2. ADVANCING PARKINSON'S DISEASE MANAGEMENT: NOVEL STRATEGIES AND THERAPEUTIC INNOVATIONS

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Introduction. Parkinson's disease is a long-term neurodegenerative condition of the central nervous system that mainly affects the control of voluntary movements due to the gradual degeneration of dopaminergic neurons in the *substantia nigra* region of the brain. The treatment of Parkinson's disease has improved continuously, with a strong focus on developing innovative methods to effectively manage the complexities of this disorder for each patient.

Aim of study. To explore the most recent concepts of Parkinson's disease pharmacotherapy based on the pathophysiological mechanism at the central nervous system (CNS) level.

Methods and materials. The current review involved carefully selecting and examining a curated set of academic literature from electronic databases such as HINARI, PubMed, NCBI, and ScienceDirect.

Results. Parkinson's disease treatment still relies on Levodopa (LD) as the gold standard. Despite this, prolonged use of levodopa has been shown to result in motor complications, known as the "on-off phenomenon", in most patients. Peripheral metabolism of LD (plasma circulating level fluctuations) may lead to systemic effects, including cardiac arrhythmias, hypotension, and vomiting. Modern strategies have been formulated to synthesize LD and dopamine prodrugs (ester, amide, cyclic prodrugs, also chemical delivery systems, enzyme models), aiming to maintain LD's effectiveness while reducing side effects. Add-on oral therapies like dopamine agonists (DAAs), monoamine oxidase Type-B inhibitors (MAO-B Is), and COMT inhibitors (COMT-Is), along with amantadine ER and adenosine A2A receptor antagonists (AA2AA), were developed to improve life expectancy and enhance the long-term response to LD therapy. In recent years, researchers have studied iron chelators as neuroprotective agents. The dopaminergic neurons of the CNS contain a significant amount of neuromelanin (NM), a dense and insoluble pigment with a strong affinity for iron. The chelator's removal of iron will prevent the excessive formation of reactive oxygen species, which leads to neuroinflammation.

Conclusion. The diligent research and continuous improvement of drug treatment for Parkinson's disease lead to a major improvement in patients' quality of life. Recreating the enzyme model in prodrug synthesis can improve the pharmacokinetic and pharmacodynamic properties, resulting in a successful drug delivery system that specifically targets them to the *substantia nigra*. Recent studies also investigate the potential neuroprotective role of iron chelators in management of Parkinson's disease.

Keywords. Parkinson's disease, therapeutic management, levodopa.