

Review Article**Microencapsulation-Based Drug Delivery Strategies for Parkinson's Disease: Recent Advances and Therapeutic Perspectives****M. Shunmuga Sundaram^{1*}, Anju. C.L², Kannan Raman³**¹*Department of Pharmaceutics, The dale view college of pharmacy and research center, Punalal 695575, Thiruvananthapuram, Kerala, India.*²*Department of Pharmaceutics, Kerala academy of pharmacy, Kandala 695512, Kattakada, Thiruvananthapuram, Kerala, India.*³*Department of Pharmacology, St.Johns College of Pharmaceutical Sciences and Research, Kattappana, Idukki-685515. Kerala, India.*Corresponding Author: **M.Shunmuga Sundaram***

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Abstract

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder characterized primarily by dopaminergic neuronal degeneration in the substantia nigra pars compacta and reduced dopamine levels in the striatum. Despite substantial advances in pharmacotherapy, conventional treatment approaches remain limited due to poor blood–brain barrier permeability, fluctuating plasma drug concentrations, reduced bioavailability, systemic adverse effects, and diminished therapeutic efficacy during long-term treatment. Microencapsulation-based drug delivery systems have emerged as a promising strategy to address these limitations by improving drug stability, prolonging release profiles, enhancing site-specific targeting, and minimizing systemic toxicity. The present review critically examines recent developments in microencapsulation approaches for Parkinson's disease management and highlights their therapeutic significance in improving treatment outcomes. Various microencapsulation techniques, including spray drying, solvent evaporation, ionic gelation, coacervation, and emulsification methods, have demonstrated substantial potential in the controlled delivery of antiparkinsonian drugs and neuroprotective agents. Additionally, polymeric and lipid-based encapsulation systems have been investigated to improve the delivery of levodopa, dopamine agonists, antioxidants, and phytoconstituents across the blood–brain barrier. Emerging evidence further suggests that microencapsulation of natural bioactive compounds may provide sustained neuroprotective effects and reduce oxidative stress associated with disease progression. Although several challenges, including scalability, formulation stability, and clinical translation, remain unresolved, recent technological advancements indicate considerable promise for future therapeutic applications. Therefore, microencapsulation-based drug delivery systems may represent an innovative and clinically relevant platform for enhancing the efficacy, safety, and long-term management of Parkinson's disease.

keywords: Parkinson's disease; Microencapsulation; Controlled drug delivery; Neuroprotective therapy

1. Introduction

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder after Alzheimer's disease and represents a major public health concern worldwide due to its increasing incidence among aging

populations [1]. The disease is primarily characterized by progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta, resulting in dopamine depletion within the striatum and subsequent impairment of motor coordination [2]. Parkinson's disease affects millions of individuals globally and imposes substantial socioeconomic and healthcare burdens due to disability, reduced quality of life, and long-term treatment dependency [3].

Clinically, Parkinson's disease is characterized by both motor and non-motor manifestations. The cardinal motor symptoms include resting tremor, bradykinesia, muscular rigidity, and postural instability, whereas non-motor symptoms comprise depression, anxiety, cognitive decline, gastrointestinal dysfunction, sleep disturbances, and autonomic abnormalities [4]. Although the precise etiology of Parkinson's disease remains incompletely understood, multiple pathogenic mechanisms, including oxidative stress, mitochondrial dysfunction, α -synuclein aggregation, neuroinflammation, excitotoxicity, and genetic susceptibility, have been implicated in disease progression [5].

Current pharmacological management of Parkinson's disease mainly focuses on symptomatic relief through dopamine replacement or modulation strategies. Among available therapies, levodopa remains the gold-standard treatment because of its superior efficacy in alleviating motor symptoms [6]. However, prolonged administration of levodopa is associated with several complications, including motor fluctuations, dyskinesia, reduced therapeutic response, and irregular plasma drug concentrations [7]. Furthermore, conventional antiparkinsonian drugs often demonstrate poor bioavailability, limited blood–brain barrier (BBB) permeability, rapid metabolism, and dose-related adverse effects, thereby restricting therapeutic efficiency [8].

The blood–brain barrier remains one of the most critical challenges in Parkinson's disease treatment. This physiological barrier protects the central nervous system by limiting the entry of toxic substances; however, it simultaneously restricts the penetration of therapeutic agents into brain tissues [9]. Consequently, many promising neuroprotective drugs fail to achieve adequate concentrations at target sites, limiting their clinical success [10].

To overcome these limitations, novel drug delivery systems have gained considerable attention in neuropharmaceutical research. Among these, microencapsulation-based drug delivery systems have emerged as a promising approach for improving the pharmacokinetic and pharmacodynamic profiles of antiparkinsonian drugs [11]. Microencapsulation refers to the process of enclosing active pharmaceutical ingredients within polymeric or lipid-based matrices to form microscale particles capable of protecting drugs from environmental degradation while enabling controlled and sustained release [12].

In Parkinson's disease therapy, microencapsulation offers several therapeutic advantages, including prolonged drug release, enhanced stability, improved bioavailability, reduction in systemic toxicity, site-specific targeting, and minimization of dosing frequency [13]. Additionally, microencapsulation techniques can facilitate the delivery of neuroprotective compounds, phytoconstituents, peptides, and dopamine agonists through alternative routes such as intranasal and targeted brain delivery systems [14]. Recent developments in biodegradable polymers, lipid-based carriers, and responsive biomaterials have further strengthened the applicability of microencapsulation in neurodegenerative disease treatment [15].

Therefore, the present review critically discusses recent advances in microencapsulation-based drug delivery strategies for Parkinson's disease, emphasizing formulation approaches, therapeutic benefits, challenges, and future prospects in enhancing clinical outcomes and disease management.

2. Pathophysiology of Parkinson's Disease

Parkinson's disease is a multifactorial neurodegenerative disorder involving complex molecular and cellular mechanisms responsible for progressive neuronal degeneration [16]. The hallmark pathological feature of Parkinson's disease is the selective loss of dopaminergic neurons in the substantia nigra pars compacta, leading to depletion of dopamine in the nigrostriatal pathway [17]. Dopamine acts as a critical neurotransmitter involved in motor control, voluntary movement regulation, reward signaling, and emotional functioning. Its depletion significantly contributes to motor impairments observed in affected individuals [18].

One of the central pathological characteristics of Parkinson's disease is the abnormal accumulation of α -synuclein protein aggregates, commonly referred to as Lewy bodies [19]. Misfolding and aggregation of α -synuclein contribute to neuronal toxicity, synaptic dysfunction, and impaired intracellular signaling pathways [20]. Growing evidence suggests that α -synuclein pathology spreads progressively across interconnected neuronal networks, thereby accelerating neurodegeneration [21].

Oxidative stress plays a substantial role in Parkinson's disease pathogenesis. Increased production of reactive oxygen species (ROS), coupled with impaired antioxidant defense mechanisms, contributes to

lipid peroxidation, DNA damage, and neuronal apoptosis [22]. Dopaminergic neurons are particularly susceptible to oxidative stress because dopamine metabolism itself generates free radicals, increasing neuronal vulnerability [23].

Mitochondrial dysfunction is another major contributor to disease progression. Defects in mitochondrial complex I activity result in impaired energy production and enhanced oxidative damage, ultimately leading to neuronal cell death [24]. Several environmental toxins, including pesticides and herbicides, have also been associated with mitochondrial impairment and increased Parkinson's disease risk [25].

Neuroinflammation further contributes to neuronal degeneration through activation of microglial cells and excessive release of pro-inflammatory cytokines such as tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and interleukin-6 (IL-6) [26]. Persistent inflammatory responses aggravate oxidative injury and accelerate dopaminergic neuronal loss [27].

Genetic factors also influence Parkinson's disease susceptibility. Mutations in genes such as *LRRK2*, *SNCA*, *PINK1*, *DJ-1*, and *Parkin* have been associated with inherited forms of the disease [28]. These mutations interfere with mitochondrial quality control, protein degradation pathways, and neuronal survival mechanisms [29].

The blood-brain barrier constitutes another critical challenge in Parkinson's disease treatment. Although essential for protecting neural tissues, the BBB limits penetration of many therapeutic molecules into the brain [30]. Consequently, effective treatment strategies increasingly focus on advanced drug delivery systems capable of improving drug transport across the BBB while maintaining therapeutic concentrations.

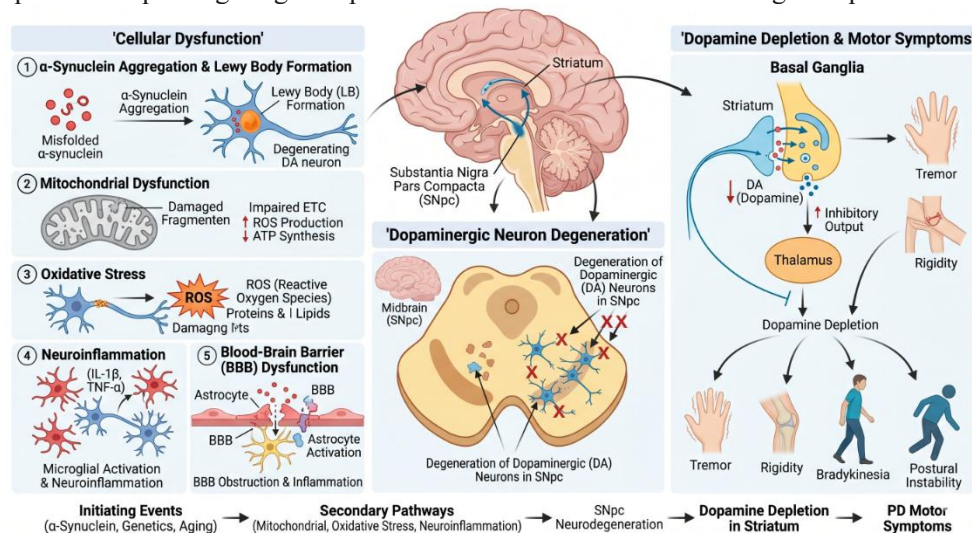


Fig 1. Pathophysiology of Parkinson Disease

3. Current Therapeutic Limitations in Parkinson's Disease

The management of Parkinson's disease primarily relies on pharmacological interventions aimed at restoring dopaminergic neurotransmission and controlling symptoms [31]. Although available therapies improve motor performance and quality of life, they do not prevent neuronal degeneration or halt disease progression [32]. Levodopa remains the cornerstone of Parkinson's disease treatment and is generally administered in combination with peripheral dopa decarboxylase inhibitors such as carbidopa or benserazide to enhance central nervous system availability [33]. Despite superior therapeutic effectiveness, long-term levodopa therapy frequently causes motor complications, including wearing-off effects, on-off fluctuations, and levodopa-induced dyskinesia [34]. These complications arise mainly from irregular dopamine stimulation and fluctuating plasma drug concentrations [35].

Dopamine agonists such as pramipexole and ropinirole are frequently used as adjunctive therapies to stimulate dopamine receptors [36]. However, these agents may cause hallucinations, impulse-control disorders, excessive daytime sleepiness, and cardiovascular adverse effects [37].

Monoamine oxidase-B inhibitors and catechol-O-methyltransferase inhibitors are also used to prolong dopamine activity but are associated with gastrointestinal disturbances, insomnia, hypotension, and hepatotoxicity in some patients [38]. Furthermore, oral administration of antiparkinsonian drugs often results in variable gastrointestinal absorption, delayed onset of action, and inconsistent therapeutic response [39].

Another major limitation of conventional therapies is poor blood–brain barrier permeability. Many neuroprotective compounds demonstrate promising activity in preclinical studies but fail clinically because they cannot effectively cross the BBB and accumulate at therapeutic concentrations [40]. In addition, repeated dosing requirements often reduce patient compliance and increase treatment burden.

These therapeutic shortcomings have highlighted the urgent need for innovative drug delivery approaches capable of improving brain targeting, prolonging drug release, minimizing systemic toxicity, and enhancing therapeutic outcomes. In this regard, microencapsulation-based drug delivery systems represent a highly promising strategy for overcoming existing treatment limitations in Parkinson's disease.

4. Microencapsulation: Concept, Principles, and Advantages

Microencapsulation is an advanced pharmaceutical technology in which active pharmaceutical ingredients are enclosed within microscopic polymeric or lipid-based protective systems to improve therapeutic performance and drug stability. Typically, the encapsulated material, known as the core substance, is surrounded by a polymeric shell or matrix to form particles ranging from one to several hundred micrometers in size. In pharmaceutical sciences, microencapsulation has attracted substantial attention because it provides controlled drug release, protects unstable compounds from environmental degradation, improves patient compliance, and enhances site-specific drug targeting [1]. In the context of Parkinson's disease, microencapsulation has emerged as a highly promising strategy to overcome limitations associated with conventional drug delivery, particularly poor bioavailability, rapid metabolism, fluctuating plasma drug concentrations, and insufficient penetration across the blood–brain barrier (BBB) [2].

The principle of microencapsulation mainly involves entrapping active pharmaceutical agents within biodegradable or biocompatible polymers to regulate drug release and maintain therapeutic drug concentrations over prolonged periods. After administration, the drug may be released through various mechanisms such as diffusion, polymer degradation, erosion, swelling, or dissolution depending on the characteristics of the carrier system and physiological environment [3]. Diffusion-controlled systems release drug molecules gradually through the polymer membrane, while erosion-controlled systems depend on the degradation of biodegradable materials for sustained liberation of therapeutic agents. Similarly, dissolution-based systems slowly release the drug through polymer dissolution, whereas stimuli-responsive systems can be designed to respond to physiological triggers such as pH, temperature, enzymatic activity, or biochemical signals [4]. These mechanisms provide greater flexibility in formulation design and make microencapsulation particularly useful for chronic neurodegenerative disorders requiring long-term therapy.

In Parkinson's disease management, microencapsulation offers several therapeutic advantages over conventional formulations. One of the major benefits is the enhancement of drug stability, particularly for compounds susceptible to oxidation, hydrolysis, or enzymatic degradation. Since antiparkinsonian agents often exhibit short biological half-lives and poor stability, encapsulation protects them from premature degradation and improves therapeutic efficiency [5]. Another important advantage is sustained and controlled drug release, which reduces sudden plasma concentration fluctuations that commonly contribute to “wearing-off” phenomena and dyskinesia during long-term levodopa therapy. By maintaining relatively stable drug concentrations, microencapsulation may improve symptom management and decrease treatment-related complications [6].

Furthermore, microencapsulation systems may facilitate improved transport across the blood–brain barrier, which remains one of the greatest obstacles in neuropharmacology. The blood–brain barrier acts as a highly selective protective interface, preventing many therapeutic molecules from reaching target brain tissues. However, advances in biodegradable polymers and nanoscale engineering have enabled the development of encapsulated formulations with enhanced permeability and targeted delivery potential [7]. In addition, microencapsulation can significantly reduce systemic toxicity and adverse effects by minimizing unnecessary drug exposure in non-target tissues. This reduction in toxicity may improve tolerability and patient adherence, particularly among elderly individuals who require prolonged treatment regimens [8]. Consequently, microencapsulation has become an increasingly important strategy in Parkinson's disease research because of its ability to optimize pharmacokinetic behavior, improve therapeutic precision, and potentially delay disease-associated complications.

5. Microencapsulation Techniques Used in Parkinson's Disease Drug Delivery

Various microencapsulation techniques have been explored to improve the delivery of antiparkinsonian drugs and neuroprotective compounds. The selection of a suitable technique generally depends on the

physicochemical properties of the active pharmaceutical ingredient, polymer compatibility, desired release profile, formulation stability, and therapeutic objectives [9]. Among the available approaches, spray drying, solvent evaporation, ionic gelation, coacervation, and emulsion-based methods are widely investigated due to their efficiency in producing controlled-release microsystems.

Spray drying is one of the most commonly utilized microencapsulation techniques because of its simplicity, reproducibility, and industrial scalability. In this method, a solution or suspension containing the drug and polymer is atomized into a heated chamber, where rapid solvent evaporation results in the formation of dry microparticles [10]. Spray drying has demonstrated significant potential in the preparation of sustained-release formulations of levodopa and antioxidant compounds intended for Parkinson's disease therapy. The process offers advantages such as uniform particle size distribution, rapid production, and suitability for large-scale pharmaceutical manufacturing. However, elevated processing temperatures may compromise the stability of heat-sensitive compounds, thereby requiring careful optimization during formulation development [11].

Another extensively investigated technique is solvent evaporation, which is particularly useful for encapsulating hydrophobic and hydrophilic compounds within polymeric matrices such as poly(lactic-co-glycolic acid) (PLGA). In this method, the drug and polymer are dissolved in an organic solvent and subsequently emulsified in an aqueous phase, followed by solvent removal to generate stable microspheres [12]. Solvent evaporation techniques have shown promising outcomes in the sustained delivery of dopamine agonists and levodopa formulations due to their high encapsulation efficiency and controlled-release capabilities. Nevertheless, concerns related to residual solvent toxicity and manufacturing complexity remain challenges that require further optimization [13].

Ionic gelation has also attracted increasing attention in neuropharmaceutical applications because of its mild preparation conditions and excellent biocompatibility. This technique generally involves ionic interactions between oppositely charged polymers such as chitosan and sodium alginate, leading to microcapsule formation without exposure to harsh processing conditions [14]. Such systems are particularly advantageous for encapsulating proteins, peptides, and phytoconstituents that may otherwise undergo degradation during formulation. Recent studies have highlighted the usefulness of ionic gelation-based microencapsulation in intranasal formulations intended to bypass the blood–brain barrier and improve drug delivery directly to the brain [15].

Coacervation is another effective microencapsulation approach involving phase separation of polymer-rich droplets around active pharmaceutical ingredients to form protective coatings. This technique has gained considerable interest for sustained drug delivery applications because of its ability to achieve high drug-loading efficiency and prolonged release profiles [16]. In Parkinson's disease treatment, coacervation-based systems have been explored for neuroprotective compounds and dopamine replacement strategies. However, process complexity and formulation instability may limit widespread industrial application [17].

Emulsion-based microencapsulation methods, including single and double emulsion techniques, are widely employed for encapsulating both hydrophilic and hydrophobic therapeutic agents. These approaches involve the dispersion of drug-containing phases into immiscible liquids to create stable microparticles with controlled-release characteristics [18]. Emulsion systems are highly flexible and adaptable for various pharmaceutical compounds; however, issues such as surfactant toxicity, batch variability, and encapsulation reproducibility remain challenges requiring continued investigation [19]. Despite these limitations, advances in formulation technology continue to improve the effectiveness of emulsion-based drug delivery systems in Parkinson's disease treatment.

6. Microencapsulation-Based Drug Delivery Strategies in Parkinson's Disease

Microencapsulation-based drug delivery systems have emerged as an innovative therapeutic strategy for improving Parkinson's disease treatment by addressing major pharmacological limitations associated with conventional formulations. Traditional antiparkinsonian therapies often suffer from poor oral bioavailability, rapid metabolism, fluctuating plasma concentrations, and inadequate blood–brain barrier penetration, which collectively reduce treatment efficiency and contribute to adverse outcomes [20]. Microencapsulation offers an alternative approach capable of improving drug retention, prolonging therapeutic action, and enabling targeted delivery to neural tissues.

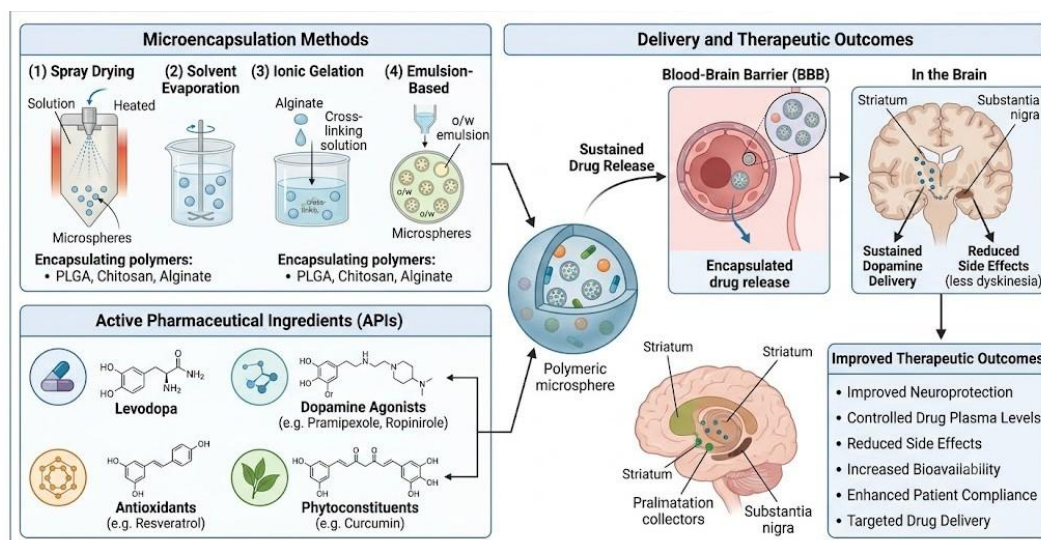


Fig 2: Microencapsulation method & Drug Delivery system in PD

Levodopa, the gold-standard treatment for Parkinson's disease, remains highly effective in improving motor symptoms; however, its short biological half-life and irregular absorption profile often lead to motor complications such as dyskinesia and wearing-off phenomena [21]. To address these limitations, researchers have explored the microencapsulation of levodopa using biodegradable polymers such as PLGA, chitosan, and alginate to develop sustained-release systems capable of maintaining more stable dopamine concentrations [22]. Controlled-release microencapsulated levodopa formulations may reduce frequent dosing requirements and improve overall motor function by minimizing fluctuations in plasma drug levels.

In addition to levodopa, dopamine agonists such as pramipexole and ropinirole have also been investigated using microencapsulation technologies to prolong therapeutic efficacy and reduce systemic adverse effects [23]. Sustained-release microspheres may provide continuous dopaminergic stimulation, potentially reducing the development of motor complications associated with intermittent receptor activation. This prolonged stimulation may improve treatment outcomes while minimizing side effects such as hallucinations, impulse-control disorders, and cardiovascular disturbances [24].

Another promising strategy involves intranasal microencapsulation systems designed to bypass the blood-brain barrier through olfactory and trigeminal neural pathways. Since conventional oral formulations face substantial challenges in achieving therapeutic brain concentrations, intranasal administration has gained increasing interest as a non-invasive alternative [25]. Chitosan-based microencapsulated formulations have demonstrated improved mucoadhesion, enhanced drug absorption, and greater brain-targeting efficiency in preclinical studies [26]. Such systems may significantly improve therapeutic outcomes by delivering drugs directly to affected neuronal regions while reducing systemic exposure.

Microencapsulation has also demonstrated considerable potential in delivering neuroprotective compounds capable of slowing Parkinson's disease progression. Oxidative stress and neuroinflammation are major contributors to neuronal degeneration; therefore, antioxidants and anti-inflammatory compounds have attracted substantial research attention [27]. Several studies have investigated the encapsulation of neuroprotective molecules to improve their stability and sustain therapeutic action. Similarly, natural phytoconstituents such as curcumin, quercetin, resveratrol, and epigallocatechin gallate possess promising antioxidant and neuroprotective properties but often exhibit poor water solubility and low oral bioavailability [28]. Encapsulation of these compounds has shown enhanced pharmacokinetic performance and improved therapeutic outcomes in experimental Parkinson's disease models, suggesting their potential role in future neuroprotective therapy [29].

7. Natural Bioactive Compounds and Neuroprotective Potential in Parkinson's Disease

Natural bioactive compounds have attracted considerable scientific attention in Parkinson's disease research due to their antioxidant, anti-inflammatory, antiapoptotic, and neuroprotective properties. Since oxidative stress and neuroinflammation play major roles in dopaminergic neuronal degeneration, naturally occurring phytochemicals have been investigated as potential therapeutic agents capable of slowing disease progression and protecting neuronal integrity [30]. However, despite promising pharmacological activities, many bioactive compounds suffer from poor aqueous solubility, low bioavailability, rapid metabolism,

limited stability, and inadequate blood–brain barrier penetration, thereby reducing their therapeutic effectiveness in clinical applications [31]. In this context, microencapsulation has emerged as an important strategy to improve the delivery and efficacy of neuroprotective phytoconstituents in Parkinson's disease therapy.

Curcumin, a polyphenolic compound isolated from turmeric (*Curcuma longa*), is one of the most extensively studied phytochemicals for neurodegenerative diseases. It possesses potent antioxidant and anti-inflammatory properties and has shown potential to inhibit α -synuclein aggregation, reduce oxidative stress, and suppress inflammatory pathways involved in Parkinson's disease pathogenesis [32]. Nevertheless, curcumin exhibits poor oral bioavailability due to low solubility and extensive first-pass metabolism. Microencapsulation of curcumin using biodegradable polymers such as PLGA, chitosan, and lipid-based carriers has demonstrated improved stability, prolonged release, and enhanced brain-targeting efficiency [33].

Similarly, resveratrol, a naturally occurring polyphenol present in grapes and berries, has gained considerable attention because of its antioxidant and mitochondrial protective effects. Resveratrol may help reduce neuronal apoptosis, attenuate inflammatory responses, and protect against mitochondrial dysfunction associated with dopaminergic neuronal loss [34]. However, its therapeutic application is restricted by poor stability and rapid metabolism. Encapsulation strategies have shown promising improvements in bioavailability and sustained drug delivery, thereby enhancing its neuroprotective effectiveness in experimental Parkinson's disease models [35].

Quercetin, a flavonoid commonly found in fruits and vegetables, has also demonstrated beneficial effects in reducing oxidative stress and inflammation. Several studies suggest that quercetin may protect neuronal cells by scavenging free radicals and modulating intracellular signaling pathways associated with neuronal survival [36]. However, poor water solubility and limited absorption significantly affect its clinical applicability. Encapsulation of quercetin within polymeric microcarriers has been shown to improve stability, absorption, and sustained therapeutic activity [37].

Epigallocatechin gallate (EGCG), a major catechin component of green tea, has demonstrated substantial neuroprotective potential through antioxidant and anti-inflammatory mechanisms. EGCG may inhibit neuronal apoptosis and reduce α -synuclein aggregation while improving mitochondrial function [38]. Similar to other phytoconstituents, encapsulation strategies have improved EGCG stability and bioavailability, thereby increasing therapeutic efficiency in neurodegenerative disease models [39]. Collectively, these findings indicate that microencapsulation of natural compounds may represent a promising complementary strategy for improving long-term Parkinson's disease management and slowing disease progression.

Natural Bioactive Compounds in Parkinson's Disease Microencapsulation Therapy

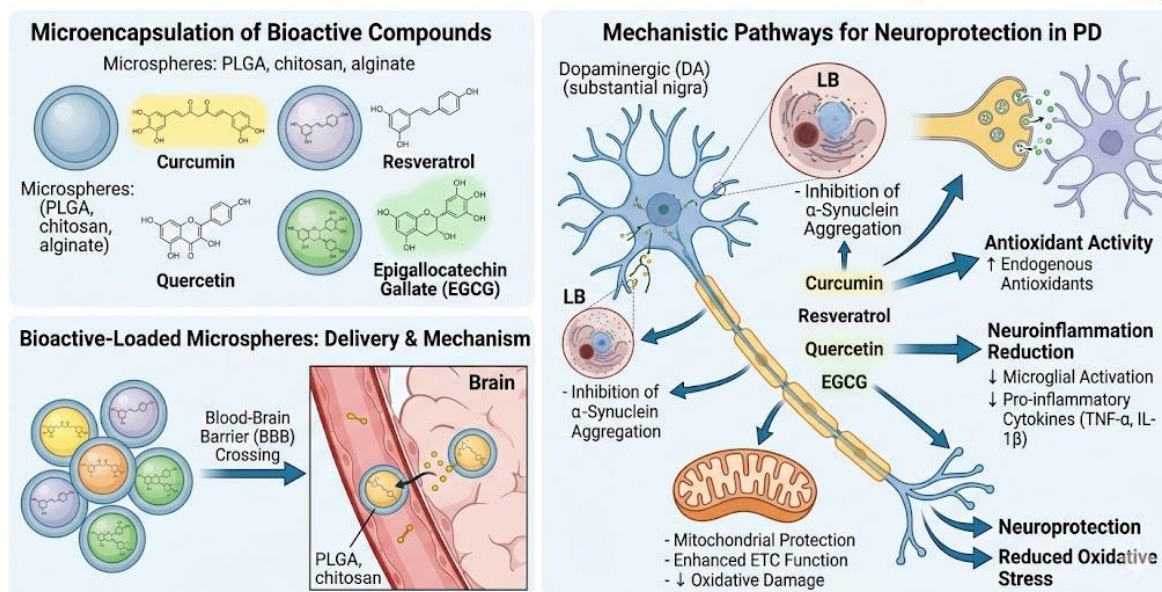


Fig 3: Natural Bioactive compounds in PD therapy

8. Challenges and Future Perspectives

Despite encouraging progress in microencapsulation-based drug delivery systems for Parkinson's disease, several scientific and technological challenges continue to limit their clinical translation. One of the primary concerns is formulation stability, as encapsulated systems may undergo aggregation, polymer degradation, premature drug leakage, or altered release characteristics during storage and administration [40]. Maintaining long-term formulation stability while preserving therapeutic efficiency remains a major challenge for pharmaceutical researchers. Another significant limitation is the difficulty associated with large-scale manufacturing and industrial reproducibility. Although several encapsulation techniques have shown excellent outcomes at laboratory scale, translating these systems into commercially viable pharmaceutical products requires optimization of manufacturing conditions, process standardization, and quality control measures [41]. Variability in particle size distribution, encapsulation efficiency, and release profiles may affect therapeutic consistency and regulatory approval.

Blood-brain barrier penetration continues to represent one of the most substantial obstacles in neuropharmaceutical development. Although microencapsulation may improve drug transport and targeting efficiency, many therapeutic molecules still demonstrate inadequate brain accumulation for achieving optimal clinical responses [42]. Therefore, future investigations should focus on developing multifunctional carrier systems capable of enhanced brain targeting through ligand-mediated transport, surface modification, receptor-mediated uptake, and stimuli-responsive release mechanisms.

Safety concerns also require careful consideration. Although biodegradable polymers such as PLGA, chitosan, and alginate are generally regarded as safe and biocompatible, comprehensive toxicity evaluations remain essential before clinical implementation [43]. Long-term safety data regarding polymer degradation products, immune responses, and repeated exposure are still limited, necessitating further preclinical and clinical investigations.

Future research may increasingly integrate nanotechnology, artificial intelligence-assisted formulation design, and personalized medicine approaches to improve Parkinson's disease treatment outcomes. Hybrid systems combining microencapsulation with nanoparticles, intranasal delivery routes, and responsive biomaterials may significantly improve brain targeting and therapeutic precision [44]. Additionally, combining neuroprotective phytochemicals with conventional antiparkinsonian agents within single encapsulated systems could offer synergistic therapeutic benefits and reduce disease progression. Therefore, continued interdisciplinary research is essential for translating experimental microencapsulation strategies into clinically effective therapies for Parkinson's disease.

9. Conclusion

Parkinson's disease remains a complex and progressive neurodegenerative disorder that significantly affects motor and non-motor functions, thereby reducing patient quality of life and increasing long-term healthcare burden. Although conventional pharmacological therapies, particularly levodopa and dopamine agonists, remain the cornerstone of treatment, several limitations such as poor bioavailability, short biological half-life, fluctuating plasma concentrations, motor complications, systemic toxicity, and inadequate blood-brain barrier penetration continue to compromise therapeutic effectiveness. These limitations emphasize the urgent need for innovative drug delivery systems capable of improving treatment outcomes and minimizing adverse effects. Microencapsulation-based drug delivery strategies have emerged as a highly promising approach for overcoming many of these therapeutic challenges. By providing controlled and sustained drug release, improving drug stability, enhancing brain-targeting efficiency, and reducing systemic toxicity, microencapsulation offers substantial advantages over conventional formulations. Various encapsulation techniques, including spray drying, solvent evaporation, ionic gelation, coacervation, and emulsion-based methods, have demonstrated encouraging outcomes in delivering antiparkinsonian drugs and neuroprotective compounds.

Furthermore, recent advances in the encapsulation of natural bioactive compounds such as curcumin, resveratrol, quercetin, and epigallocatechin gallate have shown promising neuroprotective potential by reducing oxidative stress, neuroinflammation, and neuronal degeneration. Despite remaining challenges related to scalability, formulation stability, regulatory approval, and clinical translation, ongoing technological advancements continue to strengthen the therapeutic relevance of microencapsulation systems.

Overall, microencapsulation-based drug delivery represents a promising and innovative therapeutic platform for Parkinson's disease management. Future interdisciplinary research integrating advanced biomaterials, targeted delivery technologies, and personalized therapeutic strategies may significantly enhance treatment efficacy, improve patient compliance, and potentially slow disease progression, thereby contributing to better long-term clinical outcomes.

10. References

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