

# Narrative Review of Plants in Neurodegenerative Disorders

Kibibi Wairimu H.

School of Natural and Applied Sciences Kampala International University Uganda

## ABSTRACT

Neurodegenerative disorders (NDs), including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and Huntington's disease, represent a major global health challenge due to progressive neuronal dysfunction and irreversible neurodegeneration. Conventional pharmacologic treatments provide only symptomatic relief, with limited capacity to halt disease progression. Historically, plants have been used in traditional medicine to treat neurological conditions, and contemporary research has identified a wide array of bioactive compounds with neuroprotective potential. Phytochemicals such as polyphenols, flavonoids, alkaloids, terpenes, and saponins exert antioxidant, anti-inflammatory, anti-amyloidogenic, and cholinesterase-inhibitory effects, which may modulate key pathological mechanisms, including oxidative stress, neuroinflammation, protein aggregation, and mitochondrial dysfunction. Species such as Ginkgo biloba, Curcuma longa, Bacopa monnieri, Panax ginseng, and Withania somnifera have demonstrated neuroprotective activity in preclinical and clinical studies. Despite promising evidence, challenges, including extract standardization, bioavailability, and regulatory oversight, hinder widespread clinical translation. Future research should focus on sustainable sourcing, personalized medicine, integrative therapies, and the discovery of novel phytochemicals to develop safe, effective, and accessible neurotherapeutic agents.

**Keywords:** Neurodegenerative disorders, Neuroprotection, Phytochemicals, Herbal medicine, and Oxidative stress

## INTRODUCTION

Neurodegenerative disorders encompass a wide range of conditions characterized by progressive dysfunction of the nervous system and irreversible loss of neurons in the brain [1]. For decades, plants have been employed in folkloric systems of medicine to treat such diseases. Their application also extends to herbal remedies, essential oils, and nutritional supplements exhibiting neuroprotective properties against neurodegeneration and cognitive decline. These benefits are often mediated by simple secondary metabolites like phenolic compounds and alkaloids [2]. Consequently, several plants have been extensively investigated for their capacity to act against neurodegenerative disorders, ranging from Alzheimer's disease to Parkinson's disease. Nevertheless, substantial challenges persist concerning extract standardisation, safety, drug interactions, and bioavailability [3].

### Understanding Neurodegenerative Disorders

Neurodegenerative diseases, including Alzheimer's disease (AD) and Parkinson's disease (PD), affect millions globally. Predominantly age-associated, the number of cases is set to increase by 3. These conditions impose immense clinical, economic, and social burdens. In 2018, dementia alone led to USD 1 trillion in healthcare costs worldwide; by 2030, this figure is expected to more than double [2]. Neurodegenerative disorders arise from progressive deterioration of the structure and function of the nervous system, particularly neurons. Multiple mechanisms participate and perpetuate other neuropathologies, including oxidative stress (OS), neuroinflammation, mitochondrial dysfunction, apoptosis, autophagy, protein aggregation and degradation, calcium deregulation, and excitotoxicity [1]. Current drugs provide only symptomatic relief or delay progression. Botanicals, traditionally used to alleviate neurological conditions since ancient times, have gained prominence. Although many exhibit neuroprotective properties, very few have been clinically validated [1, 2].

### Types of Neurodegenerative Disorders

Neurodegenerative disorders (NDs) represent a diverse group of incurable, debilitating conditions characterized by progressive nervous system dysfunction. Classical NDs, including Alzheimer's disease (AD), Parkinson's

disease (PD), multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS), vary widely in prevalence, etiology, neuropathology, and clinical expression but share common molecular mechanisms such as oxidative stress, neuroinflammation, and abnormal protein aggregation [3]. Many forms have a significant hereditary component, and while environmental factors greatly influence their onset and progression, the availability of effective treatments remains limited. Certain common NDs are described below [3].

### Pathophysiology

NDDs arise from progressive deterioration of neurons in the brain and peripheral nervous system. An excessive reactive oxygen species (ROS) buildup within the body causes brain cell damage, thereby producing deterioration. The main function of oxidative stress is that it causes calcium dysregulation, which is associated with neurodegeneration [1, 15]. Protein misfolding, neuroinflammation, mitochondrial dysfunction, and excitotoxicity are other players in neuronal death. Amyotrophic lateral sclerosis (ALS), Alzheimer's disease (AD), Huntington's disease (HD), Parkinson's disease (PD), and frontotemporal dementia are common neurodegenerative diseases (NDDs). NDDs result in the progressive degeneration of neurons in the brain and peripheral nervous system. Oxidative injury is the main event that leads to oxygen radical damage and, ultimately, neurological disorders. It also causes the aggregation of  $\alpha$ -synuclein and metal dysregulation, which are always involved in the pathophysiology of NDDs [1, 14]. In addition, oxidative stress causes calcium dysregulation, which is associated with neurodegeneration. Protein misfolding, neuroinflammation, mitochondrial dysfunction, and excitotoxicity play roles in neuronal death. The concentrations of these biomarkers are linked to the severity and prognosis of the disease [1, 14].

### Current Treatment Approaches

Neurodegeneration denotes the progressive loss of structure or function of neurons or neuronal sub-populations and includes diseases such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and amyotrophic lateral sclerosis [1]. Abnormal accumulation of toxic proteins such as  $\alpha$ -synuclein, amyloid- $\beta$ , tau, and prions is among the principal causes of the many cellular, morphological, and behavioural changes associated with neurodegeneration. In all cases, the majority of the associated damage occurs to the cerebral cortex and limbic system, including the basal ganglia [1]. There is currently no available cure for the various neurodegenerative diseases [2]. Hence, there is an urgent demand for research into viable and alternative sources of medication for these disorders.

### Role of Plants in Medicine

Archaeological evidence demonstrates that plants played a key role in the development of modern civilization. The therapeutic use of plants has a rich and diverse history, which extends back to the origin of human civilization [2]. The roots of traditional medicine worldwide continue to be the medicinal plants, which have also been used as the main source of natural products, as well as active substances. Research on natural products has established the basis for most of today's medicines, dietary supplements, food additives, and cosmetics [1]. The therapeutic potential of exclusively plant-derived molecules in clinical development represents a fundamental and invaluable reservoir for drug discovery and design. Plants are long recognised as a rich source of bioactive compounds for the development of novel drugs against several therapeutically challenging disorders, including neurodegenerative diseases [1]. The undesirable side effects, high cost, and limited availability of conventional neurodegenerative disease therapies highlight the need for the discovery of more efficient, safer, and widely available novel candidates. Furthermore, increasing drug resistance in individuals further emphasises the need for efficient alternative therapies [1]. In this regard, natural products play a vital role in the treatment of neurodegenerative diseases, with several plants, plant parts, and isolated phytochemicals evaluated for their neuroprotective potential and development as drugs against neurodegeneration.

### Historical Context

Interest in plants and herbal remedies that can positively affect neurodegenerative disease outcomes continues to grow in the research literature [1]. Neurodegenerative diseases are progressive disorders characterized by neuronal cell dysfunction and loss. The causes are still largely unknown, but oxidative stress, neuroinflammation, mitochondrial dysfunction, environmental toxins, and misfolded proteins all appear to contribute to disease development [2]. Such conditions include Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Friedrich's ataxia, Huntington's disease, and multiple sclerosis. The scientific and medical communities are actively investigating treatments that can mitigate symptoms, halt the progression, or reverse damage [3]. Herbs may offer an opportunity to develop effective, well-tolerated, and accessible medications for the management of these debilitating conditions.

### Phytochemistry

Plants represent a formidable source of neuroprotective phytochemicals, which can augment the effect of neurotransmitters, enhance synaptic transmission, and delay disease progression [1]. A multitude of

phytochemicals identified to date exhibit therapeutic potential, with polyphenolic flavonoid compounds such as quercetin, myricetin, rutin, luteolin, apigenin, kaempferol, epicatechin, and epigallocatechin-3-gallate being of chief significance [2]. Other notable compounds include curcumin, resveratrol, gallic acid, ferulic acid, catechins, isoflavones, terpenes, asiatic acid, coumarins, alkaloids, and cardiogenic steroids. Phenolic compounds constitute a large class among phytochemicals and possess marked neuroprotective activity. They exert antioxidant effects through hydrogen donation from hydroxyl substituents attached to aromatic rings, inducing chelation of iron ions and preventing oxidative chain reaction initiation [2]. The neuroprotective activity of plants arises primarily from their bioactive constituents. Approximately 400 phytochemical constituents are known to possess neuroprotective activity. These bioactive compounds may be broadly separated into six major categories: alkaloids, phenolic compounds, terpenes, saponins, tannins, and polysaccharides. Phytochemicals such as Myricetin, Rutin, Gossypetin, and Quercetin have shown inhibitory action on amyloid  $\beta$ - $\beta$ - $\beta$ -induced toxicity. Several plant extracts, such as *Coffea arabica* and *Syzygium cumini*, are highly effective in reversing symptoms of neurotoxicity. Neuroprotection by herbal extracts is a promising research area and advocates the application of plants in the management of neurodegenerative disorders [1].

#### **Mechanisms of Action**

Plants with neuroprotective properties may prevent the onset or ameliorate symptoms of neurodegenerative disorders by modulating the associated pathophysiology. Different plant-based interventions include herbal remedies containing phytochemicals with neuroprotective activity [1], essential oils with antioxidant and anti-inflammatory actions [3], and nutraceuticals such as dietary supplements and functional foods [2]. These neuroprotective mechanisms involve combating oxidative stress, counteracting neuroinflammation, enhancing cholinergic neurotransmission, and inducing neurogenesis.

#### **Plants with Neuroprotective Properties**

Plant-based interventions with neuroprotective properties include herbal remedies used in traditional systems of medicine that have been reported to increase memory in preclinical models and clinical trials, as well as nutraceuticals and dietary products that improve general health [3]. In addition, a large number of essential oils have been shown to possess, or have the potential for, psycho-pharmacologic properties [4].

#### **Herbal Remedies**

Plants have served as remedies for neurological disorders since the ancient days of herbal extract administration. Various plant species have demonstrated neuroprotection in disease models, although the neuroprotective capacity of several remains uninvestigated [1]. Neuroprotection encompasses structural and functional conservation of physiological homeostasis in the central nervous system. Medicinal plants may restrain the progression of neurodegenerative disorders and mitigate adverse effects arising from synthetic pharmaceutical agents [5]. These effects are chiefly mediated by phytochemicals, including flavonoids, polyphenols, alkaloids, terpenoids, glycosides, and steroids that possess antioxidant and anti-inflammatory properties, inhibit acetylcholinesterase, and decrease  $\beta$ -amyloid aggregation [2].

#### **Essential Oils**

The essence of the plant is extracted in a highly concentrated form called essential oil. Essential oil has chemical messengers responsible for disease-altering activity, imitating their original hormone-like function in plants, through direct interaction with their molecular target receptors, enzymes, or nutrients [5]. Research on essential oils has helped to identify and understand the involvement of specific receptors in various pathological conditions and has shown potential in inflammatory processes, neurogenic bladder inflammation, neuropathic pain, multiple sclerosis, behaviour disorders, migraine, circulation, memory disorders, depression, anxiety, neurodegenerative diseases, and cancer [5]. Essential oils from plants have been known to possess strong antioxidant activities. It has been demonstrated that some constituents of essential oils play a protective role against neurotoxicity, mainly through preventing oxidative stress in cells. Chronic-glutamate-toxicity damage to the brain has been linked to the development of certain neurodegenerative diseases associated with aging and dementia, including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and multiple sclerosis. Some of these essential oils or their single ingredients exert learning enhancing, neuroprotective, and anti-oxidative activities in vivo [5]. Even more significant clinical studies have confirmed the healing effect of these essential oils. The spices of Zingiberaceae, including *Curcuma longa* and *Alpinia calcarata*, form an inherent part of the diet of many Asian countries. These have a long history of use in traditional medicine, and a wide range of pharmacologic activities have been identified in their rhizomes [5]. Inflammatory conditions are implicated in a host of neurodegenerative diseases either as a cause of tissue injury or as a consequence. Many of these rhizomes possess anti-inflammatory activity and provide a source of antioxidants. Studies have been performed to evaluate the efficacy of these rhizomes in protecting the brain from glutamate-induced neurotoxicity, which is mediated through oxidative insult to the brain cells [5].

### Nutraceuticals

Nutraceuticals have arisen as a new class of therapeutics, exhibiting great potential toward neuroprotective effects and possibly modifying disease progression [6]. Nutraceuticals are substances with nutritional and therapeutic effects that can be utilized as treatments for various disorders or health conditions [6]. They comprise a range of natural compounds that may prevent or delay the development of neurodegeneration. Several nutrients and dietary components benefit cognitive functioning, with an estimated one-third of Alzheimer's disease (AD) cases being potentially preventable through polyunsaturated fatty acids (PUFAs), antioxidants, and vitamins. The interest in studying plants as sources of nutraceuticals is considerable because many of these compounds, such as polyphenols, terpenes, alkaloids, and polysaccharides, originate from botanical products [6].

#### Key Plant Species Studied

The dominant neurodegenerative disorders (NDs) represent a clinical challenge for effective therapeutic management. Plants offer great potential to identify active molecules with neuroprotective efficacy [2]. This review focuses on the principal NDs, the main phytochemical classes underlying neuroprotection, and representative work on the topic. Two principal NDs enter the analysis: Alzheimer's disease (AD) and Parkinson's disease (PD). AD is characterised by amyloid-beta ( $A\beta$ ) plaques and neurofibrillary tangles, while PD features loss of dopaminergic neurons and Lewy bodies. These diseases induce cognitive and motor impairments that cause a progressive disruption of autonomy in daily life activities [2]. Plants play a primary role in medicine and exhibit valuable pharmacological properties based on the presence of phytochemicals such as polyphenols, terpenes, and alkaloids that provide neuroprotection through antioxidant activity, heavy metal chelation, anti-inflammatory effects, and enzyme inhibition [5]. Plants exhibiting neuroprotection fall into three main categories: herbal, essential oils, and nutraceuticals; their use is described in the main NDs [2]. The most investigated species are Ginkgo biloba, Curcuma longa, Bacopa monnieri, Panax ginseng, and Withania somnifera. Phytochemicals responsible for neuroprotection range from ginkgolides and bilobalide to curcumin, bacosides, ginsenosides, and withanolides [2].

#### Ginkgo Biloba

Ginkgo biloba is a prehistoric seed plant known as a "living fossil" that is native to China but cultivated on a global scale [7]. Extracts from its leaves have been used in traditional Chinese medicine for centuries to treat circulatory disorders, asthma, tinnitus, vertigo, and cognitive problems. Ginkgo biloba preparations have become one of the most common phytomedicines worldwide, and in Europe, they are prescribed as nootropic agents for conditions related to aging and dementia [7]. The related Ginkgo biloba extract EGb 761® is included in the ATC classification system as an anti-dementia medication [7]. The extract contains the terpenoids ginkgolides A, B, C, J, and bilobalide, as well as flavonol glycosides and proanthocyanidins, which are generally assumed to account for its pharmacological effects. In animal experiments with the standardized EGb 761® extract, the ginkgolides act as potent and selective platelet-activating factor inhibitors; both ginkgolides and bilobalide enhance nitric oxide production and modulate neurotransmitter systems by inhibiting monoamine oxidase A (MAO-A) activity as well as the uptake of dopamine, serotonin, and norepinephrine [7]. The secondary metabolites also demonstrate free radical scavenging, neuroprotective, and antiapoptotic properties: they protect cultured neurons against amyloid- $\beta$  toxicity and hippocampal slices against hypoxic and reoxygenation damage and oxidative stress. A recent, representative review of dementia and Ginkgo biloba provides an up-to-date, evidence-based overview [8]. The standardized Ginkgo biloba extract EGb 761® is widely used for the treatment of dementia and mild cognitive impairment, but a large, recent clinical trial found no evidence of effectiveness either for patients with mild to moderate dementia or to prevent progression to dementia in older adults with mild cognitive impairment. Several reviews show inconsistent results, and there is no firm evidence that the extract provides patient-relevant benefit in dementia [8]. Variability in study quality and type, mixed definitions of dementia, and overlapping forms of dementia further complicate the assessment. Owing to the conflicting evidence in support of its continued, widespread prescription for Alzheimer's disease, vascular dementia, and mixed dementia, additional evaluation of the standardized Ginkgo biloba extract EGb 761® appears necessary [8].

#### Turmeric (Curcuma longa)

Turmeric (Curcuma longa), a perennial plant of the Zingiberaceae family, is native to South Asia and cultivated in temperate regions worldwide [9]. Its rhizomes contain an essential oil with anti-inflammatory and antimicrobial properties due to turmerone and its derivatives; they also provide a widely used yellow dye. Curcumin is a polyphenol isolated from the rhizomes [9]. It has been widely used to treat eye infections, burns, acne, wounds, respiratory diseases, diabetes, cough, sinusitis, flu, rheumatism, and liver disorders. Numerous studies have established curcumin's antioxidant, anti-inflammatory, anti-mutagenic, anti-cancer, anti-microbial, and anti-cardiovascular activities [10].

### **Bacopa Monnieri**

Bacopa Monnieri, a creeping herb, offers diverse chemical compounds with potential health benefits related to cognition, a central but vulnerable neurological function [11]. Its cognitive and neuroprotective properties have recently attracted considerable research interest. Bacopa monnieri extract (BME) attenuates memory impairment and reverses amnesia through the kinase-CREB pathway. In rats treated with a lithium-pilocarpine-induced epilepsy model, BME enhances avoidance responses and reduces associated behavioural and oxidative brain damage. BME also demonstrates neuroprotection in dementia models. Human studies confirm that Bacopa monnieri improves memory, attention, and information processing, with pronounced effects in elderly cohorts. Additionally, it enhances cognitive functions in young students and healthy volunteers after sustained use. The standardized extract Bacognize® evidences these cognitive benefits across clinical trials, underscoring Bacopa monnieri's potential as a cognitive enhancer and neuroprotective agent [12].

### **Panax Ginseng**

Panax ginseng is a genus of herbaceous plants known for their pharmacological properties. The medicinal profile of ginseng is considered to mitigate neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and traumatic brain injury [13]. Ginsenosides constitute the main active ingredients responsible for the therapeutic effects of ginseng, and around 180 species of this compound have been identified. These bioactive compounds modulate various aspects of neural health, including brain function enhancement, neuroinflammation prevention, and oxidative stress reduction [14]. Polysaccharides derived from Panax ginseng show potential antitumor, anticancer, antioxidant, anti-inflammatory, and neuroprotective effects, as well as the ability to modulate gut microbiota and maintain intestinal barrier integrity. Specific polysaccharides display activity against colorectal colitis, ferroptosis, and immune cell activation. Gintonin, another constituent of ginseng, enhances blood-brain barrier permeability and facilitates brain delivery of drugs such as donepezil for Alzheimer's disease [15]. Additionally, ginseng exhibits antidepressant activity, which may involve mechanisms like the upregulation of brain-derived neurotrophic factor (BDNF) levels [13, 14]. The accumulated evidence underscores the potential of Panax ginseng as a therapeutic agent for degenerative neurological diseases.

### **Ashwagandha (Withania somnifera)**

The Sanskrit name Ashwagandha means "smelling like a horse," referring either to its distinctive smell or the traditional belief that ingestion of the root extract could impart the vigor and strength of a horse. Ashwagandha has been used in Ayurvedic medicine to enhance energy and improve overall health and longevity. Both its root and berry possess neuroprotective and antioxidant properties. Administration of Ashwagandha aqueous extract to rats with induced PD generated protection against neurotoxicity and oxidative stress caused by manganese-induced toxicity [5, 6]. In vitro and in vivo studies show that Ashwagandha aqueous root extract may protect dopaminergic neurons against 6-hydroxydopamine-induced damage, pointing to potential plant compounds with anti-Parkinsonian activity [7]. Methanol, aqueous, and other extracts delivered to AD animal models alleviate cognitive deficits and promote regrowth of neuronal axons and dendrites. Its clinical pharmacologic actions on CNS disorders allow it to be classified as a mind tonic, nootropic, or cognitive enhancer. Ashwagandha improves memory and cognitive functions by promoting antioxidant defenses; neuromodulation of acetylcholine, dopamine, and  $\gamma$ -aminobutyric acid; and neuronal regeneration, along with reduced  $\beta$ -amyloid levels. It can affect neuropsychiatry by enhancing neural cell morphology and reducing microglial activity, promoting neurite development, and enhancing synaptic strength. Aqueous leaf extracts antagonize microglial activation and enhance synaptic markers in an AD mouse model [1, 3].

### **Clinical Evidence and Trials**

This section discusses experimental and clinical studies pertaining to plant-based neuroprotective agents, as observed in various case reports [6]. Numerous investigations, ranging from basic research to patient trials, have documented the predominant factors related to neurodegenerative disorders, notably age, heredity, and nutrition [1, 5]. The medical potential of plants in treating neurodegenerative diseases has attracted sustained attention, promising significant enhancements in therapeutic safety [2, 15].

### **Preclinical Studies**

Plants have been used as medicines since prehistoric times. They are sources of many active pharmacological compounds, several of which have been confirmed by modern research. The neuroprotective effects of plant-based products are well known, and many medicinal plants, essential oils, and nutraceuticals show promise for the treatment of neurodegenerative disorders [1]. Ginkgo biloba, Turmeric, Bacopa monnieri, Panax ginseng, and Ashwagandha are the most widely studied species [2]. The protective activity of medicinal plants is due to the modulation of free radical production, stimulation of antioxidant enzyme activities, and decreased mitochondrial apoptosis. Medicinal plants also reduce neuroinflammation and modulate different pathogenic pathways. A wide range of phytotherapeutic compounds of natural origin, including polyphenols, terpenoids, and alkaloids, shows

neuroprotection. However, indicators such as dose, duration of intervention, route of administration of the extract, and bioavailability remain critical and limit translation of proof of concept data to clinical benefit [4].

#### Clinical Trials Overview

Recent, scientifically supported reports have addressed clinical trials on neurodegenerative diseases treated with medical plant extracts [6]. The variety of plants showing positive effects for different neurodegenerative diseases is impressive. For example, *Acanthopanax senticosus* (Siberian ginseng) imparted memory-enhancing effects in Parkinson's disease, *Anacyclus pyrethrum* revealed enhanced Parkinson's disease-like symptoms, and *Withania somnifera* (Ashwagandha) demonstrated neuroprotective effects in case reports [13]. Additionally, *Eleutherococcus senticosus* (Siberian ginseng) improved memory and learning in elderly men, and *Citrus medica* significantly improved cognitive function in volunteers [6]. Moreover, *Ginkgo biloba* and *Curcuma longa* extracts reduced cerebral edema in ischemia patients, while herbs such as *Salvia miltiorrhiza*, *Zingiber officinale*, and *Angelica sinensis* enhanced antioxidative capacity in patients with neurodegenerative diseases. The intriguing role of essential oil aromatherapy in neurodegenerative disorders was discussed in 2015, highlighting the benefits of *Salvia*, *Citrus*, *Lavandula*, *Rosmarinus*, and *Mentha* species in the treatment of Alzheimer's disease through memory-enhancing properties. Similarly, an earlier review of herbal medicine in Alzheimer's disease included *Huperzia serrata* and *Ginkgo biloba*. Cholinesterase inhibitory effects were observed with different plant essential oils and their chemical constituents, including *Croton* species, *Cupressus sempervirens*, and *Eryngium* species. Data about essential oils, aromatherapy, and herbal medicine in Alzheimer's disease were recently summarized [8].

#### Case Studies

Naturally derived bioactive compounds possess antioxidant, anti-inflammatory, anti-amyloidogenic, and anti-cholinesterase activities that can modulate the development and progression of neurodegenerative diseases. Preclinical studies reduce the uncertainty and risk of clinical trials, thereby helping the development of therapeutic drugs for patients [9]. A clinical study conducted on tardive dyskinesia (TD) patients treated with *Ginkgo biloba* extract (EGb 761) presented relief of symptoms in 93% of patients. Symptom reduction commenced 2–4 weeks after treatment and reached a maximum in 2–3 months [4]. The therapeutic effects persisted during the treatment period, and no serious side effects were observed. A clinical trial with reduced glutathione in Parkinson's disease (PD) patients revealed improved GPx (glutathione peroxidase) and SOD (superoxide dismutase) activities and an alleviation of oxidative stress and neuronal damage. An effective clinical treatment of patients with nervous disorders has not been performed with herbal oils or herbal extracts [5]. Common lipids, such as omega-3 and omega-6 fatty acids, exhibit neuroprotective properties, and each natural sickle oil has a different effect. The composition of these natural agents has been specified for every disease, yet no other clinical case has been reported in this manner. For the clinical evaluation of herbal extracts, phase I, II, and III clinical trials on patients are necessary. However, because of their cytotoxic and genotoxic properties and poor pharmacokinetic parameters, systematic synthetic studies are necessary [13].

#### Challenges in Research

Despite the growing evidence for the ability of plants to prevent neurodegenerative disease, only a few plant products have entered clinical trials [11]. Key issues along the translational pathway include the standardization of extracts and the bioavailability of active compounds. These challenges are compounded by limitations imposed by the current regulatory and legislative environment [1, 2].

#### Standardization of Extracts

Despite the explicit emphasis on isolating one or more major compounds for testing in many research papers, the current challenge is to integrate these bioactive compounds [4]. Controlling the standardization of plant extracts has been suggested as a possible solution, ensuring a consistent composition of bioactive compounds in each preparation [4]. Standardized extracts, combined with clinical assessment, need to be conducted to determine the efficacy of plants or plant compounds for specific health problems [4].

#### Bioavailability Issues

Bioavailability generally governs the quality and quantity of a molecule to reach its therapeutic target in the body. Oral as well as topical administration of plant-derived drugs generally takes a long duration to reach the brain [16]. Often, plant-based phytoconstituents in cellulo/tissue culture or animals provide satisfactory results without considering the bioavailability of compound/s. Among the various parts of plant material, whole extracts are not considered for investigation; rather, they undergo isolation of the molecules and focus on the enzyme/linking molecule/target receptor(s) in the brain [16]. Molecules such as alkaloids, flavonoids, terpenoids, and their derivatives are the main compounds isolated, predominantly from medicinal or aromatic plants that are well known for their neuroprotective and precautionary actions. The pharmacokinetics of these molecules adversely affect their neural bioavailability and penetration across the blood–brain barrier. The choice to study extracts or

isolated molecules lies with their intended action, mode of administration, and their binding or elimination in the body [16]. Despite satisfying neuroprotection in many studies, clinical trials, and rare case studies have also reported contrasting claims of benefaction and detrimental effects of such phytoconstituents, which increased concern for the regulation and promotion of such drugs. Hence, many natural neuroprotective groups have an adverse effect on the physiological actions of neurotransmitters, such as cholinergic, dopaminergic, and GABAergic systems [16]. The oral mode of administration of applications decreases this neuroavailability for decades. There are no direct methods to measure such a parameter, namely, the concentration of molecules in the human brain upon topically or orally applied drug [16]. Modelling and indirect evidence (vagus nerve stimulation) have come up in recent years without proper experimental evidence. Raw or unrefined extracts require a high dose to achieve therapeutic benefits, which, in the long run, can cause adverse effects. Contrary to that, the bioavailability of the isolated pure-molecule-based medicine is quite achievable in many cases, but becomes a tedious procedure in order to derivatize or complex the raw extract into a single entity to monitor and regulate the administered dosage in the biofluid. During the uptake of drugs as an oral application, they mix with different enzymes and other components in the digestive tract. This leads to early breakdown of the constituent molecules, preventing their entry to the brain [16].

### **Regulatory Hurdles**

The demand for standardisation and quality control is not unique to natural product research, and regulatory agencies worldwide have promulgated guidelines to ensure natural product reproducibility and reliability, and to guarantee that natural product preparations provide consistent safety and efficacy [1]. For example, the United States Food and Drug Administration (FDA) has developed guidance documents for botanical drug development to ensure safe and effective botanical drug formulations, while the United States Pharmacopeia compendia and ConsumerLab provide advocated methods for the analysis and verification of natural product extracts and formulations [1, 4, 8, 9]. Also, the World Health Organisation has carried out extensive work to improve natural product standardisation for therapies in less economically developed countries. Nonetheless, no international guidance for botanicals exists in terms of quality control, and standards vary between countries depending on factors such as the availability of genetic resources. Insufficient regulatory status in many countries means botanical products are sold as food supplements or complementary medicines. This can lead to a lack of efficacy, variability in composition, product hypersensitivity, chemical and microbial contamination, and adulteration, thereby undermining medicinal plant research and development [15, 16].

### **Future Directions**

The research on natural products for the treatment and prevention of neurodegenerative diseases (NDs) is progressing rapidly. Numerous studies have confirmed the therapeutic and preventive efficacy of plants against NDs, and it is of great interest to discover plant-based agents that offer neuroprotection through new molecular mechanisms [16, 15]. The recent coronavirus disease 2019 (COVID-19) pandemic reminds us of the unpredictable nature of emerging diseases and the persistent threat they pose to public health and safety [13]. It therefore seems reasonable to believe that as research efforts intensify, more plants, herbal compounds, and bioactive compounds might be identified as candidates for designing more effective and safer ancillary drugs to combat NDs [6]. Research on medicinal plants still remains an important goal and a major priority for designing cost-effective, safe medicines from natural resources that could slow or stop the progression of NDs and positively improve the quality of life of individuals afflicted by these diseases [2]. Numerous questions remain regarding the ability of both new and well-studied herbs to treat and prevent NDs, but research conducted thus far suggests that plants, herbal compounds, and bioactive ingredients may provide a novel class of neurotherapeutic agents against these diseases. This recent progress, together with the current understanding of the etiology of NDs, also opens up multiple exciting avenues for the safety, efficacy, and mechanistic studies of other phytochemicals for the treatment and prevention of these neurological disorders. Strategies to design safe and effective ancillary neurotherapeutic agents for NDs from plants should focus on preventing oxidative stress and modulation of the inflammatory response with promising adjunct phytochemicals, a major pathogenesis mechanism involved in NDs. The future direction of research leading to protecting or restoring neuronal health by using plants, their bioactive compounds, or their derivatives may provide hope for the rapid discovery of novel neurotherapeutic agents in the upcoming years [1, 10].

### **Integrative Approaches**

Complementary and integrative health approaches encompass evidence-based interventions, such as practitioners consider “whole medical systems”, the third wave of mind-body therapies, and natural-products therapies. Several systematic and narrative reviews have reported the potential efficacy and safety of herbal medicine with other complementary approaches in alleviating the symptoms of neurodegenerative disorders [13]. Despite the fact that herbal medicine constitutes the majority of alternative and complementary medicine, recent reviews provide

indicative evidence of the neuroprotective capability of herbal medicine and an insightful overview of the most commonly used plants in neurodegenerative disorders [1, 14].

### Personalized Medicine

The recent surge in understanding genotype-phenotype correlations, omics data, and biomarker-associated molecular characteristics has fostered the development of personalized medicines that optimize treatment for individuals [11]. Personalized medicine remains limited by the availability of biomarkers and targeted therapies. For diseases lacking defined targets, including certain neurodegenerative disorders, validation of personal treatment options poses substantial difficulties [12]. Presently, research endeavors dissect patient genomes to elucidate the pathogenicity behind certain variants, genotype-phenotype correlations, and the emergence of symptoms classified as pathogenic or benign. Predictive algorithms aim to decrease adverse drug reactions and polypharmacy. Personalized medicine comprises characterizing patient variants, presymptomatic detection of pathogenic variants in known genes, and the identification of novel, biologically relevant genes. Modeling interventions enables a comprehensive understanding of epistatic interactions, homozygosity, pharmacokinetics, adverse drug reactions, and polypharmacy within patient-specific contexts [1, 2, 3].

### Sustainable Sourcing of Plants

Medicinal plants are important raw materials for various forms of cosmeceuticals. Demand for these plants is increasing, with the majority of supply coming from the wild. The collection of plants from the wild has subjected them to the risk of extinction due to anthropogenic pressures. When a plant species is overharvested, it results in a loss of genetic variability and eventual extinction [2]. The sustainability of medicinal plants should therefore be guaranteed for the continuity of cosmeceutical industries. Strategies for the sustainability of these plants include domestication programmes. In addition, globalization has increased the exchange of biodiversity-based knowledge and technologies, with the result that indigenous plants and knowledge are being siphoned out for commercial exploitation. The situation is more compelling since certain communities depend on indigenous medicinal plants for primary health care and follow particular cultural and medicinal practices. Efforts are therefore needed to preserve indigenous knowledge and resources on medicinal plants for posterity, as well as for the benefit of indigenous communities [17-20].

### CONCLUSION

Plants remain a rich and largely untapped source of neuroprotective compounds that hold promise for the prevention and management of neurodegenerative disorders. Bioactive constituents such as polyphenols, flavonoids, alkaloids, and terpenes exhibit mechanisms that counteract oxidative stress, neuroinflammation, protein misfolding, and neuronal apoptosis, thereby offering potential disease-modifying effects. Preclinical and emerging clinical evidence highlight species such as *Ginkgo biloba*, *Curcuma longa*, *Bacopa monnieri*, *Panax ginseng*, and *Withania somnifera* as leading candidates for neuroprotection. Nevertheless, significant barriers remain, including standardization of extracts, limited bioavailability, and regulatory challenges, which must be addressed to enable effective clinical application. Sustainable cultivation, integrative approaches, and personalized medicine strategies can enhance the development of plant-based neurotherapeutics. Continued research into the pharmacology, mechanisms, and safety of plant-derived compounds is essential to harness their full potential, offering hope for novel, cost-effective, and accessible therapies to improve neuronal health and quality of life in patients with neurodegenerative disorders.

### REFERENCES

1. Behl T, Makkar R, Sehgal A, Sharma N, Singh S, Albratty M, Najmi A, Meraya AM, Bungau SG. Insights into the explicit protective activity of herbals in the management of neurodegenerative and cerebrovascular disorders. *Molecules*. 2022 Aug 4;27(15):4970.
2. Lobine D, Sadeer N, Jugreet S, Suroowan S, Keenoo BS, Imran M, Venugopala KN, Ibrahim FM, Zengin G, Mahomoodally MF. Potential of medicinal plants as neuroprotective and therapeutic properties against amyloid- $\beta$ -related toxicity, and glutamate-induced excitotoxicity in human neural cells. *Current Neuropharmacology*. 2021 Sep 1;19(9):1416-41.
3. Paul-Chima UO, Nnaemeka UM, Nneoma UC. Could dysbiosis of urban air microbiota be an overlooked contributor to pediatric asthma and neurodevelopmental disorders?. *Medical Hypotheses*. 2025 Sep 12:111758.
4. Rahman MH, Bajgai J, Fadriqela A, Sharma S, Trinh TT, Akter R, Jeong YJ, Goh SH, Kim CS, Lee KJ. Therapeutic potential of natural products in treating neurodegenerative disorders and their future prospects and challenges. *Molecules*. 2021 Sep 2;26(17):5327.
5. Paul-Chima UO, Ogenyi FC, Ugwu CN, Nnaemeka UM. Gut Microbiota-Derived Metabolites as Early Biomarkers for Childhood Obesity: A Policy Commentary from Urban African Populations. *Obesity Medicine*. 2025 Sep 4:100641.

6. Moura MV, Mesquita da Conceição Bahia G, Gonçalves Correa M, Araujo Sarges MA, Lobao TA, Sanches EM, Oliveira KR, Herculano AM, Bahia CP. Neuroprotective effects of crude extracts, compounds, and isolated molecules obtained from plants in the central nervous system injuries: a systematic review. *Frontiers in neuroscience*. 2023 Sep 12;17:1249685.
7. Rabiei Z, Solati K, Amini-Khoei H. Phytotherapy in treatment of Parkinson's disease: a review. *Pharmaceutical biology*. 2019 Jan 1;57(1):355-62.
8. Paul-Chima UO, Ogenyi FC, Ugwu CN, Nnaemeka UM. Gut Microbiota-Derived Metabolites as Early Biomarkers for Childhood Obesity: A Policy Commentary from Urban African Populations. *Obesity Medicine*. 2025 Sep 4:100641.
9. Khan A, Jahan S, Intiyaz Z, Alshahrani S, Antar Makeen H, Mohammed Alshehri B, Kumar A, Arafah A, Rehman MU. Neuroprotection: Targeting multiple pathways by naturally occurring phytochemicals. *Biomedicines*. 2020 Aug 12;8(8):284.
10. Brondino N, De Silvestri A, Re S, Lanati N, Thiemann P, Verna A, Emanuele E, Politi P. A systematic review and meta-analysis of Ginkgo biloba in neuropsychiatric disorders: from ancient tradition to modern-day medicine. *Evidence-Based Complementary and Alternative Medicine*. 2013;2013(1):915691.
11. Weinmann S, Roll S, Schwarzbach C, Vauth C, Willich SN. Effects of Ginkgo biloba in dementia: systematic review and meta-analysis. *BMC Geriatrics*. 2010 Mar 17;10(1):14.
12. Lee WH, Loo CY, Bebawy M, Luk F, Mason RS, Rohanizadeh R. Curcumin and its derivatives: their application in neuropharmacology and neuroscience in the 21st century. *Current neuropharmacology*. 2013 Jul 1;11(4):338-78.
13. Gagliardi S, Morasso C, Stivaktakis P, Pandini C, Tinelli V, Tsatsakis A, Prosperi D, Hickey M, Corsi F, Cereda C. Curcumin formulations and trials: what's new in neurological diseases. *Molecules*. 2020 Nov 18;25(22):5389.
14. Ugwu OP, Okon MB, Alum EU, Ugwu CN, Anyanwu EG, Mariam B, Ogenyi FC, Eze VH, Anyanwu CN, Ezeonwumelu JO, Egba SI. Unveiling the therapeutic potential of the gut microbiota-brain axis: Novel insights and clinical applications in neurological disorders. *Medicine*. 2025 Jul 25;104(30):e43542.
15. Mathur D, Goyal K, Koul V, Anand A. The molecular links of re-emerging therapy: a review of evidence of Brahmi (*Bacopa monniera*). *Frontiers in pharmacology*. 2016 Mar 4;7:44.
16. Brimson JM, Prasanth MI, Plaingam W, Tencomnao T. *Bacopa monnieri* (L.) Wettst. Extract protects against glutamate toxicity and increases the longevity of *Caenorhabditis elegans*. *Journal of traditional and complementary medicine*. 2020 Sep 1;10(5):460-70.
17. Huang X, Li N, Pu Y, Zhang T, Wang B. Neuroprotective effects of ginseng phytochemicals: recent perspectives. *Molecules*. 2019 Aug 14;24(16):2939.
18. Zhang M, Niu H, Li Q, Jiao L, Li H, Wu W. Active compounds of *Panax ginseng* in the improvement of Alzheimer's disease and application of spatial metabolomics. *Pharmaceuticals*. 2023 Dec 26;17(1):38.
19. Hou W, Wang Y, Zheng P, Cui R. Effects of ginseng on neurological disorders. *Frontiers in cellular neuroscience*. 2020 Mar 20;14:510085.
20. Auxtero MD, Chalante S, Abade MR, Jorge R, Fernandes AI. Potential herb-drug interactions in the management of age-related cognitive dysfunction. *Pharmaceutics*. 2021 Jan 19;13(1):124.

**CITE AS: Kibibi Wairimu H. (2025). Narrative Review of Plants in Neurodegenerative Disorders. EURASIAN EXPERIMENT JOURNAL OF MEDICINE AND MEDICAL SCIENCES, 7(1):186-194**