Nanotechnology Used in Drug Delivery System.

Qirong Chen *

ShengHua ZiZhu Academy, ShangHai 200000, China

* Corresponding Author Email: 20210170@ntit.edu.cn

Abstract. This paper mainly focuses on exploring the connection between nanotechnology and drug delivery systems, and how these two can be combined to promote a better response. Nanomaterials are one of the most popular topics nowadays, and drug delivery systems with the help of nanomaterials will have many benefits and drawbacks. Through research, it is hopeful to address these issues to build up a safer drug delivery system. With the development of the biopharmaceutical industry and the rapid iteration of innovative drugs, the problem of insufficient utilization of drug components in the human body has always existed. Nanocarriers help drug molecules enter the body and be transported to the targeted sites in an accurate manner at the right time, improving the efficiency of drug utilization in the human body. To load drugs onto drug carriers, a series of emerging nanotechnology systems are needed. Nano drug delivery systems can increase drug solubility, alter drug distribution within the body, and improve drug targeting, thereby improving treatment efficacy and reducing the incidence of adverse reactions.

Keywords: Nanotechnology, drug delivery system, medication.

1. Introduction

Utilizing individual atoms and molecules to create materials is known as nanotechnology. The study of materials with structural sizes ranging from one nanometer to one hundred nanometers is known as nanotechnology [1]. Nanomaterials are materials with unique characteristics that differ from both macroscopic things and the initial atoms and molecules. Strong coherence induces tremendous self-organization in it, causing its characteristics to vary significantly as its size approaches the coherence length of electrons. Its scale is also about equal to that of the wavelength of light, and because of its unique effects on big surfaces, its properties—such as optics, thermal conductivity, conductivity, magnetism, and melting point—frequently differ from those of the substance in its entirety. The creation of novel materials, basic theoretical research, and application research in nanotechnology have all advanced quickly and are now widely used in a variety of industries, including coatings, medical equipment, electrical devices, and traditional materials. In addition to being successfully created, industrialized production of nano ceramic, nano textile, nano modified coatings, and other materials commonly utilized in nano powder has first been accomplished. The transition from experimental research findings to industrial production is being sped up by the use of nanopowder particles in medical diagnostic agents and microelectronics [2]. The medication delivery system and the employment of nanomaterials in it are the primary subjects of this essay.

2. Drug delivery

Traditional drugs cannot precisely act on diseased cells, tissues, and other locations, resulting in low efficiency and toxic side effects [3]. A technical system that completely controls the distribution of pharmaceuticals throughout the body in terms of time, space, and dosage is referred to as a drug delivery system. Its objective is to increase drug utilization efficiency, improve efficacy, lower costs, and lessen hazardous side effects by delivering the right amount of medication at the right time to the right place. Drug delivery also involves many types, including beauty products, and electronic products, and the types are not unique. Small molecule medications dominated the therapeutic market decades ago, but over time, new therapeutic approaches such as proteins and peptides, monoclonal antibodies, nucleic acids, and live cell therapies have emerged and fulfilled new therapeutic roles [4]. Drug delivery typically utilizes principles related to drug preparation, administration routes, site

targeting specificity, metabolism, and toxicity to optimize drug efficacy and safety, thereby improving patient convenience and compliance. The delivery of therapeutic drugs also requires processing, and strategies can be roughly divided into three types: drug modification, microenvironment modification, and drug delivery systems. Of course, both strategies must improve efficacy without compromising safety [3].

2.1. Drug modification

The purpose of drug modification is to regulate the interactions between drugs and molecules, cells, and tissues in the body, as well as between drugs and their target sites, so as to control the delivery of drugs in the body to a certain extent and achieve their expected functions. Drug modification can be used to improve the delivery of all types of treatments. The modification of drugs includes chemical changes to their structure and conjugation to known parts or targeted ligands.

For small molecules, their physicochemical properties can be regulated by introducing known molecular entities or directly altering the chemical structure of the molecule itself. Polyethylene glycol (PEG) modification can enhance the immunogenicity and duration of medication circulation for peptide and protein medicines. The development of small molecule and antibody drug modification technologies also benefits antibody drug conjugates (ADCs) [5]. The main goals of modifying live cell therapy are to introduce foreign stimuli to cells in vitro to encourage phenotypic differentiation or immune cell presentation, modify cell surfaces with conjugated drugs to enhance therapeutic effects or change cell function entirely [5].

2.2. Microenvironment regulation

Microenvironment modification is a widely used drug delivery strategy. On the one hand, microenvironment regulators can enhance the solubility of small molecules, biological agents, and nucleic acid drugs in body fluids by changing local pH values. On the other hand, microenvironment modulators can also be used to alter the process of drug action and improve its efficacy in diseased tissues [6].

2.3. Drug delivery system

Drug delivery systems refer to drug formulations, such as tablets, capsules, ointments, and solutions. Currently, most formulations can control drug release over time, known as controlled-release drug delivery systems. These systems comprise microparticles and nanoparticles, as well as hydrogels and polymer implants based on four controlled release processes (dissolution, diffusion, permeation, and ion exchange). The primary benefit of drug delivery systems is the physical shielding of medications from harmful environmental factors. The drug delivery system can integrate drug modification and environmental modification for application. The commonly used drug delivery carriers currently include artificial carriers and natural carriers [3].

Artificial carriers, such as liposomes, polymer carriers, micelles, and other nanoparticles, can be used for diverse biomedical applications. They can be controlled by adding surface modifications (including hydrophilic polymers, targeting parts, etc.), including stimulus responsive functions, or modifying their physical parameters. Natural carriers include extracellular vesicles, viral carriers, and common cellular drug delivery carriers such as red blood cells, immune cells, stem cells, and tumor cells.

3. Nanotechnology in drug delivery system

Nanodrug technology is a popular emerging technology in drug formulation technology in recent years. Nanotechnology can be used to build medication delivery systems that not only reduce hazardous side effects but also enhance the solubility, stability, and tumor targeting of pharmaceuticals. The characterization of drug delivery systems (DDS) is an important aspect of new drug development, reflecting the characteristics of DDS. Nucleic acid drugs are expected to become

the third generation of the biotechnology industry after antibody drugs, and messenger RNA (mRNA), as a part of nucleic acid drugs, is a classic application of the central principles of biology. For mRNA vaccines, one of the main obstacles is the delivery method. On the surface of the cell membrane, mRNA chains, a kind of single-stranded ribonucleic acid that contains genetic information and can direct the synthesis of proteins, are negatively charged. It is challenging for mRNA molecules to cross the cell membrane and enter the cell due to electrostatic repulsion. As a single-stranded structure, many enzymes can rapidly degrade mRNA, making mRNA delivery technology particularly crucial, requiring a balance between packaging efficiency, delivery efficiency, endosome escape, toxic side effects, stability, and a series of other aspects [7].

The adeno-associated virus (AAV) vector technology is currently one of the focuses of attention in the industry. AAV is a single-stranded DNA virus that is encapsulated in a small icosahedral symmetrical protein shell with 60 subunits. Currently, no wild-type AAV virus has been found to be pathogenic to humans. As a powerful tool for delivering gene therapy, the direct delivery efficiency of AAV vectors in vivo is very good, making them the preferred carrier for in vivo gene therapy. Some AAV vectors can also pass through the blood-brain barrier after intravenous injection, making the therapeutic effect of drugs for central nervous system diseases better. However, the development of AAV vector platforms still needs to overcome multiple challenges, such as how to turn "good viruses" into "better viruses", and how to generate a sufficient number of therapeutic AAV vectors economically and effectively. However, measuring the empty shell rate is not only a difficulty in the commercial production of AAV but also a difficulty in pharmaceutical research. Overcoming these challenges is of crucial significance for promoting AAV-mediated gene therapy. At the same time, the engineering modification of AAV capsid structure is also an important factor in the success of AAV-based vaccines and gene therapy [8].

3.1. Benefit of nanotechnology

The benefits of nanocarriers include their small size, high specific surface area, facile modification, and adjustable shape. Chemotherapy medications can create high local concentrations in the carrier due to their ability to efficiently embed, adsorb, or covalently crosslink hydrophilic/hydrophobic drug molecules. In addition, nanomaterial drug carriers can provide a stable and hidden storage space for drug molecules, effectively avoiding drug degradation and inactivation under the influence of the human physiological environment during drug delivery. Tumor treatment is more effective when anti-cancer drug concentrations are increased at the lesion site, dosages are decreased, and the likelihood of drug-resistant cells growing is decreased. All these factors help to sustain the drug's activity. At the same time, the same nano drug carrier can load two or more drugs, achieving the goal of synergistic and efficient treatment [9].

By using active or passive targeting, nanodrug carriers can provide targeted therapy. In addition to having specific size effects, nano drug delivery devices can be functionalized to increase drug treatment efficacy, decrease harmful side effects on healthy tissues and cells, and achieve targeted aggregation at the lesion site. Targeted delivery of nano drug delivery systems includes two methods: passive targeting and active targeting, Passive targeting refers to the process in which the nano delivery system preferentially enriches into the lesion tissue through tissue; Active targeting refers to the nano delivery system that couples specific ligands or antibody components to bind to cell surface specific receptors, thereby achieving accumulation in targeted tissues. The foundation for creating tailored medications with clever recognition sites is provided by this data. Currently, molecules and fragments of antibodies are frequently utilized in targeting components. The natural properties and biological functions of the outer cell membrane have been successfully retained by recently created biomimetic nanocarriers that encapsulate cell membranes, making them a useful targeted therapeutic approach. Adhesion molecules, like integrins and adhesive spot proteins, are present on the surface of cancer cell membranes and provide them with homologous recognition and homing capabilities. As a result, to improve the targeting and endocytosis capabilities of nanocarriers, cancer cell membranes are frequently employed as shells to encircle the surface of nanoparticles.

Before reaching their target site, drug molecules must cross a number of physiological barriers, including the blood, tissue, cell, and intracellular transport barriers. For instance, the endothelial cells of blood vessels and the reticular cells of organs like the liver and spleen can use pseudopodia to phagocytose foreign substances in the body once the nanomedicine delivery system has been injected intravenously into the circulation. These highly phagocytic cells are collectively referred to as the mononuclear phagocytic cell system, also known as the reticuloendothelial system. Numerous studies have shown that modifying the surface characteristics of nanoparticles, such as polyethylene glycol modification, constructing biomimetic delivery systems, and using live cells as drug carriers, can produce "invisible" nanoparticles that hinder the phagocytosis of the RES system, overcoming this barrier. When drugs enter tissues, they need to cross the plasma membrane and reach the intracellular site of action. During this process, biopolymer drugs generally cannot penetrate the cell membrane through osmotic action. T Since nanomedicine carriers are typically much smaller than cells and other organelles—between 10 and 1000 nm—than proteins, nucleic acids, and other biopolymers, it is easier to transport different biological macromolecules or medications into cells and organelles. When nanocarriers enter diseased tissue cells through endocytic pathways, endosomes/lysosomes are the main barrier for intracellular delivery. For drugs targeting the nucleus, the acidic environment in endosomes/lysosomes and the presence of multiple enzymes can easily cause drug degradation or inactivation. Functional modification of nanocarriers is necessary, the disruption, destabilization, or membrane fusion of lysosomal membranes through proton sponge effects can achieve the escape of endosomes/lysosomes from carriers and drugs [10].

The basic physical effects of nanoparticles, such as quantum effects, small size effects, and surface effects, endow nanocarriers with unique characteristics such as photothermal and magnetic properties, making them suitable as disease diagnostic probes. On the other hand, the high surface energy and surface reactivity of nanomaterials enable them to serve as drug-controlled release carriers while also integrating multiple functionalities.

3.2. Disadvantage of nanotechnology

The toxicity of nanomaterials is a major bottleneck. The US Food and Drug Administration (FDA) is the most authoritative institution in reviewing nanomedicines, and most nanomedicines it approves are liposomes. However, many materials such as magnetic beads and gold nanoparticles are only allowed for use in vitro diagnostic products and not in the human body. According to research reports, 98% of the nanoparticles injected into the mouse body will be eaten by mononuclear phagocytes in the liver and spleen, and only 2% of the nanoparticles will deposit at the tumor site. High doses of nanoparticles in organs can cause serious biological toxicity [11].

Due to the high specific surface area and small size of nanomaterials increasing their contact area with the cell membrane, the cell membrane may be chemically or physically damaged. In addition, how nanomaterials interact with cell membranes may be influenced by their surface charge, hydrophobicity, and hydrophilicity.

Cells may absorb nanomaterials and allow them to penetrate the interior of the cells. High concentrations of nanomaterials can increase the production of harmful oxygen radicals and other reactive oxygen species in cells, causing oxidative damage to various biomolecules including membrane lipids, proteins, and nucleic acids [11].

Another possible explanation for the risk of genetic mutations and harmful effects on DNA is the interaction between DNA molecules and nanoparticles. DNA nanomaterial composites are generated when nanomaterials are mixed with DNA. These complexes can cause genetic mutations and DNA changes, thereby disrupting or even killing the growth and development ability of organisms [12].

The accumulation and migration of nanoparticles are also part of the toxic process. Certain nanoparticles are clearly ineffective for living organisms as they accumulate within the body. The accumulation of the body can lead to structural problems in tissues or organs. Nanomaterials may be used as drug carriers with unique transport properties, but they also have the ability to enter the human body through transport channels and have negative effects.

In addition, the initiation of inflammatory reactions in the body is a component of the toxicity mechanism of nanomaterials. Many nanoparticles have the ability to stimulate immune cells, allowing them to release pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), I-1, and sub-6. In order to control and eradicate intracellular pathogens, promoter cytokines generally govern the development, activation, differentiation, and nesting of immune cells toward the site of infection. This can cause inflammation in organ tissues, making them unable to function properly [11].

4. Conclusion

This article mainly discusses the application of nanotechnology in drug delivery systems, explores the advantages and disadvantages of nanomaterials, and how to apply them to drug delivery systems. The current research has not effectively addressed the shortcomings mentioned in the article, as the properties of nanomaterials may cause harm to humans. Future research can continue to expand and improve on these shortcomings. These shortcomings are mainly due to the characteristics of nanomaterials themselves, and the small size of nanomaterials makes them more difficult to study and control than normal materials. Of course, this small size will also help the drug delivery system to function more accurately. And this will also help drug delivery systems to be more effective in our daily lives, and it will also help us to be simpler and more effective in treatments such as cancer.

References

[1] Baig N., et al. Nanomaterials: a review of synthesis methods, properties, recent progress, and challenges. Materials Advances, 2021, 2(6): 1821-1871.

[2] Yan T, et al. Application of composite nano-bone transplantation and massage exercise rehabilitation training in patients undergoing limb replantation. Adv Mater Sci Eng, 2022.

[3] Vargason AM, et al. The evolution of commercial drug delivery technologies. Nat Biomed Eng., 2021, 5(9): 951-96.

[4] Tiwari G, et al. Drug delivery systems: an updated review. Int J Pharm Investig, 2012, 2(1):2-11.

[5] Anselmo AC, et al. Cell-mediated delivery of nanoparticles: taking advantage of circulatory cells to target nanoparticles. J Control Release, 2014, 190:531-41.

[6] Park H, et al. Evolution of drug delivery systems: From 1950 to 2020 and beyond. J Control Release, 2022, 342: 53-65.

[7] Amy D Shapiro, et al. First-in-human phase 1/2 clinical trial of SIG-001, an innovative shielded cell therapy platform, for Hemophilia A. Blood, 2020, 136: 8.

[8] Herrmann IK, et al. Fuhrmann G. Extracellular vesicles as a next-generation drug delivery platform. Nat Nanotechnol., 2021, 16(7): 748-759.

[9] Shum T, et al. Constitutive signaling from an engineered IL7 receptor promotes durable tumor elimination by tumor-redirected T Cells. Cancer Discov., 2017, 7(11): 1238-1247.

[10] Teleanu D.M., et al. Nanomaterials for drug delivery to the central nervous system. Nanomaterials, 2019, 9(3): 371.

[11] Singh D., Gurjar B.R. Nanotechnology for agricultural applications: facts, issues, knowledge gaps, and challenges in environmental risk assessment. Journal of Environmental Management, 2022, 322: 116033.

[12] Khezri S., et al. Application of nanotechnology in the food industry and related health concern challenges. International Journal of Advanced Biotechnology and Research, 2016, 7: 1370-1382.