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Neuroprotective potency of some spice herbs, a literature review

Mohammad Reza Khazdair [a, b, *], Akbar Anaeigoudari [c], Milad Hashemzehi [c], Reza Mohebbati [d]

[a] Neurogenic Inflammation Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran
[b] Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran
[c] Department of Physiology, School of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran
[d] Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

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ABSTRACT

In recent years, growing attention has been given to traditional medicine. In traditional medicine a large number of plants have been used to cure neurodegenerative diseases such as Alzheimer's disease (AD) and other memory related disorders. *Crocus sativus (C. sativus), Nigella sativa (N. sativa), Coriandrum sativum (C. sativum), Ferula assafoetida (F. assafoetida), Thymus vulgaris* (*T. vulgaris*), *Zataria multiflora* (*Z. multiflora*) and *Curcuma longa* (*C. longa*) were used traditionally for dietary, food additive, spice and various medicinal purposes. The Major components of these herbs are carotenoids, monoterpenes and poly phenol compounds which enhanced the neural functions.

These medicinal plants increased anti-oxidant, decreased oxidant levels and inhibited acetylcholinesterase activity in the neural system. Furthermore, neuroprotective of plants occur via reduced pro-inflammatory cytokines such as IL-6, IL-1β, TNF-α and total nitrite generation.

Therefore, the effects of the above mentioned medicinal and their active constituents improved neurodegenerative diseases which indicate their therapeutic potential in disorders associated with neuro-inflammation and neurotransmitter deficiency such as AD and depression.

1. Introduction

Neurodegenerative diseases such as Alzheimer's Disease (AD), Parkinson's disease, Multiple Sclerosis (MS) results in slow neuronal death that accompanied with losing cognitive functions and sensory dysfunction.[1] Recently, these diseases associated with different multifactorial etiologies, social, and financial problems.[2] Anti-inflammatory agents have also been suggested to postpone the progression of neurodegenerative diseases such as AD. Different studies have shown that nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce the risk of developing AD.[4,5] Pathological processes including inflammation, oxidative stress, apoptosis, mitochondrial dysfunction, and genetic factors lead to neuronal degeneration in Parkinson's disease (PD).[6] It has been reported that excessive lipid peroxidation may destroy cholinergic neurons in AD[7] and dopaminergic neurons in PD.[8] Different enzymatic antioxidant such as superoxide dismutase (SOD)[9] and non-enzymatic antioxidant such as total thiol groups[10] exist in the brain. Central nervous system (CNS) also contains high level of polyunsaturated fatty acids is more sensitive to peroxidation reactions (9). Low antioxidant activity of the brain with respect to other tissues has been made the brain tissue susceptible to oxidative damage.[11]

In traditional medicine, the organs of plant such as: leaves, stems, roots, flowers, fruits and seeds were used as alternative and complementary therapy. Some derived components from herbs such as resveratrol, curcumin, ginsenoside, polyphenols, triptolide, *etc.* have neuroprotective effects.[12] Herbal products contain of complex active components or phytochemicals like flavonoids, alkaloids and isoprenoids. Therefore, it is frequently difficult to determine which component(s) of the herb(s) has more biological activity.[13,14]

In the present review study, it was aimed to highlight the useful effects of different medicinal plant which used traditionally for

* Corresponding author. Neurogenic Inflammation Research Centre, Mashhad University of Medical Sciences, Mashhad, 9177948564, Iran.
E-mail address: khazdeirmr921@mums.ac.ir (M.R. Khazdair).
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dietary, food additive, spice and various medicinal purposes on induced neurotoxicity.

2. Methods

The information's of this review were obtained from databases such as, PubMed, Web of Science, Google Scholar, Scopus, and IranMedex until the end of August 2016. The search terms were included "neuroprotective" or "neurotoxicity" and "*Crocus sativus*", "*Nigella sativa*", "*Coriandrum sativum*", "*Ferula assafoetida*", "*Thymus vulgaris*", "*Zataria multiflora*", and "*Curcuma longa*". All studies such as, *in vitro* studies, animal studies, review articles and clinical studies with the outcome of changes in the neurotransmitter releasing, behavioural changes, oxidant/anti-oxidant parameters and pro-inflammatory cytokines were included. Letter to the Editor and Unpublished data were the exclusion criteria.

3. Neuroprotective effects of medicinal plants

3.1. Crocus sativus

Crocus sativus L (*C. sativus*), commonly known as saffron belongs to the Iridaceas family, Crocoideae superfamily which is cultivated in many countries including Iran, Afghanistan, Turkey and Spain.[15] Saffron consists dried and dark-red stigma with a small portion of the yellowish style attached of *C. sativus*. It used mainly as herbal medicine in various regions in the world.[16]

Saffron possesses 150 different compounds including carbohydrates, polypeptides, lipids, H_2O, minerals and vitamins. Crocins are the main biologically active ingredients of saffron, a family of red-colored and water-soluble carotenoids, which are all glycosides of crocetin. Also, saffron has four main bioactive components such as, crocin, crocetin, picrocrocin and safranal. Another constituent of saffron was Picrocrocin which has a bitter taste.[17]

3.1.1. Medicinal properties of C. sativus

In Iranian traditional medicine, *Crocus sativus* is used to treat cognitive disorders. Recently *C. sativus* constituents were used to treat some neural disorders and to relax smooth muscle.[18–20] The anticonvulsant and anti-Alzheimer properties of saffron extract in humans and animal models have been reported.[18] The efficacy of *C. sativus* in the treatment of mild to moderate depression in clinical trial studies, and effect on brain neurotransmitter concentrations as well as its interaction with the opioid system were reviewed.[18] *C. sativus* and its main component, crocin, possess potent antioxidant effects via reducing of MDA level.[21,22] The administration of *C. sativus* extract (100 mg/kg, p.o.) before induction of cerebral ischemia by middle cerebral artery occlusion (MCAO) significantly reduced glutamate and aspartate concentrations, SOD, catalase and K-ATPase activities induced by ischemia in rats.[23] In addition, administration of *C. sativus* extract (200 mg/kg) and honey syrup for 45 days reduced the aluminum chloride-induced neurotoxicity in mice.[24]

Administration of *C. sativus* (30 mg/day) for treatment of mild-to-moderate AD in the patients of 55 years and older was found to be as effective as donepezil and the frequency of saffron extract side effects was similar to those of donepezil except for vomiting.[25] Similarly, the uses of saffron in 46 patients with mild-to-moderate AD for 16 weeks improved the cognitive functions.[26] Saffron extract (30 mg/day) for six-week was effective in the treatment of mild to moderate depression similar to the effects of fluoxetine and imipramine (100 mg/day).[27] In a double-blind clinical trial the efficacy of co-administration of hydro-alcoholic extract of *C. sativus* (40 and 80 mg) and fluoxetine (30 mg/day) for six weeks was investigated. The results showed that a dose of *C. sativus* 80 mg and fluoxetine (30 mg/day) was effective than that of *C. sativus* 40 mg to treat mild to moderate depressive disorders.[28]

3.2. Nigella sativa

Nigella sativa L. (*N. sativa*) is an annual herbaceous and belonging to Ranunculaceae family, which widely grown in the Mediterranean countries, Western Asia, Middle East and Eastern Europe. The *N. sativa* seeds have been added as a spice to range of Persian foods such as, bread, pickle, sauces and salads.[29]

Chemical components of *N. sativa* seeds include oil, protein, carbohydrate, and fiber. The fixed oil chemical compositions of *N. sativa* are linoleic acid, oleic acid, Palmitic acid, Arachidic acid, Eicosadienoic acid, Stearic acid, Linoleic acid and Myristic acid.[30] The major phenolic compounds of *N. sativa* seeds are p-cymene (37.3%), Thymoquinone (TQ) (13.7%), carvacrol (11.77%), and thymol (0.33%).[29,31,32]

3.2.1. Medicinal properties of N. sativa

N. sativa as a medicinal plant is well-known for its potent antioxidative effects.[33] It has been reported that *N. sativa* have protective effects on the renal damage.[34] *N. sativa* seeds could significantly ameliorate the spatial cognitive deficits caused by chronic cerebral hypo perfusion in rats.[35] Furthermore, *N. sativa* improved scopolamine – induced learning and memory impairment as well as reduced the AChE activity and oxidative stress of the rats brain.[36] Antioxidant effects of *N. sativa* oil on the patients with rheumatoid arthritis (RA) showed *N. Sativa* reduced the serum level of IL-10, MDA and NO. *N. sativa* also improved inflammatory responses and reduced oxidative stress in patients with RA.[37] In the other clinical trial, 40 healthy volunteers were divided into the treatment with capsules of *N. sativa* (500 mg) and placebo (500 mg) twice daily for 9 weeks. *N. sativa* enhanced memory, attention and cognition compared to the placebo group.[38] *N. sativa* (500 mg) also decrease anxiety, to stabilize mood and to modulate cognition in the human model after 4 weeks.[39] Neuroprotective effects of *N.* sativa and thymoquinone (TQ) (its major components) on various nervous system disorders such as Alzheimer disease, epilepsy and neurotoxicity have been reviewed.[40]

3.3. Coriandrum sativum

Coriander (*Coriandrum sativum* L.), is an annual herb of the parsley family (Apiaceae). This plant is generally called Geshniz in Persian. *Coriandrum sativum* is native to the Mediterranean region and is extensively grown in all over the world.[42,43]

The aliphatic aldehydes (mainly C10-C16 aldehydes) with fetid-like aroma are predominant in the fresh herb oil[44] whereas major components in the oil isolated from coriander fruit include linalool and some other oxygenated monoterpenes and monoterpene hydrocarbons.[45] Coriander is also a potential source of lipids such as petroselinic acid and a high amount of essential oils (EO) that are very important for growth and brain functions. The main coriander EO is linalool, linoleic and linolenic acids.[46] Coriander seed oil was contains linalool (60–70%) and 20% hydrocarbons but the composition of the herb oil was completely differs from the seed oil.[47]

3.3.1. Medicinal properties of C. sativum

In folk medicine, *coriandrum sativum* (*C. sativum*) was widely used as digestive agent. The seed extract of *C. sativum* was used in lotions and shampoos and exerts antimicrobial and anti-rheumatoid effects.[48] In Iranian traditional medicine, *C. sativum* has been suggested to relive insomnia.[49,50] A combination of the fresh leaves extract and tea, or crushed of plant seeds as a single dose before sleeping have been suggested to relieve anxiety and

insomnia.[49] Similar uses of *C. sativum* seed have been shown in other folk medicines.[51] The leaves extract of *C. sativum* (200 mg/kg) showed an anxiolytic effect which was presented by increasing the time spent in open arms and the percentage of open arm entries.[52] *C. sativum* fruit extract (100 and 200 mg/kg, i.p.) increased the time spent in the open arms and entries into the open arms. Locomotion activity and frequency of rearing also decreased in the groups treated by 200 mg/kg (i.p.) of the extract. Furthermore, *C. sativum* extract at 100 and 200 mg/kg increased the time spent in social interaction.[53] Anticonvulsant activity of aqueous (0.5 g/kg, i.p.) and ethenolic extracts (3.5 and 5 g/kg, i.p.) of coriander seeds were studied using pentylenetetrazole (PTZ) and the maximal electroshock seizure models. These extracts decreased the duration of tonic seizures and showed a significant anticonvulsant activity in the maximal electroshock test. In addition both extracts especially ethenolic extract (5 g/kg, i.p.) similar to phenobarbital (20 mg/kg) prolonged onset latencies of clonic convulsions.[54]

3.4. Ferula assafoetida

Asafoetida (*F. assafoetida* L.) belongs to the Apiaceae family which obtained from the exudates of the living underground rhizome or tap roots of the plant. *F. assafoetida* or gum-resin is known as “Anghouzeh”, “Khorakoma” and “Anguzakoma” in Iran.[55] It has been used in traditional medicine and as a spice in different foods in India and Nepal.[55]

E-1-propyl *sec*-butyl disulfide is a major component[56] and 25 compounds were identified in the hydrodistilled oil. E-1-propenyl *sec*-butyl disulfide (40.0%) and germacrene B (7.8%) are the major components of Ferula assa-foetida.[56]

3.4.1. Medicinal properties of F. assafoetida

F. asafoetida (Apiaceae) is considered by researchers due to its medicinal and nutritional properties. Roots, young shoots and leaves of plant are eaten as vegetable. Leaves of Ferula asafoetida possess anthelmintic, carminative and diaphoretic properties and the root of plant is used as antipyretic.[57] In addition, *F. asafoetida* is used for treatment of various diseases including asthma, epilepsy, stomachache, flatulence, intestinal parasites, weak digestion and influenza in traditional medicine.[58] It has been also reported that oleo-gum resin of *F. asafoetida* possesses sedative, expectorant, analgesic, carminative, stimulant, antiperiodic, ant-diabetic, antispasmodic, emmenagogue, vermifuge, laxative, anti-inflammatory, contraceptive and anti-epileptic effects.[59] Effects of *F. asafoetida* on muscarinic receptors and possible mechanisms for functional antagonistic of guinea-pig tracheal smooth muscle have been studied.[60,61] The relaxant effect of *F. assafoetida* on smooth muscles and its possible mechanisms have been reviewed.[62] In pharmacological and biological studies, the ole-gum- resin of *Ferula asafoetida* have been revealed to have antioxidant, antiviral, antifungal, anti-diabetic, molluscicidal, antispasmodic and antihypertensive effects.[55] In a study, acute and sub-chronic toxicity of *F. asafoetida* was evaluated and the results indicated that single oral administration (500 mg/kg) and repeated doses (250 mg/kg) for 28 days of this plant did not induce mortality and obvious toxicological signs in rats.[63] It has also been documented that oleo gum resin of *F. asafoetida* can enhance regeneration and re-myelination and decreases the rat of lymphocyte infiltration in the neuropathic tissue in mice; therefore it acts as a neuroprotective and nerve simulative agent in peripheral neuropathy.[64] Scientific evidences have also shown that *F. asafoetida* resin can potentially inhibit monoamine oxidase B (MAO-B) and it can be used in the therapy of neurodegenerative diseases such as Parkinson's and Alzheimer's diseases.[65] Meanwhile, *Ferula asafoetida* has been reported to have acetylcholinestrase (AChE) inhibiting property *in vitro* assay and *in vivo* on snail nervous system. Researchers have proposed that memory increasing effect of *Ferula asafoetida* could be attributed to inhibitory effect of this plant on AChE in the rat brain.[66] In behavioural models, such as elevated plus maz, the extract of plant dose-dependently improved memory in rats. In another behavioural model, passive avoidance test, the lower dose of extract (200 mg) could not improve memory whereas in high dose (400 mg) it ameliorated memory.[67] Additionally, it has been documented that the extract of *F. asafoetida* applies a considerable anticonvulsant effect in Pentylenetetrazol (PTZ) and amygdala-kindled rats. Researchers investigated the effect of two doses of ferula asafoetida (50 and 100 mg/kg) on parameters of seizure and the results revealed that dose 100 mg/kg exerts the better anticonvulsant effect than 50 mg.[59]

3.5. Thymus vulgaris

Thymus vulgaris (*T. vulgaris*) is a plant that is a member of Lamiaceae family which are strongly aromatic. This plant is consist of approximately 38 species and is distributed in subtropical countries.[68]

The phenols, thymol (40%) and carvacrol (15%) are main components of TV. It was contains less amounts of phenol during the winter. Also, thymol methyl ether (2%), cineol, cymen, pinene, borneol and esters are components in the essential oil.[68]

3.5.1. Medicinal properties of T. vulgaris

Thymus vulgaris (Thyme) is a subshrub native to the western Mediterranean region which is widely used as spice to add a distinctive flavour to food. In the traditional medicine, thyme is part of herbal teas and infusions.[69] It has been documented that bioactive compounds of thyme such as thyme essential oil (TEO) constituents, flavonoids and phenolic acids, natural terpenoid thymol and phenol isomer carvacrol, possess antioxidant, antimicrobial, antitussive, antispasmodic, and expectorant effects.[70,71] Researchers have reported that tocols and phenolic in thymus vulgaris oil (TO) can directly react with free radicals and inhibit lipid peroxidation.[72] It has been also reported that treatment with thymol results in improvement of antioxidant status in rat brain.[73] In addition, the results of behavioural studies have demonstrated that the extract of thyme can induce anxiolytic effects in rat when it was orally administered for 1-week. In confirmation of this report extract of thyme enhances the percentage of both the entries and the time spent in the open arms of the maze.[74] The results of animal studies also revealed that kaemfrol in thyme extract applies anxiolytic effects in the elevated plus maze (EPM) in mice.[75] Carvacrol derived from this plant has also been indicated to have anxiolytic effects in the plus maze test.[76] Bioactive monoterpenes in thyme extract such as linalool have been reported to be able to decrease the level of anxiety in animals.[77] The essential oil of thyme has also been suggested to have a dose dependent protective effect against toxicity of alfatoxins.[78] In addition, it has been documented that thymol acts centrally via mimicking or facilitating GABA action and modulates $GABA_A$ receptor.[79] Therefore, it can apply the significant anticonvulsant and antiepileptogenic effects. Recently, neuroprotective and improvement effects of thymol, a bioactive monoterpene isolated from thymus vulgaris, on amyloid β or scopolamine-caused cognitive impairment in rats was documented.[80] Researchers have suggested that neuroprotective effects of thymol can attribute to its potential effect on GABA-mediated inhibition of synaptic transmission.[81] Meanwhile, researchers reported that TO could modulate cholinergic function via enhancing synaptic acetylcholine (Ach) and nicotinic Ach receptor activity.[82] Additionally, antidepressant effects of thymol were documented. Deng et al. reported that thymol administration significantly

shortened the immobility time in tail suspension tests (TST) and forced swimming test (FST) and restored the reduction of the hippocampal levels of serotonin (5- HT) and norepinephrine (NE) in chronic unpredictable mild stress (CUMS)- induced depressive mice.[80]

3.6. Zataria multiflora

Zataria multiflora (*Z. multiflora*) is belonging to the Lamiaceae family.[83]

It have consist of p-cymene derivatives: multi-flotriol (1), multi-flrol (2), a new aromatic ester of p-hydroxy benzoic acid (3) and three known constituents: dihydroxyaromadendrane,[84] luteolin[85] and a-tocopherolquinone.[86] The main components of the plant oil were thymol (37.59%), carvacrol (33.65%); *PARA*-cymene (7.72%), γ -terpinene (3.88%) and β-caryophyllene (2.06%).[87]

3.6.1. Medicinal properties of Z. multiflora

Z. multiflora contains various compounds including terpens, luteolin, 6- hydroxyluteolin glycosides, di-, tri, and tetra-ethoxylated which could be responsible for the therapeutic effects of it[88] *Z. multiflora* Boiss essential oil (ZEO) possesses preservative effects whereas vigorous taste and aroma have limited its usage as food preservative in high amounts.[89] In Iranian traditional medicine, the plant is used for its analgesic, antiseptic and carminative effects.[88] It has also been documented that the essential oil of *Z. multiflora* has antioxidant, antibacterial and antifungal properties in *in vitro*.[89,90] The results of studies have indicated that the ZEO exhibited more potent antioxidative effect than pomegranate juice.[89] Antibacterial,[90] immunoregulatory[91,117] and anti-inflammatory[92,118] effects of this plant have also been reported. In addition, it has been reported that the Aβ-caused learning and memory impairments could be restored by i.p. administration of *Z. multiflora* essential oil in rats. Therefore zataria multiflora essential oil was considered to be as a worth source of natural therapeutic agent for attenuating cognitive symptoms of Alzheimer's disease (AD) by researchers.[93]

3.7. Curcuma longa

Curcuma longa (*C. longa*) is a member of the Zingiberaceae family and is cultivated in the countries of Southeast Asia.[94]

The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and zingiberone. Other constituents include sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprises 0.3–5.4% of raw turmeric.[95]

3.7.1. Medicinal properties of C. longa

Some plants such as *Curcuma longa* contain a natural polyphenol and non-flavonoid compound called curcumin. Curcumin is known for its several biological and medicinal effects, such as anti-inflammatory, antioxidant and so on. Curcumin therapeutic potential for neurodegenerative diseases has garnered great interest in recent years.[6] Kulkarni reported that curcumin water soluble extract is able to raise dopamine, norepinephrine and 5-HT levels in CNS.[96] Curcumin extracted from *Curcuma longa* have been reported to have inhibition effects on PD, ROS production, apoptosis, platelet aggregation, cytokines production, cyclooxygenase enzyme activity, brain oxidative damage, cognitive deficits in cell culture and animal models.[97,98] The protective effects of *C. longa* extract (1000 mg/kg, body weight, per oral) on oxidative[99] and renal damage have been reported.[100]

It has been reported that administration of curcumin (50, 100, 200 mg/kg) ameliorated cognitive deficits and mitochondrial dysfunctions symptoms in mice.[101] Curcumin has also been indicated

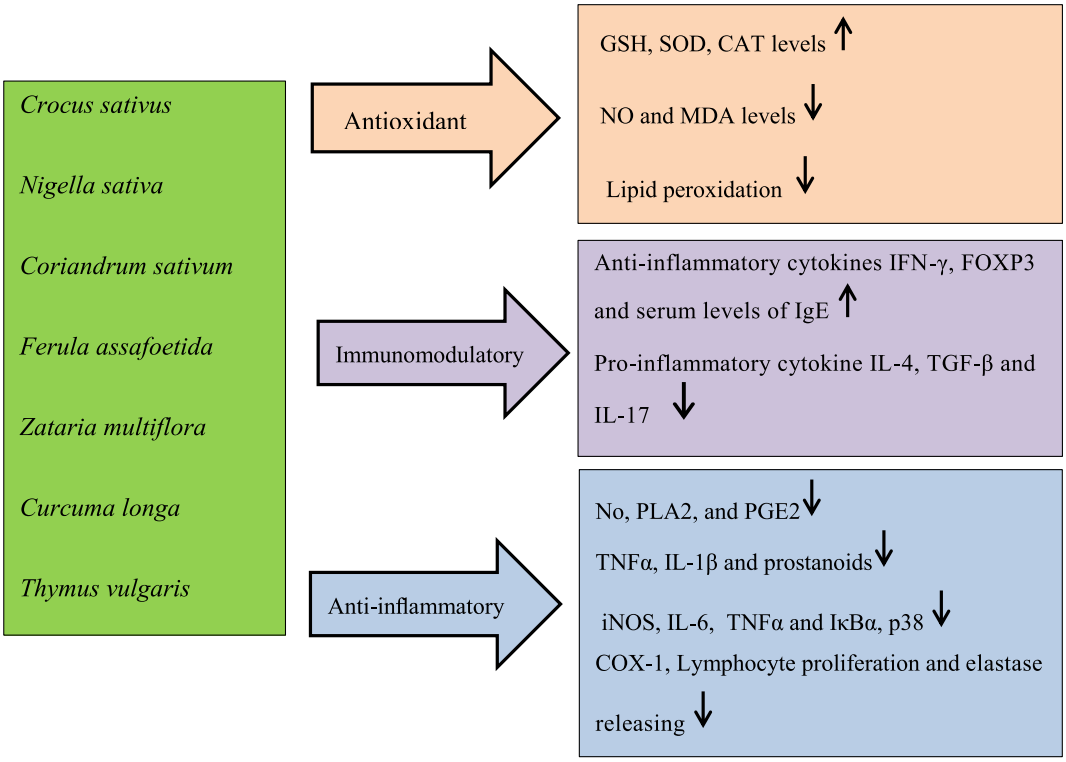

Fig. 1. Different mechanism of medical properties of medicinal herbs. GSH, glutathione; SOD, superoxide dismutase; CAT, catalase; NO, Nitric oxide; MDA, malondialdehyde; PLA2: Phospholipase A2; PGE2: Prostaglandin-E2; IL-1β, Interleukin-1β; COX-1, Cyclooxygenase-1; iNOS, Inducible nitric oxide synthase.

Table 1
The effects of medicinal plants for treatment of various disorders, a clinical evidence.

Medicinal plants	Model of study	Results	References
C. Sativus	Depressant patients	The effect of *C. Sativus* similar to imipramine in the treatment of mild to moderate depression	119
		C. Sativus could produce a significantly better the outcome on the Hamilton depression rating scale than the placebo	120
		The effect of *C. Sativus* similar to fluoxetine in the treatment depression	121
		Was effective to treatment of mild to moderate depressive disorders	122
N. sativa	Asthmatic patients	Improvement of all asthmatic symptoms, chest wheeze and pulmonary function test (PFT) values	123
		Lesser effectiveness on pulmonary function test and sGaw than theophylline	124
	Sulfur mustard espoused patients	Decreasing the use of inhaler and oral β-agonists and oral corticosteroid in the study group	125
	Allergic patients	Decreasing the IgE and eosinophil count and plasma triglycerides. Increasing the HDL cholesterol	126
C. sativum	Diabetic patients	Significant hypoglycemic activity in type-2 diabetic patients	127
C. longa	Peptic ulcer patients	The abdominal pain and discomfort satisfactorily subsided in the first and second week.	128

to exert neuroprotective effects in neuronal degenerative disorders and cerebral ischemia.[102,103] Scientific evidences demonstrate that curcumin protects the rat brain against focal ischemia through upregulation transcription factor Nrf2 and HO-1expretion.[104] Additionally, researchers suggested that curcumin debilitates glutamate neurotoxicity in the hippocampal of rat via suppressing ER stress-related TXNIP/NLRP3 inflammation activation.[105] Linlin et al. also proposed that curcumin protects rats brain against cerebral ischemia-reperfusion injury through increasing neuron survival rate, inflammatory cytokine activity and activating JAK2/STAT3 signaling pathway.[106] It has been suggested that curcumin protects the brain against oxyhemoglobin-induced neurotoxicity and oxidative stress *in vitro* model of subarachnoid hemorrhage (SAH) (Xia LI).[107]

The neuroprotective effects of curcumin in PD also are related to its antioxidant properties. Wang reported that curcumin restor ROS intracellular accumulation[108] in human cell line SH-SY5Y exposed to 6-OHDA.[109] Administration of curcumin (60 mg/kg, body weight, per oral) for three weeks has amended striatum neuronal degeneration in 6-OHDA lesioned rats.[110] Curcumin protected the neurons against ROS via restoring the GSH decreased levels.[111] Curcumin increased SOD levels in the lesioned striatum of 6-OHDA mice[112] and MES23.5 cells induced the neurotoxin 6-OHDA.[108] Curcumin has been reported to protect the axons against LPS degeneration.[113] Curcumin neuroprotective effects might be mediated by overexpression of BCl-2 which is inducible nitric oxide synthase (iNOS) antagonist. Therefore, curcumin is effective in improvement of NO-mediated degeneration.[114] Oral administration of 150 mg/kg/day curcumin for 1 week reduced pro-inflammatory cytokines such as IL-6, IL-1β, TNF-α and total nitrite generation in the striatum of MPTP-induced mice.[115] Furthermore, curcumin decreased activation of NF-κB in LPS[116] and 6-OHDA-induced inflammatory.[108]

4. Medicinal properties of medicinal herbs and their clinical application

Different medicinal plants showed the antioxidant and anti-inflammatory effects which may have potential therapeutic effects in various nervous system disorders. The results of studies also imply that beneficial effects of the plants on neurodegenerative disorders such as Alzheimer and Parkinson disease are mainly due to the interactions with the cholinergic, dopaminergic and glutamatergic systems. Regarding the anticonvulsant, analgesic effects of the plants interaction with the GABA and opioid system might be suggested. Different mechanism of medical properties of medicinal herbs was summarized in Fig. 1. The effectiveness of medicinal plants on different disorder as clinical studied were showed in Table 1.

5. Conclusion

In this review we propose to focus on neurotoxicity in various studies (*in vitro* and *in vivo*) and investigated the effects of medicinal plants on neural system. The mentioned medicinal plants play their protective roles via increased SOD and catalase levels, restoration of GSH, decreased MDA levels and also protects of neurons against ROS as antioxidant activities. Some protective effects of these natural compounds may be due to reduction of Ca^{2+}, Na^{+} and enhancement of K^{+} level or 'anti-glutamatergic' effect. The neuroprotective effects of the mentioned plants occur via reduction of inflammatory cytokines as well as enhancement of anti-inflammatory cytokines, inhibition of the acetylcholinesterase activity and decreased MDA levels in the neural system via modulating GABAergic and glutamatergic neurons, and also increasing amount of amino acids and serotonin (5-HT) in the neurotransmitters systems. Furthermore, the data of the basic and clinical evidence indicated that anti-inflammatory, antioxidant and immunoregulatory effects of some herbs on various disorders. This findings help to recommend the use of these herbs and main compound from natural resources for drug development and more investigation in the clinical studies for future were suggested.

Conflict of interest

There is no conflict of interest in this study.

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