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Editorial

Exploring the Next Generation of Novel Drug Delivery Technologies

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Conventional formulations have been often failed to achieve patient compliance due to their poor drug solubility, uncontrollable release profile, side effects, lack of site selectivity, and low bioavailability [1]. Across the laboratories, scientists are extremely committed to break down the fences between the available most promising new drug candidates and their targets towards cells or tissues. To do this, they have been developed a few novel drug delivery modalities. Eventually, the following novel drug delivery modalities intend to translate the scientific progress into clinical benefits for human welfare.

Cell-targeted delivery of therapies with lipid nanoparticles (LNPs)

LNPs have drawn a significant attention since last two decades, and achieved remarkable clinical success since the first clinical approval of Doxil in 1995 [2]. We have witnessed a great expansion in the development of nonviral systems for *in-vivo* delivery of nucleic acids in targeted manner. LNPs have been emerged as a promising and potent carriers for intracellular delivery of nucleotide-based therapeutics for production of protein in cells. LNPs can distribute mRNA into cells for generating cellular protein production after intravenous, subcutaneous and pulmonary administration [3].

Audrey Gallud, Senior Scientist, Advanced Drug Delivery, Pharmaceutical Sciences, AstraZeneca and team incubated the LNPs in serum to simulate the effects of proteins binding to the surface as the LNPs travel through the body. This novel approach has been accomplished to gain a clear concept behind the mechanism of protein accumulation on the surface of the LNPs, known as protein corona that influences the way LNPs interact with endosomal membranes [4].

Tissue-targeted delivery

Developing targeting approaches to facilitate site-specific drug delivery results in reducing off-target effects, reducing unwanted toxicities, and thereby enhancing therapeutic efficacy of a drug. Over the past few decades, a large number of literature has been reported on the understanding of biological obstructions that hinder tissue-specific drug delivery and schemes to overcome them [5].

In preclinical and clinical programs, a number of different nanosystems like polymeric nanoparticles, polymer conjugates, inorganic nanoparticles are currently evaluated. In case of polymeric nanoparticles, drug compounds are encapsulated within a polymer matrix while polymer conjugates are chemically linked to branched polymers. The nanoparticles can be connected to any drug molecule, imaging labels and an antibody to dynamically target tissues.

In association with Memorial Sloan Kettering Institute of Cancer Research and Cornell University, Zhang L et al. reported that nanoparticles comprising attached engineered antibody fragments for imaging and detection of HER2-overexpressing breast cancer, penetrated the tumour, and revealed significant accumulation within the tumour tissues [6].

Convenient treatment with controlled release formulations

Controlled drug delivery (CDD) formulations have emerged as an alternative to the conventional one, to increase the bioavailability, prolong drug release and maintain drug plasma levels within the therapeutic window with minimal side effects. CDD improves the drug solubility and stability. Controlled drug-delivery based on nanotechnology is one of the most explored science fields that collaborate biologists, chemists, physicists, pharmacists, and physicians together to improve interdisciplinary knowledge. By using controlled-release formulations, half-life of drugs can be extended inside the body to minimize dosing frequency and make treatments more convenient and patient compliance.

The future of controlled release formulations is focused on patient-specific therapy using microfluidics, 3D-printed devices and clustered regularly interspaced short palindromic repeats cas9 based delivery systems integrated with quantum sensing [7].

Developing alternative routes of administration

It is projected that the sales of biologics used for a wide range of chronic diseases like diabetes, psoriasis, rheumatoid arthritis, crohn's disease, etc will rise from $380 billion in 2022 to $416 billion in 2023, and to almost $600 billion in 2027 [8]. Of the 175 new drugs approved by the United States Food and Drug Administration during the period 2016 and 2019, most were biologics. The inconvenience of administration of numerous biologics as parenteral formulations can lead to poor patient compliance, while persistence and adherence are usually superior for oral medications compared to injections. The ongoing advancement in drug design and delivery technologies by endless effort from researchers, oral biologics are turning from a concept to reality.

Researchers have recently reported on the potential of transient permeation enhancers (TPEs) for enabling oral delivery of both peptides as well as antisense oligonucleotides. TPEs are excipients that can be co-formulated with biologics that help assist in the transportation of macromolecules across the natural barriers of the GI tract [9,10].

AstraZeneca, a British-Swedish multinational pharmaceutical and biotechnology company revealed an emerging technology named as "ingestible injectables" that aims to transfer the site of injection from subcutaneous to the gastrointestinal tract, taking the benefit of lack of pain receptors in the intestine. The purpose of ingestible injectables is to produce similar bioavailability attained in subcutaneous route but in a pain-free manner. The organization is collaborating externally for this exciting research zone to develop patient-centric delivery of biotherapeutics.

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