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REVIEW ARTICLE

Phytochemicals in Neurological Disorders Management: A Comprehensive Review

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Abstract

Neurodegenerative diseases, which cause progressive neuronal loss, are a serious global health concern. While allopathic medicine offers some remedies, limitations such as adverse effects and low efficacy have encouraged interest in alternative treatments. Phytomedicine, or the utilization of plant-based medications, has emerged as a viable alternative. Phytomedicine offers several advantages over allopathic treatments. They frequently contain a combination of bioactive compounds, which can target multiple disease processes at once. This integrative strategy may yield more thorough therapeutic outcomes. Furthermore, numerous phytomedicines exhibit neuroprotective properties including as antioxidant, anti-inflammatory, and neurotropic activity. These activities can help to decrease neuronal damage and promote neuronal regeneration. Furthermore, phytomedicine is generally well accepted and has fewer negative effects than allopathic drugs. This is especially important in chronic conditions such as neurodegenerative diseases, where continuous treatment is typically required. Studies have shown that phytomedicine isolated from plants such as *Ginkgo biloba*, curcumin (from turmeric), and *Bacopa monnieri* may be useful in the treatment of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, epilepsy, depression, and anxiety. While additional research is needed to fully understand the mechanisms of action and demonstrate efficacy, phytomedicine offers a feasible alternative or supplement to allopathic medicine for neurodegenerative diseases. The promise of natural, well-tolerated, and multi-targeted therapies makes phytomedicine an attractive field of study in the hunt for viable treatments for various chronic conditions.

Major Findings: The review demonstrates that plant-derived phytochemicals possess notable antioxidant, anti-inflammatory, and neuroprotective effects. They show potential in managing neurological disorders such as Alzheimer's, Parkinson's, and Huntington's disease. These natural compounds may serve as safer, multi-targeted alternatives or adjuncts to conventional therapies.

Keywords: Future Prospective, Management, Neurological Disorders, Phytochemicals, Treatment

1. Introduction

The majority of brain illnesses are marked by neurodegeneration[1]. Despite modern science's ongoing efforts to discover a pharmacological or surgical therapy, the outcomes have been disappointing. The vast majority of the elderly remain clinically worried regarding Neurodegenerative Diseases (NDs), such as Alzheimer's and dementia[2]. One of the biggest obstacles to effective treatment of neurodegenerative diseases (NDs) is still the Blood-Brain Barrier (BBB), which is incredibly effective. Despite numerous surgical successes and highly invasive or disruptive methods-such as focused ultrasound, intracerebral injections, convection-enhanced delivery, and osmotic BBB disruption-their clinical use is limited because of various concerns about long-term effectiveness and potential damage to the brain barrier. Because they facilitate communication, neurons are essential for the optimal functioning of the human brain[3]. Although they can be found throughout the body, the majority of neurons originate in the brain[4]. Throughout young

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adulthood, the proportion of neurons is produced by neural stem units, albeit they drastically decline as people age[5]. Neurological damage, or the slow deterioration of neurons, their form, or their activities, is a major medical concern and plays a significant part in the pathophysiology of many brain diseases, despite the fact that neurons are not permanent[6]. Synapse and networking neuron failure, as well as the development of physiologically disturbed protein changes in the brain, are all associated with neurodegeneration[7]. The most common neurodegenerative diseases include Huntington's disease, Alzheimer's disease, Parkinson's disease, prion disease, Amyotrophic lateral sclerosis, motor neuron disease, spinal cord injury, and spin cerebellar dementia[8].

Worldwide, millions of people are afflicted by neurodegenerative diseases. Although age is the most important risk factor for the development of all NDs, recent research indicates that a person's genetic makeup and environmental circumstances may also increase their risk of developing NDs. Additionally, even if a person may have certain genes that cause NDs, their immediate environment has a significant impact on the amount and timing of neurodegeneration[9,10]. Multiple illnesses may contribute to a single neurodegenerative sickness, according to more recent research[11]. Therefore, depending on the type and stage of the sickness, NDs can be severe or even fatal.

Patients with NDs exhibit with a wide range of symptoms and neurological signs, including dementia and mobility problems. Surprisingly, the bulk of these symptoms and signs are recognized as prevalent in neurodegenerative illnesses such as Alzheimer's, Parkinson's, and Huntington's[12]. Early identification of neurodegeneration may give a chance for early therapy, perhaps slowing disease progression[13]. The receptors for NMDA antagonists such as memantine, or and namzaric are used to treat Alzheimer's patients[14]. Axon has recently been used to treat Alzheimer's disease as an alternate source of energy[15]. Several medications are used to treat Parkinson's disease, Apo morphine hydrochloride; rotigotine, ropinirole, and levodopa are other examples. Levodopa is generally used to avoid Parkinson's symptoms[16].

Fruits and vegetables are currently in high demand due to their high phytochemical content[17]. Natural substances known as phytochemicals have been shown to provide defense against oxidative stress and neuroinflammation, two factors that are common in neurodegenerative diseases[18]. Common phytochemicals found in everyday life include curcumin, quercetin, diallyl trisulfide, flavonoids, and Epigallocatechin-3-Galate (EGCG). Phytochemicals change hormone metabolism, lower platelet buildup, and boost the immune system[19]. One group of researchers found that a 13% decrease in overall mortality among PD and AD patients indicates that a Mediterranean-style diet high in olive oil significantly improves well-being[20].

Though the internal mechanisms underlying this advantage are entirely unknown, cumulative research indicates that phytochemicals as nutraceuticals can improve the condition of NDs. One study claims that phytochemicals improve the situation by acting as non-traditional scavengers and antioxidants[21]. It's unclear how phytochemicals are supposed to be used in cells. However, it is anticipated that these compounds would be able to do more than simply alter gene expression and enzyme metabolism; they may also trigger stress response pathways that cells would deploy as a defense[22]. According to a different theory, phytochemicals function as ligands, binding to particular chemical receptors on cell or nucleus membranes before initiating a downward neural signaling cascade that produces their antioxidant effects[23].

The 'Green' movement in Western civilization has changed public perceptions, with many now feeling that naturally generated substances and extracts are innately safer and more attractive than synthetic chemical products, resulting in increased sales of herbal treatments[24-25]. About 80% of individuals in poor nations get their primary medical treatment from phytomedicine for both humans and animals[26]. In traditional medicine, a variety of herbs have been used to treat memory problems and neurodegenerative illnesses including Alzheimer's Disease (AD). Complex blends of organic molecules, herbal products might include fatty acids, sterols, alkaloids, flavonoids, glycosides, the saponins tannins, terpenes, and more. Herbal medicine proponents contend that the combined advantages of a plant's constituent parts, rather than the individual compounds that pharmacologists isolate, are what provide it therapeutic efficacy; as a result, traditional medicines are said to be efficient and to have few or no adverse effects. Between 25% and 50%

of contemporary medications have their origins in plants. The identification and characterization of new plants with medicinal properties for the management of neurodegenerative conditions and stroke-related brain injury has attracted an increasing amount of scientific attention in recent years. Diseases of the Central Nervous System (CNS) are treated using more than 120 traditional remedies in Asian nations[27].

A variety of illnesses have been treated using natural products, such as secondary metabolites and bioactive compounds derived from microbes, plants, and animals[28]. Both on land and at sea, nature has provided mankind with excess resources, or natural products. Natural products are essential for preserving and enhancing the health of people and animals[29]. It has been shown that these naturally occurring compounds contain a number of biological qualities, including antioxidant, anti-inflammatory, and anti-apoptotic effects[30]. Numerous preclinical neurodegenerative disorder investigations, both *in vitro* and *in vivo*, have demonstrated the value of natural compounds. Phytoconstituents such as polyphenolic antioxidants are found in freshwater and marine flora, as well as in fruits, vegetables, nuts, and herbs[31]. These phytoconstituents may enhance cognitive function and memory while preventing neurodegeneration. Additionally, they are thought to be essential in both the avoidance and management of neurological diseases including Parkinson's, Epilepsy, and Alzheimer's[32].

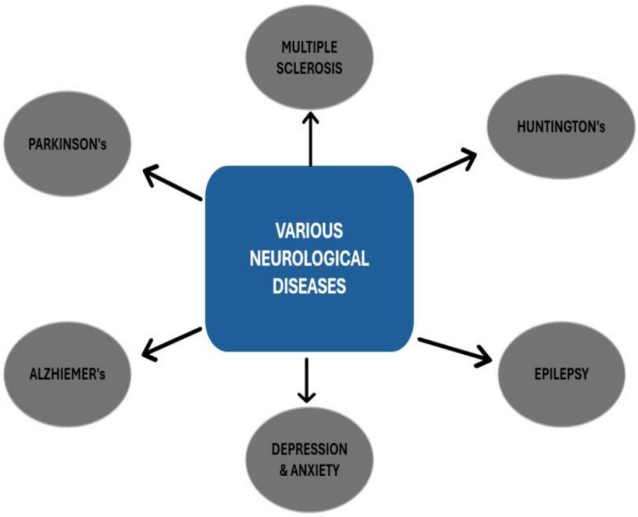


Figure 1. Overview of neurological diseases.

2. Various Neurological Diseases

While there are various neurological problems, the following ailments have caused the biggest amount of damage to human health for decades now (Figure 1).

2.1 Huntington's Diseases

Huntington's Disease (HD) is a neurological illness that is genetically transmitted and autosomal dominant. Affects muscular coordination, resulting in nerve cell loss over time, mental disorders, motor a movement disorder, cognitive impairment, and chorea and dystonia[33]. Most afflicted individuals experience symptoms throughout their mid-adult years[34]. (35-45 years), however the disorder can start earlier in life. Chorea is characterized as fast, uncontrollable writhing motions caused by the disease[35]. The unstable expanded Cytosine-Adenine-Guanine (CAG acting) three sets loop in the first domain of the transmitting diseases IT15 (Htt) gene, which codes for the protein named Huntington (Htt), is the autosomal dominant mutation that causes HD. The mutant form of Huntington's N-terminus has a mutated polyglutamine (polyQ) branch of variable length as a result of this mutation[36-37]. This dysfunction aids in expressing the clinical symptoms of HD. Because there is no treatment to prevent additional neuronal damage, a standard treatment approach is used to address mental and behavioral symptoms[38]. Currently, non-pharmacological treatments for HD include genetic counseling, therapy, and palliative care[39]. Compared to the overall population, HD patients and careers had greater suicide rates. Reasoned suicide, which has nothing to do with mental diseases, was connected to this disparity. Only 3-7 out of 100,000 persons globally are affected with HD, and there are about 20 carriers[40].

Twenty years after the discovery of Huntington's disease's genetics, were found, the cause is unknown, and no effective remedy has been developed. There are limited treatments available for HD's motor, mental, and cognitive symptoms[41]. The sole medication for chorea, Tetrabenazine (TBZ), has drawbacks, including adverse effects and drug interactions[61]. It has also been demonstrated that mood stabilizers and Selective Serotonin Reuptake Inhibitors (SSRIs) can assist treat early HD symptoms[42]. Due to a lack of therapeutic medications for treating cognitive dysfunction in

HD, a based-on research treatment strategy has been promoted. Additionally, healthcare providers and HD-affected families should have easy access to information and symptomatic therapy methods[43].

For the purpose of to properly understand the fundamental biochemical process and create treatment approaches for HD, simulations are being implemented[44]. To mimic HD, a range of molecular and mammalian models are now being used. HD has been associated with mutations in Succinate Dehydrogenase (SDH), and 3-Nitropropionic acid (3-NP), an inhibitor of cellular complex 2 and a permanent impediment of SDHr, reproduces neural degenerative conditions and morphological changes such as psychological, biochemical processes and neuropathological modifications in the creatures that are comparable to those noticed in the pathophysiology of HD[45-47]. Caenorhabditis elegans, Drosophila, mice, rats, and other transgenic species of animals that express mHtt exhibit progressive neurodegeneration and symptoms resembling Huntington's disease[48]. Researchers have gained a better understanding of HD in humans thanks to toxicological and recombinant animal models, even though no model can replicate every characteristic linked to HD etiology. Natural compounds, antioxidants, anti-inflammation, calcium antagonism, anti-apoptosis, and neurofunctional modulation can all help prevent or treat a variety of neurodegenerative disorders, including Huntington's[49]. *B. monnieri*, also known as *Herpestismonniera* and Brahmi (Family: *Scrophulariaceae*), grows throughout every part of the Indian subcontinent and is regarded by *Ayurveda* as a *Medhyarasayana*[50-51].

For thousands of years, it has been used to treat anxiety, insomnia, epilepsy, and memory loss[52,53]. Bacosides A and B and Dammarane-type saponins made from triterpenoid are the main chemical constituents of the plant[54]. Aside from these main constituents, it contains a number of saponins, including bacopasaponin A-G[54-57]. Pseudojujubogenin, jujubogenin, Bacoside I-V, X, and N1 and N2[58-60]. The herb is also claimed to contain brahmine, herpestine, and monnierin[61]. Several studies have proved the plant's memory-enhancing qualities[62]. Among the various components, it has been demonstrated that Bacoside A enhances memory[63]. *Ayurvedic* medicine has traditionally utilized the root *Withania somnifera* (WS), commonly referred to as *Ashwagandha* (*Solanaceae*), to promote vitality and longevity[64]. Antioxidant, anti-inflammatory, immune-modulating, anti-stress, memory-enhancing and anti-convulsant qualities have all been found in the plant[65-70]. WS and its active ingredients, withaferin A and sitoindosides VII-X, increase endogenous ascorbic acid, catalase, and superoxide dismutase while reducing lipid peroxidation[71]. By lowering complement, lymphocyte proliferation, and delayed-type hypersensitivity, it acts as an anti-inflammatory drug (Table 1)[72-73].

2.2 Parkinson's Disease

Parkinson's Disease (PD) is a degenerative neurological illness associated with aging[86]. Parkinson's disease is brought on by the death of nerve cells in the substantia nigra, the area of the brain that controls movement. Dopamine, a crucial neurotransmitter, cannot be produced when these nerve cells are killed or injured. Studies show that patients who have eliminated up to eighty percent of their dopamine-producing cells in the substantia nigra develop Parkinson's symptoms. It is treated separately from both motor and non-motor illnesses and often manifests between the ages of 40 and 70[87]. The primary symptoms include uncontrollably tremors, unusual posture, and slowness of movement (bradykinesia) with at least one additional resting tremor or inflexibility symptom. Other connected symptoms include loss of smell, sleep issues, emotional disorders, elevated salivation, bowel movements, and excessive a periodic function limb movement during sleep[88]. Over 40% of patients have depression, and psychotic episodes are common among Parkinson's patients[89].

The aggregation of misfolded α-synuclein in Lewy bodies one of the main clinical features of Parkinson's illness qualifies the condition as a synucleinopathy. Moreover, both familial and sporadic types of Parkinson's disease are linked to α-synuclein, which plays a unique role in the etiology of the ailment[90]. Numerous neurotoxins, such as post translational changes, neuronal inflammatory responses, oxidative stress, dysfunctional mitochondria, altered the mitochondria. Morphological neuronal problems, phosphate lipid induced Endoplasmic Reticulum (ER) strain, and metallic ions, have been connected to the buildup of A-synuclein[91]. One of the main causes of

Table 1. Therapeutic effects of plant-derived natural compounds against Huntington's disease

Compound	Source of the Plant	*In-vivo* or *in vitro* models	MOA	References
α-mangostin	*Mangostana Garcinia* L.	3-NP, CGNs	Reduce the formation of ROS, antioxidants	74
Celastrol	Hook of *Tripterygium wilfordii*	PC12, HeLa, and polyQ mutant cells	Modulation of HSP	75
Fisetin	Many plants	R6/2 HD mouse; PC12 cells producing mutant Httex1	Lower mHtt, enhance ERK stimulation	76
Galantamine	Galanthus sp.	3-NP rats	NAChR modulation promotes survival by reducing striatal lesions.	77
ginsenosides	*Panax ginseng* Meyer, C.A.	YAC128 HD mouse strokeal MSNs	Decrease glutamate-induced CA^{2+} activation	78
Hesperidin	Fruits with citrus	3-NP rats	Increased cortical striatal and hippocampus MDA, anti-inflammatory and antioxidant properties, and a spike in locomotor activity and prepulse hindering (PPI) response	79
Kaempferol	Numerous plants	3-NP plants	Reduced ephemerality and motor deficiency reduce striatal lesions and use antioxidants	80
Lutein	Numerous plants	3-NP plants	Rise in body weight, neurobehavioral enhancement, complex functions of mitochondrial enzymes, and antioxidant	81
Lycopene	various red fruits and vegetables, such as tomatoes	3-NP plants	Raise biochemistry and behavioral indicators without any modification	82
Melatonin	Numerous Plants	3-NP plants	Antioxidant	83
Trehalose	Numerous plants	PC12 and COS-7b cells expressing	Boost autophagy in opposition to mHtt	84
Fish oil alongside quercetin		3-NP plants	Decrease mitochondrial dysfunction	85

Parkinson's disease-related decrease of dopaminergic neurons is Oxidative Stress (OS). The initiation and course of neurodegenerative at the cellular level are significantly influenced by OS, which is caused by a variety of factors, including non-genetic factors (age, environment, and pre-existing disease)[92].

Numerous pathogenic processes, such as oxidative stress, inflammation, transition metal buildup, apoptosis, mitochondrial dysfunction, and protein misfolding and aggregation, can damage dopaminergic neurons. According to recent research, the most direct cause of the rise in ROS, or Reactive Oxygen Species, which triggers synaptic destruction through apoptosis, is oxidative stress[93]. Even though Parkinson's disease has no known cure, medications, surgery, and physiotherapy can help manage its symptoms. Parkinson's disease is most commonly treated with levodopa/carbidopa, a combination that increases dopamine levels in the brain. In Asia, for many years, Gastrodiaelata Blume (GE) has been used as a traditional herbal treatment for a variety of medical conditions. GE is an effective anticonvulsant, analgesic, and sedative for vertigo, general paralysis, epilepsy, and tetanus[94]. Due to their ability to combat free radicals, antioxidants have a significant impact on human health by slowing down the aging process and reducing the impacts of oxidative damage brought on, for example, by an improper diet[95].

There are currently no authorized disease-modifying medications for Parkinson's disease, and treatment for the condition is still symptomatic and frequently fraught with serious adverse effects despite much research[96]. The only drugs that now alleviate symptoms of Parkinson's disease are monoamine oxidase inhibitors, cholinesterase inhibitors, and dopamine agonists[97]. Natural antioxidants called polyphenols are becoming more well-known because of their many health advantages and the fact that they can be found in foods and supplements.

Table 2. Impact of herbal remedies on the management of Parkinson's disease

Plant	Model Used	Concentration	Impacts	References
Cordifolia Tinospora	6-OHDA-induced rat	200,400 mg\kg	High levels of dopamine. A lower ratio of iron asymmetry. Reduced MDA levels Enhanced locomotor activity.	[100]
Carthamus Tinctorius L.	A rat with an MPTP lesion	70,35 mg/kg	Optimize behavioral performance. Suppression of reacting astrogliosis.	[101]
Portulaca Oleracea	6-OHDA-induced rat	200,400 mg/kg	The open field test included more crossings and rearings.	[102]
Pruriens Mucuna	6-OHDA-induced rat	40,80,120 mg\kg	Decreased likelihood of drug-induced dyskinesias. A higher concentration of nigrostriatal catecholamines.	[103]
Hibiscus asper leaves	6-OHDA-induced rat	50,100 mg/kg	Higher levels of SOD, GPX, CAT, and overall GSH content. Lower levels of MDA.	[104]
Pentaphyllum gynostemma	6-OHDA-induced rat	10, 30 mg/kg	Dopamine, 3,4-dihydroxyphenylacetic acid, and homovanillic acid levels were recovered.	[105]
Black tea	6-OHDA-induced rat	1.5%	Reduced levels of MDA. A higher level of GSH. A rise in SOD and CAT activity. Restoration of spontaneous locomotor activity and circular behaviour caused by d-amphetamine.	[106]
Safflower	Mouse was stimulated with 1-methyl-4-phenyl-1,2,3,6-tetradropyridine.	35,70 mg/kg/day	Reversed the decline in DJ-1, dopamine transporter, and tyrosine hydroxylase protein expression. Dopamine levels that are elevated Reduced amounts of acetylcholine.	[107]
Officinalis althaea L.	6-OHDA-induced rat	10 mg/kg	Reduced rotational activity. Reduced levels of MDA.	[108]
Corniculata oxalis	Infusion of MPTP in C57 male mice	250,500 mg\kg	Reduced action of SOD. A rise in catalase activity.	[109]

Plant-based phytochemicals and herbal concoctions have been marketed as "herbal medicine" for the management of Parkinson's disease[98]. Several investigations have discovered that flavonoids bind to several key locations in Parkinson's disease to preserve their possible neuroprotective effect. While flavonoids like europinidin, capensinidin, and rosinidin have been demonstrated to be useful against Parkinson's disease, flavonoids like aspalathin and norartocarpetin have shown promise in the management of Alzheimer's disease (Table 2)[99].

2.3 Depression and Anxiety

Anxiety syndromes are a class of mental diseases distinguished by a subjective experience of discomfort or anxiety about future events, as well as a dread of engaging to current events[110,111]. About 300 million people worldwide suffer from depression, a common psychiatric disorder[112]. One in nine people worldwide experienced at least one anxiety disorder in 2013[113,114]. When people are under stress, their failure to act according to external factors causes psychological and physiological modifications that put them at risk of illness[115].

In 2011, 23.6% of Iranians aged 18-64 reported having a mental disorder in the previous 12 months, with anxiety disorders ranking second (15.6%). 2/3rd of the people suffered from moderate to severe mental illnesses[116]. According to recent studies, the prevalence of psychiatric issues among Iranians increased from

Table 3. Overview of phytomedicines employed to treat depression

Herbal Medicines	Active Compound	Mechanism of Action	Potential Applications	References
Borage	Rosmarinus acid and thesinine	Anxiolysis shown in an animal model. Anti-depressant mechanism currently unknown.	Depression and anxiety	126
Lavender	Linalool and linalyl acetate	GABA modulation. Anxiolysis shown in animal models.	A depressive disorder, anxiety, and somatic tension.	127
Korean ginseng	GinesenosideRb1 and ginsenoside Rg1	HPA-axis modulation Monoamine. modulation Nitric oxide synthase inhibitor.	Tiredness, sadness, and impaired cognition	128
Saffron	Crocin and safranal	NMDA receptor antagonist. GABA- α-agonist Increase Re-uptake inhibition of monoamines.	Depression, Anxiety	129
Roseroot	Tyrosyl, rosavin, and salidroside	Monoamine oxidase A inhibition. Monoamine modulation. Neuroendocrine modulation.	Fatigue, cognitive impairment, depression and anxiety.	130

Table 4. Overview of phytomedicines employed to treat anxiety

Herbal Medicines	Active Components	Mechanism of Action	Potential Clinical Application	Reference
Brahmi	Bacoside A Bacoside P	Metal chelation / beta-amyloid prevention Cholinesterase inhibitor. Antioxidant effects. 5HT2c stimulation.	Cognitive dysfunction, depression, anxiousness, and nervous weariness.	131
California poppy	Escholidine Cheilanthifoline	Binding attraction with GABA receptor. Anxiolysis in animal models.	Anxiety insomnia, pain	132
Chamomile	Apigenin α- bisabalide	Binding to GABA receptor. Modulates monoamine neurotransmission. Neuroendocrine modulation.	Anxiety, insomnia, stress	133
Ginkgo	Ginkolide Bilobalide	GABAergic effects. Nitric oxide activity. Modulation of cholinergic and monoamino pathway.	Cognitive, impairment, anxiety, depression	134
Gotu cola	Asiaticoside	GABA transaminase inhibition. Suppression of the human RCT's auditory startles response.	Anxiety, stress, cognitive, impairment	135
Scullcap	Baicalin Scutelaterin	GABA-α binding capacity hypothesized. Anxiolysis in a model of animal maze tests.	Anxiety, nervous exhaustion, insomnia	136
Withania	Withanolide Withaferiin	Activity of GABA-mimetic. Similar to the anxiolytic effect of lorazepam in animal models.	Anxiety, insomnia, fatigue, nervous exhaustion	137

1999-2015[117]. The prevalence of mental disorders varies by Iranian governorate and across distinct groups, ranging from 11.7 % - 38.9 %. To monitor future changes, more research on the population as a whole must be conducted, as well as validated inventories[118-119].

Compared to mature adults, younger people (12 years old) are more likely to feel depressed and anxious[120]. In 2022, severe anxiety was most prevalent among young people (16%), while depression was officially recognized in Sweden at a rate of 4%[121]. Anxiety disorders are more common in young people, women, and people with chronic illnesses, according to mounting data[122]. The etiology of depression includes a family history of depression, stressful life events, the child-parent interaction, and multiple forms of childhood maltreatment[123-124]. Death from any cause is more likely to occur in those who are depressed[125]. In the UK, the leading cause of mortality for young males is suicide. Between 25 and 34 years old (Table 3 and 4)[125].

2.4 Epilepsy

Epilepsy is a long-standing condition that has been recorded since the time of the Babylonians. Even though it strikes people of all ages, epilepsy is a prevalent neurological condition. It is true that epilepsy has a bimodal onset, with most cases developing in childhood or later in life (Institute of Medicine, 2012). It is a continuum of disorders, though, with varying degrees of severity, different seizure patterns and causes, and different outcomes for people and their families. In addition to their seizures and related medical disorders, millions of individuals diagnosed with epilepsy deal with other challenges. These include receiving high-quality healthcare, learning about and managing healthcare, finding work, living independently, and accessing other community resources, as well as struggling stigma and common public misconceptions. As a result, epilepsy has a significant impact on individuals, families, and society as a whole[138].

Herbs have been utilized to cure epilepsy for thousands of years in various civilizations[139]. China, Iran, Europe, and America have all established herbal medicine traditions. Chinese herbal medicine is a long-standing custom founded on cutting-edge medical theories that have been repeatedly proven to be effective throughout time, setting it apart from other forms. Additionally, the number of herbs used in Chinese traditional herbal medication for epilepsy is the most common in herbal medicine worldwide. Nowadays, the most popular alternative and complementary healthcare approach is herbal therapy, which is crucial for treating epileptic seizures or issues brought on by antiepileptic medications[140]. People with epilepsy who are granted the opportunity to receive herbal treatment in underdeveloped nations have different aspirations and mindsets than those in affluent ones. In developed nations, herbal medicines are the most often used type of alternate and complementary treatments. They are used to manage seizures, lessen the side effects of antiepileptic medications, and preserve general health, but most patients do not disclose their use to their physicians.

Despite the widespread acceptance and actively treating epilepsy with natural medication, most plants need adequate proof of their danger and effectiveness. Western medicine and traditional Chinese herbal medicine have rather different philosophies. The philosophy of Chinese medicine holds that the human body is an integral part of the natural universe and is not just made up of internal organs, "channels", and basic elements like essence, life-sustaining energy, blood, and bodily fluids. Through the "channel" network, organs are linked together as functional groups. Therefore, the framework of thought that ancient people collected is the foundation of traditional Chinese medicinal ideas. Western medicine places more emphasis on the basic mechanisms underlying biological functions and disease processes than doe's traditional Chinese medicine. Western-trained doctors typically don't understand traditional Chinese medicine, thus scientific explanations of the "channel's" workings and the active ingredients in herbs are necessary[141]. Despite its widespread usage, herbal treatment for epilepsy should be evaluated according to evidence-based guidelines. The great majority of the hundreds of published researches on the use of Chinese medicine to treat epilepsy were carried out on lab animals. Critical studies on the effectiveness and side effects of treating epilepsy with herbal treatments are still lacking, nevertheless. Approximately 30% of epileptic patients who take antiepileptic drugs have been shown to still have seizures (Table 5)[142].

Table 5. Therapeutic role of medicinal plants in managing epilepsy

Botanical Medicine	Region	Cells/ Animals/ Human	Target	MOA	References
Apocynaceae	Africa	*In vivo* model	GABA A receptors	Increases the affinity of GABA for the GABA A receptor.	[145]
Alba breyonia	Iran	*In vivo* model	The GABA's benzodiazepine site A receptor	Increases the responsiveness of endogenous GABA receptors	[146]
Cannabis	Asia, Europe and so on	*In vivo* and *in vitro* model	Type 1 cannabinoid receptor	Facilitates the development and localisation of cannabinoid receptor Type 1 on various pre-synapses	[147]
Herbal medicine compound	China	Human	NMDA receptors	Increase the length of time that NMDA receptor channels attenuate and change the expression of NMDA receptor subunits	[148]
Skull cap	America, Europe and China	Animal model	GABA A receptor	Strong affinity for GABA A receptor	[149]
Zingiber officinale	India and China	Animal models	NO and iNOS	Inhibits the generation of NO and lowers iNOS in mouse macrophages activated by lipopolysaccharide.	[150]
Zizyphus jujuba	India	Animal models	Channels for voltage gates	Increase the duration of Na^+ channel activation	[151]
Passiflora invarnate	America and Europe	*In vivo* and *in vitro* model	GABA	Extracts from passiflora are high in GABA.	[152]
Stoechas lavandula	Iran	Animal model	Calcium channel	Inhibits the calcium channel	[153]
Ginseng	America, China and so on	Animal models	Calcium influx and channels	Inhibit the Ca^{2+} influx caused by NMDA dependence and status epileptus.	[154]

2.5 Multiple Sclerosis

The most prevalent neurological disease, Multiple Sclerosis (MS), is an autoimmune-mediated disorder of the Central Nervous System (CNS) that frequently causes neurological problems and significant physical or mental disability in young individuals[155]. Multiple sites of inflammation brought on by oligodendrocyte death, macrophage penetration, and localized T-lymphocyte are the main reasons why the myelin sheath is destroyed[156]. These elements lead to the development of CNS plaques made up of inflammatory cells and their waste products, in both white and gray matter, as well as demyelinated and transacted axons and astrocytes. These lesions may interfere with the normal transmission of nerve impulses, resulting in neurological difficulties such as autonomic and sensory deficiencies, visual abnormalities, ataxia, fatigue, cognitive impairments, and emotional problems[157].

Environmental influences, aberrant immune responses, and genetic susceptibility are all part of the complicated etiology of multiple sclerosis[158]. Although the exact source is uncertain, it is generally accepted that aberrant immunological activation-particularly by auto reactive T cells-is crucial for initiating and maintaining the inflammatory cascade inside the central nervous system[159]. When immune cells breach the Blood-Brain Barrier (BBB) due to immunological dysregulation, cytokines is released, which heighten oxidative stress, inflammation, and the deterioration of neurons and myelin sheaths[160]. In order to reduce inflammation and delay the course of the illness, current MS therapies mostly target immunological responses[161].

Current therapy has demonstrated effectiveness in reducing relapses and postponing the development of impairment includes symptomatic medications, acute recurrence treatments, rehabilitative therapies, lifestyle changes, and Disease-Modifying Therapies (DMTs)[162]. However, their poor efficacy in progressing forms of MS and favorable safety characteristics underscore the need for alternative therapeutic options[163]. As a result, several studies on the usage of medicines made from natural sources have been conducted in the past several years. As a result, we have concluded that the substances listed below can help treat this illness (Table 6).

2.6 Alzheimer's Disease

Alzheimer's Disease (AD) is a neurodegenerative condition that progresses slowly which is caused by beta-amyloid peptide (Aβ) buildup in the medial temporal lobe and neocortex[171]. Dementia is a major decline in cognitive function that compromises with a person's daily actions. The most common kind of dementia, accounting for at least two-thirds of occurrences among those 65 and older, is Alzheimer's Disease (AD)[172]. Usually manifests as a progressive loss of cognitive function and episodic memory, leading to language and visuospatial challenges. Behavioral

Table 6: Plant compounds used in the management of multiple sclerosis

Compound	Concentration	Study Participants and Design	Properties	References
Cannabis sativa	Taking 5-25 mg of *C. sativa* extracts orally every day for 10 weeks.	Clinical studies that are double-blind and placebo-controlled.	Compared to the placebo group, tight muscles relaxed after 4, 8, and 12 weeks of therapy.	164
Oleanolic acid	Administration intraperitoneally at a dose of 50 mg/kg.	Model of EAE in C57BL/J6 mice	Alleviating neurological impairment symptoms. Decreased permeability of the blood-brain barrier; low central nervous system infiltration of inflammatory cells. Using molecular processes to aid in Th1/Th2 polarization. Blocking chemical and anti-inflammatory cytokines. Enhancing its ability to reduce inflammation.	165
Crocus sativus L.	Being gavaged with ethanol extract for 21 days.	Investigation using the c57BL/6 mice model of EAE	Lessens oxidative stress and leukocyte infiltration in the central nervous system.	166
G. biloba	8 weeks of 120 mg/kg.	Open research with 30 patients the MSIS-29, Beck Depressive disorder Inventory, and Wechsler Remembering Scale	Raising MSIS-29 and Wechsler Cognitive Scale scores.	167
Pomegranate peel extract	Ethanol extracts administered intraperitoneally for a duration of eight weeks at a dose of 100 mg/kg.	Study conducted *in vitro* using a female DA rat model of EAE	Reducing the manufacturing of IL-17 in activated T cells and blocking its production in the GALT cell line in an animal model of EAE.	168
Capparis ovata	Fraction of butanol in the hydroalcoholic extract.	Study conducted *in vitro* using the SH-SY5Y cell line	Suppressing TNF-α, NF-κB1, GFAP, CXCL10, and PTPN11 transcription in cell lines.	169
Sativex	Each spray puff of inhaled Sativex includes 2.5 mg of CBD and 2.7 mg of THC.	Double-blind clinical studies with a placebo control	160 patients	170

issues including despair, aggressiveness, and apathy are frequently present as well[173]. Alzheimer's disease happens to be one of the most serious brain disorders affecting the elderly. It is an underserved and underappreciated condition with significant public health implications[174].

The hippocampus is the first source of harm. One crucial area of the brain involved in memory formation is the hippocampus. The brain shrinks as more neurons die over time. The brain tissue has decreased greatly by the end stage. It accounts for approximately 60% of the incidence of dementia[175]. Although Alzheimer's disease can not directly cause death, it does increase a person's susceptibility to several conditions can gradually lead to death.

In accordance with the organizations for Control of Disease and Prevention (CDC), Alzheimer's disease will be the 7th greatest contributing factor to death in the United States in 2022, followed by COVID-19. Prior to the COVID-19 pandemic, Alzheimer's disease was the 6th largest cause of death, behind attack[176]. These tangled and plaque-like substances are permanent and cannot be eliminated from the brain. As a result, recognizing neural failure in the early stages of Alzheimer's disease, before permanent structural changes occur, is crucial[177]. Neuronal Damage Recent research reveals that necrosis and proptosis participate to the degenerative stages of Alzheimer's disease, including Aβ amyloid aggregation, Tau buildup, neuronal death, and alteration of the blood-brain barrier[178].

Unluckily, there is no treatment for Alzheimer's disease, and most patients are identified at a late and incurable stage, with an average survival time of 4-8 years[179]. The FDA has authorized a number of Alzheimer's medications, particularly rivastigmine, galantamine, donepezil, memantine, and memantine in conjunction with donepezil. Aside from memantine, all authorized medications contain Acetyl Cholinesterase Inhibitors (AChEI), which increase Acetylcholine (Ach) levels and improve synaptic regulation. Memantine, an NMDA receptor antagonist, mitigates the excitotoxic consequences of glutamate release[180]. These drugs merely give symptomatic relief. Medicinal herbs can help to slow the course of sickness[181].

Curcumin, resveratrol, and green tea catechins are among the phytochemicals gaining popularity, with epidemiological studies showing a link between their use and Alzheimer's disease protection (Singh *et al.*)[182]. Natural products have recently gained popularity because they have a lesser chance of side effects when compared to synthetic options. There are several herbs that have been shown to help prevent Alzheimer's disease, including *G. biloba*, *Withania somnifera, Huperzia serrata, Moringa olifera, Bacopa monnieri, Uncaria rhynchophylla, Galanthus woronowii, Curcuma longa, Panax ginseng, Centella asiatica, Glycyrrhiza glabra, and Rosmarinus officinalis*[183]. α-Tocopherol, the most readily available antioxidant form of vitamin E, has been found to aid in Alzheimer's disease. Alpha-tocopherol was found to be protective against lipid peroxidation and decreased in plasma in people having intermediate Alzheimer's disease[184]. By preventing the malfunctioning of lipid peroxidation, glutathione, catalase, Super Oxygen Dismutase (SOD), acetylcholine, and choline acetyltransferase activity caused by colchicine, *M. oleifera* has been demonstrated to have a nootropic effect on Alzheimer's disease.

It also restored the damaged brain monoamines to nearly normal levels, improved cognition, and protected against degeneration of neurons[185]. Too far, no disease-modifying medicine has been developed for Alzheimer's disease[186]. However, pharmacological therapy for this dreadful sickness is still in its early phases and does not arrest disease development[187]. However, none of these possibilities have resulted in a confirmed diagnosis or approved treatment for the disease[188]. As a result, finding safer and more effective Alzheimer's drugs remains a demanding and essential task (Table 7)[189].

3. Future Prospects for Herbal Remedies in Addressing Neurological Disorder

Many neurodegenerative diseases still have unknown etiology. Herbal medicine has long piqued people's curiosity due to its medical properties. Phytochemicals, with their anti-inflammatory, antioxidant, and anti-Cholinesterase capabilities, will be a viable treatment option for neurodegenerative diseases in the future. Alzheimer's, Parkinson's, and Huntington's diseases and other neurological conditions have cellular and subcellular features, as well as molecular signaling mechanisms that can cause apoptosis, necroptosis,

Table 7. Herbal remedies and key phytoconstituents with potential anti-Alzheimer's activity

Medicinal Plants	Active Compound	Activity against Alzheimer's Disease	References
G. biloba	Flavonoids and terpenoids	Potential anti-Alzheimer's benefits of plants with medicinal properties and their individual components.	[190]
Turmeric	Curcumin	Curcumin has excellent antioxidant and anti-inflammatory properties. It has the ability to prevent the formation and deposition of beta-amyloid plaques, a characteristic of Alzheimer's disease.	[191]
Rosemery	Rosmarinic and carnosic acids	Preclinical studies have shown that these compounds have neuroprotective characteristics by reducing oxidative stress and neurological inflammation, both of which are associated with Alzheimer's disease development.	[192]
Chinese skullcap	Baicalein and wogonin	These flavonoids have been demonstrated to reduce beta-amyloid plaque development and the death of neurons in Alzheimer's disease.	[192]
Ashwagandha	Withanolides	*Ashwagandha* is famous for its adaptogenic properties. In lab experiments, it was shown to increase cognitive performance and protect against beta-amyloid-induced neurodegeneration.	[193]
Green tea	Epigallocatechin-3-Gallate (EGCG)	EGCG, a form of catechin, is being investigated for its potential neuroprotective qualities. It is thought to inhibit beta-amyloid aggregation and lessen neurotoxicity in Alzheimer's disease.	[194]
Bacopa monnimeri	Bacosides	Bacopa has long been used in *Ayurvedic* medicine due to its cognitive-enhancing effects. Bacosides are thought to possess antioxidant and neuroprotective effects.	[195]
Ginseng	Ginsenosides	Ginsenosides are known to have both anti-inflammatory and antioxidant effects. Research suggests that these substances may improve cognitive performance and decrease the course of Alzheimer's disease.	[196]

and inflammation. Overall, botanical therapy offers a promising alternative to conventional therapies for neurodegenerative diseases. However, the effectiveness of herbal medicine or natural ingredients has been significantly compromised due to their weak pharmacokinetic properties. To overcome these limitations, botanical medicine has been integrated into a variety of pharmaceutical administration compositions[197].

The pharmacological qualities of plants with medicinal properties have been shown to be beneficial in treating a variety of neurological disorders. Although there are many different plant organisms accessible globally, just a few have been studied for neurological issues. As a result, there are several opportunities for future study into plant-based nutrients and biologically active compounds in this field. In recent years, there has been a rise in curiosity in natural alternative therapies that promote faster healing while minimizing adverse effects. The use of natural compounds in alternative and complementary treatments may lead to the discovery of innovative pharmaceutical lead molecules. The use of natural substances to treat neurodegenerative diseases has become a thriving industry. Along with contributing to serving as a scientific basis for the correct dosage and an opportunity toxicological effect on the local community, pharmacological investigations can help produce additional successful for medicinal reasons multi-targeted substances from natural sources for treating a number of neurological diseases[198].

4. Conclusion

The Medicinal use of derived from plants substances has emerged as a viable approach to treating neurological problems. Numerous studies have shown that phytochemicals can affect a variety of neurobiological processes, such as neurological inflammation, oxidative stress, and neurotransmitter imbalance. These pathways are involved in a number of neurological disorders, including Alzheimer's and Parkinson's disease, as well as anxiety and depression.

While traditional pharmaceutical methods have made great progress, they are typically associated

with negative side effects and may fail to address the underlying causes of neurological problems. Phytomedicines, on the other hand, take a more comprehensive strategy, typically addressing many pathways at once. This has the potential to improve efficacy and reduce toxicity when compared to traditional treatments.

However, it is crucial to note that the area of herbal remedies is still evolving, and more study is necessary to find the right dosage, formulation, and safety profiles of various plant-based substances. Furthermore, the complicated interactions of phytochemicals with other drugs or underlying health issues must be carefully explored.

Finally, the plants-based medicine offers a promising alternative or supplemental treatment for neurological illnesses. Researchers and physicians are attempting to find safe, effective, and long-term remedies for these severe illnesses by using plants' medicinal potential.

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6. Author's Contribution

Conceptualization: TN, SD, NB; Methodology TN, SD, NB; Data curation: TN, SD: Formal analysis: NB, MS; Writing - original draft: TN, SD, NB, AR; Supervision: NB, MS; Writing - review and editing: TN, SD, NB, MS, AR. All authors have read and agreed to the published version of the manuscript.

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