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The Magnetic Cure? Nanotechnology's Role in Parkinson's Future : A Systematic Review.

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Abstract:

Introduction: Parkinson's disease (PD) is a gradual neurodegenerative disease characterized by the loss of dopaminergic neurons in the substantia nigra. Treatments for this disease are varied; some include dopamine replacement therapy, deep brain stimulation, and MRI-guided focused ultrasound, which provides symptomatic relief. Despite extensive studies, PD still does not have a fully curable treatment. In comparison to existing treatments, magnetic nanotechnology is non-invasive and offers enhanced treatment efficiency and reduced systemic side effects. It also promises neuroregeneration and can additionally be used for imaging and disease progression. This systematic review explores the potential of magnetic nanoparticles (MNPs) in the treatment and theranostics in Parkinson's and focuses on their mechanism of action.

Methods: A systematic review using platforms such as PubMed, ScienceDirect, and Web of Science was conducted that analyzed the application of magnetic nanoparticles in PD models. The inclusion criteria were papers from the last 10 years and MNP-mediated drug delivery, neuroregeneration, stem cell therapy, or imaging in PD model animals or experimental studies. Exclusion criteria were studies without animal or experimental data and also papers that are not published in English. The initial search retrieved 20 studies, for which peer-reviewed screening was done to result in the original 12 studies meeting the inclusion criteria. Search terms used were 'Parkinson's disease,' 'magnetic nanotechnology,' 'superparamagnetic iron oxide nanoparticles,' 'targeted drug delivery,'

'neuromodulation,' and 'theranostics.' Data extraction was concentrated on nanoparticle composition, targeting mechanisms, safety profiles, and preclinical and clinical outcomes.

Results: This review studied 12 papers wherein magnetic nanotechnology shows immense potential in treatment for PD. Studies were categorized into MNPs as a direct application to PD and as a general application of MNPs. Out of these, five papers discussed the potential MNPs hold towards the treatment of PD. These findings show a promise of neurite outgrowth and regeneration in response to magnetic guidance. Two papers talk about the importance of homing adipose-derived stem cells (ADSCs) under magnetic guidance to the substantia nigra, where the ADSCs can differentiate into various cell types, including neurons and glial cells, which are relevant for PD treatment. Other studies demonstrate the usage of MNPs in theranostics and stem cell therapy in PD. Given the promising avenue for PD treatment with magnetic nanotechnology, further research needs to be conducted for human trials, its long-term safety and efficacy, and delving deeper into its neuroprotective mechanism.

Conclusion: Magnetic nanotechnology shows an innovative approach in PD treatment and also shows promise in overcoming the current therapeutic limitations seen. Advances in the engineering of magnetic nanoparticles, along with well-improved strategies in magnetic targeting, can facilitate a path for clinical applications. Clinical trials on a large scale as well as well-developed delivery systems to improve efficacy and safety should be something future researchers should concentrate on. This systematic review looks upon the necessity for interdisciplinary coordination to fast-track the translation of magnetic nanoparticles into practical Parkinson's disease treatments.

Keywords: Parkinson’s disease, magnetic nanotechnology, superparamagnetic iron oxide nanoparticles, neuromodulation.

INTRODUCTION

Parkinson’s disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra pars compacta and one that affects over 10 million people worldwide[1]. It comprises a series of neurological symptoms manifested as bradykinesia, muscle rigidity, resting tremor, and postural instability. As the disease progresses, the patient’s quality of life is negatively affected due to cognitive decline, mood disorders, and sleep disturbances. Existing therapies include levodopa-based dopamine replacement therapy, MAO-B inhibitors, deep brain stimulation (DBS), and MRI-guided focused ultrasound, although these management strategies primarily offer symptom management without altering the disease etiology[1,3].

The inability of therapeutic agents to cross the blood-brain barrier (BBB), which is a highly selective and protective layer that does not allow the entry of potentially harmful substances into the central

nervous system (CNS), is one of the main limitations in formulating impactful therapies for PD. Low drug delivery to target areas and inadvertent systemic side effects are typically the outcome of mainstream drug delivery methods[2]. Magnetic nanotechnology has established itself as a transformative solution, offering exceptional features in the design of nano-sized delivery platforms. In this set, magnetic nanoparticles (MNPs)—specifically superparamagnetic iron oxide nanoparticles (SPIONs)—have gained popularity due to their biocompatibility and efficient magnetic response. MNPs can also be altered to bind specific ligands and drugs and be guided by external magnetic fields to reach the affected brain regions. This precision paves the way for new possibilities in treating neurodegenerative disorders like PD[4]. This study explores MNPs and their various usages in PD, including targeted drug delivery, stem cell therapy, and theranostics.

METHODOLOGY

1. Search strategy and study selection

The sole purpose of this systematic review was to evaluate the use of MNPs for the therapy and diagnosis of PD, focusing on their use in drug delivery, neuroregeneration, stem cell therapy, and imaging. Following PRISMA guidelines (Figure 1) for systematic review, a search was performed on scientific databases, which included PubMed, Google Scholar, and ScienceDirect. To be included, texts had to be in English and published in the last 10 years. Only peer-reviewed experimental research articles with free full text and clear usage of MNPs in PD (either in vitro or in vivo) were selected whose measurement was therapeutic or diagnostic. The phrases searched for were Parkinson's disease, magnetic nanoparticles, superparamagnetic iron oxide nanoparticles (SPIONs), drug delivery, stem cells, neuroregeneration, and theranostics.

2. Screening and Selection Process

The initial pool of studies included 20 articles, which were carefully screened for relevance. After excluding duplicate entries and articles lacking relevant data, 12 studies were selected for full-text review.

3. Data Extraction and Categorization

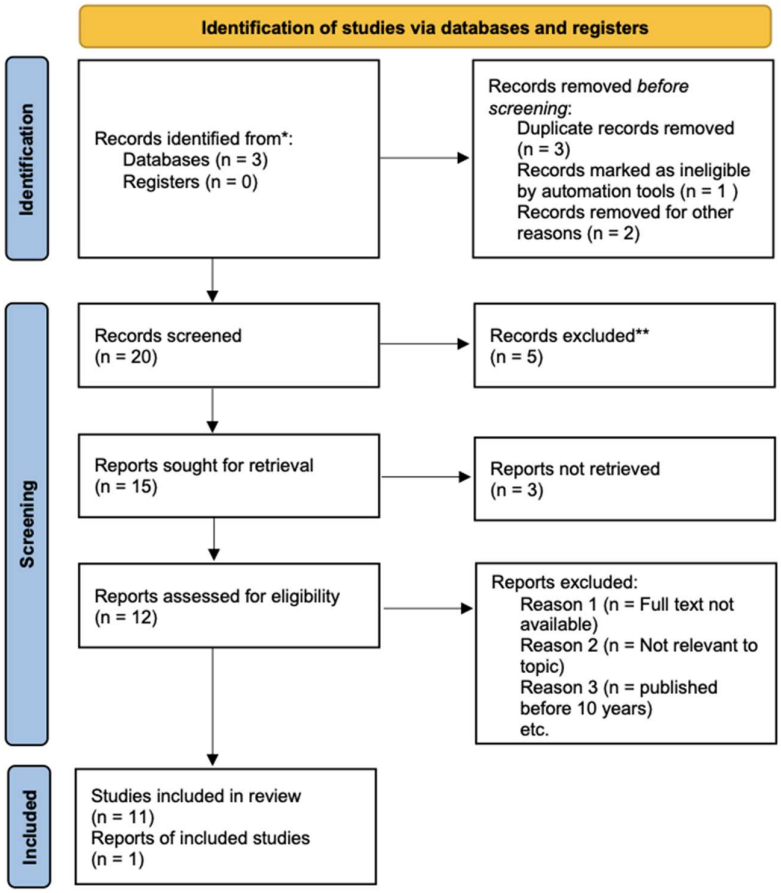
A detailed data extraction process was conducted using Excel sheets, adding the article title, author(s), year of publication, key findings, type of MNPs used, experimental model, therapeutic target, and reported outcomes. In order to design a comparison and interpretation study, the included studies were categorized by the primary function of the magnetic nanoparticles. These categories included MNP-mediated drug delivery, magnetic targeting of stem cells for neuroregeneration, MNPs used for

diagnostic imaging, and multifunctional theranostic systems. Such a design helped to provide a structural foundation for the analysis of the different approaches, therapeutic efficacy, and translational potential across each study.

No.	Author (Year)	Title	Model/Focus	MNP Strategy	Key Findings
1	Dhillon et al. (2022)[2]	Directional control of neurite outgrowth	2D cultures & brain slices	Iron oxide MNPs + magnetic gradients	Guided neurite extension toward striatum
2	Wu et al. (2020)[3]	Surface Modification of Iron Oxide	PD, Alzheimer's, gliomas	SPIONs with polymer/lipid coatings	Enhanced BBB penetration
3	Vasić et al. (2024)[4]	Multifunctional Iron Oxide Nanoparticles	Drug delivery	Chitosan/PEG-coated IONPs	Stimuli-responsive release
4	Mansour et al. (2025)[5]	Metallic nanomaterials in Parkinson's	PD models	Gold/iron oxide NPs	α-synuclein detection (0.1 nM)
5	Rahman et al. (2022)[6]	Recent advancements of nanoparticles	PD, Alzheimer's	Curcumin-loaded fus-liposomes	3.5× higher drug concentration
6	Kim & Chang (2021)[7]	Therapeutic Potential of hASCs in PD	6-OHDA mice	Silica-core MNPs	Improved motor function
7	Moayeri et al. (2020)[8]	Homing of SPION-Labeled ADSCs	6-OHDA rats	SPIONs + poly-L-lysine	96% labeling efficiency
8	Tomitaka et al. (2020)[9]	Surface-engineered multimodal	CNS diseases	IONPs + transferrin/lactoferrin	BBB crossing + imaging
9	Qiao et al. (2023)[10]	Magnetic iron oxide nanoparticles	PD, glioblastoma	Polysaccharide-coated MIONPs	40% T2 reduction (MRI)
10	Dhariwal et al. (2025)[11]	Targeted drug delivery in	Neurodegenerative diseases	Polymeric/lipid NPs	Improved BBB penetration
11	Yadav et al. (2022)[12]	Recent advances in nanotechnology	PD models	Liposomes, dendrimers	CRISPR/Cas9 delivery
12	Rajendran et al. (2025)[13]	Nano delivery systems in stem cell	Regenerative medicine	Magnetic NPs + stem cells	90% cell viability

Table 1. Summarization of all gathered papers

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Figure 1. PRISMA guidelines

RESULTS

1. Magnetic Nanoparticles for Targeted Drug Delivery

MNPSs demonstrate a novel approach to overcome the challenge of blood-brain barrier (BBB) penetration, thus providing excellent targeted drug delivery in PD. Advancements in surface-modified iron oxide nanoparticles (IONPs) demonstrate higher therapeutic efficacy due to their tailored coating. For example, polymer coatings (e.g., PEG, PLGA) and lipid hybrids (e.g., DSPE-PEG) improve biocompatibility and BBB penetration, thereby improving the targeted drug delivery system to affected brain areas (Wu et al., 2020)[3]. In addition, fus-liposomes-rhFGF20 enhance the BBB permeability and prolong the half-life of therapeutics, thus improving their bioactivity (Rahman et al. 2022)[6]. Table 2 demonstrates these studies, including the type of nanoparticle used and the therapeutic outcomes.

Study	Nanoparticle Type	Key Innovation	Therapeutic Outcome	Key Metrics
Wu et al. (2020)	Surface-modified IONPs (PEG, lipid, hybrid coatings)	Optimized surface engineering for BBB penetration	Enhanced drug delivery to brain regions	Improved stability & targeting efficiency
Rahman et al. (2022)	Multifunctional nanocarriers (fus-liposomes-rhFGF20)	Combined antioxidative & neuroprotective effects	• Prolonged therapeutic half-life • Enhanced BBB permeability	Improved bioavailability of phytochemicals

Table 2. Targeted drug delivery of magnetic nanoparticles in PD.

2. Magnetic Guidance for Stem Cell Therapy

Magnetic nanoparticle-guided stem cell therapy has shown significant potential for targeted delivery and functional recovery in PD models. In a study done by Kim & Chang, 2021[7]; successful migration of human adipose-derived stem cells (hASCs) to the substantia nigra in a saline-injected 6-OHDA-induced PD mouse model was observed by MRI and Maestro imaging. Moreover, HASCSs increase the secretion of neurotrophic factors such as brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and glial-derived neurotrophic factor (GDNF) in stem cell differentiation and neuronal growth. Motor neuron cells derived from hASCs enhance expression of microtubule-associated protein

2 (MAP2), homeobox 9 (HB9), and choline acetyltransferase (ChAT), which is used for stem cell therapy, studied by the same scientists.

In addition to these results, SPION-labeled ADSCs in rats achieved a 96% efficiency with poly-L-lysine coating and enhanced homing to the substantia nigra under external magnetic guidance. In this study, the apomorphine-induced rotation test showed a significant reduction in rotations in treated groups (Moayeri et al., 2020)[8]. Both studies demonstrated therapeutic effects and dopaminergic neuron recovery.

3. Directional Neurite Outgrowth Using Magnetic Fields

The latest advancements seen in magnetic field-guided therapy show the capability of MNPs in affecting cellular behavior, mainly neuronal extension. In the study done by Dhillon et al. (2022)[2], SPIONS were used in combination with controlled magnetic field gradients that exceeded 20 T/m to direct the pathway of neuronal growth to the striatum. In 2D cultures, confocal microscopy images revealed neurites extending preferentially along the direction of the applied magnetic field. In brain slices, enhanced neurite growth was validated using tyrosine hydroxylase immunostaining, indicating dopaminergic differentiation aligned with the magnetic gradient. These findings indicate that neuronal growth might be guided in a magnetic gradient by PD. This can help to reconstruct neural circuits in PD.

4. Theranostic Applications

MNPs, mainly SPIONs, are gaining major attention for theranostic applications in PD, combining diagnostic imaging with therapeutic potential. Recent studies show their ability to enhance MRI contrast, enabling real-time tracking of stem cell migration in preclinical PD models, which could improve cell-based therapy monitoring (Mansour et al. 2025)[5]. Another ability is that multifunctional iron oxide nanoparticles have been developed to target pathological alpha-synuclein aggregates, which is a hallmark of PD, while simultaneously delivering neuroprotective agents to reduce neurodegeneration (Kim & Chang 2021)[7]. These dual-function systems highlight a promising platform for simultaneous disease monitoring and active treatment, thereby improving therapeutic precision. However, more validation is needed to assess sensitivity, biocompatibility, and clinical scalability before widespread translation. Advances in MNP-based theranostics could revolutionize PD management by integrating real-time diagnostics with targeted drug delivery, offering a more dynamic approach to tackling this complex neurodegenerative disorder.

Mechanism of Action	Description	Molecular Targets	Reported Effects in PD Models
Neuroregeneration	MNPs promote neurite outgrowth and neural differentiation via magnetic stimulation	BDNF, GDNF, NGF pathways	Increased axonal extension; dopaminergic neuron replacement
Drug Delivery	MNPs enable crossing the BBB and release antioxidants or neuroprotective drugs	α-synuclein, ROS, mitochondria	Reduced neuroinflammation and oxidative stress; preserved neuron count
Stem Cell Homing	External magnets direct stem cells conjugated to MNPs to lesion sites	CXCR4/SDF1 axis	Enhanced migration, survival, and integration of stem cells in SNpc
Theranostics	Dual-function particles combine real-time imaging and treatment delivery	Iron-sensitive MRI regions, dopaminergic neurons	Early PD detection with therapeutic feedback monitoring

Table 3. Various usages of MNPs as a therapeutic potential in PD

DISCUSSION

PD remains a daunting neurodegenerative disorder, and emerging magnetic nanotechnology offers a promising therapeutic potential[1]. The integration of MNPs helps overcome a crucial challenge in PD treatment: the impermeability of the BBB, which poses a hurdle to PD therapy[3]. MNPs opens up a novel approach for targeted drug delivery, stem cell homing, neurite outgrowth, and theranostics[4,5,6].

Studies demonstrated SPIONs as the core structure of MNPs due to their enhanced magnetic response and biocompatibility[4]. They enabled transplanted cells (e.g., adipose-derived stem cells) to regenerate regions like the substantia nigra, hence improving motor function recovery.

More importantly, MNPs affect neuronal outgrowth, thus promoting regeneration of neurons via an external magnetic surface[2].

Functionalized MNPs also facilitate theranostic applications by using real-time MRI tracking with controlled drug release, while surface modifications optimize biocompatibility and BBB permeation [6,7]. Collectively, MNPs offer the potential to transform PD treatment beyond simple symptomatic relief.

MNPs have been studied in PD, but they also show promise in other neurodegenerative disorders, with each having distinct pathophysiological targets and therapeutics. In the case of Alzheimer's disease (AD), MNPs functionalized with anti-amyloid-beta (Aβ) ligands were used for the detection and inhibition of plaque formation, which contrasts with the case of PD, where the focus is mainly on enhancing dopaminergic survival and inhibiting aggregation of alpha-synuclein[6]. Alzheimer's-targeted nanoparticles have been studied for MRI detectability—similar to the approach utilized for SPION-enhanced stem cell tracking in PD models[6]. Huntington's disease, which researchers often do not investigate as much, has already seen the initial exploration of iron oxide nanoparticles. These may offer targeted gene therapy and antioxidant delivery to reduce the expression of mutant huntingtin protein and oxidative damage. This is similar to the MNP-based oxidative stress mitigation strategy already established in PD[6]. Most often in multiple sclerosis (MS), MNPs have been used either to deliver anti-inflammatory drugs or as MRI-visible tracers of immune cell migration, a therapeutic strategy distinct from the regenerative and neuromodulatory applications emphasized in PD research[6]. Thus, while MNP applications across neurodegenerative diseases share core advantages such as blood-brain barrier (BBB) penetration and magnetic targeting, their roles differ based on disease-specific pathology, with PD research leaning more heavily on neurorestoration and functional recovery strategies[6].

This study is limited by the number of articles selected, which followed the inclusion criteria, and the majority of the studies selected varied in their type of study design, ranging from preclinical experiments to narrative reviews. Mainly, the short-term or theoretical outcomes, with minimal clinical trial data, limited the conveyance of the findings into clinical practices. Along with the possible publication bias, the exclusion of non-English studies may have led to the omission of relevant data. Thus, these limitations emphasize the need for more long-term and intensive clinical investigations.

Future research should focus on clinical trials for preclinical success, i.e., large animal studies, and should also prioritize safety with dose optimization. Furthermore, MNPs with CRISPR-Cas9 gene editing could potentially target α-synuclein aggregates in PD more efficiently. Long-term toxicity should also be addressed to ensure these interventions are safe to use in humans.

CONCLUSION

This review establishes the various prospects of MNPs, specifically SPIONSs, in experimental models of Parkinson's disease (PD). Targeted drug delivery, guided stem cell therapy, and magnetic resonance imaging were some of the applications. In both 2D and organotypic models, high gradient fields were shown to direct neurite extension, supporting the concept of spatial control in neural circuit reconstruction. More accurate delivery of anti-inflammatory and antioxidant compounds was enabled by functionalized MNPs, and studies reported improved neuronal survival and decreased oxidative stress in the dopaminergic system. Enhanced migration and differentiation in the substantia nigra were seen from the initial results from stem cell conjugation experiments, which points towards regenerative potential in neurodegenerative settings.

The medical application of MNP-based strategies remains a substantial barrier in spite of these advances. Long-term biocompatibility, immune response, and the clearance of nanoparticles from neural tissues are some of the ongoing concerns. Variability in nanoparticle design, coating, and administration methods furthermore challenges comparisons across studies. To progress, standardized preclinical protocols, dose optimization, and long-term safety profiling should be prioritized. To confirm the therapeutic and diagnostic value of magnetic nanotechnology in PD, it is essential to have early-phase clinical trials combined with interdisciplinary collaboration across materials science, neurology, and imaging.

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