



# NATURAL NEUROPROTECTIVE AGENTS FOR NEURODEGENERATIVE DISEASES

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## ABSTRACT

Neurodegeneration, which is the progressive loss of neurons due to chronic diseases, is emerging as a significant health concern in the 21<sup>st</sup> century. Neurodegenerative conditions like alzheimer's disease, parkinson's disease, huntington's disease, dementia, amyotrophic lateral sclerosis, depression, myasthenia gravis is marked by the gradual deterioration and eventual demise of neuronal structure and function. These disorders impose substantial burdens on both individuals and society as a whole. Prominent environmental factors that have been extensively researched as potential triggers for neurodegenerative diseases include protein degradation, oxidative stress, inflammation, environmental exposures, mitochondrial dysfunction, familial predisposition, and the abnormal accumulation of proteins within neurons. An intense interest in herbal plants with long-term health-promoting or therapeutic properties has grown during the past ten years. Extensive research and exploration over recent years have revealed the substantial potential of natural products, medicinal herbs, plant extracts, and their metabolites as neuroprotective agents. These substances exhibit long-term health-promoting and medicinal qualities, contributing to their growing recognition. As shown by in vivo experiments or clinical trials, medicinal plants and natural substances, such as *Withania somnifera* (ashwagandha), Ginseng, curcumin, resveratrol, *Bacopa monnieri*, *Ginkgo biloba*, and Wolfberry,

have been used to treat neurological symptoms and to either prevent or treat neurological diseases. This review aims to spotlight the contributions of herbal plants and their phytoconstituents in addressing neurodegenerative diseases and related disorders. It will specifically delve into their mechanisms of action and therapeutic capabilities.

**Key words:** Neurodegeneration, alzheimer's disease, parkinson's disease, huntington's disease, phytoconstituents.

## INTRODUCTION

Neurodegenerative diseases are a group of deficiencies characterized by progressive degeneration of the structure and function of the nervous system. These disorders, such as alzheimer's disease, parkinson's disease, and huntington's disease present major difficulties to the affected individuals [1]. While several treatments exist, they often come with major side effects or are less efficient. This is where natural plants with their diverse chemical composition and potential therapeutic properties help in tackling neurodegenerative diseases. Acute neurodegeneration is a condition characterized by the rapid damage and death of neurons in response to sudden insults or traumatic events, such as head injuries, strokes, traumatic brain injury, cerebral or subarachnoid haemorrhages, and ischemic brain damage. In contrast, chronic neurodegeneration refers to a gradual neurodegenerative process within the nervous system that leads to the progressive and irreversible destruction of specific neuron populations. Numerous biological processes are linked to neurodegeneration, such as oxidative stress, neuroinflammation, excitotoxicity, mitochondrial dysfunction, abnormal protein folding and aggregation, and cell death [2]. These processes have been implicated in the progression and development of neurodegenerative disorders.

Natural products have been used for their therapeutic benefits since the dawn of humanity. Numerous studies have shown how these natural remedies help protect against a wide range of illnesses, including cancer, diabetes, reproductive problems, cardiovascular disease, and neurological disorders. In order to treat neurodegenerative illnesses, natural compounds have become viable neuroprotective agents. *Salvia officinalis*, *Ginkgo biloba*, *Panax ginseng*, *Curcuma longa*, and *Bacopa monnieri* are a few herbs whose plant extracts are used for neuroprotective, memory-improving, and anti-aging [3].

### Outline of neurodegenerative diseases

Neurodegenerative diseases include a spectrum of disorders caused by neuronal death, particularly in the central nervous system (CNS). This degeneration often leads to the gradual onset of progressive symptoms, of which memory loss is a tell-tale sign. Well-known neurodegenerative diseases include alzheimer's disease (AD), parkinson's disease (PD), dementia with Lewy bodies, multiple sclerosis, amyotrophic lateral sclerosis (ALS), and spongiform encephalopathies [4,5]. Among them, AD is the most common, accounting for more than 60-70% of all dementia cases. Potential mechanisms underlying these neurodegenerative diseases include factors such as protein aggregation, inflammation, excitotoxicity, oxidative stress, and neurotoxicity, which contribute to their pathophysiology [6].

## Medicinal plants in neurodegenerative diseases

Medicinal plants play a significant role in the treatment and management of neurodegenerative diseases. It is well acknowledged that medicinal plants play an important role in Unani, Siddha, and Ayurvedic systems of ancient Indian medicine. According to the World Health Organization (WHO), 80% of the population in underdeveloped nations relies on conventional medications extracted from plants for their treatment. Around 70% of India's rural population receives its medical care from traditional practitioners [4,5].

To determine the efficacy of employing these medicinal plants for the treatment of neurodegenerative diseases, it is important to appropriately look for chemical, seasonal, and geographic changes in them. When planning to use local medicinal plants for therapeutic reasons, traditional knowledge and understanding of the wealth of sources are necessary. The demand for mass manufacturing of medicinal plant remedies for the prevention of degenerative diseases has been met by the application of contemporary techniques of separation and purification. Natural products' key neuroprotective targets include mitochondrial malfunction, apoptosis, excitotoxicity, inflammation, oxidative stress, and protein misfolding [6].

In the therapy of AD, some animal products, such as omega-3 fatty acids, limit cell toxicity and have anti-inflammatory properties. Alkaloids, tannins, polyphenols, lunasin, and other plant-based substances may be effective treatments for AD. The dietary supplements resveratrol and flavonoids seem to have clear neuroprotective and other positive effects on human cognitive impairment [7].






Any substance that strengthens the cholinergic system in the brain may be helpful in treating AD and other brain disorders. Natural COX-2 inhibitors are present in herbs that inhibit Acetylcholinesterase (AChE), and these herbs have also been used as therapeutic plants for AD indication. German chamomile, Ginseng, liquorice, turmeric, and white willow bark are anti-inflammatory medicines that may lessen AD-related brain tissue inflammation [8].







Globally, herbal remedies have been used to treat illnesses. Natural products have drawn a lot of interest and contributed to the development of new drugs. Studies have shown that natural products have advantages to treat neurodegenerative diseases. They actively contribute to the maintenance of the neuronal chemicals in the brain by reducing the activity of numerous receptors via a variety of processes. For the treatment of the aforementioned neurodegenerative illnesses, certain Indian medicinal herbs have been extensively used in Indian traditional medicine (Ayurveda). These plants have been shown to have potent antioxidant properties [6,9].


Consequently, herbal remedies are seen as fresh and promising sources of prospective anti-neurodegenerative medications. Due to their cognitive advantages and, more importantly, their modes of action with regard to the basic pathophysiology of the disease, herbal medications have the potential to treat certain conditions.






Table 1: List of medicinal plants used in neurodegenerative diseases

Herb	Name of the plant	Parts used	Active constituents	Mechanism of action	Ref.
	Ginkgo ( <i>Ginkgo biloba</i> )	Leaves	Ginkgolides, quercetin, trilactonic diterpenes, kaempferol, isorhamnetin	Boosts circulation to the brain, protects neurons from oxidative damage and apoptosis.	5
	Turmeric ( <i>Curcuma longa</i> )	Root and rhizome	Curcumin, demethoxy curcumin, bisdemethoxycurcumin	Acts as neuroprotective agent, anti-inflammatory agent, antioxidant and boosts immune response.	10
	Brahmi ( <i>Bacopa monnieri</i> )	Leaves and stem	Bacoside A and bacoside B, cucurbitacin a and other phytochemicals like saponins, triterpenoids, alkaloids, sterols and polyphenols.	Enhancing neuronal synthesis, kinase activity, restoring synaptic activity and nerve impulse transmission.	11
	Ashwagandha ( <i>Withania somnifera</i> )	Root	Withaferin, withanolide	Ameliorative action against parkinson's disease and huntington's disease.	12
	Ginseng ( <i>Panax ginseng</i> )	Root and leaf	Ginsenosides and saponins	To treat neurological disorders such as PD, AD, and stroke.	5






	Saffron ( <i>Crocus sativus</i> )	Dried and dark red stigma	Crocin carbohydrates, polypeptides, lipids, vitamins and minerals	Acts as Anti-convulsant and has anti-alzheimer properties. It also treats cognitive disorders.	13
	Liquorice ( <i>Glycyrrhiza glabra</i> )	Root and rhizome	Glycyrrhizin, glycyrrhetic acid, isoliquiritin, isoflavones	Anti-inflammatory activity, reactive oxygen scavenging, enhances the integrity of blood brain barrier, prevents neuronal apoptosis.	14
	Garlic ( <i>Allium sativum</i> )	Leaves and flowers	Allicin	Neuroprotection, improve memory, anti-oxidant.	15
	Asafoetida ( <i>Ferula asafoetida</i> )	Root and rhizome	E-1- propenyl sec-butyl disulfide, carbohydrates, proteins, minerals and fibres	Neuroprotective effect on oxidative stress induced apoptosis.	13
	Grapevine ( <i>Vitis vinifera</i> )	Leaves	Resveratrol, malic acid, oxalic acid and tartaric acid.	Inhibition of arterial thrombosis, anti-oxidant, anti-inflammatory and neuroprotective effects	14





3, Tea	Volume 10, Issue 11	Leaf	Epigallocatechin-3-	Protective effect	15
	<i>(Camellia sinensis)</i>		gallate	against neurons and anti-oxidant.	
	Sweet Basil <i>(Ocimum basilicum)</i>	Leaf and flowering top	essential oils like eugenol, linalool, cineole	Treats headaches, coughs, diarrhoea, constipation and kidney malfunctions.	13
	Magnolia <i>(Magnolia officinalis)</i>	Bark	Magnolol, honokiol, obovatol lignans, alkaloids, sesquiterpenes and glycosides.	Treats neurosis, acts as anti-inflammatory, anti-bacterial and anti-allergic, neuroprotective and relaxing properties.	15
	Gotu Kola <i>(Centella asiatica)</i>	Whole plant, mainly leaves	Brahminoside, triterpenoid	Boost the memory & activities of neurons, acts as anti-inflammatory, sedative and immunostimulant.	16
	Monkshood <i>(Aconitum napellus)</i>	Seed	Aconitine, mesacotine, hypaconitine	Neuroprotective agent, anti-inflammatory & anti-rheumatic activities.	14
	St John's wort <i>(Hypericum perforatum)</i>	Stem, petals and flowers	Flavonoids Hyperforin, Rutin Hypericin	Treats depression and is used as neuroprotective agent.	16





	Black pepper ( <i>Piper nigrum</i> )	Seeds and fruits	Piperine, amides, piperidine and safrole	Multitargeting neuroprotective agent and increases blood flow to gastrointestinal tract.	15
	Peppermint ( <i>Mentha piperita</i> )	Leaf extract	Menthol, menthone, menthyl acetate	Treats insomnia, depression and acts as neuroprotective agent.	14
	Guggul ( <i>Commiphora wightii</i> )	Oily sap (Gum resin)	Guggulsterone, diterpenoids, steroids, carbohydrates and lignans	Boosts memory, anti- inflammatory agent.	16
	Sweet flag ( <i>Acorus calamus</i> )	Rhizome	Asarones, isocalamendiol, methyl eugenol sesquiterpens and flavonoids	Neuroprotective agent, enhances memory and acts as anti- convulsant.	17
	Oriental Arbor Vitae ( <i>Platycladus orientalis</i> )	Leaf extract	15-Methyl panusolidic acid, isopimarane, diterpene	It revamps agglomeration and withstands anxiety.	15
	Brazil Nuts ( <i>Bertholletia excelsa</i> )	Bark and Seed	Lecithin, Gallic acid, phenols, ferulic acid, quercetin	Antioxidant and acts as neuroprotective agent.	17







	Maritime Pine ( <i>Pinus pinaster</i> )	Bark extract	Catechin, taxifolin, procyanidins, epicatechin constituents and phenolic acids	It possesses anti-inflammatory and anti-oxidant properties.	18
	Kwao Krua ( <i>Pueraria mirifica</i> )	Dried & tuberous roots	Phytoestrogens like daidzin, genistein, deoxymiroestrol, mirificine, $\beta$ -sitosterol, campesterol and mirificoumestan	Provides protection against amyloid beta induced death of neurons and enhances development of neurites.	19
	Velvet Bean ( <i>Mucuna pruriens</i> )	Seeds	Glycoside, gallic acid, glutathione, levodopa, 5-hydroxy tryptamine, alanine, arachidic acid and arginine	Enhances motility as well as behavioural activities, relieves oxidative tension, chelation of metals and acts as anti-inflammatory.	14
	Black Oil Plant ( <i>Celastrus paniculatus</i> )	Seeds	Celastrol, palmitic acid, phytol, linalool and erucic acid	Enhances memory, anti-inflammatory, analgesic, sedative and anti-epileptic agent.	20
	Butterfly Pea ( <i>Clitoria ternatea</i> )	Extracts of root, seed and leaves	Main anthocyanin is delphinidin. also contains tannins, carbohydrates, glycosides, flavonoids, saponins, proteins, alkaloids, anthraquinones and phenols	Boosts memory, anxiolytic, anti-depressant, anti-convulsant and sedative agent.	21






	<p>Guduchi (<i>Tinospora cordifolia</i>)</p>	<p>Stem and leaf</p>	<p>Choline, tinosporin, isocolumbin, palmatine, tetrahydro palmatine, and magnoflorine, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics and polysaccharides</p>	<p>Supresses neuroinflammation, memory enhancing property and cognitive enhancement by immunostimulation and synthesis of acetylcholine.</p>	<p>22</p>
	<p>Chebulic Myrobalan (<i>Terminalia chebula L</i>)</p>	<p>Dried fruits</p>	<p>Chebulinic acid, anthraquinone glycoside, tannic acid, linoleic and stearic acid</p>	<p>Enhances memory &amp; promotes longevity.</p>	<p>23</p>
	<p>Stinging Nettle (<i>Urtica dioica L</i>)</p>	<p>Roots</p>	<p>Histaminic acid, sterols, fatty acids, alkaloids, terpenoids, flavonoids, amino acids, fibres and lignans</p>	<p>Enhances levels of estrogen, treats allergy symptoms, reduces inflammation and acts as anti-oxidant.</p>	<p>24</p>
	<p>Shankhpushpi (<i>Convolvulus pluricaulis</i>)</p>	<p>Whole plant (Mainly roots)</p>	<p>Kaempferol, beta-sitosterol, shankhapushpine, n-hexacosanol, and hydroxy cinnamic acid</p>	<p>Treats nervous disorders, acts as anti-aging agent, treats memory loss, fever and disability.</p>	<p>24</p>
	<p>Avishan-e Shirazi (Wild Marjoram) (<i>Zataria multiflora</i>)</p>	<p>Whole plant (Mainly leaves)</p>	<p>Luteolin, multiflotriol, p-hydroxy benzoic acid, thymol, carvacrol, para-cymene, alpha-tocopherolquinone</p>	<p>Restores learning and memory impairments, acts as anti-inflammatory, anti-oxidant, anti-bacterial and also has analgesic and anti-septic effects.</p>	<p>24</p>

	<p>Black Cumin (<i>Nigella sativa</i>)</p>	<p>Seeds</p>	<p>Fixed oil includes linoleic acid, oleic acid, stearic acid, palmitic acid, myristic acid and also includes thymol, carvacrol, proteins, carbohydrates and fibers</p>	<p>Anti-oxidant effect, enhances memory, decreases anxiety and reduces oxidative stress.</p>	<p>25</p>
	<p>Purple Medic (<i>Alfaalfa</i>)</p>	<p>Leaves, sprouts and seeds</p>	<p>Genistein, isoflavones, vitamins, minerals and organic acids</p>	<p>Anti-oxidant, anti-inflammatory, and proapoptotic properties.</p>	<p>26</p>
	<p>Orange (<i>Citrus sinensis</i>)</p>	<p>Peel and pulp</p>	<p>Hesperidin, flavanone-glycosides, aldehydes, esters</p>	<p>Treats mitochondrial disorders &amp; restoring GSH depletion.</p>	<p>24</p>
	<p>Fish hook vine (<i>Uncaria rhynchophylla</i>)</p>	<p>Hook bearing stems</p>	<p>Rhynchophylline, isorhynchophylline hirsutine, hirsuteine, corynanthine, corynoxine, and dihydrocorynantheine</p>	<p>Reduced neuronal cell death and ROS production, and reduces neuronal loss</p>	<p>27</p>

	Seaweed ( <i>Marine macroalgae</i> )	Blade, holdfast and stipe	Phenolic compounds like phlorotannin, phloroglucinol, eckol, dieckol, fucol, phlorethol, fuhalols, lignans, bromophenol, proteins, peptides, pigments, amino acids, and phenols	Increase cell viability, decrease oxidative stress, have a healthy mitochondrial membrane potential, and decrease caspase-3 activities.	24
	Honey ( <i>Apis mellifera</i> )	Petals and nectar	Glucose and fructose others include maltose, sucrose, isomaltose, gentiobiose, maltotriose, melezitose, isopanose, isomaltosylglucose, panose	Cancer prevention, inflammation reduction, oxidative damage attenuation, and neurodegenerative protection.	28
	Parsley ( <i>Petroselinum crispum</i> )	Aromatic leaves	Apigenin, vitamin C, iron, vitamin A	It functions as cell growth, anticarcinogenic, and enzyme inhibitor, as well as antigenotoxic, anti-inflammatory, and free radical scavenging.	27
	Arthrospira ( <i>Spirulina maxima</i> )	Blue-green algae	High quality proteins, essential amino acids, pigments, dietary fiber, minerals, fatty acids and phenolic compounds	Improved cognitive impairment	24

	Indian Snakeroot ( <i>Rauwolfia serpentina</i> )	Roots	Rescinnamine, reserpine, ajmalicine and deserpidine	Controls nerve impulses, acts as dual cholinesterase inhibitor.	27
	Canary Wood ( <i>Nauclea officinalis</i> )	Stems and leaves	Angustidine, nauclefine and angustine	Possess selective BuChE inhibitory activity and acts as anti-inflammatory, anti-tumour and anti-bacterial.	28
	Wild Rue ( <i>Peganum harmala</i> )	Seeds, bark and root	Harmol, harmalol, deoxy vasicine and vasicine	Possess cholinesterase inhibitory activities and AChE inhibitor also acts as anti-depressant.	27
	Olive ( <i>Olea europaea</i> )	Fruit, leaves and seeds	syringic acid, oleic acid and palmitoleic acid	Helps neurological dysfunction or behavioural impairments management with anti-oxidant, anti-inflammatory properties.	28
	Nigaki ( <i>Picrasma quassioides</i> )	Bark and wood	3-Ethyl-12-methoxy- $\beta$ -carboline and 6,12-dimethoxy-3-ethyl- $\beta$ -carboline	Possesses AChE inhibitory properties and acts as anti-inflammatory, anti-oxidant, anti-cancer and anti-microbial.	29
	Chinese Goldthread ( <i>Coptis chinensis</i> )	Rhizomes	Berberine chloride and 13-alkyl berberine	Treats diseases characterized by causing oxidative stress including inflammatory and neurodegenerative diseases.	30

	<p>Bay Tree (<i>Laurus nobilis</i>)</p>	<p>Leaves</p>	<p>Flavonoids like kaempferol, quercetin and isorhamnetin  tannins, eugenol, citric acid, carbohydrates, steroids, alkaloids, triterpenoids and essential oils</p>	<p>Anti-septic, anti-inflammatory, antioxidant and antimicrobial.</p>	<p>29</p>
	<p>Black chokeberry (<i>Aronia melanocarpa</i>)</p>	<p>Fruit</p>	<p>Polyphenols like proanthocyanins, anthocyanins, flavonoids and other phytochemicals</p>	<p>Immunomodulatory effect, neuroprotective agent, anti-platelet, antioxidant, anti-inflammatory.</p>	<p>30</p>
	<p>Calabar Bean (<i>Physostigma venenosum</i>)</p>	<p>Seeds</p>	<p>Physostigmine, rivastigmine (semi synthetic derivative of physostigmine)</p>	<p>Treatment of AD, rivastigmine is also indicated for the management of Lewy body dementia and PD dementia.</p>	<p>30</p>
	<p>Yuan Zhi (<i>Polygala tenuifolia</i>)</p>	<p>Dried roots</p>	<p>Tenuigenin, tenuifolin, tenuifoliside B, xanthones, polygalapyrone A</p>	<p>Tenuigenin exerts an anti-inflammatory effect by downregulating the release of NO, MMP-9, and cytokines, activation of the Nrf2-mediated HO-1 signaling pathway.</p>	<p>27</p>

### Examples of neuroprotective drugs of plant-origin and their effects:

**Polyphenols:** The ability of polyphenols to treat a variety of illness states, including as NDs and metabolic diseases, is one of the most significant structural characteristics of these compounds. NDs and other disease

states can benefit from the direct scavenging of ROS (reactive oxygen species) by polyphenolic compounds and the antioxidant effects they provide [27].

**Curcuminoids and resveratrol:** Curcumin has been shown in numerous studies to have anti-oxidant, anti-inflammatory, and anti-cancer properties. Inflammation was reduced by curcumin in *in vitro* investigations. Resveratrol is used to treat fevers, hyperlipidemia, atherosclerosis, and inflammation. Resveratrol has been demonstrated to have a variety of advantageous effects on NDs in both *in vitro* and *in vivo* experiments. The anti-oxidant activity seems to be the most significant of the various potential modes of action. The neuroprotective effect of resveratrol on dopaminergic neurons is thought to be primarily attributed to its antioxidant characteristics [28].

**Flavonoids:** In general, flavonoids have been linked to the management of AD. As a result, baicalein has been shown to protect memory losses in the AD model and A-induced impairments in hippocampus LTP through activation of Akt phosphorylation. Pinocembrin boosted the survival and mitochondrial membrane potential of cultivated rat cerebral microvascular endothelial cells, reduced brain edema, and improved cerebral blood flow. Additionally, pinocembrin exhibits anti-inflammatory and anti-oxidant properties. *In vitro*, rutin prevents neuronal damage, and *in vivo*, it helps Wistar rats with memory problems brought on by doxorubicin. Rutin has also demonstrated an ability to suppress the development of protein aggregates, depolymerize aggregates, and lessen neurotoxicity [29].

**Alkaloids:** Galantamine has very low butyryl cholinesterase (BuChE) inhibitory action but works as a selective, competitive, and reversible inhibitor of AChE (anti-cholinesterase). Rivastigmine, a potent carbamate inhibitor, slow-reversibly covalently binds to the active site of AChE to inhibit both BuChE and AChE. Rivastigmine is recommended for the treatment of Lewy body dementia and PD dementia in addition to Alzheimer's disease. According to studies, berberine is a powerful anti-oxidant that reduces oxidative stress and neuronal damage in the central nervous system. It shows neuroprotective effect in various animal models of CNS-related disorders [30].

**Terpenoids:** Ginsenosides, which come from the roots and rhizomes of *Panax ginseng* and *P. notoginseng*, are excellent examples of neuroprotective triterpenoids. In a 6-OHDA-induced nigrostriatal damage model of PD, ginsenoside was reported to have a neuroprotective impact on dopaminergic neurons through IGF<sub>1</sub> receptor signalling pathway. Tenuigenin reduces the release of NO, MMP-9, and cytokines, which has an anti-inflammatory impact. It can directly scavenge the NO radical and reduce the release of NO from LPS-activated rat microglia in a dose-dependent manner. This shows that the Nrf2-mediated HO-1 signalling pathway is the anti-inflammatory mechanism of neuroprotection. This shows that the stimulation of the Nrf2-mediated HO-1 signalling pathway is the anti-inflammatory mechanism of neuroprotection [31].

**Phenolic compounds:** According to studies on cultured rodents, carnolic acid from *R. officinalis* has neuroprotective properties on cyanide-induced brain injury. By scavenging ROS, carnolic acid shields neuronal cells from ischemia damage, whereas carnolic acid prevents Cu<sup>2+</sup>-induced LDL oxidation and chelates Fe<sup>2+</sup>. When a chemotactic stimulus was used to mobilize intracellular Ca<sup>2+</sup>, both carnolic acid and carnolic acid

inhibited the production of ROS. Carnosic acid's ability to treat AD both *in vitro* and *in vivo* is well known. It also reduced A42 production and inhibited AChE.

**Phenolic acids, alcohols and their derivatives:** In addition to many other plants, the dried, juicy stem of *Cistanche deserticola* or *C. tubulosa* (Orobanchaceae) can be used to make the glycosides acteoside and echinacoside. They have been demonstrated to have neuroprotective effects on the dopaminergic neurons of the substantia nigra in a persistently intoxicated MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) mice model of PD [32,33].

It alleviated behavioural impairments in C57BL/6 mice and raised the number of dopaminergic neurons and DA content, according to its neuroprotective effects in MPTP models of PD. Along with inhibiting a crucial APP processing enzyme, secretase (BACE-1), caffeic acid and its derivatives exhibit particular anti-inflammatory effects in the brain. Gastrodin improved bradykinesia and motor dysfunction in the sub chronic MPTP mouse PD model, demonstrating neuroprotective benefits. By controlling free radicals, Bax/Bcl-2 mRNA, caspase-3, and the cleavage of poly-ADP-ribose polymerase (PARP) in SH-SY5Y cells challenged with MPP<sup>+</sup>, it also guarded dopaminergic neurons from neurotoxicity. The substance also reduces oxidative stress, suppresses the production of neurotoxic proinflammatory mediators and cytokines such iNOS, COX-2, TNF-, and IL-1, and prevents neuronal death.

### Current scenario of pharmacotherapy

- There is currently no treatment for NDs, and all therapy approaches are intended to help patients live better lives by managing their symptoms. Treatments for AD, PD, and other neurodegenerative disorders (NDs) alleviate symptoms by a variety of ways, including raising neurotransmitter levels or regulating the metabolism of the pathogenic neurotransmitters.
- Most of the medicines used to treat cognitive impairment that are now FDA-approved in the US, including donepezil, tacrine, galantamine, and rivastigmine, work primarily by suppressing AChE.
- For the treatment of moderate to severe instances of AD, memantine was given approval. It is a non-competitive, low-affinity N-methyl-D-aspartate (NMDA) receptor antagonist that can prevent neurotoxicity brought on by glutamate excitotoxicity, the brain's main excitatory neurotransmitter, without affecting the physiological functions of glutamate required for memory and learning.
- Levodopa, a precursor to dopamine (DA), DA receptor agonists like bromocriptine and ropinirole, which can act on dopamine receptors in the central nervous system (CNS), and anticholinergic medications like benztropine, which reduce tremors and muscle stiffness symptomatically, are some of the medications for Parkinson's disease (PD). Drugs are also administered to treat the disease's non-motor symptoms. Examples include the AChE inhibitors donepezil and rivastigmine, as well as nortriptyline, which is used to treat depression-related symptoms.
- Given the overwhelming evidence that the central cholinergic system is essential for the retrieval and storage of memory objects in the mammalian CNS, the goal of several contemporary therapeutic approaches is to increase the endogenous level of Ach (acetyl choline) in order to enhance the

cholinergic deficiencies. Researchers have recently concentrated their attention mostly on one of these methods: increasing cholinergic deficiency using drugs that can block AChE.

- ACh releasers or donors, nicotinic agonists, Ach precursors, and acetylcholinesterase (AChE) inhibitors, which act by preventing the hydrolysis of ACh in the synaptic cleft and thereby restoring the levels of the neurotransmitter, are a few of these strategies to boost the levels of Acetylcholine [20,34].

## CONCLUSION

Numerous neurodegenerative illnesses are yet unknown to have a cause. For many years, the therapeutic potential of using herbal medicine has attracted a lot of attention. Phytochemicals anti-inflammatory, anti-oxidative, and anti-cholinesterase properties make them a possible treatment option for neurodegenerative diseases in the future. Molecular signalling pathways that can result in apoptosis, necroptosis, and inflammation are shared by the majority of neurodegenerative illnesses, including alzheimer's disease, parkinson's disease, huntington's disease, and others. These pathways also share common properties at the cellular and subcellular levels. The use of herbal medicine offers promising substitutes for the present treatments for neurodegenerative illnesses. Herbal medicines and natural chemicals weak pharmacokinetic qualities, however, severely limit their potential. The herbal remedy has been included into several drug delivery formulations in attempt to get around these restrictions. The mentioned plants neuroprotective benefits come about through inhibition of acetylcholinesterase activity, reduction of inflammatory cytokines, elevation of anti-inflammatory cytokines and also increasing amount of amino acids and serotonin (5-HT) in the neurotransmitters systems. It is crucial to remember that natural products, particularly those derived from plants with antioxidant properties, can serve as a trustworthy source of medication. It takes time to identify plants and use them for desired medical purposes. The synergistic action of the substances contained in herbal medicines, however, allows them to have a maximal benefit with fewer side effects after they have been discovered. To support their usage in the management of diseases, more study in this area is necessary.

## Author contributions

All authors contributed to data collection, drafting or revising the article, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

## Competing interest statement

All authors declare that there is no conflict of interests regarding publication of this paper.

## Ethical approval

Not required.

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