**ISSN- 0301-1216**
*Indian J. Prev. Soc. Med. Vol. 56, No.1, 2025*

**REVIEW ARTICLE:**

# Innovative Therapeutics in Neurodegenerative Disease: Current Advances and Future Directions

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## ABSTRACT

Neurodegenerative disorders, which are marked by gradual degeneration of the neurological system and intricate pathogenic pathways, provide a significant challenge to modern medicine. The focus of this thorough assessment is on innovative therapeutic techniques created between 2020 and 2023, with a particular emphasis on molecular therapies, biologics, and new technologies. The effectiveness of treatment has been greatly increased by recent developments in medication delivery methods, such as brain-targeting tactics and nano-carrier based ideas. The advent of disease-modifying therapies, such as Lecanemab for Alzheimer's disease and new LRRK2 inhibitors for Parkinson's disease, signifies a change in focus from treating symptoms to addressing the underlying cause of the condition. Applications of artificial intelligence and machine learning have expedited the process of finding and developing new drugs, and sophisticated biomarker platforms have made it possible to precisely stratify patients.

Not withstanding these successes, there are still major obstacles to overcome in the areas of cost control, healthcare implementation, and treatment optimization. The shift toward personalized medical methods and the integration of numerous therapeutic modalities for improved treatment outcomes are highlighted in this review, which critically examines recent advancements, cutting-edge technology, and future possibilities in neurodegenerative disease therapies.

**Keywords**: Neuro-degenerative disorders, Drug delivery systems, Disease-modifying therapies, Artificial intelligence, Biomarkers, Personalized medicine, Nanocarrier delivery, Treatment optimizatio

## Introduction

A range of debilitating neurological conditions known as neurodegenerative diseases are distinguished by the gradual loss of neuronal structure and function. Over 50 million individuals worldwide suffer from these illnesses, which include multiple sclerosis (MS), Parkinson's disease (PD), Alzheimer's disease (AD), and amyotrophic lateral sclerosis (ALS). By 2050, estimates suggest that number will have tripled.[1] There is a pressing need for efficient treatment approaches since the yearly economic burden surpasses $1.3 trillion.[2]

These diseases' pathogenic characteristics include intricate molecular processes such as protein accumulation, aggregation, and misfolding. PD is typified by α-synuclein aggregates in Lewy bodies, whereas AD is defined by tau neurofibrillary tangles and amyloid-β plaques.[3] These illnesses have similar pathogenic processes, such as oxidative stress, mitochondrial dysfunction, neuro-inflammation, and disturbed proteostasis, despite their different clinical manifestations.[4]

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| Submission | 22.01.2025 | Revision | 12.02.2025 | Accepted | 27.02.2025 | Printing | 31.03.2025 |
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***Prior Publication*: Nil*; Source of Funding:* None; *Conflicts of Interest*: None, *Article # 667/947***

Instead of modifying the condition, traditional therapy techniques have mostly concentrated on managing its symptoms.

However, new technology and a better knowledge of disease mechanisms have produced ground-breaking therapies that address the underlying pathogenic processes. New treatment approaches, enhanced drug delivery methods, and the use of artificial intelligence in drug development have all contributed to this paradigm shift.[5]

## Small Molecule Therapeutics

Because of improved blood-brain barrier (BBB) penetration and multi-target mechanisms, recent developments in small molecule research have completely changed therapy strategies. An important advancement is the creation of brain-penetrant compounds that target protein aggregation. With a 45% decrease in pathogenic protein levels, DNL151, an LRRK2 kinase inhibitor, has shown impressive effectiveness in lowering α-synuclein aggregation in PD patients.[5] By targeting both cholinesterase inhibition and monoamine oxidase modulation, multi-target-directed ligands (MTDLs) have demonstrated better cognitive results in AD trials, with a 35% increase in cognitive scores when compared to conventional single-target methods.[6]

Promising therapeutic prospects are novel tiny compounds that target tau disease. In preclinical settings, compounds such as NPT088 have demonstrated strong neuroprotective benefits by dual targeting both misfolded tau and amyloid-β.[2] Furthermore, novel scaffolds intended to enhance BBB penetration have produced brain concentrations that are up to 60% greater than those of traditional compounds.[7]

## Biologics and Immunotherapy

Unprecedented advancements have been made in the biologics area, especially in the production of monoclonal antibodies. The CLARITY AD study showed that lecanemab, which targets amyloid-β protofibrils, reduced cognitive deterioration in early-stage AD patients by 27%.[8] With a 35% reduction in cognitive decline and a notable removal of amyloid plaque, the Donanemab TRAILBLAZER-ALZ 2 study demonstrated even more encouraging outcomes.[9]

Modified protein fragments have been used in active immunization procedures to maximize beneficial effects and produce tailored immune responses. Phase II studies have demonstrated encouraging safety profiles and immunogenicity for novel vaccination methods that target misfolded proteins.[10]An inventive method of disease modification is the creation of bispecific antibodies that can target many pathogenic proteins at once.

## Advanced Delivery System

The long-standing problem of BBB penetration has been resolved by groundbreaking advancements in medication delivery technologies. Lipid nanoparticles (LNPs) and dendrimeric systems are two examples of nanocarrier-based techniques that have produced impressive brain biodistribution patterns. More sophisticated LNP formulations have shown:

- A 70% rise in the levels of brain drugs
- Extended release profiles that last more than 72 hours
- Improved target neuron cellular uptake
- A decrease in peripheral adverse effects[11]

Therapeutic delivery has been improved thanks to novel targeted techniques that make use of receptor-mediated transcytosis. The creation of dual-targeting ligands has improved cellular specificity and BBB penetration. Creative methods consist of:

- Targeting via transferrin receptors
- Delivery via glucose transporter-mediated

- Peptide conjugates that penetrate cells
- Delivery methods based on exosomes.[12]

## Disease-Specific Innovations

**Alzheimer's Disease:** New strategies concentrating on tau pathology and neuro-inflammation have surfaced in addition to amyloid-targeting treatments. TREM2 agonists have demonstrated a 40% decrease in neuro-inflammatory markers, suggesting that they may improve microglial function.[13] When compared to monotherapy treatments, combination medicines that target both tau and amyloid pathology have shown improved effectiveness, reducing disease progression indicators by 50%[14] .

**Parkinson's Disease:** Beyond conventional dopamine replacement therapy, innovation has spread. Early-phase studies of α-synuclein-targeting therapeutics have yielded encouraging results, with new antibodies reducing abnormal protein levels by up to 60%. Improved therapeutic windows and a 40% reduction in motor fluctuations have been achieved using advanced formulations of already available medications.[15]

## Emerging Technologies

**Machine learning and artificial intelligence:**

AI applications have completely changed the way that drugs are discovered and developed. Algorithms for deep learning have:

- A 60% reduction in target identification time
- Enhanced effectiveness of clinical trial design
- Increased precision in patient stratification
- Quicker procedures for lead optimization [16]

**CRISPR and Gene Editing:** The treatment of hereditary types of neurodegenerative disorders has showed great promise because to advanced gene editing methods. CRISPR systems that have been modified have attained:

- An 80% decrease in off-target impacts
- Improved tissue specificity
- Better delivery to the brain tissues [17]

**Challenges and Future Perspectives:** Despite tremendous progress, there are still many obstacles to overcome:

**Technical Challenges:**

- Optimizing the penetration of the BBB
- Decreased immunogenicity
- Enhancing the specificity of the target
- Improving the endurance of treatment

**Implementation Barriers:**

- Expensive medical care
- Adaptation of the healthcare system
- Adherence to regulations
- Concerns about access equity[18]

**Future Directions:** The field is heading in the direction of:

- Methods of personalized medicine
- Selection of treatments based on biomarkers
- Techniques for combination treatment

- More sophisticated delivery systems
- Systems for real-time monitoring

## Conclusion

Therapeutic developments for neurodegenerative diseases mark a dramatic paradigm shift away from symptomatic care and toward disease modification. The promise of focused therapeutic tactics is demonstrated by the success of innovative treatments, especially in the treatment of Parkinson's and Alzheimer's diseases. Treatment optimization has never been possible before because to the combination of cutting-edge delivery methods, new technology, and customized medical techniques. Long-standing issues with target engagement and blood-brain barrier penetration have been resolved by groundbreaking advancements in small molecules, biologics, and creative delivery methods.

The sector is still developing quickly, despite the fact that there are still many obstacles to overcome in the areas of therapeutic development, cost control, and healthcare implementation. Advanced biomarker platforms and the advent of artificial intelligence in drug discovery have sped up the creation of more potent therapies. Therapeutics for neurodegenerative diseases seem to have a bright future, with combination therapy and individualized treatment plans probably playing important roles. Millions of patients worldwide may find fresh hope as a result of the confluence of enhanced disease understanding, therapeutic innovation, and technology improvement, which points to a revolutionary age in this treatment.

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**Citation:** Joshi Priya, Singh S., Dhariyal R. Singh. Innovative Therapeutics in Neurodegenerative Disease: Current Advances and Future Directions. Indian J Prev Soc Med, 2025; 56 (1): **152-156**.