



# Current Medication Trends and Global Impact on Neurodegenerative Disorders

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## Abstract

Neurodegenerative disorders are the medical condition characterized by destruction in neuronal cells, abruption of neuronal activity and distinct involvement of the functional movement. The main neuronal disorders like Parkinson and Alzheimer disease are caused by environmental and genetic influences associated with accumulation of abnormal protein aggregation, which leads to inflammation as well as oxidative stress in the central nervous system. The AYUSH medication system considerably accepted by health-care professionals played a critical role since a decade to manage the elevated factors and continuously improving lifestyle for good survival of the patients. In which allopathic and ayurvedic medications have been precisely introduced for the management of disorders and regain of neuronal function. Unani and Siddha medicines have been widely used since ancient time and found as significantly relieving the sign and symptoms of neurodegenerative disorders, while yoga plays a perfect role for the management of these disorders. Regular yoga practice may relax the mind and calms the brain; reduces headache, fatigue and cures insomnia; increases blood circulation and maintain proper supply of oxygen to the lungs and detoxifies the internal organs. Thus, yoga plays a promising role in the improvement of mental health, releases stress, fatigue, depression and tension and also stimulating blood circulation in the brain. Finally it was concluded that, the AYUSH medication system highly accepted for relieving the neuronal complications and managing all elevated parameters in patients suffering from neuronal disorders.

**Keywords:** Neurodegenerative disorders; Parkinson; Alzheimer; Depression; AYUSH medication system

## OPEN ACCESS

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## Abbreviations

CNS: Central Nervous System; NDDs: Neurodegeneration Disorders; AD: Alzheimer's Disease; PD: Parkinson's Disease; HD: Huntington's Disease; ALS: Amyotrophic Lateral Sclerosis; RRMS: Relapsing-Remitting Multiple Sclerosis; SPMS: Secondary-Progressive Multiple Sclerosis; PPMS: Primary-Progressive Multiple Sclerosis; PRMS: Progressive-Relapsing Multiple Sclerosis; BBB: Blood Brain Barrier; ROS: Reactive Oxidative Stress; TCA: Tricarboxylic Acid; ATP: Adenosine Triphosphate; ETC: Electron Transport Chain; AYUSH: Ayurveda Yoga Unani Siddha Homoeopathy; NMDA: Methyl-D-Aspartate; MAOB: Monoamine Oxidase B; AChE: Acetyl Cholinesterase; BChE: Butyrylcholinesterase and Antibodies; NSAID: Non-Steroidal Anti-Inflammatory Drug; MRI: Magnetic Resonance Imaging

## Introduction

Neurodegenerative diseases are the brain disorders with selective loss of neuronal activity, degeneration of neuronal cells and distinct involvement of the functional systems as defined in clinical presentation [1]. The most common disorders of nervous system caused by environmental and genetic influences are Parkinson's disease and Alzheimer's disease, which have been recognized by accumulation of abnormal protein aggregate leads to inflammation and oxidative stress in the central nervous system [2,3]. The biological mechanisms associated with neurodegenerative disorders are oxidative stress, aggregates of proteins in neurons, depletion or inadequate synthesis of neurotransmitters, degradation of neurotransmitters in the synaptic cleft due to the higher activity of enzymes, abnormal ubiquitination, mitochondrial dysfunction, and excitotoxicity of neurons as well as disarrangement or damages of the Blood Brain Barrier (BBB) [4]. The human ailments associated with neurodegenerative disorders are given as follows

### Alzheimer's disease

One of the most common neurodegenerative disorders is Alzheimer's disease (AD), which

**Table 1:** Details of clinical diagnosis used for estimation of brain disorders.

S.No.	Test	Description
1	Screening measures	<ul style="list-style-type: none"> <li>• Addenbrooke's cognitive examination (ace-r)</li> <li>• Frontal assessment battery (fab)</li> </ul>
2	Tests of premorbid functions	<ul style="list-style-type: none"> <li>• National adult reading test</li> <li>• Wechsler test of adult reading</li> </ul>
3	Tests of intelligence /general ability	<ul style="list-style-type: none"> <li>• Wechsler adult intelligence scale (wais-iii &amp; iv)</li> </ul>
5	Tests of memory functions	<ul style="list-style-type: none"> <li>• Wechsler memory scale (wms-iii and iv)</li> <li>• Adult memory and information processing battery</li> <li>• Rivermead behavioral memory test</li> <li>• Doors and people test</li> <li>• Rey osterrieth complex figure</li> <li>• Recognition memory test (words and faces)</li> <li>• List learning tests (rey auditory verbal learning and california verbal learning test)</li> <li>• Autobiographical memory interview</li> </ul>
6	Tests of executive functions and attention	<ul style="list-style-type: none"> <li>• Behavioral assessment of dyse-xecutive syndrome (bads)</li> <li>• Delis-kaplan executive function system (d-kefs)</li> <li>• Wisconsin card sorting test</li> <li>• Trail making test</li> <li>• Stroop test</li> <li>• Hayling and brixton tests</li> <li>• Verbal fluency (semantic categories and fas test)</li> <li>• Test of everyday attention</li> </ul>
7	Tests of language functions	<ul style="list-style-type: none"> <li>• Confrontation naming tests (boston or graded naming test)</li> <li>• Word-picture matching peabody vocabulary test</li> <li>• Pyramids and palm trees test</li> <li>• Test for reception of grammar (trog)</li> <li>• Token test</li> <li>• Boston diagnostic aphasia examination (expression/ comprehension sub-tests)</li> </ul>
8	Tests of visuo-perceptual/spatial functions	<ul style="list-style-type: none"> <li>• Visual and object space perception battery</li> <li>• Benton line orientation test</li> <li>• Birmingham object recognition battery</li> <li>• Behavioral inattention test</li> </ul>

**Table 2:** List of selected Ayurvedic (herbal) medicines for the treatment of NDDs [48-50].

S. No.	Botanical name	Family	Part used	Dose	References
1	Ashwagandha ( <i>Withania somnifera</i> )	<i>Solanaceae</i>	Root	500 mg/kg	[48]
2	Turmeric ( <i>Curcuma longa</i> )	<i>Zingiberaceae</i>	Root	100 mg/kg	[48]
3.	Brahmi ( <i>Bacopa monnieri</i> )	<i>Scrophulariaceae</i>	Root	300 mg/kg	[48]
4.	Shankhpushpi ( <i>Convolvulus pluricaulis</i> )	<i>Convolvulaceae</i>	Root	200-400 mg/kg	[48]
5.	Gotu kola ( <i>Centella asiatica</i> )	<i>Apiaceae</i>	Root	350-400 mg/kg	[49]
6.	Jyotishmati ( <i>Celastrus paniculatus</i> )	<i>Celastraceae</i>	Root	400 mg/kg	[49]
7.	Jatamansi ( <i>Nardostachys jatamansi</i> )	<i>Caprifoliaceae</i>	Root	400 mg/kg	[49]
8.	Guggulu ( <i>Commiphora mukul</i> )	<i>Crassulaceae</i>	Root	100-300 mg/kg	[49]
9	Gingko ( <i>Gingko biloba</i> )	<i>Ginkgoaceae</i>	Root	120mg/kg	[50]
10	Lemon balm ( <i>Melissa officinalis L.</i> )	<i>Lamiaceae</i>	Root	25 mg/kg to 75 mg/kg	[50]
11	Gotu kola ( <i>Centella asiatica L.</i> )	<i>Apiaceae</i>	Root	100 mg/kg to 300 mg/kg	[50]
12	Yuan Zhi ( <i>Polygala tenuifolia willd</i> )	<i>Polygalaceae</i>	Root	100 mg/kg to 200 mg/kg	[50]

shows loss of memory, alterations in mood and behavior, often accompany most frequent cause of dementia, disorientation and aphasia. The hippocampus and cerebral cortex are preferentially and severely affected in AD [5]. Pathologically, senile or neuritic plaques (composed of amyloid- $\beta$  with peptide aggregates) and neurofibrillary tangles (filamentous bundles comprised of hyper phosphorylated tau proteins) are the main characteristic lesions in affected tissues. Tau protein is normally involved in nutrient transport along neuronal axons [6]. The prevalence of AD in the people age of  $\geq 85$  years is about 30% and the incidence rates rising upon 6% to 8% per year. It was also observed that the onset is rarely raises about 0.5% per year for the age group of 55 to 70 year population; except in familial cases, which comprises roughly 5% to 10% [7].

## Parkinson's disease

The second most common neurodegenerative disorders is Parkinson's disease (PD), associated with movement disorder like tremors, rigidity, bradykinesia and postural instability in both rest as well as working situations [8]. The mechanisms involved in PD are loss of dopamine-producing neurons of the mid-brain substantia nigra, abnormal protein aggregation with deficient clearance of aggregates, impaired mitochondrial function, oxidative stress, inflammation, necrosis and accelerated apoptosis [9]. Other pathologic condition like intracellular deposits of aggregated i.e.  $\alpha$  synuclein, ubiquitin have found in many surviving neuronal populations [10,11]. The prevalence of PD may reach 2% in persons aged  $\geq 65$  years which relatively rare with age  $\leq 50$  years and rise sharply throughout the eighth decade of life. The epidemiologic surveys, mainly in western

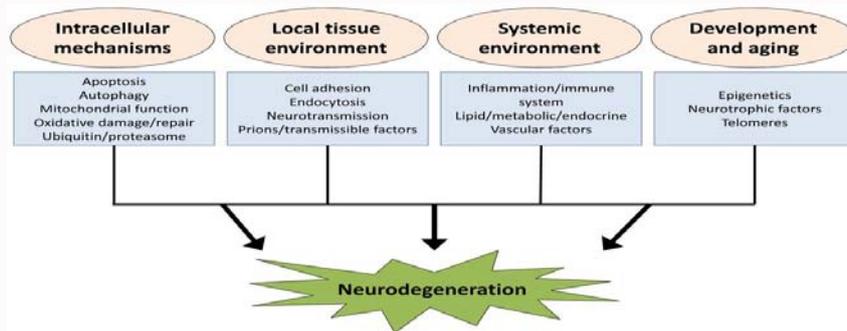


Figure 1: Conceptual model of candidate pathways contributing to neurodegeneration.

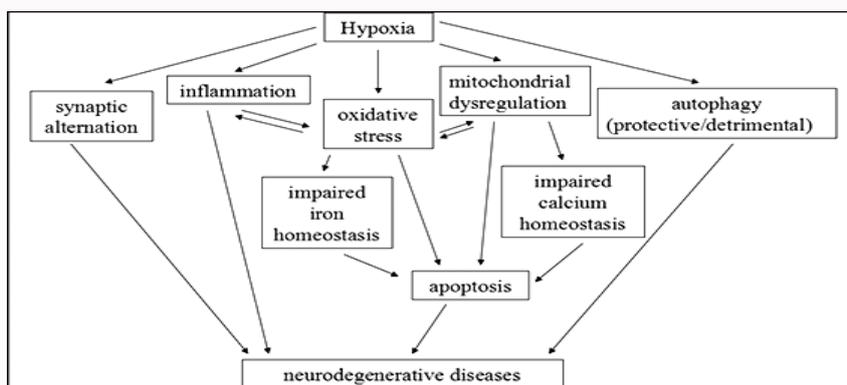


Figure 2: Pathway involve in development of neurodegenerative disorders.

countries, indicate a small (20% to 30%) excess risk in men. The worldwide annual surveys reported the incidence rates of 0.01% to 0.05% in most countries [12].

**Huntington’s diseases**

Huntington disease (HD) is atypical neurodegenerative disorder of the CNS distinguished by surplus choreatic movements, dementia, behavioral, emotional and psychiatric disturbances [13,14]. Symptoms usually begin between the ages of 35 years to 50 years, although the onset may occur at any time from childhood to old age. Death may occur an average of 15 years to 20 years after appearance of first symptoms, while some patients dying earlier surviving for 30 years to 40 years, due to falls or developed suicidal tendency [15].

**Amyotrophic lateral sclerosis**

Amyotrophic lateral sclerosis is a disease of the motor neurons in the cerebral cortex and the anterior horns of the spinal cord. ALS is generally a rapid fatal condition within 2 years to 3 years of onset usually occurs in the middle-later years of life. The major pathogenic mechanism in the neuronal death is considered to be excitotoxicity mediated by glutamate and elevated calcium ion [16]. As a consequence of neuronal cell death, neuronal muscle atrophy occurs, resulting in diminished muscle strength in bulk, fasciculation’s, and hyper-reflexia. Effects on respiratory muscles can lead to pulmonary infection, and eventually amyotrophy leads to paralysis and death [17]. The incidence is very rare approximately 0.001% to 0.002% per year, and appears to be slightly more common in men, while with the familial ALS accounting for about 10% of whole cases [18].

**Multiple sclerosis**

MS is an autoimmune and inflammatory demyelinating disease

of the central nervous system, affecting 0.03% to 0.6% of population. As per National Multiple Sclerosis Society, around 2.1 million people affected worldwide [19].

There are four types of multiple sclerosis are described as follows

**Relapsing-remitting ms (RRMS):** This is the most common form of multiple sclerosis. Around 85% people suffered with MS are initially diagnosed with RRMS. The RRMS suffered people with temporary periods called relapses, flare-up or exacerbations, when new symptoms appear [20].

**Secondary-progressive ms (SPMS):** When the conditions worsen more steadily over time, with or without occurrence of relapses and remissions known as SPMS. Most people who are diagnosed with RRMS will have transition to SPMS at some point [21].

**Primary-progressive ms (PPMS):** It is uncommon but the incidence is about 10% of people with MS and characterized by slowly worsening symptoms from the beginning with no remissions [20].

**Progressive-relapsing ms (PRMS):** It is a rare form of MS only 5% people fall in this category with acute relapses without remissions, and characterized by a steadily worsening disease state from the beginning with or without recovery [20].

Current Scenario of the human population suffered by neurodegenerative disorders in India and worldwide as per global survey report (UN news center, The Times of India news on World Alzheimer’s day and Parkinson’s news today detained in 2017) are given as follows

- Alzheimer: Incidence in India is 1.6 millions, while global incidence is 24 millions.

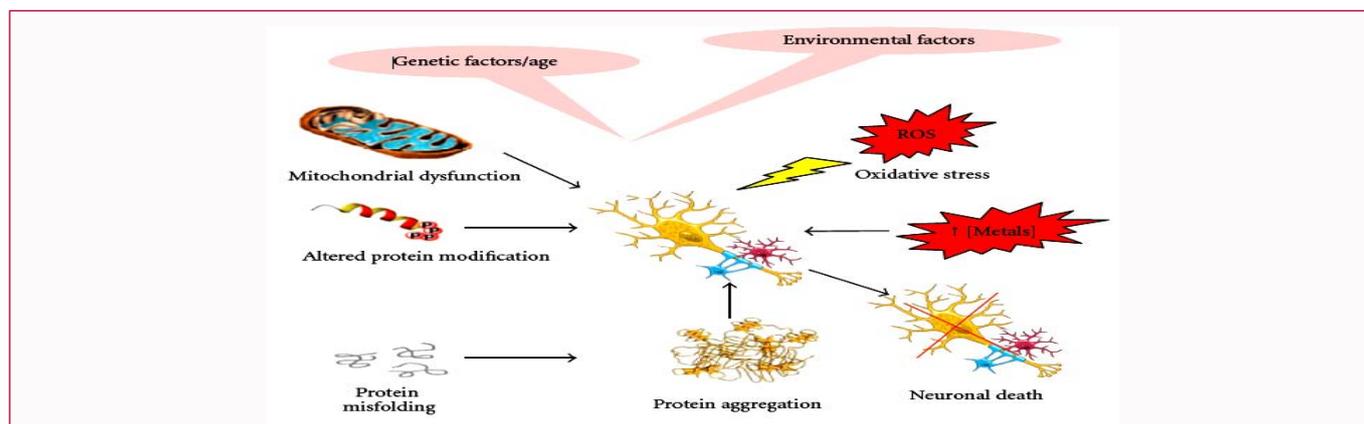


Figure 3: Mechanism involve in development of neurodegenerative disorders.

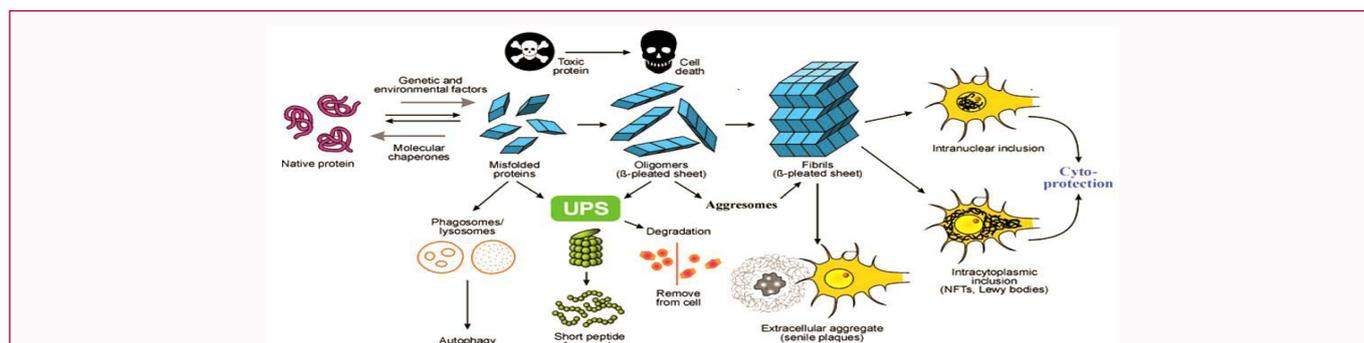


Figure 4: Model of protein misfolding and fibrillation leading to deposition of aggregated proteins in cells and extracellular spaces via actions of the UPS, phagosomes and aggresomes, either causing cell death or cytoprotection.

- Parkinsonism: Incidence in India is 7 million to 8 million, while global incidence is 7 million to 10 million.
- Dementia: Incidence in India is 04 millions, while global incidence is 50 millions.

**Symptoms**

The symptoms shown in neurodegeneration diseases are loss of memory, bradykinesia, muscular rigidity, rest tremor, postural & pace impairment [22]. Olfactory dysfunction, cognitive impairment, psychiatric symptoms, sleeps disorders, autonomic dysfunction, pain, and fatigue. [23,24]. Other symptoms like; constipation, depression, mood disorders are the characteristic of this premotor or prodromal phase of the disease [25].

**Pathophysiology**

Candidate pathways influencing the balance of neuronal survival and degeneration are displayed within broader functional groups based on their major site or mode of action (intracellular mechanisms, local tissue environment influences, systemic influences, and mechanisms related to neurodevelopment and aging). The pathways and overarching functional groups in this model are highly related and can have overlapping or interacting components which can collectively modulate neurodegenerative processes (Figure 1) [26,27].

**Etiology**

Neurodegenerative disorders are characterized by progressive dysfunction of specific characteristic of neurons and neuronal defeats associated with extra and intra cellular accumulation of misfolded proteins. The main critical processes for abnormal protein dynamics

is due to the deficiency of ubiquitin–proteosome–autophagy system, oxidative stress, free radical formation, mitochondrial dysfunction and impaired bioenergetics (Figure 2). The second most process involves in dysfunction of neurotrophins is ‘neuronal inflammation which disrupts the neuronal Golgi apparatus and axonal transport [5].

**The interrelated mechanisms leads to programmed cell death are explained as follow**

**Protein aggregation:** It plays a variety of pathological characteristic involve in neurodegenerative disorders due to abnormal interactions between intra and extra cellular deposition of self-aggregating misfolded proteins with formation of high-ordered insoluble fibrils [28-33]. The basic neurodegenerative process is the formation of several gene-gene complex and gene-environmental interaction with mutation in the genes encoding protein constituents [34]. Whereas the disintegration of neuronal networks depend on dysfunction and death of neuronal as well as glial cells, which caused by abnormal protein-protein interactions with its lesion that result from the production of vicious circles (Figure 3) [35,36]. Abnormal interaction between normal, highly soluble brain proteins alters their characteristics, properties and misfolding gradually converts them into insoluble polymers with the aggregates adopting either highly ordered (cross-pleated sheet structures) or disordered (amorphous) forms [37-39].

**Protein misfolding:** Protein aggregation resembling inappropriate folding or misfolding protein leads to structural and functional changes of a normal protein, inducing the formation of protein aggregates through different supra-molecular organizations



Figure 5: Padmasana.



Figure 6: Vajrasana.



Figure 7: Ardha Matsyendrasana.



Figure 8: Paschimottasana.

(Figure 4). Abnormal proteins resulting the production errors inherited or acquired amino acid substitutions often cannot fold correctly and will be trapped in misfolded conformations. The pathogenic pathways involve membrane permeabilization through a channel mechanism or hydrophobic interaction of prefibrillary oligomers with different cellular targets [40,41].

**Mitochondrial dysfunction and ROS:** Mitochondrial dysfunction and oxidative stress play an important role for the development of more common neurodegenerative disorders. The loss of mitochondrial function is associated with an increase in the production of reactive oxygen intermediates and a number of human diseases [42]. Mitochondria use metabolic intermediates generated during the Tricarboxylic Acid (TCA) cycle to produce Adenosine Triphosphate (ATP) during oxidative phosphorylation. Electrons are occasionally captured by oxygen to produce superoxide anion radicals

(O<sup>-2</sup>) during the ETC (electron transport chain). These superoxide radicals are converted in to hydrogen peroxide in the mitochondria through the action of manganese superoxide dismutase. In the mitochondria hydrogen peroxide is broken down to water by the action of glutathione peroxidase or peroxiredoxins. The inhibition of ETC proteins can cause a subsequent increase in ROS resulting in decrease in the mitochondrial membrane potential, loss of ATP, energy collapse and subsequent cell death [43,44].

## Diagnosis

The different types of neuropsychological diagnostic tests are commonly used in clinical evaluation of brain disorders described in Table 1 [45].

## Treatment of Neurodegeneration

### Management through 'AYUSH' medication system

The treatment goals for the management of neurodegenerative diseases are to first relieve the symptoms, prevent complications, and interruption with neurons destruction. To control neurodegenerative diseases, must treat the symptoms that disturbing the neuronal functions. Currently a novelistic medication system such as Allopath, Yoga (naturopathy), Unani, Siddha and Herbals (AYUSH) is considered cumulative therapies for the complete prevention of neurodegeneration [46]. This medication system consists of herbal/ medicinal plants possessing active chemical constituent, which is traditionally used as folk medicine that developed over generations within various societies before the era of modern medicine [47].

Selected Ayurvedic (herbal) medicines for the treatment of NDD's are listed in Table 2 [48-50].

### Yoga system of management

Yoga is antique traditional sciences which encompass yogistic physical postures (asanas), yogistic breathing practices (pranayama), meditations and relaxation techniques, highly accepted as science rather than religion or philosophy [51]. Yoga considers individual existence in five dimensions and not merely physical. These five dimensions are annamaya kosha (physical body), pranamaya kosha (vital body), manomaya kosha (Psychic body), vijanamaya kosha

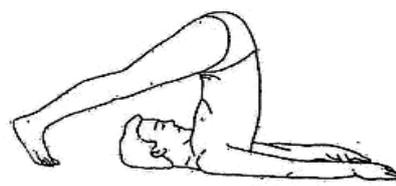


Figure 9: Halasana.

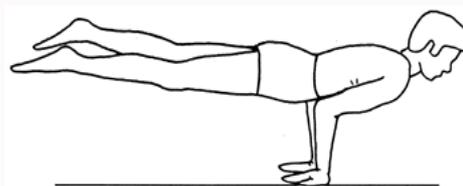


Figure 10: Mayurasana.

(intellectual body) and Anandamaya kosha (causal body) [52]. Over a short period of time, non-communicable diseases are the result of an imbalance that starts at manomaya kosha level and percolates down to the annamaya kosha level via pranamaya kosha. Therefore, yoga therapy focuses on bringing balance by all these levels of existence through a variety of techniques [53]. The components such as asanas work at the physical level; pranayama works at a vital energy level, and meditation works at psychological and intellectual levels.

The asanas are referred as poses in yoga. These particular postures help in improving the blood circulation to the vital organs like brain and prevent various types of illness to the human body. In which meditation is the most important facts about yoga and controlled breathing helps in better functioning of the brain. Researchers have observed that 20 minutes of yoga a day will improve speed and accuracy of working memory. Yoga benefits on brain are immense and the following asanas practiced on a daily basis will help in proper functioning of the brain [54].

1. Padmasana (Lotus pose)
2. Vajrasana (Diamond pose)
3. Ardha Matsyendrasana (Half spinal twist pose)
4. Paschimottanasana (Seated forward bend)
5. Halasana (Plow pose)
6. Mayurasana (Peacock pose)
7. Sirsasana (Headstand pose)
8. Shavasana (Corpse pose)
9. Sarvangasana (Bridge-bandha pose)
10. Uttanasana (Standing forward bend)
11. Vrikshasana (Tree pose)
12. Shashankasana (Hare pose)

**Padmasana:** Lotus is considered as a symbol of purity, enlightenment and detachment. Padmasana (lotus pose) is a meditative pose that works best when done in the morning with or without an empty stomach. Hold this intermediate level Hatha-Yoga pose (Padmasana) for at least 1 minute to 5 minutes [55] [Figure 5].

**Benefits:** Padmasana relaxes the mind and calms the brain; awakens the chakras in the body and increases consciousness.

**Vajrasana:** Diamond pose is a kneeling exercise, usually accompanied by breathing aerobics. Practicing the Vajrasana facilitates the body to develop into as strong as a diamond. Only Vajrasana have to be practiced after a meal for at least 5-10 minutes disparate other yogasanas [Figure 6].

**Benefits:** Vajrasana aids proper digestion and with regular practice it eliminates constipation and combats acidity. The pose helps the body to relax and increases blood circulation and also improves the flexibility of the lower body and tones the muscles.

**Ardha Matsyendrasana:** The half lord of the fishes pose is named after the sage Matsyendranath i.e. half spinal twist with numerous variations. Practice this asana either early in the morning on an empty stomach or 4-6 hours after a meal in the evening for at least 30 seconds to 60 seconds [Figure 7].



Figure 11: Sirsasana.

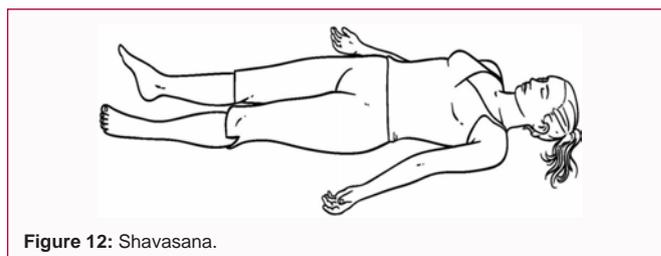


Figure 12: Shavasana.



Figure 13: Sarvangasana.



Figure 14: Uttanasana.

**Benefits:** Ardha Matsyendrasana relieves stiffness in the back and improves digestion. This pose increases the supply of oxygen to the lungs and detoxifies the internal organs and also purifies the blood which improves its circulation.

**Paschimottanasana:** The Seated forward bend is a classic Hatha-Yoga pose and very simple in performing Paschimottanasana. This asana gives the body a good stretch and concentrates on the back. Practice this pose in the morning on an empty stomach and clean bowels, also do it in the evening after 4-6 hours from the last meal. During practice, hold this basic Hatha-Yoga pose for 30 seconds to

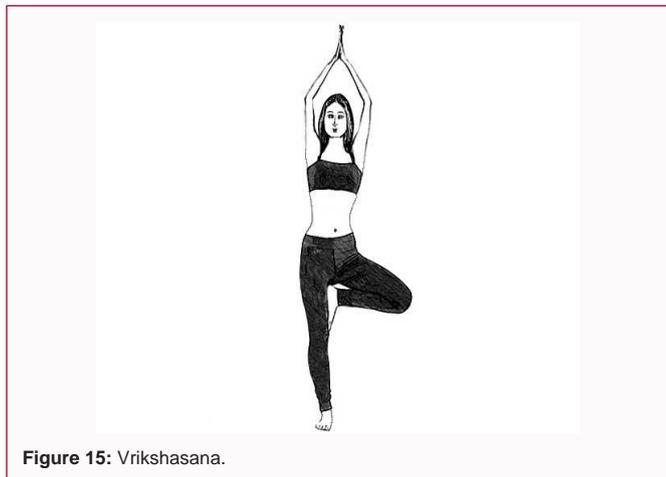


Figure 15: Vrikshasana.

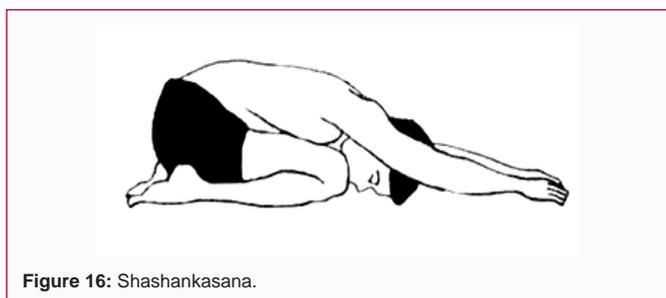


Figure 16: Shashankasana.

60 seconds [Figure 8].

**Benefits:** Paschimottanasana relieves mild depression and stress, gives a good stretch to shoulders, and activates the neurons. This asana reduces headache, fatigue; cures insomnia and maintain high blood pressure.

**Halasana:** The Plow pose uncovers the hidden capabilities of the body. The plow is a farming instrument used in many Asian countries that churns the soil in preparation for sowing seeds. Practice the pose in the morning on an empty stomach or in the evening with a gap of 4 hours to 6 hours from the last meal and hold the pose for 30 seconds to 60 seconds during practice [Figure 9].

**Benefits:** This pose releases the strain in the back and enhances the posture to reduce stress and calms the brain.

**Mayurasana:** The Peacock pose resembles a peacock when it walks around with its feathers down. It is best to practice this pose in the morning on an empty stomach as the body has the energy generated from digesting the meal of the previous night and hold this pose for 30 seconds to 60 seconds during practice [Figure 10].

**Benefits:** Mayurasana improves concentration and coordination between the mind and the body.

**Sirsasana:** The headstand is the king of all yoga poses. It requires complete inversion of the body and good upper body strength. Sirsasana needs a series of preparatory exercises over a period to do the asana. At some stage in practicing this asana It is necessary that the stomach is empty and bowels clean to. Better try to hold the pose for at least 1minute to 5 minutes [Figure 11].

**Benefits:** Sirsasana instantly calms the body and also stimulates the pituitary gland, strengthens the lungs, improves digestion, cures asthma etc. It stimulates excess blood flow to the brain which reduces

Table 3: List of appropriate Unani medicines used for the treatment of NDDs [63].

S. No.	Medicine	Unani name	Dose
1	Juglans regia	Akhrot	500 mg to 1000 mg
2	Withania somnifera	Asgand	500mg to 1000 mg
3	Cantela Asiatica	Barhami booti	250mg to 700 mg
4	Boswellia serrata	Kundur	200 mg
5	Vitis Vinefera	Maviz munaqqa	100 mg to 300mg
6	Glycyrrhiza glabera	Aslussus	100 mg to 500mg
7	Foeniculum vulgure	Badiyan	50 mg to 200mg
8	Adiantum cappilus	Parshiyawshn	125 mg to 500mg
9	Ficus carica	Injeer zarda	250mg
10	Cassia Aungustifolia	Sana Makki	12 mg to 58mg
11	Pyrethrum indicum	Bozidan	150mg
12	Cholchicum Luteum	Suranjan	2000 mg to 3000mg

the stress and recovers neuronal activity.

**Shavasana:** The ‘corpse’ pose look like relaxed sleeping pose. It is very simple and everyone can do this asana with lots of concentration on each part of the body. Better try to practice this asana for at least 10 minutes to 15 minutes [56] [Figure 12].

**Benefits:** Shavasana relaxes the whole body, which beneficial in patient suffering from neurological problem, releases stress, fatigue, depression and tension. It develops excellent concentration, cures insomnia, calms the mind; improve mental health and also stimulating blood circulation in the brain.

**Sarvangasana:** The Bridge yoga pose is a great front hip jloints opener, which strengthens spine, opens the chest, and improves spinal flexibility in addition to stimulating the thyroid. The practice become excellent while the stomach is empty with clean bowels and better tries to hold the pose for at least 2 minutes to 5 minutes [57] [Figure 13].

**Benefits:** It helps to alleviate stress and mild depression, provide calms to the brain and central nervous system. It also reduces headache, fatigue, anxiety and insomnia [57].

**Uttanasana:** This type of asana for brain requires standing straight, then bending and placing the hands outside feet, keeping the back and kneeing straight. This is better in the morning; if not possible practice it in the evening after 4-6 hours from the last meal and hold this pose for at least 2 minutes to 5 minutes [58] [Figure 14].

**Benefits:** It helps in release stress, anxiety, depression, and fatigue; provides calm to the mind and soothes the nerves. Relieves tension in the spine, neck, and back activates the abdominal muscles and also reduced symptoms of headaches, insomnia etc [58].

**Vrikshasana:** This yoga ensures benefit to the brain; stand straight and bend the right leg so that it is placed on the left thigh with its toes downwards. Raise the hands above to head as in the prayer position. Better try to practice this asana for at least 2 minutes to 5 minutes [59] [Figure 15].

**Benefits:** It gives tranquility to the mind thus good for those who are facing the problem of depression and anxiety. It increases stamina, concentration, immunity and develops esteem and self-confidence. It calms and relaxes the central nervous system and stretches the entire body from toes to fingers.

**Table 4:** List of Allopathic medicines used for the treatment of NDDs [64-66].

S. No.	Drug name	Mode of action	Dose	Rout	Reference
1	Remacemide	NMDA receptor Antagonist	300 mg/kg to 800 mg/kg	i. p.	[64]
2	Alaptid	Melanotropininhibiting factor(MIF)-1 analog	5 mg/kg to 20 mg/kg	s.c.	[64]
3	Selegiline	MAO B inhibitor	5 mg/kg to 12 mg/kg	oral	[64]
4	Ampakines	AMPA receptor Modulator	0.1-30 mg/kg	i. p.	[64]
5	Donepezil	Inhibits acetylcholinesterase	5 mg/kg to 23 mg/kg	i. p.	[65]
6	Rivastigmine	selective inhibitor of brain AChE and BChE	1.5 mg/kg to 12 mg/kg	oral	[65]
7	Galantamine	Enhances central cholinergic function and likely inhibits AChE.	40 mg/kg	oral	[65]
8	Tacrine	Cholinesterase inhibitors	10 mg/kg to 40 mg/kg	oral	[65]
9	Memantine	N-Methyl-D-Aspartate Antagonist	5 mg to 20 mg	oral	[65]
10	Amantadine	antagonism at muscarinic andN-methyl-D-aspartate (NMDA) receptors	100 mg/kg to 200 mg/kg	oral	[66]
11	Zonisamide	Inhibits MAO-B,Blocks voltage-dependent Na <sup>+</sup> channels and T-type Ca <sup>2+</sup> channels	30 mg/kg	i.p.	[66]
12	Levodopa	MAO-B inhibitors,block a major pathway in dopamine metabolism and thus increase the duration of action of dopamine	30 mg/kg	oral	[66]

**Shashankasana:** This is one of the excellent yoga asana for brain; in this horse pose start with sitting on the heels put back and neck straight. Bend the body over the thighs so that the forehead will touch the mat [60] [Figure 16].

**Benefits:** It produces calm, relaxed of mind and increasing the memory power if practice this asana regularly [60].

#### Unani medication system

In Unani system of medicine, the uses of natural sources are continued at an appropriate quantity for influencing the properties of medicine (Table 3). The common differences of unani medication system surrounded by other medication system are drugs name, doses, prescription pattern and uses in comparison to Ayurveda & Siddha medication systems [61].

Appropriate Unani medicines used for the treatment of NDDs are listed in Table 3 [62].

#### Siddha medication system

It is one of the oldest medication systems of south India, where the use of herbal medicines is arranged for the alleviation of any type of ailments in human being (Table 4). Currently, this medication system proves a rapid improvement over meticulous disease with negligible side effects.

Appropriate Siddha medicines used for the treatment of NDD's are listed in Table 4 [63].

#### Allopathic medication system

It is one of the most advanced systems of medical practice with modern medicine, which takes care of a disease using chemicals, produces different effects during treatment. Some appropriate and common medicines or chemical agents who exploit to resolve these complications are given in Table 4.

Allopathic medicines used for the treatment of NDDs are listed in Table 4 [64-66].

## Discussion

The special collection showcase of this review article facilitates our impact on understanding the mechanisms of neurodegenerative disorders. The present article spans different diseases, from commonest disorders such as Parkinson's and Alzheimer's disease to rare neurological disorders. AYUSH system is a reputed medication

system for its various pharmacological effects favorable for human health [67]. Besides the potent wound healing potential, a number of studies described the significant protective effect of the plant against several diseases of CNS. Biological effects of herbal plants have been generally attributed to the major protective effect. The neuroprotective effect of the plant has been suggested from result have dissimilar mechanisms, most of which have referred to positive influences on oxidative stress and other evaluation parameters [68]. The modulatory role of herbal products in these processes would not only lead to the discovery of novel neuroprotective agents but also help to understand complex pathophysiology of neurodegenerative diseases [69].

There are various allopathic drugs available in the global market used for the management of neurodegenerative disorders and might be reliable for modification in neuronal function. Meanwhile the patients have little compliance against these drugs after prolong exposures like insomnia, dizziness, confusion, loss of concentration etc [70]. A critical diagnosis is essential for preparation of goals to care and management of neuronal patients. The current review converses the overall symptoms, worldwide affected population, complication in management of NDDs and approaches for the most excellent treatment systems through "AYUSH" for the maintenance of these worsen condition [71].

The researchers facing serious challenges in drug discovery process for neurodegenerative diseases which becoming extremely expensive and critically incompetent. A significant shift from a single-target to a multi-target drug approach, especially for complex disorders are being observed for new drug discovery phase. Approaches based on reverse pharmacology also offer efficient development proposal for new formulations based on herbal products. The Ayurvedic system of medicine has acquired increasing recognition in recent years with help of nutritious, standard diet and new treatment approaches [72].

Early development of Ayurvedic herbal supplements which prescribed from centuries for neurodegenerative diseases (including dementias) was agreed only by Western countries health care professional as mechanistic studies on AD; however, these mechanistic points of studies addressed to the same mechanisms by the Ayurvedic therapeutics (for example, increase in nerve growth factors, neurotrophic factors, reduction in inflammation and oxidative damage), providing strong support in favor of herbal therapy for

NDDs. It was well known that, the authoritative basic knowledge of Ayurveda together with combinatorial sciences and high-throughput screening techniques continuously improving the ease with Ayurvedic formulations, which can be used in drug discovery agencies and drug development process, thereby providing new functional leads for NDDs and other age associated neurodegenerative diseases [73].

## Conclusion

The various areas of study of Yoga practices were reviewed in the present article indicated physiological benefits and effect of Yoga on nervous system, immune system, circulatory system, respiratory system, digestive system and endocrine system. Improvement in antioxidant property through Yoga treatment system are extremely utilizes in prevention of neurodegenerative disorders, cardiovascular disorders, psychosomatic disorders, analgesic effect, numerous benefits of Yoga on female population and role of Yoga on rehabilitation. Finally it was observed from the published report that, the Yoga can be adopted by a large healthy and diseased population.

There are various underlying causes of neuronal disorders, which are reliable for alteration in mood behavior and other biological activity. A significant diagnostic evaluation is essential for best possible care and management of neurodegenerative patients. The current review discuss the most excellent treatment medication systems i.e. "AYUSH" for the management of neurodegenerative condition on the basis of enormous published research proposal. Furthermore peaceful investigation and prevention on neurodegenerations are requiring for management of these challenging task to improvement of patient's life.

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## Conflicting of Interest

The authors declared no potential conflicts of interest concerning the authorship, or publication of this review article.

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