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Review Article

Exploring Neuroprotective Botanical Remedies in Neurodegenerative Conditions: A Review

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Abstract

Neuroprotection refers to the mechanisms and strategies used to protect the Central Nervous System (CNS) from neuronal injuries caused by neurodegenerative disorders. Neurodegenerative disorders are a type of chronic condition in which parts of the nervous system deteriorate over time, most notably the brain. These disorders have a slow and gradual effect on an individual. Neurodegeneration is a neuropathological condition and brain aging process. The brain pathology of neurodegenerative and cerebrovascular disease is a leading cause of death worldwide, with a death rate of approximately 8% and an incidence rate of approximately 2/1000. It is a major health issue in the twenty-first century. According to researchers, this disease affects over 50 million people worldwide. These disorders primarily affect people over the age of 65, and the World Health Organization predicts that this number will more than double in the next 30 years. Confusion, difficulty thinking, pain, muscle spasms, behavioral changes, paralysis, tremors, balance problems, coordination issues, hunched posture, and fatigue are symptoms of these disorders. These disorders are caused by age, genetics, medical history, habits, routine, and environment. This review article is focused on herbs such as Crocus sativus and Curcuma longa which are very helpful in Neurodegenerative diseases and serve as a resource for future research.

Keywords: Neurodegeneration, Medicinal Herbs, Neuroprotection, Neuroprotective plants, Parkinson, Alzheimer.

1. Introduction

Neurodegenerative disorders are a type of Chronic condition in which the parts of the nervous system get damaged and destroyed over time and it mostly happens in the brain. These disorders show their effect slowly and gradually in an individual [1]. Neurodegeneration is a process having Neuropathological conditions and brain aging. The brain pathology of Neurodegenerative and cerebrovascular disease is a leading cause of death all over the world with a Death rate of about 8% and an incidence rate is about 2/1000. For the 21st Century, it is a major health problem [2].

There are different types of Neurodegenerative disorders i.e., Alzheimer's disease, Huntington's disease, Parkinson's disease, Frontotemporal Dementia, Amyotrophic lateral sclerosis, and Spinocerebellar ataxias, Schizophrenia, Depression, Cerebrovascular Impairment[2,3].

According to Researchers, over 50 million people are affected by this disease worldwide. These disorders mostly happen to people over the age of 65 and as per the World Health Organization, this number will be doubled in the coming 30 years.

The symptoms of these disorders are Confusion, Trouble thinking, Pain, Muscle spasms, Behavioural changes, Paralysis, Tremors, Balance problems, Coordination Issues, Hunched posture, and Fatigue.

The cause of these disorders is Age, Genetics, Medical History, Habits, Routine, and Environment [1].

Neuroprotection can be defined as the mechanisms and strategies that are used to defend the Central Nervous System (CNS) from Neuronal Injuries due to Neurodegenerative disorders.

As per the studies, In Neurodegeneration, the proteins having altered physicochemical properties get deposited in the brain and are known as Misfolded proteins. It includes Accumulation and aggregation of amyloid-β (Aβ) in Alzheimer's, α-synuclein in Parkinson's, Huntingtin protein in Huntington's, and TDP-43 in Amyotrophic lateral sclerosis [4].

2. Nootropics

It is made up of Greek words, "Noo" which means thinking, and "tropein" which means to guide. Nootropics is the term which is

used for Medical Drugs and Supplements that have active cognitive functions and have positive effects on the brain.

They protect the brain from Neurotoxicity by using their Anti-hypoxic effects and improve the supply of oxygen and glucose in the brain. Nootropics don't have any direct effect on the release of neurotransmitters and Receptors.

The compounds which are having Neuroprotective properties are available in the market and are used for improving the balance of Neurotransmitters in the brain. E.g., Deanol, Meclofenoxate, Nicergoline, Piracetam, Pyritinol, Vinpocetine, Naftidrofuryl, Dihydroergotoxine, Centellic Acid, Withanolides, Methylxanthines, Rosavins [2,5].

3. Neurodegenerative Disorder

These are also known as Degenerative neurological diseases and these are progressive diseases of the cerebrospinal nervous system that affect the central and peripheral nervous system. These diseases involve neuronal cell death with gradual onset of previous symptoms such as loss of memory. The various Neurodegenerative disorders are Alzheimer's disease (AD), Parkinson's disease (PD), Lewy body dementia, Multiple sclerosis, Huntington's disease (HD), Amyotrophic lateral sclerosis (ALS), and spongiform encephalopathy. In Huntington's and Parkinson's disease, In the basal ganglia, there is a loss of neurons leading to abnormal motor control, and In Amyotrophic lateral sclerosis (AL:S), there is degeneration of spinal, bulbar, and cortical motor neurons leading to muscle weakness [6,7].

3.1. Alzheimer's Disease

Alzheimer's disease (AD) is a type of dementia that causes cognitive and functional decline with aging. Alois Alzheimer first described this in 1906. The neuropathological evaluation of Alzheimer's disease shows diffuse brain atrophy [8].

Ultimately, 44 million people around the world are living with dementia at present. One of the leading cause of death in England and Wales is Dementia. The primary pathological process says that Aβ gets accumulated due to the separation of APP in the brain by β and γ-secretase enzymes due to the imbalance of Aβ production and clearance. There is also subsequent neuronal dysfunction and neurodegeneration involved in this with NFT formation due to inflammation [9].

3.2. Parkinson Disease

Parkinson's disease is a Neurological disorder in which there is a decrease in dopaminergic neurons in the Substantia nigra pars compacta (SN) which is a part of the midbrain and Lewy bodies are also associated with this that are insoluble alpha-synuclein aggregates. The clinical features showing Parkinson's in a person are asymmetric resting tremor, cogwheel rigidity, bradykinesia, anosmia, constipation, rapid eye movement, depression, sleep behavior disorder, and autonomic dysfunction. It is also considered that before the clinical motor symptoms can appear around 50% to 70% of dopaminergic neurons have already died. Parkinson's disease results from both genetic and environmental factors which involve the exposure of a person to toxicant chemicals or a head injury which can increase the risk of Parkinson's in a person, however, lifestyle changes can help in reducing the risk factors. It has been also identified that in 5% to 10% of cases, the mutation in certain genes can also cause Parkinson's. A study has also shown that concordance in monozygotic and dizygotic twins having heritability effect is around 30% and Environmental and behavioral factors are major risk factors of Parkinson's disease [10].

3.3. Huntington's disease

Huntington's disease (HD) is a neurodegenerative disorder having autosomal-dominant inheritance with motor, cognitive, and psychiatric features. George Huntington first described this in 1872. It is caused by the expansion of CAG triplet repeat in exon 1 of the gene encoding Huntington protein which is present in the short arm of chromosome 4 resulting in the elongation of polyglutamine (PolyQ) in the mutated protein. Anticipation also occurs in this due to spermatogenesis and oogenesis when it is inherited down the paternal bloodline. Huntington's can be diagnosed in patients ranging from 2 to 87 years old [11].

3.4. Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease that is associated with the degeneration of both upper and lower motor neurons. ALS have complex genetic disorder having a Mendelian pattern of inheritance. In this, the ubiquitylated protein gets aggregated and accumulated in motor neurons [12].

4. Neuroprotective Herbs Used in Neurodegenerative Disorders

4.1. Crocus Sativus L

Crocus sativus L also known as Saffron is an herbaceous perennial plant. It belongs to the Iridaceae family. This plant can be found in the Middle East, Central Asia, India, and China. Morocco is also one of the largest producers of saffron making it the 4th largest producer in the world. Around 150,000 to 200,000 flowers are required to produce 1 kilogram of saffron.

It has around 150 volatile and non-volatile compounds present in it and out of these only 50 constituents have been identified in the chemical analysis. Crocin, Picrocrocin, and Safranal are the 3 main biologically active compounds present in this plant [13].

It has Antihypertensive activity which was investigated by Fatehi on anesthetized rats by administration of 50 mg/g aqueous extract of C. sativus petals which results in changing the blood pressure of rat from 133.5 +_ 3.9 to 117+_ 2.1(mmHg).

It shows Anticonvulsant activity by reducing the seizure duration and also Anxiolytic activity can be seen in rats. It affects depression as well as relaxant properties.

Its main active constituents such as crocin and crocetin affect the learning skills and memory of rats and mice which can be seen in ethanol-induced impairment of learning behavior in both animals and so this can be used in the treatment of memory-related disorders and Neurodegenerative disorders [14].

4.2. Nigella Sativa

Nigella Sativa is a type of yearly herbaceous plant that is part of the Ranunculaceae family. It is also known as Black cumin and black caraway seeds. It is cultivated and found in India, Pakistan, Saudi Arabia, Turkey, Syria, South Europe, and the Middle Eastern Mediterranean region. Thymoquinone (2-isopropyl-5-methylbenzo-1, 4-quinone) is the main ingredient of this plant. Thymoquinone reduces oxidative stress to protect the PC12 cells from cytotoxic agents and also has a therapeutic effect against the ethanol-induced neuronal apoptosis of the cortical neurons.

The main constituents of N. Sativa are Thymoquinone, Apinene, Sesquiterpene longifolene, Tanethol, carvacrol, p-cymene, dithymoquinone, thymohydroquinone, and 4 terpineols. Thymoquinone is the main bioactive component of N. sativa with a molar mass of 164.20 g mol−1 and molecular formula C10 H 12 O2 and consists of the keto, enol, and the mixture

forms. Keto is the main form of these 3 and is attributed to the pharmacological effects of Thymoquinone.

It is effective in Alzheimer's disease, Anxiety, Depression, Encephalomyelitis, Epilepsy, Ischemia, Parkinson's disease, Neuroinflammation, and Traumatic Brain Injury [15].

4.3. Coriandrum Sativum

It is also known as Coriander belonging to the Parsley family is an annual herb. In Persian, it is called as Geshniz. It is grown all over the world and is native to the Mediterranean region. The major components found in coriander fruit are linalool, monoterpenes, and monoterpenes hydrocarbons. The main essential oil in coriander is linalool, linoleic, and linoleic acid.

It can be used as a digestive agent according to folk medicine and the seed extract of C. Sativum can be used to make lotions and shampoos and also have antimicrobial and anti-rheumatoid effects. According to Iranian medicine, it can relieve insomnia.

The leaf extract of C. sativum shows an anxiolytic effect and the aqueous and ethanolic extracts of C. sativum seeds show Anticonvulsant activity using pentylenetetrazole (PTZ) and electroshock seizure models [16].

4.4. Withania Somnifera

Withania somnifera Dunal belongs to the Solanaceae family. It is commonly known as Ashwagandha. In the drier parts of tropical and subtropical zones, it is widely distributed ranging from the Canary Islands, the Mediterranean region, and Northern Africa to Southeast Asia. For more than 3000 years, Nigella Sativa has been a significant medicinal plant utilized in Ayurvedic and traditional medicine. Various parts of the plant, including the roots, stems, leaves, and extracts, have been employed to treat different health issues. The primary components of Nigella Sativa include alkaloids and steroidal lactones, with chemicals like withanine, somniferine, somnine, somniferinine, and withananine found within it. Withania is widely claimed to have potent aphrodisiac, sedative, rejuvenating, and life-prolonging properties.

It is also used as a general energy-enhancing tonic known as Medhya Rasayana, which means “that which promotes learning and a good memory,” and in geriatric problems. The active constituents of W. somnifera such as withanolide A, withanoside IV, and withanoside VI were shown to restore presynapses and post-synapses in addition to both axons and dendrites in cortical neurons after amyloid-β (Aβ)25–35-induced injury.

Giving mice a dose of withanolide A, withanoside IV, and withanoside VI by mouth (at 10 μmol/kg/day for 12 days) helped to enhance memory and reverse damage caused by Aβ25–35 in the brain regions responsible for memory and learning, such as the cerebral cortex and hippocampus. Oral administration of W. somnifera proved highly effective in reversing the behavioral deficits and pathological features in two mouse models of AD [17].

4.5. Thymus Vulgaris

It is a flowering plant belonging to the Lamiaceae family. It is cultivated in European Countries. Thyme is rich in oxygenated monoterpine, less amount of monoterpene hydrocarbons, and oxygenated sesquiterpene.

Thymol which is an essential oil shows neuroprotective properties against dopaminergic neurodegeneration in Rotenone-induced Parkinson’s disease on wistar albino rats. Thymol also inhibits lipid peroxidation and endogenous enzyme activity in the thymol thymol-treated animal group.

Extract of T. vulgaris has shown neuroprotective properties on experimentally induced cerebral ischemia in rats, The Neuroprotection mechanism might be associated with

antioxidant activity and inhibition of oxidative stress in rat brains [18].

4.6. Ferula Asafoetida

Asafoetida is a plant in the Apiaceae family that grows from the exudates of the plant's living subterranean rhizome or tap roots. In Iran, F. asafoetida or gum-resin is known as "Anghouzeh", "Khorakoma", and "Anguzakoma". In India and Nepal, people have long used it in traditional medicine and as a spice in various dishes.

The hydrodistilled oil contains 25 chemicals, including E-1-propyl sec-butyl disulfide, which is a substantial component. Ferula asafoetida's main components are E-1-propenyl sec-butyl disulfide (40.0%) and germacrene B (7.8%).

Ferula asafoetida leaves have anthelmintic, carminative, and diaphoretic qualities, while the plant's root is used as an antipyretic. In addition, F. asafoetida is used in traditional medicine to treat a variety of ailments such as asthma, epilepsy, stomach ache, flatulence, intestinal parasites, poor digestion, and influenza. Sedative, expectorant, analgesic, carminative, stimulant, antiperiodic, ant-diabetic, antispasmodic, emmenagogue, vermifuge, laxative, anti-inflammatory, contraceptive, and anti-epileptic properties have also been recorded for F. asafoetida oleo-gum resin.

The ole-gum resin of Ferula asafoetida has been shown in pharmacological and biological studies to have antioxidant, antiviral, antifungal, anti-diabetic, antispasmodic, and antihypertensive properties. Research also indicates that F. asafoetida resin might have the ability to block monoamine oxidase B (MAO-B), making it a possible treatment for neurodegenerative conditions like Parkinson's and Alzheimer's diseases[16].

4.7. Ginkgo Biloba

Ginkgo biloba L is an important medicinal herb that belongs to the Ginkgoceae family. It contains primarily Bilobalide, Ginkgolides A-C, Quercetin, Isorhamnetin, and Kaemferol.

In experimental animals, Ginkgo biloba extract shows neuroprotective properties against 6-hydroxydopamine (6 OHDA) induced neurotoxicity in the nigrostriatal dopaminergic system, i.e., Parkinson's disease.

Ginkgo biloba has also been reported to have antioxidant, anti-dementia, and anti-Alzheimer properties, as well as the ability to improve cognitive functions [18].

4.8. Curcuma Longa

Curcuma longa (C. longa), also known as turmeric, is a member of the Zingiberaceae family, which is widely cultivated in Asia. Curcuminoids (curcumin), ketone, sesquiterpene alcohol, and monoterpene are the main components of turmeric. Turmeric contains α and β-pinene, camphene, limonene, terpinene, linalool, curcumene, and stigmastirol, among other things.

Curcuma longa ethanolic extract (200 mg/kg) protects rats (Sprague Dawley) against trimethylation-induced oxidative stress. Prevention of oxidative stress is accomplished by lowering brain and plasma MDA concentrations while increasing SOD, CAT, and GPx enzyme activity.

Curcumin (40 mg/kg, i.p.) exhibits neuroprotective properties in an experimental model against IL-1-induced Apoptosis and depression-like behaviors caused by chronic stress. Curcumin administration to 6- and 24-month-old rats demonstrates neuroprotective and anti-aging properties[18].

Conclusion

In this review, we have focused on the different types of Neuroprotective herbs that can be used to treat different types of neurodegenerative diseases. Because of their complicated pathogenesis, neurodegenerative diseases continue to pose a challenge in modern medicine. Protein misfolding and accumulation within or outside of neurons is a key pathological feature in several neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's disease. Because of their cognitive benefits and, more importantly, their mechanisms of action about the fundamental pathophysiology of the diseases, herbal medicines are regarded as effective and promising sources of potential neuroprotective agents. Our review identified several herbal medicines with potential therapeutic effects for neurodegenerative diseases, including Crocus sativus, Nigella Sativa, Coriandrum sativum, Withania somnifera, Thymus vulgaris, Ferula Asafoetida, Ginkgo biloba, Curcuma Longa.

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Conflicts of interest

There are no conflicts of interest.

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