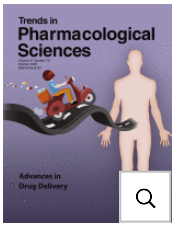
Oct 01, 2020

Volume 41, Issue 10, p679-776, e1-e2

Special Issue: Advances in Drug Delivery Systems



Drug delivery is an important aspect in drug development. Without an effective targeted and suitable delivery system, a drug cannot be useful. ... Show more

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Editorial

Kusumika Mukherjee

Drug delivery is an important aspect in drug development as, without an effective targeted and suitable delivery system, the drug would not be useful. Numerous parameters are considered towards designing successful drug delivery systems. For example, it would require understanding the properties of the drug being delivered (what), its purpose (why), and the knowledge of the target organ or tissue the drug is being delivered to (where). These in turn will help determine the type of delivery system that should be used (how).

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Spotlights

Pavimol Angsantikul, Samir Mitragotri

Fast-acting insulins are central to the regulation of prandial glucose in diabetic patients. Current fast-acting insulins require 20–30 min for the onset and longer for the peak blood concentrations. The recent work by Mann *et al*. used high-throughput synthesis and screening of polyacrylamide-based excipients to yield a formulation with pharmacokinetics that is faster than the currently available fast-acting insulins.

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Tamara Minko

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In a recent study, Saraswat and colleagues identified a novel proteolysis targeting chimera (PROTAC), ARV-825 (ARV), that efficiently degrades bromodomain-containing protein 4 (BRD4) to drug the ‘undruggable’ MYC in pancreatic cancer. ARV-loaded polyethylene glycol–poly lactic acid-co-glycolic acid (PLGA–PEG) polymeric nanoparticles (ARV-NPs) showed promising anticancer activity in both 2D cell culture and 3D multicellular tumor spheroid models of pancreatic cancer. This study demonstrates a unique therapeutic strategy in which targeting BRD4 for degradation via the E3 ubiquitin ligase cereblon (CRBN) pathway leads to sustained inhibition of oncogenic *MYC* expression for effective treatment of pancreatic cancer.

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Forum

Fluorescein Isothiocyanate Chitosan Nanoparticles in Oral Drug Delivery Studies

Anna E. Caprifico, Elena Polycarpou, Peter J.S. Foot, Gianpiero Calabrese

Oral administration of drugs is one of the most patient-friendly drug delivery routes. However, drug bioavailability via the oral route remains poor due to the harsh gastrointestinal environment. In recent years, many nanocarriers have been designed to overcome this limitation. Among those, chitosan nanoparticles (ChNPs) have proved to be a quite popular choice. Here, we highlight the use of fluorescein isothiocyanate–tagged ChNPs as an invaluable tool to monitor the fate of ChNPs encapsulating oral drugs, leading to an in-depth understanding of drug biodistribution and, in turn, shedding light on ways to improve bioavailability.

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Opinion

Modulating the Blood–Testis Barrier Towards Increasing Drug Delivery

Baiping Mao, Tiao Bu, Dolores Mruk, Chao Li, Fei Sun, C. Yan Cheng

Testicular cells produce several biologically active peptides that exert their downstream effects by activating distinct signaling proteins. These biomolecules are now known to support spermatogenesis and effectively enhance paracellular and transcellular diffusion of drugs (e.g., adjudin) across the blood–testis barrier (BTB). We briefly discuss the biomolecules that maintain the BTB: these provide new insights into how the BTB can be modulated to allow therapeutic drugs, including male contraceptives, to be transported across the BTB and more generally across blood–tissue barriers.

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Reviews

Tackling TAMs for Cancer Immunotherapy: It’s Nano Time

Yishun Yang, Jianfeng Guo, Leaf Huang

The tumor microenvironment (TME) is a highly complex environment that surrounds tumors. Interactions between cancer cells/non-cancerous cells and cells/non-cell components in the TME support tumor initiation, development, and metastasis. Of the cell types in the TME, tumor-associated macrophages (TAMs) have gained attention owing to their crucial roles in supporting tumors and conferring therapy resistance. Recent developments in nanotechnology raise opportunities for the application of nano targeted drug-delivery systems (Nano-TDDS) in cancer therapy.

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Inhaled RNA Therapy: From Promise to Reality

Michael Y.T. Chow, Yingshan Qiu, Jenny K.W. Lam

RNA-based medicine is receiving growing attention for its diverse roles and potential therapeutic capacity. The largest obstacle in its clinical translation remains identifying a safe and effective delivery system. Studies investigating RNA therapeutics in pulmonary diseases have rapidly expanded and drug administration by inhalation allows the direct delivery of RNA therapeutics to the target site of action while minimizing systemic exposure. In this review, we highlight recent developments in pulmonary RNA delivery systems with the use of nonviral vectors.

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Cancer Nanomedicines in an Evolving Oncology Landscape

Peng Guo, Jing Huang, Marsha A. Moses

Nanomedicine represents an important class of cancer therapy. Clinical translation of cancer nanomedicine has significantly reduced the toxicity and adverse consequences of standard-of-care chemotherapy. Recent advances in new cancer treatment modalities (e.g., gene and immune therapies) are profoundly changing the oncology landscape, bringing with them new requirements and challenges for next-generation cancer nanomedicines. We present an overview of cancer nanomedicines in four emerging oncology-associated fields: (i) gene therapy, (ii) immunotherapy, (iii) extracellular vesicle (EV) therapy, and (iv) machine learning-assisted therapy.

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Accessing Intracellular Targets through Nanocarrier-Mediated Cytosolic Protein Delivery

Ritabrita Goswami, Taewon Jeon, Harini Nagaraj, Shumei Zhai, Vincent M. Rotello

Protein-based therapeutics have unique therapeutic potential due to their specificity, potency, and low toxicity. The vast majority of intracellular applications of proteins require access to the cytosol. Direct entry to the cytosol is challenging due to the impermeability of the cell membrane to proteins. As a result, multiple strategies have focused on endocytic uptake of proteins. Endosomally entrapped cargo, however, can have very low escape efficiency, with protein degradation occurring in acidic endolysosomal compartments.

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Paving the Road for RNA Therapeutics

Niels Dammes, Dan Peer

Therapeutic RNA molecules possess high potential for treating medical conditions if they can successfully reach the target cell upon administration. However, unmodified RNA molecules are rapidly degraded and cleared from the circulation. In addition, their large size and negative charge complicates their passing through the cell membrane. The difficulty of RNA therapy, therefore, lies in the efficient intracellular delivery of intact RNA molecules to the tissue of interest without inducing adverse effects.

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