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EDITORIAL

Editorial of special column of hot topic reviews in drug delivery (II)



Over the past 10 years, the trend toward interdisciplinary research has become increasingly evident. Many disciplines, such as materials science, chemistry, physics, engineering, computer-aided design and artificial intelligence, mathematics, biomedicine, pathology, etc., have penetrated the field of pharmaceutical research, giving rise to many new drug delivery strategies, such as LNP and GalNAc for RNA delivery¹ and pure drug-based drug delivery². The special issue aimed to collect reviews on hot topics in drug delivery and to provide a platform for prominent scientists and scholars worldwide to communicate and share their thoughts. This special issue has garnered 22 excellent review articles and 1 research paper that cover the full spectrum of hot topics in drug delivery. First, Wu et al.³ systematically traced the technological evolution from early simple models to current advanced AI algorithms across various applications, ranging from formulation optimization to the prediction of critical formulation parameters and *de novo* material design. Understanding the *in vivo* fate of drug delivery systems is essential for translation. Zhang et al.⁴ highlight the key roles of Förster resonance energy transfer, aggregation-induced emission, and aggregation-caused quenching in revealing the nanocarrier's pharmacokinetics, biodistribution, and intracellular behavior. Xu et al.⁵ discussed the *in vivo* fate of mRNA-LNPs. Aqueous solubility remains a major challenge in drug development, severely compromising clinical performance. Chen et al.⁶ reviewed crystal engineering for poorly water-soluble drugs.

RNA-based therapeutics have emerged as attractive candidates for clinical applications, offering distinct advantages over conventional small-molecule drugs, which play an important role in the treatment of a variety of diseases. A lipid-based system has been demonstrated as one of the most promising platforms to improve RNA therapeutics. Li et al.⁷ provided a comprehensive overview of lipid-based nanosystems, from traditional formulations to cutting-edge innovations, and their evolving applications in the treatment of atherosclerosis. Dong et al.⁸ first summarized the physiological and biological barriers to the RNA inhaled platform and introduced the progress of inhaled RNA delivery systems and their therapeutic

efficiency against interstitial lung diseases. Non-invasive delivery at mucosal surfaces can deliver drugs to therapeutic sites systemically, avoiding off-target effects, reducing required drug doses, bypassing hepatic first-pass metabolism, and circumventing uncontrolled drug release. van Staden et al.⁹ discussed various liquid-based formulation approaches to cross the ocular-, nasal-, oromucosal-, and vaginal mucosal barriers, emphasizing advanced liquid drug delivery systems and the progress made toward clinical translation as a platform for future transmucosal liquid-based dosage form development. Liu and Lu et al.¹⁰ summarized recent advances in the design and functionalization of lyotropic liquid crystal systems, with a focus on their ability to overcome physiological barriers, enhance therapeutic efficacy, enable targeted delivery, and support prolonged treatment regimens. Microneedles (MNs) based delivery systems offer a promising alternative for transdermal drug administration. Chen et al.¹¹ reviewed the applications and recent advances in MN systems for treating autoimmune diseases. Yin et al.¹² introduced emerging advances in intelligent MNs for biomedical applications. Peptide- and protein-based therapeutics offer realized and potential health benefits. Liu et al.¹³ provided a comprehensive and up-to-date analysis of the structural and physiological barriers that influence peptide and protein bioavailability and therapeutic efficacy. They examined key challenges associated with various administration routes, including topical, transdermal, oral and others. Ma et al.¹⁴ summarized strategies for PEG site-specific modification of proteins, the interaction states between PEG and proteins, and the effects of PEG chains on protein spatial structure, solubility, activity, and thermal stability. Onoue et al.¹⁵ reviewed recent advancements in formulation techniques aimed at improving the biopharmaceutical properties of orally administered drugs. Chen et al.¹⁶ reviewed current developments in engineering methods and strategies for plant-derived extracellular vesicles for cancer treatment and combined cancer immunotherapies. Yang et al.¹⁷ analyzed key barriers to the clinical translation of vesicles, including endotoxin-associated safety, batch-to-batch heterogeneity, scalable manufacturing, and standardization of quality attributes. For pathology-directed drug

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delivery, Chen et al.¹⁸ analyzed how to overcome the blood–brain barrier for the treatment of brain diseases. Jiang et al.¹⁹ reviewed nanomedicine-driven tumor glucose metabolic reprogramming for enhanced cancer immunotherapy. Liang et al.²⁰ provided a cutting-edge review of novel biomedicines for the treatment of ovulatory dysfunction. Pérez-Herrero et al.²¹ summarized albumin-based nanocarriers for cancer treatment. Zhou et al.²² reviewed cuproptosis-based nanomedicine for synergistic therapy of cancer metastasis. Xu et al.²³ reviewed self-assembled nanoplateforms for cancer immunotherapy. Dunika et al.²⁴ reviewed the cannabidiol-based delivery strategies for the soft tissue wound healing.

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