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Review

A Guide to Herbal Medicines Available for Bipolar Symptoms: A Comprehensive Review

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Abstract:

Background: Because of their neuroprotective, mood-stabilizing, and anxiolytic qualities, herbal medicines have drawn more attention as an adjunctive or alternative treatment for the symptoms of bipolar disorder (BD). A thorough assessment of their mechanisms, effectiveness, and safety is still lacking despite growing interest. **Objective:** This review classifies 75 herbal medicines by biological sources, families, and pharmacological mechanisms to synthesize the evidence regarding their potential benefits for BD-related symptoms (such as mania, depression, and anxiety). **Methods:** The Cochrane Library, PubMed, and Scopus were used to perform a thorough literature search (2000–2023). Preclinical or clinical research demonstrating neuroactive effects, such as GABA modulation, antioxidant, or anti-inflammatory activity, was used to choose the herbs. To highlight therapeutic targets and mechanisms of action (MOA), data were tabulated. **Results:** Adaptogens like *Withania somnifera* and *Rhodiola rosea* may lessen mood dysregulation brought on by stress. GABAergic herbs that exhibit anxiolytic effects include *Passiflora incarnata* and *Valeriana officinalis*. Because of the possibility of interactions, dopaminergic and serotonergic modulators, such as *Mucuna pruriens* and *Hypericum perforatum*, should be used with caution. Herbs that reduce inflammation, like *Boswellia serrata* and *Curcuma longa*, may help with neuroprogression. **Conclusions:** Herbal remedies provide a variety of ways to manage the symptoms of BD. To determine efficacy, safety, and dosage, however, thorough clinical trials are necessary. Researchers and clinicians navigating integrative approaches to BD can use this review as a guide.

Keywords: neuroprotection, adaptogens, mood stabilizers, GABA, antioxidants, bipolar disorder, herbal medicine, phytotherapy

1. Introduction

The chronic mental illness known as bipolar disorder (BD) is characterized by recurrent episodes of depression and mania/hypomania, impacting roughly 1% to 2% of the world's population [1-5]. Many patients have suboptimal responses or intolerable side effects, such as metabolic disturbances, sedation, or renal toxicity, even though pharmacological treatments—such as lithium, antipsychotics, and mood stabilizers—remain first-line interventions [6]. Consequently, complementary and integrative therapies, especially herbal medicines, are gaining popularity [7].

Numerous neuropharmacological characteristics are displayed by herbal remedies, such as:

- **Neurotransmitter modulation:** *Mucuna pruriens* supplies L-DOPA, a dopamine precursor, while *Hypericum perforatum* (St. John's Wort) inhibits serotonin reuptake [4].
- **Neuroprotection:** *Ginkgo biloba* and *Curcuma longa* have anti-inflammatory and antioxidant properties that may help BD patients fight off oxidative stress and neuroprogression [10].
- **GABAergic activity:** By interacting with GABA receptors, anxiolytic herbs like *Valeriana officinalis* and *Matricaria chamomilla* may reduce anxiety associated with BD [11].

The clinical data is still dispersed despite encouraging preclinical evidence. For example, *Crocus sativus* (saffron) exhibits antidepressant activity similar to fluoxetine [12], and *Rhodiola rosea* exhibits adaptogenic effects in stress-related mood dysregulation [1]. But hazards like drug-herb interactions (e.g., *Hypericum perforatum* inducing cytochrome P450 enzymes) and difficulties with product standardization necessitate careful thought [8].

According to emerging models of bipolar disorder, oxidative stress, mitochondrial dysfunction, and chronic inflammation are characteristics of a neuroprogressive trajectory [13]. The justification for investigating phytotherapeutic agents with neuroprotective and anti-inflammatory qualities is supported by these pathophysiological characteristics. Moreover, adaptogens like *Rhodiola rosea* and *Withania somnifera*, which alter glucocorticoid responses, are relevant because dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis has been linked to the affective instability of BD [14]. Using these developing psychiatric theories as a framework, this review synthesizes herbal evidence.

Seventy-five herbal remedies that may be relevant to BD are systematically evaluated in this review, which is arranged by source, botanical family, and mode of action. The objective is to support integrative treatment frameworks by bridging the gap between traditional use and evidence-based practice.

2. Methods

A comprehensive search for articles published between January 2000 and March 2023 was carried out in the Cochrane Library, PubMed, and Scopus. The search strategy included terms such as mood stabilizers, GABA, herbal medicine, phytotherapy, bipolar disorder, antioxidants, adaptogens, and neuroprotection.

The inclusion criteria were:

- Research on herbs demonstrating neuroactive effects, either preclinical or clinical.
- English-language publications.
- Comprehensive explanations of the pharmacological mechanisms underlying BD symptoms.

Where appropriate, this review adheres to PRISMA guidelines for qualitative synthesis. Randomized controlled trials (RCTs), systematic reviews, and meta-analyses were given precedence over anecdotal and preclinical reports. Traditional usage and pharmacological relevance to BD symptoms (mania, depression, anxiety, and cognitive dysfunction) were taken into consideration when choosing the herbs. The botanical name, biological source, plant family, and mechanism of action (MOA) as documented in the literature are all included in each entry.

Table: Herbal Medicines for Mood Disorders

S.No	Herbal Name	Botanical Name	Mechanism of Action	Ref.No
1	Ashwagandha	Withania somnifera	Modulates GABAergic and serotonergic systems	[15]
2	Brahmi	Bacopa monnieri	Enhances BDNF signaling and synaptic plasticity	[16]
3	St. John's Wort	Hypericum perforatum	Inhibits serotonin, norepinephrine and dopamine reuptake	[17]

S.No	Herbal Name	Botanical Name	Mechanism of Action	Ref.No
4	Valerian	Valeriana officinalis	Enhances GABAergic transmission	[18]
5	Lavender	Lavandula angustifolia	Modulates calcium channels and serotonin receptors	[19]
6	Kava	Piper methysticum	Potentiates GABA-A receptor activity	[20]
7	Lemon Balm	Melissa officinalis	Inhibits GABA transaminase	[21]
8	Passionflower	Passiflora incarnata	Increases GABA levels	[22]
9	Chamomile	Matricaria chamomilla	Binds to benzodiazepine receptors	[23]
10	Turmeric	Curcuma longa	Inhibits monoamine oxidase and cytokine release	[24]
11	Rhodiola	Rhodiola rosea	Inhibits MAO and enhances serotonin	[25]
12	Gotu Kola	Centella asiatica	Improves hippocampal function and increases BDNF	[26]
13	Ginkgo	Ginkgo biloba	Modulates neurotransmitters and reduces oxidative stress	[27]
14	Skullcap	Scutellaria lateriflora	Binds to GABA-A receptor sites	[28]
15	Holy Basil	Ocimum sanctum	Regulates cortisol and reduces stress-induced neurotransmitter changes	[29]
16	Shankhpushpi	Convolvulus pluricaulis	Modulates cholinergic system and brain oxidative status	[30]
17	Jatamansi	Nardostachys jatamansi	Exerts neuroprotective and antidepressant activity	[31]
18	Licorice	Glycyrrhiza glabra	Modulates cortisol metabolism and MAO inhibition	[32]
19	Peppermint	Mentha piperita	Acts on CNS to alleviate tension	[33]
20	Mucuna	Mucuna pruriens	Precursor to dopamine	[34]
21	Saffron	Crocus sativus	Inhibits serotonin reuptake	[35]
22	Celastrus	Celastrus paniculatus	Enhances cognition via cholinergic mechanisms	[36]
23	Ginseng	Panax ginseng	Modulates dopamine and serotonin systems	[37]
24	Fenugreek	Trigonella foenum-graecum	Acts on monoamine neurotransmission	[38]
25	Rosemary	Rosmarinus officinalis	Modulates GABA and cholinergic function	[39]
26	Amla	Phyllanthus emblica	Antioxidant and neuroprotective	[40]
27	Guduchi	Tinospora cordifolia	Immunomodulatory and adaptogenic	[41]

S.No	Herbal Name	Botanical Name	Mechanism of Action	Ref.No
28	Mandukaparni	Centella asiatica	Enhances memory and reduces anxiety	[42]
29	Gokshura	Tribulus terrestris	Modulates testosterone and neurochemistry	[43]
30	Tagara	Valeriana wallichii	Acts as sedative and modulates GABA	[44]
31	Nagarmotha	Cyperus rotundus	Antioxidant and MAO inhibitory activity	[45]
32	Arjuna	Terminalia arjuna	Reduces cortisol, cardiotonic	[46]
33	Haritaki	Terminalia chebula	Reduces oxidative stress and inflammation	[47]
34	Bibhitaki	Terminalia bellirica	Neuroprotective, antioxidant	[48]
35	Amruth	Tinospora sinensis	Modulates immune and nervous systems	[49]
36	Shatavari	Asparagus racemosus	Enhances neuroendocrine functions	[50]
37	Bhumyamalaki	Phyllanthus niruri	Liver protective and antioxidant	[51]
38	Chitrak	Plumbago zeylanica	Anti-inflammatory, CNS active	[52]
39	Guggul	Commiphora mukul	Reduces oxidative stress and lipid peroxidation	[53]
40	Kutki	Picrorhiza kurroa	Hepatoprotective and adaptogenic	[54]
41	Neem	Azadirachta indica	Neuroprotective via antioxidant pathways	[55]
42	Pippali	Piper longum	Improves neurotransmitter balance	[56]
43	Ajwain	Trachyspermum ammi	Analgesic and neuroactive	[57]
44	Clove	Syzygium aromaticum	Neuroprotective and antioxidant	[58]
45	Fennel	Foeniculum vulgare	Spasmolytic and anxiolytic	[59]
46	Coriander	Coriandrum sativum	Antidepressant via monoamine modulation	[60]
47	Sarpagandha	Rauwolfia serpentina	Depletes catecholamines, antipsychotic	[61]
48	Bakuchi	Psoralea corylifolia	Antioxidant and neuroregenerative	[62]
49	Kalmegh	Andrographis paniculata	Reduces neuroinflammation	[63]
50	Hibiscus	Hibiscus rosa-sinensis	Antidepressant via monoamine regulation	[64]
51	Maca	Lepidium meyenii	Improves mood and sexual function	[65]
52	Magnolia	Magnolia officinalis	Acts via GABAergic and serotonergic systems	[66]
53	Blue Vervain	Verbena hastata	Anxiolytic, sedative	[67]

S.No	Herbal Name	Botanical Name	Mechanism of Action	Ref.No
54	Tilia	Tilia cordata	Binds to benzodiazepine receptors	[68]
55	Poria	Poria cocos	Antidepressant-like effect, modulates stress	[69]
56	Zizyphus	Zizyphus jujuba	Sedative and hypnotic	[70]
57	Polygala	Polygala tenuifolia	Antidepressant-like activity	[71]
58	Bupleurum	Bupleurum chinense	Antidepressant via saikosaponins	[72]
59	Schisandra	Schisandra chinensis	Antidepressant, enhances BDNF	[73]
60	Curcuma aromatica	Curcuma aromatica	Modulates HPA axis, BDNF, CREB	[74]
61	Gynostemma	Gynostemma pentaphyllum	Anxiolytic, via GABA_A and serotonin	[75]
62	Wild Yam	Dioscorea villosa	Phytoestrogenic, mood balance	[76]
63	Fumitory	Fumaria officinalis	CNS active	[77]
64	Angelica	Angelica sinensis	Neuroprotective and adaptogenic	[78]
65	Senega	Polygala senega	Contains saponins with CNS activity	[79]
66	Motherwort	Leonurus cardiaca	Neuroprotective and calming	[80]
67	Yohimbe	Pausinystalia yohimbe	Alpha-2 antagonist, CNS stimulant	[81]
68	Black Cohosh	Actaea racemosa	Mood stabilizing, hormonal balance	[82]
69	Guarana	Paullinia cupana	Improves cognition, reduces fatigue	[83]
70	Agrimony	Agrimonia eupatoria	Anti-inflammatory, anxiolytic	[84]
71	Horehound	Marrubium vulgare	Neuroprotective	[85]
72	Mistletoe	Viscum album	Immune modulation, adaptogenic	[86]
73	Club Moss	Huperzia serrata	Neuroprotective, acetylcholinesterase inhibition	[87]
74	Corydalis	Corydalis yanhusuo	Analgesic, dopaminergic activity	[88]
75	Huperzine B	Huperzia serrata	Neuroprotective, NMDA receptor antagonist	[89]

3. Discussion

The comprehensive review of 75 herbal medicines highlights their potential as adjunctive or alternative therapies for managing bipolar disorder (BD) symptoms, including mood dysregulation, anxiety, and cognitive dysfunction. These botanicals act through diverse mechanisms, such as neurotransmitter modulation, neuroprotection, and anti-inflammatory effects. However, clinical

integration requires careful consideration of efficacy, safety, and herb-drug interactions.

3.1 Neurotransmitter Modulation and Mood Stabilization

Herbs targeting monoaminergic systems, such as *Hypericum perforatum* (St. John's Wort, [17]) and *Mucuna pruriens* ([34]), demonstrate antidepressant effects but carry risks of inducing manic episodes or interacting with conventional mood stabilizers [90]. Conversely, GABAergic herbs like *Valeriana officinalis* ([18]) and *Passiflora incarnata* ([22]) show promise in alleviating anxiety and agitation without significant adverse effects [91].

3.2 Neuroprotection and Anti-Inflammatory Effects

Oxidative stress and neuroinflammation are implicated in BD progression [92]. Curcumin (*Curcuma longa*, [24]) and *Ginkgo biloba* ([27]) exhibit potent antioxidant and anti-inflammatory properties, potentially mitigating neuroprogression [93]. Adaptogens like *Rhodiola rosea* ([25]) and *Withania somnifera* ([15]) further enhance stress resilience by modulating the HPA axis [94].

3.3 Clinical Challenges and Future Directions

Despite preclinical evidence, few herbs have robust RCTs in BD populations [95]. Key limitations include:

- **Standardization:** Variability in active compound concentrations (e.g., curcumin's low bioavailability, [96]).
- **Safety:** Some herbs (e.g., *Acorus calamus*) may be neurotoxic in unrefined forms [97].
- **Herb-Drug Interactions:** *Hypericum perforatum* induces CYP450 enzymes, reducing plasma levels of psychotropics [98].

Future research should prioritize:

1. **RCTs tailored to BD**, assessing herbs like *Crocus sativus* ([35]) for depressive episodes [99].
2. **Standardized formulations** to ensure reproducibility [100].
3. **Personalized approaches** combining herbal and conventional therapies [101].

4. Clinical Recommendations

1. **For Depression:** *Crocus sativus* (saffron, [35]) or *Rhodiola rosea* ([25]) may augment SSRIs, but monitor for manic switching [102].
2. **For Anxiety:** GABAergics (*Valeriana officinalis*, [18]) or adaptogens (*Withania somnifera*, [15]) are preferable to benzodiazepines due to lower dependency risk [103].
3. **For Cognitive Dysfunction:** *Bacopa monnieri* ([16]) and *Ginkgo biloba* ([27]) may improve neuroplasticity [104].
4. **Avoid in Mania:** Dopaminergic herbs (*Mucuna pruriens*, [34]) and stimulants (*Paullinia cupana*, [83]) may exacerbate symptoms [105].

5. Conclusion

Herbal medicines offer a multifaceted approach to BD management, targeting mood, inflammation, and stress pathways. While preliminary data are encouraging, rigorous clinical trials ([106]-[110]) and standardized protocols are essential to validate their role in integrative psychiatry. Clinicians should weigh benefits against risks, particularly herb-drug interactions, to optimize patient outcomes.

6.Recognition

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