

ARTICLE ID: BTS0326028

NANOTECHNOLOGY IN DIAGNOSIS AND TREATMENT OF PARKINSON'S DISEASE

Yamini Koraganji | Nattala Santhoshini | Dama Pujitha | *Kanaka Durga Devi Nelluri

KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada, Andhra Pradesh, India.

Corresponding Author Email: Pujithadama12345@gmail.com**Received:** 15 July 2025 | **Revised & Accepted:** 13 October 2025.

Keywords: Parkinson's disease (PD); nanotechnology; nanoparticles; drug delivery; early diagnosis; quantum dots; metallic nanoparticles; biosensors; α -synuclein; dopamine detection; theranostics; L-DOPA nanoformulation; gene therapy; nanocarriers; neurodegenerative disorders.

ABSTRACT

Parkinson's disease (PD) is the second most frequent neurodegenerative condition, with dopaminergic loss in substantia nigra. It induces typical motor symptoms—bradykinesia, rigidity, tremor—and ample non-motor side effects like cognitive impairment and sleep disturbances. Levodopa and dopamine agonists are outdated therapy for which symptomatic treatment only results, and they have long-term adverse effects like dyskinesia and fluctuating efficacy. The major obstacle to the development of more potent therapies is the blood-brain barrier (BBB) that dissuades drug penetration into target sites in the brain. Nanotechnology presents a paradigm-shifting therapy for PD in the form of drug delivery in an efficient and target-specific format through the BBB. Polymeric, lipid nanoparticle, and exosomes, dendrimers, and micelles are constructed with the aim of facilitating drug stability, bioavailability, and site-specific targeting. Ligand modification of surface ligands with transferrin or lactoferrin improves their delivery across the BBB and retention at brain damage sites. They can be encapsulated in a range of agents from dopamine to neuroprotective proteins, antioxidants, and gene therapies. Nanotechnology platforms also support non-invasive routes such as intranasal or transdermal with sustained release and higher patient compliance. In addition to the therapy, nanomaterials are being used to an increasing extent for diagnosing PD at an early stage of its course with quantum dot-based systems and biosensors that can precisely measure biomarkers at ultra-low concentrations. Nanotechnology in general provides novel platforms for personalized, targeted, and minimally invasive treatment of Parkinson's disease. More clinical data and studies should be conducted to advance these promising technologies to the stage of patient treatment safely and effectively.

INTRODUCTION

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder found in around 115 of people older than 60 years there is no established cure at present and

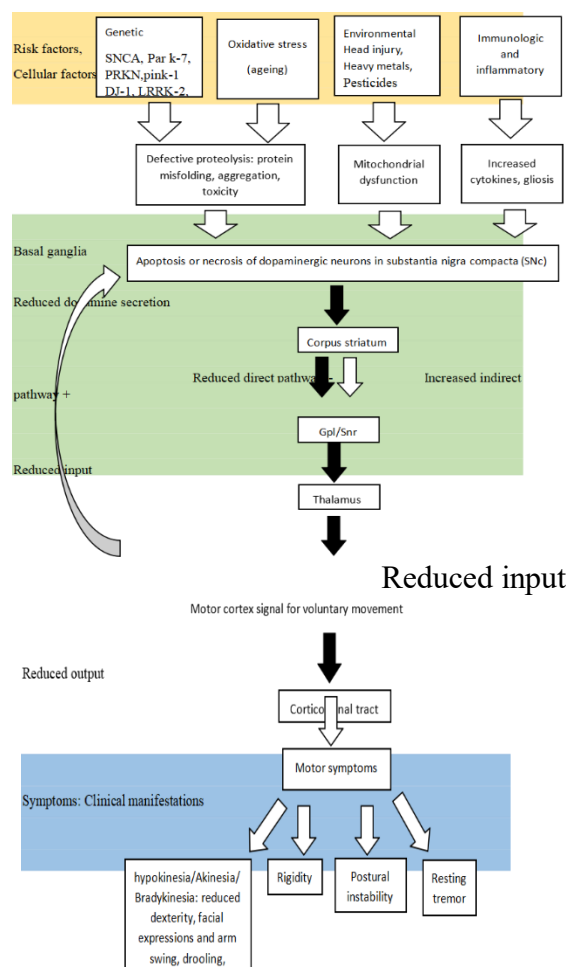
current treatments primarily have a symptomatic effect without stopping disease progression the main pharmacological treatment is to rebuild dopaminergic function with L-dopa which is

still the most successful drug in enhancing motor control and quality of life nonetheless long-term administration is associated with adverse events like dyskinesias and loss of efficacy with prolonged administration owing to its short elimination half-life and tolerance development to overcome these drawbacks researchers are investigating nondopaminergic treatments that involve adenosine glutamate serotonin and adrenergic receptors as well as calcium channel blockers iron chelators glp-1 agonists anti-inflammatory drugs neurotrophic factors and gene therapy a challenge continues to be the development of delivery systems to efficiently carry drugs across the bloodbrain barrier bbb nanoparticle-based drug delivery systems have proven to be good potential carriers because they can cross the bbb and release the drugs in a controlled fashion surface modifications like pegylation increase circulation time and reduce immune response improvements in nanoparticle design and protein corona control provide new hope for targeted as well as effective treatment of pd.

CLINICAL ASPECTS OF PARKINSON'S DISEASE

Parkinson's Disease (PD) is a progressive disorder that damages dopamine neurons in the substantia nigra, which affects how the basal ganglia work. Key motor symptoms include bradykinesia, rigidity, resting tremor, postural instability, and akinesia. In advanced stages, patients often experience freezing of gait (FOG) along with complications such as Levodopa-induced dyskinesia and motor fluctuations. PD also includes important non-motor symptoms like cognitive decline, depression, anxiety, sleep problems, and autonomic issues, such as constipation and low blood pressure. Other symptoms can include hallucinations

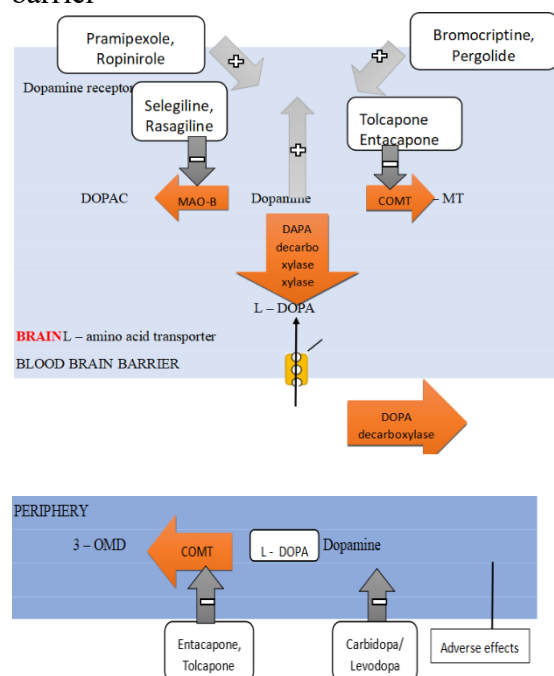
and loss of smell. Many of these non-motor signs can appear before motor symptoms, adding to the challenges of early diagnosis and overall disease impact.



1.5 CURRENT TREATMENT STRATEGY FOR PARKINSON'S DISEASE

Parkinson's disease medication such as L-DOPA, dopamine agonists, MAO-B inhibitors, and amantadine improve symptoms. L-DOPA works best but produces long-term side effects. To postpone these, therapy sometimes begins early using safer medications such as dopamine agonists or MAO-B inhibitors. More recent treatments incorporate nanoparticles to more efficiently deliver

medication through the blood–brain barrier^{1,5}



NANOTECHNOLOGY RESOURCES FOR DISTRIBUTION OF HEALING REPRESENTATIVES

Nanoparticles:

^{1,7}Nanotechnology involves nanoscale materials possessing special physical, chemical, or biological properties, which render them precious for medical purposes. Nanoparticles (NPs), normally 1–1000 nm in diameter, are most frequently applied to deliver drugs. NPs have the ability to encapsulate, adsorb, or bind active pharmaceutical ingredients to enhance solubility, minimize toxicity, improve bioavailability, and facilitate controlled drug release. In the treatment of Parkinson's disease (PD), one of the biggest challenges is to facilitate the crossing of NPs through the blood-brain barrier (BBB), arrive at the brain tissue, and release the drug efficiently. This depends upon their nature and whether they disrupt the BBB temporarily or

not. NPs pass the BBB via different mechanisms, such as endothelial cell endocytosis and transcytosis. They can also accumulate within brain capillaries, enhancing drug concentrations. Surfactants such as polysorbate 80 and poloxamer 407 facilitate by inhibiting P-glycoprotein and increasing membrane permeability or opening tight junctions. The majority of NPs employed in PD treatment are synthesized using polymeric or lipid material for more efficient delivery.

Polymeric Nanoparticles

Polymers are better than metals or ceramics at being flexible, which makes them perfect for making nanoparticles (NPs). Because of this, fullerenes, metal particles, quantum dots, carbon nanotubes, and silica NPs are not used as often. People often use biodegradable polymers like poly(lactic-co-glycolic acid) (PLGA), poly(lactic acid), poly(n-butyl cyanoacrylate) (PBCA), poly(ε-caprolactone) (PCL), human serum albumin, and chitosan. Chitosan's ionic gelation process doesn't use organic solvents, which makes it easier to add proteins and peptides. But polymeric NPs have some problems, such as leftover solvents and possibly harmful monomer byproducts. Polymers are preferred for Parkinson's disease (PD) therapy because there are well-known ways to make them and a lot of safety data that supports effective and safe drug delivery systems.

Solid Lipid Nanoparticles

Solid lipid nanoparticles (SLNs) are created by substituting liquid lipids with solid lipids, providing a small size and a high capacity for drug loading. Tsai et al. developed SLNs loaded with apomorphine utilizing glyceryl and PEG monostearate. SLNs based on PEG exhibited reduced size

attributed to increased hydrophilicity. In rats, these SLNs enhanced bioavailability by 25–28% and exhibited 5–6 times more efficacy in a Parkinson's model than an aqueous solution.^{1,7}

In inclusion, it's important to give consideration to at least three essential parameters for the development of a nanocarrier system this is certainly effective.

PARAMETER EVALUATION FOR NANOPARTICLE DESIGN

Loading capability is a vital parameter for the utilization of nanocarrier methods, simply because they offer low toxicity since it is preferable to transport high-potency medications using high-capacity loading systems, even in matrices that do not possess sufficient affinity but being utilized for vectorization. An undeniable fact that when you look at the most of situations compromises the toxic degrees of the NP matrix by contrast, low-potency drugs must certainly be transported in systems with high loading capabilities because low-capacity systems must certainly be administered at high concentrations. For PD, lots that is high right to ensure prolonged launch with a reduced quantity of matrix NP in order to prevent diminishing poisoning amounts.

Particle size

The belief that solely small nanoparticles are effective is changing. Bigger particles have demonstrated promise, providing greater drug loading and varied material application. Although there are physiological size restrictions, particles as large as 345 nm—and even greater than 400 nm—can pass through barriers such as the BBB or BRB. Performance is determined by surface properties, not only by size. Consequently, both in vitro and in vivo evaluations are crucial to confirm their

therapeutic application in treating Parkinson's disease.

Zeta potential

Zeta potential influences nanoparticle stability and blood-brain barrier interaction. Although charge affects transport, an optimal value has not been established. Reduced levels of negatively charged nanoparticles are more secure, as elevated or positive charges could interfere with the blood-brain barrier. In general, brain delivery isn't determined solely by charge. Making use of tools for medication focusing on earnestly increases the likelihood of directing the NP toward the CNS.

Active targeting mechanisms:

To enhance brain delivery in the therapy of Parkinson's, nanoparticles may be capped with ligands such as transferrin, insulin, or certain peptides. These assist the particles in crossing the blood–brain barrier by binding to natural receptors. This method is applied to both lipid and polymer-based carriers, which makes it effective for delivering drugs that are otherwise not capable of reaching the brain.¹

NANOFORMULATION STRATEGIES FOR THE TREATING PD

Numerous nanoformulations which have been examined for PD diagnosis and treatment tend to be discussed herein. Dining table 1 provides a summary of the explained techniques.

Liposomes:

^{2,9}Liposomes are lipid bilayer spheres with a water-based interior, usually created from phospholipids and cholesterol. They're already applied in many FDA-approved drugs, such as Doxil for ovarian cancer. In Parkinson's studies, transferrin-coated,

ARTICLE ID: BTS0326028

PEGylated liposomes have been utilized to transport the TH+ gene into the brain. Another study utilized dopamine-filled liposomes labeled with RVG29 to deliver to

brain cells, demonstrating better delivery to the striatum and substantia nigra and greater therapeutic effects in PD models^{2,9}

^{2,4}**Table 1:** Nanoformulation approaches in parkinson's disease treatment

Type of formulation	Drug name	Drug category	In vitro cell line	Animal model	Toxicity/side effects
Liposomes	Levodopa	Dopaminergic agonist	SH-SY5Y (human neuroblastoma)	-	Approximately 90% cell viability (3T3 and SH-SY5Y Cells)
	BPD	Dopamine precursor	Murine brain endothelial cell lines bEnd.3, human neuroblastoma SH-SY5Y cell line, mouse neuroblastoma cell line	6-OHDA-induced PD mice model	No more overactive microglial cells, no change in hippocampus, normal values for biomarkers (creatine kinase for heart, aspartate aminotransferase and alanine aminotransferase for liver, urea nitrogen and serum creatinine for kidney function)
	Dopamine	Neurotransmitter	-	MPTP-induced mouse model PD	Elevated striatal dopamine level by 40% in mice
Micelles	Catalase	Antioxidant	-	MPTP-induced PD mouse model	No hepato-, nephro- or spleen toxicity in mice and no neuronal injury, edema or breakdown of BBB

ARTICLE ID: BTS0326028

	Baicalein	Antioxidant	MDCK-MRP2 cells	MPTP-induced zebrafish model	No cytotoxicity in MDCK-MRP2 cells
Exosomes	Catalase	Antioxidant	PC 12 cell line, mouse macrophage cell line (Raw 264.7)	6-OHDA-induced PD mouse model	No microglial activation and no neurotoxic effect in mice
PLGA NPs	Dopamine	Neuroprotectant	SH-SY5Y cell line	6-OHDA-induced PD rat model	No adverse effect on dopaminergic and cardiovascular system, non-toxic to kidney, liver and spleen
	Rotigotine	Anti-parkinsonian	16 HBE, SH-SY5Y cell line	-	Non-toxic in cell line
Lactoferrin attached PEG-PLGA NPs	Urocortin	Cytoprotectant for neurons	bEnd.3 cell line	6-OHDA-induced PD rat model	Acceptable toxicity, studied through CD 68 immunohistochemistry and cell viability assay
Transferrin antibody attached PLGA NPs	Tempol	Free radical scavenger	RG2 cells	-	Not affects cell proliferation, non-toxic
Chitosan NPs	Selegiline	MAO-B receptor blocker	—	Rotenoneinduced PD rat model	—
PLGA NS	GDNF and VEGF	Neuroprotective Agent	PC 12 cell line	6-OHDA-induced PD rat model	Slight decrease in number of rotation at the end of study (10 weeks), nontoxic in cell line

Transdermal depot of microemulsion	Apomorphine	Dopaminergic agonist	-	PD patients (21)	Six patients reported sleepiness during treatment, 1 patient reported mild orthostatic hypotension, 3 patients reported transient nausea, and 1 patient discontinued owing to uncontrollable side effects
Dendrimers	hGDNF gene	Neuroprotective Gene	-	Rotenone induced PD rat model	No apparent toxicity in major organ
Solid lipid NPs	Apomorphine	Dopaminergic agonist	-	6-OHDA-induced PD rat model	No uptake in olfactory bulb, hippocampus, thalamus and cerebral cortex, non-toxic and no side effects
	Bromocriptine mesylate	Dopaminergic agonist	-	6-OHDA-induced PD rat model	-
Nanobubbles	Apomorphine	Dopaminergic agonist	-	-	Non-toxic

Exosomes

²Exosomes are lipid-encased nanovesicles featuring surface proteins that assist in their fusion with cells. Because they are naturally secreted by immune cells, they can evade phagocytic elimination, making them potential drug carriers. Haney et al. utilized exosomes to transport catalase, an antioxidant, for treating Parkinson's disease. Catalase was incorporated through techniques such as sonication, extrusion,

and the use of permeation enhancers, resulting in elevated drug loading. In vitro, neurons absorbed exosomes containing catalase, and in vivo, delivering them intranasally demonstrated neuroprotection in PD mice—results not observed with catalase alone or with empty exosomes.

Metallic NPs in PD treatment:

Metallic nanoparticles (NPs) such as gold, silver, magnetic, and cerium oxide NPs are considered for disease treatment, including Parkinson's. Targeted brain delivery was achieved using lactoferrin-coated magnetic NPs by Qiao et al. Gao et al. synthesized gold nanoclusters that inhibited fibril formation and reached the substantia nigra in PD models. Antioxidant effects of CeO₂ NPs have been demonstrated; Dillon et al. revealed they exerted protection against dopamine neurons and enhanced striatal dopamine levels in PD mice.²

^{2,6}Graphene quantum dots (GQDs) to treat PD

graphene quantum dots gqds a group of carbon-based nanomaterials possess low toxicity chemical stability high quantum confinement and stable photoluminescence they have been found to possess great promise in inhibiting and reversing the aggregation of alpha-synuclein -syn one of the primary proteins associated with parkinsons disease gqds are generally synthesized by refluxing carbon sources with strong acids nitric and sulfuric acid at elevated temperatures 800c and then rotary evaporation in vitro experiments with thioflavin t assays and tem imaging showed that gqds were able to suppress -syn fibril formation and induce disaggregation the length of the fibrils was shortened from 1 μm to 70 nm within 24 hours nuclear magnetic resonance nmr analysis demonstrated that gqds interact with -syn fibrils by electrostatic force between the carboxyl groups of gqds and the positively charged area of the protein molecular dynamics simulations also established binding to the n-terminal area with notable disruption of -sheet structures with time in vivo experiments in mouse models also confirmed the effectiveness of gqds in inhibiting and disaggregating.^{2,6}

²Polymeric NPs

Nanoparticles frequently employ polymers due to their adaptability and capacity for biodegradation. Frequently utilized materials comprise PLGA, PBCA, and chitosan, eliminating the need for toxic solvents. Although some materials can leave damaging residues, polymers remain the best choice for treating Parkinson's due to their safety and ease of use.

Polyethylenimine (PEI)

Batrakova and co-workers investigated the potential of polyethyleneimine (PEI) to construct a catalase-based nanoformulation using bone marrow-derived macrophages (BMMs) as carriers. The resulting nanozyme, with a size of about 60–100 nm, exhibited stable performance under physiological pH and maintained antioxidant activity. BMMs effectively engulfed the nanozyme within 40–60 minutes, and catalytic activity lasted for 24 hours. In an MPTP-induced Parkinson's disease mouse model, approximately 0.6% of the injected nanozyme were found to localize in the brain.

Three delivery pathways were suggested by the researchers: firstly, BMMs might travel through the blood–brain barrier (BBB) and deliver catalase directly in the substantia nigra; secondly, the nanozyme might cross the BBB independently upon release into the circulation; thirdly, catalase might be secreted into peripheral organs such as the liver and spleen, mitigating systemic inflammation and providing neuroprotection. The study underscores the promise of macrophage-mediated delivery for site-specific brain therapies.

PLGA

carroll et al created plga nps 80110 nm loaded with tempol and modified with a transferrin antibody for brain targeting such

nps penetrated the bbb exhibited considerable uptake and inhibited glioma cell viability more than free tempol pahuja et al created dopamine-loaded plga nps 120 nm that penetrated the bbb released dopamine over a period of time and alleviated pd symptoms without toxicity hu et al employed lactoferrin-conjugated peg-plga nps for bbb targeting the nps loaded with lactoferrin and urocortin demonstrated effective brain delivery through receptor-mediated endocytosis

Chitosan

Chitosan polymers with their good mucoadhesive properties have proved useful in creating nanoparticles for delivering poorly soluble drugs. One of the applications is the preparation of selegiline-loaded nanoparticles by using chitosan for nasal administration. Selegiline, a wellknown drug used in Parkinson's disease, is plagued by poor absorption when administered orally. To enhance its therapeutic efficacy, scientists developed chitosan nanoparticles for intranasal administration, which drastically increased the drug's availability in the brain and blood. This novel route of administration resulted in improved movement-related effects in animal models, including greater mobility, decreased rigidity, and increased stride length. Additionally, the preparation caused increased levels of brain glutathione, suggesting a possible antioxidant effect. The nanoparticles were of a mean diameter of around 342 nm, a moderate PDI, and more than 92% entrapment efficiency. The delivery system provides a promising, non-invasive approach for enhancing Parkinson's therapy by direct targeting the brain.

Dendrimers

Huang et al. synthesized polyamidoamine (PAMAM) nanoparticles PEGylated with lactoferrin for targeted delivery of human glial cell line-derived neurotrophic factor (hGDNF). Lactoferrin was used as a targeting ligand because its receptor is highly expressed on the blood–brain barrier (BBB). The non-viral PEGylated nanoparticle system improved brain delivery by transvascular administration, increased circulation time, and decreased immune clearance. In a rotenone-induced Parkinson's disease model of mice, the preparation restored motor function, increased levels of dopamine and other monoamines, and showed neuroprotection for dopaminergic neurons, suggesting potential as a therapeutic strategy in PD treatment.

Micelles

Micelles tend to be amphiphilic colloidal dispersions having drug-loading that is large for lipophilic and hydrophilic medications being of particle sizes within the array of 5–100 nm. Also, functionalization to micelle that is polymeric causes changes in biological along with physicochemical properties associated with medication substances. A different type of micelle, understood once the immunomicelle, is created by coupling antibody this is certainly monoclonal the hydrophilic element of micelles. Recently, Brynskikh et al. formulated a micelle-containing catalase nanozyme. This nanozyme had been more loaded into bone marrow macrophages for specific distribution towards the substantia nigra. The researchers additionally performed an in vivo study on an MPTP-caused mouse model for PD. They used macrophages for targeted distribution of

nanozyme to the mind capillary system that provided suffered launch of catalase. Catalase acts as an anti-oxidant and it is utilized being a representative this is certainly neuroprotective PD.

Nanospheres (NS)

Herran et al. formulated a neuroprotective using PLGA nanoparticles containing glial-cell-linederived neurotrophic factor (GDNF) and vascular endothelial growth factor (VEGF). Following the loading of agents, particle diameters were 235 nm for VEGF-NS and 221 nm for GDNF-NS, while zeta potential was 25 mV for both. Encapsulation efficiency was 44% in VEGF-NS and 74% in GDNF-NS. In vitro experiments with 6-OHDA-treated PC-12 cells revealed that cell viability increased by 51% upon treatment. In vivo experiments in a 6OHDA-treated rat model of Parkinson's disease (PD) were in agreement. Behavioral tests revealed significant attenuation in amphetamine-induced rotations. Immunohistochemical analysis also demonstrated neuroprotection within the striatum and substantia nigra. The dualagent nanoparticle strategy proved to have encouraging neuroprotective effects for treating PD.

Transdermal depot of microemulsion

priano et al prepared a water-in-oil wo apomorphine-containing microemulsion with a 749 nm droplet size and a pdi of 020 they topically applied 10 g of the formulation transdermally apomtd to a 100 cm area on the upper chest covered by a 1 mm thick biocompatible foam tape a polyester membrane and an occlusive layer to avoid evaporation combined with levodopa therapy this technique enhanced motor function updrs iii and maintained plasma drug concentrations recent work is focusing more on transdermal depot

systems like microemulsions polymeric nanoparticles and liposomes for sustained controlled drug release without multiple dosing

SLNs

Solid lipid nanoparticles (SLNs) are prepared by substituting solid lipids for liquid lipids and possess such benefits as small particle size, high drug loading, and high surface area. Tsai et al. prepared apomorphine-loaded SLNs with glyceryl monostearate and PEG monostearate. More hydrophilic (higher HLB value) PEG monostearate resulted in particle size being smaller.

The SLNs improved bioavailability in rats by 25–28% compared to a 2% aqueous solution. Moreover, the formulation showed a five- to sixfold enhancement in efficacy in 6hydroxydopamine-lesioned rats, demonstrating enhanced therapeutic potential.

Nanobubbles in the treatment of PD

Nanobubbles are the medication that is ultrasound-mediated system consists of perfluorocarbons and essential oils that form w/o emulsion consists of hollow liposomes having a mean diameter of 500 nm. They truly are advantageous over microbubbles (1–6 mm) due to the smaller dimensions that will help to facilitate BBB penetration after applying waves being ultrasound. Hwang et al. prepared nanobubbles using an emulsification technique with particle measurements of 150 nm to 380 nm for the delivery of apomorphine. The problem with apomorphine is an insufficient quantity of medicine can achieve mental performance following administration due to its brief half-life (41 min) and substantial metabolism that is first-pass. The prepared nanobubble formulation demonstrated a

sustained launch of apomorphine upon sonication at 1 MHz and showed two-to fourfold more medication release when compared using the team this is certainly non-ultrasound. The evolved nanobubbles also revealed an increase in the security of apomorphine in plasma as compared with the apomorphine that is free <10per cent hemolysis.

ODORRANALECTIN: A PEPTIDE THIS IS CERTAINLY LITTLE DELIVERY COMPANY' FOR PD

Odorranalectin is really a peptide that is lectin-like was identified initially from the epidermis secretions of *Odorrana grahami*. The dwelling that is standard of contains 17 amino acids having a sequence of YASPKCFRYPNGVLACT, which contains sulfur moieties that are effective at creating disulfide bonds. This can be helpful for medication distribution simply because they can very quickly conjugate or encapsulate the agents which can be healing. Overall, odorranalectin had been discovered is stable with reduced poisoning and mutagenicity this is certainly low. Wen et al. used odorranalectin for nasal distribution of urocortin peptide (UCN) towards the brain. Furthermore, to reduce the poisoning and mutagenicity of odorranalectin, it absolutely was conjugated to PEG-PLGA.

CELL-PENETRATING MITOCHONDRIA-TARGETING PEPTIDE THAT IS SYNTHETIC (CAMP):

Peptides are becoming increasingly popular in drug delivery, with more than 60 FDA-approved and numerous others in progress. Nonetheless, most target cell surfaces are affected by inadequate membrane penetration. Cell-penetrating peptides (CPPs) are being investigated for

transporting therapies into cells. In Parkinson's disease, excessive ROS-induced oxidative stress is crucial. Kang et al. utilized a CPP (CAMP) to transport the antioxidant protein metallothionein (MT1A) to mitochondria in PD cell models, where it decreased ROS and improved mitochondrial function.

^{2,12}NP-mediated inhibition of PD via a computational biology approach

Limited knowledge of PD mechanisms complicates effective treatment. Because both genetic and environmental factors are involved in PD, intricate molecular research and verified models are necessary. Kaushik et al. applied computational biology to investigate inhibition of α -synuclein by CeO₂ nanoparticles. In their study, they found that CeO₂NPs had intense interaction with essential residues of α -synuclein, exhibiting greater inhibitory activity than LDOPA. These observations underscore the potential of CeO₂NPs in PD treatment.

Current therapeutic advances in parkinson's disease L-DOPA

^{3,10}L-DOPA is still the gold standard for PD but is plagued by peripheral metabolism and waning long-term effectiveness, inducing dyskinesia and motor complications. To achieve better brain delivery and less adverse effects, nanoformulations such as PLGA, chitosan NPs, AuNFs, and thermo-reversible gels have been invented. Intranasal administration of these formulations exhibits greater brain targeting, sustained release, less systemic exposure, and enhanced therapeutic effects. Advances such as nano-scaffolds and nanosilica reservoirs exhibited extended release of dopamine and reduced dyskinesia.^{3,10}

Ropinirole

³Ropinirole, a D2 receptor agonist, is poorly absorbed orally and is painful on administration via IV. Nanocarriers such as SLNPs, PLGA, chitosan NPs, nanoemulsions, and transdermal systems improve brain targeting, prolong release, and minimize the dosing interval. These formulations indicate increased bioavailability, reduced side effects, and improved therapeutic efficacy in PD models.

Bromocriptine

Limitations of bromocriptine are poor penetration through the brain and short half-life. Chitosan NPs, SLNPs, and self-emulsifying systems improve intranasal delivery to the brain, extend the action of the drug, stabilize plasma drug level, and control PD symptoms effectively.

Pramipexole

Nanocarriers of Pramipexole, such as chitosan NPs, mesoporous silica NPs, PLGA nanosuspensions, and alginate nanodispersions, enhance intranasal

delivery to the brain, boost antioxidant activity, minimize oxidative stress, and improve PD-related motor impairment.

Selegiline

Selegiline's problems of bioavailability are overcome using chitosan NPs, nanolipid carriers, PLGA NPs, nanoemulsions, and transdermal systems. These enhance brain targeting, increase half-life, maintain release, and improve behavioral effects without reducing systemic exposure.

Urocortin

Urocortin's brain delivery is improved through lactoferrin- and odorranalectin-conjugated PLGA NPs given intranasally, exhibiting neuroprotection, decreased striatal damage, and enhanced drug retention in PD models.

Apomorphine

Limitations of apomorphine are overcome by perfluorocarbon nanobubbles and SLNPs, providing improved brain delivery, extended action, decreased frequency of dosing, and increased bioavailability through non-invasive methods.

^{3,4}**Table 2:** Few nanomedicine containing anti-parkinson's drugs in pre-clinical stages

Class	Drug	Nanoparticle type	Synthesis method	Route of administration	Animal model	Result
Dopamine precursor	L-DOPA	Chitosan nanoparticles	Cold technique	Intranasal	Wistar rat	L-DOPA loaded Chitosan nanoparticles incorporated in Pluronic PF127 gel

ARTICLE ID: BTS0326028

						prevented L-DOPA from peripheral degradation, improved its brain uptake compared to L-DOPA administered alone, and also overcame the use of carbidopa in combination.
		Poly(lactic-co-glycolic acid) nanoparticles	Double emulsion method	Intranasal	Wistar rats	The effect of nano-DOPA was long-lasting and twice as high as that of L-DOPA and LDOPA+benserazide.
Dopamine agonist	Ropinirole	Polymer-lipid hybrid nanoparticles	Emulsification solvent diffusion method	Intranasal	Albinomice	They showed high therapeutic effect even at lower doses when compared to that of higher doses of ropinirole
		Chitosan nanoemulsion	High pressure homogenization	Intranasal	Wistar rats	They showed more pronounced brain targeting potential and restored the behavioural and

ARTICLE ID: BTS0326028

						biochemical changes in Parkinson's disease.
	Bromocriptine	Nanoparticulate lipid dispersion	Emulsification	Intraperitoneal	Sprague Dawley rats	They showed pronounced improvement in the pharmacokinetic properties and prolonged the action of drug when compared to that of bromocriptine alone.
		Chitosan nanoparticles	Ionic gelation method	Intranasal	Swiss albino mice	They enhanced the brain drug targeting and reversed the catalepsy and akinesia behaviour in Parkinson's disease.
	Pramipexole	Chitosan nanoparticles	Ionic gelation method	Intranasal	Sprague-Dawley rats	They improved the motor functions and enhanced the antioxidant status when compared to that of pramipexole alone.
	Apomorphine	Solid-lipid nanoparticles	Emulsification method	Intravenous	Wistar rats	They improved bioavailability by

ARTICLE ID: BTS0326028

						severalfolds and an efficientbrain targeting was achieved.
MAO-B inhibitor	Selegiline	Chitosan nanoparticles	Ionic gelation method	Intranasal	Sprague-Dawley rats	The concentration of selegiline in plasma and brain was found to be many folds higher when compared to selegiline administered singly.
		Oil-in-water Nanoemulsion	High energy emulsification	Intranasal	Wistar rats	They enhanced brain targeting capacity andbioavailaibility of the drug, and markedly reversed the effect of haloperidol.
		Poly(lactic-co-glycolic acid) nanoparticles	Double emulsion solvent evaporation method	Transdermal	Wistar rats	They targeted the drug to the brain much more effectively than selegiline alone.

Metal Chelators

Oxidative stress induced by metal accumulation iron manganese copper zinc is responsible for dopaminergic neuron loss in parkinsons disease resulting in elevated ros generation and motor impairmentiron chelators are neuroprotective but are hampered by low bioavailability and short half-life chelators based on nanoparticles

enhance brain delivery and diminish side effectszwitterionic iron-chelating nanoparticles exhibit extended circulation and successful brain targeting alleviating symptoms in pd models citrate-coated mno nanoparticles assist against manganese toxicity by chelating excess mn and mitigating oxidative stress

α -Synuclein Inhibitors

α -Synuclein aggregation leads to PD by synaptic impairment and neurodegeneration. Aggregation is blocked, and microglial inflammation is reduced by nanoparticles. β 2-agonists in nanocarriers reduce the levels of α -synuclein expression. Phospho- α -synuclein, oxidative stress, and inflammation are reduced by metformin-loaded polydopamine nanoparticles by proteasomal degradation, which affords neuroprotection from PD development.

HORMONES

Estradiol

Estradiol a potent form of estrogen supports the survival of dopaminergic neurons by stimulating estrogen receptor- and exerting both antioxidant and anti-apoptotic actions although it is well-absorbed through oral routes its overall bioavailability is significantly reduced due to extensive first-pass liver metabolism additionally long-term use at higher doses is associated with an increased risk of cancer making low-dose formulations preferable to overcome these challenges nanocarrier-based delivery systems have been developed to enhance brain targeting for instance intranasal administration of estradiol encapsulated in chitosan nanoparticles has demonstrated greater accumulation in brain tissue compared to traditional intravenous delivery similarly plga polylactic-co-glycolic acid nanoparticles given orally have shown improved systemic availability minimized adverse effects and better therapeutic compliance in parkinsons disease model.

Progesterone

Progesterone a steroidal steroid hormone has significant neuroprotective roles in parkinsons disease pd progesterone

increases 3-hydroxysteroid oxidoreductase activity and ipsilateral expression especially when treated early its neuroprotection is associated with brain-derived neurotrophic factor and glial fibrillary acidic protein progesterone further increases the density of dopaminergic neurons and inhibits proinflammatory macrophages in the myenteric plexus yet its therapeutic use is hampered by low bioavailability and side effects like decreased hdl cholesterol and possible teratogenic effects nanotechnology has enhanced progesterone delivery to the brain for example trimethyl chitosan hydrogel nanoparticles synthesized through polyelectrolyte complexation and ionotropic gelation greatly enhanced brain bioavailability showing a threefold increase in progesterone level in comparison to non-nanocarrier formulations melatonin a pineal gland-derived neurohormone also provides neuroprotection in pd its antioxidant activities decrease the formation of hydroxyl radicals modulate mitochondrial function and sustain circadian rhythm it also possesses anti-inflammatory and anti-apoptotic activities melatonin-loaded polydopamine nanostructures have been reported to provide greater brain targeting prolonged drug release and prevention of neurodegeneration by reverting mitochondrial function and blocking both caspase-dependent and independent apoptotic pathways in rotenone-induced pd models.

Dexamethasone

Dexamethasone a glucocorticoid hormone with strong anti-inflammatory and immunosuppressive functions is commonly employed in the treatment of various inflammatory diseases chronic

administration may lead to side effects such as osteoporosis hypertension and metabolic disorders liposomal dexamethasone nanoformulations using nanotechnology to target cd163 macrophages have been shown to have efficient microglial modulation and neuroprotection the nanoparticles significantly enhanced the motor activities of 6-ohda-induced pd rat models which indicates their therapeutic interest in the treatment of pd.

GROWTH ELEMENTS

Growth factors such as NGF, BDNF, IGF-1, VEGF, and GDNF are vital for safeguarding dopaminergic neurons and slowing the progression of Parkinson's disease (PD). Yet, a major hurdle remains: these molecules struggle to cross the blood-brain barrier, which limits their clinical use. Recent advances in nanotechnology have started to address this challenge. For example, nanoparticles like PBCA and PLGA, when coated with agents such as polysorbate 80 or poloxamer 188, have shown promise in ferrying growth factors across the blood-brain barrier in PD models. These nano-carriers provide sustained, targeted delivery, leading to improved neuroprotection, support for neuron survival, better cognitive function, and reduced PD symptoms. Overall, nanotechnology offers a promising strategy to enhance the effectiveness of growth factor-based therapies for Parkinson's disease.

FUTURE PERSPECTIVES

★ ^{3,11}Nanomedicine approaches to therapy of parkinsons diseasenew studies identify the promise of nanomedicine-based approaches for treating parkinsons disease pd particular focus is given to maximizing drug delivery and minimizing side

effects various nanocarrier systems have been investigated for enhancing bioavailability brain targeting and therapeutic performance parenteral delivery of nanoparticles provides immediate systemic drug exposure and improved brain delivery even at reduced doses dopamine-loaded plga nanoparticles .

- ★ when administered intravenously to pd rats showed greater resistance to oxidation and improved brain targeting compared to bulk dopamine these nanoparticles demonstrated low cytotoxicity in sh-sy5y cells and effective intrastriatal delivery restoring motor deficits in 6-ohda-lesioned rats without notable toxicity plga is also fda and ema-approved for parenteral use due to its biocompatibility.
- ★ biodegradability and sustained-release capabilities solid-lipid nanoparticles slns of bromocriptine provided extended drug release and stability due to the tristearin-tricaprin lipid matrix the system is capable of maintaining constant plasma levels which could improve compliance with fewer side effects in patients their applications can be further developed for delivery of l-dopa and dopamine agonists nerve growth factor ngf administered through pbca nanoparticles.
- ★ surface-modified with polysorbate 80 facilitated increased cellular uptake by brain endothelial cells inducing cognitive improvement in animal models the approach has the potential to alleviate age-related cognitive impairment in pd and lower peripheral toxicity with enhanced targeting efficiency intranasal delivery provides a non-invasive option for crossing the blood-brain barrier chitosan nanoparticles characterized by muco

adhesion and controlled-release ability have been employed in l-dopa delivery although the use of thermo reversible gels reduced permeation .

- ★ chitosan nanoparticles alone gave 747 drug recovery providing better neuroprotection pegpla nanoparticles modified with wheat germ agglutinin were the first to deliver intranasally neuropeptides with greatly enhanced drug absorption the method is promising for delivering proteins and peptides straight to the brain oral drug delivery is still prevalent but is restricted by first-pass metabolism.
- ★ apomorphine possesses poor oral bioavailability 17 because it is degraded in the gastrointestinal tract but apomorphine-loaded slns enhanced oral bioavailability to 25 preserved the drug from degradation and demonstrated greater therapeutic efficacy in pd models slns also possess high drug loading low toxicity and upscalable productiontransdermal delivery is beneficial for long-term release and patient compliance but is hindered by the skin barrier a ropinirole transdermal nanoformulation with capryol 90 and tween 20 enhanced skin permeability 75-fold without inducing irritation bioavailability of ropinirole increased dramatically.
- ★ compared to oral tablets or gels showing superior motor symptom control in pdfinally solgel silica nanoparticles containing dopamine enabled controlled release particularly in the larger pore sizes intrastriatal implantation in rats with pd resulted in behavioral improvement and holds potential for site-specific drug delivery at low costoverall these nanotechnology advancements offer

varied promising solutions for improved drug delivery and therapeutic efficacy in parkinsons disease further in vivo analysis and clinical translation are necessary to confirm their long-term safety and efficacy^{3,11}

^{2,6}Nanotechnology in the diagnosis of Parkinson's disease

Early pd diagnosis is still difficult even with unmistakable motor symptoms of bradykinesia rigidity and tremor specific biomarkers for pd pathophysiology are needed mutations in the genes nurr1 lrrk2 uch-l1 autosomal-dominant and dj1 pink1 parkin autosomal-recessive are crucial diagnostic markers imaging techniques used for detection include cranial ct pet fluorine-18-labeled dopa mri spect and cranial ultrasound spect tracers of presynaptic dopamine transporters facilitate early pd detection the michael j fox foundation-funded parkinsons progression marker initiative ppmi funds blood urine csf and imaging-based research for identifying early-stage pd biomarkers.

Diagnosis using metallic NPs

Carbon-paste electrodes with carbon nanotube and silver nanoparticle (AgNP) incorporation are able to measure dopamine and ascorbic acid at high sensitivity (micromolar levels).Zinc oxide nanowire arrays (with ~100 nm diameter) measure dopamine at ~1 nM concentrations employing differential pulse voltammetry.Uric acid concentration is lower in PD patients, making it a possible early biomarker.Macrocyclic polyamine monolayers on gold electrodes simulate ligand-gated ion channels; dopamine binding evokes charge changes, enabling picomolar-level detection.Iron-oxide nanoparticles (PEGylated) linked with

oligomeric amyloid antibodies permeate the blood–brain barrier and act both as early PD detectors and MRI contrast agents. α -Synuclein detection, an important PD biomarker, has been amplified by gold-doped titanium oxide nanotube arrays with sensitivity in picogram/ml levels. Volatile organic compounds (VOCs) such as styrene and hydroxytoluene in the breath of PD patients were detected through sensors fabricated with carbon nanotubes and AgNPs. Such sensors distinguished PD from Alzheimer's patients with 78% accuracy.

Diagnosis using quantum dots

Quantum dots are minuscule semiconductors as well as a area this is certainly huge of is going on in this area for their used in the analysis also therapy of many diseases. Quantum dots behave as a core by which medicine molecules may be affixed. The mitochondrial complex I of neurons will not function properly during PD progression. This complex we has a connection that is direct NADH: ubiquinone oxidoreductase and reduced total of the amount of NADH, ubiquitin is associated with the loss of dopaminergic neurons. In one research, Ma et al. Formulated quantum dots (CdSe/ZnS) after which conjugated them with ubiquinone. This bioconjugate surely could replace the fluorescence to locate the mitochondrial complex we stage in SHSY5Y cells. Ergo, out of this scholarly study, it could be figured quantum-dotubiquinone could become an in vitro biosensor for early PD detection.^{2,6}

^{2,8}Nanotechnology breath test for early-stage PD

The first reported account of PD analysis through exhaled air before therapy (de novobreath) was captured into the study work of Feinberg et al. The detectives

described a break-through trial that is clinical to distinguish between de novo PD and control topics having an electronic system when it comes to recognition of volatile particles in exhaled breathing (sensor range). They further investigated various other common PD diagnostic examinations such as for instance odor, ultrasound and symptom recognition this is certainly non-motor. The sensitiveness accuracy and, specificity values associated with the sensor array to detect PD fom settings was discovered becoming 79%, 84% and 81%, respectively, when comparing to the odor recognition test (62%, 89%, 73%). Because of the convenience and power to identify PD at an stage this is certainly early this method is certainly expected to create a brand new arena in the diagnosis of PD.^{2,8}

CONCLUDING REMARKS

²Within the review that is current we've explained the role and importance of nanotechnology in PD. There's a amount that is huge of getting on to find a cure for PD along with improved methods for its analysis. Additionally, many different types of NPs such as liposomes, exosomes, SLNs, exosomes, nanobubbles and polymeric NPs have-been created so that you can establish nanotechnology this is certainly theranostic for PD therapy. In current PD that is traditional, lectin (a unique strategy) is also employed for medication delivery in PD. Because, genetic fluctuations in α -synuclein will be the reason that is main PD development, considerable research is ongoing in gene delivery via nanotechnology. PD detection takes place after 10–15 years of onset when motor symptoms tend to be observable. Not enough technique for the first recognition of PD is just a challenge this is certainly major the road of PD

treatment. The detection this is certainly current as well as treatment of PD on the basis of the non-motor symptoms are difficult, because these are common signs for other brain conditions too. Consequently, early-stage analysis of PD is a major task for researchers make it possible for the perfect remedy associated with infection. As previously mentioned previous, for the intended purpose of analysis scientific studies are continuous nanotechnology that is utilizing includes the application of quantum dots, metallic NPs, among others. This manuscript expounds the advances which are notable in unique nanoformulation approaches reported in the published literature. After thinking about these nanoformulation approaches as well as the advantages connected it could be concluded that nanotechnology keeps immense potential to resolve the ongoing dilemmas from the diagnosis in addition to treatment of PD together with them².

REFERENCES

1. Gerardo Leyva-Gómez, Hernán Cortés, Jonathan J. Magaña, Norberto Leyva-García, David Quintanar-Guerrero, Benjamín Florán, Nanoparticle technology for treatment of Parkinson's disease: the role of surface phenomena in reaching the brain, *Drug Discovery Today*, Volume 20, Issue 7, 2015, Pages 824-837.
2. Sunita Chawla, Dnyaneshwar Kalyane, Vishakha Tambe, Pran Kishore Deb, Kiran Kalia, Rakesh K. Tekade, Evolving nanoformulation strategies for diagnosis and clinical interventions for Parkinson's disease, *Drug Discovery Today*, Volume 25, Issue 2, 2020, Pages 392-405.
3. Jyotsna Shankar, Geetha K.M, Barnabas Wilson, Potential applications of nanomedicine for treating Parkinson's disease, *Journal of Drug Delivery Science and Technology*, Volume 66, 2021, 102793, ISSN 1773-2247.
4. Garbayo E, Ansorena E, Blanco-Prieto MJ. Drug development in Parkinson's disease: from emerging molecules to innovative drug delivery systems. *Maturitas*. 2013 Nov;76(3):272-8. doi: 10.1016/j.maturitas.2013.05.019. Epub 2013 Jul 1. PMID: 23827471.
5. nkita Paul, Khushwant S. Yadav, Parkinson's disease: Current drug therapy and unraveling the prospects of nanoparticles, *Journal of Drug Delivery Science and Technology*, Volume 58, 2020, 101790, ISSN 1773-2247, <https://doi.org/10.1016/j.jddst.2020.101790>.
6. Esraa Ghazy, Abbas Rahdar, Mahmood Barani, George Z. Kyzas, Nanomaterials for Parkinson disease: Recent progress, *Journal of Molecular Structure*, Volume 1231, 2021, 129698, ISSN 0022-2860, <https://doi.org/10.1016/j.molstruc.2020.129698>.
7. Soursou, Georgia & Alexiou, Athanasios & Ashraf, Ghulam & Siyal, Asad & Mushtaq, Gohar & Kamal, Mohammad. (2015). Applications of Nanotechnology in Diagnostics and Therapeutics of Alzheimer's and Parkinson's Disease. *Current Drug Metabolism*. 16. 705-712. 10.2174/138920021608151107125049.
8. Gunay MS, Ozer AY, Chalon S. Drug Delivery Systems for Imaging and Therapy of

- Parkinson's Disease. *Curr Neuropharmacol.* 2016;14(4):376-91. doi: 10.2174/1570159x1466615123012490
4. PMID: 26714584; PMCID: PMC4876593.
9. Kumar B, Pandey M, Potttoo FH, Fayaz F, Sharma A, Sahoo PK. Liposomes: Novel Drug Delivery Approach for Targeting Parkinson's Disease. *Curr Pharm Des.* 2020;26(37):4721-4737. doi: 10.2174/138161282666620012814512
4. PMID: 32003666.
10. García-Pardo J, Novio F, Nador F, et al. Bioinspired Theranostic Coordination Polymer Nanoparticles for Intranasal Dopamine Replacement in Parkinson's Disease. *ACS Nano.* 2021;15(5):8592-8609. doi:10.1021/acsnano.1c00453.
11. Sharma S, Rabbani SA, Agarwal T, Baboota S, Potttoo FH, Kadian R. Nanotechnology Driven Approaches for the Management of Parkinson's Disease: Current Status and Future Perspectives. *Curr Drug Metab.* 2021;22(4):287-298. doi: 10.2174/138920022166620112412340
5. PMID: 33234098.
12. Kaushik AC, Bharadwaj S, Kumar S, Wei DQ. Nano-particle mediated inhibition of Parkinson's disease using computational biology approach. *Sci Rep.* 2018 Jun 15;8(1):9169. doi: 10.1038/s41598-018-27580-1. PMID: 29907754; PMCID: PMC6003935.