortem research has shown elevated levels of stimulatory G proteins (GSA) and increased adenylate cyclase activity in the brains of individuals with the disorder. The role of monoaminergic neurotransmitters in the development of mood disorders gained significant

attention in the 1960s through the amine hypothesis. According to this theory, a deficiency in noradrenaline and serotonin was thought to cause depression, while an excess of these biogenic amines was linked to mania. The impact of noradrenergic and serotonergic substances on treating depressive symptoms, and their potential to trigger manic episodes, supported the idea that catecholamines are crucial to the pathology of mood disorders. However, while studies measuring key neurotransmitters and their metabolites in the cerebrospinal fluid or plasma of bipolar patients suggest dysfunctions in noradrenergic and serotonergic systems, the findings remain inconsistent, and a comprehensive neurochemical model for bipolar disorder has yet to be fully established⁽⁵⁾.

Trauma

Mental health conditions like bipolar disorder often have a complex etiology, with childhood trauma being a significant contributing factor. Research suggests that between 16% and 39% of individuals with bipolar disorder also meet the criteria for post-traumatic stress disorder (PTSD). Furthermore, it is estimated that approximately 50% of patients with bipolar disorder have experienced childhood trauma. Interestingly, many individuals with bipolar disorder who do not meet the full criteria for PTSD still report experiencing childhood trauma. This suggests that early life trauma may play a critical role in shaping the development and progression of bipolar disorder. The exact mechanisms by which childhood trauma influences bipolar disorder are not yet fully understood, but ongoing research aims to elucidate this complex relationship. Only four evaluations have addressed childhood trauma thus far. There is strong evidence linking childhood trauma to the development and progression of bipolar disorder. Trauma can take many different forms, including emotional and physical abuse, sexual abuse, and physical



violence. There are few comprehensive data on the trauma types' epidemiology and how they affect the development and progression of bipolar illness. The majority of this field's study focused on both physical and sexual abuse. However, among the trauma subtypes, there are signs that emotional abuse and neglect are more common. The literature appears to overlook emotional maltreatment. The challenge of identifying emotional abuse in assessment surveys is one argument that could apply. It is important to note that trauma suffered by bipolar patients occurs not only from early life trauma but also from their own disruptive behavior during manic episodes ⁽⁶⁾.

Chemical Imbalance ⁽⁷⁾

Types of chemicals (neurotransmitters)

- 1) Norepinephrine
- 2) Serotonin
- 3) Dopamine
- 4) Acetylcholine

1. Norepinephrine

Assessing noradrenergic (NE) activity in the human central nervous system (CNS) poses methodological challenges, yet a substantial body of research suggests that individuals with bipolar disorder (BD) exhibit abnormalities in their NE systems. Studies employing in vivo techniques have revealed that plasma levels of NE and its primary metabolite, 3-methoxy-4-hydroxyphenylglycol (MHPG), are lower in BD patients compared to those with unipolar depression. Furthermore, NE levels are elevated during manic episodes relative to depressive episodes. Postmortem analyses have uncovered amplified NE turnover in the cortical and thalamic regions of Bipolar disorder. Additionally, urinary MHPG levels are decreased in individuals with bipolar disorder experiencing depressive episodes, whereas longitudinal studies indicate that MHPG excretion is elevated during manic episodes. Notably, cerebrospinal fluid (CSF) NE and MHPG levels exhibit a consistent pattern

2. Serotonin

Emerging evidence from several studies, including cerebrospinal fluid (CSF) evaluates, neuroendocrine challenge tests, serotonin receptor and reuptake site binding studies, pharmacological investigations, and brain imaging research, suggests that alterations in serotonergic neurotransmission may contribute to the development of major depressive episodes. Notably, a subset of patients exhibiting impulsivity, violence, and suicidal tendencies have shows lower levels of 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite. However, studies examining CSF 5-HIAA levels in manic individuals have yielded inconsistent and variable results. A review of the literature reveals that baseline CSF 5-HIAA levels in manic patients have been reported to be lower in some studies, unchanged in others, and even higher in a few instances, compared to non-depressed controls. In contrast, the majority of studies have found no significant difference in CSF 5-HIAA levels between manic and depressed patients

3. Dopamine

The notion that bipolar disorder can be modulated through the dopaminergic system is further substantiated by pharmacological evidence. Dopamine agonists, for instance, have shown promise as antidepressants, but can also induce mania in certain individuals with bipolar disorder. Recent studies employing a catecholamine depletion method in euthymic bipolar patients treated with lithium have yielded intriguing results. Researchers used the tyrosine hydroxylase inhibitor methylparatyrosine (AMPT) to deplete catecholamines, and found that while AMPT did not adversely affect mood, a significant proportion of patients exhibited "rebound hypomania." These preliminary findings suggest a dysregulated signaling system, wherein an "overshoot" occurs due to compromised homeostatic mechanisms resulting from compensatory adaptation to

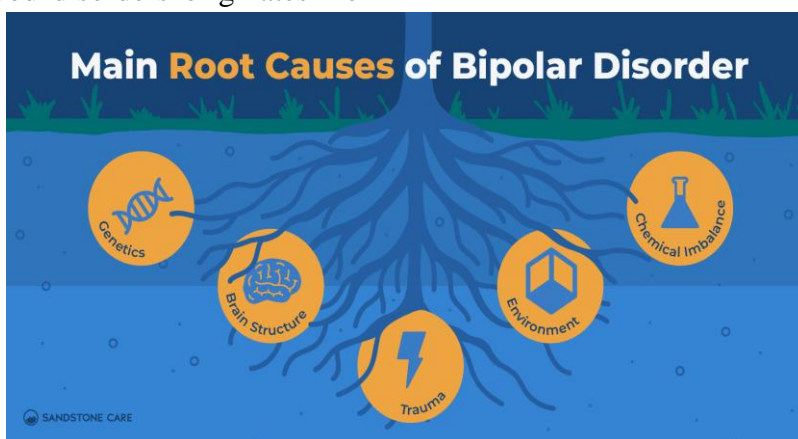


catecholamine depletion. A recent study investigated the effects of a tyrosine-free combination on manic symptoms and psychostimulant effects of methamphetamine. The results showed that reducing tyrosine availability diminished manic ratings and both subjective and objective assessments of methamphetamine's psychostimulant effects. These early findings imply that the brain's ability to regulate tyrosine levels may play a crucial role in mitigating abnormal dopamine neurotransmission following methamphetamine treatment, and potentially in manic episodes as well.

4. Acetylcholine

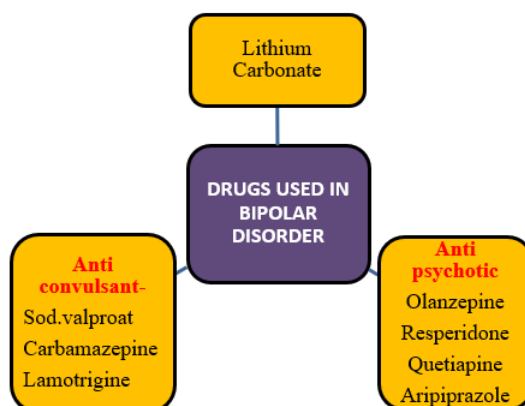
The majority of the data indicating the cholinergic system's role in mood disorders originates from

behavioral, neurochemical, and physiological research on how the body reacts to pharmacological interventions. These investigations, conducted in the early 1970s, demonstrated that mania was linked to noradrenergic tone's relative inferiority over cholinergic tone, and depression to the opposite. Further evidence for this comes from a study on the intravenous administration of the central cholinesterase inhibitor physostigmine, which showed that it might temporarily modify symptoms in manic cases and induce depression in euthymic bipolar patients who had stabilized on lithium.

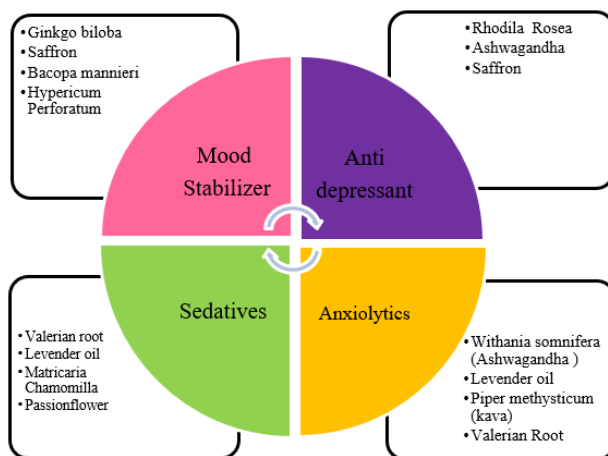


Drugs Used in Bipolar Disorder: -

1) Synthetic Drugs: -



2) Herbal Drugs Used In Bipolar Disorder: -



1) Ashwagandha: -

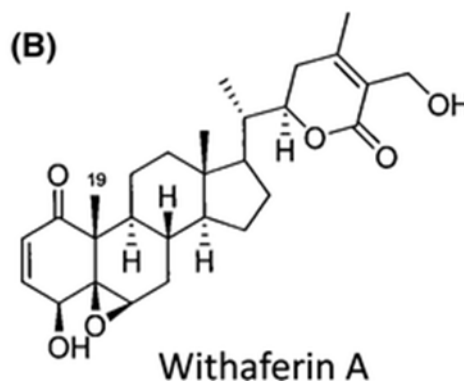
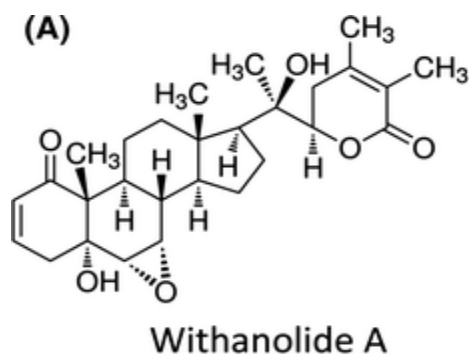


- Synonym :- Indian Gingseng ,Withania root ,Withania somnifera , Winter cherry
- Biological Source:- Ashwagandha consist of dried mature roots of *Withania somnifera*.
- Family :- Solanaceae
- Chemical Constituents of Withania Somnifera
Withania somnifera, commonly known as ashwagandha, contains a diverse range of biologically active compounds. These include:

Alkaloids:- Isopelletierine, anaferrine, cuseohygrine, and anahygrine are some of the key alkaloids present in WS.

Steroidal lactones:- Withanolides and withaferins are the primary steroidal lactones found in WS, contributing to its therapeutic properties.

Saponins:- WS also contains a variety of saponins, which play a crucial role in its biological activity.



IUPAC Name:

A) 1-Oxo-5,6-epoxyergosta-2,24-diene-4,20,22-triol-26-oic acid

B) $5\beta,6\beta$ -Epoxy- $4\beta,27$ -dihydroxy-1-oxowitha-2,24-dienolide

Ashwagandha is known as a "rasayana" in Ayurvedic medicine, which is a medication used to prevent illness and improve mental and physical function, ashwagandha has been included into Western herbal therapy. Potential application in endocrine and neurological illnesses. An investigation involving animals was noted that

ashwagandha has adaptogenic properties through a stress-inducing process, demonstrating a decrease in stress-related variables (cortisol levels, depressive symptoms, and dysfunctional sexual behavior). Withanolides are the active ingredients of ashwagandha because they have been demonstrated to GABA-mimetic properties. Ashwagandha is a natural supplement that have shown to improve memory function and memory in people with bipolar disorder^(10,15,16).

2) Ginkgo Biloba:



- Synonyms:- maiden hair tree , kew tree
- Biological source:- It consist of the dried leaves of *Ginkgo biloba linn*
- Family:- ginkgoaceae
- Chemical Constituents of Ginkgo Leaves:-

The medicinally valuable leaves of the Ginkgo biloba tree contain a diverse array of bioactive compounds. Key constituents include:

1. Terpene trilactones: Ginkgolides A, B, C, J, and bilobalide, which contribute to the plant's therapeutic properties.
2. Flavonoids: Numerous flavonol glycosides, biflavones, and proanthocyanidins, which possess antioxidant and other biological activities.
3. Phenolic compounds: Alkylphenols, simple phenolic acids, and other phenolic derivatives, which may contribute to the plant's medicinal effects.

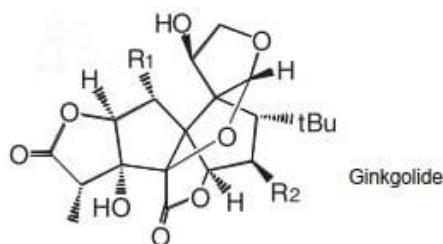
4. Amino acid derivatives: 6-Hydroxykynurenic acid and 4-O-methylpyridoxine, which may play roles in neurological and other physiological processes.

5. Polyphenols: A class of compounds that may contribute to the plant's adaptogenic and other biological activities.

Research has demonstrated that ginkgo biloba can modulate mood in individuals with cognitive impairment, even when used therapeutically for conditions such as tinnitus, peripheral vascular disease, and cognitive decline. Animal studies have shown that ginkgo extract and its four primary terpenoid components – ginkgolide A, ginkgolide B, ginkgolide C, and bilobalide – exhibit anxiolytic effects. A 2006 clinical trial investigated the efficacy of EGb 761 extract (480 or 240 mg daily) versus placebo in individuals with adjustment disorder or generalized anxiety disorder (GAD) experiencing anxious mood

swings, as diagnosed using the DSM-III-R criteria.

The study lasted for four weeks.



Compound	R ₁	R ₂
Ginkgolide A	H	H
Ginkgolide B	OH	H
Ginkgolide C	OH	OH

The precise mechanism of action of ginkgo biloba remains unclear, but research suggests it exerts several beneficial effects, including:

1. Enhanced vaso-regulatory activity, leading to increased cerebral blood flow.
2. Antagonism of platelet activating factor, which may contribute to its anti-inflammatory properties.
3. Modulation of neuronal metabolism, influencing neurotransmitter balance and neuronal health.

4. Antioxidant activity, characterized by free radical scavenging properties.

These effects collectively contribute to the potential therapeutic benefits of ginkgo biloba, although further research is needed to fully elucidate its mechanisms of action^(11,14).

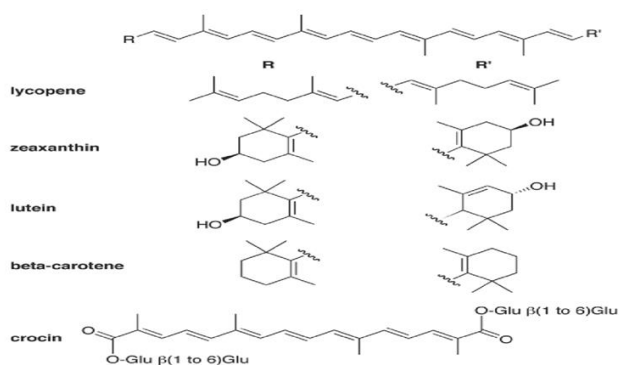
3) Saffron



- Synonyms :-Saffron , Hay Saffron,Kesar
- Biological Source:- Saffron is derived from the dried stigmas and upper portions of the styles of the *Crocus sativum* flower
- Family:- Iridaceae

Chemical Composition of Saffron:-Saffron's complex chemical profile comprises over 150 compounds, including:

1. Carotenoids: Crocetin, crocin, β -carotene, lycopene, and zeaxanthin contribute to its vibrant color and potential health benefits.
2. Monoterpene aldehydes: Picrocrocin and safranal are responsible for saffron's distinctive aroma and flavor.
3. Monoterpenoids and isophenons : These compounds add to the diversity of saffron's chemical constituents and indicate chemical makeup.



- Neurological Effects of Saffron :- Saffron has been observed to have a profound impact on mood and cognitive function. However, it may also have adverse effects on individuals with bipolar disorder, potentially triggering excitability and impulsive behavior.
- Neuroprotective Mechanisms:- Research suggests that saffron's neuroprotective properties are mediated through the activation of key cellular signaling pathways, including:

1. Mitogen-activated protein kinase (MAPK) pathway: Saffron's bioactive compounds may modulate the MAPK pathway, influencing neuronal survival and function.
2. Phosphatidylinositol 3-kinase (PI3K) pathway: Saffron's neuroprotective effects may also be attributed to its ability to activate the PI3K pathway, promoting neuronal health and resilience (12,13).

4) Bacopa Monnieri

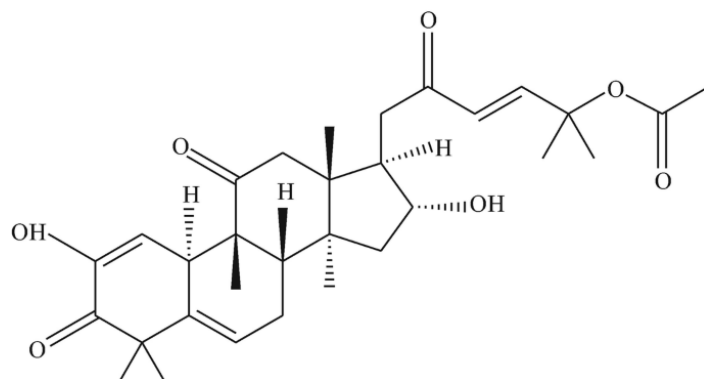


- Synonyms:- water hyssop, water hyssop, brahmi, thyme-leaved gratiola, herb of grace, and Indian pennywort (17,18).
- Biological Source :- It is a small perennial herbaceous plant of *Bacopa monnieri*
- Family:- Scrophulariaceae.
- Chemical Composition of Bacopa Monnieri:- Bacopa monnieri, a renowned herb in traditional medicine, boasts a diverse array of bioactive compounds, including:

1. Alkaloids: Brahmine, nicotine, and herpestine contribute to its pharmacological properties.
2. Saponins: Bacosides A and B, saponins A, B, and C, and triterpenoid saponins are key constituents.
3. Sterols: Stigmastanol, β -sitosterol, and stigmasterol are present in the herb.
4. Triterpenes: Betulinic acid and pseudojujubogenin glycoside add to its chemical complexity.

5. Amino Acids: α -Alanine, aspartic acid, glutamic acid, and serine are among the amino acids found in *Bacopa monnieri*.

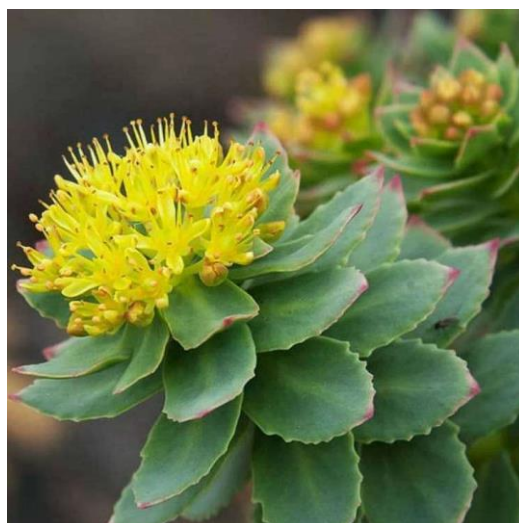
6. Other Compounds: D-mannitol is also present in the herb..



Bacoside

Bacopa Monnieri having procholinergic effects, It produce GABAminergic modulation, and causes modulation of brain stress hormones and reduction of beta amyloid protein

5) *Rhodiola Rosea*



- Synonyms:- *Sedum rhodiola*, *Sedum roseum*, also known as “roseroot”, “golden root” or “arctic root”⁽¹⁹⁾.

- Biological Source:-It is a dried extract of plant *Rhodiola rosea*

- Family:- Crassulaceae

- Chemical Constituents:-

Rhodiola roots are rich in a diverse array of bioactive compounds, including:

1. Phenolic compounds: Phenols, rosavin, rosin, and rosarian contribute to its adaptogenic properties.

2. Organic acids: Various organic acids are present, adding to the herb's chemical complexity.

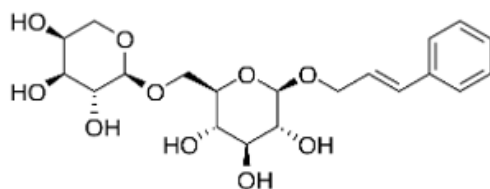
3. Terpenoids: *Rhodiola* roots contain terpenoids, which may contribute to its therapeutic effects.

4. Flavonoids: Flavonoids, known for their antioxidant properties, are also present.

5. Anthraquinones: Anthraquinones, a class of compounds with potential medicinal applications, are found in *Rhodiola* roots.

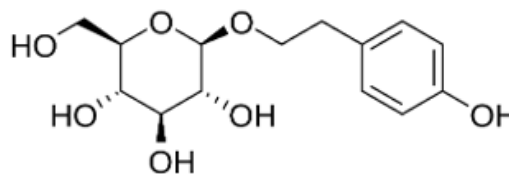
6. Alkaloids: Alkaloids, including tyrosol and salidroside, are among the root's bioactive constituents.

7. Phenolic acids and derivatives: Rhodiola roots also contain phenolic acids and their derivatives, which may contribute to its pharmacological properties.



Rosavin

- Rhodiola inhibits the activity of the enzymes monoamine oxidase A and B. the dopamine, norepinephrine, and serotonin are broken down by these enzymes. Neurotransmitter levels rise when these enzymes are prevented



Salidroside

from breaking down, which aids in mood regulation⁽²⁰⁾.

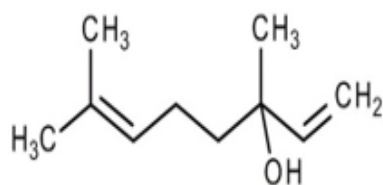
6) *Lavandula Angustifolia*:-



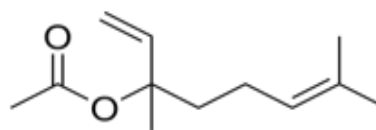
- Synonyms:-Levender
- Biological Source:- It is the volatile oil obtained by steam distillation of flowering tops of plant *Lavandula angustifolia*
- Family:- Labiatae
- Chemical Constituents:- *Lavandula angustifolia* contain following chemicals plays major role in management of bipolar disorder

1. Linalool
2. Linalyl acetate
3. Geraniol
4. β -Caryophyllene
5. Lavandulyl acetate

These compounds contribute to the oil's distinct aroma and potential therapeutic properties.



Linalool



Linalyl Acetate

Lavender essential oil interacts with various well-established targets in the central nervous system, including:

1. Monoamine oxidase A (MAO-A)
2. Serotonin transporter (SERT)
3. Gamma-aminobutyric acid type A (GABAA) receptors

4. N-methyl D-aspartate receptors

These interactions contribute to the oil's anxiolytic (anxiety-reducing) and antidepressive properties, influencing mood regulation and emotional well-being ⁽²¹⁾.

7) Valerian Root :-

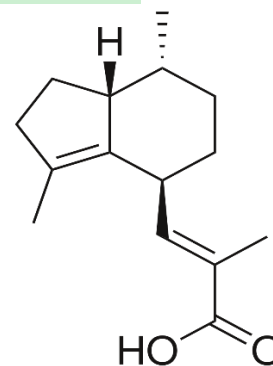


Synonyms:- Indian valerian , Valerian rhizome , European valerian

Biological Source:-It consists of dried roots , rhizome , and stolons of *Valeriana officinalis*

Family:-Valerianaceae ⁽²²⁾.

Chemical Constituents:- Valerian root (*Valeriana* sp.) possesses a multifaceted phytochemical profile, encompassing valerenic acids, monoterpenes, sesquiterpenes, and iridoid glycosides. This intricate constellation of bioactive compounds confers the root's sedative and antispasmodic properties, which have been leveraged in traditional medicine to mitigate stress, promote relaxation, and enhance sleep quality.



Valerenic acids

It is believed to enhance GABA (gamma-aminobutyric acid) activity, which can promote relaxation and reduce anxiety. Additionally, valerian may modulate neurotransmitter systems and exert anti-inflammatory effects, potentially stabilizing mood.

Other Herbal Drugs Used to Cure Bipolar Disorder

Sr No.	Name	Part Used	Mechanism Of Action
1.	Hypericum perforatum	Flowers and Leaves	<ol style="list-style-type: none"> 1. Inhibition of Reuptake Neurotransmitter 2. MAO Inhibition 3. Anti-Inflammatory Effects 4. Neuroprotective Effects
2.	Passiflora incarnata	Flower	<ol style="list-style-type: none"> 1. GABAergic Activity 2. Antioxidant Properties

			<ol style="list-style-type: none"> 3. Sedative Effects 4. Modulation of Neurotransmitters
3.	L-Theanine	–	<ol style="list-style-type: none"> 1. GABA Modulation 2. Increase in Serotonin and Dopamine 3. Reduction of Stress
4.	Omega-3 fatty acid	–	<ol style="list-style-type: none"> 1. Neurotransmitter Regulation 2. Neuroprotective Effect 3. Reduction of Anxiety and Depression Symptoms
5.	Piper methysticum	Root	<ol style="list-style-type: none"> 1. GABAergic Activity 2. Anxiolytic Effects 3. Neuroprotective Properties 4. Mood Stabilization 5. Cognitive Function
6.	Matricaria chamomilla	Flower	<ol style="list-style-type: none"> 1. Anxiolytic Effects 2. GABAergic Activity 3. Anti-Inflammatory Properties 4. Mood Stabilization
7.	Curcuma longa	Root	<ol style="list-style-type: none"> 1. Anti-Inflammatory Effects 2. Neurotransmitter Modulation 3. Neuroprotective Properties 4. Stress Reduction

CONCLUSION: -

In conclusion, enormous herbal plants show promise in preventing and treating bipolar disorder. Bipolar disorder is intricately linked to changes in intracellular substances affecting neurotransmitters and neurological processes. While various treatments exist for dealing bipolar disorder, their pharmacokinetic parameters are incompletely evaluated due to limited clinical trials and studies. The toxicological profile of these treatments is also not fully examined, raising concerns about potential adverse drug reactions. Uncertainties persist regarding the appropriate dosage for these drugs in bipolar disorder, necessitating further investigation into their quality, efficacy, and safety. Many phyto-active constituents have shown probable in preventing and treating manic and depressive episodes in bipolar disorder, offering hope for improved management of this challenging condition.

ACKNOWLEDGMENTS

We extend our deepest gratitude to the numerous researchers, scholars, and authors whose new work

has laid the foundation for this review. Their contributions have been instrumental in shaping our understanding and guiding the development of this manuscript. Our heartfelt thanks to J.E.S'S College of Pharmacy, Nandurbar due to generously provided access to essential resources and unwavering support throughout this research endeavor. Without their assistance, this project would not have been possible. Special appreciation goes to Farhan Ahamad Pinjari ,Gayatri Rajput, Prachi Pote, Neha Pursnani, Dipali Mali, whose insightful guidance, constructive feedback, and relentless encouragement have significantly enriched the quality of this work. Their profound expertise in phytochemistry and mental health has been invaluable in advancing the scope and depth of this review. Finally, we acknowledge the tireless efforts of researchers worldwide who continue to explore innovative approaches to mental health care, particularly in the realm of alternative therapies for conditions such as bipolar disorder. It is our hope that this review will inspire further



investigation into the therapeutic potential of herbal remedies and their bioactive components, paving the way for new discoveries and improved treatment options.

REFERENCES

1. Rao PG. An overview of Indian research in bipolar mood disorder. *Indian J Psychiatry*. 2010 Jan.
2. Müller, J. K., & Leweke, F. M. (2016). Bipolar disorder: clinical overview. *Klinik bipolarer Erkrankungen. Medizinische Monatsschrift für Pharmazeuten*, 39(9), 363–369.
3. <https://my.clevelandclinic.org/health/diseases/9294-bipolar-disorder>
4. Smith, D. J., Whitham, E. A., & Ghaemi, S. N. (2012). Bipolar disorder. *Handbook of clinical neurology*, 106, 251–263.
5. Freund, N., & Juckel, G. (2019). Bipolar Disorder: Its Etiology and How to Model in Rodents. *Methods in molecular biology* (Clifton, N.J.), 2011, 61–77.
6. Aldinger, F., & Schulze, T. G. (2017). Environmental factors, life events, and trauma in the course of bipolar disorder. *Psychiatry and clinical neurosciences*, 71(1), 6–17.
7. Manji, H. K., Quiroz, J. A., Payne, J. L., Singh, J., Lopes, B. P., Viegas, J. S., & Zarate, C. A. (2003). The underlying neurobiology of bipolar disorder. *World psychiatry : official journal of the World Psychiatric Association* (WPA), 2(3), 136–146.
8. Alda, M. (2015). Lithium in the treatment of bipolar disorder: pharmacology and pharmacogenetics. *Molecular psychiatry*, 20(6), 661-670.
9. Sarris J. (2018). Herbal medicines in the treatment of psychiatric disorders: 10-year updated review. *Phytotherapy research : PTR*, 32(7), 1147–1162.
10. Singh, N., Bhalla, M., de Jager, P., & Gilca, M. (2011). An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. *African journal of traditional, complementary, and alternative medicines : AJTCAM*, 8(5 Suppl), 208–213.
11. Noor-E-Tabassum, Das, R., Lami, M. S., Chakraborty, A. J., Mitra, S., Tallei, T. E., Idroes, R., Mohamed, A. A., Hossain, M. J., Dhama, K., Mostafa-Hedeab, G., & Emran, T. B. (2022). Ginkgo biloba: A Treasure of Functional Phytochemicals with Multimedicinal Applications. *Evidence-based complementary and alternative medicine : eCAM*, 2022.
12. Siddiqui, M. J., Saleh, M. S. M., Basharuddin, S. N. B. B., Zamri, S. H. B., Mohd Najib, M. H. B., Che Ibrahim, M. Z. B., Binti Mohd Noor, N. A., Binti Mazha, H. N., Mohd Hassan, N., & Khatib, A. (2018). Saffron (*Crocus sativus* L.): As an Antidepressant. *Journal of pharmacy & bioallied sciences*, 10(4), 173–180.
13. Gohari, A. R., Saeidnia, S., & Mahmoodabadi, M. K. (2013). An overview on saffron, phytochemicals, and medicinal properties. *Pharmacognosy reviews*, 7(13), 61–66.
14. Isah T. (2015). Rethinking Ginkgo biloba L.: Medicinal uses and conservation. *Pharmacognosy reviews*, 9(18), 140–148.
15. Saleem, S., Muhammad, G., Hussain, M. A., Altaf, M., & Bukhari, S. N. A. (2020). *Withania somnifera* L.: Insights into the phytochemical profile, therapeutic potential, clinical trials, and future prospective. *Iranian journal of basic medical sciences*, 23(12), 1501–1526.
16. Mikulska, P., Malinowska, M., Ignacyk, M., Szustowski, P., Nowak, J., Pesta, K., Szelağ, M., Szklanny, D., Judasz, E., Kaczmarek, G., Ejiohuo, O. P., Paczkowska-Walendowska, M., Gościniak, A., & Cielecka-Piontek, J. (2023). Ashwagandha (*Withania somnifera*)-Current Research on the Health-Promoting



Activities: A Narrative Review.
Pharmaceutics, 15(4), 1057.

17. Lansdown, R.V.; Knees, S.G.; Patzelt, A. (2013). . IUCN Red List of Threatened Species. 2013 Retrieved 19 November 2021
18. "Bacopa monnieri". Germplasm Resources Information Network. Agricultural Research Service, United States Department of Agriculture. Retrieved 2008-03-13.
19. Ivanova Stojcheva, E., & Quintela, J. C. (2022). The Effectiveness of *Rhodiola rosea* L. Preparations in Alleviating Various Aspects of Life-Stress Symptoms and Stress-Induced Conditions-Encouraging Clinical Evidence. *Molecules* (Basel, Switzerland), 27(12), 3902.
20. Whig R, Leo RJ. Mania associated with *Rhodiola rosea*: an adaptogen with antidepressant effects. *Prim Care Companion CNS Disord.* 2022;24(2):21cr02980.
21. López, V., Nielsen, B., Solas, M., Ramírez, M. J., & Jäger, A. K. (2017). Exploring Pharmacological Mechanisms of Lavender (*Lavandula angustifolia*) Essential Oil on Central Nervous System Targets. *Frontiers in pharmacology*, 8, 280.
22. Nandini Sundaresan *Valeriana Officinalis: A Review Of Its Traditional Uses, Phytochemistry And Pharmacology* , jan 2018.

HOW TO CITE: Farhan Ahamad. N. Pinjari*, Gayatri. B. Rajput, Prachi. N. Pote, Neha. J. Pursnani, Dipali. R. Mali, *Phytochemical Approaches to Bipolar Disorder: A Systematic Review of Herbal Remedies and Their Bioactive Constituents*, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 2, 425-440.
<https://doi.org/10.5281/zenodo.14825911>

