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MINI-REVIEW article

Natural products as of nutraceuticals treatment for neurological disorders: An overview

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Abstract: Natural products play a major role in maintaining healthy people and animals and in preventing sickness. Experiments have shown that these natural compounds have several biological properties, including anti-inflammatory, anti-apoptotic, and antioxidant effects. Using Google Scholar, PubMed, and Science Direct database searches, current recorded information was incorporated in this review. The databases listed above were searched using the following Medical Subject Headings (MeSH) terms for data extraction: preventative, natural product, phytoconstituents, natural products for Parkinson's illness, Alzheimer's disease, and natural products for the brain. The effectiveness of natural products in a variety of preclinical models of neurodegenerative diseases has been demonstrated by *in vitro* and *in vivo* studies. Phytoconstituents, such as polyphenolic antioxidants, are present in freshwater and marine flora, as well as in fruits, vegetables, nuts, and herbs. These phytoconstituents may help the brain's memory and cognitive processes while preventing neurodegeneration. Moreover, they are essential in the prevention and treatment of various neurodegenerative diseases, including Parkinson's disease, epilepsy, Alzheimer's disease, and other neurological conditions. This review briefly highlights a few neurodegenerative diseases, emphasizing how natural products and nutraceuticals function against neurological disorders.

Introduction

Food and synthetic products made from food have been used for a long time because of their health benefits. The safety profile of nutraceuticals is primarily responsible for the recent increase in their use [1]. The foundation of nutritional psychiatry is the use of nutraceuticals to treat, prevent, and cure mental illnesses [2]. Numerous indications pointed to the possible use of several foodstuffs in the treatment of neuropsychiatric and neurodegenerative diseases [3, 4]. Also, clinical research has indicated that nutraceuticals may be a potential treatment for many conditions [5]. Numerous studies have suggested that these organic compounds may be important in the pharmacotherapy of neurodegenerative illnesses [6].

Human beings are the most frequently used natural items as a primary source of therapeutic substances to treat a wide range of illnesses, diseases, and frailty. However, the adverse effects and toxic nature of some natural compounds are unknown to those using these medications. Sumerian and Akkadian civilizations were the first to use plants that contained these medicinal compounds for therapeutic purposes [7]. Ayurvedic, Chinese, and

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Unani traditional medicine systems-all of which are still widely practiced today, rely heavily on natural materials. Secondary metabolites with a great deal of structural diversity and a variety of novel and intriguing pharmacophores have primarily been isolated from plants. Of nearly 250,000 plants or higher, less than 1% have thoroughly investigated their phytochemistry or pharmaceutical potential [8]. The World Health Organization (WHO) reported that 75% of people worldwide still receive their primary medical treatment from plant-based traditional medicines, which primarily use plant extracts or their bioactive secondary metabolites. Nature contains an infinite supply of molecules for improving human health in the form of food, spices, and plants. Phytochemicals derived from plants can exert antagonistic, synergistic, or additive effects on organisms [9]. The term "nutraceuticals," which was initially used by Stephen L. DeFelice, is a combination of the terms pharmaceutical and nutrition. A nutraceutical is any food particle (whole) or portion (purified food product) that provides health or medical advantages, such as illness prevention and treatment [10, 11]. Nutraceuticals and herbal medicines are significant and beneficial resources for neurological disease prevention rather than treatment [12]. It has been observed that phytoconstituents have modulatory effects on the nervous system in a variety of experimental models of neurological illnesses [13]. The majority of research on various neural problem models that mimic essential aspects of disease has identified significant components such as oxidative stress, mitochondrial malfunction, and neuro-inflammation, however, the pathophysiology of nervous system disorders is still not fully understood [14, 15]. Neurotoxicity models are a valuable resource for creating new treatment plans and evaluating the benefits and drawbacks of symptomatic therapies [16]. Numerous published studies indicate that chromatin remodeling and epigenetic changes are the mechanisms by which natural products exert a variety of biological effects [17]. Because of their broad range of biological and pharmacological properties, they are good options for treating neurological conditions and neurodegenerative diseases [18]. Numerous studies on the identification and development of new neuroprotective medications have demonstrated the great potential of plant extracts and their bioactive chemicals [19], in conjunction with nutraceuticals, as neuroprotective candidates against a variety of neuro-degenerative diseases. This review briefly describes a few neurodegenerative illnesses and emphasizes how natural products and nutraceuticals might be used. Up-to-date documented information was included in this review by conducting database searches using Google Scholar, PubMed, and Science Direct until June 2024. Only English-language publications were included in the search. The databases listed above were searched using the following Medical Subject Heading (MeSH) terms for data extraction: preventive, natural product, phytoconstituents, natural products for Alzheimer's disease, natural remedies for brain, and natural goods natural products for Parkinson's diseases, Huntington's illness, natural remedies natural products for epilepsy damage to the peripheral nerve, natural products studies for the prevention of neurological illnesses in vivo and in vitro, and motor behavior abnormalities. The original articles were acquired in nearly every instance, and relevant information was extracted.

Nutraceuticals promise better neuronal health: Numerous compounds produced from plant foods have been shown to have neuroprotective effects [20]. Polyunsaturated fatty acids and antioxidants, which are found in foods such as fruits, vegetables, and seafood, can help lower the risk of Alzheimer's disease [21]. Piperine, an alkaloid found in Piper nigrum fruits, can contribute to neurodegeneration and memory loss [22]. Carotenoids and flavonoid-like substances exhibit neuroprotective properties [23]. Ascorbic acid and carotenes reduce lipid peroxidation, which in turn reduces the risk of Alzheimer's disease [24]. In Alzheimer's disease, caffeine can protect against oxidative damage [25]. Age-related changes in motor function can be improved by dietary supplements [26]. Research indicates that in a model of Parkinson's disease, capsaicin, an alkaloid present in the fruit of the Capsicum genus, protects against dopamine neuron loss and promotes behavioral recovery by preventing oxidative stress [27]. Additionally, sesamin from sesame oil increases dopamine levels and has a neuroprotective effect on dopaminergic neurons [28]. Numerous foods, including blueberries and grapes, contain the antioxidants resveratrol and pinostilbene, which have neuroprotective properties. Epigallo-

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catechin-3-gallate, an antioxidant in green tea, also exhibits a neuroprotective effect [25]. Fructose, a rich constituent of honey, sugar cane, and sugar beet produced anxiolytic and memory-enhancing effects in rat models after a six-week treatment [29]. The consumption of olive oil as the primary source of monounsaturated fat can reduce the incidence of neurodegenerative disease [30]. Curcumin belongs to the ginger family and has been shown to have a variety of biological functions, including neuroprotective effects [31]. Black cumin, and *Nigella sativa*, have also been shown to improve memory and learning in rats [32]. Thymoquinone, an active ingredient in *Nigella sativa*, may have antioxidant properties and protect against the early pathogenic effects of prevalent neurodegenerative diseases [33]. Flavonoids are abundant in fruits, vegetables, nuts, herbs, and beverages made from plants. According to reports, the majority of flavonoids have powerful antioxidant properties that protect cells from oxidative damage [34]. Medicinal plants are receiving particular attention as a means of preventing epilepsy and oxidative stress [35]. The flavone glycoside baicalin preserves endogenous enzyme levels, increases GABA levels in the brain, and suppress oxidative stress [36]. Rutong et al. verified that kaempferol 3-O-rutinoside enhances behavioral performance in a mouse model of Parkinson's disease induced by 6-hydroxydopamine, in part by suppressing reactive astrogliosis and α-synuclein overexpression or aggregation [37, 38]. *Bacopa monnieri* is a well-known nootropic species. Administration of an alcoholic extract of *Bacopa monnieri* enhances memory and cognitive function while reducing retrograde amnesia. It has also been demonstrated to protect against cognitive deficits caused by phenytoin [39]. Alpha-asarone, also known as α-asarone, is a naturally occurring chemical extracted from the Chinese herbal medicinal plant *Acorus gramineus* and is frequently used in clinical settings to treat epilepsy. Additionally, it has been demonstrated to have neuroprotective properties and increase glutamate uptake while reducing synaptic excitement. The sedative and anticonvulsant effects of α-asarone on the central nervous system have already been clinically demonstrated. Using in-vitro and in-vivo models, a study was carried out to clarify the mechanism of action and therapeutic targets of α-asarone to understand its anti-epileptic effects. α-asarone was discovered to be an inhibitor of hippocampal neuronal activity, which increases neuronal tonic Gamma-aminobutyric acid (GABA) inhibition and has anti-epileptic effects in the central nervous system [40]. Memory and cognitive deficiencies in the brain have been corrected using natural products. The therapeutic benefits of these products are mostly attributable to the way phytonutrients interact with several signaling pathways linked to neuroinflammation and protein folding [41]. Cinnamaldehyde, eugenol, cinnamyl acetate, and cinnamyl alcohol are largely responsible for its anti-Alzheimer disease activity by blocking oligomer and amyloid fibril formation [42]. The natural nutraceutical compounds listed here act against neurological problems and prevent cognitive dysfunction (**Tables 1-5**, respectively), epilepsy, Alzheimer's disease, Parkinson's disease, and antidepressant action.

Table 1: Natural product components' roles in cognitive deterioration

Natural product	Common name	Phytoconstituents	Functions	Reference
Ginkgo biloba	Maidenhair tree	Quercetin glucopyranoside, quercetin rutinoside, quercetin 3-O-α-L-[6‴-p-coumaroyl-(β-D)-glucopyranosyl-(1,2)-rhamnopyranoside]	Improves memory and acts as an antioxidant	[43]
Withania somnifera	Indian ginseng	Withanone	Withanone reduces oxidative stress and inflammation, which improves cognitive decline	[44]
Bacopa monnieri	Brahmi, Thankuni	Bacosides, Bacopasides	Boost in retaining capability	[45]
Vaccinium angustifolium	Lowbush, Blueberry	Anthocyanins	Enriched memory and motor performance	[46]
Tinospora cordifolia	Gulbel	Whole plant/ Ethanolic extract	Enhancement of cognition	[47]

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Table 2: Functions of natural product ingredients against epilepsy

Natural product	Common name	Phytoconstituents	Functions	Reference
Ferula gumosa	Galbanum	Pinene	Protection against (Pentylenetetrazole) PTZ provoked seizures.	[48]
Ficus platyphylla	Broadleaf fig	Saponin rich fraction	Defense against seizures triggered by strychnine and PTZ	[49]
Ficus religiosa	Sacred fig	Saponin rich fraction	Modification of cerebral neurotransmitter levels	[50]
Myristica fragrans	Nutmeg	Oil from kernels	Anticonvulsant activity against Strychnine and PTZ stimulated seizure	[51]
Citrus fruits	-	Naringenin	Reduction in the intensity of seizures	[52]

Table 3: Functions of natural product ingredients against Alzheimer's disease

Natural product	Common name	Phytoconstituents	Functions	Reference
Ananas comosus	Pine apple	Bromelain	Breaks down amyloid-β42 monomers and oligomers seen in AD patients' (cerebrospinal fluid) CSF.	[53]
Vitis vinifera	Grape vine	Resveratrol	Reduction of oxidative stress and inflammation by sirtuin 1 activation, which in turn reduces NF-kB activity and FOXO protein apoptotic activity.	[54]
Vaccinium angustifolium	Lowbush, Blueberry	Anthocyanins	Lowering of oxidative injury and drop in the expression of age-linked protein, such as NF-kB	[55]
Magnolia officinalis	Houpo	Magnolol, honokiol, obovatol and 4-O methylhonokiol	Acetylcholine esterase inhibitory and memory boosting capacity	[56]
Juglans regia	Persian walnut	Fatty acids, alpha-tocopherol, vitamins, and polyphenols, especially ellagic acid	Inhibition of amyloidogenic activity, defibrillation of produced Aβ, and Aβ fibril formation	[57]

FOXO: Forkhead box protein O1, and NF-kB: Nuclear Factor-kappa B

Table 4: Functions of natural product ingredients against Parkinson's disease

Natural product	Common name	Functions	Reference
Epigallocatechin-3-gallate	-	↑TH-positive cells in the Substantia nigra region ↑CD3+CD4+ to CD3+CD8+ T-cell lymphocyte ratio in the peripheral blood ↓TNF-α and IL-6 cytokine expression in serum	[58]
Chrysin	-	↑Behavioral functions, ↑TH-positive cells in the Substantia nigra and Striatum	[59]
Thymoquinone	Rotenone	↑Behavioral functions, ↑Parkin, Drp1, TH-positive cells in the Substantia nigra and Striatum	[60]
Estrogenic compounds	-	Neuroprotective effects	[61]
Panax ginseng	Five fingers	Maintenance of neuronal constitutional stability, improvement of cognitive capacity	[62]

IL-6: Interleukin-6**,** TNF-α: Tumor necrosis factor-alpha, and TH: Tyrosine hydroxylase

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Table 5: Functions of natural product ingredients act as antidepressant

Natural product	Common name	Phytoconstituents	Functions	References
Curcuma longa	Haldi	Curcumin	Inhibition of the enzymes monoamine oxidase A and B	[63]
Scutellaria baicalensis	-	Baicalin	Inhibits neuroinflammatory response as well as oxidative stress.	[64]
Crocus sativus	Saffron	Crocetin, safranal	Decrease in Beck inventory scores for anxiety and despair	[65]
Rosmarinus officinalis	Rosemary	Rosmarinic acid	Increases tyrosine hydroxylase and pyruvate carboxylase.	[66]
Malus domestica	Apple	Quercetin	Decreases neuroinflammation via iNOS and BDNF regulation	[67]

BDNF: Brain-derived neurotrophic factor and Drp1: Dynamin-related protein 1

Conclusion: Naturally derived phytochemicals and their derivatives play a potential neuroprotective role in their multidimensional ability to regulate and modulate chronic inflammation, oxidative stress, and downstream signaling, which are hallmarks of Parkinson's disease. These phytoconstituents may prevent neurodegeneration and improve memory and cognitive functions in the brain. They are also crucial in the prevention and management of several neurodegenerative diseases, such as epilepsy, Parkinson's disease, Alzheimer's disease, and other neurological diseases. Therefore, future research should search for novel classes of natural compounds that could offer novel methods for preventing a range of neurodegenerative and mood disorders.

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