SENNOS

Journal of Drug Delivery and Biotherapeutics (JDDB)

Journal homepage: https://sennosbiotech.com/JDDB/1

Mini Review Article

Nanotechnology-Based Approaches for Parkinson's Disease: Progress in Drug Delivery and Regenerative Medicine

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ARTICLEINFO

ABSTRACT

Nanotechnology is emerging as a promising frontier in the development of next-generation drug delivery systems, offering innovative solutions to address the challenges associated with Parkinson's Disease (PD). PD, a neurodegenerative disorder characterized by the loss of dopaminergic neurons, poses significant therapeutic obstacles, including poor drug solubility and stability, low permeability across the blood-brain barrier (BBB), and a lack of treatment specificity. Nanotechnology-based approaches provide opportunities to overcome these limitations by improving drug delivery, enhancing neuroprotection, and supporting neuronal regeneration. This review focuses on several nanotechnology-driven strategies, including lipid- and polymeric-based nanoparticles that improve drug solubility, stability, and targeted delivery across the BBB. It also examines the application of CRISPR-Cas9 delivery systems for precise gene editing, offering disease-modifying potential, and explores the integration of stem cell-based regenerative therapies for restoring dopaminergic neurons and repairing damaged neural networks. Beyond these approaches, the potential for nanotechnology to enable personalized treatments and novel therapeutic interventions is discussed. While nanotechnology holds significant promise in advancing PD management, critical challenges remain, including concerns about safety, reproducibility, scalability, and clinical adaptation.

Keywords: Nanotechnology; Parkinson's Disease (PD); Drug Delivery Systems; Blood-Brain Barrier (BBB); Lipid Nanoparticles; Polymeric Nanoparticles

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Received date: 10-Sep-2024 Revised date: 29-SEP-2024, Accepted date: 19-Oct-2024

Crossref DOI: https://doi.org/10.61920/jddb.v1i02.148

1. Introduction

The introduction of a review article titled "Nanotechnology-Based Approaches for Parkinson's Disease: The introduction "Current Directions in Drug Delivery and Regenerative Medicine" will serve to introduce the most important problems and prospects of the topic addressing the treatment of Parkinson's disease (PD). It provides a brief and general outlook of the disease, previous therapeutic dilemmas and how nanotechnology could revolutionize the treatment.

1.1 Overview of Parkinson's Disease (PD)

Parkinson's disease is a multifactorial movement disorder of central nervous system origin characterized by progressive deterioration of dopaminergic neurons in the substantia nigra region of the brain.[1] This involves for example ataxia, akinesia, bradykinesia, rigidity; involvement of balance; and non-motor aspects such as dementia, depression, and dysfunction of the autonomic nervous system.

PD has a multifaceted etiology mechanistically that include formation of Lewy bodies through aggregation of alpha-synuclein, free radical-induced oxidative stress, mitochondrial dysfunctions, and pro-inflammatory glial activation.[2] PD is a disease that affects millions of people all over the world and its stat is projected to increase with ageing population. Given its significant socio-economic cost, compounded by the PD patients' diminished quality of life, new treatment approaches are required [4].

1.2 Limitations of Current Therapies

Most available treatments for Parkinson's disease are symptomatic, and none of them has neuroprotective or neurodegenerative effects.[5] The mainstay of treatment which is levodopa provides only short-term benefit and is accompanied by side effects that include motor fluctuations and dyskinesia on long-term use.[6] This is significantly less effective over time and in one case is invasive with no regeneration properties or really even neuroprotective effect in PD.[7] In addition these treatments do not attack the specific cause of PD such as the neuronal loss and protein aggregation.[8] A major problem in drug delivery is the presence of BBB that only allows a limited number of agents to penetrate through to the brain. Therefore, an urgent call to enhance new treatment type genres that can help overcome these barriers and afford long-term, specific, and effective treatments.[9]

1.3 The Role of Nanotechnology in Advancing PD Treatment

The innovation of technologies with action on a nanometer scale has become the focus of hope in combating neurological disorders such as Parkinson's disease. This technology provides novel strategies for diagnosis and therapy through nanomaterials and nanocarriers in drug delivery and regenerative medicine.[10] The use nanoparticles can enhance drug solubility, chemical stability, and capability to cross the BBB when delivers a target drug.[11] Polymeric nanoparticles, liposomes, solid lipid nanoparticles and dendrimers are some recent progresses in treatment delivery, which possesses combined ability to encapsulate therapies and administer these into the affected regions of the brain. Apart from drug delivery nanotechnology is also involved in regenerative medicine.[12] Carbon nanotubes, graphene and nanofibers may act as a template for neurite extension for the purpose of neurodegeneration. secondly, it is encapsulated neuroprotective agents, gene medicine, or stem cell which aims to stop disease development or even reversal.[13]

This section also reveals cross disciplinary nature of nanotechnology: involving materials science, biology, and pharmacology for enhancing interventions for PD.[14] Through here, nanotechnology-based therapy shows the promising ability to overcome the shortcomings of the current conventional therapies in evolving the treatment of PD and enhancing the quality of the patient's life.[15]

2. Fundamentals of Nanotechnology in Medicine

2.1 Definition and Principles of Nanotechnology

Nano-technology is the science of engineering and manipulating structures and devices at the scale of one to hundred nanometers. These properties allow control of the dispersion state of particles to improve solubility, chemical stability, and bioavailability of the drug.[16] Nanotechnology in medicine is more or less centered on developing nanoscale carriers such as nanoparticle, liposome, and nanogel to enhance the effectiveness of the treatment by targeting effective sites in the body.[17]

2.2 Advantages of Nanotechnology in Drug Delivery Systems

This is because nanotechnology increases drug availability, not only does it provide targeted delivery of drug but also the dynamics of controlled and sustained release of drugs.[18] That is why it is effective for CNS disorders that need to pass the blood-brain barrier (BBB). Furthermore, nanocarriers lower the impact of the side effects since they help target delivery of the drugs to particular tissues or cells.[19]

2.3 Previous Applications in Neurodegenerative Disorders

Neurodegenerative diseases such as, Alzheimer's and Huntington's disease have been contexts frequently investigated with nanotechnology.[20] Various neuroprotective agents-releasing nanocarriers including antioxidants and neurotrophic factors have been effectively delivered to the brain through crossing the BBB.[21] For instance, polymeric nanoparticles and liposomes for enhanced drug delivery and therapeutic efficacy have been demonstrated for this disorder, thus, providing a basis for such application in Parkinson's disease.[22]

3. Nanotechnology-Enhanced Drug Delivery for PD

3.1 Nanoparticle Platforms

The drug delivery problems are illustrated in Parkinson's disease by nanoparticles in regulating controlled delivery to the brain.[23]

3.1.1 Lipid-Based Nanoparticles (Liposomes, Solid Lipid Nanoparticles):

Lipid based systems seem to be biocompatible and can cross the BBB proficiently. It is with respect to these parameters that liposomes encapsulate drugs for controlled release while solid lipid nanoparticles enhance stability and prolonged drug circulation.[24]

3.1.2 Polymer-Based Nanoparticles:

Polymeric research such as PLGA and chitosan provide controlled drug release and increase the bioavailability in the brain; in addition, it as a multifunctional carrier to target dopaminergic neurons.[25]

3.1.3 Metal and Magnetic Nanoparticles:

Au and Fe2O3 nanoparticles, among others, are employed due to theranostics properties where the drug delivery and imaging functions are combined. Magnetic nanoparticles facilitate targeted delivery with external magnetic field.[26]

3.2 Targeting the Blood-Brain Barrier (BBB)

Transportation of drugs across the BBB is an important factor for treating PD.[27]

3.2.1 Strategies to Enhance BBB Permeability:

Preferred tactics of nanocarriers are the use of functional groups such as ligands or surfactants for enhancement of BBB crossing.[28]

3.2.2 Receptor-Mediated Transport Mechanisms:

Nanoparticles functionalized with specific ligands like transferrin or insulin receptors receptors are selectively internalized by endocytosis thus carrying the therapeutic agent directly to the brain.[29]

3.3 Controlled and Sustained Drug Release

Nanotechnology allows for controlled release of drugs applied in the treatment of PD and thus improving the results obtained.[30]

3.3.1 Stimuli-Responsive Nanocarriers:

These systems utilize stimuli including pH; temperature or enzymes to release drugs at the site of action and not before consequently reducing and mitigating side effects.[17]

3.3.2 Nanogels and Dendrimers:

Nanogels offer large surface area and encapsulation efficiency and release property and dendrimers are well known for their branched structure and molecular target delivery property.[31]

4. Nanotechnology in Regenerative Medicine for PD

4.1 Nanomaterials for Neuroprotection

Parkinson's disease can be protected from damaged neurons by nanomaterials through the reduction of oxidative stress and inflammation.[5]

4.1.1 Antioxidant Nanoparticles:

Cerium oxide nanoparticles and selenium nanoparticles eradicate ROS and decrease oxidative stress, promoting neuronal function.[19]

4.1.2 Anti-inflammatory Nanostructures:

Anti-inflammatory agents are carried within nanocarriers that directly target microglial activation to manage neuro inflammation and decelerate disease advancement.[32]

4.2 Nano scaffolds in Neural Tissue Engineering

Nano scaffolds also present a favorable substrate for neural regeneration in PD.[33]

4.2.1 Nanofibers and Hydrogels:

Below are some of the approaches that are used in the repair of nerve tissue: Nanofibers and hydrogels replicate the matrix surrounding a neuron and encourages the growth of axonal whereas they offer support to damaged neuron.[34]

4.2.2 Enhancing Stem Cell Differentiation and Survival:

Nanomaterials promote cellular survival and differentiation of stem cells into dopaminergic neurons to increase functional regeneration in PD.[20]

4.3 Gene Therapy and Nanocarriers

Nanotechnology enhances the method of transferring genetic material for a corrective or constructive purpose in PD.[29]

Polymeric and lipid based NPs have ability to protect the genetic material such as DNA or RNA from degradation to maintain the delivery and effective expression of therapeutic genes to the target cells.[35]

4.3.1 Nanoparticle-Mediated Gene Delivery:

4.3.2 CRISPR/Cas9 Systems and Nanotechnology:

Nanocarrier systems allow CRISPR/Cas9 systems to be targeted to dopaminergic neurons that can then reverse genetic mutations and stop the progression of PD. [36]

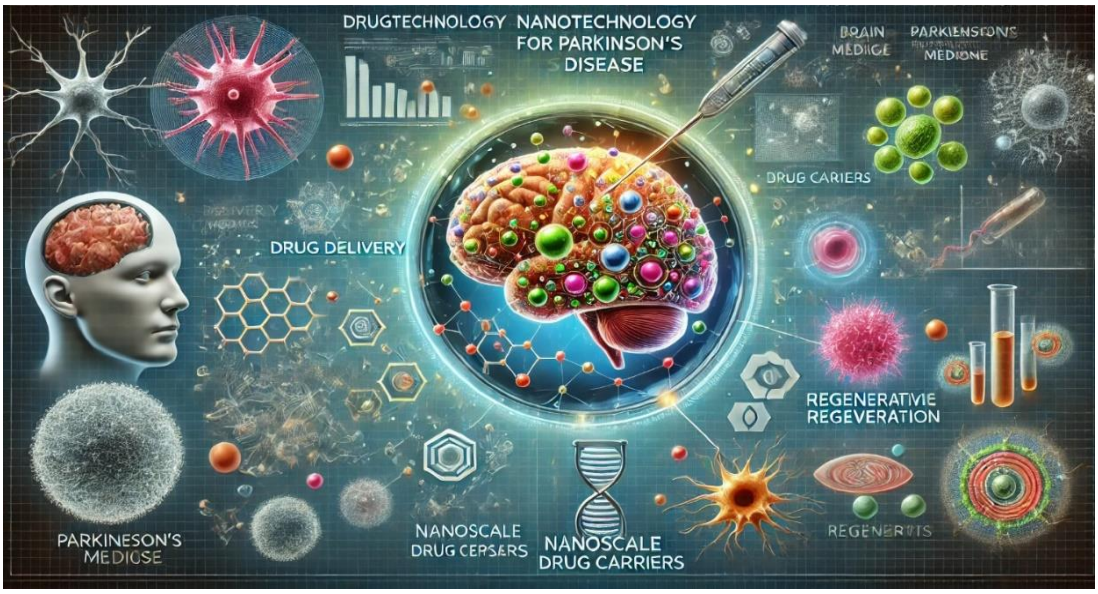

Fig.1: Nanotechnology-Based Approaches for Parkinson's Disease: Progress in Drug Delivery and Regenerative Medicine

5. Clinical Progress and Challenges

5.1 Preclinical Studies and Outcomes

The current reviews show that preclinical approaches of employing nanotechnology-based therapies can be effective in managing Parkinson's disease (PD).[30] Hence different animal models have been established where they have improved drug delivery through BBB, neuroprotective effect through antioxidant nanoparticles and better NEURO regeneration through Nano scaffolds. The results reported here offer a substrate for exploring in clinical setting.[33]

5.2 Ongoing Clinical Trials Involving Nanotechnology for PD

There are multiple ongoing clinical trials for nanocarrier mediated drug delivery for PD and regenerative therapeutics. Lipid and polymeric nanoparticles are used for attempting efficient delivery of dopamine agonists or a neuroprotective agent. The promising direction of joint work is to make stem cell therapies optimized with nanomaterials and nanoparticles to develop gene delivery systems.[17]

5.3 Safety, Biocompatibility, and Ethical Considerations

This issue authorizes safety and ethical factors that stay vital while transmuting nanotechnology to clinical practice.[37]

5.3.1 Toxicological Assessments:

Some challenges are observed, including the toxicity of nanoparticles, immune response and the behavior of nanoparticles in organs. Due to these properties, it can be pointed out that extensive in vitro and in vivo investigations are necessary in order to guarantee the safety of such materials.[38]

5.3.2 Long-Term Effects and Clearance:

Fundamental knowledge of the enduring consequences of nanomaterials through biodegradability and elimination from the body are important to avoid negative effects of nanomaterials. Steady state nanomaterials may be hazardous to the

well being of an individual and therefore, calls for fully biodegradable as well as urinary antiseptics systems.[39]

6. Future Perspectives and Directions

6.1 Personalized Nanomedicine in PD

The current and future treatment strategies for PD are in the area of advanced nanomedicine where nanotechnology fits patient profile. [15]New scientific needs in genomics and biomarkers will allow for the creation of nanocarriers that will act selectively on key pathways thus increasing the effectiveness and reducing post-therapy side effects.[29]

6.3 Regulatory Hurdles and Standardization

The translation of nanotechnology to clinical practice has also some limitations; these are high steer control regulatory needs, safety measures that have to be fulfilled, readiness recognition protocols of nanoparticles where on how to synthesize, characterize, and test are rare. Overcoming these barriers is important for the population-based implementation.

6.2 Integration of Nanotechnology with Other Emerging Therapies

Integrating nanotechnology with such treatments as stem cell therapy, gene editing with CRISPR and immunotherapy is complementary. These approaches can be improved further using nanocarriers, and the avenues for neurodegeneration and disease modification in PD have been expanded.

6.4 Collaborative Research and Interdisciplinary Approaches

It is important for this field that researchers, clinicians, and industries work together to move nanotechnology forward for PD. The synergy of collaborative areas of neuroscience, material science, and biomedical engineering will pull together innovation and enhance translational research [36].

7. Conclusion

7.1 Summary of Key Findings

Nanotechnology has tremendously demonstrated its capability in offsetting the drawbacks of conventional approaches towards the treatment of Parkinson's disease (PD) [13]. New generation nanocarriers such as lipid-based, polymeric, and metal nanoparticles have enhanced prospects in drug delivery across the BBB, targeted drug delivery and controlled release. Furthermore, it has provided new therapeutic paths in the areas of regenerative medicine in which nanotechnology already served in neuroprotection, tissue engineering, and gene therapy [19].

7.2 The Potential Impact on PD Management

As a result of application, nanotechnology may drastically change therapeutics distribution and the hasten neuro degradation. There is great potential of symptomatic treatments extending to change the course of a disease leading to better patients care and quality life [39].

7.3 Final Thoughts on the Road Ahead

However, there are still many issues that despite early noticeable progress, remain unsolved such as safety issue, regulatory issues, and scalability. [40] Further studies, strong cooperation, and ongoing development are required to make these advances become realistic choices in clinical treating. The adoption of nanotechnology with other novel medical practices such as personalized medicine and other therapies are

a clear indication of the progressive future that patient suffering from PD must look forward to [30].

Acknowledgement

The authors sincerely thank all researchers and institutions whose pioneering work in the fields of nanotechnology and neurodegenerative disease management has contributed to the advancement of knowledge in this area. We extend our gratitude to the funding agencies and academic bodies that have supported research efforts aimed at improving therapeutic strategies for Parkinson's Disease. Special thanks are due to colleagues and collaborators for their valuable insights and discussions, which have greatly enriched the development of this review. We also acknowledge the contributions of the publishers and journals that have provided a platform for disseminating innovative research in nanotechnology and regenerative medicine. Finally, we are deeply grateful to our families and mentors for their unwavering encouragement and support throughout this academic endeavour.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest associated with this manuscript. The preparation, writing, and publication of this review were carried out independently without any financial or personal relationships that could potentially influence the work reported.

Authorship Contribution Statement

All authors contributed to the conception, drafting, and critical revision of the manuscript. [Alka Pawar] conducted the primary literature review and prepared the initial draft, [Anil Patil] provided expertise on nanotechnology and regenerative medicine, reviewed and finalized the manuscript. All authors approved the final version for submission.

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