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Leading Trends in Pharmaceutical Research: Top Cited Articles in Molecular Pharmaceutics

M. Kishore Babu[1], M. Vamshi Krishna[2], N. Jansi Rani[3], P. Chandra Sekhar[4]

1.Professor , Department of pharmaceutics , QIS College of pharmacy , Ongole , A.P

2.Associate Professor , Department of Pharmaceutics , QIS College of pharmacy , Ongole , A.P

3Assistant Professor , Department of Pharmaceutics , QIS College of pharmacy , Ongole , A.P

4.Assistant Professor , Department of Pharmaceutics , QIS College of pharmacy , Ongole , A.P

Abstract

Several Molecular Pharmaceutics publications that garnered a lot of citations in 2023 are highlighted in this collection. These widely referenced publications provide insightful information about the study areas that readers are presently most interested in. They showcase ground-breaking findings in addition to pertinent analyses and viewpoints on important topics of the day.

- Corresponding Author
Kishore babu
kishorebabu@gmail.com

Introduction

Both the area of vaccine research in general and articles on the COVID-19 pandemic and the novel vaccines that sprang from it continue to get a lot of interest. Salian et al. provide a summary of the many methods and tools employed in the creation of COVID-19 vaccines, as well as initiatives to recycle various medication classes and investigate cutting-edge treatment techniques. According to Chatzikleanthous et al., COVID-19 vaccines that use lipid nanoparticles for mRNA encapsulation demonstrate the enormous potential of lipid-based delivery methods. Their study provides a summary of the many approaches that may be used to create lipid-based vaccination adjuvants and delivery systems for antigens based on proteins, carbohydrates, and nucleic acids. It also looks at how these approaches may be combined to make vaccines with several components. The quick development of mRNA vaccines in response to the COVID-19 pandemic is highlighted by Webb et al. A modular strategy that allows for quick adaption to different targets is the use of lipid nanoparticle (LNP) technology for mRNA protection and delivery into cells. The authors also talk about how the need for both RNA drug ingredient and LNP drug product is putting pressure on COVID vaccine manufacturing facilities. They stress the necessity of improving manufacturing methods to fulfill future demands in the manufacture of RNA medicines. LNPs are crucial for mRNA transport, but they are also becoming a nonviral delivery system for CRISPR/Cas9-mediated genome editing, especially for the treatment of cancer and genetic disorders. The difficulties in delivering CRISPR components and the need for advanced delivery methods to guarantee safe and efficient genome editing are covered by Kazemian et al. in their review. They provide a summary of LNPs, CRISPR-mediated gene therapy, and the prerequisites for CRISPR component delivery. There is also discussion of potential future directions for the clinical use of LNP-CRISPR gene editing.

Indo-American Journal of Life Sciences and Biotechnology

Numerous tumors and methods are being investigated in an effort to improve cancer detection and treatment. One of the best targets for cancer theranostics has been found to be fibroblast activation protein (FAP). A novel family of FAP inhibitors was investigated by Ma et al. using an N-(4-
131I was used to label the quinolinoyl)-Gly-(2-cyanopyrrolidine) scaffold. In U87MG xenograft mice, intratumor injection of one of the iodine-labeled derivatives markedly inhibited tumor development while avoiding severe toxicity. The scientists came to the conclusion that this compound's therapeutic effectiveness in tumor-bearing animals points to its potential for use in glioma brachytherapy. One common first-line chemotherapeutic treatment for colorectal cancer (CRC) is oxaliplatin (OX). The problem is that CRC cells often become resistant to treatment. It is believed that tumor-associated macrophages (TAMs) are essential for OX resistance. According to Lan et al., OX-resistant patients had a larger density of tumor-associated macrophages infiltrating their CRC tissues than OX-sensitive individuals. They came to the conclusion that one potential treatment approach for OX-resistant CRC patients would be to target the tumor-associated macrophages. Ali Sayyed et al. investigated chemotherapy resistance using a new medication and methodology. They assessed cisplatin resistance in relation to oral squamous cell cancer (OSCC). A cisplatin-resistant OSCC 3D tumor spheroid model was made more sensitive to cisplatin by using exosomes loaded with a microRNA-155 inhibitor. This positive result opens the door for exosome-based treatments in the future to treat patients with resistant oral cancer. When chemotherapy medications are delivered specifically to cancer cells, local drug concentrations inside tumors rise, killing more cancer cells and reducing side effects, improving treatment results and quality of life. To target cancer cells, Pramanik et al. used cubosomes, which are liquid crystal lipid nanoparticles with a surface functionalized with hyaluronic acid. In CD44-positive cells, the scientists discovered that the hyaluronic acid-tagged cubosomes loaded with copper acetylacetonate caused noticeably more cell death than untargeted cubosomes, indicating that this might be a viable therapeutic approach in the future. As "magic bullets," antibody-drug conjugates are utilized to cure cancer. A monoclonal antibody delivers a cytotoxic payload to a particular cell. However, they are difficult to
Combine. Using a family of IgG Fc-affinity reagents, Matsuda et al. created a technological platform for site-specific antibody conjugation. After creating a thiol intermediate, they conjugated it with several payloads. By raising the maximum tolerated dosage and demonstrating an enhanced therapeutic index, these conjugates performed well in performance evaluation tests. There is potential for the technique to facilitate the synthesis of next-generation ADCs with less heterogeneity.

Nanotechnology

continues to play a prominent role in drug delivery innovations. Farr and Xiong discuss the limitations of conventional formulations of the iron chelator, deferoxamine mesylate, which is used to treat iron poisoning and chronic iron overload. Iron accumulation has also been linked to Alzheimer's disease, Parkinson's disease, and secondary damage following intracerebral hemorrhage and consequently reducing iron levels in the brain is of great current interest. In their review, the authors describe how both intranasal and systemic nanoformulations of deferoxamine show promise in addressing iron overload in the brain. Arora et al. also studied the potential of nanoformulations for addressing a neuro-degenerative disease, focusing their research on developing a liposomal ApoE2 gene delivery system for treatment of Alzheimer's disease. They achieved efficient brain-targeted delivery of ApoE2 encoding plasmid DNA using liposomes targeted at glucose transporter-1 (GLUT-1). The liposomes were surface-functionalized with a GLUT-1 targeting ligand, mannose, and a cell-penetrating peptide to enhance brain targeting and cellular internalization, respectively. Despite the numerous challenges associated with gene delivery to the brain, the dual-functionalized liposomes proved effective in targeting the brain and facilitating the expression of genetic cargo in brain cells in a mouse model. The review by Spada et al. details the reasons why albumin is such an attractive carrier in nanomedicine. They note

Indo-American Journal of Life Sciences and Biotechnology

that albumin has high biocompat- ibility and biodegradability, is nonimmunogenic, and is safe for clinical application. Furthermore, albumin interacts with many different drugs, which can in some instances protect them from elimination and metabolism, leading to improvements in their pharmacokinetic properties. Importantly, albumin can also interact with receptors overexpressed in many diseased tissues and cells, facilitating active targeting without requiring the use of specific ligands appended to the nanocarrier. In particular, the authors focus on the role of albumin in carrying anticancer drugs such as paclitaxel. Nanoparticles are also attracting attention for delivery to the lung. Pramanik et al. focus their review on the potential benefits of using nanoparticle drug delivery systems for the treatment of chronic lung diseases. The authors highlight the use of nebulized formulations of nanoparticles, as well as the production and delivery of composite particles composed of nanoparticles using a dry powder inhaler device. They also provide an overview of commercial pulmonary drug delivery systems. Showcasing the diverse application of nano drug delivery systems, Sharifi et al. discuss the opportunities and challenges of using nano- medicines in healing chronic wounds. Nanomedicine can activate various cellular and molecular mechanisms within the wound microenvironment via angiogenetic, antimicrobial, and anti-inflammatory properties, which may turn nonhealing wounds into ones that heal. In addition to highlighting current studies on the potential and difficulties of using nanomedicine to the treatment of chronic wounds, this study offers a succinct summary of wound healing processes and pathology. Additionally, Gondaliya et al. reported on wound healing, investigating the effects of using exosomes generated from mesenchymal stem cells (MSC) to deliver an inhibitor of miR-155. They showed how MSC-derived exosomes loaded with an inhibitor of miR-155 might be used therapeutically to promote wound healing in diabetics. Their work lays the groundwork for a potential therapeutic approach that encapsulates miRNAs and antibiotics in MSC-derived exosomes, ultimately leading to better results for diabetic wounds that are chronic and nonhealing.

Conclusion

Another current topic of study is the use of polymers as important excipients in sophisticated drug delivery formulations. Lai discussed a particular kind of polymeric system that is crucial for drug delivery: hydrogels, which are made up of cross-linked hydrophilic polymers that can expand and absorb a lot of water. In particular, the paper explains the hydrogel's self-healing characteristic, which allows it to mend physical harm caused by physiological circumstances when the damage stems from its low mechanical strength. In turn, self-healing may lessen the possibility of the medication put into the hydrogel releasing uncontrollably. The most recent developments in the creation of self-healing hydrogels are reviewed by the author. Hiew et al. assessed the drug crystallization propensity and associated drug and polymer release rates in lumefantrine amorphous solid dispersions (ASDs) made with various polymers. In contrast to ASDs with better drug-polymer connections, the scientists discovered that ASDs with lower drug-polymer contacts exhibited excellent release but poor stability against crystallization. ASDs were also examined by Yang et al., who concentrated on the creation of drug-rich nanodroplets upon release. In contrast to ASDs containing high glass transition temperature medications, they discovered that low glass transition temperature pharmaceuticals, when manufactured as an ASD, produced a greater nanodroplet yield during release trials.

Reference

We conclude our examination of popular subjects with machine learning, which is now receiving a lot of attention. Lai et al. used machine learning to assist identify the molecular characteristics that contribute to certain therapeutic antibodies' high solution viscosity. By combining machine learning with molecular modeling

Through feature selection, the scientists found that the monoclonal antibody's net charge and the amino acid composition of the Fv region are important factors that determine the viscosity behavior. Miljković

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and colleagues used machine learning to predict human pharmacokinetics (PK). They created machine learning algorithms to forecast specific PK end points based only on chemical structure data and dosage. The model was constructed utilizing over 1000 distinct medications' worth of publically accessible human PK data. The authors deduced from the results that their machine learning models are probably helpful in drug discovery and might be used to impact choices made in drug development initiatives and the advancement of therapeutic candidates. Kudos to each and every author of a highly referenced publication in 2023. We're excited to see how popular subjects in pharmaceutical research develop in the future.