



Review

Herbal medicines in obsessive-compulsive disorder: Pre-clinical and clinical evidence

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Abstract: Background: Obsessive-compulsive disorder (OCD) is a chronic and debilitating neuropsychiatric disorder characterized by recurrent obsessions and compulsions that significantly impair quality of life and daily functioning. Although cognitive behavioural therapy (CBT) and pharmacotherapy remain the mainstay of treatment, many patients experience incomplete response, relapse, or adverse effects associated with long-term therapy. Consequently, increasing attention has been directed toward herbal medicines and phytochemicals as potential alternative or adjunctive therapeutic approaches for OCD. **Objective:** This review summarizes the available evidence regarding herbal medicines and phytoconstituents investigated for OCD, with emphasis on their therapeutic potential, proposed mechanisms of action, and findings from preclinical and clinical studies. **Methods:** Relevant articles were retrieved from PubMed, Scopus, Web of Science, Open Access Journals, and Google Scholar up to 31st December 2025 using keywords including “obsessive-compulsive disorder”, “OCD”, “medicinal plants”, “herbal medicine”, and “phytomedicine”. **Discussion:** Clinical studies, particularly randomized controlled trials, suggest that *Crocus sativus*, *Withania somnifera*, *Valeriana officinalis*, and *Echium amoenum* may reduce OCD symptom severity, primarily assessed using Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores. Preclinical studies further demonstrated anti-obsessive effects of several medicinal plants through modulation of serotonergic, dopaminergic, and glutamatergic pathways, along with antioxidant, anti-inflammatory, and neuroprotective activities. However, the current evidence remains limited by small sample sizes, short follow-up duration, lack of replication studies, and

methodological heterogeneity involving variations in herbal preparations, dosages, and study designs. In addition, mechanisms related to immune regulation, neuroinflammation, oxidative stress, and gut–brain interactions remain insufficiently explored. **Conclusions:** Herbal medicines demonstrate promising therapeutic potential in OCD management; however, the existing clinical evidence remains insufficient to support routine clinical use. Future research should prioritize large double-blind randomized controlled trials with standardized herbal formulations, longer follow-up periods, and comprehensive safety evaluation, along with mechanistic studies investigating immune, inflammatory, and gut–brain pathways involved in OCD pathophysiology.

Keywords: obsessive-compulsive disorder; phytoconstituents; pre-clinical study; bioactive compounds; clinical trials; cognitive- behavioural therapy

1. Introduction

Obsessive-compulsive disorder (OCD) is a chronic and debilitating neuropsychiatric disorder characterized by intrusive and recurrent thoughts, urges, or images (obsessions) accompanied by repetitive behaviours or mental acts (compulsions) performed to reduce anxiety or distress [1–4]. Common manifestations include excessive washing and cleaning associated with contamination fears, repetitive checking behaviours related to fear of harm, intrusive aggressive or sexual thoughts accompanied by mental rituals, and compulsive arranging or counting behaviours linked to symmetry concerns [4]. Although OCD affects approximately 1–3% of the global population, it is considered one of the most disabling psychiatric disorders because of its chronic nature, functional impairment, and profound impact on quality of life [5]. Many patients spend several hours each day performing compulsions, leading to significant disruption in academic, occupational, and social functioning. OCD is also associated with substantial psychological, social, and economic burden on affected individuals, caregivers, and healthcare systems and has been recognized among the leading causes of disability in the developed world [6].

OCD frequently coexists with other psychiatric disorders, including major depressive disorder, bipolar disorder, psychosis, and substance use disorders, which further complicate disease management and worsen prognosis [6]. Emerging evidence also suggests that stressful environmental conditions may exacerbate OCD symptoms. During the COVID-19 pandemic, the prevalence and severity of obsessive-compulsive symptoms increased considerably, particularly among vulnerable populations such as pregnant women, individuals diagnosed with COVID-19, students, and healthcare professionals [7–9]. However, despite these observations, the clinical burden of OCD extends beyond prevalence alone and includes persistent distress, impaired interpersonal relationships, reduced productivity, and increased healthcare utilization.

The precise ethology and pathophysiology of OCD remain incompletely understood and are believed to involve complex interactions between neurobiological, genetic, immunological, endocrine, and environmental factors [10]. Dysfunction of the cortico-striato-thalamo-cortical (CSTC) circuitry has long been implicated in OCD pathogenesis [11]. In addition, abnormalities involving the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), amygdala-cortical pathways, and associated limbic networks have also been reported [12]. Neurotransmitter dysregulation involving serotonin, dopamine, glutamate, and gamma-aminobutyric acid (GABA) systems has been extensively associated with obsessive-compulsive symptoms [13,14]. Structural neuroimaging studies have further

demonstrated grey matter and white matter abnormalities in frontal brain regions of patients with OCD as shown in Figure 1 [15,16].

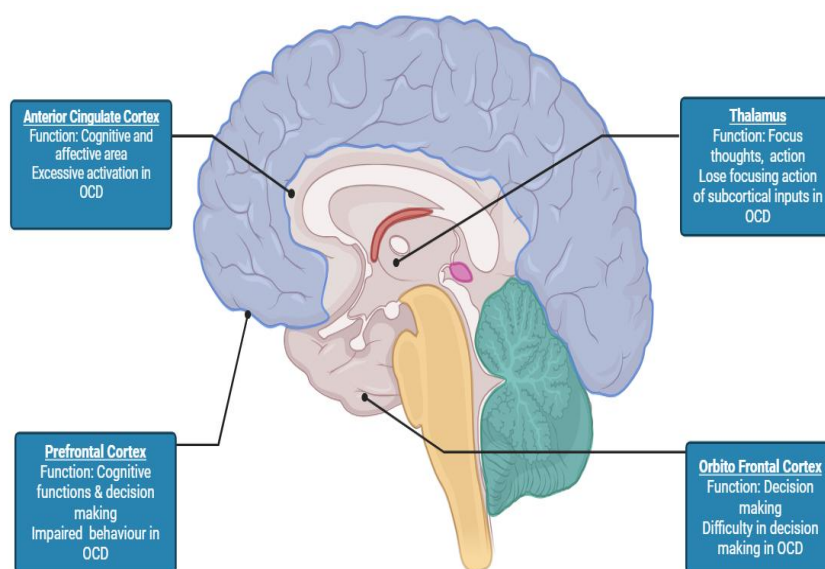


Figure 1. Association of various areas of the brain with OCD.

Recent evidence indicates that OCD pathophysiology extends beyond classical neurotransmitter abnormalities and neural circuitry dysfunction. Dysregulation of the autonomic nervous system, particularly altered sympathetic-parasympathetic balance and impaired stress responsiveness, has been implicated in OCD. Furthermore, disturbances in the hypothalamic-pituitary-adrenal (HPA) axis and abnormal cortisol regulation suggest an important role of endocrine dysfunction in disease progression [17]. Neuroinflammatory mechanisms, immune dysregulation, oxidative stress, and altered cytokine profiles have also been increasingly recognized as contributors to OCD pathology. In addition, growing interest has been directed toward the gut-brain axis and intestinal microbiota, which may influence neuroinflammation, neurotransmitter synthesis, and behavioural regulation. These multifactorial mechanisms provide a strong rationale for exploring therapeutic agents with multimodal pharmacological activities [18,19].

Current management strategies for OCD primarily include selective serotonin reuptake inhibitors (SSRIs), clomipramine, and cognitive behavioural therapy (CBT), particularly exposure and response prevention therapy. Although these approaches are considered effective for many patients, a substantial proportion exhibit partial response, treatment resistance, relapse after discontinuation, delayed therapeutic onset, or poor treatment adherence due to adverse effects and long-term medication use [20,21]. Accessibility and affordability of specialized psychotherapeutic interventions also remain major limitations in many healthcare settings. Consequently, there is increasing interest in complementary and alternative therapeutic approaches, including herbal medicine, because of their perceived safety, lower incidence of adverse effects, multitarget pharmacological actions, affordability, and holistic therapeutic potential [22,23].

Herbal medicines have gained increasing importance in the management of obsessive-compulsive disorder (OCD) because of their potential to modulate multiple biological pathways involved in the disorder while producing comparatively fewer adverse effects than conventional pharmacotherapy. OCD is associated with dysregulation of serotonergic, dopaminergic, glutamatergic, inflammatory, oxidative stress, and neuroendocrine pathways, and many medicinal plants possess anxiolytic, antidepressant, antioxidant, anti-inflammatory, neuroprotective, and neuromodulatory properties that may help alleviate obsessive-compulsive symptoms. Several herbal agents, including *Crocus sativus*, *Withania somnifera*, *Valeriana officinalis*, *Hypericum perforatum*, and *Bacopa monnieri*, have demonstrated promising anti-OCD effects in preclinical and clinical studies through modulation of neurotransmitter systems and reduction of oxidative stress and neuroinflammation [24–27].

The growing interest in herbal medicine is also driven by the limitations of conventional OCD treatments, including incomplete response, delayed onset of action, relapse, and adverse effects associated with long-term pharmacotherapy. In addition, limited accessibility to specialized psychotherapeutic interventions may further affect treatment outcomes. Herbal medicines may therefore serve as potential alternative or adjunctive therapies because of their multitarget pharmacological actions, perceived safety, affordability, and holistic therapeutic approach. Although further large-scale clinical studies are required, the existing evidence highlights the therapeutic potential of herbal plants in OCD management [28].

Several medicinal plants and phytoconstituents possessing anxiolytic, antioxidant, anti-inflammatory, neuroprotective, adaptogenic, and neuromodulatory properties have demonstrated promising effects in preclinical and clinical studies of OCD. However, the available evidence remains fragmented, and there is limited comprehensive synthesis integrating mechanistic insights, experimental findings, clinical evidence, and therapeutic challenges associated with herbal medicine in OCD management. Therefore, this narrative review aims to critically summarize the current understanding of OCD pathophysiology and comprehensively evaluate the available preclinical and clinical evidence regarding herbal medicine for OCD. This review may provide valuable insights for clinicians, pharmacologists, neuroscientists, researchers, and mental health professionals interested in the development of safer and more effective therapeutic strategies for OCD [29,30].

2. Materials and methods

A narrative literature review was conducted to evaluate the available preclinical and clinical evidence on herbal medicine for obsessive-compulsive disorder (OCD). Electronic databases including PubMed, Scopus, Web of Science, Google Scholar, and Open Access Journals were searched for relevant studies published up to 31st December 2025.

The search strategy was adapted according to individual database requirements using both basic and advanced search options. Keywords used included “obsessive-compulsive disorder”, “OCD”, “herbal medicine”, “medicinal plants”, “traditional medicine”, “traditional plant”, “phytotherapy”, and “plant extract” using Boolean operators (“AND”, “OR”) in titles, abstracts, and keywords.

Retrieved articles were screened for relevance through title, abstract, and full-text assessment, and reference lists of eligible studies were manually searched to identify additional relevant publications. Preclinical studies, clinical studies, narrative reviews, systematic reviews, case reports, and expert opinion articles related to herbal interventions for OCD were included.

Extracted information included plant names, plant parts used, study type, intervention details, treatment duration, experimental or clinical models, and major therapeutic outcomes. As this study was conducted as a narrative review, formal quality assessment and meta-analysis were not performed.

3. Results

3.1. *Colocasia esculenta*

Colocasia esculenta, belonging to the *Araceae* family and commonly referred to as Taro, Yam, and Elephant ear, is indigenous to the warmer regions of India. It has been conventionally employed for various ailments and is considered a "nerve tonic" [31]. In an animal experiment, the hydroalcoholic extract of *C. esculenta* leaves showed improvement in symptoms of OCD. It produced both antidepressant and anxiolytic effects supporting common claims. [32]. It also demonstrated the anti-compulsive effect in mouse model using the marble-burying test. Similar to the effects of the antidepressant "fluoxetine," the extract administered intraperitoneally reduced the number of buried marbles in a dose-dependent manner. Flavonoids in *C. esculenta* are thought to have neuroprotective properties that might have raised 5-HT levels in the hippocampus [31,33]. There is still uncertainty regarding the exact mechanism of *C. esculenta* anti-compulsive effects.

3.2. *Hypericum perforatum*

H. perforatum, often referred to as "St. John's Wort", millepertuis, or hypericum, is a herbaceous perennial plant native to northern Africa, western Asia, and Europe. It belongs to the *Hypericaceae* family [34–36] *H. perforatum* is effective in treating skin wounds, eczema, burns, gastrointestinal ailments, and psychological disorders. Currently, it has been demonstrated to be effective in treating mild to moderate depression [37–40] The therapeutic preparation comprises the flowering tops and leaves, with the primary compounds of attention being phloroglucinols, naphthodianthrones, xanthenes, and flavonoids (e.g., hyperforin) and hypericin [41]. In a 12-week double-blind randomized controlled trial, sixty participants with obsessive-compulsive disorder were administered a placebo or St John's wort (LI 160). No significant differences were observed between the placebo and St John's Wort groups regarding mean alteration on Y-BOCS, its subscales, or the proportion of individuals deemed "much" or "very much" improved at the endpoint. Outcomes indicate that St John's wort offers no benefit in comparison to a placebo in the treatment of OCD [42]. In an open-label trial, twelve individuals with a primary DSM-IV diagnosis of OCD persisting for a minimum of 12 months were administered a fixed dosage of an extended-release preparation of hypericin (0.3% hypericin; 450 mg *bid* for 12 weeks). "Clinical Global Impression of Improvement Scale" (CGI), "Y-BOCS", and "Patient Global Impression of Improvement Scale" were employed for weekly assessments, whereas the "Hamilton Rating Scale for Depression" was utilized monthly. A notable alteration from reference to endpoint was noted, with an average Y-BOCS change of 7.4 points. A substantial change transpired in one week and progressively intensified throughout the trial. At the conclusion, 5 (42%) of 12 were rated as "much" or "very much improved" on the clinician-assessed CGI, 6 (50%) were "minimally improved," and 1 (8%) exhibited "no change." It produces an anti-OCD effect by inhibition of 5-HT reuptake. The most common side effects were diarrhoea and disrupted sleep [43].

3.3. *Lagenaria Siceraria*

L. siceraria, a member of the *Cucurbitaceae* family and commonly referred to as Bottle gourd, is a popular Indian vegetable. It is a trailing or pubescent plant with fruits shaped like a bottle [44,45]. In India, its fruits are commonly utilized for treating a wide range of illnesses and symptoms associated with hyperlipidaemia and atherosclerosis. Traditionally, *L. siceraria* fruit has been utilised for its cardioprotective, diuretic, besides cardiotonic properties. It also relieves fever, jaundice, pain, and ulcers, and is useful for treating asthma, chest cough, along with several bronchial illnesses [44]. *L. siceraria* fruits contain cucurbitacin saponins and flavonoids [44–47]. Total buried marbles were lowered by administering a methanolic extract of *L. siceraria* fruits intraperitoneally at doses of 25 and 50 milligrams per kilogram. Effects were analogous to 10 mg/kg fluoxetine (i.p.). Fruit extract of *L. siceraria* combined with Fluoxetine does not induce motor impairment. A preliminary phytochemical assessment of methanolic extract of *L. siceraria* identified tannins, flavonoids, sterols, saponins, carbohydrates, and proteins [44].

3.4. *Benincasa hispida*

B. hispida, often known as the wax gourd, is a member of the *Cucurbitaceae* family. In semi-tropical countries like Thailand and India, this vegetable is well-liked. In Ayurveda, it is used to treat peptic ulcers, internal organ haemorrhages, epilepsy, and other neurological disorders [48,49]. *B. hispida* fruits contain minerals, vitamins, flavonoids, saccharides, glycosides, volatile oils, carotenes, uronic acid, proteins, and β -sitosterin [50,51]. This herb influenced CNS and showed anxiolytic [52] as well as anticonvulsant [53] characteristics. It produces anti-OCD effect by inhibition of serotonergic reuptake. Methanolic extracts of fruits (600 and 400 milligrams per kilogram) demonstrated anti-compulsive effects by preventing marble-burying behaviour, akin to fluoxetine; furthermore, the extract did not affect motor activity. Furthermore, simultaneous administration of a sub-efficacious dosage of its extract (200 milligrams per kilogram) with a sub-efficacious dosage of fluoxetine (5 milligram per kilogram) significantly reduced marble-burying behaviour without impacting mobility. The administration of p-chlorophenyl alanine (PCPA), a serotonin-depleting agent, moderately but considerably reduced the inhibitory effect of the extract, while fully abolishing the influence of fluoxetine on burying behaviour [50]. Tryptophan was found in the methanolic extract of *B. hispida*, according to preliminary phytochemical analyses [50]. Tryptophan is an essential precursor of serotonin in serotonergic neurons [54,55] and may increase serotonin production to enhance the methanolic extract's anti-compulsive effectiveness.

3.5. *Withania somnifera*

W. somnifera comes from the family *Solanaceae* and is often referred to as Indian ginseng or Ashwagandha. For thousands of years, people have turned to this herb for its restorative and revitalizing medicinal properties [56,57]. Aqueous and methanolic *W. somnifera* extract (50 milli gram per kilogram) decreased marble-burying behaviour in animals without affecting mobility, according to an investigation. Parachlorophenylalanine, ritanserin, and fluoxetine all had comparable effects [58]. Phytochemical analysis of the extract revealed the presence of tryptophan, a precursor of 5-hydroxytryptamine (5-HT) in serotonergic neurons. The anti-obsessive qualities of *W. somnifera*

may be explained by this discovery. According to certain studies, *W. somnifera* may also enhance serotonergic transmission by affecting post-synaptic 5-HT_{2A/2C} receptors [59–60]. Thirty people with OCD were divided into 2 clusters for this randomized, double-blind, placebo-controlled trial: 1 cluster received 120 milligrams of *W. somnifera* extract daily, while the other group received a placebo. Take four capsules of the extract or a placebo daily, ideally with food, for six weeks; all subjects were on selective serotonin reuptake inhibitors. At the start and finish of the experiment, the Y-BOCS was utilized to evaluate the intensity of OCD symptoms. When tested for OCD symptoms, researchers discovered that *W. somnifera* extract was safe and effective [60].

3.6. *Tabernaemontana divaricata*

In traditional medicine, *T. divaricata*, also known as crepe jasmine, which is a member of the Apocynaceae family, has long been used to cure fever, pain, and diarrhoea. Extracts from this herb may be employed as pharmacological therapies for a variety of disorders [61]. *T. divaricata* extracts have significant antioxidant properties. *T. divaricata*'s antioxidant properties could be due to its phenolic and flavonoid levels [62]. Chanchal et al. examined the impact of an ethanolic extract of *T. divaricata* leaves on adult Swiss albino mice to assess their burying behaviour. Cluster 1 got normal saline orally, clusters 2, 3, and 4 got 100, 200, and 300 milligrams per kilogram of *T. divaricata*, and clusters 5, 6, and 7 got 5, 10, and 30 milligrams per kilogram of fluoxetine, respectively. Mice treated acutely with fluoxetine and *T. divaricata* at doses ranging from very low to very high showed a reduction in marble-burying behaviour but no change in motor activity. In addition, there were no notable adverse effects [63].

3.7. *Clitoria ternatea*

C. ternatea, *Fabaceae*, frequently referred to as Butterfly pea, is a popular Ayurvedic medication that has been utilized for treating a variety of diseases, including anxiety and sadness. "Sankhapushpi," an Ayurvedic medication made from *C. ternatea* roots and seeds, has been utilized as a neurotoxic agent [64]. Recent research suggests it has anxiolytic and antidepressant properties [65]. Although the specific method by which *C. ternatea* exerts its neuropsychiatric effects is still unknown, current investigations show that it could be due to its serotonergic action and may impact 5-HT reuptake [66,67]. An animal study found that ethanolic extracts of aerial parts might regulate OCD by significantly reducing marble-burying behaviour, analogous to that of fluoxetine. In addition, combining a subeffective dosage of extract with a subeffective dosage of fluoxetine may greatly enhance fluoxetine's anti-OCD efficacy [68]. There is still an inadequate number of scientific trials on its efficacy in psychiatric illnesses like OCD.

3.8. *Citrus aurantium* (Bitter orange)

Bitter orange is a frequent name for the aromatic herb *Citrus aurantium*, which belongs to the Rutaceae family. Immature dried fruit or peel has been used in traditional Chinese medicine to treat neurological conditions like epilepsy, anxiety, and insomnia, as well as indigestion, diarrhoea, and dysentery [68,69]. Bitter oranges are utilised in a variety of food products, including juices, syrups, and marmalades [70,71]. It contains bioactive components like phenols, vitamins, and flavonoids.

The essential oil of *C. aurantium* is primarily composed of linalyl acetate (23%) and linalool (59%) [72]. Augmented time spent in open arms of an elevated plus maze [73] demonstrated that essential oils had anxiolytic effects after a single dose in mice. One research examined the efficacy of *C. aurantium* L. peel essential oil using two standardized tests for GAD and OCD: the light-dark box and the marble-burying test. For 15 days before the trial, mice in a study were given a single oral dose either 30 minutes before the trial or once daily. In a light-dark box test, an essential oil treatment by itself significantly lengthens the duration spent in the light chamber and increases the number of chamber changes. The parameters of the light-dark box remained unchanged after several treatments. Aside from that, both one-time and repeated applications of essential oil treatments reduced marble-burying behaviour. Mice administered single or repeated treatments of essential oil at doses shown to be effective in behavioural tests demonstrated no motor impairment when tested using the rotarod method. Compared to the light-dark box, the marble burial test seems to be more in line with obsessive-compulsive disorder. [74].

3.9. *Crocus Sativus*

Saffron, or *C. sativus*, is a perennial herb that is a member of the Iridaceae family. India, Spain, Iran, Greece, and Italy are among the countries that cultivate this plant [75–76]. Safranal, Picrocrocin, and Crocin are its primary components [77–78]. Crocin had a protective effect on several models of psychiatric illnesses, incorporating depression as well as anxiety [79]. mCPP is a non-selective 5-HT receptor agonist that causes OCD-like behaviour in mice (extreme self-grooming) and intensifies symptoms in OCD patients [80]. One study examined the potential influence of crocin on unnecessary self-grooming produced by 0.6 milligrams per kilo gram mCPP (i.p.) in rats. 30 and 50 milligrams per kilogram of Crocin (i.p.) was found to reduce excessive self-grooming caused by mCPP [81].

3.10. *Curcuma longa* (Turmeric)

A member of the family *Zingiberaceae*, *Curcuma longa* has a long history of flavouring foods. Curcumin, a phytochemical with multiple health benefits that is safe to consume, is its principal active ingredient. It is a naturally occurring polyphenol and has a yellow hue [82–86]. Several reactive oxygen species (ROS) can be neutralized by curcumin. Inhibiting lipid peroxidation in numerous animal models, curcumin demonstrates great promise as a lipid-soluble antioxidant [87–89]. In an investigation, Chimakurthy and Murthy looked at the effects of curcumin on OCD induced by quinpirole. They found that curcumin protects against OCD. Group 1 rats were given a placebo of peanut oil (0.1 milli litre per 100 milligram). Group 2 rats were given no treatment at all. Groups 3, 4, and 5 rats were given oral treatments with 5 and 10 milligrams per kilogram of curcumin and 1.8 milligrams per kilogram of paroxetine, respectively. Except for a control group, all clusters were given quinpirole (0.5 milligrams per kilogram, PO). Curcumin alleviated the OCD symptoms in rats, including the recurrent cleaning and grooming of the snout and the total duration and rate of recurrence of stopping at objects. Dopamine levels were lower in rats given 5 or 10 mg/kg of curcumin, whereas serotonin levels rose only with the 10 mg/kg dose [90].

3.11. *Cannabis Sativa*

C. sativa contains a distinctive group of chemicals referred to as plant cannabinoids or phytocannabinoids. For thousands of years, traditional medicine has employed cannabinoids (CBD) to treat menstruation pain, malaria, rheumatism, and constipation. Cannabinoids have recently been demonstrated to depict hypothermia, catalepsy, anti-inflammatory, and antinociception characteristics [91,92]. The hemp plant's second most prevalent ingredient is cannabinoids. Cannabidiol has shown protective effects in various animal models of mental illness and neurodegeneration, and clinical trials have indicated probable advantages in the treatment of Multiple sclerosis, Amyotrophic lateral sclerosis, Alzheimer's disease, and Parkinson's disease [93]. In a study done by Deiana et al. [94], cannabidiol at a dosage of 120 milligram per kilo gram at 2 hours post-injection reduced marble-burying behaviour, consistent with its pharmacokinetic profile [94].

3.12. *Echium amoenum*

E. amoenum, commonly referred to as *Boraginace* comes from the family *Boraginaceae*. Oxtongue is the Iranian name for this wild annual plant. This herb contains high levels of antioxidants such as rosmarinic acid and flavonoids [95,96]. *E. amoenum* has been demonstrated to have analgesic as well as anti-inflammatory properties, and it is utilized in traditional medicine as an anxiolytic, sedative, and obsessive. Furthermore, it has been suggested to improve mood [97,98]. In a double-blind, parallel-group trial, 44 participants were randomly given either a placebo or *E. amoenum* aqueous extract (500 milligram per kilo gram) for six weeks. Participants were tested before trial and during weeks 1, 2, 4, and 6 by Y-BOCS, the HAM-A, and a score sheet for adverse results. After 4 as well as 6 weeks of treatment, the extract significantly surpassed the placebo group in reducing obsessive, compulsive, and anxious symptoms. There was no statistically substantial variance in side effects between the groups [98].

3.13. *Silybum Marianum*

Milk thistle, or *S. marianum*, has a record of medicinal usage dating back more than two thousand years. The plant exhibited a wide range of beneficial effects, including protecting the liver, reducing inflammation, warding off cancer, and preventing diabetes. The southern regions of Europe, North Africa, and Iran cultivate this native Mediterranean plant [99–101]. Participating in a pilot double-blind randomized study were 35 adults who met diagnostic and statistical manual-IV standards for OCD as determined by a structured clinical interview. Everyone who took the Yale-Brown Scale for OCD had to get a score of 21 or above. Both the extract (600 mg daily) and fluoxetine (30 mg daily) were given to subjects at random for eight weeks. Milk thistle and fluoxetine both had similar therapeutic effects, according to the research. Concerning the reported side effects, there was no statistically substantial variance between two sets of subjects [101].

3.14. *Valeriana Officinalis*

V. officinalis L. (Valerian) comes from the family *Valerianaceae* and possesses sedative [102] and anti-anxiety properties [103]. >400 goods in Germany and a minimum 25 of goods in the UK including

valerian [104]. Valerian's anxiolytic properties have been linked to the existence of sesquiterpenes and monoterpenes [105]. Several putative pathways for *V. officinalis* pharmacological activity have been hypothesized on the basis of its agonistic activities at benzodiazepine, barbiturate, adenosine, and GABA receptors [106,107]. In a double-blind controlled trial, its extract was found to be beneficial in treating OCD may be because of key constituents (shown in Figure 2.) present in the plant. The extract performed more effectively than the placebo. Substantial effects were detected in the extract group on days 28, 42, and 56, indicating the extract's rapid beginning of action. Furthermore, the lower prevalence of libido impairment could be a significant benefit of *V. officinalis* extract. In addition, there was no substantial differentiation in the overall incidence of side effects between the extract and the placebo [108–116].

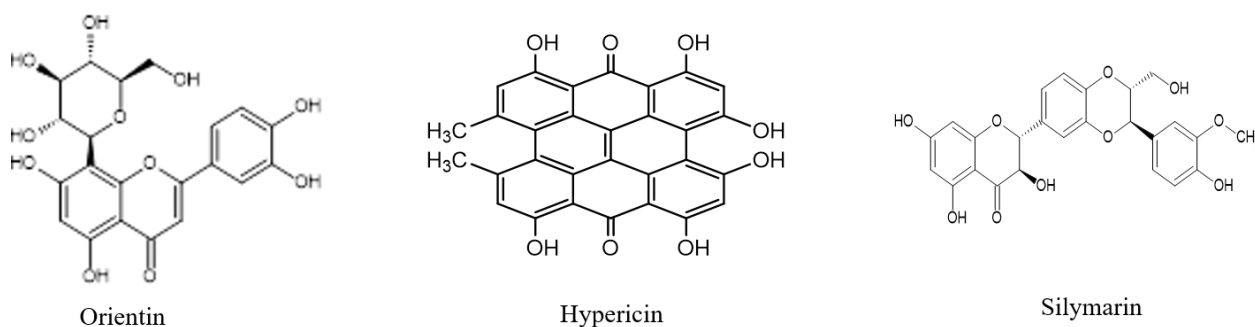


Figure 2. Chemical Structure of some key constituents.

4. Mechanism of Action of OCD active plants

Obsessive-compulsive disorder (OCD) is associated with dysregulation of multiple neurotransmitter systems, particularly serotonin, dopamine, and glutamate within cortico-striato-thalamo-cortical (CSTC) circuits [117–119]. The clinical effectiveness of selective serotonin reuptake inhibitors (SSRIs) strongly supports the involvement of serotonergic dysfunction in OCD pathophysiology [117]. Similarly, the beneficial effects of dopamine D2 receptor antagonists and evidence of glutamatergic abnormalities further indicate the contribution of dopaminergic and glutamatergic systems in disease progression [118,119]. Altered serotonin metabolites in cerebrospinal fluid and genetic variations involving serotonergic pathways have also been linked with OCD susceptibility [117].

Serotonin synthesis begins from tryptophan, which is converted into 5-hydroxytryptophan and subsequently serotonin through the action of tryptophan hydroxylase and aromatic L-amino acid decarboxylase enzymes. Released serotonin is either reabsorbed by serotonin transporters (SERT) or metabolized by monoamine oxidase-A (MAO-A) to maintain neurotransmitter homeostasis [120].

Several medicinal plants exert anti-obsessive effects through modulation of serotonergic neurotransmission (Figure 3). Certain plants enhance serotonin levels, whereas others improve serotonergic signaling by inhibiting serotonin reuptake or MAO activity. In addition to serotonergic modulation, many herbal agents also exhibit antioxidant, anti-inflammatory, anxiolytic, neuroprotective, and adaptogenic properties, which may contribute to their therapeutic potential in

OCD. These multitarget pharmacological actions suggest that plant-based therapies may represent promising alternative or adjunctive approaches for OCD management.

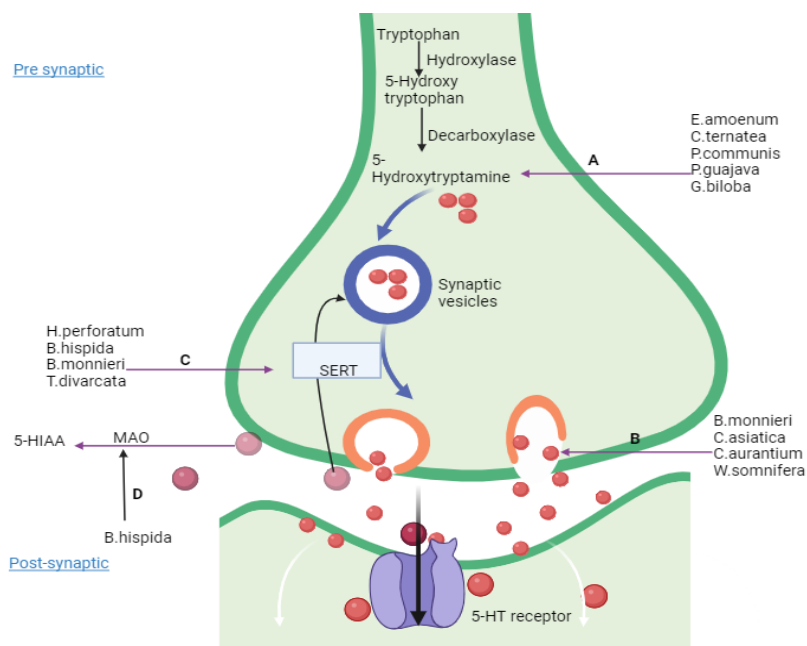


Figure 3. Mechanism of plants having anti-OCD potential. (A-Represents plants that increase serotonin levels, B-Represents plants that increase serotonergic neurotransmission, C- Represents plants that inhibit the reuptake of serotonin, D-Represents plants which inhibit MAO enzyme).

4.1. Preclinical Studies on plants having anti-OCD potential

Herbal medicinal products have recently garnered heightened attention for their application in diverse medical conditions. This renewed interest is largely due to their promising profile of reduced complications and adverse effects compared to conventional synthetic drugs, highlighting their potential as a safer alternative in modern therapeutic regimens [121]. Tables 1 and 2 present a comprehensive summary of plants effective at both pre-clinical and clinical levels for the treatment of OCD. Table 1 includes the plant's scientific name, specific plant part utilized, and extract of plant employed. Additionally, information such as dosage, and the animal models utilized in pre-clinical studies is also provided.

For clinical trials, Table 2 specifies the total number of patients involved, treatment duration, interventions, as well as tolerability and efficacy assessment of treatment. Nineteen studies on animals and six on humans have investigated OCD-active plants thus far. On average, 37 people participated in the trials, and the duration of the trials ranged from 6 to 12 weeks. Y-BOCS was employed to assess the severity of OCD in all clinical trials. Y-BOCS is a valid tool for gauging the intensity as well as the frequency of symptoms in individuals suffering from OCD. Relevant data regarding distress, amount of time spent, resistance, and control over all compulsions and obsessions can be found on this 10-item scale. With a total possible score between 0-40 (no to extremely severe symptoms), each item is given a score between 0 and 4 [122].

Table 1. Pre-clinical studies on using herbal plants for OCD treatment.

Plant	Animal model	Change in number of marbles buried or other changes	Refs
Hydroalcoholic extract of <i>Colocasia esculenta</i> (leaves) 25 and 50 mg/kg i.p.	Marble burying test in male Swiss albino mice	Decreased ($P \leq 0.05$)	31,32
Hydroalcoholic extract of <i>Hypericum perforatum</i> (aerial part) 150 and 300 mg/kg p.o.	Marble burying test in male Swiss albino mice	Substantial reduction ($P < 0.02$)	110
Methanolic extract of <i>Lagenaria siceraria</i> (fruit) 25 and 50 mg/kg i.p.	Marble burying test in male Swiss albino mice	Substantial reduction ($P < 0.001$)	44
Methanolic extract of <i>Benincasa hispida</i> (fruit) 200, 400 and 600 mg/kg i.p.	Marble burying test in male Swiss albino mice	Substantial reduction ($P < 0.001$)	50
Ethanolic extract of <i>Bacopa Monnieri</i> (leaves) 100, 200 and 400 mg/kg p.o.	Marble burying test in male Swiss albino mice	Substantial reduction ($P \leq 0.01$)	128
Methanolic and aqueous extract of <i>Withania somnifera</i> (root) 10, 25, 50 and 100 mg/kg i.p.	Marble burying test in Swiss albino mice	Substantial reduction ($P < 0.001$)	55
Juice of <i>Pyrus communis</i> (fruit) 50% v/v and 100% v/v p.o.	Flickering Light Induced Obsessive-Compulsive behavior in adult Swiss mice	Increase in Serotonin and GABA brain levels and enhanced scavenging of free radicals in brain	58
Ethanolic extract of <i>Tabernaemontana divaricata</i> (leaves) 100, 200 and 300 mg/kg p.o.	Marble burying test in male Swiss albino mice	Substantial reduction ($P < 0.0001$)	63
Ethanolic extract of <i>Psidium guajava</i> (leaves) 200 and 400 mg/kg p.o.	Marble burying test in mice	Elevated the levels of dopamine and 5-HT	129
Extract of <i>Ginkgo biloba</i> (leaf) 50, 100 and 200 mg/kg p.o.	Quinpirole-induced compulsive checking in rats	Increase in serotonin and decrease in dopamine levels in brain	113
Ethanolic extract of <i>Clitorea ternatea</i> (aerial part) 100, 200 and 400 mg/kg p.o.	Marble burying test in male Swiss albino mice	Substantial reduction ($*p \leq 0.05$)	68
Aqueous and ethanolic extract of <i>Centella asiatica</i> (whole plant) 50 and 100 mg/kg p.o.	Marble burying test in mice	Increase serotonergic transmission	130,131
Aqueous extract of <i>Citrus aurantium</i> (fruit) 500 and 1000 mg/kg p.o.	Marble burying test in male Swiss mice	Substantial reduction ($P \leq 0.05$)	74
<i>Crocus sativus</i> 30, 50 mg/kg i.p.	mCPP-induced OCD-like behavior in male Wistar rats	Substantial reduction in number and duration of grooming ($P \leq 0.05$)	81

Continued on next page

Plant	Animal model	Change in number of marbles buried or other changes	Refs
<i>Curcuma longa</i> 5, 10 mg/kg oral	Quinipirole-induced obsessive-compulsive model in male Wistar rats	Substantial reduction in repetitive grooming and cleansing, and rate of recurrent stops at objects ($P < 0.05$)	90
<i>Cannabis sativa</i> 15, 30 and 60 mg/kg i.p.	Marble burying test in male mice	Substantial reduction ($P \leq 0.05$)	132
<i>Psophocarpus tetragonolobus</i> 10, 20 and 40 mg/kg i.p.	Marble burying test in male Swiss albino mice	Substantial reduction ($P < 0.0001$)	133
<i>Vitis vinifera</i> 60 mg/kg i.p.	Marble burying test in male NMRI mice	Activity due to the noradrenergic system	134

While the majority of clinical trials had an equal number of men and women participating, a small number had a significantly higher representation of one gender [123]. Five of the six clinical trials took place in Iran, while the sixth took place in the US. The marble-burying model was utilized in 14 of the 19 pre-clinical studies that examined OCD behaviours. There is no behavioural training necessary to use this famous animal model to evaluate OCD-like behaviours [124]. The animals were housed in a conventional cage with a depth of 5 cm of wood chip bedding and 20 marbles arranged on top for the marble-burying test. Number of marbles buried was recorded after 30 min [125]. One study examined the effects of m-CPP, a non-selective serotonin receptor agonist, on OCD-like behaviour in rats and assessed their level of excessive self-grooming [126]. Using quinpirole-induced compulsive checking, researchers in two separate animal studies recorded and analyzed the animals' behaviours, including how often they stopped, for how long, how many times they visited other objects, and how often they engaged in ritualistic behaviour [127]. Two rat studies evaluated the effectiveness of anti-OCD plants; one used a flickering light model and the other an open field test.

Among the investigated herbal interventions, *Crocus sativus*, *Withania somnifera*, *Valeriana officinalis*, and *Echium amoenum* demonstrated encouraging clinical outcomes, particularly in randomized double-blind placebo-controlled trials using validated assessment tools such as the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Some studies reported reductions in OCD symptom severity comparable to conventional pharmacotherapy, suggesting potential therapeutic benefit and acceptable tolerability. The major strengths of these studies include the use of randomized controlled designs, placebo or active comparator groups, and standardized clinical outcome measures. However, despite these promising findings, the current evidence remains insufficient to support routine clinical use [128,129]. Most studies were limited by relatively small sample sizes, short follow-up duration, single-center study settings, and lack of replication studies. In addition, variability in herbal preparations, extraction methods, dosage regimens, and study methodologies limits comparability and reproducibility across studies. Long-term safety data, pharmacokinetic evaluation, and detailed assessment of herb–drug interactions are also lacking. Therefore, larger multicenter randomized controlled trials with standardized herbal formulations and extended follow-up periods are necessary before these herbal therapies can be routinely recommended in clinical practice [130–133]

Table 2. Clinical studies on the use of herbal plants for OCD treatment.

Drug	Plant extract or part	Study design	Dosage (daily)	Control group	Clinical outcome	No. of participants	Ref
<i>Crocus Sativus</i>	Stigma/extract	10 weeks RDBCT	30 mg ($\pm$ mg fluvoxamine)	Fluvoxamine treated group	Effective and Safe as fluvoxamine ($P = 0.47$)	50	135
<i>Echium amoenum</i>	Flowers/aqueous extract	6 weeks RDBPCT	500 mg	Placebo	Significant Reduction in Y-BOCS score ($P = 0.35$) when compared with placebo	44	98
<i>Silybum marianum</i>	Leaves/methanol extract	Case report (6,8,4 weeks)	300 mg	Fluoxetine treated group	Improved OCD symptoms when compared with fluoxetine treated group	3	136
<i>Valeriana officinalis</i>	Root/ extract	8 weeks RDBPCT	765 mg	Placebo	Significantly improved OCD symptoms ($P < 0.0001$) when compared with placebo	31	108
<i>Withania somnifera</i>	Root/ethanol extract	6 weeks RDBPCT	120 mg	Placebo	Significant reduction in Y-BOCS scale ($P < 0.001$) when compared with placebo	30	60

Note: OCD: Obsessive-compulsive disorder; RDBCT: Randomized double-blind controlled trial; RDBPCT: Randomized, double-blind, placebo-controlled trial. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is a 10-item clinician-administered tool used to rate the severity of obsessive-compulsive disorder (OCD) symptoms. The total score ranges from 0 to 40. If the score is from **0 to 7**: Sub-clinical or minimal symptoms.

5. Discussion

The present review summarizes the available preclinical and clinical evidence regarding herbal medicines and phytochemicals investigated for obsessive-compulsive disorder (OCD). Several medicinal plants, including *Echium amoenum*, *Crocus sativus*, *Valeriana officinalis*, and *Withania somnifera*, demonstrated promising anti-OCD effects in clinical studies, while herbs such as *Hypericum perforatum*, *Centella asiatica*, *Cannabis sativa*, and *Curcuma longa* showed encouraging findings in preclinical models. Most investigated herbal agents appeared to exert their effects through modulation of serotonergic, dopaminergic, and glutamatergic pathways, along with antioxidant, anti-inflammatory, anxiolytic, and neuroprotective activities [134,135].

Among the clinical evidence, *Crocus sativus* demonstrated efficacy comparable to fluvoxamine in a randomized controlled trial, while *Withania somnifera*, *Valeriana officinalis*, and *Echium amoenum* significantly reduced Y-BOCS scores compared with placebo groups. However, despite these encouraging findings, the current evidence remains insufficient to support routine clinical use. Most studies involved small sample sizes, single-center designs, lack of long-term follow-up, and limited replication studies. Although some studies reported significant findings with approximately 30 participants, the statistical power may still be inadequate to reliably detect moderate treatment effects or generalize findings to broader patient populations. In addition, treatment durations of 6–12 weeks may not be sufficient to evaluate long-term efficacy, relapse prevention, and safety in a chronic disorder such as OCD [136–138].

Interestingly, several herbal medicines investigated for OCD are already known for anxiolytic and antidepressant properties. This observation may be clinically relevant, as conventional pharmacotherapy for OCD also commonly utilizes antidepressants, particularly SSRIs. Therefore, medicinal plants with antidepressant and anxiolytic activities may provide therapeutic benefit in OCD through overlapping neurobiological mechanisms.

The review also identified important methodological limitations in existing studies. Considerable heterogeneity exists in herbal preparation methods, extract composition, dosages, outcome measures, and experimental models. Furthermore, several herbs have been evaluated in only a single study, limiting reproducibility and confidence in findings. Mechanisms involving immune modulation, neuroinflammation, oxidative stress, autonomic regulation, and the gut–brain axis remain poorly investigated despite increasing evidence of their involvement in OCD pathophysiology. Future preclinical studies should therefore explore these emerging biological pathways using mechanistic and translational approaches [139].

Safety considerations should also be carefully addressed before integration of herbal medicine into routine OCD management. Although many investigated plants were generally well tolerated, limited data are available regarding long-term toxicity, herb–drug interactions, pharmacokinetic properties, and safety during chronic administration. This is particularly important because herbal therapies may be used alongside SSRIs or other psychotropic medications, increasing the possibility of adverse interactions [140–144].

This review has several strengths. It provides an updated overview of both preclinical and clinical studies on herbal therapies for OCD and summarizes their potential mechanisms of action. In addition, both herbal medicines and isolated phytochemicals were critically evaluated. However, certain limitations should also be acknowledged. The review included only English-language articles and was

conducted as a narrative review rather than a systematic review; therefore, selection bias and incomplete retrieval of all relevant literature cannot be excluded [145–147].

Future research should prioritize well-designed multicenter randomized controlled trials with larger sample sizes, standardized outcome measures, longer follow-up periods, and detailed safety evaluation. Herbs with preliminary positive clinical evidence, such as *Crocus sativus*, *Withania somnifera*, *Valeriana officinalis*, and *Echium amoenum*, require larger confirmatory randomized controlled trials before clinical recommendations can be made. In contrast, herbs currently supported only by animal studies, including *Curcuma longa*, *Cannabis sativa*, *Centella asiatica*, and *Citrus aurantium*, first require phase I safety studies followed by controlled human trials. Further investigations should also focus on mechanisms related to neuroinflammation, immune dysfunction, oxidative stress, and gut microbiota alterations to better understand the therapeutic potential of herbal medicine in OCD management [148–150].

7. Conclusions

Several herbal medicines and phytochemicals, including *Crocus sativus*, *Withania somnifera*, *Valeriana officinalis*, and *Echium amoenum*, demonstrated promising anti-OCD effects in both preclinical and clinical studies. The reported therapeutic effects were primarily associated with modulation of serotonergic and dopaminergic pathways, antioxidant activity, anti-inflammatory effects, and neuroprotective properties. However, the current evidence remains limited because most studies involved small sample sizes, short follow-up periods, single-center designs, and lack of replication studies. In addition, several herbal agents have only been evaluated in animal models, while mechanisms involving immune regulation, neuroinflammation, oxidative stress, and gut–brain interactions remain insufficiently explored.

Future studies should prioritize large multicenter randomized controlled trials with standardized herbal preparations, longer treatment duration, detailed safety evaluation, and consistent outcome measures. Further mechanistic studies investigating immune, inflammatory, endocrine, and microbiota-related pathways may also improve understanding of the therapeutic potential of herbal medicine in OCD management.

Author contributions

Anjali Saini and Sarita Khatkar led the conception and writing of the manuscript, Priyanka Rathee writing review, Sunil Sharma provided background information and contributed to figure design and preparation, Anurag Khatkar and Neelam Malik revised and edited the manuscript. All authors read and approved the final manuscript.

Use of Generative-AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

All authors declare no conflicts of interest in this paper.

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