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Review Article

Parkinson's Disease: A Challenge to Budding Young Pharmacists

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ABSTRACT

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized primarily by tremors, rigidity, bradykinesia, and postural instability. The disease occurs mainly due to degeneration of dopaminergic neurons in the substantia nigra region of the midbrain, resulting in dopamine deficiency within the central nervous system. Parkinson's disease is considered one of the major non-communicable neurological disorders affecting the elderly population worldwide. Various environmental and lifestyle-related risk factors such as chronic stress, excessive alcohol consumption, tobacco use, and exposure to toxic substances may contribute to disease progression. The present review highlights the biochemical role of dopamine, dopaminergic pathways, natural and plant sources of L-DOPA, and currently available therapeutic approaches for Parkinson's disease. Levodopa combined with carbidopa remains the gold standard treatment for symptomatic management of PD. Dopamine functions both as a neurotransmitter and as a precursor for norepinephrine and epinephrine synthesis. Several plant species including Mucuna pruriens, Vicia faba, and Cassia species contain significant quantities of L-DOPA and may serve as potential natural therapeutic sources. Recent advances in neuropharmacological research indicate that mitochondrial dysfunction, α-synuclein aggregation, and cardiolipin-mediated protein refolding mechanisms may play important roles in disease progression. Understanding these molecular mechanisms may contribute to the development of novel therapeutic strategies. Furthermore, computational approaches such as QSAR studies and virtual screening tools may assist in identifying innovative neuroprotective agents for Parkinson's disease management.

INTRODUCTION

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder that primarily affects movement and motor coordination. The disease is mainly associated with degeneration of dopamine-producing neurons located in the substantia nigra pars compacta of the

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midbrain. Reduction in dopamine levels disrupts normal neuronal signaling within the basal ganglia, resulting in impaired motor function. Common clinical manifestations of Parkinson's disease include resting tremors, muscular rigidity, bradykinesia, impaired posture, slow movement, and reduced olfactory sensation. In advanced stages, cognitive dysfunction and psychiatric disturbances may also occur. Diagnosis is commonly performed through clinical examination supported by neuroimaging techniques such as Magnetic Resonance Imaging (MRI). Dopamine was first synthesized in 1910 by George Barger and James Ewens at Wellcome Laboratories in London. It was later identified in the human brain in 1957 by Kathleen Montagu. The neurotransmitter role of dopamine was subsequently recognized by Arvid Carlsson and Nils-Åke Hillarp. Dopamine belongs to the catecholamine and phenethylamine families and functions both as a neurotransmitter and as a precursor in the biosynthesis of norepinephrine and epinephrine.

Biochemistry Of Dopamine

Dopamine (3,4-dihydroxyphenethylamine) is synthesized in the body from the amino acid L-tyrosine through enzymatic pathways.

Biosynthetic Pathway

Primary Pathway

L-Phenylalanine → L-Tyrosine → L-DOPA → Dopamine

Minor Pathways

L-Phenylalanine → m-Tyrosine → p-Tyramine → Dopamine

L-Phenylalanine → m-Tyrosine → m-Tyramine → Dopamine

Dopamine is converted into norepinephrine by the enzyme dopamine β-hydroxylase in the presence of oxygen and L-ascorbic acid as cofactors. Norepinephrine is further converted into epinephrine by phenylethanolamine N-methyltransferase using S-adenosyl-L-methionine as a cofactor.

Dopaminergic Pathways

Dopaminergic pathways are neuronal projections in the brain responsible for synthesis and release of dopamine. These pathways regulate movement, cognition, reward, and emotional responses.

The major dopaminergic pathways include:

1. Nigrostriatal pathway – regulates voluntary motor control and is primarily affected in Parkinson's disease.

2. Mesolimbic pathway– associated with reward, motivation, and emotional behavior.

3. Mesocortical pathway – transmits dopamine from the ventral tegmental area (VTA) to the prefrontal cortex and regulates cognition and executive functions.

4. Tuberoinfundibular pathway – regulates prolactin secretion from the pituitary gland.

Altered dopamine activity has also been associated with schizophrenia, attention deficit hyperactivity disorder (ADHD), and restless leg syndrome.

Current Therapeutic Approaches

Levodopa (L-DOPA) combined with carbidopa remains the most effective pharmacological therapy for symptomatic treatment of Parkinson's disease. Levodopa acts as a dopamine precursor capable of crossing the blood-brain barrier,

whereas carbidopa inhibits peripheral metabolism of levodopa and enhances its bioavailability.

Other therapeutic approaches include:

* Dopamine agonists

* Monoamine oxidase-B inhibitors

* Catechol-O-methyltransferase inhibitors

* Anticholinergic agents

* Deep brain stimulation therapy

Despite current treatments, no therapy has yet been able to completely stop neuronal degeneration in Parkinson's disease.

Natural And Plant Sources Of L-Dopa

Several plant species naturally contain L-DOPA or dopamine-like compounds.

Table 1: Plant Sources of L-DOPA

Sr.No.	Plant	Part of plant	Uses
01.	Mucuna pruriens	Velvet beans	As a source for L-DOPA as a drug.
02.	Vicia faba	Broad beans	Rich source of L-DOPA
03.	Cassia and Bauhinia trees	Seeds	Substantial amount of L-DOPA
04.	Marine green algae Ulvaria obscura	Algal blooms	Dopamine present in very high concentration.

Bananas, potatoes, avocados, broccoli, oranges, tomatoes, spinach, and beans also contain measurable quantities of dopamine and related catecholamines. However, dietary dopamine cannot directly influence brain dopamine levels because dopamine itself does not effectively cross the blood-brain barrier.

Role Of Mitochondria And Cardiolipin In Parkinson's Disease

Recent studies suggest that mitochondrial dysfunction plays an important role in Parkinson's disease pathogenesis. α-Synuclein aggregation leads to formation of toxic protein deposits within neuronal cells. Cardiolipin, a phospholipid present in mitochondrial membranes, may assist in refolding toxic α-synuclein aggregates into less toxic conformations. Understanding the molecular role of cardiolipin in protein refolding may contribute to development of future neuroprotective therapies aimed at slowing disease progression.

Future Research Perspectives

Future advances in neuropharmacology and molecular neuroscience may improve understanding of neuronal degeneration and dopamine regulation in Parkinson's disease. Potential research areas include:

* Development of neuroprotective drugs

* Blood-brain barrier targeted drug delivery systems

* Plant-derived L-DOPA formulations

* Mitochondrial protective therapies

* Protein refolding mechanisms

* QSAR-based drug discovery

* Virtual screening using computational tools such as PyRx

Innovative pharmaceutical research by young pharmacists may contribute significantly toward the discovery of safer and more effective therapeutic agents for Parkinson's disease management.

CONCLUSION

Parkinson's disease remains one of the most challenging neurodegenerative disorders affecting the aging population. Dopamine deficiency caused by degeneration of substantia nigra neurons is the principal pathological hallmark of the disease. Although levodopa-carbidopa therapy provides symptomatic relief, currently available treatments cannot completely prevent neuronal death or disease progression. Recent findings involving mitochondrial dysfunction, α-synuclein aggregation, and cardiolipin-mediated protein refolding have opened new directions for neuropharmacological research. Continued efforts in medicinal chemistry, computational drug design, and neuroprotective therapy development may provide improved treatment strategies in the future.

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