WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 6.041
Volume 5, Issue 5, 580-595 Review Article ISSN 2278 – 4357

A REVIEW ON PARKINSON'S DISEASE

Zeenath Banu*, Azra Fatima, Sarwar Fatima, Syeda Fatimuz Zohra, Tabassum Sultana

*Assistant Professor, Shadan Women's College of Pharmacy, Khiartabad, Hyderabad.

Article Received on
11 March 2016,
Revised on 01 April 2016,
Accepted on 21 April 2016
DOI: 10.20959/wjpps20165-6741

***Corresponding Author**
Zeenath Banu
Assistant Professor,
Shadan Women's College of Pharmacy, Khiartabad, Hyderabad.

ABSTRACT

Parkinson's disease, first described by James Parkinson in 1817, is a neurodegenerative ailment resulting from the damage of nerve cells in the brain. It is a chronic, progressive, neurodegenerative disorder with an estimated prevalence of 31 to 328 per 100,000 people worldwide. It is estimated that more than 1 percent of the population over age 65 are afflicted with Parkinson's disease; incidence and prevalence increase with age. There are numerous unanswered questions regarding the diagnosis and management of Parkinson's disease. Worsening mobility, causing problems with activities of daily living, pain and communication problems due to rigidity of facial muscles, are the main reasons of their decreasing quality of life. This study is focused on the role of psychological variables, which could be associated with quality of life in PD patients. After their identification a discussion about opportunities of improvement patient's quality of life can be opened. Current drug therapies for human PD with Levodopa or various dopamine receptor agonists offer symptomatic relief and appear to have little effect on the neurodegenerative process. More than 50% of patients with PD treated over 5 years with Levodopa will develop complications such as motor fluctuations and dyskinesia's. In this scenario, slowing the progression of PD through neuroprotective or restorative therapy is a major focus of research. From a pharmacologic standpoint, current strategies involve interrupting the cascade of biochemical events that leads to death of dopaminergic cells. The significance of many indigenous medicinal plants and their phytoconstitutents in the management of Parkinsonism with minimal side effect profile arise in this context.

KEYWORDS: Parkinson's disease, Dopamine, Lewy bodies.

INTRODUCTION

Parkinsonism is a clinical syndrome consisting of four cardinal features: bradykinesia (slowness and poverty of movement), muscular rigidity, resting tremor (which usually abates during voluntary movement), and an impairment of postural balance leading to disturbances of gait and falling (Lang, 1998). The most common cause of Parkinson's disease is idiopathic PD, first described by James Parkinson in 1817 as *paralysis agitans*, or the "shaking palsy."

The pathological hallmark of PD is a loss of the pigmented, dopaminergic neurons of the substantia nigra pars compacta, with the appearance of intracellular inclusions known as *Lewy bodies* (Gibb, 1992; Fearnley and Less, 1994). Progressive loss of dopamine-containing neurons is a feature of normal aging; however, most people do not lose the 70% to 80% of dopaminergic neurons required to cause symptomatic PD. Without treatment, PD progresses over 5 to 10 years to a rigid, akinetic state in which patients are incapable of caring for themselves**.** Death frequently results from complications of immobility, including aspiration pneumonia or pulmonary embolism. The availability of effective pharmacological treatment has altered radically the prognosis of PD; in most cases, good functional mobility can be maintained for many years, and the life expectancy of adequately treated patients is increased substantially. [1]

EPIDEMIOLOGY

Parkinson disease is recognized as one of the most common neurologic disorders, affecting approximately 1% of individuals older than 60 years. The incidence of Parkinson disease has been estimated to be 4.5-21 cases per 100,000 populations per year, and estimates of prevalence range from 18 to 328 cases per 100,000 1222wpopulations, with most studies yielding a prevalence of approximately 120 cases per 100,000 populations.[2]

ETIOLOGY

- **Dopamine:** When dopamine levels decrease, it causes abnormal brain activity, leading to signs of Parkinson's disease.
- **Aging:** aging causes defective electron transfer in mitochondria. Hence, Parkinsonism mostly occurs in individual above 60years of age.
- **Genes:** Certain gene variations appear to increase the risk of Parkinson's disease but with a relatively small risk of Parkinson's disease for each of these genetic markers.

- **Environmental triggers:** Exposure to certain toxins or environmental factors may increase the risk of later Parkinson's disease, but the risk is relatively small. These changes include:
- **Neurotoxins:** A synthetic neurotoxin agent called MPTP can also cause immediate and permanent Parkinsonism. The compound was discovered in the 1980s in individuals who injected themselves with a synthetic form of heroin contaminated with MPTP.
- **The presence of Lewy bodies:** Clumps of specific substances within brain cells are microscopic markers of Parkinson's disease. These are called Lewy bodies, and researchers believe these Lewy bodies hold an important clue to the cause of Parkinson's disease.
- **Alpha-synuclein is found within Lewy bodies.** Although many substances are found within Lewy bodies, scientists believe an important one is the natural and widespread protein called alpha-synuclein (A-synuclein). It's found in all Lewy bodies in a clumped form that cells can't break down. This is currently an important focus among Parkinson's disease researchers.
- **Free radicals:** Production of free radicals such as hydroxyl and peroxynitrite in the metabolism of neurotransmitters. These free radicals damage brain cells and reduce dopamine levels. [3]

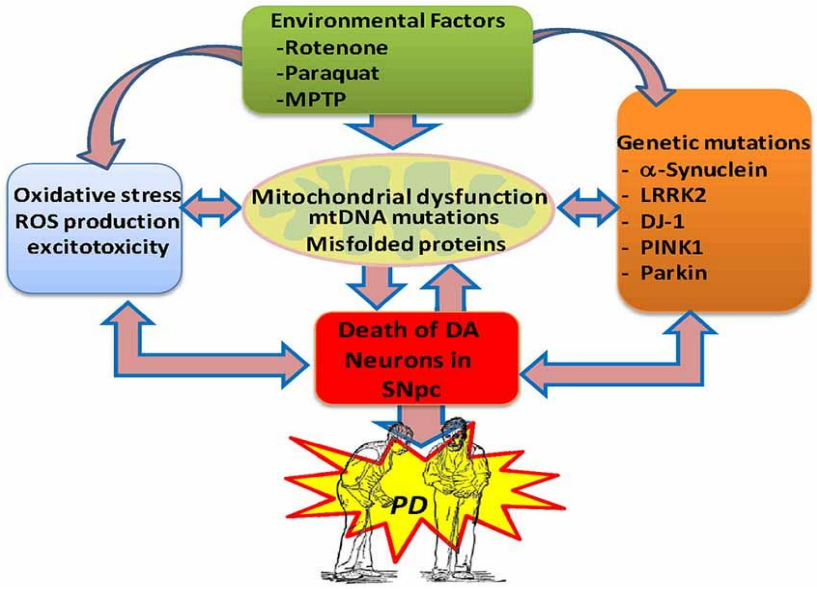

Fig 01: Etiology of Parkinsonism

ANATOMY OF BASAL GANGLIA (HUMAN BRAIN)

The extrapyramidal system consists of a series of functionally related nuclei in the telencephalon, diencephalon and midbrain. The basal ganglia represent the largest component, and include the caudate, putamen and globus pallidus. The pars reticulata and pars compacta of the substantia nigra of the midbrain as well as the subthalamic nucleus, which is located in the caudal diencephalon are functionally connected to this system. [4]

The extrapyramidal system has historically been viewed as a part of the motor system, since damage to these areas affect muscle tone, posture, and voluntary movements and can also produce abnormal movements. It has become increasingly clear that this system is also used for control of behavioural "tone" and emotional "posture" of the animal as a whole

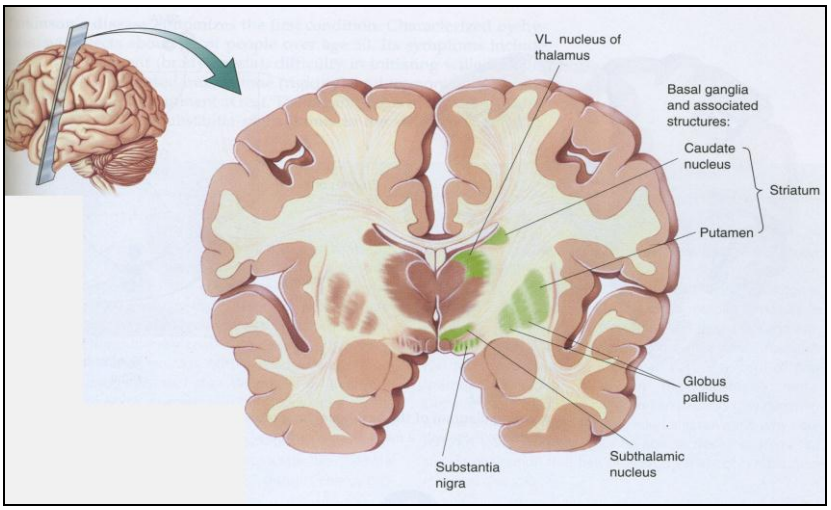

Fig 02: Basal Ganglia

NEURO CHEMISTRY OF BASAL GANGLIA

Neurotransmitters

The most well recognized transmitter of the circuitry in midbrain is dopamine (DA), released at the terminals of the nigrostriatal projections in the striatum. According to the classical concept, DA is inhibitory to striatal neurons. However the newer scheme of connections of basal ganglia predicts that DA, in addition to its known inhibitory effect, it also excitatory to a subset of striatal neurons that project to the medial globus pallidus and substantia nigra pars reticulate. Other neurotransmitter used by the circuitry includes the excitatory neurotransmitter glutamate and the inhibitory neurotransmitter, GABA.

The striatum also contains cholinergic “interneurons” that release acetylcholine and activate GABA containing inhibitory neurons that project to the pallidum. It is believed that these interneurons are also under the inhibitory influence of DA release at the endings of the nigrostriatal pathway.

Dopamine metabolism

Dopamine is one of the three catecholamine neurotransmitter in the brain, the others being noradrenaline and adrenaline. Dopamine is metabolized by two enzymes, catechol-O-methyl transferase (COMT) and mono amino oxidase-B (MAO-B). Newly synthesized DA is taken up into the storage vesicles and transported to the axon terminals of nigrostriatal pathway. It is released by sodium mediated, calcium-dependent mechanisms. [4]

PATHOPHYSIOLOGY OF PARKINSON’S DISEASE

The basal ganglia represent a system of several discrete collections of neurons within the brain. The term "basal ganglia" encompasses several separate, but interrelated neuron populations. The putamen, caudate, Globus Pallidus Internus (GPI), Globus Pallidus Externus (GPE), substantia nigra (SN), and Subthalamic Nucleus (STN) are all discrete neuron populations that, as a whole, compose the "basal ganglia". These named populations of neurons work together to achieve a common goal. The term "striatum" includes the caudate and putamen only, and the term "lentiform nuclei" includes the putamen and globus pallidus. The basal ganglia modulate movement through a complex loop of inhibitory and excitatory signals.

Direct Pathway

When we decide to move, our frontal lobes send an excitatory signal via the neurotransmitter glutamate to the striatum (i.e.: caudate and putamen).The neurons in the striatum then send an inhibitory signal to the globus pallidus internus (GPi) and the substantia nigra pars reticulata (SNPR). As a result, GPi and SNPR are no longer able to inhibit the thalamus, which is their normal "resting" function. The thalamus now finds itself "un-inhibited", or "dis-inhibited", and is able to send a message back to the cortex saying it is "ok" to allow the desired movement to occur. The motor cortex then sends a message down the spinal cord causing the desired movement. Dopamine is secreted by a different part of the substantia nigra known as the "pars compacta". These neurons secrete dopamine onto specific cells in the striatum. The dopamine interacts with the D1 (dopamine-1) receptors on these cells causing them to become more active (i.e.: dopamine has a stimulatory effect via the D1 receptor).

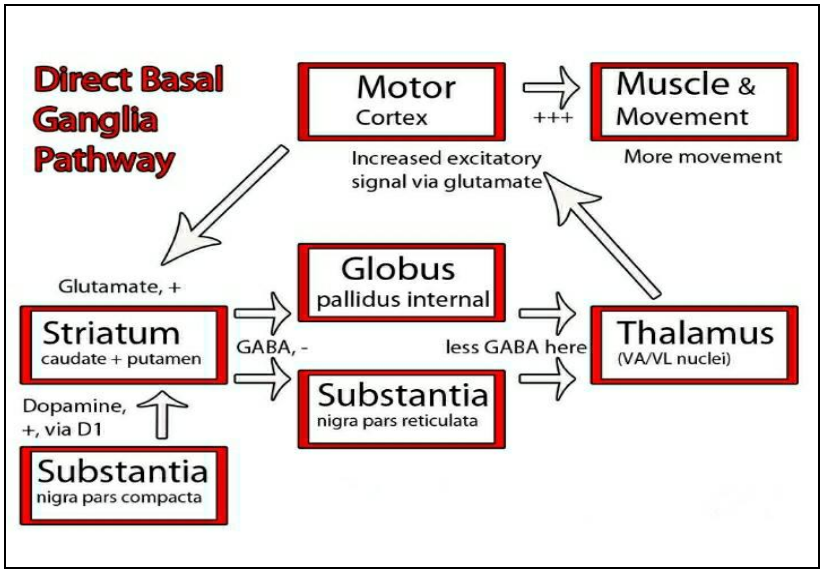

Fig 03: Direct Pathway

Indirect Pathway

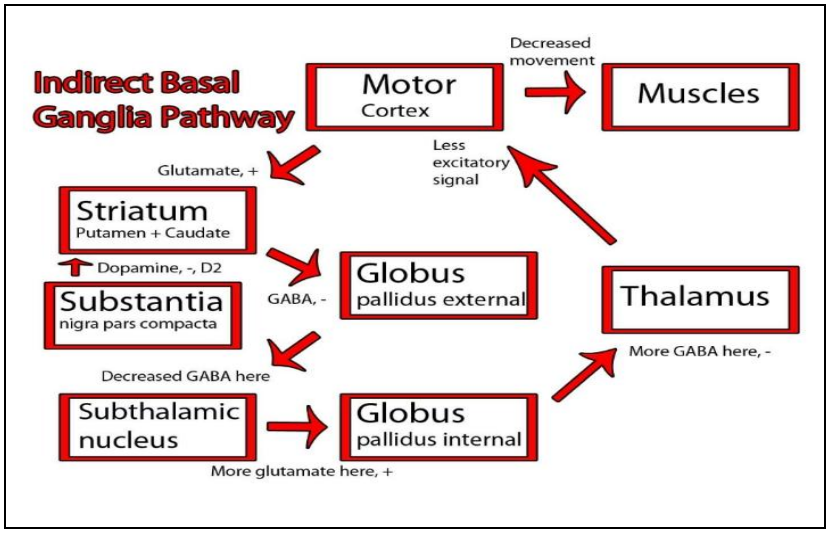

Fig 04: Indirect Pathway

In the indirect basal ganglia pathway the striatum then sends an inhibitory signal via the neurotransmitter GABA to the external segment of the globus pallidus. This is different from the direct pathway where the striatum sends a signal to the internal segment of the globus pallidus. The external segment of the globus pallidus normally indirectly inhibits its internal counterpart. Thus, when the striatum inhibits the external segment, it is, in effect, releasing the internal segment from inhibition. At this point, the internal segment of the globus pallidus is able to send its inhibitory signals to the thalamus, which causes thalamic neurons to stop sending excitatory signals to the motor cortex. The cortex is then unable to send an impulse down the spinal cord and, ta-da, the net result is a decrease in movement. It would be slightly

easier to understand if the external segment of the globus pallidus "talked" directly to the internal segment, but that is not how it works. The message is relayed through another nucleus known as the subthalamic nucleus. The subthalamic nucleus is usually inhibited by the external segment of the globus pallidus. Therefore, when the striatum inhibits the external globus pallidus, it causes the cells in the STN to become more active (i.e.: the STN is released from the inhibitory effects of the external globus pallidus).The sub thalamic nucleus, in turn, is able to send an excitatory signal to the neurons in the internal segment of the globus pallidus. The cells in GPi then become more active, which means that they suppress the activity of the thalamus more robustly. The thalamus is then unable to send its normal excitatory messages to the motor cortex. When the basal ganglia malfunction it causes unwanted movements, or a failure to initiate movements. The classic basal ganglia disease is Parkinson's disease, which has elements of both unwanted movements (resting tremors) and difficulty initiating movement (bradykinesia).[5]

TYPES OF PARKINSON'S DISEASE

I. Primary (Idiopathic) Parkinson's Disease

Idiopathic Parkinson's disease - or Parkinson's - is the most common type of Parkinson's disease. Unlike some other forms which have specific causes it is not known why idiopathic Parkinson's occurs. Idiopathic means that the cause is unknown. The main symptoms of idiopathic Parkinson's are tremor, rigidity and slowness of movement.

II. Secondary (Drug-Induced) Parkinson's Disease

A small number (around 7%) of people diagnosed with Parkinson's disease have developed their symptoms following treatment with particular medication. Drugs - known as neuroleptic drugs - used to treat schizophrenia and other psychotic disorders block dopamine. These drugs are thought to be the biggest cause of drug-induced Parkinsonism. Dopamine is a chemical in the brain which allows messages to be sent to the parts of the brain that co-ordinate movement. The symptoms of Parkinson's appear when the level of dopamine falls. The symptom of drug-induced Parkinsonism tends to be static. Only in rare cases do they change in the manner that the symptoms of Parkinson's do.[6]

III. Vascular Parkinson's Disease

Vascular Parkinson's disease is one of the atypical forms of Parkinson's disease. It affects people with restricted blood supply to the brain, usually older people who have problems

with diabetes. People who have had a stroke may experience vascular Parkinson. Symptoms include difficulty speaking, making facial expressions or swallowing.

IV. Inherited Parkinson's Disease

There is no conclusive evidence that Parkinson's is a hereditary condition that can be passed on within families, apart from in exceptionally rare cases. It is thought that although it is not directly inherited, some people may have genes that increase the possibility of developing Parkinson's.

V. Juvenile Parkinson's Disease

Juvenile Parkinson's is a term used when the condition affects people under the age of 20. [6]

CLINICAL MANIFESTATIONS

The distribution of age at onset of PD assumes a bell shaped curve. Symptoms usually appear after the age of 50. The mean age at onset is 55-75 years in both sexes. The young are no except and onset before age of 30 does not preclude a diagnosis of PD.

The symptoms are:

I. MOTOR SYMPTOMS

A. Cardinal Symptoms

- **Tremor:** Tremor is defined as rhythmic oscillation of a body part. There are more than 20 kinds of tremor. The most useful distinction is between resting and action tremors. Rest tremor occurs when a body part, such as hand is not in use. Typical rest tremor has frequency of 3 to 6 cps and will disappear with any movement.
- **Rigidity:** Stiffness, increased muscular tone. In combination with resting tremor, this produces ratchety, “cog wheel” rigidity when the limb is passively moved
- **Bradykinesia/Akinesia**: Respectively, slowness or absence of movement.
- **Postural instability**: Failure of postural reflexes, which leads to impaired balance and falls.[7]

B. Other Motor Symptoms

- Gait and posture disturbance
- Shuffling.
- Decreased arm swing.
- Difficulty in turning head.

- Dystonia (In about 20% of cases) – Abnormal, sustain, painful twisting muscle contractions, usually affecting the foot and ankle.
- Fatigue (up to 50% cases).
- Masked faces, with infrequent blinking.
- Difficulty rolling in bed or raising from seated position.
- Micrographia (small, cramped hand writing).
- Impaired motor coordination.

C. Non – Motor Systems

- Mood disturbances:
- Cognitive disturbance:
- Sleep disturbances:
- Sensational disturbances [8]

DIAGNOSIS

There are currently no blood or laboratory tests that have been proven to help in diagnosis PD. Therefore the diagnosis is based on medical history and a neurological examination. The disease can be difficult to diagnose accurately. "The unified Parkinson's disease rating scale" is primary clinical tool used to assist in diagnosis and determine severity of PD. Indeed only 75% of clinical diagnosis of PD is confirmed at autopsy. Easy signs and symptoms of PD may sometimes be dismissed as the effects of normal aging. The physician may need to observe the person for some time until it is apparent that the symptoms are consistently present. Usually doctors look for shuffling of feet and lack of swing in the arms. Doctors may sometimes request brain scans or laboratory tests in order to rule out other diseases. However CT and MRI brain scans of people with PD usually appear normal, but PET scan shows decreased dopamine activity in basal ganglia, a pattern which aids in diagnosing Parkinson's disease.

Clinical stages: There are five clinical stages.

Stage 1- PD patients with unilateral signs (usually tremor and rigidity) have stage 1 disease, according to the staging system of Hoehn and Yahr (1967).

Stage 2- Bilateral symptoms and signs, in the absence of gait or balance problems, constitute stage 2 diseases.

Stage 3- Once patient develop unsteadiness of gait or being falling, they have stage 3 Parkinson's disease.

Stage 4- Stage 4 patients require assistance with ambulation (a cane, walker, or another person).

Stage 5- Patients are either wheel chair-bound or bed bound comes under stage.[9]

TREATMENT OF PARKINSONISM

Treatment approaches include medication, surgery, general lifestyle modifications (rest and exercise), physical therapy (UK: Physiotherapy), support groups, occupational therapy and speech therapy.[10, 11]

Drug Classification

I. Drugs Affecting Brain Dopamine Systems

Dopamine precursor:	Levodopa (DA does not cross BBB)
Peripheral decarboxylase inhibitors:	Carbidopa, Benserazide.
Dopaminergic agonist:	Bromocriptine, Pergolide, Piribedi, Ropinirole,
MAO-B inhibitors:	Seligiline.
COMT inhibitors:	Entacopone, Tolcapone.
Dopamine facilator:	Amantadine.

II. Drugs Affecting Brain Cholinergic System

Central anticholinergics:	Trihexyphenidyl, Procyclidine, Biperiden.

OTHER TREATMENTS

A. Surgical Procedures

Deep Brain Stimulation

In deep brain stimulation (DBS), surgeons implant electrodes into a specific part of your brain. The electrodes are connected to a generator implanted in your chest near your collarbone that sends electrical pulses to your brain and may reduce your Parkinson's disease symptoms. Deep brain stimulation is most often offered to people with advanced Parkinson's disease who have unstable medication (levodopa) responses. DBS can stabilize medication fluctuations, reduce or halt involuntary movements (dyskinesias), reduce tremor, reduce rigidity, and improve slowing of movement.

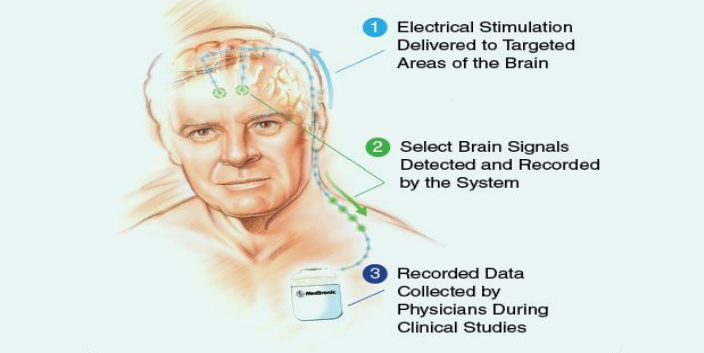

Fig 05: Deep Brain Stimulation

B. Maintaining A Healthy Life Style

Certain lifestyle changes may help make living with Parkinson's disease easier.

➢ Healthy Eating

Eating foods high in fibres and drinking an adequate amount of fluids can help prevent constipation that is common in Parkinson's disease. A balanced diet also provides nutrients, such as omega-3 fatty acids, that may be beneficial for people with Parkinson's disease.

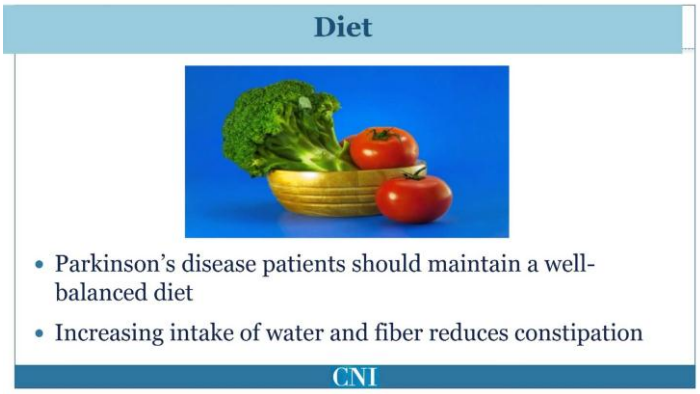

Fig 6: Diet

➢ Exercise

Exercising may increase your muscle strength, flexibility and balance. Exercise can also improve your well-being and reduce depression or anxiety.

C. NON PHARMACOLOGICAL TREATMENT

It includes the following:

- ➢ Education
- ➢ Support
- ➢ Exercise and physical therapy
- ➢ Speech therapy [11]

Table I: Plants With Anti Parkinsonism Activity.

S. No	Plant	Family	Plant Part Used	Extract	Animal Used	Model	Parameter	P Value	References
01	Gentisic Acid	_	_	_	Swiss Albino Mice	Haloperidol Induced Catalepsy	Cataleptic Behaivour	<0.01	M.P.Kabra et.al 2015
02	Elaenocarpus Ganitrus	Elaeocarpacaeae	Seeds	Ethanolic extract of Elaenocarpus Ganitrus seeds	Albino Mice	Rota Rot Method	Dyskinesis Activity	<0.001	Harish. G. Bagewadi et.al 2015
03	P.Zeylancia	Plumbaginaceae	Root	Hydroalcoholic extract of P.Zeylancia roots	Albino Wistar Rats	Haloperidol Induced Catalepsy	Dyskinesis Activity	<0.001	S.P.Ittiyavirah et.al 2014
04	Nelumbo Nucifera	Nelumbonaceae	Seeds	Methanolic extract of Nelumbo Nucifera seeds	Adult Wistar Rats	Haloperidol Induced Catalepsy	Catalepsy	<0.001	I.Pal et.al 2014
05	Nigella Sativa	Ranunculaceae	Seeds	Ethanolic extract of Nigella Sativa Seeds	Wistar Rats	Chlorpromazine Induced Experimental Animal Model	Catalepsy	<0.001	K.S.Sandhu et.al 2013
06	Ocimum Sanctum	Lamiaceae	Seeds	Aqeous extract of Ocimum Sanctum	Albino Mice	Haloperidol Induced Catalepsy	Catalepsy	<0.001	L.A.Latiff et.al 2012
07	Juniperus Communis	Cumessaceae	Leaves	Methanolic extract of Juniperus Communis	Wistar Rats	Chlorpromazine Induced Experimental Animal Model	Catalepsy, Muscule rigidity	<0.001	S.Bias et.al 2011
08	Mucuna Pruriens	Fabaceae	Seeds	Methanolic extract of Mucuna Pruriens	Albino Wistar Rats	Haloperidol Induced Catalepsy	Catalepsy	<0.001	J.G.Longhi et.al 2011
09	T.Cordifolia	Menispermieaceae	Seeds	Ethanolic extract of T.Cordifolia seeds	Wistar Rats	Haloperidol Induced Catalepsy	Dopamine Level, Oxidative stress	<0.001	J.Kosaraju et .al 2010
10	Phyllanthus Emlica	Euphorbiaceae	Seeds	Ethanolic extract of Phyllanthus Emlica seeds	Albino Mice	Chlorpromazine Induced Experimental Animal Model	Catalepsy	<0.001	S.Chanda et.al 2009
11	Glycrrhiza	Glycrrhiza uralensis	Roots and Rhizomes	Ethyl acetate	Swiss albino mice	Haloperidol In duced Catalepsy	Cataleptic behavior	<0.01	Alok batra et.al 2006

12	Dimeresculentin	Viola yedoensis	Dried whole plant	Acetate extract	Albino mice	Chlorpromazine Induced Experimental Animal Model	Dyskinesis activity	<0.001	Ashis Bhowmick et.al 2007
13	Polygala Radix	PolygalaTenuiolia	Roots	Dimethyl Thiazole	Albino rabbit Wilstar rat	Haloperidol Induced Catalepsy	Dyskinesis Ativity	<0.001	Basanta.K et.al2007
14	Gum Arabica	Senegalin senega	Gum layer	Polyvinyl Acetate	Adult wilstar rat	Haloperidol Induced Catalepsy	Catalepsy	<0.001	Veena Bhatra et.al 2008
15	Ergot alkaloid	Claviciptaceae	Roots	Bromocryptine	Wistar Rats	Chlorpromazine Induced Experimental Animal Model	Catalepsy	<0.001	K.S.Sandhu et.al 2008
16	Ergot alkaloid	Clavicipitaceace	Roots an shoots	Polyphenols	Albino Mice	Haloperidol Induced Catalepsy	Catalepsy	<0.001	Schin P.Patil et.al 2009
17	Gypnosides	Gynostemma pentaphyllum	Leaves	Ethanol	Wistar Rats	Chlorpromazine Induced Experimental Animal Model	Catalepsy muscle rigidity	<0.001	Jayanth S et.al 2010
18	Ericaceae	Cyanoccocus	fruits	Polyphenols	Albino Wistar Rats	Haloperidol Induced Catalepsy	Catalepsy	<0.001	Shushruta Koppula et.al 2010
19	Lingusticum	Lingusticum Officinale	Roots and Leaves	Ethanol	Wistar Rats	Haloperidol Induced Catalepsy	Dopamine Level Oxidative stress	<0.001	Catherine E et .al 2011
20	Synuclein	Centella asiatica	Seeds	Methanolic	Albino Mice	Chlorpromazine Induced Experimental Animal Model	Catalepsy	<0.001	Husnul Kohtimah et.al 2011

EXPERIMENTAL MODELS OF PARKINSON'S DISEASE

RESERPINE MODELS

Systemic administration of reserpine, a pharmacological compound causes a depletion of catecholamine in the brain, led to an akinetic (absence of movement) state. Administration of L-DOPA reverses the akinetic state, indicating that behavioural recovery wasdependent on dopamine replacement. The signs of motor dysfunction associated with PD results from striatal dopamine depletion prompt application of reserpine in other species. Administration of reserpine to rodents induces a hypokinetic state due to depletion of dopamine at nerve terminals. These motor changes due to loss of dopamine storage capacity in the intracellular vesicles. The motor deficits induced by these compounds are temporary and reversed by L-DOPA administration. The major drawback of these models is, these agents do not produce morphological changes which resemble human parkinsonism.[12]

MPTP MODELS

Administration of MPTP results in depletion of striatal dopamine and nigrostriatal death in a wide variety of animal species, including mice, cats, dogs, sheep and nonhuman primates. Even though almost all species of animals develop some neurochemical or morphological effects of MPTP, the degree of susceptibility among species varies on basis of differences in susceptibility to MPTP. The rats are essentially resistant to MPTP, where as mice are somewhat sensitive. Difference strains of animals are differing in sensitivity to MPTP.[13]

Methamphetamine models

The administration of methamphetamine (METH) to rodents results in long term depletion of striatal dopamine and serotonin. The action of this toxin is differing from that of MPTP in that dopamine is depleted at the level of dopaminergic terminals, not in cell bodies. The mechanism of action of METH is unclear. Studies indicate that METH exerts its neurotoxic effects through the dopamine receptor and transporter because selective antagonists are able to produce toxicity [14]

Genetic models

In addition to experimental models developed using neurotoxin agents, several genetic rodent models have been discovered or engineered. The best characterized spontaneous genetic mouse degenerative model is the weaver mouse. An autosomal recessive mutation in the potassium channel leads to neuronal cell death in the cerebellum and the nigrostriatal system.

But the major drawbacks of these models are the high cost and less success rate in experimental pharmacology.[15]

6-HYDROXYDOPAMINE MODEL

It was the first agent discovered that has specific neurotoxic property in the dopeminergic nervous systems. 6-Hydroxydopamine uses the same catecholamine transport system as do dopamine leading to specific damage via oxidative stress to dopaminergic neurons. To be neurotoxic to brain, 6-OHDA must be administered by intracerebral or intraventricular injections because it is unable to cross the blood brain barrier. The specificity is achieved by stereotactically targeting 6-OHDA to the substantia nigra, the ventral tagmental area, the nigrostriatal tract or the striatum. Loss of dopaminergic cells lead to loss of dopamine content.[16]

NEUROLEPTIC INDUCED CATALEPSY

Neuroleptics that are commonly used in the treatment of schizophrenia and other affective disorders are often associated with distressing extrapyramidal side effects. The phenomenon of cataleptic immobility induced in rodents by typical neuroleptic (eg; Haloperidol) is a robust behavioral model to study nigrostriatal function and its modulation by dopaminergic, cholinergic and serotonergic systems. Haloperidol-induced catalepsy occurs due to the blockade of dopamine and reduced dopaminergic transmission [17]

REFERENCES

1. K.D.Tripathi, essentials of Medical Pharmacology, seventh edition.
2. David A, Prevelance of Parkinsonism signs and associated mortality in a community population of older people, The New England journal of medicine, 1996; 334: 71-76.
3. Forno, Neuropathology of P. D, Journal of neuropathology and experimental neurology, 1996; 55: 259-272.
4. Swenson, Review of clinical and functional neuroscience, Basal ganglia.
5. Joseph Jankvoic, P.D clinical features and diagnosis, Journal of neurology, neurosurgery and pyschiatry, 2008; 79: 368-376.
6. Peter Brown Md, oscillatory nature of human basal ganglia: relationship to the pathophysiology of P. D, movement disorders, 2003; 18: 357-363.
7. Dek Tredici, where does P.D pathology begin in the brain , Journal of neuropathy and experimental neurology, 2002; 61: 413-426.
8. Hagai bergman Md, pathophysiology of P.D , movement disorders, 2002; 17: S28-S40.

9. K.D.Tripathi, Essentials of Medical Pharmacology (7 th Edition), 2013; 425-435.
10. K.D.Tripathi, Essentials of Medical Pharmacology (7 th Edition), 2013; 425-435.
11. M.Wagel et.al Physical therapy of PD, Journal of Neurosciences, 2008; 23: 191-193.
12. Kaakkola S, Teravainen H. Animal models of Parkinsonism. *Pharmacol Taxicol,* 1990; 67(2): 95-100.
13. Schimidt CJ, Ritter JK, Sonsalla PK. Role of dopamine in neurotoxic effects of methamphetamine. *J pharmacol Exp Ther,* 1985; 233: 539-544.
14. Tarlov SR, Martin SB, Graybiel AM. Cell death in midbrain of the murine mutation weaver. *J Neurosci,* 1996; 16: 1819-1826.
15. Ryan RE, Ross SA, Drago J, Loiacono RE. Dose related neuroprotective effects of chronic nicotine in 6-hydroxydopamine treated rats and loss of neuroprotection in α4 nicotinic receptor subunit knockout mice. *British Journal of Pharmacology,* 2001; 132: 1650-1656.
16. Calne D, Chaste TN, Barbeau A. Dopaminergic antagonist-induced parkinsonism. *Advances in Neurology* Volume 9, Raven press, publishers, 156-163. Assis TS, Almeida RN, Barbosa-Filho JM, Medeiros IA. CNS pharmacological effects of the total alkaloidal fraction from *Albizia inopinata* leaves. *Fitoterapia,* 2001; 72: 124-130.