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Nanocarriers for Crossing the Blood Brain Barrier in the Treatment of Alzheimer and Parkinson Diseases

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Abstract

Neurodegenerative diseases such as Alzheimer's and Parkinson's present formidable therapeutic challenges due to the restrictive nature of the blood-brain barrier (BBB), which significantly limits the passage of pharmacological agents into the central nervous system. Recent advancements in nanotechnology have led to the emergence of nanocarrier-based drug delivery systems capable of overcoming these barriers with enhanced precision and efficiency. This chapter critically explores the design, functionalization, and application of various nanocarriers—including polymeric nanoparticles, lipid-based systems, dendrimers, and inorganic nanoparticles—for effective transport across the BBB. Emphasis is placed on the mechanisms of BBB penetration, such as receptor-mediated transport, adsorption-mediated transcytosis, and carrier-mediated pathways, which are exploited through strategic surface modifications and ligand conjugation. The integration of stimuli-responsive features and theranostic functionalities enables not only targeted delivery but also real-time monitoring and diagnosis of neurodegenerative pathology. Additionally, the chapter addresses the translational hurdles including safety, biocompatibility, pharmacokinetics, and regulatory frameworks that must be navigated for clinical success. Interdisciplinary approaches involving computational modeling, systems biology, and AI-driven optimization are discussed as future directions for refining nanocarrier design and achieving personalized neurotherapeutics. This comprehensive evaluation highlights the transformative potential of nanocarriers in revolutionizing the management of Alzheimer's and Parkinson's diseases through targeted, non-invasive, and sustained therapeutic delivery to the brain.

Keywords: Blood-Brain Barrier, Nanocarriers, Neurodegenerative Diseases, Targeted Drug Delivery, Alzheimer's Disease, Parkinson's Disease.

Introduction

Neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD) represent some of the most pressing medical challenges of the 21st century due to their chronic progression, increasing prevalence with age, and absence of curative treatments [1]. These disorders are characterized by progressive neuronal loss, accumulation of misfolded proteins,

neuroinflammation, oxidative stress, and dysfunction in neurotransmitter systems [2]. Despite extensive research, therapeutic outcomes remain limited, primarily because conventional drugs fail to achieve adequate concentrations within the brain [3]. A critical factor contributing to this failure is the presence of the blood-brain barrier (BBB), a dynamic and highly selective interface that tightly regulates the movement of substances between the bloodstream and the central nervous system (CNS) [4]. This barrier protects the brain from toxins and pathogens but also severely restricts the entry of most pharmacological agents, including large molecules and neuroprotective compounds, thereby complicating the treatment of neurological conditions [5].

To address these challenges, researchers have increasingly turned to nanotechnology, which offers a suite of innovative tools for enhancing drug delivery across the BBB [6]. Nanocarriers—engineered delivery systems typically ranging from 1 to 100 nanometers—enable drugs to be encapsulated, protected from degradation, and selectively delivered to targeted brain regions [7]. Their unique physicochemical properties, such as high surface area, tunable size, and modifiable surface characteristics, allow them to interact favorably with biological membranes and exploit natural transport mechanisms at the BBB [8]. These include receptor-mediated transcytosis, adsorptive-mediated uptake, and transport via endothelial cell channels [9]. Through functionalization with targeting ligands, peptides, antibodies, or polymers, nanocarriers can be engineered to recognize and bind to specific receptors overexpressed on BBB endothelial cells, thereby facilitating precise and efficient drug delivery to the brain parenchyma [10].

Among the various nanocarrier systems investigated, polymeric nanoparticles, liposomes, dendrimers, solid lipid nanoparticles, and metallic nanoparticles have shown significant promise in preclinical studies [11]. Each class offers distinct advantages in terms of drug loading capacity, biocompatibility, release kinetics, and potential for functionalization. Polymeric nanoparticles, for instance, can be tailored for sustained release, while lipid-based systems closely mimic biological membranes, enhancing their cellular uptake [12]. Dendrimers offer highly branched, multivalent architectures ideal for targeted delivery, and metal-based carriers, particularly those using gold or iron oxide, can serve dual purposes in drug delivery and imaging [13]. These systems not only facilitate the delivery of conventional drugs but also enable the transport of genetic materials, neurotrophic factors [14], and small interfering RNAs (siRNAs), further broadening their therapeutic applications in neurodegenerative conditions [15].