Application of Cell Membrane-Coated Nanoparticles in the Medical Field

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Abstract. Since the advent of nanotechnology, nanomaterials have found extensive application in the medical industry. The application of nanoparticles is currently constrained by their low biosafety, limited blood circulation period, and poor targeting capacity. Cell membranes have been continually replicated and employed for encapsulation and camouflage of nanoparticles, to improve their biological features. Cell membranes serve as a window and interface for communication within the human body. Nanomedicine has recently advanced to a new level of development thanks to coating technology that completely grafts cell membranes onto the surface of nanoparticles. The nanoparticles' cover helps them adapt better to challenging physiological settings. They considerably improve their targeting capabilities and avoid immune system clearance through homologous recognition, broadening their spectrum of applications in drug transportation, biological detoxification, and other fields. This article mainly introduces the research progress of the emerging nanoprobe technology of cell membrane packages, as well as the preparation pathway of cell membrane wrapped nanoparticles and the analysis and research of the application value and development prospects in the med.

Keywords: Cell membrane, nanoparticles, cell membrane coating technology, medical field.

1. Introduction

In 1952, French scientist Dr. Paul Boudart produced platinum nanocrystals for the first time, ushering in the era of nanomaterials. Materials that have one or more dimensions in three dimensions that are between one and one hundred nanometers in size are referred to be nanomaterials. Compared to traditional materials, nanomaterials have unique advantages in strength, hardness, toughness, conductivity, thermal conductivity, and other properties. They also exhibit specific surface effects, tiny size effects, quantum size effects, and macroscopic quantum tunneling effects, according to studies on nanomaterials [1]. Nanomaterials offer exceptional physical and chemical characteristics because of their high surface activity, tiny size, and huge specific surface area. For example, nanomaterials have better strength, hardness, toughness, conductivity, and thermal conductivity than traditional materials. It can also be used in fields such as catalytic reactions, adsorption separation, and electrochemical sensing. Nanomaterials are now a hotbed for cutting-edge research in many areas, and they have a wide range of uses in the biomedical sector.

Due to the excellent controllability and plasticity of nanomaterials, their size, morphology, structure, and other characteristics can be controlled through controlling reaction conditions, additives, and other means during the preparation process, which can better meet the material requirements of different shapes, sizes, and characteristics required for various diseases and treatment processes. Its potential applications in the realm of biomedicine are unparalleled. Nanomaterials, on the other hand, have a greater specific surface area and smaller size, which may allow them to pass through cell membranes and reach the inside of cells, thus causing risks to the environment and human health. Following investigation, a novel technique known as the cell membrane encapsulation nanoparticle technology was discovered to address this issue. The idea is to wrap the cell membrane around nanoparticle surfaces using technology for cell membrane coating. The encased nanoparticles can more easily adapt to challenging physiological settings because of this layer of "camouflage". Through homologous recognition, they can not only avoid immune system clearance but also significantly enhance targeting properties. There are many areas where this technology has potential applications, including drug delivery, biological detoxification, immune regulation, and other areas [2]. This technology is anticipated to address the issue of the traditional nanoparticle modification's limited scope and advance the development of monotherapy as a monotherapy for several diseases. Therefore, this article introduces the technology for encapsulating nanoparticles in cell membranes, analyzes the preparation of relevant cell membranes and nanomaterials, and explores their applications in the field of biomedicine.

2. Cell membrane and nanoparticles

2.1. Cell membrane for encapsulating nanoparticles

The majority of the cell membrane is an elastic, semi-permeable phospholipid membrane with a thickness of 7-8nm. The outside of the membrane is in touch with the outside world in animal cells. Its primary duties include exchanging chemicals selectively, absorbing nutrients, eliminating metabolic waste, and secreting and transporting proteins. Cells, the most fundamental building block of life, rely on their outermost membrane, which is made up of proteins, lipids, and carbohydrates, to react to their surroundings and control the extracellular environment. There isn't any conclusive proof that the cell membrane can sometimes undertake some specialized tasks, including regulating the entry and departure of substances, in place of the live cells. The complete coverage of the function of the straight cell membrane on nanoparticles indicates that they can effectively evade immune clearance in the body, extend their circulation and service life in the body, and enhance the targeting effect of drugs. At present, there are various cell membranes or artificial fusion cell membranes being used for research on nanoparticle encapsulation and camouflage. Commonly used cell membranes include plasma membranes of red blood cell membranes, white blood cells, stem cells, cancer cells, platelets, and bacteria [3].

Animals typically have red blood cells, which are in charge of delivering oxygen and nutrients throughout the body. They have a 120-day lifetime on average when in blood circulation. For nanoparticles that require long-term work, the red blood cell membrane is an excellent encapsulation of the cell membrane. Moreover, immune-labeled molecules such as CD47 located on the surface of red blood cell membranes also have good biocompatibility and nonimmunogenicity, which are necessary specific conditions for the preparation of long-circulating nanoparticles. Due to the immune system's rejection and clearance effects being effectively avoided, nanoparticles can greatly prolong their blood circulation period and the potential damage caused by their powerful body penetration. Research has shown that there has been a breakthrough and progress in the research of nanovaccinenano vaccines made from polymer nanoparticles encapsulated in red blood cell membranes. Through experiments, it has been found that such nanovaccinenano vaccines stimulate specific immune responses and are expected to be applied in the immunotherapy of melanoma. Secondly, there is a significant breakthrough in targeted delivery of nanoparticles encapsulated in red blood cell membranes, which can effectively transport specific molecules to specific locations within the cell. For example, using red blood cell membranes to encapsulate monoclonal antibody nanoparticles against human telomerase reverse transcriptase effectively avoids macrophage phagocytosis and transports them to tumor areas for clearance and treatment of cancer cells.

2.2. Nanoparticles for cell membrane encapsulation

Due to the diverse shapes of nanoparticles, they are given many informal names, such as nanospheres, nanocapsules, nanorods, nanowhiskers, nanostars, nanoflowers, nanofibers, etc. Currently, most of them are referred to as nanospheres and nanocapsules. Nanospheres are drugs that are uniformly dispersed in a nucleated solid matrix or covalently connected to nanoparticles, while nanocapsules are drugs that are encapsulated in a cavity by a polymer film.

Commonly used nanoparticles include natural nanoparticles, polymer nanoparticles, and inorganic nanoparticles. The naturally formed nanoparticles include common types such as lipoproteins, viruses, and ferritin. There are many types of polymer nanoparticles, such as polylactic acid (PLGA), polylactic acid (PLA), chitosan, and gelatin. Inorganic nanoparticles mainly include gold, silicon, iron, copper, and their compounds, many of which are magnetic and photosensitive, and have potential value in imaging, photothermal therapy, and photodynamic therapy. These diverse and diverse types of nanoparticles have laid the foundation for the development of coated nanoparticles [4].

3. The principle of cell membrane encapsulation of nanoparticles

3.1. Culture of the cell membrane and preparation of nanoparticles

Firstly, collect the cells with the required cell membrane and create a culture medium suitable for the growth and reproduction of the cells. Then, separate the cells' cell membranes. For instance, the DMEM medium with 10% fetal bovine serum (FBS), 1% antibiotic antifungal solution, and a humidified incubator with 5% carbon dioxide is used to cultivate human ovarian cancer cell line OVCAR3 at a constant temperature and humidity. The commonly used separation methods currently involve cell lysis, mechanical destruction, and differential centrifugation to clear intracellular components. The commonly used preparation methods nowadays include ultrasonic fragmentation, centrifugation, dissolution, and membrane method. The preparation methods of nanoparticles mainly include physical methods, chemical methods, and physicochemical methods. The vacuum condensation method, physical crushing method, mechanical ball milling method, solid phase method, gas phase method, precipitation method, liquid phase method, electrolysis method, etc. are some of the most used preparation techniques. Commonly employed for preparation, the nanoprecipitation process may dissolve medicines and nanoparticles in acetone to accomplish encapsulation [5].

3.2. Preparation of cell membrane encapsulated nanoparticles

The extraction and preparation of the cell membrane, the synthesis of the nanoparticles, and the fusing of the cell membrane and the nanoparticles are the three main processes in the preparation of traditional cell membrane encapsulated nanoparticles. To verify that the cell membrane has been effectively coated on the surface of the nanoparticles, it is also required to evaluate the characterization of the cell membrane-encapsulated nanoparticles, such as physicochemical and biological features. During the coating process, attention needs to be paid to the integrity and stability of the cell membrane to ensure the effective transfer of its function. The size, surface charge, and protein makeup of nanoparticles all affect how well they encapsulate cell membranes. Cell membrane coating technology is the process of encasing cell membranes in nanoparticles. A method for coating and separating cell membranes on the surface of other materials is called cell membrane coating technology. These days, a wide range of applications for this technology exist, such as the creation of cell models, the study of cell signal transduction, and the study of interactions between cells and materials. At present, the commonly used cell membrane coating technologies mainly include mechanical separation, high-pressure spray, electrotransfer, and covalent crosslinking. Among them, the covalent crosslinking method is the most commonly used method, which can prepare highly stable and high-quality cell membrane coatings. In addition, with the development of nanotechnology, biomaterials, tissue engineering, and other fields, cell membrane coating technology is expected to be widely applied in fields such as medicine, biology, and materials science.

A variety of cell types, including red blood cells, platelets, white blood cells, cancer cells, stem cells, and bacteria, can now be employed in experiments and research as sources of cell membranes to encapsulate nanoparticles. The use of cell membrane-encapsulated nanoparticle technology in the medical industry is widespread. For instance, coating the membrane of a white blood cell on the surface of nanoparticles allows for the identification and targeted treatment of tumor cells [6], coating the membrane of a liver cell on the surface of a synthetic liver scaffold allows for the simulating and replacement of liver cells [7]. Taking the application in tumor treatment as an example, the research paper on the application of nanoparticles based on biomimetic strategies of cell membranes in tumor treatment shows that. Many types of nanoparticles can emit light through photoluminescence or upconversion, exhibiting significant fluorescence in living organisms, and are widely used in the field of biological imaging. On the other hand, nanoparticles can effectively load pharmaceuticals by physical adsorption, electrostatic interactions, covalent linkages, and other techniques due to their huge specific surface area and unique chemical composition. To obtain high-dose drug loading, they can even directly inject medications into cavities. Additionally, the unique environment at the tumor site and the size effect of nanoparticles facilitate the convergence of nanosystems for precise targeting. Research has demonstrated that building a nanomedicine delivery system using the superior physical and chemical characteristics of nanoparticles and the EPR effect may considerably increase the distribution and utilization rate of small molecule medications and enhance the therapeutic impact of treating illnesses. The primary research focus of nanomedicines is now on building therapeutic platforms that integrate several therapies by fusing the biological properties of cell membranes with the functional properties of nanomaterials themselves.

4. Applications in the Medical Field

4.1. Drug transportation

Transporting drugs into nanoparticles encapsulated in cell membranes can build a controllable and efficient drug delivery system in the body, targeting drug delivery to diseased areas for targeted release, which is beneficial for improving drug efficacy and reducing drug toxicity. Many drugs have high cytotoxicity, killing viral cells while also severely damaging normal human cells. Therefore, using cell membrane nanoparticles to transport drugs should not only have good biocompatibility, high drug loading, and utilization rates, as well as targeted properties but also enable drug release at an appropriate rate at the site of action. For example, mesoporous SiO_2 nanoparticles can undergo continuous regulation of uniform mesoporous pore size, regular pore channels, and stable skeleton structure within the range of 2-50nm. They are easy to modify on internal and external surfaces and have no physiological toxicity, making them excellent carriers for drug molecules [8].

Drug delivery is severely hampered by the immune system's ability to collect and eliminate nanoparticles. A possible method for interacting and negotiating with the immune system is to conceal nanoparticles in cell membranes. These biomimetic nanoparticles are a new class of nanotherapeutic agent that take on specific biological properties from the source cells (such as platelets, immune cells, cancer cells, and red blood cells) to evade immune elimination, extend circulation time, and even target disease areas based on the homing trend of cell membrane proteins.

4.2. Tumor vaccine

Nowadays, radiotherapy and chemotherapy are still the main treatment methods for cancer, and chemotherapy is mainly achieved through chemotherapy drugs. Inhibiting the growth and metastasis of cancer cells, thereby promoting cancer cell apoptosis. However, currently commonly used chemotherapy drugs in clinical practice have poor tumor targeting, which not only kills cancer cells but also damages normal cells in the human body, leading to adverse drug reactions. Through research, it has been found that magnetic nanoparticles of iron oxide are excellent carriers for delivering chemotherapy drugs due to their small particle size, high biosafety, large surface curvature, high relaxation performance, superparamagnetism, easy surface modification and functionalization, and other advantages. Therefore, they have received widespread attention. Nowadays, the combination of magnetic iron oxide nanoparticles and anti-tumor drugs to achieve targeted diagnosis and treatment of cancer is the main development direction and research hotspot [9].

For highly targeted and effective tumor therapy, a new tumor derived fragment (TDF) interference nanotechnology-based anti-tumor method has recently been developed. On the one hand, TDF-based nanoparticles and nanoparticles that cause immunogenic death in tumor cells can be used as in situ or ectopic vaccines to elicit immune responses during cancer immunotherapy. On the other side, it can also act as a medication delivery system for the treatment and detection of cancer.

4.3. Phototherapy

In recent years, the number of cancer patients has shown a continuous growth trend, but traditional surgical procedures have caused shortcomings such as innovation and incomplete treatment; Chemotherapy also difficult to eradicate tumor cells, while also killing normal cells and damaging the human immune system; Radiotherapy lacks selectivity. Therefore, new treatment methods are needed to treat cancer. The advantage of nanomaterials lies in their unique advantages in cancer treatment due to their small size effects, surface effects, volume effects, and quantum effects. Phototherapy is mainly focused on photothermal therapy (PTT) and photodynamic therapy (PDT), which have become potential alternatives to traditional tumor therapy due to their advantages of low uncertainty, good targeting, and controllability. PTT is based on the thermal energy generated by photothermal agents under light conditions to achieve therapeutic effects; PDT can generate ROS under NIR laser irradiation to kill cancer cells [10]. The primary issues with traditional phototherapy drugs, however, are immune system identification, blood circulation clearance, and limited accumulation at target areas. Since many of the proteins on the cell membrane's surface may be passed on to nanoparticles covered by the cell membrane, cell membrane coating has emerged as a promising strategy to get around these restrictions. Different coating techniques can be employed to coat nanoparticles with cell membranes from various sources. The photophysical characteristics of the initial phototherapy nanoparticles are mostly unaltered after cell membrane encapsulation. Additionally, during laser irradiation, the coated cell membrane can be ablated from the phototherapy nanoparticles, causing medication release and synergistic therapy. Combining with additional adjuvants will help to normalize the tumor microenvironment.

4.4. Immunology

Nanoparticles enclosed in cell membranes for use in immunotherapy and vaccinations. Nanoparticles can enhance the immunogenicity of the antigen and shield it against deterioration. Numerous studies have demonstrated that certain nanoparticles can aid in boosting antigen recruitment in lymph nodes, the primary locations for immunological surveillance and activation. Nanoparticles are promptly discharged into the lymphatic system after being injected into the skin through the first lymphoid vesicles in the stroma, where they interact with local dendritic cells in lymph nodes. Additionally, because nanoparticles are eliminated from our bodies more slowly than free antigens, they have more time to engage with dendritic cells. Moreover, antigen-presenting cells present antigens encapsulated in nanoparticles to T cells in a more free form. So far, nano carrier-related immunotherapy strategies have shown great potential, such as adjuvant lipid substituted lipid nanoparticles to enhance the immunogenicity of novel coronavirus mRNA vaccine.

5. Summarize

These days, the creation of pharmaceuticals may be made more and more precisely by utilizing nanotechnology. pharmaceuticals with particular functionalities can now be made by directly utilizing the arrangement of atoms and molecules at the size of nanomaterials. The technology of cell membrane encapsulation of nanoparticles will make the transportation of drugs in the human body more convenient. Various cell membranes in the human body can be used as encapsulation materials to participate in the assembly of membrane coating platforms, endowing nanoparticles with new characteristics. Its unique advantages provide new ideas for targeted drug delivery and personalized treatment in vivo. Although this technology has broad application prospects in fields such as biomedicine, biosensing, and drug delivery, research on cell membrane-encapsulated nanoparticles is still in the laboratory stage, and many cells have insufficient sources. Large-scale in vitro cell culture requires high cost. At the same time, the manufacturing process is relatively cumbersome and requires high technical requirements, which cannot be widely applied to meet the needs of continuous clinical treatment. Therefore, the main direction of current development is to continuously screen cell membrane camouflage nanoparticles with higher biocompatibility, stronger specificity, and wider application, reduce the manufacturing cost of nanoparticles, and make breakthroughs in coating technology.

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