Chapter-1: Herbal Remedies for Neurodegeneration

Introduction:

Neurodegeneration refers to the progressive loss of structure and function of neurons, leading to the dysfunction and death of nerve cells in the central nervous system (CNS) or peripheral nervous system (PNS). It is a complex and debilitating process that underlies various neurological disorders, including Parkinson's disease, Alzheimer's disease, Huntington's disease, Amyotrophic lateral sclerosis (ALS), and multiple sclerosis.

Definition:

Neurodegeneration is a condition characterized by the accumulation of abnormal protein aggregates, oxidative stress, inflammation, mitochondrial dysfunction, impaired neurotransmission, and neuronal death. These pathological processes contribute to the gradual decline in cognitive, motor, and sensory functions associated with neurodegenerative diseases [(1)].

Types and Classification:

Neurodegenerative diseases can be broadly categorized based on the affected region of the CNS, the molecular mechanisms involved, or the predominant clinical symptoms. Some common types of neurodegenerative diseases include:

1. **Parkinson's disease (PD):** PD primarily affects the dopaminergic neurons in the substantial nigra of the brain, leading to motor symptoms such as tremors, rigidity, bradykinesia, and postural instability.

2. **Alzheimer's disease (AD):** AD is characterized by the accumulation of amyloid-beta plaques and neurofibrillary tangles in the brain, resulting in memory loss, cognitive decline, and behavioural changes.

3. **Huntington's disease (HD):** HD is caused by a genetic mutation that leads to the progressive degeneration of neurons in the basal ganglia and cerebral cortex. It manifests with motor symptoms, cognitive impairment, and psychiatric disturbances.

4. **Amyotrophic lateral sclerosis (ALS):** ALS affects the motor neurons, leading to muscle weakness, paralysis, and eventually respiratory failure. It can be classified as sporadic (without a known cause) or familial (inherited).

5. **Multiple sclerosis (MS):** MS is an autoimmune disease characterized by inflammation and demyelination of the CNS. It results in a wide range of symptoms, including fatigue, muscle weakness, difficulties with coordination, and sensory disturbances [(2)].

Mechanisms of Neurodegeneration:

The exact mechanisms underlying neurodegeneration are still not fully understood, and different diseases may involve distinct molecular pathways. However, several common mechanisms have been identified:

1. **Protein misfolding and aggregation**: Abnormal folding of proteins, such as alpha-synuclein, tau, amyloid-beta, and Huntington, leads to the formation of protein aggregates or inclusion bodies that are toxic to neurons.

2. **Oxidative stress:** Increased production of reactive oxygen species (ROS) in neurons and impaired antioxidant defense mechanisms result in oxidative damage to cellular components, including proteins, lipids, and DNA.

3. **Mitochondrial dysfunction:** Impaired mitochondrial function and energy metabolism lead to the generation of ROS and the release of pro-apoptotic factors, eventually causing cell death.

4. **Neuroinflammation:** Activation of immune cells and the release of inflammatory mediators, such as cytokines and chemokines, contribute to chronic inflammation and further neurodegeneration.

5. **Excitotoxicity:** Excessive activation of glutamate receptors, particularly NMDA receptors, leads to an influx of calcium ions into neurons, causing excitotoxicity and cell death [(3)].

Symptoms:

The symptoms of neurodegenerative diseases vary depending on the affected region of the CNS and the specific disease. However, common symptoms include:

a) Cognitive decline (e.g., memory loss, impaired thinking, confusion)
b) Motor impairments (e.g., tremors, muscle weakness, coordination problems, gait disturbances)
c) Sensory abnormalities (e.g., vision or hearing loss, altered sensations)

d) Behavioural and mood changes (e.g., depression, anxiety, personality changes)
e) Autonomic dysfunction (e.g., bladder or bowel problems, orthostatic hypotension) [4].

Causes:

- The greatest risk factor for neurodegenerative diseases is aging. Mitochondrial DNA mutations as well as oxidative stress both contribute to aging.
- Many of these diseases are late-onset, meaning there is some factor that changes as a person ages for each disease. One constant factor is that in each disease, neurons gradually lose function as the disease progresses with age. It has been proposed that DNA damage accumulation provides the underlying causative link between aging and neurodegenerative disease [5].

Treatment:

Most of the neurodegenerative diseases have no cure, and treatment primarily focuses on managing symptoms and slowing disease progression. However, various approaches are being explored for potential therapeutic interventions:

1. Pharmacological Interventions:

- Dopamine agonists (e.g., levodopa) for Parkinson's disease to alleviate motor symptoms.
- Cholinesterase inhibitors (e.g., donepezil, rivastigmine) for Alzheimer's disease to enhance cognition.
- Immune modulators (e.g., interferon-beta, monoclonal antibodies) for multiple sclerosis to reduce inflammation and immune-mediated damage

2. Gene Therapy:

- Gene-based therapies aim to correct or replace defective genes responsible for certain neurodegenerative diseases. For instance, gene silencing techniques like RNA interference are being investigated for treating Huntington's disease.

3. Stem Cell Transplantation:

- Stem cells have the potential to differentiate into various cell types, including neurons. Transplanting stem cells or their derivatives into the damaged areas of the CNS holds promise for replacing damaged or lost neurons.

4. Targeting Protein Aggregation:

- Strategies to prevent or clear abnormal protein aggregates include immunotherapy, small molecule inhibitors, and gene therapies aimed at breaking down or preventing the formation of toxic protein aggregates.

5. Lifestyle Modifications:

- Regular exercise, a balanced diet, and mental stimulation by yoga and meditation will help reduce the risk of neurodegenerative diseases and slow disease progression. These lifestyle interventions promote overall brain health[(6)].

Neurodegenerative diseases are characterized by the progressive decline of the structure and function of the nervous system. While modern medicine offers various treatment options, the use of herbal remedies has gained significant attention due to their potential efficacy and fewer side effects. In this chapter, we explore some herbal drugs that have been traditionally used and studied for their potential in managing neurodegenerative diseases.

Sl.No	Common Name	Botanical Name	Family	Mechanism of action	References
1.	Ginkgo	*Ginkgo biloba*	Ginkgoaceae	Antioxidant property, improves blood circulation and provides neuroprotective effects	(7)
2.	Ashwagandha	*Withania somnifera*	Solanaceae	Anti-inflammatory properties and aids in stress reduction, potentially beneficial in Alzheimer's disease.	(8)
3.	Turmeric	*Curcuma longa*	Zingiberaceae	Antioxidant and anti-inflammatory properties and may help combat neurodegenerative diseases	(9)

4.	Sage	*Salvia officinalis*	Lamiaceae	Enhance memory and cognitive abilities.	(10)
5.	Rosemary	*Salvia rosmarinus*	Lamiaceae	Antioxidant and anti-inflammatory properties, potentially protecting against neurodegeneration	(11)
6.	Lemon Balm	*Melissa officinalis*	Lamiaceae	Neuroprotective effects and improves cognitive function.	(12)
7.	Green Tea	*Camellia sinensis*	Theaceae	Antioxidants, it protects against oxidative stress and neurodegeneration	(13)
8.	St. John's Wort	*Hypericum perforatum*	Hypericaceae	Elevate symptoms of depression and anxiety in neurodegenerative diseases.	(14)
9.	Ginseng	*Panax ginseng*	Araliaceae	Neuroprotective effects	(15)
10.	Licorice root	*Glycyrrhiza glabra*	Leguminosae	Calming effects and potential protection against neurodegeneration.	(16)
11.	Brahmi	*Bacopa monnieri*	Plantaginaceae	Enhances cognitive performance and improves memory and learning abilities.	(17)
12.	Lions Mane Mushroom	*Hericium erinaceus*	Hericiaceae	Stimulate nerve growth factor production, aiding in the regeneration and repair of damaged neurons	(18)
13.	Gotu Kola	*Centella asiatica*	Apiaceae	Supports cognitive function and may improve memory, attention, and mood	(19)
14.	Peony	*Paeonia lactiflora*	Paeoniaceae	Neuroprotective and anti-inflammatory properties	(20)
15.	roseroot	*Rhodiola rosea*	Crassulaceae	Supports cognitive function and reduces fatigue	(21)
16.	Chamomile	*Matricaria recutita*	Asteraceae	Reduces inflammation and stress	(22)
17.	Huperzine	*Huperzia bernh*	Lycopodiaceae	Improve memory and cognitive function	(23)
18.	Passionflower	*Passiflora edulis*	Passifloraceae	Calming properties and aids in reducing anxiety and stress	(24)
19.	Sagebrush	*Artemisia tridentata*	Asteraceae	Improve cognitive abilities and memory.	(25)
20.	Peppermint	*Mentha piperita*	Lamiaceae	Exhibits antioxidant and anti-inflammatory effects, potentially beneficial in neurodegeneration.	(26)
21.	Holy Basil	*Ocimum tenuiflorum*	Lamiaceae	Reduces stress and supports cognitive health	(27)
22.	Astragalus	*Astragalus membranaceus*	Fabaceae	Shows neuroprotective effects and enhances brain functions	(28)
23.	Skullcap	*Scutellaria lateriflora*	Lamiaceae	Potentially reduces anxiety and promotes relaxation	(29)
24.	Kava Kava	*Piper methysticum*	Piperaceae	Relieves stress and anxiety, and promotes relaxation	(30)

25.	Hawthorn	*Crataegus monogyna*	Rosaceae	Improves blood circulation and provides antioxidant effects	(31)
26.	Moringa	*Moringa oleifera*	Moringaceae	Contains antioxidants and anti-inflammatory compounds, potentially beneficial in neurodegenerative diseases	(32)
27.	Oat Straw	*Avena sativa*	Poaceae	Supports cognitive function and may enhance memory and attention	(33)
28.	Reishi Mushroom	*Ganoderma lucidum*	Ganodermataceae	Exhibits neuroprotective effects and boosts the immune system	(34)
29.	Valerian Root	*Valeriana officinalis*	Caprifoliaceae	Calming herb that aids in reducing anxiety and improving sleep	(35)
30.	Lemon Verbena	*Aloysia citrodora*	Verbenaceae	Provides antioxidants and may have neuroprotective effects	(36)
31.	Yerba Mate	*Ilex paraguariensis*	Aquifoliaceae	Conatain caffeine and antioxidants, promoting alertness and providing neuroprotective effects.	(37)
32.	Nettle Leaf:	*Urtica dioica*	Urticaceae	Shows antioxidant and anti-inflammatory properties, potentially beneficial in neurodegenerative diseases	(38)
33.	Cat's Claw	*Uncaria tomentosa*	Bignoniaceae	Exhibits antioxidant and anti-inflammatory effects, potentially protecting against neurodegeneration	(39)
34.	Milk Thistle	*Silybum marianum*	Asteraceae	Contains antioxidant and anti-inflammatory compounds, potentially supporting brain health.	(40)
35.	Dandelion Root	*Taraxacum officinale*	Asteraceae	Rich in antioxidants, it may protect against oxidative stress in the brain	(41)
36.	Black Cohosh	*Cimicifuga racemosa*	Ranunculaceae	Traditionally used for its calming effects, potentially beneficial in managing neurodegenerative diseases	(42)
37.	baikal	*Scutellaria Baicalensis*	Lamiaceae	Exhibits potential neuroprotective effects and reduces inflammation in the brain.	(43)
38.	Poria Mushroom	*Wolfiporia extensa*	Polyporaceae	Possesses antioxidant and anti-inflammatory effects, potentially protecting against neurodegeneration	(44)
39.	Dong Quai	*Angelica sinensis*	Apiaceae	Traditionally used for its calming and cognitive-enhancing properties	(45)

40.	White Willow Bark	*Salix alba*	Salicaceae	Exhibits potential anti-inflammatory effects, potentially aiding in neurodegenerative diseases	(46)
41.	Oregano	*Origanum vulgare)*	Lamiaceae	Rich in antioxidants, it may protect against oxidative stress in the brain	(47)
42.	Marshmallow Root	*Althaea officinalis*	Malvaceae	Shows anti-inflammatory effects and potentially supports cognitive health	(48)

It is essential to note that herbal remedies should always be used under proper guidance, and consulting with a healthcare professional is advised before incorporating them into any treatment plan.

1. **BRAHMI**

Botanical name: *Bacopa monnieri* (Linn.)

Common name: water hyssop, waterhyssop, brahmi, thyme-leafed gratiola, herb of grace, and Indian pennywort.

Family: Scrophulariaceae

Description: *Bacopa monnieri* is a perennial, creeping herb native to the wetlands of southern and Eastern India, Australia, Europe, Africa, Asia, and North and South America. *Bacopa monnieri* is a non-aromatic herb. The leaves of this plant are succulent, oblong, and 4–6 mm (0.16–0.24 in) thick. Leaves are oblanceolate and are arranged oppositely on the stem. The flowers are small, actinomorphic and white, with four to five petals. It can even grow in slightly brackish conditions. Propagation is often achieved through cuttings

Chemical constituents: The best characterized phytochemicals in *Bacopa monnieri* are dammarane-type triterpenoid saponins known as bacosides, with jujubogenin or pseudo-jujubogenin moieties as aglycone units. The alkaloids brahmine, nicotine, and

herpestine have been catalogued, along with D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacin and plantainoside B [49] .

2. JATAMANSI

Botanical name: *Nardostachys jatamansi* (Linn.)

Common name: Spikenard, nard, nardin, or muskroot.
Family: Caprifoliaceae

Description: ***Nardostachys jatamansi*** is a flowering plant of the valerian family that grows in the Himalayas. The plant grows 10–50 cm (4–20 in) in height and has pink, bell-shaped flowers.[4] It is found at an altitude of 3,000–5,000 m (9,800–16,400 ft). Rhizomes (underground stems) can be crushed and distilled into an intensely aromatic amber-colored essential oil, which is very thick in consistency. Nard oil is used as a perfume, an incense, a sedative, and a herbal medicine said to fight insomnia, birth difficulties, and other minor ailments.

Chemical constituents:

- Acaciin
- Ursolic Acid
- Octacosanol
- Kanshone A
- Nardosinonediol
- Nardosinone
- Aristolen-9beta-Ol
- Oleanolic Acid
- Beta-Sitosterol [50]

3. TULSI

Botanical name: *Ocimum tenuiflorum* (Linn.)
Family: Lamiaceae
Common name: holy basil, tulsi or tulasi, and tamole, damole, or domole
Description: *Ocimum tenuiflorum*, commonly known as in Fiji, is an aromatic perennial plant in the family Lamiaceae. It is native to tropical and subtropical

regions of Australia, Malesia, Asia, and the western Pacific.[3] It is widely cultivated throughout the Southeast Asian tropics. basil is an erect, many-branched subshrub, 30–60 cm (12–24 in) tall with hairy stems. Leaves are green or purple; they are simple, petioled, with an ovate blade up to 5 cm (2 in) long, which usually has a slightly toothed margin; they are strongly scented and have a decussate phyllotaxy. The purplish flowers are placed in close whorls on elongated racemes.

Chemical constituents: The plant and its oil contain diverse phytochemicals, including tannins, flavonoids, eugenol, caryophyllenes, carvacrol, linalool, camphor, and cinnamyl acetate, among others.[9][10] One study reported that the plant contains an eponymous family of 10 neolignan compounds called *tulsinol A-J* (51).

4. FENNEL

Botanical name: *Foeniculum vulgare* (Linn.)
Common name: Saunf
Family: Apiaceae
Description: Fennel (Foeniculum vulgare) is a flowering plant species in the carrot family. It is a hardy, perennial herb[3] with yellow flowers and feathery leaves. It is indigenous to the shores of the Mediterranean but has become widely naturalized in many parts of the world, especially on dry soils near the sea-coast and on riverbanks.It is a highly flavorful herb used in cooking

Chemical constituents: The aromatic character of fennel fruits derives from volatile oils imparting mixed aromas, including trans-anethole and estragole (resembling

liquorice), fenchone (mint and camphor), limonene, 1-octen-3-ol (mushroom). Other phytochemicals found in fennel fruits include polyphenols, such as rosmarinic acid and luteolin, among others in minor content [52].

5. HIBISCUS

Botanical name: *Hibiscus rosasinensis* (Linn.)
Common name: **rose mallow**, **hardy hibiscus**, **rose of sharon**, and **tropical hibiscus**
Family: Malvaceae
Description:**Hibiscus** is a genus of flowering plants in the mallow family, Malvaceae. The genus is quite large, comprising several hundred species that are native to warm temperate, subtropical and tropical regions throughout the world. Member species are renowned for their large, showy flowers and those species are commonly known simply as "hibiscus", or less widely known as . The leaves are alternate, ovate to lanceolate, often with a toothed or lobed margin (dentate). The flowers are large, conspicuous, trumpet-shaped, with five or more petals, colour from white to pink, red, blue, orange, peach,[7] yellow or purple,[8] and from 4–18 cm broad.

Chemical constituents: Flavonoids, anthocyanins, terpenoids, steroids, polysaccharides, alkaloids, amino acids, lipids, sesquiterpene, quinones, and naphthalene groups [53].

6. PEPPER

Botanical name: *Piper nigrum* (Linn.)
Common name: Black pepper
Family: Piperaceae
Description: The pepper plant is a perennial woody vine growing up to 4 m (13 ft) in height on supporting trees, poles, or trellises. It is a spreading vine, rooting readily where trailing stems touch the ground. The leaves are alternate, entire, 5 to 10 cm (2.0 to 3.9 in) long and 3 to 6 cm (1.2 to 2.4 in) across. The flowers are small, produced on pendulous spikes 4 to 8 cm (1.6 to 3.1 in) long at the leaf nodes, the spikes lengthening up to 7 to 15 cm (2.8 to 5.9 in) as the fruit matures.

Chemical constituents: Black pepper contains about 5–9% of the alkaloids Piperine and Piperettine and about 1.2– 5% of volatile oil.It contains a variety of chemical constituents, such as Piperolides, Propenylphenols, Amides, Neolignans,Llignans, Flavonoids, Terpenes, and Steroids [(54)].

7. GINGER

Botanical name: *Zingiber officinale* (Linn.)
Common name: Ginger,Zingiber
Family: Zingiberaceae
Description: **Ginger** (Zingiber officinale) is a flowering plant whose rhizome, **ginger root** or ginger, is widely used as a spice and a folk medicine.[2] It is a herbaceous perennial which grows annual pseudostems (false stems made of the rolled bases of leaves) about one meter tall, bearing narrow leaf blades. The inflorescences bear flowers having pale yellow petals with purple edges, and arise directly from the rhizome on separate shoots

Chemical constituents: The characteristic fragrance and flavor of ginger result from volatile oils that compose 1–3% of the weight of fresh ginger, primarily consisting of sesquiterpenes, such as beta-bisabolene and zingiberene, zingerone, shogaols, and gingerols with [6]-gingerol (1-[4'-hydroxy-3'-methoxyphenyl]-5-hydroxy-3-decanone) as the major pungent compound [(55)].

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