

# Brain Drug Delivery Systems

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At present, major central nervous system (CNS) disorders, including neurodegenerative diseases, cerebrovascular diseases, and brain tumors, are serious threats to human health due to the aging of the general population. For example, more than 24 million people worldwide are currently suffering from Alzheimer's disease, and approximately 15 million injuries and 5 million deaths were caused by stroke each year. However, drug delivery for the treatment of these brain diseases is far from efficient. The main obstacle for brain drug delivery is the blood–brain barrier (BBB), which is composed of polarized endothelial cells, astrocytes, microglial cells, and pericytes, and which separates the blood from the underlying brain cells, providing protection to neurons and preserving CNS homeostasis. Essentially, nearly 100% of large-molecule drugs and >98% of small-molecule drugs do not penetrate the BBB. Nanotechnology-based drug delivery systems could bring hope to brain drug delivery for the treatment of brain diseases and have become a hot topic in the field of drug delivery. Tremendous efforts have been made in the treatment of CNS disorders, and some impressive developments have been achieved.

The aim of this theme issue is to address the latest important developments of brain drug delivery systems in the diagnosis and treatment of Alzheimer's disease, Parkinson's disease, stroke, and brain tumors. It contains six review articles and seven research papers written by eminent experts from Europe, the United States, and Asia. In this theme

issue, readers will find a general review of nanotherapeutics for major diseases in central nervous systems (Jiang *et al.*). Considering that brain drug delivery strategies could be adapted according to the unique pathological features of different brain diseases, more specialized reviews in nanotechnology-based drug delivery systems for the diagnosis and treatment of neurodegenerative diseases (Bozdağ-Pehlivan), brain tumors (Yang *et al.*), and ischemic stroke (Lee *et al.*) are also provided. For instance, recent work indicates that the perturbation of axonal transport is an early marker in the pathological process of many neurodegenerative diseases. Thus, developing novel therapeutics targeting this early precursor in neuronal dysfunction is critical for the treatment of neurodegenerative diseases. The review by Gunawardena discusses the potential of a novel nanotechnology-based approach to targeting this early defect in neurodegenerative diseases to maximize the therapeutic effects. As a noninvasive way to deliver drugs to the CNS, intranasal delivery offers a direct nose-to-brain pathway bypassing the BBB and represents a promising therapeutic strategy for the treatment of CNS diseases (Benedict *et al.*).

Novel strategies for brain drug delivery are also presented in original papers of this theme issue. Jiang *et al.* designed angiopep-conjugated nanoparticles for the targeted long-term gene therapy of Parkinson's disease, and Peura *et al.* explored a large amino acid transporter 1-based strategy for the brain delivery of dopamine. A fatty acid-based strategy was used for efficient brain gene delivery (Lu *et al.*), and small-interfering RNA (siRNA) was delivered into neurons to knock down protein expression by means of a dendrimer (Cena *et al.*). In addition to the above-mentioned receptor-mediated, carrier-mediated approaches, the rational design of nanotechnology-based brain drug delivery system including the optimization of particle size and surface modification

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(Feng *et al.*), the multivalent effect of targeting moieties (Li *et al.*), and small-molecule enhancers such as borneol (Wang *et al.*) to up-regulate the BBB permeability of nanoparticles are also discussed. After exploring these novel strategies and the latest important developments of brain drug delivery systems provided in each paper of this theme issue, the reader is encouraged to foster innovative cross-disciplinary thinking and open up new avenues in designing effective brain drug delivery systems for treating brain diseases.

The guest editor and all authors of this thematic issue are deeply grateful to special features editor Ram I. Mahato and editorial assistant Ms. Rachel D. Lucke for their valuable suggestions and editorial board for their foresight in encouraging an issue on this topic.



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