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Nanotechnology Based Drug Delivery and Marine Diet Derived Compounds in Alpha-Synuclein-Linked Parkinson's Disease

Authors: 1. Snegaa Sathasivan
snegaasatha@gmail.com (+995 599268234)
2. Jessica Annamalai
Jessica.annamalai@gmail.com (+995 559258261)
3. Shaheen Kauser Sadhik Bathcha
shahk18022003@gmail.com (+995 599319728)
4. Joshua Annamalai
Joshua.annamalai19@gmail.com (+995 595775631)
Affiliation: Tbilisi State Medical University, Georgia.

INTRODUCTION

Parkinson's Disease (PD) is the second most prevalent neurodegenerative disorder, and is defined by a progressive loss of dopaminergic function in the substantia nigra pars compacta (SNpc) neurons. Symptomatically, the neurodegeneration is paired with a wide array of motor symptoms—bradykinesia, rigidity, and postural instability—along with heterogeneous non-motor afflictions consisting of olfactory impairment, gastrointestinal disease, REM sleep behavior disorder, autonomic dysfunction, and cognitive decline. [1] [2]

The histopathological hallmark of PD is the Lewy bodies, intracellular aggregates consisting predominantly of masses of misfolded alpha-synuclein (AS) protein. Pathologic inclusions are instrumental in spreading neuronal death and dysfunction through mechanisms of oxidative stress, mitochondrial damage, neuroinflammation, and apoptosis [3] [6]

Even though levodopa is the standard symptomatic PD therapy, its bioavailability is restricted within the systemic circulation and its action is hindered by poor BBB penetration. Drug delivery systems with nanoparticles have been proposed as efficient systems in minimizing such problems for improving the pharmacokinetics and therapeutic activity of anti-Parkinsonian drug. A number of nanoparticle classes such as carbon nanotubes, silver, gold, and graphene have been found to be promising candidates for potential application both as drug therapeutic delivery as well as PD biosensing.[4]

The worldwide prevalence of Parkinson's Disease has increased over the past few decades, now affecting over 10 million individuals globally. The illness is a significant contributor to disability-adjusted life years (DALYs) and has a large healthcare cost. In spite of the development of pharmacologic and neurosurgical treatments—such as levodopa, dopamine agonists, and deep brain stimulation (DBS)—existing treatment is still largely palliative and cannot halt the target

neurodegenerative cascade.[5]

Moreover, chronic treatment with levodopa is associated with the onset of motor fluctuations, levodopa-induced dyskinesias, and time-dependent decline in drug efficacy.

One of the significant challenges to the manufacturing of disease-modifying drugs for PD is the BBB effect, which restricts most therapeutic agents from diffusing into the CNS. Most neurotherapeutic drugs possess lipophilic nature that also reduces their effective CNS bioavailability, thereby necessitating other types of viable drug delivery.

Nanotechnology emerged as an agitative platform to solve these issues of delivery. Nanoparticle (NP)-based platforms hold unique strengths due to their nanoscale nature, tunable surface chemistry and ability to be functionalized with targeting ligands so that they can penetrate through the BBB and deliver therapeutic loads directly within neural tissue [7]

Certain NP formulations like metal (e.g., gold, cerium oxide), polymer (e.g., PLGA, chitosan), lipid-based, and hybrid nanocarriers have been revealed to be able to deliver drugs, peptides, and nucleic acids effectively with improved targeting specificity, controlled release profiles, and diminished systemic toxicity. (Figure 1) [8] [5]

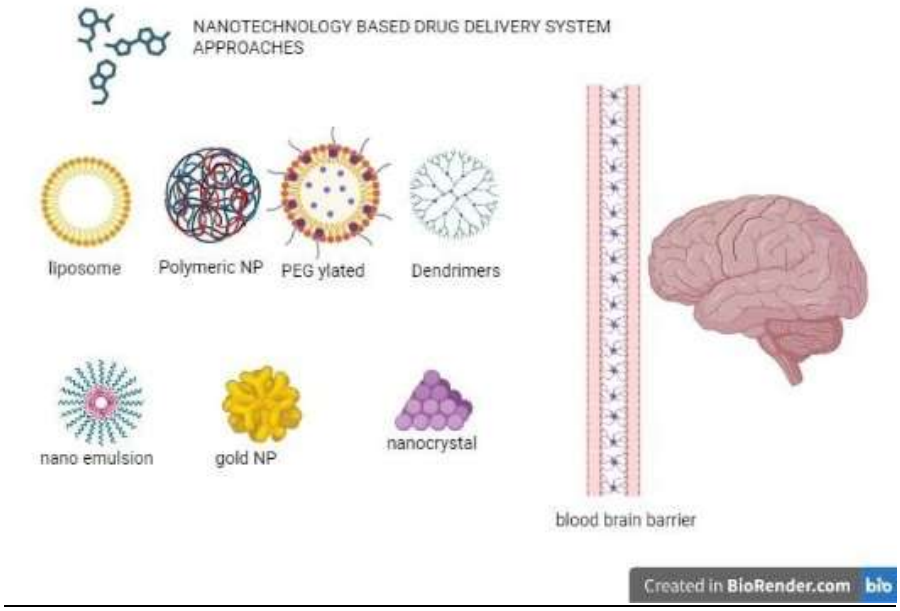

Figure 1: The different approaches in nanotechnology based drug delivery system can be classified into organic (liposomes, RBC membranes, SLN, nanoemulsions etc), Inorganic (metals, graphene quantum dots etc)

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These drug delivery systems not only provide enhanced penetration but also exhibit therapeutic potential through relief from oxidative stress (ROS), AS aggregation inhibition, improved mitochondrial activity, and attenuation of neuroinflammatory responses.[3]

Apart from the therapy, nanoscale biosensing technology is also revolutionizing the diagnostic front

of PD. The traditional diagnostic modalities are either insensitive in the early disease or invasive. Ultra-sensitive, real-time, and minimally invasive measurement of PD biomarkers such as alpha-synuclein, dopamine content, and mitochondrial metabolites in biological fluids can be achieved with nanomaterial-based biosensors.[5]

Penetration through the BBB remains an issue for nanotherapeutic delivery in the CNS. Available solutions are broadly categorized as noninvasive, invasive, and alternative approaches.

Noninvasive Strategies include:

- Transcellular Transport Mechanisms: Nanoparticles can traverse endothelial barriers by receptor interaction with subsequent internalization followed by transcytosis through receptor-mediated endocytosis, if they have ligand-functionalized surfaces.
- Intranasal delivery via neural pathways: Intranasal delivery has the potential for direct delivery of nanoparticles into the brain via the olfactory and trigeminal nerves without entering systemic circulation and BBB.
- Cell-Penetrating Peptide (CPP)-mediated transport: CPPs are a category of short peptides that allow cellular membrane translocation by enabling nanoparticle-drug conjugates to penetrate through the BBB effectively.

Invasive procedures include:

- Focused Ultrasound-Mediated BBB Disruption (FUS-BBB): Uses ultrasound and microbubbles to temporarily inactivate tight junctions in BBB, allowing localized nanoparticle delivery. The oscillating microbubbles induces mechanical stress on the tight junctions, thus disrupts the BBB integrity.
- Magnetic Field-Induced Permeabilization: Magnet-activated nanoparticles, under the control of an external magnetic field, exert mechanical forces, temporarily increasing BBB permeability
- Implantable Biodegradable Polymeric Matrices: Surgical implantation of drug-loaded polymeric scaffolds provides sustained and localized delivery of nanotherapeutics into brain parenchyma.

Alternatives strategies include:

- Osmotic BBB Disruption: Hyperosmotic agents such as mannitol, Fructose or glycerol temporarily open the BBB by shrinking endothelial cells and loosening tight junctions. Although very effective, the method is nonspecific and systemic side effects occur.

Each of these newer methods collectively comprises the cutting edge of nanomedicine approaches to cross the BBB and improve the efficacy of CNS drug delivery in neurodegenerative diseases such as PD.[9]

Neuroinflammation is also a key etiologic impetus behind PD progression that is encouraged by

enhanced reactive oxygen species (ROS) and monoamine oxidase-B (MAO-B) activity that encourages dopaminergic neuron damage.[10] [11]

Unlike MAO-A, MAO-B readily metabolizes dopamine to produce neurotoxic byproducts (ROS). Neurotrophic factors, particularly glial cell line-derived neurotrophic factor (GDNF), play an essential neuroprotective role through dopaminergic neuron survival maintenance and synaptic efficacy promotion. Neurotrophic factors are being explored as adjunct therapeutic modalities in PD [12] [13].

This review aims to synthesize new evidence from latest peer-reviewed literature on nanotechnology for PD treatment in therapeutic and diagnostic uses with complementary nutritional therapies through marine-based compounds. By describing the mechanistic underpinnings of nanoparticle action, biosensing platforms, and dietary neuroprotection, the article tries to guide next-generation multimodal treatment paradigms for the motor and non-motor features of Parkinson's Disease.

METHODS

This research was structured as a Literature review. Literature was collected using PubMed, MEDLINE, Google Scholar, ScienceDirect, MDPI, and Scopus, targeting peer-reviewed articles from 2003 to 2023. The primary keywords used in various combinations included: "Parkinson's Disease," "Nanoparticles,", “Innovations in Parkinson’s”, “Nanotechnology”, "Blood-Brain Barrier," "Alpha-synuclein," "Oxidative Stress," "Neuroinflammation," and ”Marine derived compounds”.

Eligibility criteria for inclusion encompassed:

1. Studies involving PD patients, animal models.

2. Articles written in English.

3. Research focused on nanotechnology-based therapeutic or diagnostic interventions.

Exclusion criteria included:

1. Non-PD neurodegenerative disorders.

2. Editorials, opinion pieces and conference abstracts.

In total, over 2000 articles were initially screened by title and abstract. Approximately 180 full-text articles were evaluated, out of which 37 were selected based on relevance, methodological rigor, and novelty. Snowball referencing was also applied to identify additional eligible studies.

Data was extracted using a standardized matrix capturing NP type, delivery method, target mechanism (e.g., AS inhibition, anti-oxidative effect), therapeutic payload, model type (animal or in vitro), outcome measures (e.g., TH levels, motor performance), and limitations noted by the original authors.

The review also incorporated key parameters such as dopaminergic neuronal survival, BBB permeability, and reduction in inflammatory markers, where data allowed. Descriptive statistics were used for trend identification. Figures and schematic representations were adapted from studies to

summarize NP mechanisms and pathways.

RESULT

Recent studies emphasize the drug-treating potential of nanotechnology for Parkinson's Disease (PD) through facilitation of enhanced drug delivery, inhibition of pathological protein aggregation, and greater neuroprotection. Nanoparticles (NPs), with the ability to cross the blood-brain barrier (BBB), are a promising approach to targeted therapy of PD.

1. Nanoparticle-Mediated Drug Delivery

Functionalized liposomes and polymer nanoparticles such as PEG-PLGA (polyethylene glycol-poly lactic acid-co-glycolic acid) systems show efficient uptake by dopaminergic neurons. Controlled release of drugs from NPs decreases systemic toxicity. Shape, size, polymer and surfactant composition, and physicochemical drug properties are the determinants of NP efficiency. Various NPs such as organic NPs, Inorganic NPs, polymeric NPs and Lipid based vesicles are used to provide therapeutic effects of PD.

- Liposomes :

They offer biocompatibility, hydrophilic and hydrophobic drug encapsulation capacity, transportation and immune clearance protection[14]

PEGylated liposomes decrease Reticuloendothelial system (RES) uptake and prolong systemic circulation time. This kind of liposomes have steric stabilization[7].

Kahana et al. published another article where a new brain-targeted drug carrier target liposome and used it to treat Parkinson's disease (PD) in a mouse model. The liposomes contained a diacylglycerol moiety and were conjugated through a linker to a 5-amino acid peptide of the amyloid precursor protein (APP) that was recognized by certain BBB receptors. The delivery of APP-targeted liposomes via injection with an 800 μg/kg DA dose yielded a significant striatal DA increase in amphetamine-treated mice within 5 min. The rise in striatal DA content was sustained following dosing for a duration of at least 3 h, which indicates slow release of DA from the delivery system. [5]

- Solid Lipid Nanoparticles (SLNs): They exhibit advantages of high drug loading ability, controlled release, enhanced stability, and reduced toxicity. SLNs were effective in delivering CNS-active drugs like bromocriptine in the treatment of PD [15] [16]
- Nanoemulsions: oil-in-water stabilized systems in the 20–200 nm droplet size range, improve drug solubility, nasal delivery increases bioavailability by avoiding first-pass effect compared to other delivery systems. In a mouse model of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced PD, an ibuprofen nanoemulsion with mucoadhesive properties showed dopaminergic neuroprotection and behavioral recovery [7] [17] [18] [19]

Mandal et al. explored the neuroprotective potential of Ibuprofen loaded sodium hyaluronate based mucoadhesive nano-emulsion (MNEI) via intranasal delivery against inflammation caused by dopaminergic neurodegeneration in 1-methyl- 4-phenyl-1,2,3,6- tetrahydropyridine (MPTP) mice model of PD. The nanoemulsion formulation was optimized with 3Labrafil M 1944 CS, Accenon CC,

and Transcutol P as oil phase, surfactant, and co-surfactant, respectively. The average globule size was found to be 46.3 ± 2.28 nm with low size distribution. Pharmacokinetic studies demonstrated significant reduction of MPTP-induced dopamine after nasal delivery of nanoemulsion. Pharmacodynamic studies showed significant improvement in PD symptoms. [20].

- Cerium oxide, CeO_2 (Metal NPs): they possess antioxidant and anti-aggregate activity. Ruotolo et al. have shown that CeO_2 NPs decreases the toxicity caused by α-synuclein through protein absorption on the particle surface, ROS removal, and preservation of mitochondrial function in yeast and mice models [21]

Brain-targeted liposomes (BTLs) explores whether BTL has the potential to suppress AS aggregation in the brain. With respect to the immunohistochemistry that was employed to examine the AS aggregation and dopaminergic neurons in substantia nigra of mice models, we divided the adeno-associated virus (AAV) inoculated mice into 4 groups: control PD mice, PD mice injected with free SynO4 mAbs, PD mice injected with BTL, and normal mice (control group). Each group was injected intravenously every other day for two or four weeks.

Two weeks following initiation of treatment, Comparing the cell number with aggregated AS and total aggregated AS accumulation (intracellular + extracellular), BTL-treated mice had reduced cell numbers of AS-positive cells (≈2.8-fold, $p = 0.0006$) and total AS accumulation (≈2.5-fold, $p = 0.0005$) compared to untreated PD mice. The BTL-treated group presented with a survival disparity in dopaminergic neurons (81 ± 9% survival vs 76 ± 12%-healthy: $p = 0.0147$) relative to the free SynO4-treated group (73 ± 12% survival vs 76 ± 12%-healthy: $p = 0.0002$).

After four weeks of viral AS inoculation, PD untreated had 60 ± 11% survival of dopaminergic neurons. BTL retarded loss of dopaminergic neurons with 70 ± 10% neuronal survival rate, but free SynO4 mAb therapy had only a survival rate of 53 ± 26%, therefore trending towards the survival of dopaminergic neurons.

According to the motor behavior and motor learning in the PD mice, the treatment groups were intravenously injected every other day for four weeks and were tested by the rotarod apparatus at two and four weeks after treatment. Post-treatment, the BTL group demonstrated motor function performance comparable to that of the healthy control group ($p < 0.7607$). Mice treated with Free SynO4 mAb had decreased latency to fall compared to mice treated with BTL ($p < 0.0074$). We also tested the short-term motor learning capacity of mice. Healthy and BTL-treated mice showed progressive improvement in performance with greater latency to fall (Healthy and BTL day 1 v Day 3: $p < 0.0001$). Free SynO4-treated and control groups of PD exhibited impaired motor learning with no difference in capacity for performance (PD Day 1 v Day 3: $p < 0.0497$; free SynO4 Day 1 v Day 3: $p < 0.0138$).

To describe the safety profile of BTL, the assay was conducted on blood samples of mice obtained 40 days post-treatment. No difference was found when comparing the control group and the BTL-treated group. The free SynO4 treatment indicated mild rises in levels of hepatic enzymes and bilirubin. PD, free SynO4, and BTL-treated groups all had elevated WBC and lymphocytic antibody levels, which are most probably due to increased AS levels with the potential of generating inflammation and immune response. Free SynO4 treatment lowered neutrophil counts. All the above findings as a whole mean that BTL for 4 weeks was very well tolerated without inducing organ toxicity [22]

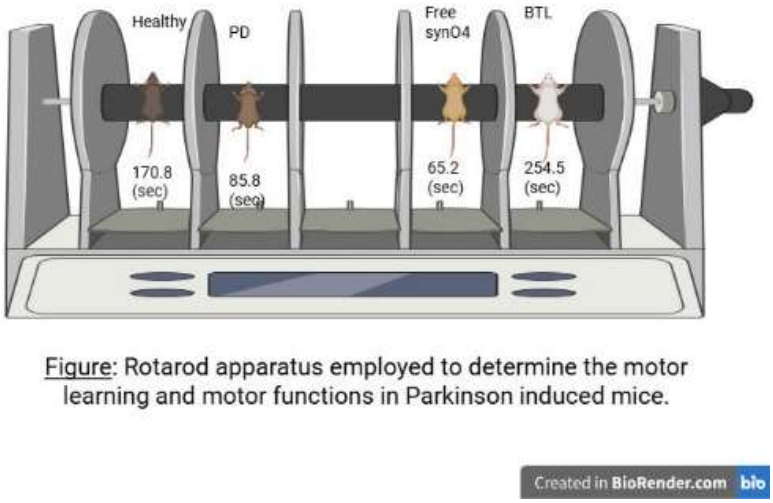

Figure: Rotarod apparatus employed to determine the motor learning and motor functions in Parkinson induced mice.

Figure 2: Rotarod apparatus experiment.

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2. **Alpha-Synuclein Aggregation Inhibition**

Metal and carbon-based NPs have been useful in inhibiting α-synuclein aggregation.

- Gold nanoclusters (AuNCs) inhibit α-synuclein fibrillation, enhance neuronal viability, and rescue dopaminergic neurons in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mice models.

Gao et al. reported that AuNCs prevented alpha-synuclein fibrillation and enhanced neuronal viability in 1-methyl-4-phenylpyridinium (MPP+) induced PD models.

Gold NPs and iron oxide NPs (IO-NPs) magnetic NPs are the most common metallic nanoparticle used for PD treatment.

According to GAO and colleagues research, Gold nano-clusters (AuNCs) would suppress accumulation and fibrillation of a-Synuclein and induce cell survival in Parkinson's disease (PD) lesioned cell model MPP+18. Assay on MPTP mice model of PD revealed AuNCs rescuing dopaminergic neurons and improving mental issues of ill mice. This research introduced a novel possibility for preparation of anti-PD medicine and proposes another direction in medication applications of AuNCs. [23]

- Graphene quantum dots (GQDs) penetrate the BBB, destabilize mature α-synuclein fibrils, suppress Lewy pathology, and thereby improve motor behavior and neuronal viability.

Kim et al have shown that graphene quantum dots (GQDs) can suppress α-syn fertilization. GQDs directly influence mature fibrils to trigger their dis-aggregation. Kim's in vivo group discovered GQDs penetrating through to the BBB and rescue from dopamine neurons loss, behavior

abnormalities, and Lewy neuritis pathology induced by α-syn formed fibrils. [24]

These findings hold promise for the creation of NP-based inhibitors of pathologic protein aggregation.

3. Anti-inflammatory and Antioxidant Effects

- Polymeric nanoparticles: like Poly(lactic-co-glycolic acid (PLGA), chitosan,, poly(ethylene glycol) (PEG), Polydopamine NPs and and amphiphilic block copolymers systems restrict neuroinflammation and oxidative stress in PD models. They have been reported to suppress dyskinesia and restore mitochondrial activity are utilized in different architectures for Parkinson therapy.

Bi et al. also synthesized a lactoferrin (Lf) surface-modified biodegradable poly(lactic-co-glycolic acid)-poly(ethylene glycol) (PLGA-PEG) nanoparticles (NPs) in another research work to intranasally deliver rotigotine to the brain for the treatment of PD [23]

4. Biosensing and Diagnostic Advancements

Nanotechnology has transformed the diagnosis of PD through the sensitive detection of biomarkers such as dopamine and α-synuclein in bodily fluids.

Gold NP-based, single-walled carbon nanotube-based, and ZnO nanowire-based biosensors have been reported to be extremely sensitive in their ability to detect these markers from saliva, blood, and CSF.

A 40-gold NP sensor array with 40 sensors discriminated PD patients from controls at 81% accuracy via breath Volatile compound (VOC) analysis, which was tantamount to the diagnostic efficacy of midbrain ultrasound.

In another study, Finberg et al. reported a clinical trial of a diagnostic device consisting of a cascade of gold nanoparticle or single-walled carbon nanotube sensors to detect volatile molecules in breath, and differentiate between control subjects and de novo PD. After initial screening by an expert neurologist the study population comprised 29 PD patients vs. 19 controls of matched age. The sensitivity, precision, and accuracy of the biosensor for detecting PD in controls were 79, 84, and 81%, respectively, compared to midbrain ultrasonography (93, 90, 92%) and odor detection (62, 89, 73%), significantly better than a diagnostic odor test and as good as nearly a brain ultrasound scan. [26]

These diagnostic platforms enable early detection and continuous monitoring of disease progression.

Method	Sensitivity (%)	Precision (%)	Accuracy (%)
Biosensor (40 sensors: gold nanoparticles/single-walled carbon nanotubes)	79	84	81
Midbrain Ultrasonography	93	90	92
Odor Detection	62	89	73

Table 1- Use of Biosensors (Gold Nanoparticles/ Carbon Nanotubes) to detect patients with Parkinson's Disorder.

5. Effects on enzymatic and chemical degradation

SLNs are formulated by a combination of lipids and surfactants or co-surfactants having some properties such as solidity at room and body temperature and low melting point.

Importantly, SLNs will guard drugs from enzymatic and chemical degradation, deliver the active ingredient to the target site with a significant decrease in toxic side effects on adjacent tissue and cross physiological barriers to increase bioavailability of included compounds [29].

In the palliative treatment of PD, Marine compounds would be likely to possess the property of incorporating reactive functional groups like -OH, -NH2, and -SH, which could make them antioxidants. These marine compounds may have other functional moieties which could make them targetable to the significant determinants of Parkinson's disease like alpha-synuclein, MAO-B, and other such proteins involved in the disease's signaling pathways.
Omega-3 fatty acids are being researched in many clinical trials at present, and two of them are associated with Parkinson's disease. One double-blind, randomized, placebo-controlled trial with 29 patients with Parkinson's disease, where there was a control group that received omega 3 fatty acid supplementation and a placebo group that received mineral oil. The trial validated that 12-week treatment with omega-3 fatty acids supplement along with antidepressant drug resulted in significant reduction of depressive symptoms. 14 patients exhibited </= 50% reduction of MADRS score (Montgomery Asberg Rating score), 7 patients exhibited remission with </= 12% reduction of MADRS score and 2 dropped out of experiment. Reduction of CGI score (Clinical Global Impression) and MADRS score was noted across all.
This demonstrates that omega-3 fatty acid supplementation is well tolerated in such patient populations and is likely to be a useful addition to the conventional pharmacotherapies.
Another double-blind, randomized, placebo-controlled study on 60 patients with Parkinson's disease identified that supplementation with omega-3 fatty acids in combination with vitamin E yielded favorable results according to the Unified Parkinson's Disease Rating Scale (UPDRS). [27] [28]

CONCLUSION

Parkinson's Disease (PD) is presently still not curable and a progressively disabling neurodegenerative disorder; however, nanotechnology is coming up as a promising multi-faceted strategy towards management of the disorder's complex pathophysiologic mechanisms. Nanoparticle (NP)-mediated delivery systems have specific advantages in overcoming BBB permeability, in addition to being capable of delivering targeted delivery of neuroprotective drugs and AS aggregation inhibitors [30].

A variety of NP formulations—e.g., liposomes, nanoemulsions, polymeric, metal, and hybrid nanoparticles—exhibited encouraging preclinical results with the prevention of oxidative stress, preservation of mitochondrial function, and inhibition of dopaminergic neuronal degeneration in PD animal models. Additionally, nanoparticle-assisted biosensing platforms offer highly sensitive and non-invasive diagnostics for the early detection of PD, which is required for timely therapeutic intervention [3] [31]

Aside from these advances, bench-to-bedside translation is yet to be realized. The main challenges are NP-induced toxicity, immunogenicity, scalability of production of NPs, and inexperience with long-term biological activity. These issues need to develop complete regulatory guidelines to evaluate the safety and efficacy of nanomaterials as an instrument in clinical intervention. Regulatory, as well as ethical, aspects and proper preparation of corresponding animal models and corresponding preclinical assay sensitivity are crucial in advancement for NP-based therapeutics against PD. Accurate forecasting of nanoparticle pharmacokinetics, biodistribution, metabolism, and excretion profiles in the human body are major milestones to advance these technologies from preclinical to clinical trials [32]

Future research will aim to develop multi-functional nanoparticle platforms that capture therapeutic and diagnostic functions (theranostics), customize nanomedicine to the patient's genetic profile, and incorporate artificial intelligence so that disease and treatment can be tracked in real-time. Thus, nanotechnology offers an inexpensive yet efficient alternative to conventional PD diagnosis techniques [30]

Nanoparticle effects on pathological protein aggregation are all described as extremely variable as a function of their composition, size, shape, and charge. Additional research is required to establish the relative contributions of such sets of physical and chemical variables towards controlling NP activity in a physiological environment. Both in vivo and in vitro systems have crucial roles for the optimization of NP-based therapeutic intervention in the prevention of neurodegenerative disease.

Nanomaterials are also increasingly changing therapeutic frameworks in neurology both by improving the efficiency of delivery of therapeutic agents and by making whole new classes of therapy for traditionally treatable neurological diseases possible. [32]

Nanomedicine has the potential to improve the efficacy of therapy as well as diagnostic accuracy. Nanoparticles, due to their special property of crossing the BBB, offer great promise for the treatment of brain diseases of greater complexity.

However, higher clinical effectiveness and safety are necessary against increasingly instrumented nanoparticle toxicity and bioaccumulation. Non-toxicity should also take precedence for the next

generation of therapeutic nanoparticles. Better NP formulation, including those that are antibody-conjugated, could conceivably further enhance the targeting of biomarker and therapeutic agents in neurological disease.

Lifestyle interventions independent of medication, including a healthy diet, exercise, cognitive and social constituents, were associated with better brain function. Those nonpharmacologic approaches, including rehabilitation treatments such as physiotherapy, occupational, speech and cognitive therapies, all have a positive impact on the maintenance of functional capacity and Quality of life (QoL) in neurologic patients. Combination of nanotechnology with these multi-pronged approaches may result in comprehensive treatment of neurodegenerative disorders [33]

In earlier studies, new treatments like BTL-based therapies have been shown to slow down the progression of Parkinson's Disease (PD) in animal tests. For example, BTL worked better than free SynO4 in stopping the build-up of AS and the death of neurons. Additionally, giving BTL through an IV for two to four weeks led to big reductions of AS accumulation both inside and outside cells. This treatment also helped maintain movement abilities and thinking skills with a commendable safety record.

Although natural substances are safe for the brain, they have not been used widely in clinics yet because there are no well-designed randomized controlled trials to confirm their effectiveness and safety. However, their ability to reduce oxidative stress—a common cause of nerve degeneration—offers hope for use alongside other treatments.

Given the various causes of PD, there is a chance to develop drugs that target multiple issues. Most current PD medications target only one issue, which often leads to less effective results and side effects. The approval of GV-971, a compound from the ocean, for phase III clinical trials for Alzheimer's disease in China shows the treatment possibilities of marine-based substances in nerve-related diseases and highlights the need to investigate these substances for PD. [34]

Nevertheless, although BBB remains the most potent protector against CNS drug delivery, mounting concern regarding NP-induced neurotoxicity also makes clinical translation more difficult. Neurotoxicity—predominantly ROS-mediated—is severely influenced by the physicochemical properties of nanoparticles including shape, size, surface area, solubility, concentration, exposure duration, and delivery route. For example, evidence has suggested that iron oxide nanoparticles have been shown to provoke oxidative stress, neuronal apoptosis, and behavioral abnormalities in animal models.

Since extensive data on NP neurotoxicity are not currently available, further in vitro and in vivo investigations are required. Up-to-date tools like in silico modeling, computational biology, and bioinformatics can be used to design optimized NP preparations and optimize safety assessments.

Despite such barriers, incorporation of marine compound analogs into standard PD treatment is a natural and persuasive route towards neuroprotection. Further, the crossover of nanotechnology into PD treatment is not as much an upgrade as a change of treatment paradigm. With constant verification and inter-disciplinary working, nanomedicine holds not only to the quelling of symptoms but the redesign of disease progression at its most fundamental level.

Future Perspectives

During the recent decades, numerous approaches have been studied to enable effective delivery of drugs to the CNS. Despite tremendous progress, impermeability of the BBB remains a major limitation, and many attempts are needed to create new delivery platforms for therapeutic and diagnostic medicines.

Gene therapy holds great promise for the treatment of neurodegenerative disorders, based on the understanding of disease-specific gene mutations. The employment of neural stem cells (NSCs) and the control of their differentiation to therapeutic neurogenesis is another innovative strategy. Combination of gene therapy and nanomedicine can offer a platform for the treatment of numerous monogenic and complex neurological disorders. Designing targeted therapeutic regimens with minimal off-target effects requires deep understanding of the genetic architecture of these disorders. [35]

While considerable progress in research has been made in neurodegenerative diseases, it remains a far-fetched challenge, particularly early diagnosis. There is an urgent need to create dependable biomarkers and cutting-edge imaging methods that will facilitate simple and accurate detection of the disease in its early stages. [36] [37]

At the same time, there is increasing evidence for the role of non-pharmacological interventions in enhancing traditional therapies. Cognitive stimulation, exercise, dietary changes, and lifestyle modification overall have all been shown to help in the restoration of brain health and can be valuable adjuncts in the overall management of neurodegenerative disease. [33]

Conflicts of Interest

The authors declare no conflicts of interest.

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