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Phytotherapy and Plant-derived Bioactive Compounds in Schizophrenia: Preclinical Evidence, Clinical Trials, and Mechanistic Insights: Review

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Abstract

Background: Schizophrenia is a chronic and debilitating neuropsychiatric disorder characterised by positive symptoms, negative symptoms, and cognitive impairments that significantly affect quality of life and functional outcomes. Although antipsychotic medications remain the cornerstone of treatment, their limited efficacy against negative and cognitive symptoms and their associated adverse effects have prompted interest in complementary therapeutic approaches such as phytotherapy. **Aim:** This review aims to critically evaluate the current preclinical and clinical evidence regarding the therapeutic potential of phytotherapeutic agents and plant-derived bioactive compounds in the management of schizophrenia. **Methods:** Relevant literature on phytotherapy in schizophrenia was examined, focusing on preclinical studies, clinical trials, and mechanistic investigations. Key botanical extracts and phytochemicals, including *Withania somnifera*, *Ginkgo biloba*, *Curcuma longa*, *Panax ginseng*, *Bacopa monnieri*, Cannabidiol, and *Centella asiatica*, were assessed for their pharmacological mechanisms, efficacy, safety, and translational relevance. **Results:** The reviewed evidence indicates that several phytotherapeutic agents exhibit antioxidant, anti-inflammatory, neuroprotective, and neuromodulatory properties that target multiple pathways implicated in schizophrenia pathophysiology. Clinical and preclinical studies suggest potential benefits in improving negative symptoms, cognitive deficits, and overall symptom management. Among the reviewed agents, Cannabidiol and *G. biloba* demonstrated the strongest clinical support, while other compounds showed promising but preliminary outcomes. **Conclusion:** Phytotherapy represents a promising adjunctive strategy for schizophrenia by targeting pathophysiological mechanisms inadequately addressed by conventional antipsychotics. However, methodological limitations, including small sample sizes, heterogeneous study designs, and a lack of standardised formulations, limit definitive conclusions. Large-scale randomised controlled trials incorporating standardised extracts, pharmacokinetic assessments, and biomarker-guided outcomes are required to establish the clinical utility of phytotherapeutic interventions in schizophrenia.

Major Findings: The review highlights the therapeutic potential of plant-derived bioactive compounds from medicinal plants as adjunctive therapies for schizophrenia. These agents alleviate cognitive deficits by modulating neurotransmission, and neuroplasticity.

Keywords: Herbal Medicine, Health Risk, Mental Health, Phytotherapy, Psychological Well-being, Schizophrenia

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1. Introduction

Schizophrenia is a complex and disabling psychiatric disorder that affects approximately 1% of the global population and represents one of the leading causes of years lived with disability worldwide. The disorder typically emerges in late adolescence or early adulthood and follows a chronic, relapsing course marked by profound disturbances in perception, cognition, emotion, and behaviour. Clinically, schizophrenia is characterised by three major symptom domains: positive symptoms (hallucinations, delusions, and thought disorder), negative symptoms (blunted affect, anhedonia, avolition, and social withdrawal), and cognitive deficits involving attention, working memory, processing speed, and executive function. Among these, negative and cognitive symptoms are particularly resistant to pharmacological treatment and are strongly associated with poor functional outcomes[1].

Since the introduction of chlorpromazine in the mid-20th century, antipsychotic medications have remained the cornerstone of schizophrenia treatment. Both first-generation and second-generation antipsychotics exert their primary therapeutic effects through antagonism or partial agonism at dopamine D_2 receptors. While these agents are effective in reducing positive symptoms, their impact on negative and cognitive symptoms is modest, and up to one-third of patients are considered treatment-resistant. Furthermore, long-term antipsychotic use is frequently associated with adverse effects such as extrapyramidal symptoms, metabolic syndrome, weight gain, cardiovascular risk, sedation, and hyperprolactinemia, which contribute to poor adherence and reduced quality of life[2].

Growing recognition of the limitations of conventional pharmacotherapy has led to an increased interest in complementary and integrative approaches for schizophrenia. Among these, phytotherapy, the therapeutic use of plants, plant extracts, and plant-derived bioactive compounds, has gained particular attention. Traditional medical systems, including *Ayurveda*, Traditional Chinese Medicine, and various ethnomedical practices, have long utilised botanical agents for mental and cognitive disorders. Advances in phytochemistry, neuropharmacology, and molecular neuroscience have enabled systematic investigation of these agents within modern scientific frameworks[3].

Importantly, phytotherapeutic agents often exert multi-target effects, simultaneously modulating oxidative stress, neuroinflammation, neurotransmitter systems, mitochondrial function, and neuroplasticity. Such pleiotropic actions are particularly relevant to schizophrenia, which is increasingly understood as a disorder involving widespread neurobiological dysregulation rather than a single neurotransmitter imbalance. As a result, phytotherapy has been explored primarily as an adjunctive strategy aimed at enhancing symptom control, improving cognitive function, reducing adverse effects, and potentially modifying disease progression[4]. The present review provides a comprehensive and critical overview of phytotherapy research in schizophrenia, encompassing both botanical extracts and isolated phytochemicals. By integrating evidence from preclinical models, clinical trials, and mechanistic studies, this review aims to clarify the therapeutic potential, limitations, and future directions of phytotherapeutic interventions in schizophrenia.

2. Materials and Methods

2.1 Literature Search Strategy

A comprehensive and systematic literature search was conducted to identify relevant studies investigating phytotherapeutic agents in schizophrenia. Electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, were searched for articles published up to January 2025. Search terms included combinations of the following keywords: schizophrenia, psychosis, phytotherapy, herbal medicine, plant extract, phytochemical, nutraceutical, clinical trial, randomised controlled trial, animal model, and mechanism. Boolean operators ("AND", "OR") were applied to refine the search. In addition, reference lists of relevant review articles and meta-analyses were manually screened to identify additional studies not captured by database searches. Clinical trial registries were also reviewed to identify ongoing or unpublished trials.

2.2 Inclusion and Exclusion Criteria

Studies were included if they met one or more of the following criteria:

i. Randomised controlled trials or open-label clinical studies evaluating phytotherapeutic agents in patients

diagnosed with schizophrenia or schizoaffective disorder.
ii. Preclinical studies using validated animal or cellular models relevant to schizophrenia pathophysiology.
iii. Mechanistic studies elucidating molecular, biochemical, or neuropharmacological actions of plant-derived compounds relevant to schizophrenia.

Studies were excluded if they:

i. Focused exclusively on non-psychotic psychiatric disorders.
ii. Investigated synthetic compounds not derived from plant sources.
iii. Lacked relevance to schizophrenia symptom domains or mechanisms.
iv. Were case reports without experimental or clinical rigour.

2.3 Data Extraction and Synthesis

Data extracted from relevant studies included study design, sample size, intervention type and dosage, treatment duration, outcome measures, key findings, and reported adverse effects. Due to the substantial heterogeneity in study designs, interventions, and outcome assessments, the findings were synthesised using a narrative approach rather than a quantitative meta-analysis.

3. Results

Consistent with the predefined inclusion criteria and narrative review methodology, the selected literature provided converging evidence from randomised controlled trials, open-label clinical studies, and validated preclinical models. The literature search identified methodologically relevant studies investigating standardised botanical extracts and isolated phytochemicals as adjunctive therapeutic interventions for schizophrenia. Across the included studies, outcomes were evaluated using symptom rating scales, cognitive performance assessments, and biological markers associated with oxidative stress and neuroinflammation. Overall, the findings indicated modest yet consistent improvements in negative symptoms and cognitive function, accompanied by reductions in oxidative and inflammatory biomarkers. Although heterogeneity in study designs, interventions, and outcome measures precluded quantitative meta-analysis, the structured study selection and synthesis approach ensured a comprehensive evaluation of clinically and mechanistically relevant evidence.

3.1 Pathophysiological Basis for Phytotherapy in Schizophrenia-Neurotransmitter Dysregulation

The classical dopamine hypothesis of schizophrenia posits that hyperactivity of mesolimbic dopamine pathways contributes to positive symptoms, while hypoactivity in mesocortical pathways underlies negative and cognitive symptoms. However, this model does not fully account for the complexity of the disorder. Glutamatergic dysfunction, particularly hypofunction of N-Methyl-D-Aspartate (NMDA) receptors, has been implicated in both positive and cognitive symptoms, while Gamma-Aminobutyric Acid (GABA) interneuron deficits contribute to impaired cortical synchronisation. Serotonergic and cholinergic systems further modulate these networks[5]. Phytochemicals frequently interact with multiple neurotransmitter systems. For example, ginsenosides influence dopaminergic and glutamatergic signalling, withanolides modulate GABAergic tone, and cannabidiol (CBD) indirectly affects dopamine transmission through endocannabinoid pathways. Such multi-system modulation may complement the narrow receptor targets of conventional antipsychotics[5].

3.2 Oxidative Stress and Mitochondrial Dysfunction

Accumulating evidence indicates that schizophrenia is associated with elevated oxidative stress and impaired antioxidant defence mechanisms. Increased lipid peroxidation, reduced glutathione levels, and mitochondrial abnormalities have been reported in patients, particularly during early stages of illness. Oxidative damage can impair synaptic plasticity, neuronal integrity, and neurotransmission, contributing to cognitive decline and disease progression. Many plant-derived compounds, including flavonoids, polyphenols, and terpenoids, possess potent antioxidant properties. Flavonoids of *C. longa*, and *G. biloba*, bacosides from *B. monnieri* have been shown to scavenge reactive oxygen species, enhance endogenous antioxidant enzymes, and protect mitochondrial function[1,5].

3.3 Neuroinflammation and Immune Dysregulation

Neuroinflammation is increasingly recognised as a key contributor to the pathophysiology of schizophrenia. Elevated concentrations of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ), have been reported in the peripheral blood and cerebrospinal fluid of individuals with schizophrenia. Furthermore, microglial activation and dysregulated immune signalling are thought to contribute to aberrant synaptic pruning, impaired neurodevelopment, and altered neuronal connectivity, particularly during critical developmental periods. Several phytotherapeutic agents exhibit immunomodulatory and anti-inflammatory properties that may mitigate these pathological processes. Curcumin has been shown to suppress nuclear factor-kappa B (NF-κB) signalling, *W. somnifera* attenuates stress-induced inflammatory responses, and ginsenosides from *P. ginseng* regulate microglial activation. Collectively, these mechanisms highlight the potential of phytotherapeutic interventions as neuroprotective strategies for schizophrenia, particularly in the context of early intervention and disease modification[3].

3.4 Neuroplasticity and Neurotrophic Factors

Deficits in neuroplasticity and reduced expression of brain-derived neurotrophic factor (BDNF) have been implicated in the pathophysiology of schizophrenia, particularly in relation to cognitive impairment. Enhancing neurotrophic signalling represents a promising therapeutic strategy for improving cognitive outcomes. Several phytochemicals have been shown to increase BDNF expression and promote synaptic plasticity in preclinical models. These neuroprotective effects may contribute to the observed improvements in learning, memory, and cognitive flexibility associated with certain botanical interventions[4,6].

4. Phytotherapeutic Agents Investigated in Schizophrenia

Phytotherapeutic research in schizophrenia encompasses a diverse range of botanical medicines and isolated plant-derived bioactive compounds. These agents are primarily investigated as adjunctive therapies to conventional antipsychotic medications, with the objectives of improving symptom management, particularly negative and cognitive symptoms, reducing treatment-related adverse effects, and targeting underlying pathophysiological mechanisms beyond dopaminergic dysfunction. Among the most extensively studied phytotherapeutic agents are *W. somnifera* (*Ashwagandha*), *G. biloba*, curcumin derived from *C. longa*, ginsenosides from *P. ginseng*, *B. monnieri*, CBD, and *C. asiatica*. The following sections discuss these agents with respect to their pharmacological properties, preclinical evidence, clinical efficacy, and potential translational significance in schizophrenia management.

4.1 *Withania somnifera* (*Ashwagandha*)

4.1.1 Botany and Phytochemistry

Withania somnifera (Family: *Solanaceae*) is a medicinal plant widely used in *Ayurvedic* medicine owing to its adaptogenic, anxiolytic, and neuroprotective properties. Its principal bioactive constituents are steroidal lactones, collectively known as withanolides, including withaferin A and withanoside IV. These compounds exert diverse pharmacological effects through the modulation of neurotransmission, stress-response pathways, and immune function effectively.

4.1.2 Mechanistic Rationale

Multiple mechanisms support the putative utility of *Withania* in schizophrenia:

4.1.2.1 Modulation of GABAergic and Cholinergic Systems

Withanolides exhibit affinity for $GABA_A$ receptors and may modulate acetylcholine release, which is relevant to anxiety and cognition.

4.1.2.2 Hypothalamic-Pituitary-Adrenal (HPA) Axis Regulation

Ashwagandha has been shown to reduce stress-induced elevations in corticosterone in animal models, potentially alleviating stress-related exacerbations of schizophrenia symptoms.

4.1.2.3 Antioxidant and Anti-inflammatory Actions

By attenuating oxidative stress and pro-inflammatory cytokines, *Withania* may counteract neurobiological disturbances implicated in schizophrenia.

4.1.3 Preclinical Evidence

In rodent models, *Withania* extracts demonstrate antipsychotic-like effects. In the amphetamine-induced hyperlocomotion model, which mimics positive symptoms via dopaminergic hyperactivity, withanolide-rich extracts attenuated hyperlocomotion comparably to low-dose haloperidol, suggesting dopamine-modulatory effects. Furthermore, in NMDA receptor antagonist (Ketamine or Phencyclidine (PCP)) models, which recapitulate negative and cognitive symptoms, *Withania* normalised social interaction deficits and preserved working memory in maze-based tasks. Finally, biomarker studies indicate reductions in lipid peroxidation products and an increase in superoxide dismutase activity, supporting neuroprotective effects.

4.1.4 Clinical Evidence

Clinical research on *Withania* as adjunctive therapy, though limited, is encouraging. Randomised controlled trials involving *ashwagandha* extract - Standardised by withanolide content - added to antipsychotic therapy have reported significant improvements in negative symptom scores on standardised scales - Positive and Negative Syndrome Scale (PANSS) and Scale for the Assessment of Negative Symptoms (SANS) compared with placebo. Reports also note enhanced cognitive performance, specifically in working memory, processing speed and reduced stress/anxiety symptoms. Finally, safety and tolerability are generally favourable, with sedation and mild gastrointestinal discomfort being the most common adverse events.

4.1.5 Summary and Integration

Ashwagandha's multi-target pharmacology-spanning neurotransmitter modulation, stress-axis regulation, antioxidant activity, and anti-inflammatory effects make it a compelling candidate for adjunctive treatment, particularly for negative symptoms and cognitive deficits, which are poorly addressed by current antipsychotics[7,8]. However, larger, multicenter randomised controlled trials (RCTs) with standardised extracts and biomarkers are required to confirm efficacy.

4.2 *Ginkgo biloba*

4.2.1 Botanical Profile and Active Components

Ginkgo biloba is an ancient tree species whose leaf extracts contain flavonoid glycosides and ginkgolides with potent antioxidant and vasoprotective properties. Standardised preparations, particularly *G. biloba* extract 761 (EGb761), provide reproducible concentrations of these bioactive constituents, ensuring consistency in pharmacological activity and clinical efficacy.

4.2.2 Mechanisms of Action

The proposed mechanisms of *G. biloba* relevant to schizophrenia include the antioxidant and free radical scavenging activity, which may counteract the elevated oxidative stress associated with disease progression. Additionally, its role in neurovascular modulation and enhancement of microcirculation can potentially improve cerebral perfusion and support cognitive function. Finally, the herb is thought to modulate neurotransmitter systems, including mild inhibition of monoamine oxidase activity and regulation of dopaminergic and serotonergic signalling pathways.

4.2.3 Preclinical Evidence

Preclinical studies have demonstrated that *G. biloba* extracts reduce N-methyl-D-aspartate (NMDA) receptor antagonist-induced cognitive deficits and social withdrawal behaviours, normalise biomarkers of oxidative damage - such as malondialdehyde levels, in the prefrontal cortex and hippocampus and also enhance hippocampal brain-derived neurotrophic factor (BDNF) expression, thereby promoting neuroplasticity and neuronal survival.

4.2.4 Clinical Evidence

Clinical investigations of *G. biloba* in schizophrenia have primarily focused on its use as an adjunctive therapy. Meta-analyses of randomised, double-blind, placebo-controlled trials have shown that *G. biloba* supplementation, when combined with antipsychotic treatment, improves both positive and negative symptom scores compared with placebo. Several studies have reported improvements in cognitive performance, particularly in attention and executive function; however, findings remain inconsistent across trials. Available safety data indicate that the extract is generally well tolerated. Nevertheless, it may interact with antiplatelet and anticoagulant medications, potentially increasing the risk of bleeding and warranting careful clinical monitoring.

4.2.5 Summary and Integration

The strength of evidence for *G. biloba* lies in moderate-sized clinical RCTs demonstrating symptom reduction when used adjunctively. Its multimodal mechanisms-including antioxidation, neurovascular enhancement, and weak neurotransmitter modulation-are well aligned with schizophrenia's pathobiology. Future studies should stratify participants by symptom profiles and include cognitive endpoints as primary outcomes[9,10].

4.3 Curcumin (*Curcuma longa*)

4.3.1 Phytochemistry and Pharmacokinetics

Curcumin, the principal polyphenolic constituent of *C. longa* (turmeric), possesses potent antioxidant, anti-inflammatory, and neuroprotective properties. However, its clinical application is limited by poor oral bioavailability, rapid metabolic degradation, and restricted penetration across the blood-brain barrier. To overcome these limitations, several advanced formulations, including piperine-enhanced preparations, liposomal systems, and nanoparticle-based delivery platforms, have been developed to improve its absorption, bioavailability, and central nervous system (CNS) distribution.

4.3.2 Mechanistic Rationale

In the context of schizophrenia, curcumin's mechanisms include the inhibition of Nuclear Factor Kappa B (NF-κB) signalling, which reduces pro-inflammatory cytokines implicated in neuroinflammation. Its potent antioxidant actions counteract free radical-mediated neuronal damage. Furthermore, it upregulates the modulation of BDNF and Cyclic Adenosine Monophosphate (cAMP) response Element-Binding Protein (CREB) pathways, which support synaptic plasticity and cognitive function. Finally, it is involved in neurotransmitter modulation, including potential regulation of glutamatergic and dopaminergic systems.

4.3.3 Preclinical Evidence

Preclinical models demonstrate that curcumin attenuates ketamine-induced cognitive and social deficits in rodents. It reduces oxidative markers and restores antioxidant enzyme levels in the prefrontal cortex and hippocampus region. Furthermore, it normalises dopamine turnover ratios and modulates glutamate receptor expression in key brain regions, thereby enhancing performance in memory and executive function tests, including T-maze and novel object recognition tasks.

4.3.4 Clinical Evidence

While curcumin's clinical study in schizophrenia remains limited, small pilot trials have investigated adjunctive curcumin formulations in early-stage schizophrenia. This preliminary evidence shows modest improvement in negative symptoms and cognitive scales, making these bioavailability-enhanced formulations more promising; however, replication in larger RCTs is necessary. Curcumin is generally well tolerated, although gastrointestinal discomfort and interactions with anticoagulants have been reported.

4.3.5 Summary and Integration

Curcumin's pleiotropic actions, particularly anti-inflammatory and neuroplasticity-enhancing properties, directly address mechanistic targets increasingly recognised in schizophrenia. However, the bioavailability challenge and paucity of large clinical trials represent significant translational hurdles. Curcumin may be most promising as part of multi-component treatment regimens[11].

4.4 *Panax ginseng* and Ginsenosides

4.4.1 Phytochemistry

Panax ginseng contains a group of bioactive steroidal saponins known as ginsenosides, which are primarily responsible for its pharmacological activities. These compounds exert diverse effects on the central nervous system, including antioxidant, anti-inflammatory, neuroprotective, and neuromodulatory actions. Furthermore, ginsenosides have been shown to regulate neurotransmitter signalling, enhance neuroplasticity, and improve cognitive functions such as learning, memory, and attention, making them promising candidates for the management of neuropsychiatric disorders, including schizophrenia.

4.4.2 Mechanistic Rationale

Ginsenosides of *P. ginseng* exert neuroprotective actions through antioxidation and anti-inflammatory pathways, as well as the modulation of neurotransmitter

systems, including dopamine and glutamate, potentially mitigating dysregulated signalling implicated in schizophrenia. Furthermore, these bioactive compounds enhance synaptic plasticity, possibly via upregulation of neurotrophic factors like BDNF.

4.4.3 Preclinical Evidence

In animal models relevant to schizophrenia, ginsenosides reverse amphetamine-induced hyperlocomotion and validate improvements in social interaction deficits. These behavioural improvements in cognitive tasks are accompanied by reductions in oxidative stress and normalisation of glutamate receptor expression. Specifically, Ginsenoside Rb1 and Ginsenoside Rg3 (Rb1 and Rg3) have demonstrated anti-inflammatory effects in microglial cultures, reducing cytokine release.

4.4.4 Clinical Evidence

Clinical investigations in schizophrenia are sparse but suggest adjunctive *ginseng* extracts may improve subjective cognitive outcomes and global functioning when added to antipsychotics. Positive symptom reduction trends were observed in open-label studies, but require confirmation in controlled trials.

4.4.5 Summary and Integration

Panax ginseng contains bioactive steroidal saponins, known as ginsenosides (particularly Rb1 and Rg3), which possess neuroprotective, antioxidant, and anti-inflammatory properties. Preclinical studies using schizophrenia-relevant models have demonstrated that ginsenosides can attenuate amphetamine-induced hyperlocomotion, improve social interaction deficits, and enhance performance in cognitive tasks. Mechanistically, these compounds modulate dopaminergic and glutamatergic neurotransmission, suppress microglial activation, and upregulate neurotrophic factors such as BDNF, thereby promoting neuroplasticity and neuronal survival. Although clinical evidence remains limited, available studies suggest that *P. ginseng* may improve cognitive performance and overall functional outcomes when used as an adjunct to antipsychotic therapy. Its pharmacological profile aligns closely with the multifactorial pathophysiology of schizophrenia by targeting oxidative stress, neuroinflammation, neurotransmitter dysregulation, and impaired neuroplasticity. These effects may be particularly beneficial for cognitive deficits and negative symptoms, which are often inadequately addressed by conventional dopamine receptor antagonists. However, current clinical findings are preliminary, and variability in extract composition and standardisation limits direct comparisons across studies. Therefore, large-scale, randomised, placebo-controlled clinical trials employing chemically standardised ginseng preparations and well-defined cognitive endpoints are required to establish its therapeutic efficacy and translational potential in schizophrenia management[12].

4.5 *Bacopa monnieri*

4.5.1 Phytochemistry

Bacopa monnieri is a medicinal herb widely used in *Ayurvedic* medicine for its cognitive-enhancing and neuroprotective properties. Its principal bioactive constituents, known as bacosides, exhibit potent antioxidant, anti-inflammatory, and neuromodulatory activities. Preclinical and clinical studies suggest that *B. monnieri* may improve learning, memory, attention, and overall cognitive performance through the modulation of neuroplasticity and neurotransmitter function.

4.5.2 Mechanistic Rationale

Bacosides may enhance synaptic transmission and plasticity by modulating cholinergic and glutamatergic pathways, which reduce oxidative stress, protecting neurons from free radical-induced damage and stimulate hippocampal neurogenesis, supporting memory and learning processes.

4.5.3 Preclinical Evidence

In animal models, *Bacopa* extracts improve performance in learning and memory tasks impaired by NMDA antagonists, where reductions in oxidative biomarkers have been correlated with cognitive improvements. Some studies suggest enhancement of cholinergic transmission, relevant to cognitive symptoms.

4.5.4 Clinical Evidence

Clinical evidence in schizophrenia remains limited; however, preliminary adjunctive studies suggest potential cognitive benefits of *B. monnieri*. Small clinical trials have reported improvements in cognitive

performance when *B. monnieri* is administered alongside standard antipsychotic therapy. The most consistently reported benefits include enhanced memory recall, attention, and information-processing speed. These findings indicate the potential utility of *B. monnieri* in addressing cognitive deficits associated with schizophrenia, although larger randomised controlled trials are needed to confirm its efficacy.

4.5.5 Summary and Integration

Bacopa monnieri is an *Ayurvedic* medicinal herb rich in bacosides, a class of bioactive compounds known for their cognitive-enhancing, antioxidant, and neuroprotective properties. Preclinical studies have demonstrated that *B. monnieri* attenuates NMDA receptor antagonist-induced cognitive deficits, improves learning and memory performance, and reduces oxidative stress in the hippocampus and prefrontal cortex. Mechanistically, bacosides modulate cholinergic and glutamatergic neurotransmission, enhance synaptic plasticity, and promote neurotrophic signalling. Limited clinical studies suggest that adjunctive *B. monnieri* may improve memory recall, attention, and information-processing speed in individuals receiving antipsychotic therapy. Given its ability to target cognitive dysfunction and oxidative stress, two key features inadequately addressed by conventional antipsychotics. *B. monnieri* represents a promising adjunctive therapeutic candidate. However, further large-scale, randomised controlled trials employing standardised formulations and clinically relevant cognitive endpoints are required to establish its efficacy in schizophrenia management[13].

4.6 Cannabidiol (CBD)

4.6.1 Phytochemistry

CBD is a non-intoxicating phytocannabinoid derived from *Cannabis sativa*. Unlike Δ^9-tetrahydrocannabinol (THC), the principal psychoactive constituent of *Cannabis*, CBD does not produce psychotomimetic or euphoric effects. Emerging preclinical and clinical evidence suggests that CBD possesses antipsychotic, anti-inflammatory, antioxidant, and neuroprotective properties, making it a promising therapeutic candidate for the management of schizophrenia and related neuropsychiatric disorders.

4.6.2 Mechanistic Rationale

The proposed mechanisms of CBD relevant to schizophrenia include modulation of the endocannabinoid system, primarily through inhibition of fatty acid amide hydrolase (FAAH), resulting in increased anandamide levels and indirect regulation of cannabinoid receptors (CB_1 and CB_2). Additionally, CBD exhibits serotonergic modulation, including partial agonistic activity at 5-hydroxytryptamine 1A (5-HT1A) receptors, which may contribute to its anxiolytic and antipsychotic effects. It also attenuates glutamatergic excitotoxicity and neuroinflammation, thereby reducing neuronal damage and inflammatory responses associated with schizophrenia. Finally, its neuroprotective and antioxidant effects are potentially mediated through activation of peroxisome proliferator-activated receptor gamma (PPARγ) and other intracellular signalling pathways involved in neuronal survival and plasticity.

4.6.3 Preclinical Evidence

Rodent models show that CBD reduces amphetamine- and PCP-induced hyperlocomotion, improves social interaction and cognitive performance and normalises aberrant firing patterns in prefrontal cortex neurons.

4.6.4 Clinical Evidence

CBD has one of the strongest clinical profiles among phytotherapeutics. Randomized, double-blind studies demonstrated that oral CBD (600-800 mg/day) significantly reduces positive and negative symptoms compared with placebo. Furthermore, some trials reported improved cognitive scores and enhanced global functioning. Noteably, CBD displays an excellent safety profile with minimal sedation or metabolic adverse effects.

4.6.5 Summary and Integration

Cannabidiol (CBD) is a non-intoxicating phytocannabinoid derived from *C. sativa* with demonstrated antipsychotic-like properties. Preclinical models show that CBD reduces amphetamine and PCP-induced hyperlocomotion, improves social behaviour, and normalises cognitive deficits. Mechanistically, CBD modulates endocannabinoid signalling, indirectly influences CB_1/CB_2 receptors, enhances 5-HT1A

serotonergic activity, reduces neuroinflammation, and may regulate glutamatergic transmission. Randomised controlled trials in schizophrenia report significant improvements in positive and negative symptoms, with emerging evidence for cognitive benefits. CBD is generally well tolerated, with minimal extrapyramidal or metabolic adverse effects. CBD demonstrates the strongest clinical support among phytotherapeutic agents in schizophrenia. Its multi-system modulation aligns with contemporary neurobiological models extending beyond dopamine dysregulation. Importantly, its favourable safety profile and lack of psychotomimetic effects distinguish it from Δ^9-THC. While adjunctive use shows promise, further large-scale trials, dose-optimisation studies, and pharmacokinetic evaluations are needed to clarify long-term efficacy and integration into evidence-based schizophrenia management[14].

4.7 *Centella asiatica*

4.7.1 Phytochemistry

Centella asiatica contains bioactive triterpenoid saponins, including asiaticoside, madecassoside, asiatic acid, and madecassic acid, which are responsible for its pharmacological activities. These compounds exhibit potent antioxidant, anti-inflammatory, and neuroprotective properties and have been shown to promote neurite outgrowth, synaptic plasticity, and neuronal regeneration. Furthermore, *C. asiatica* may enhance cognitive function and memory by modulating neurotrophic signalling pathways and reducing oxidative stress-induced neuronal damage.

4.7.2 Mechanistic Rationale

Proposed actions include augmentation of antioxidant defences, neurotrophic support, and potentially enhancing neuronal repair and connectivity.

4.7.3 Preclinical Evidence

Animal studies indicate improvement in cognitive and social behaviours in NMDA antagonist models. However, clinical evidence is currently limited.

4.7.4 Summary and Integration

Centella asiatica is a medicinal herb containing triterpenoid saponins such as asiaticoside and madecassoside, which exhibit antioxidant, anti-inflammatory, and neuritogenic properties. In preclinical schizophrenia-relevant models, *Centella* improves cognitive performance, enhances social behaviours, and reduces oxidative stress markers in cortical and hippocampal regions. Mechanistically, it supports neurotrophic signalling, promotes dendritic growth, and may enhance synaptic plasticity. Human evidence in schizophrenia remains limited, though cognitive-enhancing effects have been observed in other neuropsychiatric populations. *Centella asiatica* aligns with therapeutic strategies targeting cognitive impairment and neuroplastic deficits in schizophrenia. Its antioxidant and neurotrophic actions address mechanisms poorly targeted by conventional antipsychotics. However, the absence of robust randomised clinical trials in schizophrenia limits definitive conclusions. Standardised extracts, biomarker-guided studies, and cognitive-focused endpoints are needed to clarify its adjunctive role and translational relevance in schizophrenia treatment[15].

4.8 Comparative Analysis of Phytotherapeutic Agents

The present review highlights the growing potential of phytotherapeutic agents as adjunctive interventions for schizophrenia, a complex neuropsychiatric disorder characterised by positive symptoms, negative symptoms, and cognitive impairments. The evidence gathered from preclinical and clinical studies indicates that plant-derived compounds possess diverse pharmacological properties that target multiple pathological mechanisms implicated in schizophrenia. Unlike conventional antipsychotic medications, which primarily modulate dopaminergic pathways and often show limited efficacy against cognitive and negative symptoms, phytotherapeutic agents exhibit broader biological activities, including antioxidant, anti-inflammatory, neuroprotective, and neuromodulatory effects.

Among the reviewed agents, CBD and *G. biloba* demonstrate the strongest clinical support, with controlled studies reporting improvements in symptom severity, cognitive performance, and overall tolerability. Other phytotherapeutic candidates, including *W. somnifera*, *C. longa*, *P. ginseng*, *B. monnieri*, and *C. asiatica*, have shown promising outcomes in experimental and early clinical investigations. These

agents exert their therapeutic effects through modulation of oxidative stress, attenuation of neuroinflammation, regulation of neurotransmitter systems, enhancement of neuroplasticity, and promotion of neurotrophic signalling pathways. Such multi-target mechanisms are particularly advantageous in schizophrenia, where the underlying pathophysiology involves complex interactions among oxidative imbalance, immune dysregulation, neurotransmitter abnormalities, and impaired neuronal connectivity.

The review further suggests that phytotherapeutic agents with neurotrophic and cholinergic activities, particularly *B. monnieri*, *C. asiatica*, and *P. ginseng*, may offer additional benefits in addressing cognitive dysfunction, one of the most disabling and treatment-resistant aspects of schizophrenia. Improvements in memory, attention, and executive function observed in preclinical studies support their potential role in enhancing functional outcomes and quality of life. Furthermore, the favourable safety profiles associated with many plant-derived compounds make them attractive candidates for long-term adjunctive use alongside conventional antipsychotic therapies.

Despite these encouraging findings, several challenges continue to limit the clinical translation of phytotherapy in schizophrenia. Variability in plant sources, extraction methods, formulation composition, dosage regimens, and bioavailability contributes to inconsistencies across studies. Standardisation remains a critical concern, particularly for complex herbal extracts and compounds such as curcumin, which exhibit poor pharmacokinetic properties. Additionally, many existing clinical studies are constrained by small sample sizes, short treatment durations, heterogeneous methodologies, and insufficient evaluation of long-term efficacy and safety.

Overall, the collective evidence supports the therapeutic promise of phytotherapeutic agents as multi-target adjunctive strategies for schizophrenia management. As illustrated in Figure 1, phytotherapeutic agents including *W. somnifera*, *G. biloba*, *C. longa*, *P. ginseng*, *C. asiatica*, CBD, and *B. monnieri* exert antioxidant, anti-inflammatory, neuroprotective, and neuromodulatory effects that collectively target key pathological pathways involved in schizophrenia. By modulating oxidative stress, neuroinflammation, neurotransmitter dysregulation, and impaired neuroplasticity, these agents may contribute to improvements in positive symptoms, negative symptoms, and cognitive deficits. However, definitive clinical recommendations require validation through large-scale, rigorously designed randomised controlled trials employing standardised formulations, pharmacokinetic assessments, biomarker-guided

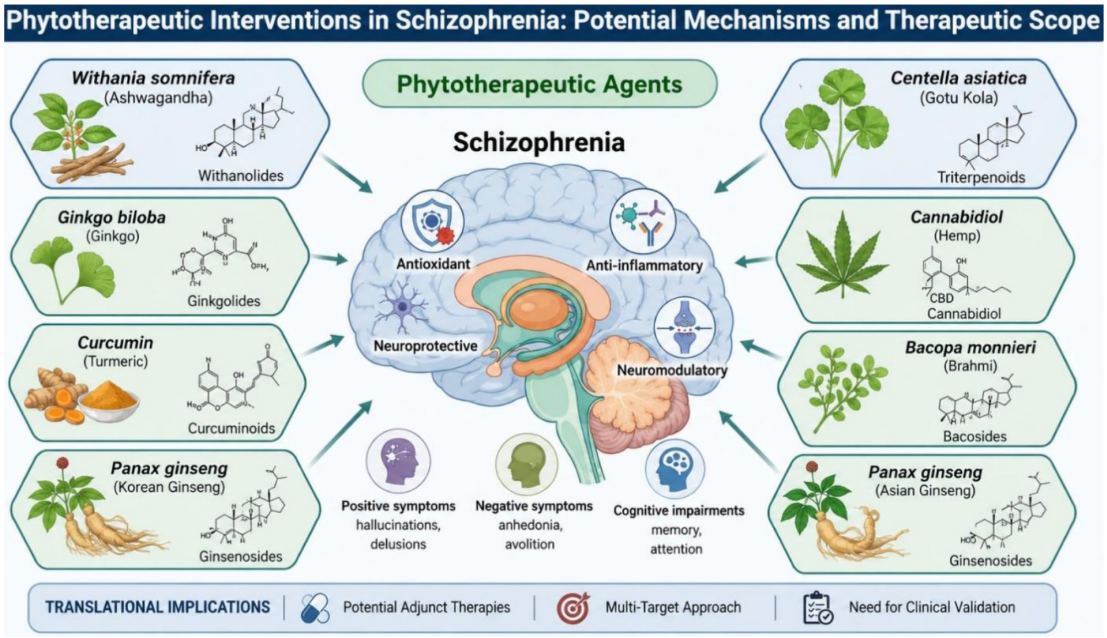


Figure 1. The schematic illustrates the potential therapeutic role of phytotherapeutic agents in schizophrenia.

approaches, and clinically meaningful outcome measures. Addressing these limitations will be essential for integrating phytotherapy into evidence-based psychiatric practice and realising its full therapeutic potential[16-18].

5. Discussion

The present review synthesises available preclinical and clinical evidence supporting the potential role of phytotherapy and plant-derived bioactive compounds in the management of schizophrenia. Collectively, the findings indicate that several botanical agents possess antipsychotic, neuroprotective, antioxidant, and anti-inflammatory properties, with the potential to improve symptom domains that are often inadequately addressed by conventional pharmacotherapy, particularly negative symptoms and cognitive deficits. Importantly, the therapeutic value of phytotherapy lies not in replacing standard antipsychotic medications but in complementing existing treatment strategies through multi-target mechanisms that address the complex and multifactorial neurobiology of schizophrenia.

5.1 Multi-target Mechanisms and Pathophysiological Relevance

Unlike conventional antipsychotic medications, which primarily exert their therapeutic effects through dopamine D_2 receptor antagonism, phytotherapeutic agents target multiple neurobiological pathways implicated in the pathogenesis of schizophrenia. Growing evidence indicates that oxidative stress, neuroinflammation, glutamatergic dysregulation, impaired neuroplasticity, mitochondrial dysfunction, and abnormalities in stress-response systems contribute significantly to disease onset and progression. In this context, several plant-derived compounds offer a broader pharmacological spectrum that may complement existing therapeutic approaches.

Phytotherapeutic agents such as curcumin, *G. biloba*, and *W. somnifera* possess potent antioxidant and anti-inflammatory properties that can mitigate neuronal damage associated with chronic oxidative and inflammatory stress. Similarly, CBD and ginsenosides derived from *P. ginseng* modulate glutamatergic, serotonergic, and endocannabinoid signalling pathways, which are increasingly recognised as key contributors to schizophrenia-related symptomatology. Furthermore, several botanical compounds have demonstrated the ability to enhance BDNF expression, promote synaptic plasticity, and support neuronal survival, thereby addressing cognitive dysfunction and impaired neuroplasticity.

The pleiotropic nature of these phytochemicals may offer particular advantages in schizophrenia, a disorder characterised by considerable symptom heterogeneity and complex underlying pathophysiology. By simultaneously targeting multiple molecular and cellular mechanisms, phytotherapeutic agents have the potential to improve not only positive symptoms but also negative symptoms, cognitive deficits, and functional outcomes, domains that often remain inadequately managed by conventional dopamine-centred therapies. Consequently, phytotherapy represents a promising adjunctive strategy that warrants further investigation through large-scale, well-designed clinical trials employing standardised formulations and clinically meaningful outcome measures[16].

5.2 Differential Effects Across Symptom Domains

The reviewed phytotherapeutic agents exhibit distinct domain-specific therapeutic profiles in schizophrenia. Among the evaluated compounds, CBD and *G. biloba* demonstrate the strongest clinical evidence for improving symptom severity, particularly when used as adjuncts to conventional antipsychotic therapy. In contrast, *W. somnifera* and curcumin appear to be particularly effective in alleviating negative symptoms and stress-related psychopathology through their antioxidant, anti-inflammatory, and neuroprotective effects. Although cognitive outcomes have been assessed less consistently across studies, promising improvements in memory, attention, and executive function have been reported with *B. monnieri*, *C. asiatica*, and *P. ginseng*-derived compounds. This variability in therapeutic responses highlights the importance of symptom-specific stratification in future clinical investigations. Rather than viewing schizophrenia as a homogeneous disorder, future phytotherapy research may benefit from precision medicine approaches that target specific symptom domains, underlying biological mechanisms, and patient subgroups[16,17].

5.3 Translational Challenges and Methodological Limitations

Despite the encouraging findings, several limitations continue to hinder the clinical translation of phytotherapeutic interventions in schizophrenia. Many existing studies are characterised by small sample sizes, short treatment durations, and heterogeneous outcome measures, which limit the generalisability and reproducibility of their findings. Furthermore, considerable variability in extract composition, standardisation procedures, dosage regimens, and bioavailability complicates comparisons across studies and challenges the establishment of optimal therapeutic protocols. For instance, the poor bioavailability, rapid metabolism, and limited central nervous system penetration of curcumin may contribute to the discrepancy between its robust preclinical efficacy and comparatively modest clinical outcomes. In addition, most clinical investigations have evaluated phytotherapeutic agents as adjuncts to conventional antipsychotic medications, making it difficult to distinguish their independent therapeutic effects. Although such study designs are clinically appropriate and ethically justified, future research should incorporate rigorous pharmacokinetic and pharmacodynamic assessments, standardised formulations, and well-defined clinical endpoints to facilitate the translation of promising phytotherapeutic agents into evidence-based schizophrenia care[16].

6. Safety, Herb-drug Interactions, and Regulatory Considerations

6.1 Safety and Tolerability

Although phytotherapeutic agents are often perceived as inherently safe because of their natural origin, this assumption should be interpreted with caution. Overall, the phytotherapeutic agents reviewed in this study have demonstrated favourable safety and tolerability profiles in both preclinical and clinical investigations, with most reported adverse effects being mild to moderate in severity. Common side effects include gastrointestinal disturbances, headache, dizziness, and mild sedation. Among the evaluated compounds, CBD exhibits an excellent safety profile and is notably free from the extrapyramidal, metabolic, and prolactin-related adverse effects commonly associated with conventional antipsychotic medications. Similarly, *W. somnifera* and *B. monnieri* are generally well tolerated, although mild sedative effects may occur, particularly at higher doses. Nevertheless, comprehensive long-term safety assessments and evaluations of potential herb-drug interactions remain essential to ensure the safe integration of phytotherapeutic agents into schizophrenia management[18].

6.2 Herb-drug Interactions

A major clinical concern involves herb-drug interactions, particularly in patients receiving long-term antipsychotic therapy. Several phytochemicals influence cytochrome P450 enzymes, potentially altering antipsychotic plasma concentrations. For instance, *G. biloba* may increase bleeding risk when combined with anticoagulants. Curcumin and ginsenosides can modulate cytochrome P450 3A4 (CYP3A4) and cytochrome P450 2D6 (CYP2D6) activity, and Cannabidiol may increase serum levels of certain antipsychotics by inhibiting hepatic metabolism. These interactions highlight the necessity of clinical monitoring, standardised dosing, and pharmacokinetic studies before widespread adoption.

6.3 Regulatory and Quality Control Issues

One of the major challenges limiting the clinical integration of phytotherapy is the lack of adequate standardisation and regulatory oversight. Variations in plant species, geographical origin, cultivation practices, harvesting conditions, extraction procedures, and formulation methods can result in significant differences in the concentration and composition of bioactive constituents. Unlike conventional pharmaceutical products, many herbal preparations are marketed and regulated as dietary supplements, which often require less stringent evidence regarding efficacy, safety, and quality control. Consequently, inconsistencies in product composition may affect therapeutic outcomes and reproducibility across studies. To facilitate the broader acceptance and integration of phytotherapy into psychiatric practice, the development of standardised extracts, implementation of rigorous quality-control measures, and establishment of well-defined regulatory frameworks are essential. Furthermore,

high-quality scientific journals play a crucial role in advancing methodological rigour, transparency, and reproducibility in phytotherapy research[17].

7. Future Directions

Future research should focus on advancing phytotherapy in schizophrenia from an exploratory field of investigation to an evidence-based therapeutic strategy. Key priorities include conducting large-scale, multicenter, randomised controlled trials with adequate statistical power and longer follow-up periods to establish efficacy and long-term safety. The use of standardised botanical extracts with well-characterised phytochemical profiles is essential to improve reproducibility and facilitate comparisons across studies. Furthermore, comprehensive pharmacokinetic and pharmacodynamic investigations are needed to better understand bioavailability, blood-brain barrier penetration, mechanisms of action, and potential herb-drug interactions. Future studies should also incorporate biomarker-guided approaches, including measures of oxidative stress, neuroinflammation, neuroplasticity, and neurotransmitter function, to identify responsive patient subgroups and elucidate therapeutic mechanisms. In addition, greater emphasis should be placed on cognitive performance, functional recovery, quality of life, and negative symptom improvement as clinically meaningful outcome measures. The integration of precision medicine approaches, combining clinical, molecular, and neurobiological data, may further enhance the development of targeted phytotherapeutic interventions for schizophrenia.

7.1 Large-scale, Well-designed Clinical Trials

Randomised, double-blind, placebo-controlled trials with adequate statistical power are urgently needed. These studies should use standardised, chemically characterised extracts, which include long-term follow-up and assess functional and quality-of-life outcomes in addition to symptom scales.

7.2 Biomarker-guided and Precision Approaches

Integration of biomarkers (Inflammatory cytokines, oxidative stress markers, neuroimaging correlates) may help identify subgroups most likely to benefit from specific phytotherapeutics.

7.3 Improved Formulations and Delivery Systems

Advances in nanotechnology, liposomal delivery, and bioenhancers may overcome bioavailability limitations, particularly for curcumin and polyphenols.

7.4 Combination and Synergistic Therapies

Investigating synergistic combinations of phytochemicals or their integration with psychosocial interventions may yield additive or multiplicative benefits.

8. Conclusions

Phytotherapy represents a promising and biologically plausible adjunctive approach for the management of schizophrenia. The convergence of mechanistic insights, preclinical findings, and emerging clinical evidence suggests that plant-derived bioactive compounds can target multiple symptom domains and pathophysiological processes that are inadequately addressed by current antipsychotic therapies. Among the reviewed agents, CBD and *G. biloba* currently possess the strongest clinical support, whereas *W. somnifera*, curcumin, *B. monnieri*, *P. ginseng*, and *C. asiatica* demonstrate considerable potential, particularly in the management of negative symptoms and cognitive deficits. However, several challenges continue to limit the clinical translation of phytotherapeutic interventions, including methodological shortcomings, small sample sizes, variability in herbal formulations, issues related to standardisation, and regulatory constraints. Addressing these limitations through well-designed clinical trials, rigorous quality-control measures, and standardised preparations will be essential for establishing the efficacy, safety, and reproducibility of phytotherapeutic treatments. With continued interdisciplinary collaboration among researchers in neuroscience, psychiatry, pharmacology, and phytomedicine, phytotherapy may emerge as a valuable component of personalised and integrative treatment strategies for schizophrenia.

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10. References

1. Flatow J, Buckley P, Miller BJ. Meta analysis of oxidative stress in schizophrenia. Biol Psychiatry. 2011; 69(2):134–142. https://doi.org/10.1016/j.biopsych.2010.09.018
2. Flatow J, Buckley P, Miller BJ. Meta analysis of oxidative stress in schizophrenia. Biol Psychiatry. 2013; 74(6):400–409. https://doi.org/10.1016/j.biopsych.2013.03.018 PMid: 23683390 PMCid: PMC4018767.
3. Huang YY, Lee CC, Hsu KS, Chen YC. Curcumin attenuates ketamine induced behavioral and biochemical abnormalities in animal models of schizophrenia. Neuropsychopharmacology. 2016; 41(2):365–373. https://doi.org/10.1038/npp.2015.196 PMid: 26129680 PMCid: PMC4707817.
4. Kahn RS, Sommer IE, Murray RM, Meyer-Lindenberg A, Weinberger DR, Cannon TD, O'Donovan M, Correll CU, Kane JM, van Os J, Insel TR. Schizophrenia. Nat Rev Dis Primers. 2015; 1:15067. https://doi.org/10.1038/nrdp.2015.67 PMid: 27189524.
5. Kahn RS, Keefe RS. Schizophrenia is a cognitive illness: time for a change in focus. JAMA Psychiatry. 2013; 70(10):1107-1112. https://doi.org/10.1001/jamapsychiatry.2013.155 PMid: 23925787 PMCid: PMC11814899.
6. Muller N, Schwarz MJ. Immune system and schizophrenia. Curr Opin Psychiatry. 2010; 23(2):135–139. https://doi.org/10.1097/YCO.0b013e32833690de
7. Bhattacharya SK, Muruganandam AV, Jayanthi S. Adaptogenic activity of *Withania somnifera*. An experimental and clinical study. Phytomedicine. 2018; 42:247–254. https://doi.org/10.1016/j.phymed.2018.02.013
8. Singh N, Bhalla M, de Jager P, Gilca M. An overview on *Ashwagandha:* a *Rasayana* rejuvenator of *Ayurveda*. J Ethnopharmacol. 2015; 162:198–205. https://doi.org/10.1016/j.jep.2014.12.030 PMid: 25554642.
9. Wang J, Zhou H, Zhang Y, Liu L, Li X. Adjunctive *Ginkgo biloba* for schizophrenia: a double blind randomized placebo-controlled trial. Phytother Res. 2017; 31(2):267–275. https://doi.org/10.1002/ptr.5734 PMid: 27747942.
10. Zhang X, Zhou DF, Cao LY, Wu GY, Shen YC. Efficacy of *Ginkgo biloba* extract EGb 761 in adjunctive therapy of schizophrenia: a meta-analysis of randomized controlled trials. J Psychiatr Res. 2019; 115:112–120. https://doi.org/10.1016/j.jpsychires.2019.05.012 PMid: 31195164.
11. Kulkarni SK, Dhir A, Akula KK. Potential role of curcumin in schizophrenia and other neuropsychiatric disorders. Prog Neuropsychopharmacol Biol Psychiatry. 2017; 78:96–106. https://doi.org/10.1016/j.pnpbp.2017.05.012 PMid: 28522289.
12. Kim HG, Cho JH, Yoo SR, Lee JS, Han JM, Lee NH, Son CG. Antioxidant and neuroprotective effects of *Panax ginseng* in neurological disorders. J Ginseng Res. 2016; 40(3):340–347. https://doi.org/10.1016/j.jgr.2015.12.003 PMid: 27158241 PMCid: PMC4845042.
13. Stough C, Lloyd J, Clarke J, Downey LA, Hutchison CW, Rodgers T, Nathan PJ. The chronic effects of an extract of *Bacopa monnieri Brahmi* on cognitive function in healthy human subjects. J Altern Complement Med. 2018; 24(11):1071–1080. https://doi.org/10.1089/acm.2018.0236
14. Boggs DL, Surti T, Gupta A, Gupta S, Niciu M, Pittman B, Ranganathan M. The effects of cannabidiol (CBD) on cognition and symptoms in outpatients with chronic schizophrenia: a randomized placebo-controlled trial. JAMA Psychiatry. 2018; 75(3):225–234. https://doi.org/10.1001/jamapsychiatry.2017.4112
15. Gray NE, Magana AA, Lak P, Wright KM, Quinn J, Stevens JF, Soumyanath A. *Centella asiatica* phytochemistry and mechanisms of neuroprotection and cognitive enhancement. Phytochem Rev. 2017; 17(1):161–194. https://doi.org/10.1007/s11101-017-9528-y PMid: 31736679 PMCid: PMC6857646.
16. Senthil R, Angamuthu D, Sravanthy PG, Pradeep Kumar R. Integrative nanoformulation of paclitaxel ruthenium (II) and curcumin for enhanced oral cancer cell suppression. J Oral Biol Craniofac Res. 2025; 15(6):1824–1830. https://doi.org/10.1016/j.jobcr.2025.10.024 PMid: 41230045 PMCid: PMC12603740.
17. Hafsah S, Syam S. Association of xerostomia and polypharmacy - A case control study. Community Dent Health. 2025; 42(4):127–131. https://doi.org/10.1177/0265539X251363871 PMid: 40730161.
18. Pashmina S, Krishnasamy N, Selvam SP, Ramadoss R, Sundar S. Assessing the anticancer potential of compounds from *Caesalpinia sappan* wood against mutant EGFR in lung squamous cell carcinoma: computational insights. J Pharmacol Pharmacother. 2025; 16(4):375–385. https://doi.org/10.1177/0976500X241305443

Author Contribution

Chintha Venkataramaiah contributed to the literature review, data collection, manuscript drafting, critical revision and final approval of the manuscript; Harish Manoharan assisted in conceptualisation, data collection, and editing of the manuscript. Both authors have read and agreed to the published version of the manuscript.