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SCREENING OF MEDICINAL PLANTS USED FOR PREVENTION AND TREATMENT NEURODEGENERATIVE DISEASES: A REVIEW

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ABSTRACT: Amyotrophic lateral sclerosis (ALS), Parkinson's disease, Alzheimer's disease, and Huntington's disease occur as a result of the neurodegeneration process. No specific treatment was found to reduce or stop neurodegenerative diseases. In conventional medicine, many plants have been used to treat neurodegenerative diseases. Natural products play an important role in the prevention and treatment of various neurodegenerative diseases, as well as neuronal dysfunction. Different studies suggest that natural products, such as polyphenolic and plant-separated alkaloids, may delay neurodegeneration and improve memory and cognitive function. Ethnopharmacological studies have provided data to identify potential new drugs in plant sources. Recently many drugs found in medicines have been isolated from plants or their origin, including anticholinesterase (Anti-ChE) isolated plant alkaloids that have been investigated in terms of their potential in the treatment of Alzheimer's disease (AD). The anti-inflammatory and antioxidant activities of plants and soluble components of plants are used to improve inflammation, anxiety, seizures, and more. Medicinal plants have beneficial properties due to the presence of complex chemical compounds to treat toxins in the nervous system. This review article explored the use of medicinal plants to treat neurodegenerative diseases.

INTRODUCTION: Neurodegeneration is the progressive loss of the neuron structure or functions in the brain. Neurons are the building blocks of the nervous system which include the brain and spinal cord. Neurons normally don't replicate or restore themselves, so when they become injured or die they cannot be replaced by the body. Many neurodegenerative diseases are caused by a genetic mutation, protein misfolding, protein degradation pathway, membrane damage, mitochondrial dysfunction.

Neurodegenerative diseases including amyotrophic lateral sclerosis (ALS), Parkinson's disease, Alzheimer's disease, and Huntington's disease (HD) occurs as a result of neurodegeneration process ^{1,2}. Alzheimer's disease (AD) has been hypothesized to be a protein misfolding disease caused by an accumulation of abnormally folded A-beta and tau proteins in the brain characterized by loss of neurons and synapses in involving the basal forebrain cholinergic system, amygdala, hippocampus, and several cortical areas.

Alzheimer's disease is the most common form of dementia. Alzheimer's disease develops differently for every individual. The most common symptoms are difficulty in remembering recent events, known as short-term memory loss. As the disease advances symptoms can include confusion, irritability,

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aggression, mood swings trouble with language and long term memory loss progressively bodily functions are lost finally leading to death. Most of the autosomal dominant familial Alzheimer's disease can be attributed to mutations in one of three genes those encoding amyloid precursor protein (APP) presenilins³. Alzheimer's disease (AD) affects approximately 5.4 million people in the United States, with its prevalence expected to increase dramatically over the next 20 years.

Currently, about 34 million people worldwide have Alzheimer's disease, and lifestyle factors that are modifiable in principles, such as physical inactivity and obesity are associated with a heightened risk for Alzheimer's disease. There is no cure for Alzheimer's disease, and there are no accessible treatments that stop or reverse the succession of the disease⁴. Accessible treatments offer relatively small symptomatic advantage but remain palliative in nature. Donepezil, Galantamine, Tacrine, Rivastigmine, Memantine, Piracetam. etc., are some drugs available for the treatment of Alzheimer's disease. Some medicinal plants also available for it, having neuroprotective activity⁵. Huntington's disease (HD) is a rare inherited progressive neurodegenerative disorder resulting caused by a single mutation in the gene those codes for the protein Huntingtin. HD is primarily characterized by selective neuronal loss, primarily in the cortex and striatum, cognitive abnormality, psychiatric deterioration, and loss of medium spiny neurons. Nrf2 is the redox-sensitive transcription factor necessary for the synthesis of glutathione a natural antioxidant that play an imperative role in HD. BDNF also plays a significant role in the survival and activity of the neurons that die in Huntington's disease⁶.

The incidence of HD is much higher in European populations than in East Asia. Presently, the Maracaibo region of Venezuela has the uppermost reported worldwide prevalence at 700 cases per 100,000 people. There is no cure for Huntington's disease but different symptomatic drugs are available for it. Hence enormous progress has been made in laboratories throughout the world. There are diverse drugs that may become treatments that can relieve some symptoms and, in some, improve the quality of life in Huntington's disease. Novel advancement also takes place as the use of

genetically altered stem cells. Different models are available for Huntington's disease like excitotoxic models, genetic models, metabolic models^{7,8}.

Parkinson's disease (PD) is the second most chronic progressive neurodegenerative disorder characterized by the clinical feature are resting tremor, bradykinesia, rigidity and postural instability caused by early prominent death of dopaminergic neurons in the *Substantia nigra* pars compacta (SNpc) and widespread occurrence of alpha-synuclein (aSyn), an intracellular protein. PD is also related to non-motor symptoms, which may lead to motor symptoms by more than a decade. These non-motor symptoms become difficult symptoms in the later stages of PD⁹. The incidence and prevalence of PD increase with advancing age, with a prevalence of 160/ 100000 in Europe rising to 4% of the population over 80. Currently, the mainstay of PD management is pharmacological therapy; however, these symptomatic therapies have the most important limitations in advanced disease. Numerous disabling features increase later in the course of the disease, including non-motor symptoms, dopamine resistant motor symptoms, and motor complications of long-term dopamine therapy. Although there have been significant advances in the medical and surgical treatment for PD, ultimate disease-modifying therapy is lacking. However, researchers are optimistic that they will be able to identify the potential targets for disease modification^{10,11}.

Amyotrophic lateral sclerosis (ALS) is an adult-onset fatal devastating neurodegenerative disease that results in progressive obliteration of neurons of the spinal cord and motor neurons of the cortical brain leading to fatal paralysis. Patients typically die from respiratory failure within 3 years of symptom onset. The incidence of ALS in Europe is 2–3 cases per 100,000 individuals in the general population, and the generally lifetime risk of developing the disease is 1:400. ALS is familial in 5% of cases and shows a Mendelian pattern of inheritance¹². ALS is recognized to overlap with front temporal dementia. Multiple cell types and mechanisms are likely involved in ALS pathogenesis, which makes the progress of conventional drug therapies difficult. The cause of ALS is not yet elucidated; however, mutations in genes SOD1, C9orf72, TDP-43, FUS/TLS,

angiogenin, and others have been associated with ALS. Riluzole remains the only efficient drug and extends the average survival of patients by 3–6 months. Optimal treatment is based on symptom organization and protection of the quality of life,

provided in a multidisciplinary setting. The discovery of further successful disease-modifying therapies remains a critical need for patients with this devastating condition¹³.

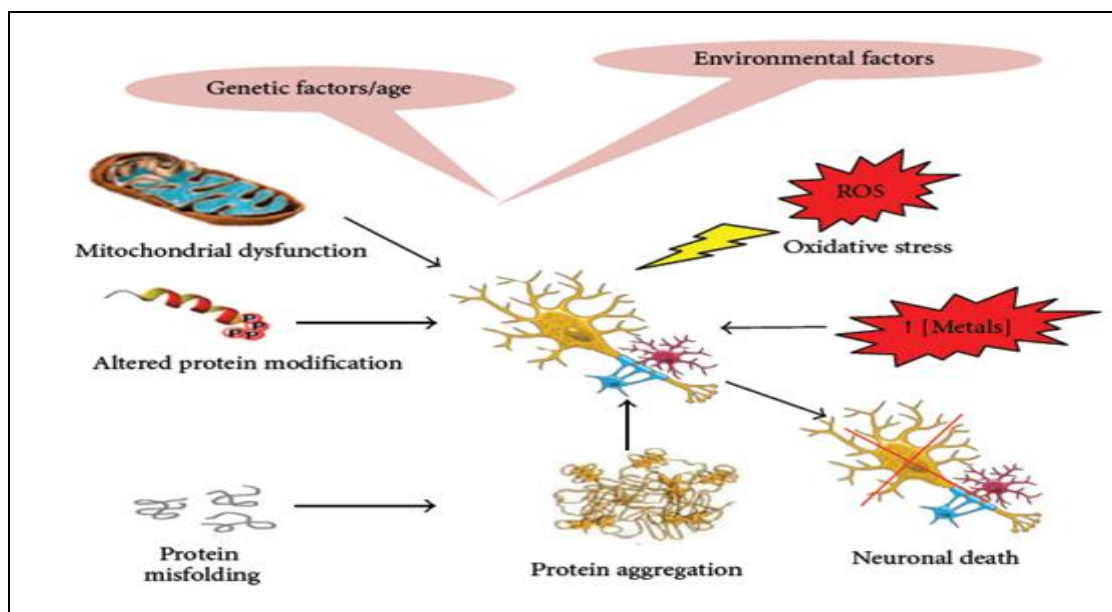


FIG. 1: DIFFERENT FACTOR ASSOCIATED WITH NEURODEGENERATIVE DISEASE

There is no drug to cure neurodegenerative diseases, but in Ayurveda, there are such remedies that slow down the disease. Ayurveda system is one of the world's oldest medical systems. It originates in India more than 3000 years ago and remains one of the country's traditional health care systems. Its concepts about health and disease are to promote the use of herbal compounds, to eliminate the root cause of the disease by restoring balance and also prevent the recurrence of the imbalance¹⁴. Herbal medicine has existed world with the long recorded history and they were used in ancient Chinese, Greek, Egyptian and Indian medicine for various therapies purposes. The world health organization (WHO) estimated that 80% of the world's population still uses herbal medicines

for their health care. In Ayurveda, single or multiple herbs are used for the treatment. The Ayurveda literature „Sarangdhar Samhita“ dominates the concept of polyherbalism to achieve greater therapeutic efficacy. According to Ayurveda, neuro-degenerative disease is an imbalance of Vata Pitta and Kapha¹⁵. It was found that herbal medicinal drugs have great importance for the treatment of various diseases. It was also found that out of total medicinal drugs, 50% are natural in origin also, according to Ayurveda, there is great importance to natural drugs¹⁶. In the present review study, it was aimed to highlight the following information of different plants are useful in the treatment of neurodegenerative diseases like AD, PD, HD and ALS.

TABLE 1: LIST OF MEDICINAL PLANT USE IN TREATMENT OF NEURODEGENERATIVE DISEASES

S. no.	Plant Name	Family	Part Used	Use in neurodegenerative diseases	Ref.
1	<i>Acanthopanax senticosus</i> Harms	Araliaceae	Leaves	PD, AD	17, 18
2	<i>Acorus Calamus</i>	Acoraceae	Dried Rhizome	AD, PD	19,20
3	<i>Aframomum melegueta</i> K. Schum	Zingiberaceae	Seed	AD	21
4	<i>Allium sativum</i>	Amaryllidaceae	Rhizome	PD	22
5	<i>Alpinia Officinarum</i>	Zingiberaceae	Rhizome	AD	22
6	<i>Alpinia galangal</i>	Zingiberaceae	Rhizomes	AD	24
7	<i>Angelica sinensis</i>	Umbelliferae	Root	AD, PD	25, 26, 27
8	<i>Artemisia vulgaris</i>	Asteraceae	Leaves	AD	28
9	<i>Bacopa Floribunda</i> wetts.	Scrophuliaceae	Aerial parts	AD	29, 30, 31

10	<i>Bacopa Monnieri</i>	Plantaginaceae	Aerial parts	HD, PD AD	32, 33, 34
11	<i>Bergenia ciliata</i>	Saxifragaceae	Rhizome	AD	35, 36
12	<i>Calendula Officinalis</i>	Asteraceae	flower	HD, AD	37,38
13	<i>Camellia sinensis Kuntze</i>	Theaceae	Leaves	HD, AD, PD	39, 40
14	<i>Carica papaya Linn</i>	Caricaceae	Leaves and root	AD	41
15	<i>Cassia obtusifolia</i>	Fabaceae	Seed	PD, AD	42, 43
16	<i>Cassia occidentalis</i>	Fabaceae	Seed	HD, AD	44, 45
17	<i>Celastrus Paniculatus</i>	Celastraceae	Seed Oil	HD, AD	46, 47
18	<i>Centella Asiatica</i>	Apiaceae	Aerial Parts	AD, HD	48, 49
19	<i>Chaenomeles speciosa</i>	Rosaceae	Fruit juice	PD, AD	50, 51
20	<i>Chrysanthemum morifolium Ramat</i>	Asteraceae	Flower	PD	52
21	<i>Citrus sinensis</i>	Rutaceae	Fruit	PD, AD	53
22	<i>Cocos nucifera Linn</i>	Arecaceae	Fiber	AD	54, 55
23	<i>Coffea Arabica L.</i>	Rubiaceae	Seeds	AD, PD	56, 57, 58
24	<i>Cola acuminata</i>	Sterculiaceae	seeds	AD	59, 60
25	<i>Convolvulus pluricaulis</i>	Convolvulaceae	Root	AD, HD	61, 62
26	<i>Crataegus pinnatifida</i>	Rosaceae	Fruits	AD, PD	63, 64
27	<i>Crocus Sativus</i>	Iridaceae	Dried stigma and Part of the style	AD, PD	65, 66
28	<i>Curcuma longa</i>	Zingiberaceae	Rhizome	AD, PD	67, 68, 69
29	<i>Dalbergia Sissoo</i>	Fabaceae	Leaves	HD, AD	70, 71
30	<i>Detarium Microcarpum Guill</i>	Caesalpiniaceae	Fruits	AD	72, 73
31	<i>Elaeis guineensis Jacq.</i>	<u>Arecaceae</u>	Fruits	AD	74
32	<i>Elettaria cardamomum</i>	Zingiberaceae	Dried seeds, Oil	AD	75
33	<i>Evolvulus Alsinoideslin</i>	Convolvulaceae	Whole plant	AD	76, 77
34	<i>Ficus capensis Thunb</i>	Moraceae	Leaves	AD	78,79
35	<i>Ficus religiosa Linn</i>	Moraceae	Leaves	HD, PD, AD	80, 81, 82
36	<i>Galanthus nivalis</i>	Amaryllidaceae	Crude drug	AD	83
37	<i>Garcinia kola Heckel</i>	Clusiaceae	Seed	HD, AD, PD	84, 85, 86
38	<i>Gastrodia elata blume</i>	Orchidaceae	Root	AD, PD	87, 88
39	<i>Ginkgo Biloba</i>	Ginkgoaceae	Leaves	AD, PD	89, 90
40	<i>Huperzia serrata</i>	Lycopodiaceae	moss	AD, PD	91, 92
41	<i>Hypericum perforatum</i>	Clusiaceae	Root	AD, PD	93, 94
42	<i>Ilex paraguariensis</i>	Aquifoliaceae	Leaves	AD, PD	95, 96, 97
43	<i>Indigo naturalis</i>	Apiaceae	Plant based powder	AD	98
44	<i>Lavandula angustifolia</i>	Lamiaceae	Aerial part, Oil	PD, AD	99, 100
45	<i>Lawsonia inermis Linn.</i>	Lythraceae	Leaves	AD	101
46	<i>Lipidium Meyenii Walp.</i>	Brassicaceae	Dried Hypocotyls	AD, PD	102, 103
47	<i>Luehea Divaricata Mart.</i>	Malvaceae	Leaves	HD, AD	104, 105
48	<i>Lycium Barbarum</i>	Solanaceae	Berries	AD, PD	106, 107
49	<i>Lycopersicon esculentum</i>	Solanaceae	fruits	PD, AD	108, 109
50	<i>Lycoris chejuensis</i>	Amaryllidacea	Whole plant	AD	110
51	<i>Lycoris longituba Linn.</i>	Amaryllidaceae	Whole plant	AD	111
52	<i>Magnolia Officinalis Rehd</i>	Magnoliaceae	Bark	AD, PD	112, 113, 114
53	<i>Melissa officinalis</i>	Lamiaceae	Aerial part	PD, AD	115, 116
54	<i>Monordica Charantia</i>	Cucurbitaceae	Fruits	HD, PD, AD	117,118,119
55	<i>Morinda Citrifolia</i>	Rubiaceae	Fruits	HD, AD	120,121
56	<i>Morus alba</i>	Moraceae	Whole Plant	PD, AD	122,123
57	<i>Mucuna pruriens</i>	Fabaceae	Seeds	PD, AD	124, 125
58	<i>Musa Sapiantum linn.</i>	Musaceae	Stem	AD	126, 127
59	<i>Myristica fragrans</i>	Myristicaceae	Seed kernel	AD	128
60	<i>Narcissus confuses</i>	Amaryllidacea	Crude drug	AD	129
61	<i>Nardostachys jatamansi</i>	Valerianaceae	Whole plant	AD, PD	130, 131
62	<i>Nicotiana tabaccum</i>	Solanaceae	Leaves	AD, PD	132, 133
63	<i>Nigella sativa</i>	Ranunculaceae	Seed Oil	PD, AD	134, 135, 136
64	<i>Panax ginseng</i>	Araliaceae	Roots	AD, HD, PD	137, 138, 139, 140
65	<i>Petroselinum crispum</i>	Umbelliferae	Leaves, root, stem	AD	141, 142
66	<i>Physostigma vennosam Balf</i>	Leguminosae	Beans	AD	143
67	<i>Picralima nitida Staff</i>	Apocynaceae	Fruits and seeds	AD	144
68	<i>Piper betel Linn</i>	Piperaceae	Leaf	AD,	145
69	<i>Piper methysticum frost</i>	Piperaceae	Whole plant	AD, PD	146, 147, 148

70	<i>Plumbago scandens</i>	Plumbaginaceae	Whole plant	PD	149
71	<i>Polygala tenuifolia wild</i>	Polygalaceae	Rhizome	AD, PD	150, 151
72	<i>Polygonum cuspidatum</i>	Polygonaceae	Roots	PD, AD	152, 153
73	<i>Portulaca oleracea</i>	Portulacaceae	Seed	PD, AD	154, 155
74	<i>Prunus dulcis</i>	Rosaceae	Nuts	PD, AD	156, 157
75	<i>Psoralea corylifolia</i>	Fabaceae	Fruits	HD, AD	158, 159
76	<i>Pueraria thomsonii</i>	Fabaceae	Roots	PD, AD	160, 161
77	<i>Puwraria tuberosa Roxb.</i>	Fabaceae	Tubers	AD	162
78	<i>Quassia undulata</i>	Simaroubaceae	Leaves	AD	163
79	<i>Rhizoma acori tatarinowii</i>	Araceae	Leaf	AD, PD	164, 165
80	<i>Rice Bran</i>	Poaceae	Oil	HD, PD, AD	166, 167, 168
81	<i>Ricinus communis Kinn.</i>	Euphorbiaceae	Beans	AD	169
82	<i>Rosa Canina</i>	Rosaceae	Berries	AD	170, 171
83	<i>Rosmarinus officinalis</i>	Lamiaceae	Leaves	AD, PD	172, 173, 174
84	<i>Rubus Idaeus</i>	Rosaceae	Berries	AD	175, 176
85	<i>Saffron crocus</i>	Iridaceae	Stigmas	AD, PD	177, 178
86	<i>Salvia Officinalis</i>	Lamiaceae	Leaves	AD	179
87	<i>Salvia miltiorrhiza Bunge</i>	Lamiaceae	Rhizome	AD, PD	180, 181
88	<i>Schisandra chinensis (Turcz.)</i>	Schisandraceae	Fruit	AD, PD	182, 183
89	<i>Scoparia dulcis L</i>	Scrophulariaceae	Leaves	AD	184, 185
90	<i>Scutellaria baicalensis Georgi</i>	Lamiaceae	Roots	AD, PD	186, 187
91	<i>Senecio abyssinicus</i>	Asteraceae	Aerial parts	AD	188
92	<i>Sesame indicum</i>	Pedaliaceae	Seeds	PD	189, 190
93	<i>Silybum Marianum</i>	Asteraceae	Seeds	AD, PD	191, 192
94	<i>Solanum incanum L</i>	Solanaceae	Leaves, Fruits	AD	193
95	<i>Solanum xanthocarpum</i>	Solanaceae	Fruits	ME, AD	193
96	<i>Spondias mombin L</i>	Anacardiaceae	Leaves	AD	194
97	<i>Terminalia chebula linn</i>	Combretaceae	Rhizome	AD	119
98	<i>Tetrapleura Tetraptera</i>	Mimosaceae	Fruits	AD	195
99	<i>Thuja orientalis</i>	Cupressaceae	Fruits	PD, AD	196, 197
100	<i>Tinospora Cordifolia</i>	Menispermaceae	Whole plant	AD, PD	198, 199
101	<i>Trifolium pretense</i>	Leguminosae	Flower heads	PD, AD	200, 201
102	<i>Tripterygium Wilfordii Hook F</i>	Celastraceae	Whole plant	PD, AD	202, 203
103	<i>Uncaria rhynchophylla</i>	Rubiaceae	Whole plant	PD, AD	204, 205
104	<i>Uncaria tomentosa Willd</i>	Rubiaceae	Aerial parts	PD, AD	206
105	<i>Uraria Picta (Jacq.)</i>	Leguminosae,	Stem	AD	207
106	<i>Vanilla planifolia</i>	Orchidaceae	Seed	AD, PD, HD	208
107	<i>Vicia faba</i>	Fabaceae	Seed	PD	209, 210, 211
108	<i>Vinca minor</i>	Apocynaceae	Aerial part	AD	212
109	<i>Vitis Vinifera</i>	Vitaceae	Fruit	AD, PD	213, 214
110	<i>Vitis vinifera Linn.</i>	Vitaceae	Seed	AD	215
111	<i>Withania Somnifera</i>	Solanaceae	Roots	HD, PD	216, 217,
112	<i>Zingibar Officinale Roscoe</i>	Zingiberaceae	Rhizomes	AD, HD, PD	218, 219, 220,

Note: - AD – Alzheimer’s disease, PD - Parkinson’s disease, HD- Huntington’s disease

CONCLUSION: Neurodegenerative diseases appear to share several common multifactorial degenerative processes that contribute to neuronal death, leading to functional impairments in the fields of AD, PD, HD, and ALS. No treatment is available to slow or stop neurodegenerative diseases like AD, PD, HD, and ALS. The Food and Drug Administration has approved five drugs that temporarily improve symptoms. The effectiveness of these drugs varies crossways the population. None of the treatments available today alters the underlying path of this terminal disease. Plant-derived bioactive compounds, also of directly being developed as drugs. Natural products will continue to be enormously significant as sources of

medicinal agents. Thus natural products have emerged as promising hope in the drug discovery programs in neurodegenerative diseases. In the future, more emphasis should be given to finding new targets for neurodegenerative disease therapies. Targets for new neurodegenerative diseases therapies to be emphasized include preventing building up of amyloid plaques, preventing building up of paired helical segments and preventing brain cell dysfunction and death. In this paper, we reviewed various medicinal plants which show the use of neurodegenerative diseases treatment were collected from the different investigations and were reported above as we can say these medicinal plants are responsible for

treating neurodegenerative diseases like AD, PD, HD, and ALS under several investigators studied.

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