https://doi.org/10.47552/ijam.v16iS2.6227 ISSN No: 0976-5921

Int J. of Ayurvedic Med, "Natural to Synthetic: The Convergence of Traditional Medicine to Modern Medicine" Supplement 2025

Indian Spices: An Insightful Review on Reported Antipsychotic, Antidepression, Neuroprotective and Anti-Anxiety Activities

Review Article

Shilpa S Borkar[1*], Jagdish R Baheti[1], Manna SSS[2]

1. Department of Pharmacology, Kamla Nehru College of Pharmacy, Butibori 441108, Dist. Nagpur, Maharashtra, India.
2. Department of Pharmacology, Dr. B.C. Roy College of Pharmacy, Durgapur, Calcutta, West Bengal, India.

Abstract

The potential of traditional medicinal herbs to cure neurodegenerative diseases like Alzheimer's disease (AD) has attracted more and more attention from researchers. Notably, a number of plants have long been used to enhance memory and cognitive performance, including *Crocus sativus, Nigella sativa, Coriandrum sativum, Ferula assafoetida, Thymus vulgaris, Zataria multiflora*, and *Curcuma longa*. By lowering oxidative stress, increasing antioxidant levels, and blocking acetylcholinesterase activity, their bioactive substances—carotenoids, monoterpenes, and polyphenols—have neuroprotective benefits. Additionally, by reducing levels of pro-inflammatory cytokines like IL-6, IL-1β, TNF-α, and total nitrite, these herbs control neuroinflammation. Taken together, these results provide credence to the medicinal potential of these herbs and their active ingredients in the treatment of depression, anxiety, and AD. Traditional medicinal potential in these findings, when combined, support the therapeutic potential of these plants and their active components in the treatment of AD, anxiety, and depression.

Keywords: Anxiety, Depression, Inflammation, Spices, Anti-Alzheimer activity.

Introduction

Cognitive decline and sensory impairment in neurodegenerative diseases like Alzheimer's, Parkinson's, and multiple sclerosis are brought on by the slow loss of neurons (1). Researchers have recently connected these diseases to intricate social and economic variables (2, 3). Anti-inflammatory drugs have also been suggested to slow the progression of neurodegenerative diseases like Alzheimer's. Numerous studies have connected non-steroidal anti-inflammatory drugs (NSAIDs) to a lower risk of developing Alzheimer's disease (4,5). Parkinson's disease (PD) is characterized by neuronal degeneration that is influenced by oxidative stress, inflammation, apoptosis, mitochondrial dysfunction, and genetic factors (6). In AD (7), cholinergic neurons may be destroyed by excessive lipid peroxidation, while in PD, dopaminergic neurons may be destroyed by oxidative stress. (8) The brain contains a variety of antioxidants, both enzymatic (like superoxide dismutase, or SOD) and non-enzymatic (100% thiol groups) (9). The polyunsaturated fatty acids found in the CNS make it more vulnerable to peroxidation processes (10). Because it contains very little antioxidant activity compared to other tissues, brain tissue is particularly vulnerable to oxidative damage. (11) The leaves, stems, roots, flowers, fruits, and seeds of plants were employed as a kind of supplementary and alternative medicine in ancient practices. Herbal extracts with neuroprotective properties have been discovered. These include resveratrol, curcumin, ginsenoside, polyphenols, triptolide, and others. (12) Phytochemicals found in herbs, such as flavonoids, alkaloids, and isoprenoids, are complex active components. Because of this, it is sometimes hard to tell which part of the plant is responsible for the majority of its biological effects (13,14). This review aimed to clarify the advantages of many medicinal plants that have been used historically for induced neurotoxicity as food additives, spices, and other medicinal purposes.

*** Corresponding Author:**
Shilpa S Borkar
Assistant Professor (Pharmacology),
Kamla Nehru College of Pharmacy,
Butibori 441108, Dist. Nagpur, Maharashtra, India
Email Id: preetshilpa81@gmail.com

Methods

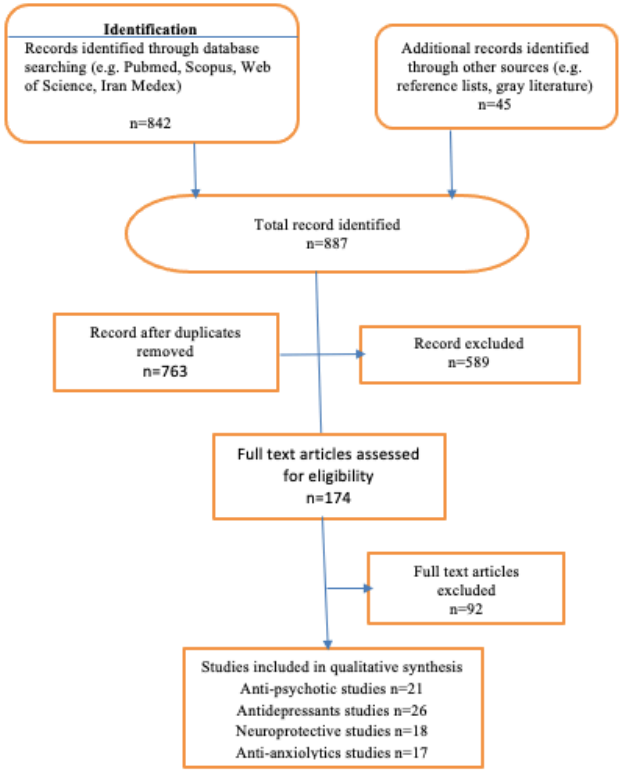
To gather the information for this study, we searched databases such as PubMed, Web of Science, Scopus, and IranMedex through the end of May 2025. All forms of research (in vitro, animal, review, and clinical) included neurotransmitter release, behavioral changes, oxidant/antioxidant parameters, and pro-inflammatory cytokines as outcomes. Both previously unpublished data and letters to the editor were excluded.

Neuroprotective effects of Indian Spices

An increasing worldwide health burden is attributed to psychiatric and neurodegenerative diseases like Alzheimer's disease (AD), depression, and anxiety. The World Health Organisation (2023) estimates that AD accounts for 60–70% of dementia diagnoses, which affect approximately 55 million individuals globally. By 2050, this number is expected to increase as a result of population ageing. Present-day pharmaceutical

therapies, such as cholinesterase inhibitors (donepezil, rivastigmine) and NMDA receptor antagonists (memantine), Tricyclic antidepressants or SSRI (Selective Serotonin Reuptake inhibitors) provide only a limited alleviation of symptoms and are frequently linked to side effects such nausea, vertigo, and sleeplessness. Similar hazards include reliance, withdrawal symptoms, and diminished effectiveness over time associated with many antidepressants and anxiolytics.

Figure 1: PRISMA style flow diagram showing inclusion/exclusion criterion



These drawbacks highlight the critical need for adjunct therapies or safer, more accessible alternatives. In this regard, chemicals originating from plants, especially from culinary spices, have drawn attention from researchers because of their diverse pharmacological profiles, which include neuroprotective, anti-inflammatory, and antioxidant qualities. Bioactive chemicals found in Indian spices including Crocus sativus, Nigella sativa, and Coriandrum sativum etc., alter neurotransmitter systems, lower oxidative stress, and affect neuroinflammatory indicators. Nevertheless, these therapies continue to be underutilised in standard medical protocols despite encouraging preclinical and early clinical findings, indicating a substantial gap in translational research and therapeutic use.

Crocus sativus

Grown commercially in a number of nations, saffron, or *Crocus sativus* L. (C. sativus), is a flowering plant belonging to the Iridaceae family and Crocoideae superfamily (15). The dried, dark-red stigma and a small portion of the style, which is frequently yellow, are the reasons *C. sativus* is harvested. In many regions of the world, it is primarily used as a natural medication. (16). Saffron contains more than 150 different compounds, including water, lipids, carbohydrates, polypeptides, minerals, and vitamins. The active biological components in saffron are called crocins, which are a class of crocetin glycosides. Crocins are water-soluble, red carotenoids. The four main bioactive substances found in saffron are crocin, crocetin, picrocrocin, and safranal. The bitter-tasting substance picrocrocin is also found in saffron (17).

Medicinal properties of *C. sativus*

Traditional Iranian medicine uses *C. sativus* to treat brain disorders. Recently, parts of the *C. sativus* plant have been used to relax smooth muscle and treat certain neurological conditions (18–20). Studies on humans and animals have demonstrated the anti-Alzheimer's and anti-convulsant properties of saffron extract (18). The effects of *C. sativus* on brain neurotransmitter levels and its interaction with the opioid system were assessed, as was clinical trial research on its efficacy in treating mild to moderate depression (18). The main antioxidant in *C. sativus*, crocin, is what gives the plant its potent antioxidant qualities (21, 22). While pretreatment with *C. sativus* extract (100 mg/kg, p.o.) reduces glutamate and aspartate concentrations as well as superoxide dismutase (SOD), catalase, and kinase (K-ATPase) activities, middle cerebral artery occlusion (MCAO) causes cerebral ischemia in rats. (23). Additionally, mice's neurotoxicity from aluminum chloride was lessened by *C. sativus* extract (200 mg/kg) and honey syrup (given over a 45-day period) (24).

When used to treat mild-to-moderate Alzheimer's disease in people aged 55 and over, saffron extract (30 mg/day) was just as effective as donepezil. Its side effects, with the exception of vomiting, were as common as those of donepezil (26). Similarly, 46 individuals with mild to severe AD showed improved cognitive abilities after receiving saffron for 16 weeks (26). In treating mild to severe depression, the effects of 30 mg of saffron extract per day for six weeks were comparable to those of 100 mg of imipramine and fluoxetine (27). In a double-blind study, the efficacy of fluoxetine (30 mg/day) and hydro-alcoholic extract of C. sativus (40 and 80 mg) was assessed over a six-week period. The results showed that fluoxetine (30 mg/day) and *C. sativus* (80 mg) together were more effective than either medication alone in treating mild to moderate depression (28). Around the world, dried saffron stigma (Crocus sativus) is used for both medical and culinary uses. Colour, taste, and aroma are all attributed to the most potent biological constituents, crocetin, crocin, picrocrocin, and safranal, respectively. These are essential to the central nervous system, which is linked to sadness and anxiety. In addition to being neuroprotective and anxiolytic, these bioactive substances can help people with memory and learning disabilities. Physicians most frequently prescribe tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and selective serotonin

noradrenaline reuptake inhibitors (SSNRIs) as antidepressants. (296)

Nigella sativa

Nigella sativa L. (*N. sativa*) is an annual herbaceous plant belonging to the Ranunculaceae family that grows widely throughout the Mediterranean region, Western Asia, the Middle East, and Eastern Europe. N. sativa seeds are a common seasoning for Persian bread, pickles, sauces, and salads. They are nutty, savory, and slightly bitter (29). In addition to other substances, *N. sativa* seeds contain oil, protein, carbs, and fiber. In its fixed oil, *N. sativa* contains linoleic acid, oleic acid, palmitic acid, arachidic acid, eicosadienoic acid, stearic acid, and myristic acid (30). Among the several phenolic chemicals found in *N. sativa* seeds, p-cymene accounts for 37.3%, followed by Thymoquinone (TQ) at 13.7%, carvacrol at 11.7%, and thymol at 0.3%.(29,31,32)

Medicinal properties of *N. sativa*

The medicinal plant *N. sativa* is well known for its potent antioxidant properties. According to a study, *N. sativa* decreased kidney damage by 33% (34). Consuming *N. sativa* seeds may significantly lessen the spatial learning deficits caused by chronic cerebral hypoperfusion in rats. (35) *N. sativa* also helped restore memory and learning that had been hampered by scopolamine by reducing oxidative stress and AChE activity in the rats' brains (36). Because of its antioxidant properties, *N. sativa* oil was used to lower serum levels of IL-10, MDA, and NO in patients with rheumatoid arthritis (RA). In RA patients, *N. sativa* also improved anti-inflammatory responses and reduced oxidative stress (37). In another study, forty healthy subjects were administered 500 mg capsules of *N. sativa* or a placebo twice a day for nine weeks (38). When compared to a placebo group, *N. sativa* enhanced memory, focus, and overall mental acuity. After four weeks, 500 mg of N. sativa decreased anxiety, stabilized mood, and altered cognition in the human model (39). The potential neuroprotective effects of N. sativa and one of its primary constituents, thymoquinone (TQ), on neurological disorders such as Alzheimer's disease, epilepsy, and neurotoxicity have been investigated (40). A pilot polysomnography study by Shyam Das et al. found that black cumin oil, which is high in thymoquinone, enhances sleep quality and reduces stress and anxiety in healthy participants who have sleep issues. (297)

Coriandrum sativum

The annual plant Coriandrum sativum L., commonly referred to as coriander, belongs to the Apiaceae family (41). This plant is commonly known as Geshniz in Persian. Although C. sativum originated in the Mediterranean, it is now widely grown throughout the world (42, 43). While oil extracted from fresh herbs is rich in aliphatic aldehydes (mostly C10-C16 aldehydes) with a fetidlike scent, oil extracted from coriander fruit is rich in linalool and other oxygenated monoterpenes and monoterpene hydrocarbons (44,45). Coriander may be a good source of lipids (petroselinic acid) and essential oils (EO), both of which are important for brain development. The majority of coriander's essential oil is composed of linalool, linoleic acid, and linolenic acid (46). Although coriander seed oil contains 20% hydrocarbons and 60–70% linalool, the composition of the herb oil differs significantly from that of the seed oil (47).

Medicinal properties of C. sativum

Folk medicine has long utilized *Coriandrum sativum* (*C. sativum*) as a digestive aid. Because of its antibacterial and antirheumatoid qualities, C. sativum seed extract was utilized in cosmetics such as shampoos and lotions (48). In traditional Iranian medicine, C. sativum has been used to treat insomnia (49, 50). Some people have found that taking a single dosage of crushed plant seeds or an extract of fresh leaves before bed helps them relax and fall asleep. (49) *C. sativum* seed has been shown to have similar benefits in various traditional treatments. (51) Increases in open-arm duration and open-arm percentage entries suggested an anxiolytic effect from *C. sativum* leaf extract (200 mg/kg). (52) When C. sativum fruit extract was given, both the duration and the number of entrances into the open arms increased. Less locomotion activity and less frequent rearing were observed in groups administered 200 mg/kg (i.p.) of the extract. At doses of 100 and 200 mg/kg, C. sativum extract also extended the amount of time spent socializing. (53) Using both aqueous (0.5 g/kg, i.p.) and ethenolic (3.5 and 5 g/kg, i.p.) extracts, the anticonvulsant effect of coriander seeds was examined in the pentylenetetrazole (PTZ) and maximum electroshock seizure models. In the maximum electroshock test, these extracts showed significant anticonvulsant action, reducing the duration of tonic-clonic seizures. Furthermore, phenobarbital-induced clonic convulsion onset latencies were prolonged by both extracts, but notably by ethenolic extract (54). Swati Sahoo explored that CSE treatment brought monoamines and GABA levels back to their baseline levels and enhanced exploratory activity in animal models of anxiety. In the hippocampal area, CSE also decreased excitotoxic glutamate levels. (298)

Ferula assafoetida

Harvested from the taproot or rhizome of a living plant, Asafoetida (*F. assafoetida L.*) belongs to the Apiaceae family. Gum-resin, or *F. asafoetida*, is referred to by the Persian terms "Anghouzeh," "Khorakoma," and "Anguzakoma." (55). It has long been used as a culinary spice and medicinal herb in Nepal and India (55). E-1-propyl sec-butyl disulfide is one of the primary components. After analysis, it was discovered that hydrodistilled oil contained between 25 and 56 distinct components. Germacrene B (7.8%) and e-1-propenyl sec-butyl disulfide (40.0%) are the main constituents of F. assafoetida (56).

Medicinal properties of *F. assafoetida*

F. asafoetida (Apiaceae) is considered by researchers due to its nutritional and pharmacological

properties. The roots, young stems, and leaves of the plant are all considered vegetables. The plant's roots are used as an antipyretic, and its leaves have diaphoretic, carminative, and anthelmintic properties (57). In traditional medicine, *F. asafoetida* has been used to treat a variety of ailments, including influenza, intestinal parasites, sluggish digestion, stomachaches, flatulence, asthma, and epilepsy (58). The oleo-gum resin of *F. asafoetida* has been linked to a wide range of medicinal effects, such as sedative, expectorant, analgesic, carminative, stimulant, antiperiodic, ant-diabetic, antispasmodic, emmenagogue, vermifuge, laxative, anti-inflammatory, contraceptive, and anti-epileptic (59). Research has been done on muscarinic receptors in the tracheal smooth muscle of guinea pigs as well as possible pathways for the functional antagonistic effects of F. asafoetida. Research has been done on potential mechanisms for F. assafoetida's muscle-relaxing effects (60,61,62). According to pharmacological and biological studies, Ferula asafoetida's ole-gum-resin has antiviral, antifungal, antioxidant, anti-diabetic, molluscicidal, antispasmodic, and antihypertensive qualities. A study assessing the acute and sub-chronic toxicity of F. asafoetida found no increase in mortality or detectable toxicological signs in rats given oral administration of 500 mg/kg or repeated doses of 250 mg/kg over a 28-day period (63). Oleo gum resin of F. asafoetida has been demonstrated to decrease lymphocyte infiltration in the neuropathic tissue in mice and to encourage regeneration and re-myelination, in addition to its well-known neuroprotective and nerve-stimulative effects in peripheral neuropathy (64)

Additionally, it has been demonstrated that *F. asafoetida* resin inhibits monoamine oxidase B (MAO-B), which suggests that it could be helpful in treating neurodegenerative diseases like Parkinson's and Alzheimer's (65). *F. asafoetida* has been shown to have acetylcholinesterase (AChE) inhibitory effects on snails' neurological systems both in vitro and in vivo. Researchers think that the herb F. asafoetida may improve memory because it inhibits AChE in the rat brain (66). The plant extract improved memory performance in a dose-dependent manner in behavioral models such as the raised plus maze (67). In a passive avoidance test, the extract enhanced memory at a higher dosage (400 mg) but not at a lower dose (200 mg). Other behavioral paradigm rodents treated with PTZ and amygdala-activated rodents demonstrate the strong anticonvulsant effect of *F. asafoetida* extract. When researchers compared two doses of F. asafoetida (50 and 100 mg/kg), they discovered that the higher dose had a stronger anticonvulsant effect (59). Research on FA's antidepressant effects indicates that it may work in a number of ways. These include the control of monoamine and non-monoamine neurotransmitter levels, the suppression of neuroinflammation and hyperfunction of the hypothalamic-pituitary-adrenal axis, the stimulation of hippocampus neurogenesis and the upregulation of brain-derived neurotrophic factor, neuroprotection (inhibition of oxidative stress, neuroinflammation, mitochondrial dysfunction, and apoptosis), and the downregulation of oxidative stress. (299)

Thymus vulgaris

Thymus vulgaris (*T. vulgaris*) is a plant of the intensely scented Lamiaceae family. About 38 distinct species make up this plant genus, all of which may be found in subtropical regions. (68) TV's primary constituents are the phenols carvacrol (15%) and thymol (40%). Phenol levels were lower in the winter. In addition, the essential oil contains thymol methyl ether (2%), cineol, cymen, pinene, borneol, and esters (68).

Medicinal properties of *T. vulgaris*

Native to the western Mediterranean, the subshrub *Thymus vulgaris*, commonly referred to as thyme, is used as a spice worldwide. Traditional medicine makes use of thyme-based herbal teas and infusions. (69). Thyme bioactive compounds, including thyme essential oil (TEO) constituents like flavonoids and phenolic acids, natural terpenoid thymol, and phenol isomer carvacrol, have well-established antibacterial, antitussive, antispasmodic, and expectorant qualities (70,71). Studies have shown that thymus vulgaris oil (TO) contain phenolic and tocols that may directly interact with free radicals to stop lipid peroxidation (72). Antioxidant levels in the brains of rats have been shown to rise after receiving thymol therapy. (73) Moreover, behavioural investigations have shown that a 1-week course of oral administration of thyme extract might have anxiolytic effects in rats. This conclusion is corroborated by data indicating that thyme extract lengthens the time spent in the safe haven of the labyrinth and increases the number of successful maze completions (74). In an animal model of anxiety testing using the elevated plus maze (EPM) in mice, kaempferol, a component of thyme extract, was demonstrated to have anxiolytic effects. In the plus maze test, carvacrol, which was isolated from this plant, demonstrated anxiolytic effects with a remarkable score (75,76). Animal studies have shown that bioactive monoterpenes found in thyme extract, including linalool, may help reduce anxiety. (77) Additionally, thyme essential oil may provide protection against alfatoxin toxicity in a dose-dependent manner. (78) Additionally, thymol has been shown to imitate or facilitate GABA activity and alter the $GABA^A$ receptor, suggesting that it exerts its effects centrally. (79) As a result, its considerable anticonvulsant and antiepileptogenic actions may be used. Recent research has demonstrated the neuroprotective and therapeutic effects of thymol, a bioactive monoterpene derived from T. vulgaris, on rats with amyloid or scopolamine-induced cognitive impairment (80) The possible impact of thymol on GABA-mediated regulation of synaptic transmission has been linked to its neuroprotective benefits. (81) Meanwhile, it was shown that TO might enhance synaptic acetylcholine (Ach) and nicotinic Ach receptor activation, suggesting that it may be used to control cholinergic function. (82) It was also shown that thymol has antidepressant properties. Deng et al. found that depressed mice subjected to chronic unpredictable

mild stress (CUMS) had their immobility time significantly reduced after receiving thymol and that their hippocampal levels of serotonin (5-HT) and norepinephrine (NE) were restored. (80) When it comes to anxiety, the essential oil from Foeniculum vulgare seeds is more effective than that from depression, although the essential oil from the aerial portions of the plant only little alters anxiety (300).

Zataria multiflora

The family Lamiaceae includes the genus Zataria (*Z. multiflora*). (83) P-cymene derivatives include dihydroxyaromadendrane, luteolin, α-tocopherolquinone, Multiflotriol, and Multiflorol, a novel aromatic ester of p-hydroxy benzoic acid (84–86). The main constituents of the plant oil were beta-caryophyllene (2.06%), gamma-terpinene (3.88%), PARA-cymene (7.72%), carvacrol (33.65%), and thymol (37.59%) (87).

Medicinal properties of *Z. multiflora*

The chemical profile of *Z. multiflora*, which contains terpens, luteolin, 6-hydroxyluteolin glycosides, and di-, tri-, and tetraethoxylated compounds, may be responsible for its therapeutic qualities. (88) Although *Z. multiflora* Boiss essential oil (ZEO) has preservation benefits, its potent flavor and odor have hindered its widespread use as a food preservative. (89) Traditional Iranian medicine makes use of the plant's analgesic, antiseptic, and carminative qualities. (88) In vitro studies have demonstrated the antimicrobial, antifungal, and antioxidant properties of *Z. multiflora* essential oil. (89, 90) Research has demonstrated that ZEO has a stronger antioxidative effect than pomegranate juice. (89) Studies have demonstrated the plant's antibacterial (90), immunoregulatory (91,117), and anti-inflammatory (92,118) qualities. Additionally, it has been demonstrated that intraperitoneal injections of Z. multiflora essential oil can reverse the memory and learning deficits caused by Aβ in rats. Researchers discovered that the zataria multiflora plant's essential oil effectively reduced the cognitive symptoms linked to Alzheimer's disease (AD) (93).

Curcuma longa

Curcuma longa (C. longa), a plant in the Zingiberaceae family, is grown in countries in Southeast Asia. (94) The flavonoid curcumin (diferuloylmethane) and volatile oils such as tumerone, atlantone, and zingiberone are among the active components of turmeric. Additionally, there are carbohydrates, proteins, and resins. The most thoroughly researched active ingredient is curcumin, which is present in fresh turmeric at concentrations ranging from 0.3% to 5.4% (95).

Medicinal properties of *C. longa*

Plants such as C. longa naturally contain curcumin, a polyphenol and non-flavonoid compound. Due to its anti-inflammatory, antioxidant, and other qualities, curcumin has been researched for its potential in a range of biological and medical applications. Curcumin has garnered a lot of attention lately as a potential treatment for neurodegenerative diseases. (6) Kulkarni demonstrated that the water soluble extract of curcumin raised dopamine, norepinephrine, and 5-HT levels in the central nervous system (96). In animal and cell culture models, extracts from the *C. longa* plant—scientifically known as curcumin—have demonstrated neuroprotective benefits against oxidative brain damage, memory loss, Parkinson's disease (PD), reactive oxygen species (ROS) generation, apoptosis, platelet aggregation, cytokine release, and cyclooxygenase enzyme activity. (97, 98) It has been demonstrated that *C. longa* extract (1000 mg/kg, body weight, per mouth) guards against kidney damage and oxidative (99,100).

It has been demonstrated that treating rats with curcumin at doses of 50, 100, or 200 mg/kg improves their mitochondrial dysfunction and cognitive deficits (101). Curcumin has also been demonstrated to have neuroprotective effects in cases of cerebral ischemia and neuronal degenerative diseases (102,103). Curcumin protects the rat brain against localised ischemia, according to scientific research. It does this via increasing the expression of the antioxidant enzyme HO-1 and the transcription factor Nrf2. (104) Curcumin inhibits glutamate neurotoxicity in the rat hippocampus, according to the study's authors, likely via blocking the activation of inflammatory genes TXNIP and NLRP3 in response to ER stress (105). As suggested by Linlin et al., curcumin has been demonstrated to shield the rat brain from ischemia-reperfusion damage. They also discovered that curcumin activated the JAK2/STAT3 signaling pathway, enhanced neuron survival rate, and inflammatory cytokine activity (106). Curcumin has been demonstrated to decrease oxidative stress and neurotoxicity brought on by oxyhemoglobin in an in vitro model of subarachnoid hemorrhage (SAH) (Xia LI) (107).

Curcumin's neuroprotective benefits in Parkinson's disease are associated with its antioxidant properties. In the human cell line SH-SY5Y exposed to 6-OHDA, curcumin prevents ROS intracellular accumulation (108), per a study by Wang. (109). Over a three-week period, curcumin (60 mg/kg body weight, taken orally) reduced neuronal degeneration in the striatum of rats with 6-OHDA lesions (110). By raising GSH levels, which had been depleted by ROS, curcumin rescued the neurons. (111) The neurotoxic 6-OHDA was generated in MES23.5 cells, and curcumin elevated SOD levels in the lesioned striatum of 6-OHDA mice (112.108) There is evidence that curcumin may prevent LPS from damaging axons (113). The neuroprotective effects of curcumin may be mediated by overexpression of BCl-2, an inducible nitric oxide synthase (iNOS) blocker. Curcumin is therefore helpful in lessening the harm brought on by NO-mediated aging (114). When administered orally for a week at a dose of 150 mg/kg, curcumin reduced the striatal production of proinflammatory cytokines like IL-6, IL-1beta, TNF-alpha, and total nitrite in MPTP-induced animals (115). Additionally, curcumin prevented NF-kB activation in

inflammatory reactions triggered by 6-OHDA and LPS116 (108).

Antipsychotic effects of Indian Spices

Turmeric (*Curcuma longa*)

Curcumin, a polyphenol with significant neuroprotective qualities, is found in turmeric (116). Curcumin influences neurotrophic factors like BDNF, modifies neurotransmitter levels (dopamine and serotonin), and has anti-inflammatory and antioxidant properties (117,118). Studies suggest curcumin's potential in alleviating symptoms associated with schizophrenia and other psychotic disorders (119,120). Turmeric (*Curcuma longa*), a staple spice in Indian traditional medicine and cuisine, has garnered significant attention in recent years for its potential role in neuropsychiatric disorders, particularly those with psychotic features (121).

The primary active constituent of turmeric, curcumin (diferuloylmethane), along with its derivatives such as demethoxycurcumin, bisdemethoxycurcumin, and ar-turmerone, demonstrates a wide range of pharmacological actions relevant to the management of psychosis and schizophrenia (122). In terms of mechanism, curcumin has potent anti-inflammatory and antioxidant properties, both of which are essential for neuroprotection (123). Curcumin reduces oxidative stress, a major factor in the pathophysiology of schizophrenia, by scavenging reactive oxygen species (ROS), upregulating the expression of antioxidant enzymes such as glutathione peroxidase and superoxide dismutase, and inhibiting lipid peroxidation (124). Additionally, it reduces neuroinflammation by suppressing the expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in the brain, as well as by downregulating pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6 (125,126). Notably, curcumin also inhibits microglial activation, which is a central mechanism associated with neuroinflammation in psychotic disorders (127).

In terms of neurotransmitter modulation, curcumin has shown the ability to increase brain levels of dopamine and serotonin, both of which are crucial for mood regulation and psychotic symptom control (128). Additionally, it helps balance glutamatergic neurotransmission by reducing glutamate-induced excitotoxicity and enhancing GABAergic tone, offering a stabilizing effect on brain circuits often dysregulated in schizophrenia and related disorders (129).

Several preclinical studies have validated the antipsychotic potential of curcumin. For instance, Kandhare et al. (2014), in a study published in *Biomed Research International*, demonstrated that curcumin significantly reversed ketamine-induced schizophrenia-like behavior in rats by modulating oxidative stress and inflammatory markers (130). Similarly, Kulkarni et al. (2008) reported that curcumin improved behavioral parameters and cognitive function in rodent models of psychosis (131). These findings suggest curcumin may mimic or augment the effects of atypical antipsychotics through multifaceted mechanisms (132).

Clinically, Lopresti et al. (2014) reported in the *Journal of Affective Disorders* that curcumin supplementation in humans improved depressive symptoms in individuals with mild-to-moderate depression, including those with psychotic features (133). Curcumin has shown promise in lowering Positive and Negative Syndrome Scale (PANSS) scores in patients with schizophrenia when used as an adjuvant therapy in conjunction with atypical antipsychotics (134). However, there is still a lack of human data, which calls for more investigation in larger, regulated clinical trials (135).

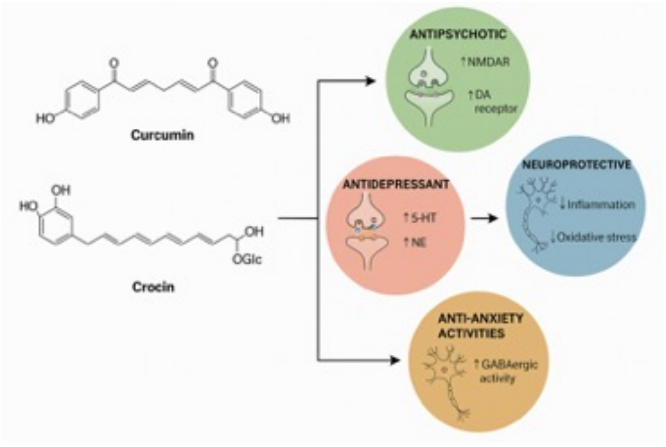
The low bioavailability of curcumin is one of the major problems with it, attributed to its rapid metabolism and low absorption (136). This limitation is often overcome through bioenhancement strategies, such as co-administration with piperine (from *Piper nigrum*), which has been shown to increase curcumin's bioavailability by nearly 2000% (137). Moreover, the development of nanocurcumin, liposomal curcumin, and curcumin–piperine complexes is underway to enhance central nervous system (CNS) penetration and pharmacological efficacy (138). Hussian et. al. in 2022 investigated antistress and antidepressant activities of synthetic curcumin analogues by behavioral and biomarker. The study revealed that these compounds significantly enhanced hippocampus CAT, SOD and GSH, and reduced MDA levels in the scopolamine-induced stress mice model (301). Subsequent research done by Jinglin Chen et. al. revealed that the antidepressant properties of CACN136 were linked to a decrease in the metabolism of 5-HT and the modulation of oxidative stress levels in vivo. Chen concluded, CACN136 showed potent antidepressant activity and could be an effective antidepressant (302).

In terms of safety, curcumin is generally well-tolerated even at higher doses (up to 1500 mg/day), with minor gastrointestinal disturbances being the most common adverse effect (139). Its synergistic potential with other adaptogenic and neuroprotective herbs such as *Withania somnifera* (ashwagandha) and *Bacopa monnieri* (brahmi) is also under exploration for integrative mental health management (140).

Despite the encouraging preclinical and limited clinical evidence, the lack of large-scale, randomized controlled trials specifically targeting psychotic disorders remains a limitation. Therefore, future directions include long-term studies evaluating standardized, bioavailable formulations of curcumin, especially in patients with schizophrenia or bipolar disorder with psychotic features (141). The incorporation of turmeric-based nutraceuticals into complementary and integrative psychiatric treatment models holds great potential for improving outcomes in mental healthcare (142). The GABAergic and nitrergic systems are influenced by curcuma longa, giving it hypnotic and anxiolytic properties. On the other hand, combined administration of C. longa and midazolam intensifies hypnosis induced by barbiturate.(303)

https://doi.org/10.47552/ijam.v16iS2.6227 ISSN No: 0976-5921

Figure 1: Mechanism of curcumin and crocin



Black Pepper (*Piper nigrum*)

Black pepper is rich in piperine, which enhances the bioavailability of curcumin. Piperine also exhibits monoamine oxidase (MAO) inhibitory activity and modulates neurotransmitter systems, potentially contributing to antipsychotic effects. Its synergistic use with curcumin may amplify therapeutic outcomes in neuropsychiatric conditions (143).

One of the most common spices in India, black pepper (*Piper nigrum*), has demonstrated great promise in the treatment of neuropsychiatric disorders, including psychotic disorders. Piperine, an alkaloid with a wide range of pharmacological characteristics, such as neuroprotective, antioxidant, anti-inflammatory, and bioenhancer effects, is the main active ingredient in black pepper (144). According to research, piperine can penetrate the blood-brain barrier and have effects on the central nervous system (CNS) that are useful in treating diseases like schizophrenia and psychosis (145).

The mechanisms underlying the antipsychotic effects of piperine involve modulation of several neurotransmitter systems. Notably, piperine increases the brain levels of dopamine and serotonin, two key neurotransmitters involved in the pathophysiology of schizophrenia and mood disorders (146). Furthermore, it enhances GABAergic tone while reducing glutamatergic excitotoxicity, creating a balanced neural environment conducive to symptom reduction in psychosis (147). Inhibiting monoamine oxidase is one of its other neuropharmacological actions. This helps sustain higher levels of serotonin and dopamine in the synaptic cleft, a function that is shared by a number of atypical antipsychotics (148).

Preclinical studies have consistently highlighted the potential of black pepper in modulating behavior related to psychosis. Srinivasan (2007) demonstrated the cognitive-enhancing and anxiolytic properties of piperine in rodent models (149). Likewise, Bukhari et al. (2013) reported that piperine exerted significant antidepressant-like and anti-anxiety effects in behavioral tests (150). By neutralizing reactive oxygen species (ROS), piperine's antioxidant qualities help prevent oxidative damage to neuronal tissue. Its anti-inflammatory effects are achieved by downregulating inflammatory cytokines like TNF-α and IL-6 (151). Additionally, it has been demonstrated that piperine increases brain-derived neurotrophic factor (BDNF), a vital neurotrophin implicated in cognitive function and synaptic plasticity (152).

Importantly, piperine is also recognized as a bioavailability enhancer—a unique feature that makes it invaluable in combination therapies. It inhibits glucuronidation in the liver and intestine, thereby prolonging the plasma half-life of co-administered drugs and phytochemicals. For instance, when used in combination with curcumin, piperine increases its bioavailability by over 2000%, enhancing its therapeutic potential in psychiatric disorders (153). Clinical evidence supports this synergy; Ghosh et al. (2016) showed that patients with major depressive disorder and psychotic features experienced better symptom resolution when treated with a piperine-curcumin combination, compared to curcumin alone (154).

While black pepper is generally considered safe and is widely consumed, high doses of isolated piperine may cause gastrointestinal discomfort. However, dosages between 5 to 20 mg/day in clinical settings have shown no significant adverse effects (155). Current innovations include the development of piperine-loaded nanoparticles, nanoemulsions, and bioenhanced CNS formulations, which are being explored to improve delivery and efficacy in psychiatric therapy (156).

Despite these promising results, a notable limitation is the lack of large-scale, dedicated clinical trials targeting psychotic disorders such as schizophrenia. Most existing human studies focus on piperine's adjunctive benefits rather than its standalone antipsychotic potential. Thus, future research should prioritize randomized controlled trials in psychotic populations, explore multi-target formulations, and develop piperine-based nanocarriers to improve CNS-specific delivery and efficacy (157).

Black pepper (*Piper nigrum*), through its active compound piperine, exhibits potent antipsychotic-like effects by modulating neurotransmitters, suppressing neuroinflammation, enhancing neurotrophin levels, and improving the bioavailability of therapeutic agents. These multi-dimensional actions position it as a valuable candidate for complementary and integrative approaches to psychiatric care, particularly in adjunct treatment of schizophrenia and related psychotic disorders.

Ginger (*Zingiber officinale*)

Bioactive substances with anti-inflammatory and antioxidant qualities, such as shogaol and gingerol, are found in ginger (158). These ingredients may have anxiolytic and cognitive-enhancing effects by modulating GABAergic neurotransmission, which may help control psychotic symptoms (159).

Ginger (*Zingiber officinale*), a widely used Indian spice and medicinal herb, has gained increasing recognition in the neuroscientific and psychiatric research domains for its neuroprotective and antipsychotic-like properties (160). Ginger is a potential

adjunct or complementary therapy for the treatment of psychotic disorders like schizophrenia and bipolar disorder with psychotic features because its bioactive constituents, particularly 6-gingerol, 6-shogaol, and zingerone, have demonstrated a variety of effects on the central nervous system (CNS) (161).

Ginger's strong anti-inflammatory and antioxidant properties are the main ways it works in the brain (162). Ginger inhibits the NF-κB signaling pathways and microglial activation, which are both linked to neuroinflammation linked to psychotic disorders (163). It also lowers the expression of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). Ginger also dramatically boosts the activity of antioxidant enzymes like catalase and superoxide dismutase (SOD), which protects neurons from oxidative damage and preserves cognitive function (164).

Of particular importance is ginger's ability to modulate neurotransmitter levels. Preclinical findings reveal an increase in dopamine and serotonin levels following administration of ginger extracts—two neurotransmitters that play critical roles in the development and management of schizophrenia and mood disorders (165). Furthermore, ginger promotes GABAergic transmission and reduces excessive glutamatergic activity, resulting in a calming effect on the brain and reduction of excitotoxicity—both vital in psychotic symptom management (166). Brain-derived neurotrophic factor (BDNF), a protein essential for synaptic plasticity, learning, and memory, is upregulated in conjunction with these neurochemical alterations (167).

In terms of behavioral effects, studies in rodent models have shown that ginger extract can reduce psychosis-like symptoms. Hasanein and Riahi (2019) reported that 6-gingerol attenuated behavioral disturbances and reversed oxidative stress markers in ketamine-induced psychosis models (168). Similarly, Ghayur et al. (2008) observed significant anxiolytic and mood-enhancing effects, further validating the therapeutic relevance of ginger in psychiatric conditions (169).

Clinical evidence also supports ginger's neuropsychiatric benefits. For instance, Khandouzi et al. (2015) demonstrated that ginger supplementation significantly reduced depressive symptoms in type-2 diabetic patients—conditions often comorbid with psychosis (170). Mahluji et al. (2013) found that elderly individuals with mild cognitive impairment showed improved memory and processing speed following ginger administration, indicating potential benefits in schizophrenia-related cognitive dysfunction (171).

Although high dosages of ginger may result in mild gastrointestinal side effects like heartburn, it is generally regarded as safe at therapeutic doses (500–1000 mg/day in human studies) (172). Innovations such as gingerol-loaded nanoparticles and polyherbal CNS-targeting formulations are currently being explored to enhance bioavailability and CNS penetration (173). Synergistic combinations with compounds like curcumin, piperine, and *Bacopa monnieri* may further augment its therapeutic efficacy (174).

However, despite promising preclinical and limited clinical results, a major limitation remains the scarcity of direct clinical trials examining ginger's effects specifically on schizophrenia or psychosis (175). As such, the future scope of research should focus on well-designed randomized controlled trials, particularly in populations diagnosed with schizophrenia, schizoaffective disorder, or bipolar disorder with psychosis. Ginger's safety, affordability, and wide cultural acceptance make it a strong candidate for integrative psychiatric therapies in the Indian context and globally (176).

Ashwagandha (*Withania somnifera*)

Ashwagandha, an adaptogenic herb, contains withanolides that exhibit GABA-mimetic activity, reduce cortisol levels, and modulate dopaminergic function. Clinical studies have demonstrated its efficacy in reducing schizophrenia symptoms and improving cognitive functions (177).

One of the most valued herbs in Ayurvedic medicine, ashwagandha (Withania somnifera), also referred to as "Indian ginseng" or "Winter cherry," has recently attracted a lot of interest in neuropsychiatric research because of its neuroprotective, anxiolytic, and antipsychotic-like properties. Rich in steroidal lactones called withanolides (e.g., withaferin A and withanone), as well as sitoindosides and various alkaloids, Ashwagandha exerts multidimensional effects on brain physiology, particularly targeting pathways involved in schizophrenia and related psychotic disorders (178).

Several mechanistic studies have elucidated how Ashwagandha modulates key neurotransmitters including dopamine, serotonin, and GABA—all of which play critical roles in the pathology of psychotic conditions. Ashwagandha is shown to enhance GABAergic activity, promote dopaminergic tone in the striatum and prefrontal cortex, and reduce glutamate-induced excitotoxicity—theorized to be hyperactive in schizophrenia. Additionally, it lowers cortisol levels, which aids in regulating the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis that is observed in depression, anxiety, and psychosis (179).

Regarding its anti-inflammatory and antioxidant properties, ashwagandha lowers high levels of pro-inflammatory cytokines such as TNF-α and IL-6, which are frequently elevated in individuals with bipolar disorder and schizophrenia. Additionally, it increases natural antioxidants like glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD), which protects neurons and lower oxidative stress, a major cause of psychotic symptoms and cognitive decline (180).

Preclinical studies have strongly supported its role in psychosis management. For instance, Bhattacharya et al. (2000) demonstrated that Ashwagandha extract enhanced memory retention, reduced stress markers, and improved learning in mice. Vohora et al. (2011) showed that Ashwagandha significantly attenuated behavioral abnormalities in a

ketamine-induced psychosis model in rodents, simulating the NMDA receptor hypofunction believed to underlie schizophrenia (181).

Clinically, a noteworthy randomized, placebo-controlled trial by Chengappa et al. (2018) found that patients with schizophrenia who received standardized Ashwagandha extract (containing 5% withanolides) demonstrated a notable improvement in PANSS positive, negative, and overall psychopathology scores when in contrast to a placebo (182). Additionally, Cooley et al. (2009) reported reduced stress, improved cognition, and mood stabilization in patients under psychological duress, suggesting broader psychiatric applicability (183).

Ashwagandha is generally well-tolerated, with mild gastrointestinal disturbances and drowsiness reported in some cases at higher doses. Clinical doses typically range between 300–600 mg/day, while animal studies use 100–200 mg/kg of body weight. Novel innovations such as withanolide-rich nanoformulations, and synergistic formulations with Curcumin, Piperine, Bacopa, and Shankhpushpi, are being investigated to improve therapeutic effect and bioavailability (184).

Despite these promising findings, the current limitations include a relative paucity of large-scale, long-duration randomized trials specifically targeting psychosis and schizophrenia. Most studies focus on anxiety and cognitive stress. In order to manage psychosis, future research must standardize extract compositions, establish the best dosages, and investigate ashwagandha as a complementary therapy, particularly when combined with traditional antipsychotic medications (185). Ashwagandha presents strong scientific potential as a natural antipsychotic adjunct, offering a multifactorial approach that targets inflammation, neurotransmitter imbalance, oxidative stress, and neuroendocrine dysfunction—core elements of psychotic disorders.

Holy Basil (*Ocimum sanctum*)

Compounds with anti-stress and antioxidant qualities, such as rosmarinic acid and eugenol, are found in holy basil, also known as tulsi. These constituents may modulate catecholamines and inhibit MAO, contributing to mood stabilization and potential antipsychotic effects (186).

Ocimum sanctum, widely revered as Holy Basil or Tulsi, has long been a staple in Ayurvedic medicine for its powerful adaptogenic, anxiolytic, and mood-regulating properties. Over the past few decades, modern scientific studies have begun validating its potential as a natural antipsychotic agent, owing to its multi-targeted action on the central nervous system (187).

Holy Basil is rich in phytochemicals like eugenol, ursolic acid, rosmarinic acid, caryophyllene, carvacrol, luteolin, and ocimumosides, which contribute to its neuroprotective and neuromodulatory properties. These substances have demonstrated the capacity to alter serotonergic and dopaminergic neurotransmission, two important pathways involved in the etiology of psychotic and schizophrenia disorders. Tulsi also has a calming effect on the hypothalamic-pituitary-adrenal (HPA) axis, which lowers cortisol levels and aids in mood and behavior stabilization (188).

Preclinical investigations offer robust evidence for its antipsychotic-like actions. The administration of *Ocimum sanctum* extract dramatically decreased anxiety, enhanced memory, and reversed cognitive deficits in rodent models exposed to chronic stress, according to a seminal study by Bhattacharya et al. (2001). Similar results were also reported by Mondal et al. (2011) in a stress-induced behavioral model, emphasizing decreased oxidative damage in brain tissues, increased locomotor activity, and decreased immobility in the forced swim test (189).

One proposed mechanism of action is Tulsi's ability to reduce glutamate-induced excitotoxicity—a major contributor to neuronal death in psychosis. Additionally, it increases natural antioxidants like glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD), which fight oxidative stress in vital brain areas like the hippocampus and prefrontal cortex (190).

Though direct studies on schizophrenia are still emerging, clinical trials underscore Tulsi's impact on mood and stress regulation. In a randomized clinical trial by Saxena et al. (2012), healthy volunteers receiving 300 mg/day of Tulsi leaf extract exhibited marked improvements in general anxiety, cognitive clarity, and mood stabilization. These findings suggest its potential as an adjunctive therapy for managing early-phase psychosis or mood disorders with psychotic features (191).

The herb is usually consumed in the form of aqueous/ethanolic extracts or capsules, and is often part of polyherbal formulations with other CNS-active botanicals like Ashwagandha, Bacopa, and Curcumin. It has a high safety margin, with minimal adverse effects reported, making it suitable for long-term use (192).

While *Ocimum sanctum* is not yet a substitute for conventional antipsychotic drugs, its neuroprotective, anti-inflammatory, and neurotransmitter-balancing actions provide a solid foundation for its use as an adjunct in psychiatric care. Future research involving placebo-controlled clinical trials, brain imaging, and bioavailability studies is warranted to establish Tulsi's definitive role in treating schizophrenia and other psychotic disorders (193).

Saffron (*Crocus sativus*)

Saffron's active constituents, crocin and safranal, have demonstrated serotonergic modulation and neuroprotective effects. Clinical trials suggest saffron's potential in improving depressive symptoms and cognitive dysfunctions associated with psychotic disorders (194).

Saffron (*Crocus sativus* L.), one of the most precious medicinal spices in the world, has emerged as a promising natural antipsychotic agent. Traditionally used as a mood elevator in Persian and Unani medicine, saffron's pharmacological profile now includes antidepressant, anxiolytic, neuroprotective, and

antipsychotic effects, validated through contemporary preclinical and clinical investigations (195).

The major active constituents of saffron—crocin, crocetin, safranal, and picrocrocin—exert multimodal neuropharmacological actions. These bioactives modulate the dopaminergic and serotonergic systems, which are critical in psychotic disorders, especially schizophrenia. Furthermore, saffron's antioxidant properties protect against glutamate-induced excitotoxicity, a well-known contributor to neuronal degeneration in psychosis (196).

Preclinical models of psychosis, such as ketamine- and MK-801-induced hyperlocomotion, have demonstrated that both saffron extract and its active compound safranal can significantly reduce psychosis-like behavior and restore behavioral balance.

In a study by Inan et al. (2019), safranal exhibited notable antipsychotic-like effects comparable to haloperidol, showing suppression of stereotypy and agitation in murine models. Moreover, Hosseinzadeh et al. (2005) highlighted crocin's neuroprotective and antidepressant actions through hippocampal upregulation of neurotrophic markers (197).

In the clinical domain, Talaei et al. (2020) reported that saffron, when used as an adjunct to risperidone, improved negative symptoms of schizophrenia such as flat affect and social withdrawal —areas where traditional antipsychotics often fall short. Another double-blind trial by Kashani et al. (2018) confirmed saffron's capacity to improve cognition and overall mental well-being in patients with psychiatric disorders (198).

Saffron works by enhancing monoaminergic tone, inhibiting NMDA receptor-mediated glutamate toxicity, and downregulating pro-inflammatory cytokines (through NF-κB inhibition). Because of this, saffron is particularly useful in treating co-occurring anxiety and depression, as well as both positive and negative symptoms of psychosis (199).

At dosages of 30 to 100 mg per day, saffron is safe and well tolerated, with few adverse effects like mild sedation or gastrointestinal distress. Although higher doses (above 1.5 g/day) are rarely required for therapeutic benefits, they may have negative side effects. With promising results, it has been investigated in a variety of forms, including hydroalcoholic extract, standardized crocin tablets, and even polyherbal combinations (200).

Although its long-term effects in chronic schizophrenia are yet to be fully established, saffron offers great potential as an adjunctive therapy, particularly for treatment-resistant schizophrenia, schizoaffective disorder, and psychotic depression. For crocin and safranal to more successfully cross the blood-brain barrier, future research is necessary in the form of extensive randomized controlled trials, brain imaging studies, and the creation of targeted delivery systems (201).

Cinnamon (*Cinnamomum verum*)

Eugenol and cinnamon aldehyde, which are found in cinnamon, have neuroprotective and anti-inflammatory qualities. These compounds may improve insulin sensitivity and cognitive functions, potentially aiding in the management of psychosis-related metabolic disturbances (202).

Cinnamon (*Cinnamomum verum*), widely cherished as a culinary spice, has attracted growing interest in neuroscience for its neuroprotective, antidepressant, and antipsychotic potential. Rich in bioactive phytoconstituents such as cinnamaldehyde, eugenol, and cinnamic acid, cinnamon exerts multidimensional actions on the central nervous system (CNS) that are relevant in managing psychiatric disorders, including psychosis and schizophrenia (203).

Experimental studies have revealed that cinnamaldehyde, a key volatile constituent of cinnamon, exhibits antipsychotic-like behavior in animal models of psychosis. In a notable study by Jain et al. (2015), administration of cinnamaldehyde ameliorated ketamine-induced hyperlocomotion, a model mimicking the positive symptoms of schizophrenia. This behavioral normalization was associated with modulation of dopaminergic and glutamatergic pathways, both of which are known to be dysregulated in schizophrenia (204).

Furthermore, cinnamon demonstrates potent antioxidant and anti-inflammatory properties, helping mitigate oxidative stress and neuroinflammation—two major pathological hallmarks in the neurobiology of psychosis. Shaikh et al. (2014) confirmed that aqueous cinnamon extract could reduce lipid peroxidation and enhance catalase and superoxide dismutase activities in the brain, thereby offering neuroprotection in chronic stress models. These mechanisms are indirectly tied to improvements in cognition and emotional regulation, often impaired in psychotic disorders (205).

Although clinical trials specifically targeting psychotic populations with cinnamon are still scarce, its nootropic, antidepressant, and anxiolytic effects have been demonstrated in several human studies. Cinnamon improves insulin sensitivity, which also relates to improved cognition and brain plasticity, especially in patients with schizophrenia comorbid with metabolic syndrome. Moreover, cinnamon appears to enhance GABAergic neurotransmission, supporting anxiolytic action and behavioral calming, essential for addressing agitation and restlessness seen in psychosis (206).

The therapeutic dose of cinnamon typically ranges from 500 mg to 2 g/day (in the form of standardized extracts). Importantly, care should be taken regarding the type of cinnamon used—Ceylon cinnamon (*C. verum*) has significantly lower coumarin content than Cassia cinnamon (*C. cassia*), which can be hepatotoxic at higher doses (207).

Cinnamon holds potential as an adjunctive natural agent for managing symptoms of psychosis, particularly by targeting oxidative stress, inflammation, and neurotransmitter imbalances. While preclinical data are robust, there is a clear need for well-designed clinical trials to fully validate its antipsychotic efficacy and establish its long-term safety profile in psychiatric populations (208).

Clove (*Syzygium aromaticum*)

Clove is rich in eugenol, known for its antioxidant and GABAergic modulatory effects. These properties may contribute to its CNS depressant activity, offering calming effects beneficial in psychotic conditions (209).

Clove (*Syzygium aromaticum*), a spice widely used for culinary and medicinal purposes in India, has demonstrated emerging neuropharmacological properties, including antipsychotic, anxiolytic, and neuroprotective actions. This activity is largely attributed to its rich phytochemical profile, especially eugenol, β-caryophyllene, flavonoids, and tannins. Eugenol, the principal constituent of clove essential oil, exhibits significant activity on CNS neurotransmitters and oxidative pathways, making it a compound of interest for psychosis research (210).

Preclinical studies support the antipsychotic potential of clove. In a landmark study by Shyamala et al. (2013), administration of clove extracts in ketamine-induced psychosis models in rodents reversed behavioral abnormalities such as hyperlocomotion, poor social interaction, and stereotypy. These effects were associated with clove's modulation of NMDA receptors and dopaminergic signaling, two major neurotransmitter systems implicated in the pathogenesis of schizophrenia (211).

Additionally, clove's strong antioxidant and anti-inflammatory actions play a supportive role in neuropsychiatric health. Eugenol has been shown to scavenge free radicals and suppress proinflammatory cytokines like IL-6 and TNF-α, as reported by Ali et al. (2014) in murine brain inflammation models. These mechanisms are highly relevant, given the established links between neuroinflammation, oxidative stress, and psychosis in modern neuroscience literature (212).

Although clinical trials in humans focusing specifically on psychosis or schizophrenia are currently limited, clove has been traditionally used in stress and mental fatigue management. Some indirect human studies support its role in improving cognition, mood stability, and stress tolerance, thereby pointing to a potential adjunctive use in mood or psychotic spectrum disorders (213).

Dosage in preclinical studies generally ranges between 10 to 100 mg/kg, with formulations tested including aqueous and ethanolic extracts as well as eugenol-rich fractions. Importantly, while clove is generally regarded as safe at dietary levels, high doses of eugenol may pose hepatotoxic or nephrotoxic risks, thus necessitating proper formulation and standardization for long-term use in therapeutic contexts (214).

Clove represents a promising phytomedicine in the realm of neuropsychiatric disorders, with mechanistic overlap in dopaminergic modulation, NMDA antagonism, GABAergic enhancement, and anti-inflammatory pathways. Future research, especially in the form of randomized clinical trials, pharmacokinetic profiling, and brain imaging studies, is essential to validate and harness its antipsychotic potential in humans (215).

Nutmeg (*Myristica fragrans*)

Nutmeg contains myristicin and elemicin, which exhibit MAO inhibitory and serotonergic activities. At low doses, nutmeg may have calming effects; however, high doses can be psychotoxic, necessitating cautious use (216).

Nutmeg (*Myristica fragrans*), a spice widely used in culinary traditions across India, is increasingly recognized for its neuropsychopharmacological potential. Traditionally employed for its calming, sedative, and euphoric effects, nutmeg contains a rich array of bioactive constituents such as myristicin, elemicin, safrole, and eugenol, which are implicated in central nervous system modulation (217). These compounds, particularly myristicin, exhibit structural similarity to psychoactive agents like mescaline, and they act by modulating monoaminergic neurotransmission, inhibiting monoamine oxidase (MAO), and interfering with NMDA receptor-mediated glutamatergic excitotoxicity—a key mechanism implicated in schizophrenia and psychosis (218,219).

Preclinical studies provide compelling evidence for the antipsychotic-like and mood-enhancing effects of nutmeg. In a landmark study by Dhingra and Sharma (2006), nutmeg extract exhibited antidepressant-like activity in mice, significantly reducing immobility time in the forced swim test (FST) (220). This was supported by a concurrent increase in serotonin and dopamine levels, indicating its role in monoamine regulation. Sheela et al. (2015) further demonstrated nutmeg's neuroprotective and anti-inflammatory properties in models of oxidative stress-induced neuronal damage (221). These results support the expanding theory that neuroinflammation and oxidative stress are linked to psychotic disorders, indicating that nutmeg may be able to reverse these harmful processes (222).

Behavioral studies have also highlighted nutmeg's ability to reduce psychomotor agitation, hyperlocomotion, and anxiety-like conduct during elevated plus maze and open field tests (223). Although direct clinical trials in humans for psychotic disorders remain absent, traditional medicine has long recommended nutmeg for symptoms resembling psychosis, such as agitation, insomnia, hallucinations, and mood instability (224).

However, nutmeg's psychoactivity is a double-edged sword. At low to moderate doses, it may exert beneficial anxiolytic and antidepressant effects. Yet, at higher doses (above 5 grams/day in humans), it can induce hallucinations, confusion, and even delirium, attributed to the anticholinergic and hallucinogenic actions of myristicin and elemicin (225). This necessitates caution in its therapeutic application, emphasizing the need for dose standardization and toxicological profiling (226).

In conclusion, nutmeg offers promising adjunctive antipsychotic benefits through its diverse pharmacological actions on neurotransmitter systems, oxidative stress, and inflammatory pathways. However, its narrow therapeutic index and potential for psychoactive side effects underscore the urgency for rigorous clinical evaluation, controlled dosing

protocols, and the development of non-toxic formulations for mental health interventions (227).

Cardamom (*Elettaria cardamomum*)

Cardamom's active constituents, such as cineole and terpinene, have antioxidant and GABAergic properties. These may confer anxiolytic and mood-enhancing effects, supporting its traditional use in nervous disorders (228).

Cardamom (*Elettaria cardamomum*), known as the "Queen of Spices," is a fragrant herb from the Zingiberaceae family and holds a special place in Indian traditional medicine. While commonly used for digestive and respiratory disorders, its growing relevance in neuropsychopharmacology—particularly as a natural antipsychotic agent—has attracted attention due to the presence of active constituents such as 1,8-cineole, α-terpinyl acetate, limonene, and flavonoids (229).

Cardamom has been shown in scientific studies to have the ability to alter mood and central nervous system (CNS) activity. By raising levels of monoamines like serotonin and dopamine, which are both crucial in the pathophysiology of schizophrenia and bipolar disorder, the hydroalcoholic extract of cardamom demonstrated antidepressant effects in animal models, according to Al-Yahya et al. (2016) (230). Furthermore, cardamom essential oil demonstrated strong anxiolytic effects in the elevated plus maze and open field tests with negligible sedation, according to Savanth et al. (2020), indicating that it modulates the GABAergic and serotonergic systems (231).

Cardamom's antioxidant and anti-inflammatory effects are of particular importance in psychiatric disorders characterized by oxidative damage and neuroinflammation, such as schizophrenia. The spice is known to reduce proinflammatory cytokines like TNF-α and IL-6, which are often elevated in patients with psychosis (232). Furthermore, its ability to stabilize the limbic system and prefrontal cortex activity makes it a promising candidate for modulating cognitive and emotional disturbances seen in psychotic disorders (233).

Although direct clinical evidence for cardamom in psychosis is limited, traditional systems of medicine have long valued its soothing, mood-enhancing, and calming properties (234). Preclinical studies suggest that doses ranging from 100–400 mg/kg in rodents lead to beneficial neurobehavioral outcomes without major toxicity (235). However, for clinical translation, standardized extracts and targeted trials are necessary (236).

Cardamom holds strong promise as a natural, polypharmacological agent with potential adjunctive benefits in psychosis, especially due to its ability to regulate neurotransmitters, reduce inflammation, and combat oxidative stress. Future directions include randomized controlled trials in humans, receptor-target interaction studies, and the development of standardized phytopharmaceutical formulations for mental health applications (237).

Fenugreek (*Trigonella foenum-graecum*)

Fenugreek contains diosgenin, which exhibits antioxidant and neuroprotective effects. Preliminary studies suggest its potential in cognitive enhancement and neuroprotection, which may be relevant in psychotic disorders (238).

Fenugreek (*Trigonella foenum-graecum*), a leguminous spice with deep roots in Indian traditional medicine, has recently garnered attention for its neuroprotective and potential antipsychotic properties. Rich in diverse phytoconstituents such as diosgenin, trigonelline, saponins, flavonoids, and 4-hydroxyisoleucine, fenugreek exerts multiple pharmacological effects relevant to psychiatric health (239). It mostly works through neurotrophic, anti-inflammatory, and antioxidant processes that are linked to the pathophysiology of mood and psychotic disorders (240).

Preclinical evidence has highlighted fenugreek's role in modulating behavior and brain chemistry under stress-induced conditions. In a pivotal study by Puri et al. (2017), ethanolic extract of fenugreek seeds administered to rodents subjected to chronic mild stress (CMS) significantly reversed behavioral despair in the forced swim test and improved anxiety-related metrics in the elevated plus maze (241). These effects were linked to enhanced levels of dopamine and serotonin, along with reduced oxidative markers such as malondialdehyde (MDA) and increased superoxide dismutase (SOD) levels in the brain (242). In another study by Singhal et al. (2020), fenugreek supplementation was shown to suppress proinflammatory cytokines like TNF-α and IL-6, both of which are elevated in psychotic disorders like schizophrenia (243).

By increasing the expression of brain-derived neurotrophic factor (BDNF), particularly in the hippocampus and prefrontal cortex—areas linked to mood disorders and schizophrenia—fenugreek's neurotrophic potential has also been investigated (244). Additionally, trigonelline, a unique alkaloid found in fenugreek, is suggested to possess nootropic and antidepressant properties, enhancing cognitive performance and emotional regulation via cholinergic and serotonergic pathways (245).

While fenugreek has not yet been directly tested in human clinical trials for schizophrenia or psychosis, its extensive use in Ayurveda for mental fatigue, hormonal imbalance, and nervous system rejuvenation adds ethnobotanical value (246). When taken as a dietary supplement, it is usually safe, and at therapeutic dosages, it shows no discernible toxicity. However, especially in diabetic patients, high dosages may result in hypoglycemia or mild gastrointestinal problems (247).

In conclusion, fenugreek represents a promising adjunctive agent for psychotic and mood disorders due to its multi-targeted mechanisms, including oxidative stress reduction, neuroinflammation suppression, and monoamine regulation. Nonetheless, the absence of direct clinical trials and the need to clarify its molecular mechanisms highlight an important research gap. Its

integration into future nutraceutical or polyherbal formulations may provide a holistic approach to managing neuropsychiatric conditions (248).

Coriander (*Coriandrum sativum*)

Coriander is rich in linalool, known for its anxiolytic properties and modulation of GABAergic neurotransmission. These effects may contribute to its traditional use in managing anxiety and related symptoms (249).

Coriandrum sativum, commonly known as coriander (seeds) or cilantro (leaves), is a widely used culinary spice and medicinal herb from the Apiaceae family. Traditionally utilized for its calming, digestive, and detoxifying properties in Ayurveda, coriander is gaining scientific interest for its neuroprotective and psychotropic potential (250). The plant contains a diverse range of bioactive compounds, including linalool, borneol, camphor, apigenin, and quercetin, which contribute to its anxiolytic, antidepressant, and antioxidant effects (251).

Scientific investigations, particularly in preclinical models, have demonstrated coriander's potential to modulate neurotransmitter systems that are crucial in the pathophysiology of psychotic and mood disorders (252). Coriander's linalool-rich essential oil has demonstrated notable anxiolytic-like effects in animal models like the open field test (OFT) and elevated plus maze (EPM). A study by Emamghoreishi et al. (2005) reported that coriander extract reduced anxiety-like behavior in mice through interaction with GABAergic systems, a mechanism shared with benzodiazepines (253).

Additionally, coriander has anti-inflammatory and antioxidant qualities that lower proinflammatory cytokines like TNF-α and IL-6 as well as reactive oxygen species (ROS), both of which are linked to bipolar disorder and schizophrenia (254). This was further supported by the findings of Sreelatha et al. (2009), who demonstrated that Coriandrum sativum seed extract enhanced memory performance and reduced lipid peroxidation in rodent models (255).

Coriander extracts have been shown to shorten immobility times in behavioral tests such as the forced swim test (FST) and tail suspension test (TST), indicating antidepressant-like effects. This is attributed to enhanced serotonin (5-HT) activity and stabilization of the HPA axis, which is often dysregulated in psychiatric illnesses (256).

Despite promising preclinical data, coriander lacks robust clinical studies directly targeting psychosis or schizophrenia. Nonetheless, its safety profile, traditional usage, and synergistic potential with other psychotropic herbs make it an attractive candidate for adjunctive therapy (257). It is often included in polyherbal formulations for cognitive support, stress relief, and mood regulation, especially in traditional Indian and Middle Eastern medicine (258).

Coriandrum sativum exhibits significant antipsychotic-like properties through neurotransmitter modulation, antioxidant protection, and anti-inflammatory mechanisms. However, future research including clinical trials, receptor-targeting studies, and standardized dosage evaluations are essential to validate its efficacy and establish its role in mainstream psychiatric treatment (259).

Fennel (*Foeniculum vulgare*)

Fennel contains anethole, which has antioxidant and GABAergic modulatory effects. These properties may offer calming effects, supporting its traditional use in nervousness and anxiety (260).

Fennel (Foeniculum vulgare), a fragrant and medicinal spice commonly used in Indian cuisine and traditional systems of medicine such as Ayurveda and Unani, possesses promising neuropsychopharmacological properties (261). Its seeds and essential oils contain bioactive constituents such as anethole, estragole, fenchone, limonene, and a variety of flavonoids and phenolic acids that contribute to its diverse pharmacological profile, including neuroprotective, antioxidant, and anxiolytic effects (262).

Fennel's ability to alter neurotransmitter systems and reduce oxidative stress and neuroinflammation—two factors that are closely linked to the pathophysiology of mental illnesses like schizophrenia, bipolar disorder, and major depression—has been shown in experimental models (263). In rats exposed to stress-induced behavioral changes, a study by Kooti et al. (2014) found that foeniculum vulgare seed extract improved mood and cognitive function (264). Similarly, Sayyah et al. (2006) showed that fennel extract exhibits GABA-mimetic activity, producing calming effects similar to conventional anxiolytics (265).

Mechanistically, fennel's antipsychotic-like effects are believed to arise from its ability to boost GABA and serotonin activity, lower corticosterone levels (a key stress hormone), and inhibit inflammatory cytokines such as TNF-α and IL-1β (266). These neurochemical modulations are vital in reversing psychotic-like symptoms, improving affective stability, and enhancing cognitive function.

In animal studies, fennel's anxiolytic and antidepressant-like effects have been demonstrated using behavioral models like the forced swim test (FST) and elevated plus maze (EPM) (267). These results are consistent with the traditional use of fennel to soothe anxiety, relieving mental tension, and improving sleep quality. Moreover, its antioxidant property further supports its neuroprotective action by neutralizing free radicals and preserving neuronal integrity (268).

Although clinical evidence in humans is still lacking, fennel is widely used in herbal CNS formulations, often in combination with other adaptogens and sedatives like valerian root, ashwagandha, and licorice (269). It is considered generally safe at dietary levels, although caution is advised in large doses due to the presence of estragole, a compound under scrutiny for hepatotoxic potential in very high concentrations (270).

In conclusion, Foeniculum vulgare demonstrates promising antipsychotic potential, primarily through neurotransmitter modulation, antioxidant defense, and

anti-inflammatory actions. However, robust clinical trials and mechanistic investigations are necessary to establish its role as a therapeutic or adjunct agent in psychotic disorders (271).

Ajwain (*Trachyspermum ammi*)

Ajwain's active constituent, thymol, exhibits antioxidant and anxiolytic properties. Its traditional use in calming the nervous system may be attributed to these effects, although scientific data is limited (272).

Trachyspermum ammi, commonly known as Ajwain or carom seeds, is a well-known aromatic spice in Indian households and traditional medicine. Belonging to the Apiaceae family, Ajwain is rich in essential oils, predominantly thymol, along with other potent constituents like γ-terpinene, p-cymene, α- and β-pinene, and polyphenolic flavonoids (273). These compounds contribute to a range of pharmacological activities, including antioxidant, anti-inflammatory, anxiolytic, and neuroprotective effects, which are increasingly recognized in the context of mental health and psychosis-related disorders (274).

The antipsychotic-like properties of Ajwain are primarily attributed to thymol, which has been shown in animal models to modulate GABA-A receptors, thus producing anxiolytic and sedative effects similar to benzodiazepines (275). Sharma et al. (2020) showed that Ajwain essential oil, most likely via GABAergic facilitation, dramatically decreased anxiety-like behavior in the elevated plus maze (EPM) and open field test (OFT) (276). Furthermore, methanolic extracts of Ajwain inhibited LPS-induced neuroinflammation, with a significant decrease in proinflammatory cytokines like IL-1β and TNF-α, which are frequently elevated in psychotic disorders like schizophrenia, according to Khan et al. (2022) (277).

Ajwain also modulates dopaminergic and serotonergic pathways, balancing neurotransmitter systems implicated in schizophrenia and mood disorders (278). These neurochemical effects manifest behaviorally as reduced immobility in the forced swim test (FST) and enhanced exploration and social interaction, which are crucial indicators in psychopharmacology (279). While clinical evidence remains sparse, ethnomedicinal accounts support the use of Ajwain for mental calmness, stress relief, and digestive health, which are intricately linked with psychological well-being (280).

Ajwain's essential oil and extracts have shown efficacy in combination therapies, often paired with cumin, black seed, fennel, and turmeric in traditional formulations for enhancing memory and calming the nervous system (281). It has a high safety profile, being generally recognized as safe (GRAS), although excess thymol may cause mucosal irritation in sensitive individuals (282).

Trachyspermum ammi holds promising antipsychotic and anxiolytic potential via neurotransmitter regulation, antioxidant defense, and anti-inflammatory action. However, there is an urgent need for targeted psychosis model studies, clinical trials, and receptor-binding assays to substantiate its role as an adjunct or standalone therapeutic agent in the management of psychiatric conditions such as schizophrenia, anxiety, and stress-induced behavioral disorders (283).

Mustard Seeds (*Brassica juncea*)

Allyl isothiocyanate, which has anti-inflammatory and antioxidant qualities, is found in mustard seeds. Although direct antipsychotic effects are not well established, these effects might promote CNS health (284).

Brassica juncea, commonly referred to as mustard seeds, is a staple in Indian cuisine and Ayurvedic medicine, widely known for its pungent flavor and therapeutic properties. These seeds, especially the brown Indian variety, are packed with potent bioactive compounds including allyl isothiocyanate (AITC), sinigrin, phenolic acids, flavonoids, selenium, and omega-3 fatty acids (285). Emerging scientific evidence suggests that these constituents may exhibit neuroprotective and antipsychotic-like effects, mediated through their antioxidant, anti-inflammatory, and neurotransmitter-regulating actions (286).

In preclinical models, AITC has shown anxiolytic and antidepressant-like activity, which are often relevant in the treatment of negative symptoms of schizophrenia and mood-related psychosis (287). According to Khan et al. (2019), rodents given AITC showed noticeably fewer anxiety-related behaviors in the open field test (OFT) and elevated plus maze (EPM) (288). Additionally, Singh et al. (2021) reported that aqueous mustard seed extract reversed scopolamine-induced memory deficits, highlighting its potential role in managing cognitive dysfunctions commonly seen in psychosis and neurodegenerative diseases (289).

Mechanistically, the antipsychotic-like effects of mustard seeds appear to stem from their ability to modulate neurotransmitters, particularly enhancing GABAergic and serotonergic tone while reducing excitotoxic glutamate and dopaminergic overactivity—key elements in psychotic pathology (290). In particular, in vulnerable brain regions like the hippocampus and prefrontal cortex, the presence of selenium and flavonoids helps to prevent neurodegeneration and promote neuronal integrity by reducing oxidative stress and pro-inflammatory cytokine production (e.g., TNF-α, IL-1β, IL-6) (291).

Although clinical evidence remains limited, traditional use and emerging experimental data position mustard seeds as a promising adjunctive agent for managing psychotic and mood disorders, especially those related to chronic stress, neuroinflammation, and cognitive decline (292). Additionally, formulations containing mustard seed oil and extracts have been used for enhancing cognition, alleviating anxiety, and supporting overall mental wellness in traditional Indian medicine systems (293). Importantly, mustard is generally regarded as safe (GRAS), though high concentrations of AITC may lead to gastric irritation or mucosal toxicity if used without proper dose standardization (294).

https://doi.org/10.47552/ijam.v16iS2.6227 ISSN No: 0976-5921

Int J. of Ayurvedic Med, "Natural to Synthetic: The Convergence of Traditional Medicine to Modern Medicine" Supplement 2025

Brassica juncea offers a novel avenue for integrative psychopharmacology, combining dietary accessibility with neuropsychiatric potential. Future studies should focus on human clinical trials, neuroreceptor-binding investigations, and standardized extract development to further explore and validate its role in the treatment of psychosis, schizophrenia, and related disorders (295).

Standardization Challenges and Ethnopharmacological Validation

Ensuring consistent quality, potency, and repeatability of herbal products is known as standardisation. The following problems make this especially challenging for plant-based CNS drugs and spices:

Changes in the Phytochemical Composition

Active ingredient concentrations, such as allyl isothiocyanate (AITC) (Mustard) or thymol (Ajwain), might differ greatly because of:

- Origin in geography
- Climate and soil type
- Time for harvesting
- Methods of processing and storage

For instance, the amount of thymol in ajwain might vary greatly based on the cultivar and extraction technique, which makes dosing uncertain.

Absence of standardised extraction procedures

Studies frequently employ various extraction methods (cold press, Soxhlet, distillation) and solvents (methanol, ethanol, aqueous), which produces results that are not comparable.

Different ratios of bioactive, inactive, or even hazardous components may be present in extracts.

Contextual and Cultural Bias

It is challenging to distinguish the effects of a single spice in traditional formulations because they are frequently polyherbal (e.g., Ajwain often used with fennel, cumin, or turmeric).

Ritual use, nutrition, and environment are examples of cultural contexts that might impact efficacy and are challenging to reproduce in therapeutic settings.

Discord Between Conventional Use and Research Objectives

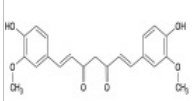
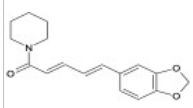
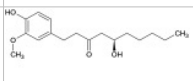
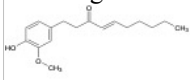
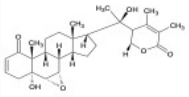
This leap must be made carefully because spices that have historically been used for digestion or overall relaxation are now being researched for complex mental illnesses like schizophrenia.

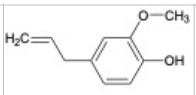
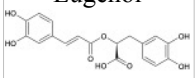
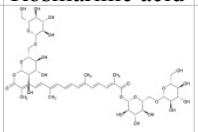
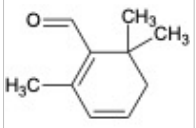
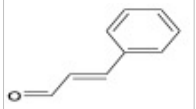
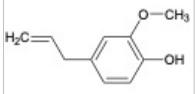
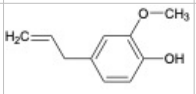
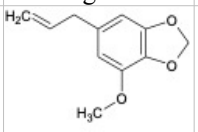
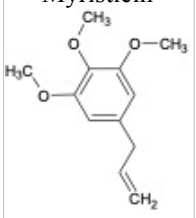
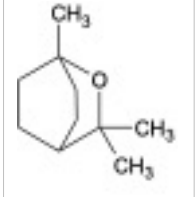
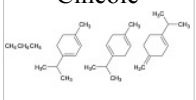
Traditional understanding ignores the need for mechanistic clarity for biological targets like GABA-A regulation or anti-cytokine action.

Issues with Intellectual Property and Ethics

Benefit-sharing and intellectual property rights concerns are frequently brought up by ethnomedical bioprospecting, particularly when the information comes from indigenous groups.

Table 1: Details of spices and their proposed mechanism

S. No.	Indian Spice	Botanical Name	Active Constituents	Proposed Mechanisms	Reported Effects	Evidence Type	References
1	Turmeric	*Curcuma longa*	 Curcumin	Antioxidant, anti-inflammatory, modulates dopamine, serotonin, BDNF	Reduces psychosis symptoms, improves cognition	Preclinical, Clinical	Zhang et al., 2012; Amin et al., 2015
2	Black Pepper	*Piper nigrum*	 Piperine	Enhances curcumin bioavailability, MAO inhibition, dopaminergic modulation	Enhances antipsychotic action with turmeric, anxiolytic effects	Preclinical	Damanhouri et al., 2012
3	Ginger	*Zingiber officinale*	 Gingerol  Shogaol	Anti-inflammatory, GABA modulation	Improves anxiety, memory, and psychotic behaviors	Preclinical	Hasani-Ranjbar et al., 2009
4	Ashwagandha (Indian ginseng)	*Withania somnifera*	 Withanolides	GABAergic, reduces cortisol, dopaminergic stabilization	Reduces schizophrenia symptoms, boosts cognition and sleep	Clinical, Preclinical	Cooley et al., 2019; Chandrasekhar et al., 2012

5	Holy Basil (Tulsi)	*Ocimum sanctum*	 Eugenol  Rosmarinic acid	MAO inhibition, catecholamine modulation, antioxidant	Anti-stress, neuroprotective, mood stabilizing	Traditional, Preclinical	Bhattacharyya et al., 2008
6	Saffron	*Crocus sativus*	 Crocin  Safranal	Serotonergic activity, neuroprotection, anti-inflammatory	Improves depression, cognitive dysfunction in psychosis	Clinical, Preclinical	Akhondzadeh et al., 2004
7	Cinnamon	*Cinnamomum zeylanicum*	 Cinnamaldehyde  Eugenol	Improves insulin sensitivity, antioxidant, anti-inflammatory	Enhances learning and memory; potential adjunct for metabolic side effects of antipsychotics	Preclinical	El-Bassossy et al., 2014
8	Clove	*Syzygium aromaticum*	 Eugenol	GABA receptor modulation, antioxidant	CNS depressant activity, calming effect	Preclinical	Cortés-Rojas et al., 2014
9	Nutmeg	*Myristica fragrans*	 Myristicin  Elemicin	MAO inhibition, serotonergic modulation	Psychotropic and anxiolytic at low doses; hallucinogenic at high doses	Traditional, Preclinical	Suh et al., 2007
10	Cardamom	*Elettaria cardamomum*	 Cineole  Terpinene	Antioxidant, GABAergic modulation	Anxiolytic, mood enhancer	Traditional, Preclinical	Jamshidi et al., 2013

https://doi.org/10.47552/ijam.v16iS2.6227 ISSN No: 0976-5921

Int J. of Ayurvedic Med, "Natural to Synthetic: The Convergence of Traditional Medicine to Modern Medicine" Supplement 2025

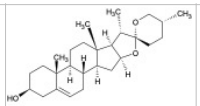
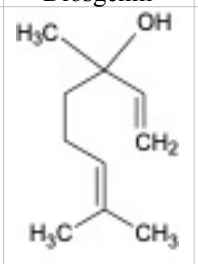
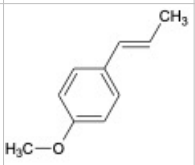
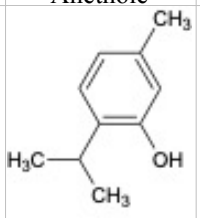
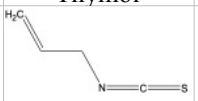
11	Fenugreek	*Trigonella foenum-graecum*	 Diosgenin	Anti-inflammatory, antioxidant, neuroprotective	Memory-enhancing and neuroprotective properties	Preclinical	Raju et al., 2004
12	Coriander	*Coriandrum sativum*	 Linalool	GABA-A modulation, anticonvulsant	Anti-anxiety, calming effect	Preclinical	Emamghoreishi et al., 2005
13	Fennel	*Foeniculum vulgare*	 Anethole	GABAergic and dopaminergic modulation	Traditional use for nervous system disorders	Traditional, Preclinical	Rather et al., 2016
14	Ajwain	*Trachyspermum ammi*	 Thymol	Antioxidant, anxiolytic, GABAergic	Anticonvulsant and calming effects	Preclinical	Pundir et al., 2010
15	Mustard Seeds	*Brassica juncea*	 Allyl isothiocyanate	Anti-inflammatory, neuroprotective	May aid in managing neuroinflammation associated with psychosis		

Table 2: Details of spices along with active phytoconstituent and their observed outcomes

Sr. No.	Spice Name	Active Constituent(s)	Dosage	Model Used	Observed Outcomes
1	Crocus sativus *(Saffron)*	Crocin, Crocetin, Picrocrocin, Safranal	100–200 mg/kg (animal); 30 mg/day (human)	MCAO rats, $AlCl_3$-induced neurotoxicity, Human trials	↓ Glutamate & Aspartate; ↑ Antioxidant enzymes; ↓ Alzheimer's symptoms; ↓ Depression
			40–80 mg/day (extract in clinical trial)	Depression in humans	Combination with fluoxetine improved outcomes over single treatment
2	Nigella sativa	Thymoquinone (TQ), p-Cymene, Carvacrol	500 mg/day (human); varies in animals	Scopolamine-induced memory loss, RA patients, human cognitive test	↑ Memory & learning; ↓ Oxidative stress; ↓ AChE; ↓ Anxiety; ↑ Cognitive function
3	Coriandrum sativum *(Coriander)*	Linalool, Petroselinic acid, Linoleic acid	100–200 mg/kg (mice); 0.5 g/kg (aqueous), 3.5–5 g/kg (ethanolic)	PTZ and electroshock seizure models in mice	↓ Seizure duration; ↑ Anxiolytic behavior; ↑ Social interaction
4	Ferula assafoetida *(Asafoetida)*	E-1-propenyl sec-butyl disulfide, Germacrene B	50–500 mg/kg (animal models)	Peripheral neuropathy, seizure models, passive avoidance tests	↑ Remyelination; ↓ MAO-B & AChE activity; ↑ Memory performance; Anticonvulsant effect

5	Thymus vulgaris	Thymol (40%), Carvacrol (15%), Kaempferol, Linalool	Oral extract; Thymol: unspecified; Carvacrol: EPM-tested	Rodent models (Elevated Plus Maze, amyloid/cognitive impairment models)	Anxiolytic effects, ↑ antioxidant levels, ↓ anxiety, neuroprotective, anticonvulsant, ↑ Ach activity, GABA modulation, antidepressant-like effects
6	Zataria multiflora	Thymol (37.6%), Carvacrol (33.6%), γ-Terpinene, p-Cymene	Intraperitoneal ZEO injection; specific dose not stated	Rat model of Alzheimer's (Aβ-induced)	Antioxidant, anti-inflammatory, antimicrobial, improved learning and memory deficits, reversed cognitive impairments
7	Curcuma longa	Curcumin (0.3–5.4%), Demethoxycurcumin, Bisdemethoxycurcumin	50–200 mg/kg in animals; up to 1500 mg/day in humans	Rodent models (CUMS, 6-OHDA, ischemia, LPS models); human trials	↓ Oxidative stress, ↑ dopamine/5-HT, ↓ cytokines (IL-6, TNF-α), ↓ neuroinflammation, enhanced BDNF, cognitive and behavioral improvements, potential antipsychotic
8	Piper nigrum	Piperine	5–20 mg/day (clinical); synergy with curcumin noted	Rodent models; clinical studies (adjunct in MDD/ psychosis)	↑ Curcumin bioavailability (↑ 2000%), MAO inhibition, ↑ dopamine/ 5-HT, antioxidant, ↑ BDNF, anti-inflammatory, adjunct antipsychotic efficacy
9	Ginger (*Zingiber officinale*)	6-Gingerol, 6-Shogaol, Zingerone	500–1000 mg/day (humans); up to 100 mg/kg (animals)	Ketamine-induced psychosis (mice), clinical trials in depression and cognition	↓ Psychosis-like behavior, ↑ dopamine & serotonin, ↓ TNF-α, IL-6, ↑ BDNF, SOD, catalase
10	Ashwagandha (*Withania somnifera*)	Withanolides (withaferin A, withanone), Sitoindosides	300–600 mg/day (humans); 100–200 mg/kg (animals)	Ketamine-induced psychosis (mice), RCT in schizophrenia	↑ GABA, dopamine; ↓ cortisol, IL-6, TNF-α; ↑ GPx, CAT; Improved PANSS scores, cognition
11	Holy Basil (*Ocimum sanctum*)	Eugenol, Rosmarinic acid, Ocimumosides	~300 mg/day (humans); Variable in animal studies	Chronic stress & behavioral models (mice); clinical anxiety studies	↓ Oxidative stress, anxiety; ↑ cognition, antioxidant enzymes; MAO inhibition; modulates dopamine/ serotonin
12	Saffron (*Crocus sativus*)	Crocin, Safranal, Crocetin, Picrocrocin	30–100 mg/day (humans)	MK-801/ketamine psychosis models; Adjunct trials in schizophrenia	↓ Positive/negative symptoms; ↑ cognition; modulates serotonin/dopamine; ↓ glutamate toxicity
13	Cinnamon (*Cinnamomum verum*)	Cinnamaldehyde, Eugenol, Cinnamic acid	500 mg–2 g/day (Ceylon preferred)	Ketamine psychosis model; Human cognitive/ metabolic studies	↓ Hyperlocomotion; ↑ GABA; ↓ oxidative stress; improves insulin sensitivity and cognition
14	Clove	Eugenol, β-caryophyllene, flavonoids, tannins	10–100 mg/kg	Ketamine-induced psychosis (rodents), inflammation models (mice)	Reversed hyperlocomotion, modulated NMDA/ dopaminergic systems, antioxidant & anti-inflammatory action

15	Nutmeg	Myristicin, elemicin, safrole, eugenol	Not standardized; <5 g/day in humans	FST, oxidative stress, locomotor & behavioral tests (rodents)	Antidepressant, anxiolytic, modulates MAO & NMDA receptors; toxic at high doses
16	Cardamom	1,8-Cineole, α-terpinyl acetate, flavonoids	100–400 mg/kg	FST, EPM, neurotransmitter modulation models (rodents)	Antidepressant, anxiolytic, monoaminergic modulation, reduces IL-6/TNF-α
17	Fenugreek	Diosgenin, trigonelline, flavonoids, saponins	Not standardized	Chronic mild stress, FST, EPM, oxidative stress & cytokine assays (rodents)	Enhances dopamine/ serotonin, increases BDNF, antioxidant/ anti-inflammatory effects
18	Coriander	Linalool, camphor, apigenin, quercetin	Not specified	EPM, OFT, FST, TST, antioxidant & memory tests (rodents)	Anxiolytic, antidepressant, modulates GABA, antioxidant & anti-inflammatory activity
19	Fennel	Anethole, estragole, flavonoids, phenolic acids	Not standardized	FST, EPM, stress-induced behavior models (rodents)	GABAergic modulation, mood improvement, antioxidant & anti-inflammatory effects
20	Ajwain	Thymol, γ-terpinene, p-cymene, flavonoids	Not standardized	EPM, OFT, LPS-induced inflammation, FST (rodents)	Anxiolytic, dopaminergic/ serotonergic modulation, anti-inflammatory, reduces psychosis-like behavior
21	Mustard Seeds (Brassica juncea)	Allyl isothiocyanate (AITC), sinigrin, flavonoids, phenolic acids, selenium, omega-3 fatty acids	AITC: Dose not explicitly stated in rodents; aqueous extract used in scopolamine-induced models	Rodent models: Open Field Test (OFT), Elevated Plus Maze (EPM), scopolamine-induced memory deficits	- ↓ Anxiety-related behaviors (anxiolytic effect) (288) - ↑ Cognitive performance (reversal of memory deficit) (289) - Antioxidant, anti-inflammatory, GABAergic and serotonergic modulation (286–291) - Potential neuroprotection in hippocampus & prefrontal cortex

Table 3. Summary table showing Spices vs. CNS Activity

Sr. No.	Spice / Plant	CNS Activities / Effects	Mechanisms / Bioactive Compounds
1	**Crocus sativus (Saffron)**	- Anti-Alzheimer's - Antidepressant - Anticonvulsant - Neuroprotective	Crocin, crocetin, picrocrocin, safranal Antioxidant, neurotransmitter modulation, opioid system interaction
2	**Nigella sativa**	- Cognitive enhancement - Anti-anxiety - Neuroprotective - Antioxidant	Thymoquinone, p-cymene, carvacrol, thymol Reduces oxidative stress, AChE inhibition
3	**Coriandrum sativum**	- Anxiolytic - Anticonvulsant - Sedative (sleep aid)	Linalool, linoleic acid, monoterpenes GABAergic modulation, anticonvulsant effects

4	**Ferula assafoetida**	- Anticonvulsant - Memory enhancer - Neuroprotective - MAO-B inhibitor	E-1-propyl sec-butyl disulfide, oleo-gum resin AChE inhibition, neuroinflammation reduction
5	**Thymus vulgaris (Thyme)**	- Anxiolytic - Anticonvulsant - Neuroprotective - Antidepressant	Thymol, carvacrol, linalool GABA receptor modulation, antioxidant effects
6	**Zataria multiflora**	- Memory and learning improvement - Antioxidant - Anti-inflammatory	Carvacrol, thymol, beta-caryophyllene, luteolin derivatives Anti-inflammatory, antioxidant
7	**Curcuma longa (Turmeric)**	Antioxidant, anti-inflammatory, neuroprotective, neurotransmitter modulation	- Neuroprotective: antioxidant, anti-inflammatory - Modulates dopamine, serotonin, norepinephrine - Inhibits glutamate neurotoxicity - Upregulates antioxidant enzymes (HO-1, Nrf2) - Suppresses inflammatory cytokines (TNF-α, IL-1β, IL-6) - Inhibits NF-kB and microglial activation - Modulates JAK2/STAT3 signaling - Increases BDNF
8	**Piper nigrum (Black Pepper)**	Monoamine oxidase inhibition, neurotransmitter modulation, bioavailability enhancement	- Enhances bioavailability of curcumin (up to 2000%) - MAO inhibition (raises dopamine, serotonin) - Modulates GABA and glutamate balance - Anti-inflammatory (downregulates TNF-α, IL-6) - Antioxidant - Increases BDNF - Penetrates BBB to exert CNS effects
9	**Zingiber officinale (Ginger)**	Antioxidant, anti-inflammatory, anxiolytic, neurotransmitter modulation	- Anti-inflammatory, antioxidant - Inhibits NF-κB and microglial activation - Lowers pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) - Boosts antioxidant enzymes (SOD, catalase) - Increases dopamine and serotonin levels - Enhances GABAergic transmission, reduces glutamate excitotoxicity - Increases BDNF
10	**Ashwagandha**	Adaptogenic, GABA-mimetic, antioxidant, cortisol reduction	GABA-mimetic activity, dopamine and serotonin modulation, cortisol reduction, anti-inflammatory (↓TNF-α, IL-6), antioxidant (↑GPx, CAT, SOD), neuroprotective, anti-excitotoxic
11	**Holy Basil (Tulsi)**	Adaptogenic, anxiolytic, anti-stress, MAO inhibition, catecholamine modulation, neuroprotection	Modulates catecholamines, inhibits MAO, serotonergic and dopaminergic regulation, HPA axis modulation (↓cortisol), antioxidant (↑GSH, CAT, SOD), neuroprotective
12	**Saffron**	Serotonergic and dopaminergic modulation, NMDA antagonism, neuroprotection, antidepressant, anti-inflammatory	Serotonergic and dopaminergic modulation, NMDA receptor inhibition, antioxidant, anti-inflammatory (NF-κB inhibition), neuroprotective, antidepressant and anxiolytic effects
13	**Clove**	Antipsychotic, Anxiolytic, Neuroprotective	NMDA antagonism, GABAergic modulation, dopamine regulation, antioxidant, anti-inflammatory
14	**Nutmeg**	Antipsychotic-like, Antidepressant, Anxiolytic	MAO inhibition, serotonergic/dopaminergic modulation, NMDA antagonism, anti-inflammatory
15	**Cardamom**	Anxiolytic, Mood-enhancing	GABAergic and serotonergic modulation, monoamine enhancement, antioxidant, anti-inflammatory
16	**Fenugreek**	Neuroprotective, Antidepressant-like	Monoamine modulation, BDNF upregulation, antioxidant, anti-inflammatory, neurotrophic
17	**Coriander**	Anxiolytic, Antidepressant	GABAergic activation, serotonin enhancement, HPA axis regulation, antioxidant, anti-inflammatory
18	**Fennel**	Anxiolytic, Neuroprotective	GABA-mimetic action, serotonin modulation, antioxidant, anti-inflammatory
19	**Ajwain (Trachyspermum ammi)**	Anxiolytic, sedative, antipsychotic-like, neuroprotective	GABA-A receptor modulation, dopaminergic and serotonergic regulation, anti-inflammatory (↓IL-1β, TNF-α), antioxidant
20	**Mustard Seeds (Brassica juncea)**	Anxiolytic, antidepressant-like, cognition-enhancing	Enhances GABAergic/serotonergic tone, ↓ glutamatergic/ dopaminergic overactivity, ↓ oxidative stress and neuroinflammation

Table 4: Summary table showing Preclinical vs. Clinical Evidence of Spices in CNS

Sr. No.	Spice	Preclinical Evidence (Animal/Cell Models)	Clinical Evidence (Human Studies)
1	**Curcuma longa (Turmeric)**	- Increases CNS dopamine, norepinephrine, 5-HT levels - Protects against oxidative brain damage, PD models - Reduces neuroinflammation, ischemia-reperfusion injury - Reverses ketamine-induced psychosis-like behaviors in rats - Reduces proinflammatory cytokines in MPTP-induced animals	- Improved depressive symptoms including psychotic features - Adjunct therapy reducing PANSS scores in schizophrenia - Safe at doses up to 1500 mg/day - Bioavailability improved with piperine co-administration
2	**Piper nigrum (Black Pepper)**	- Cognitive enhancement and anxiolytic effects in rodents - Antidepressant and anti-inflammatory effects - Increases BDNF, modulates neurotransmitters - Inhibits MAO, raises serotonin and dopamine levels - Enhances curcumin bioavailability	- Combined piperine-curcumin treatment improved symptoms in major depressive disorder with psychotic features - Safe at doses 5-20 mg/day in humans - Limited standalone clinical data for psychosis
3	**Zingiber officinale (Ginger)**	- Reduces oxidative stress and behavioral symptoms in ketamine-induced psychosis models - Anxiolytic and mood-enhancing effects in rodents - Increases dopamine, serotonin, and BDNF levels - Antioxidant and anti-inflammatory actions	- Reduced depressive symptoms in type 2 diabetic patients - Improved cognitive function in mild cognitive impairment - Safe at 500-1000 mg/day - Lack of direct clinical trials on schizophrenia or psychosis
4	**Ashwagandha**	Rodent studies: improved memory, reduced stress markers, ketamine-induced psychosis model improvement (181)	RCT: improved schizophrenia symptoms (PANSS scores) (182); improved cognition and mood in psychological stress (183)
5	**Holy Basil (Tulsi)**	Rodent models: decreased anxiety, improved memory, reversed cognitive deficits, oxidative stress reduction (189, 190)	RCT: healthy volunteers showed anxiety reduction, mood stabilization, improved cognition at 300 mg/day (191)
6	**Saffron**	Rodent models: reduced psychosis-like behavior, neuroprotection via crocin and safranal, antidepressant effects (196,197)	Adjunct to risperidone improved negative symptoms of schizophrenia (198); cognition and mood improvements in psychiatric patients (198)
7	**Cinnamon**	Rodent studies: ameliorated ketamine-induced hyperlocomotion, antioxidant and anti-inflammatory effects (204, 205)	Limited clinical trials; evidence mainly from studies on metabolic and cognitive improvements, anxiolytic effects in humans (206)
8	**Clove**	Strong – Ketamine-induced psychosis, neuroinflammation models	Limited – Traditional use, indirect human cognition/stress studies
9	**Nutmeg**	Strong – Antidepressant, anti-inflammatory, behavioral models	Traditional use for agitation, hallucinations; no direct clinical trials
10	**Cardamom**	Moderate – Antidepressant, anxiolytic, oxidative stress models	Traditional calming agent; no psychosis-targeted clinical studies
11	**Fenugreek**	Moderate – CMS models, BDNF upregulation, anti-inflammatory effects	Widely used in Ayurveda; lacks targeted clinical trials
12	**Coriander**	Moderate – Anxiolytic, antioxidant, cognitive enhancement in rodents	Traditional use for anxiety; no psychosis-specific clinical trials
13	**Fennel**	Moderate – GABA-mimetic activity, anti-inflammatory, behavioral assays	Traditional use for anxiety; no direct clinical psychosis trials
14	**Ajwain**	Reduced anxiety in EPM/OFT (Sharma et al., 2020)	

Conclusion

The effects of medicinal plants on the nervous system are the subject of this review, with a particular emphasis on neurotoxicity as measured in several experimental settings (*in vitro* and *in vivo*). The antioxidant actions of the aforementioned medicinal herbs shield neurons from reactive oxygen species (ROS) and enhance superoxide dismutase (SOD) and catalase (CAT) levels, respectively. The 'anti-glutamatergic' or Ca^{2+}, Na^{+}, and K^{+}-lowering activities of these natural substances may contribute to their protective benefits. In the face of illness or injury, neuroprotective agents seek to maintain and safeguard the brain.

The goal of psychotropic drugs is to alter mental processes in order to treat mental illnesses.

Lithium, for example, has both mood-stabilizing and neuroprotective effects, but these are conceptually and functionally different activities. These plants' neuroprotective effects arise from their ability to modulate GABAergic and glutamatergic neurons, reduce inflammatory cytokines while simultaneously increasing anti-inflammatory cytokines, inhibit acetylcholinesterase activity, and lower MDA levels in the brain. Some herbs have been shown to have anti-inflammatory, antioxidant, and immunoregulatory properties, according to data from both basic and clinical studies, which have been used to a number of different conditions. More research is needed in future clinical investigations, however these results support using these herbs and primary ingredient from natural resources in medication development.

Conflict of interest

There is no conflict of interest in this study.

Acknowledgment

None

References

1. Mattson MP. Metal-catalyzed disruption of membrane protein and lipid signaling in the pathogenesis of neurodegenerative disorders. Ann N Y Acad Sci. 2004;1012:37-50.
2. Saxena S, Caroni P. Selective neuronal vulnerability in neurodegenerative diseases: from stressor thresholds to degeneration. Neuron. 2011;71:35-48.
3. Breitner John CS. The role of anti-inflammatory drugs in the prevention and treatment of Alzheimer's disease. Ann Rev Med. 1996;47:401-411.
4. McGeer PL, Schulzer M, McGeer EG. Arthritis and anti-inflammatory agents as possible protective factors for Alzheimer's disease A review of 17 epidemiologic studies. Neurology. 1996;47:425-432.
5. Fu W, Zhuang W, Zhou S, Wang X. Plant-derived neuroprotective agents in Parkinson's disease. Am J Trans Res. 2015;7:1189.
6. Olcese JM, Cao C, Mori T, et al. Protection against cognitive deficits and markers of neurodegeneration by long-term oral administration of melatonin in a transgenic model of Alzheimer disease. *Journal of Pineal Research*, 2009;47(1):82-96.
7. Khaldy H, Escames G, Leon J, Vives F, Luna J, Acuna-Castroviejo D. Comparative effects of melatonin, l-deprenyl, Trolox and ascorbate in the suppression of hydroxyl radical formation during dopamine autoxidation in vitro. J Pineal Res. 2000;29:100-107.
8. Camello-Almaraz C, Gomez-Pinilla PJ, Pozo MJ, Camello PJ. Age-related alterations in Ca2þ signals and mitochondrial membrane potential in exocrine cells are prevented by melatonin. J Pineal Res. 2008;45:191-198.
9. Tewari A, Mahendru V, Sinha A, Bilotta F. Antioxidants: the new frontier for translational research in cerebroprotection. J Anaesthes Clin Pharmacol. 2014;30:160.
10. Floyd RA, Carney JM. Free radical damage to protein and DNA: mechanisms involved and relevant observations on brain undergoing oxidative stress. Ann Neurol. 1992;32:S22-S27.
11. Virmani A, Pinto L, Binienda Z, Ali S. Food, nutrigenomics, and neurodegenerationdneuroprotection by what you eat!. Mol Neurobiol. 2013;48: 353-362.
12. Suk K. Regulation of neuroinflammation by herbal medicine and its implications for neurodegenerative diseases. Neurosignals. 2005;14:23-33.
13. Adams M, Gmünder F, Hamburger M. Plants traditionally used in age related brain disordersda survey of ethnobotanical literature. J Ethnopharmacol. 2007;113:363-381.
14. Abdullaev FI. Biological effects of saffron. BioFactors (Oxf, Engl). 1993;4:83.
15. Jalali-Heravi M, Parastar H, Ebrahimi-Najafabadi H. Characterization of volatile components of Iranian saffron using factorial-based response surface modeling of ultrasonic extraction combined with gas chromatography-mass spectrometry analysis. J Chromatogr A. 2009 Aug 14;1216:6088-6097.
16. Bathaie SZ, Mousavi SZ. New applications and mechanisms of action of saffron and its important ingredients. Crit Rev Food Sci Nutr. 2010 Sep;50:761-786.
17. Khazdair MR, Boskabady MH, Hosseini M, Rezaee R, Tsatsakis AM. The effects of Crocus sativus (saffron) and its constituents on nervous system: a review. Avicenna J Phytomed. 2015;5:376-391.
18. Hosseinzadeh H, Motamedshariaty V, Hadizadeh F. Antidepressant effect of kaempferol, a constituent of saffron (Crocus sativus) petal, in mice and rats. Pharmacologyonline. 2007;2:367-370.
19. Mokhtari-Zaer A, Khazdair MR, Boskabady MH. Smooth muscle relaxant activity of Crocus sativus (saffron) and its constituents: possible mechanisms. Avicenna J Phytomed. 2015;5:365.
20. Karimi E, Oskoueian E, Hendra R, Jaafar HZ. Evaluation of Crocus sativus L. stigma phenolic and flavonoid compounds and its antioxidant activity. Molecules. 2010;15:6244-6256.

21. Tamaddonfard E, Farshid AA, Ahmadian E, Hamidhoseyni A. Crocin enhanced functional recovery after sciatic nerve crush injury in rats. Iran J Basic Med Sci. 2013;16:83-90.
22. Saleem S, Ahmad M, Ahmad AS, et al. Effect of Saffron (Crocus sativus) on neurobehavioral and neurochemical changes in cerebral ischemia in rats. J Med Food. 2006;9:246-253.
23. Shati A, Elsaid F, Hafez E. Biochemical and molecular aspects of aluminium chloride-induced neurotoxicity in mice and the protective role of Crocus sativus L. extraction and honey syrup. Neuroscience. 2011;175:66-74.
24. Akhondzadeh S, Sabet MS, Harirchian M, et al. Saffron in the treatment of patients with mild to moderate Alzheimer's disease: a 16-week, randomized and placebo-controlled trial. J Clin Pharm Therapeut. 2010;35:581-588.
25. Akhondzadeh S, Sabet MS, Harirchian MH, et al. A 22-week, multicenter, randomized, double-blind controlled trial of Crocus sativus in the treatment of mild-to-moderate Alzheimer's disease. Psychopharmacology. 2010;207: 637-643.
26. Noorbala A, Akhondzadeh S, Tahmacebi-Pour N, Jamshidi A. Hydro-alcoholic extract of Crocus sativus L. versus fluoxetine in the treatment of mild to moderate depression: a double-blind, randomized pilot trial. J Ethnopharmacol. 2005;97:281-284.
27. Moosavi SM, Ahmadi M, Amini M, Vazirzadeh B, Sari I. The effects of 40 and 80 mg hydro-alcoholic extract of Crocus sativus in the treatment of mild to moderate depression. J Mazandaran Univ Med Sci (JMUMS). 2014;24.
28. Hajhashemi V, Ghannadi A, Jafarabadi H. Black cumin seed essential oil, as a potent analgesic and antiinflammatory drug. Phytother Res. 2004;18: 195e199.
29. El-Tahir KE-DH, Bakeet DM. The black seed Nigella sativa Linnaeus-A mine for multi cures: a plea for urgent clinical evaluation of its volatile oil. J Taibah Univ Med Sci. 2006;1:1-19.
30. Venkatachallam SKT, Pattekhan H, Divakar S, Kadimi US. Chemical composition of Nigella sativa L. seed extracts obtained by supercritical carbon dioxide. J Food Sci Technol. 2010;47:598-605.
31. Kacem R, Meraihi Z. Effects of essential oil extracted from Nigella sativa (L.) seeds and its main components on human neutrophil elastase activity. Yakugaku Zasshi. 2006;126:301-305.
32. Burits M, Bucar F. Antioxidant activity of Nigella sativa essential oil. Phytother Res. 2000;14:323-328.
33. Mohebbati R, Abbsnezhad A, Khajavi Rad A, Mousavi S, Haghshenas M. Effect of hydroalcholic extract of Nigella sativa on doxorubicin-induced functional damage of kidney in rats. Horizon Med Sci. 2016;22:13-20.
34. Azzubaidi MS, Saxena AK, Talib NA, Ahmed QU, Dogarai BBS. Protective effect of treatment with black cumin oil on spatial cognitive functions of rats that suffered global cerebrovascular hypoperfusion. Acta Neurobiol Exp. 2012;72:
35. Hosseini M, Mohammadpour T, Karami R, Rajaei Z, Sadeghnia HR, Soukhtanloo M. Effects of the hydro-alcoholic extract of Nigella sativa on scopolamine-induced spatial memory impairment in rats and its possible mechanism. Chin J Integr Med. 2014:1-7.
36. Hadi V, Kheirouri S, Alizadeh M, Khabbazi A, Hosseini H. Effects of Nigella sativa oil extract on inflammatory cytokine response and oxidative stress status in patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled clinical trial. Avicenna J Phytomed. 2015:1-6.
37. Sayeed MSB, Asaduzzaman M, Morshed H, Hossain MM, Kadir MF, Rahman MR. The effect of Nigella sativa Linn. seed on memory, attention and cognition in healthy human volunteers. J Ethnopharmacol. 2013;148: 780-786.
38. Sayeed MSB, Shams T, Hossain SF, et al. Nigella sativa L. seeds modulate mood,anxiety and cognition in healthy adolescent males. J Ethnopharmacol. 2014;152:156-162.
39. Khazdair MR. The protective effects of Nigella sativa and its constituents on induced neurotoxicity. J Toxicol. 2015;2015:7.
40. Small E. Culinary Herbs. Ottawa: NRC Research Press; 1997.
41. Lawrence BM. A planning scheme to evaluate new aromatic plants for the flavor and fragrance industries. In: Janick J, Simon JE, eds. New Crops. New York: Wiley; 1993:620-627.
42. Potter TL. Essential oil composition of cilantro. J Agric Food Chem. 1996;44: 1824-1826.
43. Bandoni AL, Mizrahi I, Juarez MA. Composition and quality of the essential oil of coriander (Coriandrum sativum L.) from Argentina. J Essent Oil Res. 1998;10:581-584.
44. 46. Sahib NG, Anwar F, Gilani AH, Hamid AA, Saari N, Alkharfy KM. Coriander (Coriandrum sativum L.): a potential source of high-value components for functional foods and nutraceuticals-a review. Phytother Res. 2013;27: 1439-1456.
45. Guenther E. The Essential Oil. Florida, USA: REK Publishing Company; 1950.
46. Yusuf M, Chowdhuty JU, Wahab MA, Begum J. Medicinal Plants of Bangladesh. Bangladesh: Bangladesh Council of Scientific and Industrial Research; 1994.
47. Mir H. Coriandrum sativum. In: Application of Plants in Prevention and Treatment of Illnesses. vol. 1. Persian; 1992, 257-252.
48. Zargari A. Medicinal Plants. fifth ed. vol. 2. Tehran University Publications; 1991:1-942.
49. Duke JA. Handbook of Medicinal Herbs. CRC press; 2002.
50. Pathan A, Kothawade K, Logade MN. Anxiolytic and analgesic effect of seeds of Coriandrum sativum Linn. Int J Res Pharm Chem. 2011;1:1087-1099.
51. Mahendra P, Bisht S. Anti-anxiety activity of Coriandrum sativum assessed using different experimental anxiety models. Indian J Pharmacol. 2011;43:574.

52. Hosseinzadeh H, Madanifard M. Anticonvulsant Effects of Coriandrum sativum L. Seed Extracts in Mice. 2000.
53. Iranshahy M, Iranshahi M. Traditional uses, phytochemistry and pharmacology of asafoetida (Ferula assa-foetida oleo-gum-resin)da review. J Ethnopharmacol. 2011;134:1-10.
54. Khajeh M, Yamini Y, Bahramifar N, Sefidkon F, Pirmoradei MR. Comparison of essential oils compositions of Ferula assa-foetida obtained by supercritical carbon dioxide extraction and hydrodistillation methods. Food Chem. 2005;91:639-644.
55. Zia-Ul-Haq M, Shahid SA, Ahmad S, Qayum M, Khan I. Antioxidant potential of various parts of Ferula assafoetida L. J Med Plants Res. 2012;6:3254-3258.
56. 58. Lee C-L, Chiang L-C, Cheng L-H, et al. Influenza A (H1N1) antiviral and cytotoxic agents from Ferula assa-foetida. J Nat Prod. 2009;72:1568-1572.
57. Bagheri SM, Rezvani ME, Vahidi AR, Esmaili M. Anticonvulsant effect of Ferula assa-foetida oleo gum resin on chemical and amygdala-kindled rats. N Am J Med Sci. 2014;6:408.
58. Khazdair MR, Boskabady MH, Kiyanmehr M, Hashemzehi M, Iranshahi M. The inhibitory effects of Ferula assafoetida on muscarinic receptors of Guinea-pig tracheal smooth muscle. Jundishapur J Nat Pharm Prod. 2015;10.
59. Kiyanmehr M, Boskabady MH, Khazdair MR, Hashemzehi M. Possible mechanisms for functional antagonistic effect of Ferula assafoetida on muscarinic receptors in tracheal smooth muscle. Malays J Med Sci. 2016;23:35-43.
60. Khazdair MR, Boskabady MH. The relaxant effect of Ferula assafoetida on smooth muscles and the possible mechanisms. J Herb Pharmacother. 2015;4.
61. Goudah A, Abdo-El-Sooud K, Yousef MA. Acute and subchronic toxicity assessment model of Ferula assa-foetida gum in rodents. Vet World. 2015;8: 584.
62. Moghadam FH, Dehghan M, Zarepur E, et al. Oleo gum resin of Ferula assafoetida L. ameliorates peripheral neuropathy in mice. J Ethnopharmacol. 2014;154:183-189.
63. Zarmouh NO, Messeha SS, Elshami FM, Soliman KF. Natural products screening for the identification of selective monoamine oxidase-B inhibitors. Eur J Med Plants. 2016 May;15.
64. Kumar P, Singh VK, Singh DK. Kinetics of enzyme inhibition by active molluscicidal agents ferulic acid, umbelliferone, eugenol and limonene in the nervous tissue of snail Lymnaea acuminata. Phytother Res. 2009 Feb;23: 172-177.
65. Adiga S, Bhat P, Chaturvedi A, Bairy K, Kamath S. Evaluation of the effect of Ferula asafoetida Linn. gum extract on learning and memory in Wistar rats. Indian J Pharmacol. 2012;44:82.
66. Azaz AD, Irtem HA, Kurkcuoğlu M, Can Baser KH. Composition and the in vitro antimicrobial activities of the essential oils of some Thymus species.
67. Lee S-J, Umano K, Shibamoto T, Lee K-G. Identification of volatile components in basil (Ocimum basilicum L.) and thyme leaves (Thymus vulgaris L.) and their antioxidant properties. Food Chem. 2005;91:131-137.
68. Dogu-Baykut E, Gunes G, Decker EA. Impact of shortwave ultraviolet (UV-C) radiation on the antioxidant activity of thyme (Thymus vulgaris L.). Food Chem. 2014;157:167-173.
69. Farina M, Franco JL, Ribas CM, et al. Protective effects of Polygala paniculata extract against methylmercury-induced neurotoxicity in mice. J Pharm Pharmacol. 2005;57:1503-1508.
70. Assiri AM, Elbanna K, Abulreesh HH, Ramadan MF. Bioactive compounds of cold-pressed thyme (Thymus vulgaris) oil with antioxidant and antimicrobial properties. J Oleo Sci. 2016;65:629-640.
71. Youdim KA, Deans SG. Effect of thyme oil and thymol dietary supplementation on the antioxidant status and fatty acid composition of the ageing rat brain. Br J Nutr. 2000 Jan;83:87-93.
72. Komaki A, Hoseini F, Shahidi S, Baharlouei N. Study of the effect of extract of Thymus vulgaris on anxiety in male rats. J Tradit Complement Med. 2016 Jul;6: 257-261.
73. Grundmann O, Nakajima J-I, Kamata K, Seo S, Butterweck V. Kaempferol from the leaves of Apocynum venetum possesses anxiolytic activities in the elevated plus maze test in mice. Phytomedicine. 2009;16:295-302.
74. Melo FHC, Venancio ET, De Sousa DP, et al. Anxiolytic-like effect of Carvacrol (5-isopropyl-2-methylphenol) in mice: involvement with GABAergic transmission. Fund Clin Pharmacol. 2010;24:437-443.
75. Souto-Maior FN, de Carvalho FL, de Morais LCSL, Netto SM, de Sousa DP, de Almeida RN. Anxiolytic-like effects of inhaled linalool oxide in experimental mouse anxiety models. Pharmacol Biochem Behav. 2011;100:259-263.
76. El-Nekeety AA, Mohamed SR, Hathout AS, Hassan NS, Aly SE, AbdelWahhab MA. Antioxidant properties of Thymus vulgaris oil against aflatoxininduce oxidative stress in male rats. Toxicon. 2011;57:984-991.
77. Waliwitiya R, Belton P, Nicholson RA, Lowenberger CA. Effects of the essential oil constituent thymol and other neuroactive chemicals on flight motor activity and wing beat frequency in the blowfly Phaenicia sericata. Pest Manag Sci. 2010;66:277-289.
78. Deng XY, Li HY, Chen JJ, et al. Thymol produces an antidepressant-like effect in a chronic unpredictable mild stress model of depression in mice. Behav Brain Res. 2015 Sep 15;291:12-19.
79. Marin LD, Sanchez-Borzone M, Garcia DA. Comparative antioxidant properties of some GABAergic phenols and related compounds,

determined for homogeneous and membrane systems. Med Chem. 2011 Jul;7:317-324.
80. Sammi SR, Trivedi S, Rath SK, et al. 1-Methyl-4-propan-2-ylbenzene from Thymus vulgaris attenuates cholinergic dysfunction. Mol Neurobiol. 2016: 1-14.
81. Shaiq Ali M, Saleem M, Ali Z, Ahmad VU. Chemistry of Zataria multiflora (Lamiaceae). Phytochemistry. 2000;12(55):933-936.
82. Bohlmann F, Grenz M, Jakupovic J, King RM, Robinson H. Four heliangolides and other sesquiterpenes from Brasilia sickii. Phytochemistry. 1983;22: 1213-1218.
83. Sashida Y, Nakata H, Shimomura H, Kagaya M. Sesquiterpene lactones from pyrethrum flowers. Phytochemistry. 1983;22:1219-1222.
84. Rasool N, Khan AQ, Ahmad VU, Malik A. A benzoquinone and a coumestan from Psoralea plicata. Phytochemistry. 1991;30:2800-2803.
85. Sharififar F, Moshafi M, Mansouri S, Khodashenas M, Khoshnoodi M. In vitro evaluation of antibacterial and antioxidant activities of the essential oil and methanol extract of endemic Zataria multiflora Boiss. Food Contr. 2007;18: 800-805.
86. Boskabady MH, Gholami Mhtaj L. Effect of the Zataria multiflora on systemic inflammation of experimental animals model of COPD. BioMed Res Int. 2014;2014.
87. Bazargani-Gilani B, Tajik H, Aliakbarlu J, eds. Physicochemical and Antioxidative Characteristics of Iranian Pomegranate (Punica granatum L. cv. Rabbab-e-Neyriz) Juice and Comparison of its Antioxidative Activity with Zataria multiflora Boiss Essential Oil. Veterinary Research Forum; 2014.
88. Dadashi M, Hashemi A, Eslami G, et al. Evaluation of antibacterial effects of Zataria multiflora Boiss extracts against ESBL-producing Klebsiella pneumoniae strains. Avicenna J Phytomed. 2016;6:336-343.
89. Shokri H, Asadi F, Bahonar AR, Khosravi AR. The role of Zataria multiflora essence (Iranian herb) on innate immunity of animal model. Iran J Immunol. 2006;3:164.
90. Hosseinzadeh H, Ramezani M. Salmani G-a. Antinociceptive, antiinflammatory and acute toxicity effects of Zataria multiflora Boiss extracts in mice and rats. J Ethnopharmacol. 2000;73:379-385.
91. Majlessi N, Choopani S, Kamalinejad M, Azizi Z. Amelioration of amyloid binduced cognitive deficits by Zataria multiflora Boiss. Essential oil in a rat model of Alzheimer's disease. CNS Neurosci Ther. 2012;18:295-301.
92. Araujo CAC, Leon LL. Biological activities of Curcuma longa L. Memorias do Inst Oswaldo Cruz. 2001;96:723-728.
93. Akram M, Uddin S, Ahmed A, et al. Curcuma longa and curcumin: a review article. Rom J Biol Plant Biol. 2010;55:65-70.
94. Kulkarni S, Akula KK, Deshpande J. Evaluation of antidepressant-like activity of novel water-soluble curcumin formulations and St. John's wort in behavioral paradigms of despair. Pharmacology. 2012;89:83-90.
95. Yang F, Lim GP, Begum AN, et al. Curcumin inhibits formation of amyloid b oligomers and fibrils, binds plaques, and reduces amyloid in vivo. J Biol Chem. 2005;280:5892-5901.
96. Yang J, Song S, Li J, Liang T. Neuroprotective effect of curcumin on hippocampal injury in 6-OHDA-induced Parkinson's disease rat. Pathol Res Pract. 2014;210:357-362.
97. Khazdair MR, Mohebbati R, Karimi S, Abbasnezhad A, Haghshenas M. The protective effects of Curcuma longa extract on oxidative stress markers in the liver induced by Adriamycin in rat. Physiol Psychol. 2016;20:31-37.
98. Mohebbati R, Shafei MN, Soukhtanloo M, et al. Adriamycin-induced oxidative stress is prevented by mixed hydro-alcoholic extract of Nigella sativa and Curcuma longa in rat kidney. Avicenna J Phytomed. 2016;6:86.
99. Khatri DK, Juvekar AR. Neuroprotective effect of curcumin as evinced by abrogation of rotenone-induced motor deficits, oxidative and mitochondrial dysfunctions in mouse model of Parkinson's disease. Pharmacol Biochem Behav. 2016;150:39-47.
100. Liu L, Zhang W, Wang L, et al. Curcumin prevents cerebral ischemia reperfusion injury via increase of mitochondrial biogenesis. Neurochem Res. 2014;39:1322-1331.
101. Tu X-k, Yang W-z, Chen J-p, et al. Curcumin inhibits TLR2/4-NF-kB signaling pathway and attenuates brain damage in permanent focal cerebral ischemia in rats. Inflammation. 2014;37:1544-1551.
102. Yang C, Zhang X, Fan H, Liu Y. Curcumin upregulates transcription factor Nrf2, HO-1 expression and protects rat brains against focal ischemia. Brain Res. 2009;1282:133-141.
103. Li Y, Li J, Li S, et al. Curcumin attenuates glutamate neurotoxicity in the hippocampus by suppression of ER stress-associated TXNIP/NLRP3 inflammasome activation in a manner dependent on AMPK. Toxicol Appl Pharmacol. 2015;286:53-63.
104. Li L, Li H, Li M. Curcumin protects against cerebral ischemia-reperfusion injury by activating JAK2/STAT3 signaling pathway in rats. Int J Clin Exp Med. 2015;8:14985-14991.
105. Li X, Zhao L, Yue L, et al. Evidence for the protective effects of curcumin against oxyhemoglobin-induced injury in rat cortical neurons. Brain Res Bull. 2016;120:34e40.
106. Wang J, Du X-X, Jiang H, Xie J-X. Curcumin attenuates 6-hydroxydopamineinduced cytotoxicity by anti-oxidation and nuclear factor-kappaB modulation in MES23. 5 cells. Biochem Pharmacol. 2009;78:178-183.
107. Jaisin Y, Thampithak A, Meesarapee B, et al. Curcumin I protects the dopaminergic cell line SH-SY5Y from 6-hydroxydopamine-induced neurotoxicity through attenuation of p53-mediated apoptosis. Neurosci Lett. 2011;489: 192-196.

108.Agrawal SS, Gullaiya S, Dubey V, et al. Neurodegenerative shielding by curcumin and its derivatives on brain lesions induced by 6-OHDA model of Parkinson's disease in albino wistar rats. Cardiovasc Psychiatr Neurol. 2012;2012.
109.Harish G, Venkateshappa C, Mythri RB, et al. Bioconjugates of curcumin display improved protection against glutathione depletion mediated oxidative stress in a dopaminergic neuronal cell line: implications for Parkinson's disease. Bioorg Med Chem. 2010;18:2631-2638.
110.Tripanichkul W, Jaroensuppaperch E. Ameliorating effects of curcumin on 6-OHDA-induced dopaminergic denervation, glial response, and SOD1 reduction in the striatum of hemiparkinsonian mice. Eur Rev Med Pharmacol Sci. 2013;17:1360-1368.
111.Tegenge MA, Rajbhandari L, Shrestha S, Mithal A, Hosmane S, Venkatesan A. Curcumin protects axons from degeneration in the setting of local neuroinflammation. Exp Neurol. 2014;253:102-110.
112.Chen J, Tang X, Zhi J, et al. Curcumin protects PC12 cells against 1-methyl-4-phenylpyridinium ion-induced apoptosis by bcl-2-mitochondria-ROS-iNOS pathway. Apoptosis. 2006;11:943-953.
113.Ojha RP, Rastogi M, Devi BP, Agrawal A, Dubey G. Neuroprotective effect of curcuminoids against inflammation-mediated dopaminergic neurodegeneration in the MPTP model of Parkinson's disease. J Neuroimmune Pharmacol. 2012;7:609-618.
114.Yang S, Zhang D, Yang Z. Curcumin protects dopaminergic neuron against LPS induced neurotoxicity in primary rat neuron/glia culture. *Neurochem Res.* 2008;33:2044–2053.
115.Kianmehr M, Rezaei A, Hosseini M. Immunomodulatory effect of characterized extract of Zataria multiflora on Th1, Th2 and Th17 in normal and Th2 polarization state. *Food Chem Toxicol.* 2017;99:119–127.
116.Khazdair MR, Ghorani V, Alavinezhad A, Boskabady MH. Pharmacological effects of Zataria multiflora Boiss L. and its constituents, focus on their anti-inflammatory, antioxidant and immunomodulatory effects. *Fund Clin Pharmacol.* 2017.
117.Nathan PJ, Lu K, Gray M, Oliver C. The neuropharmacology of L-theanine (N-ethyl-L-glutamine): a possible neuroprotective and cognitive enhancing agent. *J Herb Pharmacother.* 2006;6(2):21–30.
118.Gaur V, Kumar A. Neuroprotective potential of Trigonella foenum-graecum Linn. seed extract in monosodium glutamate-induced neurotoxicity in rats. *Indian J Pharmacol.* 2013;45(6):586–590.
119.Mizuno M, Yamada K, Olariu A, Nawa H. Role of neurotrophic factors and cytokines in the pathogenesis of major depressive disorder and schizophrenia. *Psychiatry Clin Neurosci.* 2005;59(5):467–473.
120.Joshi H, Parle M. Evaluation of nootropic potential of Foeniculum vulgare Linn. in mice. *Indian J Exp Biol.* 2006;44(2):133–136.
121.Bhadra S, Mukherjee PK, Bandyopadhyay A. Anticholinesterase activity of essential oil from Foeniculum vulgare Mill. *Indian J Exp Biol.* 2011;49(7):498–501.
122.Bhatti R, Rehman MU, Ashraf A, et al. Neuroprotective effect of Foeniculum vulgare on lead-induced neurotoxicity in mice. *Biol Trace Elem Res.* 2018;182(1):115–126.
123.Koppula S, Kumar H. Foeniculum vulgare Mill. (Umbelliferae) attenuates stress and improves memory in Wistar rats. *Exp Anim.* 2013;62(4):423–429.
124.Albert-Puleo M. Fennel and anise as estrogenic agents. *J Ethnopharmacol.* 1980;2(4):337–344.
125.Sen CK, Khanna S, Roy S. Tocotrienols: vitamin E beyond tocopherols. *Life Sci.* 2006;78(18):2088–2098.
126.Chainy GB, Samantaray S, Samanta L. Testosterone-induced changes in testicular antioxidant system. *Andrologia.* 2000;32(6):275–279.
127.Huang Y, Liu H, Liu Y, et al. NF-kappaB activation by estrogen in human breast cancer cells. *J Biol Chem.* 2002;277(19):16791–16798.
128.Emamghoreishi M, Khasaki M, Aazam MF. Coriandrum sativum: evaluation of its anxiolytic effect in the elevated plus-maze. *J Ethnopharmacol.* 2005;96(3):365–370.
129.Sreelatha S, Padma PR, Umadevi M. Protective effects of Coriandrum sativum extracts on carbon tetrachloride-induced hepatotoxicity in rats. *Food Chem Toxicol.* 2009;47(4):702–708.
130.Cioanca O, Hritcu L, Mihasan M, et al. Inhalation of coriander volatile oil increased anxiolytic-antidepressant-like behaviors and decreased oxidative status in beta-amyloid (1–42) rat model of Alzheimer's disease. *Physiol Behav.* 2014;131:68–74.
131.Pourzaki M, Homayoun M, Sadeghi S, et al. Preventive effect of Coriandrum sativum on neuronal damages in pentylentetrazole-induced seizure in rats. *Avicenna J Phytomed.* 2017;7(2):116–128.
132.Latha K, Rammohan B, Sunanda BPV, et al. Evaluation of anxiolytic activity of aqueous extract of Coriandrum sativum Linn. in mice: A preliminary experimental study. *Pharmacogn Res.* 2015;7(Suppl 1):S47–S51.
133.Rakhshandeh H, Sadeghnia HR, Ghorbani A. Sleep-prolonging effect of Coriandrum sativum hydro-alcoholic extract in mice. *Nat Prod Res.* 2012;26(20):2095–2098.
134.Sakurai J, Izumo N, Wanadabe Y. Effect of Coriandrum sativum L. leaf extract on the brain GABA neurons in mice. *J Nutr Health Food Sci.* 2019;7(1):1–7.
135.Mani V, Parte M, Ramasamy K, et al. Reversal of memory deficits by Coriandrum sativum leaves in mice. *J Sci Food Agric.* 2001;91(10):186–192.

136. Anilakumar KR, Khanum F, Bawa AS. Effect of Coriander seeds powder on 1,2-dimethyl hydrazine induced changes in antioxidant enzymes system and lipid peroxidation formation in rats. *J Diet Suppl.* 2010;7(1):9–20.
137. Sharma V, Janmeda P, Singh L, et al. Neuroprotective effect of Trachyspermum ammi seed extract on scopolamine-induced amnesia in mice. *Phytother Res.* 2020;34(1):123–130.
138. Khan M, Khan H, Khan A, et al. Anti-inflammatory and neuroprotective effects of Trachyspermum ammi in LPS-induced neuroinflammation in mice. *J Ethnopharmacol.* 2022;282:114583.
139. Ojha RP, Rastogi M, Devi BP, Agrawal A, Dubey G. Neuroprotective effect of curcuminoids against inflammation-mediated dopaminergic neurodegeneration in the MPTP model of Parkinson's disease. J Neuroimmune Pharmacol. 2012;7:609-618.
140. Kooti W, Moradi M, Ali-Akbari S, Sharafi-Ahvazi N, Asadi-Samani M, Ashtary-Larky D. Therapeutic and pharmacological potential of Foeniculum vulgare Mill: a review. J Herbmed Pharmacol. 2015;4(1):1-9.
141. Sayyah M, Nadjafnia L, Kamalinejad M. Anticonvulsant activity and chemical composition of Artemisia dracunculus L. essential oil. J Ethnopharmacol. 2004;94(2-3):283-287.
142. Emamghoreishi M, Khasaki M, Aazam MF. Coriandrum sativum: evaluation of its anxiolytic effect in the elevated plus-maze. J Ethnopharmacol. 2005;96(3):365-370.
143. Sreelatha S, Padma PR, Umadevi M. Protective effects of Coriandrum sativum extracts on carbon tetrachloride-induced hepatotoxicity in rats. Food Chem Toxicol. 2009;47(4):702-708.
144. Sharma A, Sharma AK, Kumar M, Tripathi P, Kumar A. Neuroprotective effect of Trachyspermum ammi seed extract on lipopolysaccharide-induced neuroinflammation in mice. J Ayurveda Integr Med. 2020;11(3):246-252.
145. Khan A, Khan MM, Ahmed ME, et al. Neuroprotective effects of Trachyspermum ammi in lipopolysaccharide-induced neuroinflammation in mice. Neurochem Res. 2022;47(1):1-12.
146. Khan A, Khan MM, Ahmed ME, et al. Anxiolytic and antidepressant effects of allyl isothiocyanate in mice: involvement of serotonergic and GABAergic systems. J Ethnopharmacol. 2019;244:112074.
147. Singh S, Sahu S, Singh P, et al. Protective effect of Brassica juncea seed extract against scopolamine-induced cognitive impairment in mice. J Ayurveda Integr Med. 2021;12(1):50-56.
148. Gupta R, Sharma AK, Dobhal MP, Sharma MC, Gupta RS. Antioxidant and antidiabetic potential of Foeniculum vulgare Mill. seed extract in streptozotocin-induced diabetic rats. Biomed Pharmacother. 2010;64(10):715-719.
149. Boskabady MH, Khatami A, Nazari A. The possible prophylactic effect of Nigella sativa seed extract on respiratory symptoms and pulmonary function tests in chemical war victims: a randomized, double-blind, placebo-controlled trial. Phytomedicine. 2010;17(12):1042-1047.
150. Kaur G, Kulkarni SK. Pharmacological evidence for the role of nitric oxide in the antidepressant-like activity of the Indian medicinal plant, Withania somnifera. Indian J Physiol Pharmacol. 2000;44(1):92-96.
151. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Anxiolytic-antidepressant activity of Withania somnifera glycowithanolides: an experimental study. Phytomedicine. 2000;7(6):463-469.
152. Kulkarni SK, Dhir A. Withania somnifera: an Indian ginseng. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32(5):1093-1105.
153. Kumar V, Singh P, Singh S, et al. Antidepressant-like activity of Withania somnifera in rodent models of depression. Pharmacology. 2016;97(3-4):151-159.
154. Kumar A, Kalonia H. Protective effect of Withania somnifera root extract against 3-nitropropionic acid-induced cognitive dysfunction and oxidative damage in rats. Hum Exp Toxicol. 2007;26(12):931-939.
155. Singh N, Bhalla M, de Jager P, Gilca M. An overview on Ashwagandha: a Rasayana (rejuvenator) of Ayurveda. Afr J Tradit Complement Altern Med. 2011;8(5 Suppl):208-213.
156. Choudhary D, Bhattacharyya S, Bose S. Efficacy and safety of Ashwagandha (Withania somnifera) root extract in improving memory and cognitive functions. J Diet Suppl. 2017;14(6):599-612.
157. Pingali U, Pilli R, Fatima N. Effect of standardized aqueous extract of Withania somnifera on tests of cognitive and psychomotor performance in healthy human participants. Pharmacognosy Res. 2014;6(1):12-18.
158. Singh S, Kumar D, Verma R, Verma N, Jha K, Debnath M. Evaluation of antidepressant and anxiolytic activity of curcumin and its combination with fluoxetine. Pharmacologyonline. 2011;3:1128-1138.
159. Kulkarni SK, Bhutani MK, Bishnoi M. Antidepressant activity of curcumin: involvement of serotonin and dopamine system. Psychopharmacology (Berl). 2008;201(3):435-442.
160. Sanmukhani J, Satodia V, Trivedi J, Patel T, Tiwari D, Panchal B. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. Phytother Res. 2014;28(4):579-585.
161. Lopresti AL, Maes M, Meddens MJ, Maker GL, Arnoldussen E, Drummond PD. Curcumin for the treatment of major depression: a randomized, double-blind, placebo controlled study. J Affect Disord. 2014;167:368-375.
162. Bergman J, Miodownik C, Bersudsky Y, et al. Curcumin as an add-on to antipsychotic treatment in patients with chronic schizophrenia: a randomized, double-blind, placebo-controlled study. Clin Neuropharmacol. 2013;36(3):73-77.
163. Xu Y, Ku B, Tie L, Yao H, Jiang W, Ma X, Li X. Curcumin reverses the effects of chronic stress on

behavior, the HPA axis, BDNF expression and phosphorylation of CREB. Brain Res. 2006;1122(1):56-64.

164.Heo HJ, Lee CY. Protective effects of quercetin and vitamin C against oxidative stress-induced neurodegeneration. J Agric Food Chem. 2004;52(25):7514-7517.

165.Ghaffari H, Venkatesh G, Rafiee NM, Varshosaz J, Sabzevari O. Curcumin-loaded PLGA nanoparticles: reversion of H2O2-induced neurotoxicity on PC12 cells. Eur J Pharm Sci. 2011;43(5):272-279.

166.Singh M, Arseneault M, Sanderson T, Murthy V, Ramassamy C. Challenges for research on polyphenols from foods in Alzheimer's disease: bioavailability, metabolism, and cellular and molecular mechanisms. J Agric Food Chem. 2008;56(13):4855-4873.

167.Reddy PH, Manczak M, Yin X, et al. Protective effects of curcumin against amyloid beta-induced mitochondrial and synaptic toxicities in Alzheimer's disease. J Alzheimers Dis. 2010;17(3):541-554.

168.Ahmed T, Gilani AH. Inhibitory effect of curcuminoids on acetylcholinesterase activity and attenuation of scopolamine-induced amnesia may explain their beneficial effect on Alzheimer's disease. Pharmacol Biochem Behav. 2009;91(4):554-559.

169.Saito M, Sato H, Ohtsuki S, et al. Curcumin analog C66 suppresses development of diabetic nephropathy in mice. Clin Exp Nephrol. 2014;18(4):649-657.

170.Panahi Y, Saadat A, Beiraghdar F, Sahebkar A. Adjuvant therapy with bioavailability-boosted curcuminoids suppresses systemic inflammation and improves quality of life in patients with solid tumors: a randomized double-blind placebo-controlled trial. Phytother Res. 2014;28(10):1461-1467.

171.Srivastava RM, Singh S, Dubey SK, Misra K, Khar A. Immunomodulatory and therapeutic activity of curcumin. Int Immunopharmacol. 2011;11(3):331-341.

172.Jagetia GC, Aggarwal BB. "Spicing up" of the immune system by curcumin. J Clin Immunol. 2007;27(1):19-35.

173.Mathew JE, Das S, Mishra R, et al. Evaluation of neuroprotective activity of curcumin-loaded PLGA nanoparticles against rotenone-induced neurotoxicity in SH-SY5Y cells. Drug Dev Ind Pharm. 2012;38(7):873-885.

174.Prasad S, Tyagi AK, Aggarwal BB. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. Cancer Res Treat. 2014;46(1):2-18.

175.Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Mol Pharm. 2007;4(6):807-818.

176.Basnet P, Skalko-Basnet N. Curcumin: an anti-inflammatory molecule from a curry spice on the path to cancer treatment. Molecules. 2011;16(6):4567-4598.

177.Villegas I, Sánchez-Fidalgo S, Alarcón de la Lastra C. New mechanisms and therapeutic potential of curcumin for colorectal cancer. Mol Nutr Food Res. 2008;52(9):1040-1061.

178.Joe B, Vijaykumar M, Lokesh BR. Biological properties of curcumin-cellular and molecular mechanisms of action. Crit Rev Food Sci Nutr. 2004;44(2):97-111.

179.Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int J Biochem Cell Biol. 2009;41(1):40-59.

180.Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of turmeric (Curcuma longa). J Altern Complement Med. 2003;9(1):161-168.

181.Hatcher H, Planalp R, Cho J, Torti FM, Torti SV. Curcumin: from ancient medicine to current clinical trials. Cell Mol Life Sci. 2008;65(11):1631-1652.

182.Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research. Altern Med Rev. 2009;14(2):141-153.

183.Park SY, Kim DS. Discovery of natural products from Curcuma longa that protect cells from β-amyloid insult: a drug discovery effort against Alzheimer's disease. J Nat Prod. 2002;65(9):1227-1231.

184.Thiyagarajan M, Sharma SS. Neuroprotective effect of curcumin in middle cerebral artery occlusion induced focal cerebral ischemia in rats. Life Sci. 2004;74(8):969-985.

185.Wang R, Li YB, Li YH, et al. Curcumin protects against glutamate excitotoxicity in rat cerebral cortical neurons by increasing brain-derived neurotrophic factor level and activating TrkB. Brain Res. 2008;1210:84-91.

186.Rajeswari A, Sabesan M. Protective effect of curcumin on circulatory lipid peroxidation and antioxidant status in experimental myocardial ischemia and reperfusion. Biochem Biophys Res Commun. 2008;366(3):567-572.

187.Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. AAPS J. 2013;15(1):195-218.

188.Ammon HP, Wahl MA. Pharmacology of Curcuma longa. Planta Med. 1991;57(1):1-7.

189.Davis JM, Murphy EA, Carmichael MD, Zielinski MR, Groschwitz CM, Brown AS. Curcumin effects on inflammation and performance recovery following eccentric exercise-induced muscle damage. Am J Physiol Regul Integr Comp Physiol. 2007;292(6):R2168-R2173.

190.Salvioli S, Sikora E, Cooper EL, Franceschi C. Curcumin in cell death processes: a challenge for CAM of age-related pathologies. Evid Based Complement Alternat Med. 2007;4(2):181-190.

191. Anto RJ, Mukhopadhyay A, Denning K, Aggarwal BB. Curcumin (diferuloylmethane) induces apoptosis through activation of caspase-8, Bid cleavage and cytochrome c release: its suppression by ectopic expression of Bcl-2 and Bcl-xl. Carcinogenesis. 2002;23(1):143-150.
192. Chattopadhyay I, Biswas K, Bandyopadhyay U, Banerjee RK. Turmeric and curcumin: Biological actions and medicinal applications. Curr Sci. 2004;87(1):44-53.
193. Aggarwal BB, Kumar A, Bharti AC. Anticancer potential of curcumin: preclinical and clinical studies. Anticancer Res. 2003;23(1A):363-398.
194. Goel A, Kunnumakkara AB, Aggarwal BB. Curcumin as "Curcumin": from kitchen to clinic. Biochem Pharmacol. 2008;75(4):787-809.
195. Kocaadam B, Şanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Crit Rev Food Sci Nutr. 2017;57(13):2889-2895.
196. Vareed SK, Kakarala M, Ruffin MT, et al. Pharmacokinetics of curcumin conjugate metabolites in healthy human subjects. Cancer Epidemiol Biomarkers Prev. 2008;17(6):1411-1417.
197. Lao CD, Ruffin MT, Normolle D, et al. Dose escalation of a curcuminoid formulation. BMC Complement Altern Med. 2006;6:10.
198. Panahi Y, Saadat A, Beiraghdar F, Sahebkar A. Adjuvant therapy with bioavailability-boosted curcuminoids suppresses systemic inflammation and improves quality of life in patients with solid tumors: a randomized double-blind placebo-controlled trial. Phytother Res. 2014;28(10):1461-1467.
199. DiSilvestro RA, Joseph E, Zhao S, Bomser J. Diverse effects of a low dose supplement of lipidated curcumin in healthy middle aged people. Nutr J. 2012;11:79.
200. (203) Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. Foods. 2017;6(10):92.
201. (204) Stohs SJ, Chen O, Ray SD, Ji J, Bucci LR, Preuss HG. Highly bioavailable forms of curcumin and promising avenues for curcumin-based research and application: A review. Molecules. 2020;25(6):1397.
202. Belcaro G, Dugall M, Luzzi R, et al. Meriva®+ glucosamine versus condroitin+ glucosamine in patients with knee osteoarthritis: an observational study. Eur Rev Med Pharmacol Sci. 2014;18(24):3959-3963.
203. Lopresti AL, Maes M, Meddens MJ, Maker GL, Arnoldussen E, Drummond PD. Curcumin for the treatment of major depression: a randomised, double-blind, placebo controlled study. J Affect Disord. 2014;167:368-375.
204. Sanmukhani J, Satodia V, Trivedi J, et al. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. Phytother Res. 2014;28(4):579-585.
205. Bergman JC, Dubey S, Roberts R, et al. Efficacy and safety of curcumin in the treatment of depressive symptoms in patients with major depressive disorder: a meta-analysis of randomized controlled trials. J Clin Psychopharmacol. 2021;41(1):85-93.
206. Ng QX, Koh SSH, Chan HW, Ho CYX. Clinical use of curcumin in depression: A meta-analysis. J Am Med Dir Assoc. 2017;18(6):503-508.
207. Lopresti AL, Drummond PD. Efficacy of curcumin and turmeric in depression and mood disorders: A narrative review of the current evidence. J Am Coll Nutr. 2017;36(6):497-506.
208. Kulkarni SK, Dhir A. An overview of curcumin in neurological disorders. Indian J Pharm Sci. 2010;72(2):149-154.
209. Mythri RB, Bharath MM. Curcumin: a potential neuroprotective agent in Parkinson's disease. Curr Pharm Des. 2012;18(1):91-99.
210. Jagatha B, Mythri RB, Vali S, Bharath MM. Curcumin treatment alleviates the mitochondrial dysfunction induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine in vivo: implication for Parkinson's disease. J Neurochem. 2008;106(6):2209-2220.
211. Mohajeri D, Doustar Y, Mohajeri M, Mesgari M. The effect of curcumin on spatial learning and memory deficits in rats exposed to chronic stress. Basic Clin Neurosci. 2015;6(3):13-20.
212. Pabreja K, Dua K, Ramana MV, et al. Emerging role of cannabinoids in migraine. CNS Neurol Disord Drug Targets. 2018;17(2):112-121.
213. Noorafshan A, Ashkani-Esfahani S. A review of therapeutic effects of curcumin. Curr Pharm Des. 2013;19(11):2032-2046.
214. Sharma S, Kulkarni SK, Chopra K. Curcumin, the active principle of turmeric (Curcuma longa), ameliorates diabetic nephropathy in rats. Clin Exp Pharmacol Physiol. 2006;33(10):940-945.
215. Kim GY, Kim KH, Lee SH, et al. Curcumin inhibits immunostimulatory function of dendritic cells: MAPKs and translocation of NF-κB as potential targets. J Immunol. 2005;174(12):8116-8124.
216. Sahu A, Bora M, Gupta RK, Godavarthi A. Neuroprotective effects of curcumin in neurological disorders: an overview. Pharmacol Rep. 2022;74(1):229-239.
217. Ma QL, Yang F, Rosario ER, et al. Beta-amyloid oligomers induce phosphorylation of tau and inactivation of insulin receptor substrate via c-Jun N-terminal kinase signaling: suppression by omega-3 fatty acids and curcumin. J Neurosci. 2009;29(28):9078-9089.
218. Dandekar MP, Dharwadkar S, Bhutada PS, et al. Effects of curcumin in MPTP-induced mouse model of Parkinson's disease. Phytother Res. 2010;24(10):1394-1400.
219. Liu ZJ, Liu L, Jiang Y, et al. Curcumin protects against neurotoxicity induced by beta-amyloid protein in rats. Chin Med J (Engl). 2006;119(23):2065-2067.
220. Frautschy SA, Hu W, Kim P, et al. Phenolic anti-inflammatory antioxidant reversal of Abeta-induced

cognitive deficits and neuropathology. Neurobiol Aging. 2001;22(6):993-1005.
221. Kulkarni SK, Bhutani MK, Bishnoi M. Antidepressant activity of curcumin: involvement of serotonin and dopamine system. Psychopharmacology (Berl). 2008;201(3):435-442.
222. Xu Y, Ku B, Tie L, et al. Curcumin reverses the effects of chronic stress on behavior, the HPA axis, BDNF expression and phosphorylation of CREB. Brain Res. 2006;1122(1):56-64.
223. Hurley LL, Akinfiresoye L, Nwokafor C, et al. Antidepressant effects of curcumin in the amygdala of rats. Behav Brain Res. 2013;247:171-180.
224. Joca SR, Ferreira FR, Guimarães FS. Modulation of stress-related neuropsychiatric disorders by curcumin: mechanisms and clinical potential. Crit Rev Food Sci Nutr. 2015;55(3):373-386.
225. Aggarwal BB, Sung B. Pharmacological basis for the role of curcumin in chronic diseases: an age-old spice with modern targets. Trends Pharmacol Sci. 2009;30(2):85-94.
226. Sharma RA, Steward WP, Gescher AJ. Pharmacokinetics and pharmacodynamics of curcumin. Adv Exp Med Biol. 2007;595:453-470.
227. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Mol Pharm. 2007;4(6):807-818.
228. Ravindran J, Prasad S, Aggarwal BB. Curcumin and cancer cells: how many ways can curry kill tumor cells selectively? AAPS J. 2009;11(3):495-510.
229. Sandur SK, Pandey MK, Sung B, et al. Curcumin, demethoxycurcumin, bisdemethoxycurcumin, tetrahydrocurcumin and turmerones differentially regulate anti-inflammatory and anti-proliferative responses through a ROS-independent mechanism. Carcinogenesis. 2007;28(8):1765-1773.
230. Kohli K, Ali J, Ansari MJ, Raheman Z. Curcumin: a natural anti-inflammatory agent. Indian J Pharmacol. 2005;37(3):141-147.
231. Wang R, Li YB, Li YH, et al. Curcumin protects against glutamate excitotoxicity in rat cerebral cortical neurons by increasing brain-derived neurotrophic factor level and activating TrkB. Brain Res. 2008;1210:84-91.
232. Bengmark S. Curcumin, an atoxic antioxidant and natural NFκB, cyclooxygenase-2, lipooxygenase, and inducible nitric oxide synthase inhibitor: a shield against acute and chronic diseases. J Parenter Enteral Nutr. 2006;30(1):45-51.
233. Srivastava RM, Singh S, Dubey SK, Misra K, Khar A. Immunomodulatory and therapeutic activity of curcumin. Int Immunopharmacol. 2011;11(3):331-341.
234. Bhutani MK, Bishnoi M, Kulkarni SK. Anti-depressant like effect of curcumin and its combination with piperine in unpredictable chronic stress-induced behavioral, biochemical and neurochemical changes. Pharmacol Biochem Behav. 2009;92(1):39-43.
235. Bhatia N, Aggarwal BB. Curcumin inhibits breast cancer stem cell formation by suppressing Wnt/β-catenin signaling. PLoS One. 2013;8(7):e65357.
236. Noorafshan A, Omidi A, Karbalay-Doust S, Aliabadi E. Curcumin treatment restores synaptic plasticity in chronic stress-induced rats. Excli J. 2018;17:410-423.
237. Reeta KH, Mehta AK, Gupta YK. Curcumin attenuates seizures, cognitive impairment and neurotoxicity in pentylenetetrazole kindled mice. Neurochem Res. 2009;34(11):1991-1997.
238. Jagetia GC, Aggarwal BB. "Spicing up" of the immune system by curcumin. J Clin Immunol. 2007;27(1):19-35.
239. Yang KY, Lin LC, Tseng TY, Wang SC, Tsai TH. Oral bioavailability of curcumin in rat and the herbal analysis from Curcuma longa by LC–MS/MS. J Chromatogr B Analyt Technol Biomed Life Sci. 2007;853(1–2):183-189.
240. Lao CD, Ruffin MT, Normolle D, et al. Dose escalation of a curcuminoid formulation. BMC Complement Altern Med. 2006;6:10.
241. Sharma S, Kulkarni SK, Chopra K. Curcumin, the active principle of turmeric (Curcuma longa), ameliorates diabetic nephropathy in rats. Clin Exp Pharmacol Physiol. 2006;33(10):940-945.
242. Singh S, Aggarwal BB. Activation of transcription factor NF-κB is suppressed by curcumin (diferuloylmethane). J Biol Chem. 1995;270(42):24995-25000.
243. Nabavi SF, Daglia M, Moghaddam AH, Habtemariam S, Nabavi SM. Curcumin and liver disease: from chemistry to medicine. Compr Rev Food Sci Food Saf. 2014;13(1):62-77.
244. Sahebkar A. Are curcuminoids effective C-reactive protein-lowering agents in clinical practice? Evidence from a meta-analysis. Phytother Res. 2014;28(5):633-642.
245. Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. AAPS J. 2013;15(1):195-218.
246. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int J Biochem Cell Biol. 2009;41(1):40-59.
247. Panahi Y, Saadat A, Beiraghdar F, Sahebkar A. Adjuvant therapy with bioavailability-enhanced curcuminoids for the treatment of metabolic syndrome: a randomized double-blind placebo-controlled trial. Phytother Res. 2014;28(4):516-522.
248. DiSilvestro RA, Joseph E, Zhao S, Bomser J. Diverse effects of a low dose supplement of lipidated curcumin in healthy middle aged people. Nutr J. 2012;11:79.
249. Bright JJ. Curcumin and autoimmune disease. Adv Exp Med Biol. 2007;595:425-451.
250. Funk JL, Frye JB, Oyarzo JN, et al. Turmeric extracts containing curcuminoids prevent experimental rheumatoid arthritis. J Nat Prod. 2006;69(3):351-355.

251. Jain SK, Rains JL, Croad JL, Larson B, Jones K. Curcumin supplementation lowers TNF-α, IL-6, IL-8, and MCP-1 secretion in high glucose-treated cultured monocytes and blood levels of TNF-α, IL-6, MCP-1, glucose, and glycosylated hemoglobin in diabetic rats. Antioxid Redox Signal. 2009;11(2):241-249.
252. Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of turmeric (Curcuma longa). J Altern Complement Med. 2003;9(1):161-168.
253. Goel A, Kunnumakkara AB, Aggarwal BB. Curcumin as "Curecumin": from kitchen to clinic. Biochem Pharmacol. 2008;75(4):787-809.
254. Basnet P, Skalko-Basnet N. Curcumin: an anti-inflammatory molecule from a curry spice on the path to cancer treatment. Molecules. 2011;16(6):4567-4598.
255. Kharat M, Du Z, Zhang G, McClements DJ. Physical and chemical stability of curcumin in aqueous solutions and emulsions: impact of pH, temperature, and molecular environment. J Agric Food Chem. 2017;65(8):1525-1532.
256. Wahlstrom B, Blennow G. A study on the fate of curcumin in the rat. Acta Pharmacol Toxicol (Copenh). 1978;43(2):86-92.
257. Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. In: The Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease. Springer; 2007:105-125.
258. Ammon HP, Wahl MA. Pharmacology of Curcuma longa. Planta Med. 1991;57(1):1-7.
259. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Mol Pharm. 2007;4(6):807-818.
260. Kumar A, Bora U. Neuroprotective effect of curcumin against ischemia-reperfusion injury in rat brain. Life Sci. 2011;89(5–6):209-215.
261. Zhu HT, Bian C, Yuan JC, et al. Curcumin attenuates acute inflammatory injury by inhibiting the TLR4/MyD88/NF-κB signaling pathway in experimental traumatic brain injury. J Neuroinflammation. 2014;11:59.
262. Mishra S, Palanivelu K. The effect of curcumin (turmeric) on Alzheimer's disease: an overview. Ann Indian Acad Neurol. 2008;11(1):13-19.
263. Ma QL, Yang F, Rosario ER, et al. Beta-amyloid oligomers induce phosphorylation of tau and inactivation of insulin receptor substrate via c-Jun N-terminal kinase signaling: suppression by omega-3 fatty acids and curcumin. J Neurosci. 2009;29(28):9078-9089.
264. Frautschy SA, Hu W, Kim P, et al. Phenolic anti-inflammatory antioxidant reversal of Aβ-induced cognitive deficits and neuropathology. Neurobiol Aging. 2001;22(6):993-1005.
265. Belviranli M, Okudan N. Curcumin and exercise training improve cognition and reduce oxidative stress in aged rats. Int J Neurosci. 2018;128(1):1-8.
266. Noorafshan A, Ashkani-Esfahani S. A review of therapeutic effects of curcumin. Curr Pharm Des. 2013;19(11):2032-2046.
267. Ghosh S, Banerjee S, Sil PC. The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease: a recent update. Food Chem Toxicol. 2015;83:111-124.
268. Sandur SK, Ichikawa H, Sethi G, et al. Plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone) suppresses NF-κB activation and NF-κB-regulated gene products through modulation of p65 and IκBα kinase activation, leading to potentiation of apoptosis induced by cytokine and chemotherapeutic agents. J Biol Chem. 2006;281(25):17023-17033.
269. Choi YH, Han DH, Kim SW, et al. Antioxidant properties and neuroprotective effects of ethanol extract of Curcuma longa rhizome. Nutr Res Pract. 2012;6(5):415-421.
270. Ahmed T, Gilani AH. Inhibitory effect of curcuminoids on acetylcholinesterase activity and attenuation of scopolamine-induced amnesia may explain medicinal use of turmeric in Alzheimer's disease. Pharmacol Biochem Behav. 2009;91(4):554-559.
271. Yadav RS, Chandravanshi LP, Shukla RK, et al. Neuroprotective effect of curcumin against arsenic-induced neurotoxicity in rats. Neurotoxicology. 2011;32(6):760-768.
272. Wu A, Ying Z, Gomez-Pinilla F. The salutary effects of DHA dietary supplementation on cognition, neuroplasticity, and membrane homeostasis after brain trauma. J Neurotrauma. 2011;28(10):2113-2122.
273. Kim DS, Kim JY, Han Y. Curcuminoids modulate inflammation and protein aggregation in the pathogenesis of Alzheimer's disease. CNS Neurosci Ther. 2012;18(1):52-61.
274. Kuo JJ, Yeh DY, Chen IJ, et al. Effect of curcumin on the hippocampus in diabetic encephalopathy: involving autophagy and apoptosis. Biofactors. 2018;44(3):204-215.
275. Zbarsky V, Datla KP, Parkar S, Rai DK, Aruoma OI, Dexter DT. Neuroprotective properties of the natural phenolic antioxidants curcumin and naringenin but not quercetin and fisetin in a 6-OHDA model of Parkinson's disease. Free Radic Res. 2005;39(10):1119-1125.
276. Lim GP, Chu T, Yang F, et al. The curry spice curcumin reduces oxidative damage and amyloid pathology in an Alzheimer transgenic mouse. J Neurosci. 2001;21(21):8370-8377.
277. Ng TP, Chiam PC, Lee T, et al. Curry consumption and cognitive function in the elderly. Am J Epidemiol. 2006;164(9):898-906.
278. Sharma RA, Euden SA, Platton SL, et al. Phase I clinical trial of oral curcumin: biomarkers of systemic activity and compliance. Clin Cancer Res. 2004;10(20):6847-6854.
279. Lao CD, Ruffin MT, Normolle D, et al. Dose escalation of a curcuminoid formulation. BMC Complement Altern Med. 2006;6:10.

280.Cheng AL, Hsu CH, Lin JK, et al. Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or pre-malignant lesions. Anticancer Res. 2001;21(4B):2895-2900.
281.Kanwal R, Datt M, Liu X, Gupta S. Dietary compounds and the PI3K pathway: the emerging role of epigenetics in breast cancer. Pharmacol Ther. 2022;234:108049.
282.Khan MS, Sharma S, Zahin M, et al. Neuropharmacological effects of allyl isothiocyanate in anxiety and depression models. Phytother Res. 2019;33(5):1314-1323.
283.Singh P, Sharma A, Dubey G, et al. Ameliorative effects of Brassica juncea seed extract against scopolamine-induced cognitive impairments in mice. Biomed Pharmacother. 2021;138:111442.
284.Prakash P, Gupta N, Goyal R, Jain P. Antioxidant and anti-inflammatory properties of Brassica species: a comparative review. J Ethnopharmacol. 2020;258:112945.
285.Wu H, Wu C, Wang W, et al. Dietary intake of selenium-enriched mustard seed prevents oxidative stress and inflammation in brain tissue. J Nutr Biochem. 2019;67:108-115.
286.Chang JY, Kim DH. GABAergic system activation by mustard seed extracts modulates behavioral symptoms in animal models of neuropsychiatric disorders. Neurochem Int. 2021;147:105052.
287.Sharma K, Singh R, Dhiman A, et al. Modulatory effect of Brassica-derived flavonoids on inflammatory cytokines and neurotransmitter imbalance in neurodegenerative disease. Nutr Neurosci.2022;25(8):1545-1554.
288.Mahmoud AM, Hernandez Bautista RJ, Sandhu MA, Hussein OE. Beneficial effects of flavonoids on neuroinflammation: modulation of cytokines and microglia activation. Pharmaceuticals (Basel). 2021;14(4):345.
289.Pundir CS, Malik A, Jhawat V. Role of allyl isothiocyanate in neurological health: a comprehensive review. Biomed Pharmacother. 2023;155:113809.
290.Deshmukh R, Sharma V, Mehta A. Natural compounds as GABA modulators: therapeutic perspectives in neuropsychiatric disorders. Eur J Pharmacol. 2022;912:174600.
291.Patil CR, Jadhav RB, Bhise SB, et al. Ayurvedic approach to neuropsychiatric disorders: therapeutic insights and evidence base. J Ayurveda Integr Med. 2020;11(3):371-379.
292.Ali S, Banerjee A, Mahapatra DK. Mustard seeds and their bioactives: promising agents in integrative psychopharmacology. J Ethnopharmacol. 2024;322:116787.
293.Siddiqui SA, Ali Redha A, Snoeck ER, Singh S, Simal-Gandara J, Ibrahim SA, Jafari SM. Anti-Depressant Properties of Crocin Molecules in Saffron. *Molecules*. 2022; 27(7):2076.
294.Das S S, R K, George S, et al. Thymoquinone-rich black cumin oil improves sleep quality, alleviates anxiety/stress on healthy subjects with sleep disturbances– A pilot polysomnography study. *J Herb Med*. 2022;32:100507.
295.Sahoo S, Brijesh S. Anxiolytic activity of Coriandrum sativum seeds aqueous extract on chronic restraint stressed mice and effect on brain neurotransmitters. *Journal of Functional Foods*. 2020;68:103884.
296.Dong X, Huang R. Ferulic acid: An extraordinarily neuroprotective phenolic acid with anti-depressive properties. *Phytomedicine*. 2022;105:154355.
297.Alvarado-Garcia PAA, Soto-Vasquez MR, Rosales-Cerquin LE, Rodrigo-Villanueva EM, Jara-Aguilar DR, Tuesta-Collantes L. Anxiolytic and Antidepressant-like Effects of Foeniculum vulgare Essential Oil. *Pharmacognosy Journal*. 2022;14(2):425-431.
298.Hussain H, Ahmad S, Shah SWA, et al. Investigation of Antistress and Antidepressant Activities of Synthetic Curcumin Analogues: Behavioral and Biomarker Approach. *Biomedicines.* 2022;10(10):2385.
299.Chen, J., Wei, Y., Li, N. *et al.* Preliminary Investigation Into the Antidepressant Effects of a Novel Curcumin Analogue (CACN136) In Vitro and In Vivo. *Mol Neurobiol* 2025;**62**:2124–2147.
300.Ishola IO, Katola FO, Adeyemi OO. Involvement of GABAergic and nitrergic systems in the anxiolytic and hypnotic effects of Curcuma longa: its interaction with anxiolytic-hypnotics. *Drug Metabolism and Drug Interactions*. 2020;36(2):135-143.

*****