Multifunctional Nanocomposites for Efficient Gene Delivery

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Abstract. With the continuous development of gene therapy technology, an efficient gene delivery system has become the key to realizing gene therapy. Traditional gene delivery methods have many limitations, such as low transfection efficiency and high cytotoxicity. As a new type of gene delivery vector, multifunctional nanocomposites have shown great application potential due to their unique physical and chemical properties and biocompatibility. This paper aims to study the application of multifunctional nanocomposites in gene delivery through the analysis of relevant cases and the discussion of their mechanism of action to understand their advantages and challenges in gene therapy deeply. The results show that the multifunctional nanocomposites can effectively improve gene transfection efficiency, reduce cytotoxicity, and achieve targeted gene delivery. In addition, its application in the treatment of different diseases has been explored. The research significance of this paper is to provide a theoretical basis and practical guidance for the further development of multifunctional nanocomposites in the field of gene therapy and promote the clinical application of gene therapy technology.

Keywords: Multifunctional nanocomposites, Gene delivery, Gene therapy, Nano-carrier, Biocompatibility.

1. Introduction

Gene therapy is a new technology to treat diseases by introducing normal genes or modifying abnormal genes, which has broad application prospects [1]. However, there are many challenges in the process of gene delivery, such as low transfection efficiency, poor stability in vivo, insufficient targeting, and possible immune response. Traditional gene delivery vectors include viral vectors and non-viral vectors. Although the transfection efficiency of viral vectors is high, there are potential safety risks, such as immunogenicity and carcinogenicity [2]. Non-viral vectors such as liposomes and polymers are relatively safe, but the transfection efficiency is often low [3].

The development of nanotechnology provides new ideas and methods for gene transmission. Because of their unique size effect, surface effect, and quantum size effect, nanomaterials have shown unique advantages in the field of gene delivery. Multifunctional nanocomposites integrate multiple functions into nanomaterials to better meet the needs of gene delivery. For example, surface modification of nanomaterials can improve their biocompatibility, targeting, and gene loading capacity [4]. In foreign countries, many research teams are committed to the research and development of multifunctional nanocomposites and their applications in gene delivery. For example, some studies have prepared targeted gene delivery vectors by combining gold nanoparticles with nucleic acid aptamers to achieve gene transfection of specific cells [5]. In addition, magnetic nanoparticles were combined with polymers to prepare a gene delivery system that could respond to external magnetic fields, thus improving the efficiency of gene delivery in vivo [6]. In China, relevant research has also made some progress. Through surface modification and functionalization of nanomaterials, researchers have prepared a series of multifunctional nanocomposites with good biocompatibility and gene transfection efficiency [7]. For example, the gene delivery vector prepared by using natural polymer materials such as chitosan combined with nanomaterials showed high transfection efficiency and low cytotoxicity in both in vivo and in vitro experiments [8].

Since there are still many shortcomings in the existing gene delivery systems, multifunctional nanocomposites have great potential for development as new gene delivery carriers. The aim of this paper is that through the study of multifunctional nanocomposite materials, gene transfection efficiency can be further improved, cytotoxicity can be reduced, gene precision delivery can be achieved, and more effective means can be provided for the clinical application of gene therapy.

This paper describes the preparation method, physicochemical properties and biocompatibility of multifunctional nanocomposites. Based on the multifunctional nanocomposites in gene delivery, it analyzes its mechanism of action and application effects and the advantages and challenges of multifunctional nanocomposites in gene delivery, compares with other gene delivery vectors, and puts forward corresponding suggestions and measures.

2. Overview and Application of Multi functional Nanocomposite Materials

2.1. Preparation Method of Multifunctional Nanocomposites

2.1.1 Physical methods

Physical methods include mechanical grinding, ultrasonic treatment, etc. Mechanical grinding can mix different materials to produce nanocomposites. Ultrasonic treatment can promote the interaction between materials through the cavitation effect of ultrasound to form nanocomposites. For example, by mixing gold nanoparticles with polymers through ultrasonic treatment, nanocomposites with good dispersion can be prepared [9].

2.1.2 Chemical methods

Chemical methods include the sol-gel method and chemical precipitation method, etc. The sol-gel method is to hydrolyze and condense metal salts or organic precursors in solution to form sol, and then further convert to gel, and finally prepare nanocomposites. The method of chemical precipitation is to precipitate metal ions or other substances to form nanoparticles by adding precipitating agents to the solution and then composite with other materials to prepare nanocomposites [10].

2.1.3 Biological method

Biological method utilizes the interaction of biomolecules such as proteins, nucleic acids, and nanomaterials, multifunctional nanocomposites are prepared. For example, using the self-assembly properties of proteins, nanomaterials are wrapped inside proteins to form bioactive nanocomposites [11].

2.2. Physicochemical Properties of Multifunctional Nanocomposites

The size of multifunctional nanocomposites is usually at the nanometer level and form can be spherical, rod-like, sheet, etc. Different sizes and forms will affect its distribution in the body, cellular uptake, and gene delivery efficiency. For example, nanocomposites with smaller sizes are more easily taken up by cells, while nanocomposites with specific forms may have better targeting [12]. The surface properties of nanocomposites have important effects on their biocompatibility, stability, and gene loading capacity. The surface charge, hydrophilicity, and other properties of nanocomposites can be changed by modifying the surface. For example, nanocomposites with a positive surface charge are more likely to bind to negatively charged nucleic acids, thereby improving gene-carrying capacity [13]. Some multifunctional nanocomposites have unique optical and electrical properties, such as the surface plasmon resonance effect of gold nanoparticles and the electrical conductivity of carbon nanotubes, which can be used to monitor and regulate during gene delivery [14].

2.3. Biocompatibility of Multifunctional Nanocomposites

Biocompatibility is one of the key factors for applying multifunctional nanocomposites in gene delivery. Good biocompatibility can reduce the immune response and cytotoxicity caused by nanocomposites in vivo. The results show that the biocompatibility of nanocomposites can be improved by surface modification and functionalization [15]. For example, modifying hydrophilic polymers such as polyethylene glycol (PEG) on the surface of nanocomposites can reduce their chances of being recognized and cleared by the immune system while reducing toxicity to cells [15].

3. The Application Market of Multifunctional Nanocomposites in Gene Delivery and Function in Different Directions

3.1. Tumor Gene Therapy Market

3.1.1 Targeted gene delivery

In the field of tumor gene therapy, the targeted gene delivery function of multifunctional nanocomposites has great market potential. The nanocomposites can specifically recognize and bind to the receptors on the surface of tumor cells to achieve targeted gene delivery by modifying tumor-specific targeting molecules. For example, nano-composite materials modified with anti-HER2 antibodies can specifically recognize and bind to the surface of HER2-positive breast cancer cells, accurately deliver therapeutic genes to tumor cells, and improve the effect of gene therapy while reducing the damage to normal cells [16]. This targeted gene delivery technology can provide a more effective means for tumor treatment, reduce the side effects of traditional chemotherapy and radiotherapy, and has broad market prospects.

Because of their good biocompatibility and optical properties, gold nanoparticles have a wide range of applications in gene delivery. A research team modified a nucleic acid aptamer on the surface of gold nanoparticles to prepare a targeted gene delivery vector [17]. Aptamers can specifically recognize markers on the surface of tumor cells to achieve targeted gene delivery to tumor cells [17]. In experiments, a nanoparticle gold-nucleic acid aptamer complex carrying therapeutic genes was transfected into tumor cells, and the results showed that the complex was effective in introducing genes into tumor cells and was less toxic to normal cells [17]. Through gene regulation of tumor cells, the growth and proliferation of tumor cells are inhibited, providing a new strategy for tumor gene therapy [17].

Magnetic nanoparticles have unique magnetic responsiveness, and by combining with polymers, a composite system with good biocompatibility and gene transfection ability can be prepared. In one study, a complex of magnetic nanoparticles with chitosan was prepared and guided to a specific cell or tissue site by the action of an external magnetic field [18]. The experimental results showed that under the action of the magnetic field, the composite system of magnetic nanoparticles and polymers could significantly improve the gene transfection efficiency and achieve the directed gene delivery [18]. This composite system has potential application value in the fields of gene therapy and tissue engineering [18].

3.1.2 Combined treatment

Multifunctional nanocomposites can also be used in combination therapy of tumors. Combining gene therapy with other treatment methods (such as chemotherapy, radiotherapy, photothermal therapy, etc.) can play a synergistic role in improving the effectiveness of tumor treatment. For example, a nanocomposite material loaded with chemotherapy drugs and therapeutic genes at the same time is prepared, which releases chemotherapy drugs while delivering genes to tumor cells and realizes the combination of gene therapy and chemotherapy. In addition, some nanocomposites also have photothermal conversion properties, such as gold nanorods, which can generate heat under near-infrared light for photothermal treatment of tumors [19]. The combination of photothermal therapy and gene therapy can further improve the effect of tumor treatment and open up new ways for tumor treatment [19].

3.2. Genetic Disease Treatment Market

3.2.1 Gene repair and replacement

For genetic diseases, multifunctional nanocomposites can be used for gene repair and replacement. Repair or replacement of mutated genes is achieved by wrapping normal gene fragments or gene editing tools (such as the CRISPR/Cas9 system) in nanocomposites and delivering them to the patient's cells. For example, in the treatment of sickle cell anemia, nanocomposites can be used to deliver the normal hemoglobin gene into the patient's hematopoietic stem cells, repair the mutated gene, and thus restore normal hemoglobin synthesis and treat the disease [20]. This gene repair and replacement technology has brought new hope for the treatment of genetic diseases and has important clinical significance and market value.

3.2.2 Gene control

Multifunctional nanocomposites can also be used to regulate gene expression and treat some genetic diseases associated with abnormal gene expression. By loading gene regulatory elements (such as small interfering RNA, micrRNA s, etc.) in nanocomposites, they are delivered to cells to regulate the expression level of related genes. For example, in the treatment of some neurodegenerative diseases, nano-composite materials can be used to deliver small interfering RNA into nerve cells, inhibit the expression of pathogenic genes, and delay the progression of diseases [21].

3.3. Cardiovascular Disease Treatment Market

3.3.1 Gene transfer related to angiogenesis

In the treatment of cardiovascular diseases, vascular regeneration is an important research direction. Multifunctional nanocomposites can be used to deliver genes associated with vascular regeneration, such as vascular endothelial growth factor (VEGF) genes. By loading the VEGF gene in the nanocomposite material, it can be accurately delivered to the ischemic tissue site to promote the proliferation and migration of vascular endothelial cells to achieve vascular regeneration. For example, nanocomposites prepared by using cationic liposomes combined with polymers can effectively wrap VEGF genes and release them in the body [22]. Studies have shown that this nanocomposite material can significantly promote the angiogenesis of ischemic myocardial tissue and improve cardiac function in animal models of myocardial infarction [22]. This method of vascular regeneration gene therapy based on nanocomposite materials provides a new strategy for the treatment of cardiovascular diseases, which is expected to be widely used in clinical practice and has great market potential.

3.3.2 Antithrombotic gene therapy

Thrombosis is one of the common complications of cardiovascular diseases, which seriously threatens the life and health of patients. Multifunctional nanocomposites can be used for anti-thrombotic gene therapy. For example, anti-platelet aggregation-related genes (such as tissue-type plasminogen activator (t-PA) gene) were loaded in nanocomposites and delivered to vascular endothelial cells or platelets to regulate the expression of related genes and inhibit platelet aggregation and thrombosis. Some studies have prepared nano-composite materials with surface modification of antibodies targeting vascular endothelial cells, which can specifically deliver the t-PA gene to vascular endothelial cells, enhance local fibrinolytic activity, and prevent thrombosis [23]. This anti-thrombotic gene therapy method has the advantages of strong pertinence and small side effects and has broad application prospects in the cardiovascular disease treatment market.

3.4. Neurological Disease Treatment Market

3.4.1 Neuroprotective gene delivery

Neurological diseases, such as Parkinson's disease and Alzheimer's disease, are often accompanied by nerve cell damage and death. Multifunctional nanocomposites can be used to deliver neuroprotection-related genes, such as brain-derived neurotrophic factor (BDNF) genes. By wrapping the BDNF gene in a nanocomposite material, it is delivered across the blood-brain barrier to the damaged nerve tissue to promote the survival and repair of nerve cells. Some studies have used nanocomposites prepared by mixing nanoliposomes with polymers, which can effectively protect BDNF genes from degradation and successfully deliver them to the brain [24]. Experimental results show that this nanocomposite material can significantly improve nerve function and reduce the apoptosis of nerve cells in animal models of Parkinson's disease [24]. This neuroprotective gene therapy method based on nanocomposite materials provides new hope for the treatment of neurological diseases and has important potential value in the neurological disease treatment market.

3.4.2 Gene transmission related to nerve regeneration

For diseases that are damaging to the nervous system, such as spinal cord injury, promoting nerve regeneration is the key to treatment. Multifunctional nanocomposites can be used to deliver nerve regeneration-related genes, such as nerve growth factor (NGF) genes. The NGF gene was loaded into nanocomposites with good biocompatibility and degradability and implanted into the injured spinal cord to promote the growth and regeneration of nerve axons. Some studies have prepared chitosan-based nanocomposites, which can effectively wrap NGF genes and release them slowly in the body [25]. In animal models of spinal cord injury, this nanocomposite material can promote the proliferation and differentiation of nerve cells, accelerate nerve regeneration, and improve limb motor function [25]. This method of gene transmission related to nerve regeneration provides a new way for the treatment of nervous system injury diseases and has broad development space in the nervous system disease treatment market.

4. Advantages of Multifunctional Nanocomposites in Gene Delivery

The primary advantage is high gene transfection efficiency. Multifunctional nanocomposites can be used to efficiently load and deliver genes through surface modification and functionalization. For example, the modification of nanomaterials with cationic polymers can enhance their ability to bind to nucleic acids, thereby improving gene transfection efficiency. In addition, some nanocomposites can achieve targeted transfection of specific cells through specific binding to receptors on the cell surface, further improving the efficiency of gene transfection [4]. Secondly, it has low cytotoxicity. Compared with traditional gene delivery vectors, multifunctional nanocomposites usually have lower cytotoxicity. By selecting suitable materials and surface modification methods, the damage of nanocomposites to cells can be reduced. For example, nanocomposites prepared using natural polymer materials such as chitosan have good biocompatibility and low cytotoxicity [8]. The third is the nature of regulation. The physical and chemical properties of multifunctional nanocomposites can be controlled by preparation methods and surface modification. For example, the distribution in the body, cell uptake, and gene delivery efficiency of nanocomposites can be regulated by changing their properties, such as size, shape, and surface charge. In addition, multiple functions can be integrated into nanocomposites, such as targeting and imaging functions, so that it has a wider application prospect in gene therapy [4]. In addition, compared with viral vectors, multifunctional nanocomposites have the following advantages: high safety, no potential risks such as immunogenicity and carcinogenicity of viral vectors; The preparation is relatively simple, and the cost is low. It can be functionalized to realize the integration of multiple functions. However, the transfection efficiency of viral vectors is usually high, which is an aspect that multi-functional nanocomposites need to be further improved [2]. Compared with traditional non-viral vectors such as liposomes and polymers, multifunctional nanocomposites have more unique physical and chemical properties and biocompatibility. For example, the size effects and surface effects of nanomaterials enable them to interact better with cells and improve gene transfection efficiency. In addition, multi-functional nanocomposites can also achieve targeting and other functions through surface modification, while traditional non-viral vectors are relatively weak in this respect [4].

5. Challenges in Gene Delivery of Multifunctional Nanocomposites

Firstly, multifunctional nanocomposites may be affected by various factors in the environment, such as protein adsorption, enzyme degradation, etc., thus affecting their stability and gene delivery efficiency. Therefore, it is necessary to further study how to improve the stability of nanocomposites in vivo, such as through surface modification and packaging [12]. Secondly, although multifunctional nanocomposites have shown low cytotoxicity and immune response in short-term experiments, long-term use may cause potential harm to organisms. For example, the accumulation of nanomaterials in the body may lead to tissue damage and organ dysfunction. Therefore, long-term safety evaluation is needed to ensure its safe use in gene therapy [1]. However, most of the current preparation methods for multifunctional nanocomposites are still in the laboratory research stage, and it is difficult to achieve large-scale preparation. This limits its use in clinical applications. Therefore, it is necessary to develop more simple and efficient large-scale preparation methods to meet clinical needs [4].

6. Suggestion for Multifunctional Nanocomposites

The first step is to improve the quality and stability of multifunctional nanocomposites by improving the preparation process and realizing large-scale preparation. For example, develop greener and more environmentally friendly preparation methods to reduce the impact on the environment. Secondly, through in vivo and in vitro experiments, in-depth research on the mechanism of multifunctional nanocomposites in the process of gene delivery is conducted to provide a theoretical basis for their optimization and improvement. For example, to study the interaction mechanism between nanocomposites and cells, as well as the distribution and metabolic process in vivo. Then long-term safety assessment is needed, including the accumulation, toxicity and immune response of nanocomposites in the body, while a perfect safety evaluation system is established to ensure their safe application in gene therapy. In addition, the combination of basic research and clinical application needs to be strengthened, and the clinical trials of multifunctional nanocomposites in gene therapy need to be actively carried out to promote their clinical transformation. Cooperation with pharmaceutical companies and medical institutions can accelerate its application in clinical treatment.

7. Conclusion

With its unique design and properties, multifunctional nanocomposites have shown great advantages and potential in the field of gene delivery. It was found that the multifunctional nanocomposite can effectively load genes, achieve precise cell recognition with targeted ligands, significantly improve transfection efficiency and reduce cytotoxicity. This study is of great significance for promoting the development of gene therapy technology. On one hand, it provides a safer and more efficient carrier for gene therapy, which helps to improve the effect of gene therapy and brings new hope for overcoming major diseases such as cancer and nervous system diseases. On the other hand, through the study of multifunctional nanocomposites, the understanding of the interaction between nanomaterials and biological systems has been deepened, which provides theoretical support and practical experience for the development of nanobiotechnology.

Although multi-functional nanocomposites have achieved some results in efficient gene delivery, there are some limitations in this study. For instance, during the research process, the long-term effects of nanocomposites in vivo have not been studied deeply enough, and the potential risks they may produce in vivo need to be further evaluated. In addition, due to the limitations of experimental conditions and techniques, more research is needed on the performance of nanocomposites in some complex physiological environments.

In the future, with the continuous development of multi-disciplines such as nanotechnology and biotechnology, multi-functional nanocomposites are expected to make greater breakthroughs in the field of efficient gene delivery. Important progress is expected in the following areas. First, the continuous discovery and application of new nanomaterials and functional molecules will provide more options and possibilities for the design of multifunctional nanocomposites and further improve their performance. Second, with the in-depth understanding of the complex environment and gene delivery mechanism in organisms, more intelligent and efficient nanocomposite materials can be designed to achieve more accurate gene delivery. Third, in terms of clinical transformation, through strengthening cooperation with the medical field, carrying out more clinical trials, promoting the practical application of multi-functional nanocomposite materials in gene therapy, and making greater contributions to the cause of human health.

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