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Breaking Barriers: Advances In Nanocarrier-Based Therapies For Neurodegenerative Diseases

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ABSTRACT:

Because of the protective nature of the blood-brain barrier (BBB), the intricacy of their pathophysiology, and gradual neuronal dysfunction, neurodegenerative illnesses like Alzheimer's and Parkinson's pose a serious problem. Promising methods for getting past these obstacles and improving medication delivery to the central nervous system have been made possible by recent developments in nanotechnology. The potential of several nanocarriers, such as liposomes, polymeric nanoparticles, dendrimers, and solid lipid nanoparticles, to enhance the results of treatment for Parkinson's and Alzheimer's illnesses is examined in this paper. The creation of surface-modified, stimuli-responsive nanoparticles that target important disease characteristics such dopaminergic neuronal degeneration and amyloid-beta aggregation is given particular attention. Prospects for the future emphasize how biocompatible, multipurpose, and customized nanomedicine techniques are becoming more and more important in improving the safety and effectiveness of treatments. Nanocarrier-based drug delivery systems have enormous promise to redefine neurotherapeutic approaches, notwithstanding the difficulties associated with clinical translation.

Keywords: Nanocarriers, Neurodegenerative diseases, Alzheimer’s disease, Parkinson’s disease, Targeted drug delivery, Controlled drug release.

INTRODUCTION:

As demonstrated by Alzheimer's, Huntington's, and Parkinson's illnesses, neurodegenerative disorders (ND) are typified by increasing neuronal malfunction and death, frequently impacting particular systems because of selective sensitivity, and being influenced by a variety of circumstances[1][2]. Neurodegenerative diseases are largely influenced by genetics. Additional significant factors that contribute to neuronal damage include the accumulation of amyloid fibrils, oxidative stress, chronic inflammation, aging cells, genomic instability, issues with protein balance, excess metal accumulation (such as copper, zinc, lead, and iron), and mitochondrial dysfunction[2]. Stroke is the second most prevalent disease after Alzheimer's in the United States and is ranked as the third leading cause of mortality worldwide, according to data. It causes severe brain cell destruction and ultimately death[2].

As of right now, 95% of all novel drug candidates have subpar biopharmaceutical and pharmacokinetic characteristics. Therefore, it is imperative to create appropriate drug delivery systems that would only convey the drug molecule to the target region, sparing healthy organs and tissues[1]. The size and shape of materials have an impact on their functionality in nanotechnology, which deals with structures at the billionth of a meter

scale. Drug delivery nanoparticles, which are usually less than 100 nm and composed of biodegradable substances like metals, lipids, or polymers, enhance the kinetics and bioavailability of drugs. For various biological uses, these nanoparticles can transport a range of active substances, including proteins, nucleic acids, and chemotherapeutics[1][2][3]. Nanoparticles (NPs), nanotubes, nanomedicines, nanocarriers, microparticles (MPs), and polymeric nanomaterials (NMs) are examples of recent significant advancements in novel technological inventions that have greatly improved the management of neurodegenerative diseases by enabling precise drug delivery to particular molecular targets and sites of action[2]. Drug bioavailability, site-specific targeting, and the uptake of poorly soluble medications can all be enhanced by the use of nanoparticles in targeted drug delivery at the site of disease. Figure provides a schematic comparison of targeted and untargeted medication delivery systems[3].

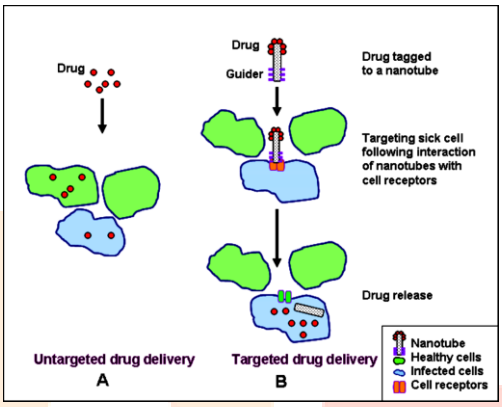

Fig. 1: targeted and untargeted medication delivery systems[3]

There are currently no clinical treatments for neurodegenerative illnesses, and the mechanism underlying their onset and progression remains unclear. This is mostly because of the Blood-Brain Barrier (BBB), Blood-Cerebrospinal Fluid Barrier (BCFB), and P-glycoproteins, which function as defense mechanisms and stop most medications from penetrating the body, resulting in peripheral (side) effects[2].

The blood–brain barrier (BBB):

The structured interface between the peripheral circulation and the central nervous system is known as the blood–brain barrier (BBB). Even though astrocytes and pericytes play a significant role, the BBB is primarily made up of the special characteristics of endothelial cells:

i) the tight junctions that physically limit solute flux between the blood and the brain by joining adjacent endothelial cells, which results in limited passive diffusion to the brain for small lipophilic compounds (optimal log P is 1-3) with molecular weights less than 400–500 Da;

ii) transport proteins allow for the selective influx transport of hydrophilic compounds,

iii) Metabolic barriers supply the biotransformation and detoxification system, and

iv) little pinocytotic activity[1].

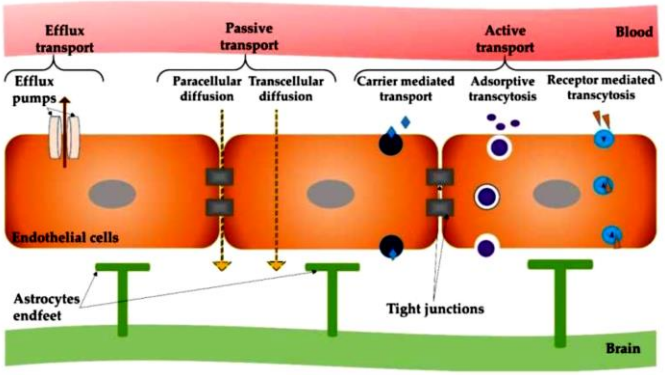

Fig. 2: Different modes of transport across the blood-brain barrier (BBB) [2]

The Blood-Cerebrospinal Fluid Barrier (BCFB):

Prior to accessing the brain, a medication molecule delivered systemically must pass through the Blood-Cerebrospinal Fluid Barrier (BCFB), which is the second barrier (after the BBB) 54. The choroid plexus's (CP) epithelial cells are responsible for this. A secretory epithelium of the highest caliber, the choroid plexus epithelium (CPE) has special cellular transport systems. When it comes to secretory rate, the CPE cells are among the most effective tissues[2].

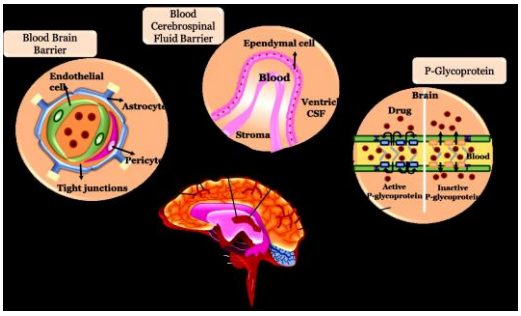

Fig. 3: The schematic representation of the main barriers for drug delivery to the brain targeting[2]

Type of nanoparticles/nanomaterials:

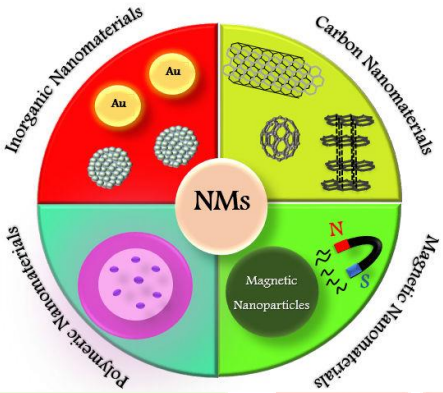

Fig. 4: types of nanomaterials [2]

Table 1: Different type of nanoparticles/nanomaterials and their application in drug delivery [2]

Types of NPs and or NMs		Size	Advantage or Application
Inorganic NPs	Gold NPs	1–150 nm	Inhibit formation of amyloid fibrils, Neural survival by increasing the expression of brain-derived neurotrophic factor
	Silver NPs	1-100 nm	Alter gene and protein expressions of Aβ deposition
Magnetic NMs		1 nm to 0.5 μm	Regulate the metal homeostasis in the brain, carry a large dose of drug to achieve high local concentration and avoid toxicity, Target and detect amyloid plaques in AD
Polymeric NMs		1–1000 nm	Cross the BBB and enhance the viability of brain cell, Improved oral bioavailability, Increased brain uptake, Enhanced the bioactivity of drugs
Carbonic NMs	Graphene	1-100 nm	Neuronal cell survival, assist in neuronal regeneration
	Fullerene	0.4-1.6 nm	Antioxidant activity against cytotoxicity of oxidative stress, induce neural stem cell

			(NSC) proliferation and rescue the function of injured CNS
	Carbon Nanotubes	1-100 nm	Promoting functional recovery of neurons after brain damage, Promote the neuronal activity, Network communication and Synaptic formation

ALZEIMER'S DISEASE:

More than 90 percent of the 50 million instances of dementia that occur globally are caused by Alzheimer's disease (AD), the most prevalent and deadly neurodegenerative illness[4]. The parts of the brain in charge of memory, learning, and higher executive functions are methodically destroyed[5].

Fig. 5: Factors increasing risk for Alzheimer's disease[5]

There are noticeable cognitive impairments linked to Alzheimer's disease. Amyloid plaques, which are extracellular deposits of amyloid-beta (Aβ) peptide, and intracellular hyperphosphorylated neurofibrillary tangles are significant contributors to the early start of AD[2].

Pathophysiology:

Stages of AD: AD Stages: Preclinical disease, MCI, and AD-caused dementia are the three main categories into which AD clinical stages can be separated. People spend different amounts of time in each stage of the continuum, even though the beginning and end points—preclinical AD and severe Alzheimer's dementia—are known. In this sense, the duration of each phase of the continuum is influenced by age, gender, heredity, and other factors. Biomarker progression begins before symptoms manifest, yet both cognitive decline and biomarker values rise with time[6].

Preclinical disease: At this stage, people show detectable brain biochemical changes that are the frst symptoms of AD including raised levels of some biomarkers, but these patients have not yet shown symptoms like memory loss [5].

MCI: Patients with MCI have minor issues with their memory and thinking capacity that may not be immediately obvious or cause interference with their aptitude to perform their daily living activities, in addition to the existence of biomarkers [5].

Dementia due to Alzheimer's disease: Dementia is categorized by a pattern of memory loss specifed as intra-individual and reasoning impairment afecting at least two cognitive areas [5].

Nanoparticles based drug delivery system:

Liposomes are lipid bilayer-based vesicles that range in size from 20 nm to several micrometers; their nanoscale variants are referred to as nanoliposomes. Because they can penetrate cell membranes and lipid bilayers, both are effective drug delivery methods that increase bioavailability [7]. It is hypothesized that oxidative stress and the 39–43 amino acid peptide amyloid-β (Aβ) are key factors in the pathophysiology of Alzheimer's disease (AD)[8]. Using either a covalent or non-covalent conjugation process, four distinct chelating ligands (CuAc, EDTA, histidine, and ZnAc) have been conjugated onto nanoliposome formulations. The results have been assessed for particle size, zeta potential, resolubilization of Aβ(1–42) peptides, neurotoxicity analysis, and ex vivo uptake by PC12 neuronal cells. It has been established that CuAβ(1–42)

and ZnAβ(1–42) aggregates can be resolubilized in vitro using formulations of EDTA, histidine, or ZnAc coupled nanoliposomes [9].

According to some theories, Nano-N2PY successfully prevents the production of Aβ aggregates, shielding human brain cells from the harmful effects of Aβ. Nanoparticles with the same core but a BSA coating were created as control nanovehicles (CNVs). SNVs had particle sizes between 221.6 ± 22.5 nm and 894.0 nm, while CNVs had particle sizes between 235.7 ± 16.3 nm and 956.1 ± 23.3 nm. Furthermore, the zeta potential values for CNVs and SNVs varied from 12.8 ± 3.0 to 37.2 ± 5.5 mV and 32.7 ± 2.4 to 41.6 ± 2.6 mV, respectively[1]. To increase drug accumulation in the brain by targeting the low-density lipoprotein-receptor (LDLr) on the BBB's capillary endothelial cells, nanoliposome formulations containing phosphatidic acid (PA) or cardiolipin (CL) have been prepared and conjugated with apolipoprotein E (ApoE) derived peptides (mApoE or dApoE) in another study to design newer drugs for the treatment of AD[10].

Deeper drug penetration through epidermal layers is made possible by ethersomes, which are innovative liposomal drug delivery systems made of soft phospholipid vesicles with a high ethanol concentration [11]. In models of Alzheimer's disease caused by D-galactose, a synthetic substance called lipotrazine phosphate (LP) has been demonstrated to improve learning and memory, decrease oxidative damage, and increase hippocampus cholinergic function[12]. Because of their nanosize, ease of synthesis, and functional diversity, dendrimers—highly branched three-dimensional macromolecules made up of different linkages such as polyamines and polyamides—are perfect for targeted drug delivery[13].

Table 2: Nanosystems for therapeutic applications in Alzheimer's disease.[14]

Disease	Nanocarrier Platform	Composition	Bioactive Agent	Active Targeting Ligand	References
Alzheimer	Polymeric NPs	PS80-coated PLGA NPs	Donepezil, cholinesterase inhibitor		[29]
	Polymeric NPs	PS80-coated PLGA NPs	Tacrine, cholinesterase inhibitor		[30]
	Polymeric NPs	PS80-coated PLGA NPs	Rivastigmine, cholinesterase inhibitor		[31]
	Polymeric NPs	PLGA and PBCA NPs	Rivastigmine, cholinesterase inhibitor		[32]
	Micelles	PHEA-EDA-Sq17-PS80 amphiphilic copolymer	Rivastigmine, cholinesterase inhibitor		[33]
	Polymeric NPs	PEG-PLGA NPs	Memantine, glutamate antagonist		[34]
	Polymeric NPs	Chitosan	F(ab') portion of the anti-amyloid antibody IgG4.1		[35]
	Liposomes	PEG-DMPC and PEG-EYPC	Amyloid beta binding llama single-domain antibody fragments (VHH-pa2H)	GSH	[36]
	Liposomes	Sm/Chol in 1:1 molar ratio		PA and CL	[37]

	SLNs	Stearic acid (internal phase), phospholipon 90G (surfactant) and sodium taurocholate (co-surfactant)		PA and CL	[38]
	Liposomes	Sm/Chol in 1:1 molar ratio		PA and mApoE peptide	[39],[40]
	Polymeric NPs	PEG-PLA NPs		TGN and QSH peptides	[41]
	Polymeric NPs	PLGA NPs with pluronicF127 (0.1%) as stabilizer	iAβ5 peptide, Aβ aggregation inhibitor	Anti-TfR mAb OX26 and anti-Aβ mAb DE2B4	[42]
	Polymeric NPs	PLGA NPs	Ac-LVFFARK-NH2 , Aβ aggregation inhibitor		[43]
	Dendrimers		KLVFF peptide, Aβ aggregation inhibitor		[44]
	Gold NPs		LCA10 and VCD10 peptides, Aβ aggregation inhibitors		[45]
	Polymeric NPs	PLGA NPs	Vitamin D-binding protein		[46]
	Nanospheres	Oxidized mesoporous carbon nanospheres	Protoporphyrin IX, Aβ and tau aggregation inhibitor	RVG peptide	[47]
	Nanocrystals	CeNC/IONC/ MSN-T807	Methylene blue, tau aggregation inhibitor	T807 ligand	[48]
	Magnetic NPs	Dextran coated-Fe3O4 NPs	Osmotin protein, neuroprotective		[49]
	Liposomes	MPB-PE or PDP-PE	D-penicillamine, copper chelator		[50]
	Polymeric micelles	PEG-PLA	R-flurbiprofen (or tarenflurbil), anti-inflammatory	FBA, RNA aptamer	[51]
	Liposomes	DOTAP/DOPE/Chol/DSPE-PEG (4.5:4.5:2:4 molar ratio)	BDNF	Mannose and penetratin or rabies virus	[52]

				glycoprotei n	

PARKINSON'S DISEASE:

Degeneration of pigmented neurons in the substantia nigra is a common feature of Parkinson's disease (PD), a chronic and progressive movement illness that lowers the neurotransmitter dopamine's (DA) nigrostriatal availability. Levodopa (also known as L-dopa or LDA), the levorotatory isomer of dihydroxyphenylalanine, the metabolic precursor of dopamine, has long been used to treat Parkinson's disease (PD) because DA cannot pass the blood-brain barrier on its own because it is hydrophobic and lacks a certain transporter [15].

Parkinson's disease (PD), which affects more than 2% of those over 65, is the most prevalent movement disorder and the second most frequent age-related neurodegenerative illness [14]. The fact that PD is a complex multisystem ND with both motor and non-motor signs and symptoms is now well acknowledged[16]. The hallmarks of the Parkinson's disease motor phenotype—brady-hypokinesia, stiffness, tremors, impaired balance, and gait difficulties—are caused by dopamine's involvement in motor processes[17]. The quality of life of PD patients is greatly impacted by non-motor symptoms, which are quite noticeable, particularly in advanced stages of the disease, and are caused by various neurotransmitter deficiencies in both the central and peripheral nerve systems. These symptoms include mood depression, pain, dysautonomia (constipation, urgency, orthostatic hypotension), behavioral (hallucinations, delusions), cognitive (dysexecutive syndrome, moderate cognitive impairment to dementia), sleep, and vigilance problems[18][19].

Pathophysiology:

Lewy bodies, which are eosinophilic intracellular inclusions made of aggregation of the α-synuclein (SNCA) protein, and a decreased number of dopaminergic neurons in the substantia nigra pars compacta are pathological characteristics of this ND. According to Braak's six-stage explanation, these aggregates start in the medulla and olfactory bulbs and gradually expand to the pons, midbrain, limbic lobe, amygdala, and neocortex[20,14]. Adrenergic, cholinergic, and serotonergic neurotransmitter systems eventually malfunction as a result of Lewy body proliferation[21]. It is typified by a gradual decline in motor abilities brought on by the death of dopamine-releasing neurons in the brain's substantia nigra, however the presence of nonmotor symptoms corroborates the death of neurons in nondopaminergic regions[22]. Since severe motor deficits are the primary cause of this illness, diagnosis is sometimes delayed, making care more challenging[23].

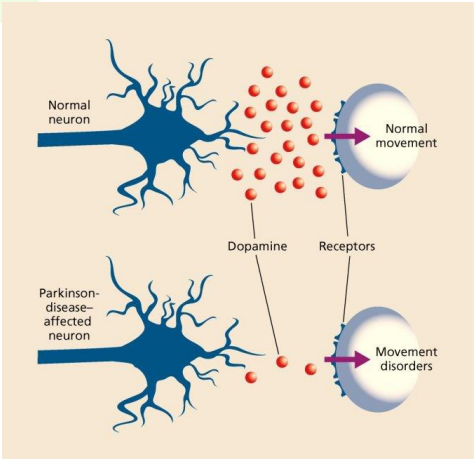

Fig. 6: Dopamine levels in a normal and Parkinson disease-affected neuron[2].

Nanoparticles based drug delivery system:

Over the past 20 years, research has concentrated on creating NBDDS to transport drugs to specific areas for the treatment of Parkinson's disease (PD) [1]. In this case, dopamine-loaded chitosan nanoparticles (NPs) were made. They had positive Z-potential values and a particle size between 110 and 150 nm. It was

discovered that these NPs reduced dopamine's overall toxicity in Madin-Darby canine kidney (MDCKII-MDR1) cells. Furthermore, dopamine-loaded chitosan nanoparticles decreased the generation of ROS and enhanced dopamine transport in the chosen cell line. Brain microdialysis investigations in rats showed that dopamine-loaded NPs caused a dose-dependent increase in striatal dopamine production after intraperitoneal acute injection. This was consistent with a rapid and pulsatile release of the neurotransmitter[24].

Dopamine-loaded PLGA nanosystems in the setting of polymeric NPs were distinguished by a steady and gradual release of the neurotransmitter. The hydrodynamic diameter of the dopamine-containing NPs was around 120 nm, and their Z-potential values were marginally negative. When compared to cells treated with free dopamine, treatment of SH-SY5Y cells with these nanoformulations did not result in morphological alterations or a decrease in cell survival. In a rat model of Parkinson's disease produced by 6-hydroxydopamine (6-OHDA), these NPs also shown the ability to penetrate the blood-brain barrier and capillary endothelium in the striatum and substantia nigra. The striatum of parkinsonian rats showed markedly elevated dopamine levels and decreased dopamine-D2 receptor supersensitivity following intravenous NP treatment [25].

Particle sizes of around 200 nm were obtained by loading the dopamine agonist ropinirole (RP) onto both uncoated and PS80-coated chitosan NPs. Both formulations showed a biphasic release pattern, releasing RP in bursts at first and then continuously throughout a 10-hour period. After three months, coated NPs were found to be stable. When compared to uncoated NPs and free RP, coated NPs showed reduced accumulation in the liver, spleen, and kidney and greater RP concentrations in the brain after one hour of intravenous treatment in Wistar rats [26]. Ropinirole has more recently been encapsulated in SLNs, NLCs, and the hydrogel formulations that go with them (RP-SLN-C and RP-NLC-C). The RP-SLN and RP-NLC systems demonstrated stability over three months, a negative surface charge, and a particle size of around 200 nm. Carbopol 934 was then used as a gelling polymer to transform these NPs into hydrogels. Studies on in vitro and ex vivo permeation revealed improved penetration and sustained release characteristics when compared to the control, a solution of free RP. Pharmacokinetic investigations revealed that when compared to suspensions of free RP, the oral administration of RP-SLN and RP-NLC was enhanced by 2.1 and 2.7 times, while the topical administration of RP-SLN-C and RP-NLC-C was enhanced by 3.0 and 3.3 times. Moreover, topical application of RP-SLN-C and RP-NLC-C increased their bioavailability by 1.4 and 1.2 times, respectively, in comparison to oral administration.[27]

Bromocriptine, an antiparkinsonian medication, was added to two distinct nanoformulations: NLCs and monoolein aqueous dispersions (MADs). The mean diameter of both MADs and NLCs was less than 200 nm. In 6-OHDA-hemilesioned rats, NLCs significantly reduced motor deficit in comparison to MAD-based formulations, exhibiting long-lasting therapeutic benefits in relation to free bromocriptine. Therefore, only NLCs increased the dopamine agonist's half-life in vivo, even though both formulations were able to effectively encapsulate it. [28]

Table 3: Nanosystems for therapeutic applications in Parkinson's disease.[14]

Disease	Nanocarrier Platform	Composition	Bioactive Agent	Active Targeting Ligand	References
Parkinson	Liposomes	PC/Chol (7:3 molar ratio) with DSPE-PEG2000-COOH (2.5 mol %)	Dopamine	Transferrin	[53]
	Polymeric NPs	Chitosan	Dopamine		[54]
	Polymeric NPs	PLGA NPs	Dopamine		[55]
	Polymeric NPs	PBCA NPs and poloxamer 188 as stabilizer	Dopamine		[56]
	Nanogels	PVP/PAAc	Dopamine		[57]
	Liposomes	HSPC/Chol/DSPE-PEG 20:10:2 molar ratio	L-DOPA, dopamine precursor	Chlorotoxin peptide	[58]
	Microspheres	PLGA NPs	Rotigotine, dopamine agonist		[59]
	Polymeric NPs	PS80-coated chitosan	Ropinirole, dopamine agonist		[60]
	SLNs	Dynasan-114 (solid lipid), soylecithin (primary surfactant) and poloxamer 188 (secondary surfactant)	Ropinirole, dopamine agonist		[61]
	NLCs	Dynasan-114 (solid lipid), Caproyl 90 (liquid lipid) soylecithin (primary surfactant) and poloxamer 188 (secondary surfactant)	Ropinirole, dopamine agonist		[61]
	MADs	Glyceryl monooleate and poloxamer 407	Bromocriptine, dopamine agonist		[62]
	NLCs	Tristearin/Miglyol 2:1 molar ratio with poloxamer	Bromocriptine, dopamine agonist		[62]
	Polymeric NPs	PLGA and PEG-PLGA NPs	Urocortin	Lactoferrin	[63]
	Zwitterionic polimers	PMPC-coated acrylated BSA	Non-Fe hemin, iron chelator	TAT peptide	[64]
	Micelles	PTS	Coenzyme Q10, antioxidant		[65]
	Nanocrystals	Pluronic F68	schisantherin A, antioxidant		[66]
	Polymeric NPs	mPEG–PLGA NPs	schisantherin A, antioxidant		[67]
	Micelles		Curcumin	Lactoferrin	[68]
	Cerasomes	PS80-modified cerasome-forming lipid N-[N-(3-triethoxysilyl)propylsuccinamoyl]- di-hexadecylamine	Curcumin		[69]

	Polymeric NPs	Sodium alginate	Curcumin		[70]
	Liposomes	Glyceryl monooleate NPs coated with Pluronic F-68 and vitamin E−TPGS	Curcumin and piperine		[71]
	Spongosomes and cubosomes	Monoolein	Curcumin and fish oil		[72]
	Polymeric NPs	PS80-coated PLA NPs	Resveratrol		[73]

Many studies have been conducted on nanoparticles to transfer dopamine (DA) to the brain for the treatment of Parkinson's disease (PD), in addition to liposome investigations. Researchers have examined the impact of administration routes on levodopa methyl ester (LDME)/benserazide-loaded nanoparticles in rats with LDA-stimulated dyskinetic behavior [15]. The axial, limb, orolingual (ALO), and locomotive aberrant involuntary movement scores (AIMs) of dyskinetic rats treated with LDME/benserazide-loaded nanoparticles were found to be lower than those of dyskinetic rats treated with LDME + benserazide. The findings showed that rats' expression of LID can be decreased by LDME/benserazide-loaded nanoparticles.[1]

FUTURE PERSPECTIVES ON NANOCARRIERS FOR BRAIN DRUG DELIVERY IN ALZHEIMER'S AND PARKINSON'S DISEASES:

Enhanced Blood–Brain Barrier (BBB) Penetration:

Through surface modification approaches that increase their permeability, nanocarriers that are intended to pass the blood-brain barrier are developing. The creation of functionalized nanocarriers that use ligands or peptides for receptor-mediated transcytosis is one exciting field. Targeting the insulin or transferrin receptors, for example, can improve the brain's absorption of nanocarriers. In order to improve BBB penetration and drug release at the target region, researchers are also investigating stimuli-responsive nanocarriers, in which the characteristics of the carrier (such as size, shape, and charge) alter in reaction to external variables like pH, temperature, or magnetic fields. Solid lipid nanoparticles (SLNs), lipid-based nanocarriers, and polymer-based nanocarriers are also being studied because of their enhanced capacity to target the brain. [74]

Targeted and Controlled Drug Release:

More sophisticated nanocarriers that react to disease-specific biomarkers will be used in tailored medication delivery systems in the future. For instance, functionalized nanoparticles can be used to target certain markers expressed by cancer cells or brain tissue in Parkinson's and Alzheimer's diseases. Additionally, sophisticated nanocarriers are being developed to release medications in reaction to certain environmental signals, such as the oxidative stress linked to neurological illnesses or the acidic environment of malignancies. In order to reduce side effects and improve the therapeutic efficacy, smart nanocarriers might be designed to deliver controlled release over extended periods of time. Biodegradable nanocarriers are designed to safely exit the body without collecting harmful consequences [75]

Multifunctional Nanocarriers (Theranostics):

For Parkinson's and Alzheimer's illnesses, the theranostic method, which combines therapy and diagnostics on a single platform, has enormous promise. Drug distribution and treatment effects may be tracked in real time by loading nanocarriers with both therapeutic medicines and diagnostic markers (such as imaging agents). To follow the nanocarriers in vivo, for example, nanoparticles can be engineered to carry MRI contrast agents or fluorescent probes. This will increase the accuracy of treatment by helping to understand the drug's pharmacokinetics and tissue localization. For a more thorough approach to therapy, multifunctional nanocarriers can also target several disease pathways, such as oxidative stress and inflammation in AD and PD.[76]

Biocompatible and Biodegradable Materials:

Nanocarriers composed of biocompatible and biodegradable materials will be essential in lowering the toxicity of drugs delivered to the brain. Future studies will concentrate on creating nanocarriers from naturally occurring biopolymers that are both biocompatible and biodegradable, such as lipids, albumin, and chitosan. Following medication administration, these substances decompose into non-toxic metabolites and guarantee safe removal from the body. Furthermore, developments in liposomes, micelles, and polymeric nanoparticles may provide improved control over drug release, decreased immunogenicity, and increased durability.[77]

Clinical Translation and Personalized Medicine:

Customizing treatment regimens will be essential to the practical implementation of nanocarrier-based treatments for Parkinson's and Alzheimer's illnesses. More individualized methods of nanomedicine are emerging, in which the nanocarriers are customized based on the patient's genetic profile, the course of the illness, and how well the patient responds to treatment. In this sense, choosing the most effective treatment will be largely dependent on genetic screening and biomarker discovery. Large-scale clinical studies that concentrate on the long-term safety and effectiveness of these nanocarriers are also required. Integrating patient-specific data with nanomedicine to develop medicines that maximize benefits while minimizing negative effects is a future objective.[78]

CONCLUSION:

By providing safer, more effective, and more focused drug delivery methods, nanotechnology has paved the way for new developments in the treatment of neurodegenerative illnesses. Different kinds of nanoparticles, including dendrimers, liposomes, and polymeric nanoparticles, have shown promise in delivering therapeutic medicines to certain brain areas impacted by Parkinson's and Alzheimer's illnesses by overcoming the blood-brain barrier. These cutting-edge medication delivery methods allow for regulated release and less systemic toxicity in addition to increasing bioavailability. In the future, research will concentrate on creating multifunctional, biocompatible nanocarriers that can react to disease-specific indicators. With the use of genetic profiling and biomarker analysis, personalized nanomedicine is set to emerge as a crucial therapeutic approach. Nanotechnology presents a revolutionary way to treat the intricate pathophysiology of neurodegenerative diseases and enhance patient outcomes, despite ongoing obstacles including long-term safety, large-scale production, and regulatory approval.

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