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Research Progress and Prospects of Marine Polysaccharide-Based Nanocarriers in Cancer Therapy

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Abstract. Cancer therapy remains a major and intractable challenge in the global public health field. Various traditional treatment methods generally suffer from numerous problems such as insufficient targeting ability, obvious toxic and side effects, and frequent occurrence of tumor drug resistance. With the continuous iteration and improvement of nanotechnology, nanomedicine delivery systems have opened up a brand-new research direction for precise cancer treatment. Marine polysaccharides themselves possess excellent biocompatibility, biodegradability, extremely low biological toxicity, and diverse biological activities. These natural materials can be used to prepare nanocarriers with outstanding performance. This paper sorts out the specific classification methods, chemical structures and core physicochemical properties of marine polysaccharides, summarizes the commonly used preparation processes of marine polysaccharide-based nanocarriers at the present stage, and analyzes the practical application of such carriers in cancer treatment directions including chemotherapy, gene therapy, immunotherapy and theranostics. The article dissects various shortcomings and limitations existing in current related research, and also discusses the future development trend and clinical transformation potential of this type of nanocarriers. It can provide a reliable reference basis for the technical optimization and industrial application of marine polysaccharide-based nanocarriers, and help achieve further upgrading and development of precise cancer treatment technologies.

Keywords: Marine polysaccharides, Nanocarriers, Cancer therapy, Drug delivery, Applied research

1. Introduction

According to data from the 2023 Global Cancer Statistics Report released by the World Health Organization (WHO), there are more than 20 million new confirmed cancer cases worldwide every year, and the number of deaths caused by cancer has exceeded 10 million. Malignant tumors have now become one of the leading causes of human death [1]. At present, the mainstream clinical methods for treating tumors include surgical resection, chemotherapy and radiotherapy, and each of these treatment methods has inherent limitations in practical clinical application. Surgical treatment has a relatively limited scope of application. It can only act on early-stage localized tumors and is difficult to achieve ideal therapeutic effects on advanced metastatic tumors. Moreover, the

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probability of tumor recurrence after surgery is relatively high. Chemotherapeutic drugs are typical cytotoxic agents. These agents do not have the ability to target and recognize tumors. In the process of killing cancer cells, they will damage normal human tissues and organs, thereby causing a series of serious adverse reactions such as myelosuppression and gastrointestinal discomfort [2]. Although radiotherapy technology can complete the clearance of local cancer cells, it is easy to cause irreversible damage to surrounding normal human tissues and can also induce cancer cells to develop radiation resistance. In addition, the inherent multidrug resistance (MDR) of tumor cells will continuously reduce the actual effect of clinical treatment, which is also the core bottleneck restricting the development of the tumor treatment industry at present [3]. Therefore, developing tumor treatment regimens with high efficiency, low toxicity and high targeting has become the research focus of many scholars in the field of biomedicine.

The continuous maturity of nanotechnology can effectively make up for various defects existing in traditional tumor treatment methods. Nanocarriers have a particle size ranging from 1 to 1000 nm, possess a large specific surface area, and their surfaces can be artificially modified. These advantages give them extremely high application value in the field of drug delivery [4]. Compared with conventional drug delivery systems, nanocarriers can achieve passive drug accumulation relying on the inherent enhanced permeability and retention effect (EPR effect) of tumor tissues. Researchers can also endow nanocarriers with active targeting ability by modifying specific ligands on their surfaces, thereby increasing the accumulation of drugs in tumor lesions and reducing the distribution of drugs in healthy human tissues, ultimately achieving the goals of optimizing therapeutic effects and reducing drug toxic and side effects. At the same time, nanocarriers can isolate enzymatic hydrolysis and metabolic processes in the human body, effectively protect the biological activity of the loaded drugs, improve the bioavailability of the drugs themselves, and can also realize sustained and controlled release of drugs.

Among various existing carrier preparation materials, marine polysaccharides have extremely high research and application value due to their unique biological characteristics. The ocean is the largest biological resource bank on Earth, which contains a large number of natural macromolecular polysaccharides. Most of these polysaccharides are extracted from seaweeds, crustaceans and mollusks. Compared with terrestrial polysaccharides, marine polysaccharides have better biocompatibility, can be degraded in the natural environment, and have almost no biological toxicity. Some marine polysaccharides also have inherent biological activities such as anti-tumor, anti-virus and immunomodulatory effects, which can achieve the effect of "carrier-drug" synergistic therapy [5]. For example, two common polysaccharides, fucoidan and chitosan [6], can assist in tumor treatment by regulating human immune function, inhibiting cancer cell proliferation and inducing cancer cell apoptosis, providing a brand-new research idea for the development of the tumor diagnosis and treatment industry.

In recent years, significant progress has been made in the research of marine polysaccharide-based nanocarriers in cancer therapy. A variety of novel carrier systems have been developed and applied in preclinical studies. However, there is still no systematic review that comprehensively sorts out their research progress, existing problems and development prospects. The purpose of this paper is to sort out the preparation technologies, applications in cancer therapy and targeting mechanisms of marine polysaccharide-based nanocarriers, analyze the challenges faced by current research, provide directions for subsequent related research, promote the clinical translation of marine polysaccharide-based nanocarriers, and offer new strategies and methods for precise cancer treatment.

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2. Types, structures and properties of marine polysaccharides

2.1. Main categories and sources of marine polysaccharides

Marine polysaccharides are extremely diverse in types and have a wide range of sources. According to their sources, they can be divided into seaweed-derived polysaccharides, crustacean-derived polysaccharides, mollusk-derived polysaccharides, etc. Among them, seaweed-derived and crustacean-derived polysaccharides are the two most widely studied categories at present [6]. Brown algae are one of the important sources of marine polysaccharides. The main polysaccharide contained in brown algae is fucoidan, which is mainly found in brown algae such as kelp, wakame and fucus. It is an acidic polysaccharide with fucose as the main sugar unit and also contains sulfate groups. The shells of crustaceans (such as shrimp, crabs and lobsters) are rich in chitosan, which is an alkaline polysaccharide obtained by deacetylation of chitin and is also the most abundant alkaline polysaccharide in nature. Polysaccharides derived from red algae mainly include carrageenan and porphyran. Carrageenan is mainly extracted from red algae such as Eucheuma and Gracilaria. According to the degree of sulfation and the type of glycosidic bonds, it can be divided into κ-carrageenan, ι-carrageenan and λ-carrageenan. Porphyran is mainly extracted from laver and is a neutral polysaccharide with galactose and guluronic acid as the main sugar units. Polysaccharides derived from green algae mainly include alginate and ulvan. Alginate is mainly extracted from green algae such as Ulva lactuca and Enteromorpha. It is a linear polysaccharide formed by the connection of guluronic acid and mannuronic acid through glycosidic bonds. Ulvan is mainly extracted from green algae of the genus Ulva and has good water solubility and biological activity [7].

2.2. Correlation between structural characteristics and biological activities

The biological activities of marine polysaccharides are closely related to their own chemical structures. Monosaccharide composition, glycosidic bond type, degree of sulfation and molecular weight are the core structural parameters affecting the properties of polysaccharides, among which the degree of sulfation and monosaccharide composition have the most significant effects on biological performance [7]. The anti-tumor and anti-viral abilities of fucoidan are positively correlated with its degree of sulfation. Sulfate groups can bind to surface receptors on cancer cells, which can not only inhibit the proliferation process of cancer cells, but also activate immune cells, thereby enhancing the body's own anti-tumor immune capacity. The degree of deacetylation of chitosan determines the amino content in the molecule and directly affects its water solubility, biocompatibility and biological activity. Chitosan with a higher degree of deacetylation exhibits better water solubility and stronger tumor inhibitory effect.

Different types of carrageenan exhibit different biological activities due to differences in glycosidic bond connection modes and sulfate modification sites. First, κ-carrageenan has excellent gelling properties and biocompatibility and is often used to prepare various nanocarriers. Second, ι-carrageenan can exert good anti-inflammatory and anti-tumor effects. In addition, molecular weight also has a critical impact on the properties of polysaccharides. Low-molecular-weight marine polysaccharides are more easily absorbed and utilized by organisms and can exhibit more prominent anti-tumor and immunomodulatory activities [8].

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2.3. Core properties of marine polysaccharides

Biocompatibility is the most fundamental and core advantage of marine polysaccharides when used as nanocarriers. These polysaccharides are natural biological macromolecules with good compatibility with human cells and tissues, and generally do not cause immune rejection reactions. At the same time, they can be gradually metabolized and decomposed in the organism without producing toxic residues [7]. Chitosan and alginate have been widely used in the biomedical field at present, and their biological safety has been verified through clinical trials. Biodegradability is another major advantage of marine polysaccharides. These polysaccharides can be decomposed by biological enzymes such as lysozyme and glycosidase, and can also be hydrolyzed in acidic and alkaline environments. The small-molecule sugars produced by degradation can be absorbed and metabolized by the organism without long-term accumulation in the body to cause toxicity. Researchers can also rely on this property to achieve controlled drug release.

The molecular chains of marine polysaccharides carry a large number of active groups such as hydroxyl groups, amino groups, carboxyl groups and sulfate groups. Researchers can optimize the water solubility, structural stability and tumor targeting ability of polysaccharides through chemical modification methods such as polyethylene glycol modification and ligand grafting. Some marine polysaccharides also have pH, temperature and redox-sensitive stimulus-response properties, which can adapt to the special microenvironment of tumors with acidity and high glutathione, thereby achieving intelligent drug release. For example, alginate can depolymerize in an acidic environment to release the internally encapsulated drugs; chitosan modified with disulfide bonds can achieve targeted drug release in tumor tissues with high glutathione [9].

3. Preparation technologies of marine polysaccharide-based nanocarriers

3.1. Common preparation methods

There are many preparation methods for marine polysaccharide-based nanocarriers, which can be divided into physical methods, chemical methods and biological methods according to the preparation principles. Among them, ionic crosslinking method, self-assembly method, emulsion-solvent evaporation method and green synthesis method are the most commonly used preparation methods at present. The principles, advantages, application scopes and typical applications of various preparation methods are shown in Table 1:

Table 1. Principles, advantages, applicable scopes, and typical applications of various preparation methods for marine polysaccharide-based nanocarriers

Preparation Method	Core Principle	Main Advantages	Application Scope	Typical Applications
Ionic Cross-linking Method	Electrostatic interaction between charged groups of polysaccharides and counterions to form stable nanoparticles	Simple operation, mild reaction, no toxic organic solvents, low cost	Hydrophilic polysaccharides (chitosan, alginate), loading of hydrophilic drugs	Chitosan-TPP nanoparticles loaded with doxorubicin and siRNA

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Table 1. (continued)

Self-assembly Method	After hydrophobic modification, polysaccharides self-assemble to form core-shell structures through hydrophobic interactions, hydrogen bonds, etc.	Stable carrier structure, capable of efficient loading of hydrophobic drugs	Hydrophobic/amphiphilic polysaccharides, loading of hydrophobic chemotherapeutic drugs	Cholesterol-grafted chitosan nanomicelles loaded with paclitaxel
Emulsification-Solvent Evaporation Method	Drugs are dissolved in organic solvents, mixed with polysaccharide aqueous solution to form emulsions, and nanoparticles are formed after solvent evaporation	High drug loading rate, wide application scope, and capable of preparing composite carriers	Various polysaccharides, mainly hydrophobic drugs, preparation of composite carriers	Carrageenan-PLGA composite nanoparticles loaded with paclitaxel
Green Synthesis Method	Using the reducibility of marine polysaccharides to reduce metal ions to form metal nanoparticles, with polysaccharides as stabilizers	Environmentally friendly, no additional reducing agents needed, and good biocompatibility of carriers	Polysaccharides with reducibility, photothermal/chemotherapy synergistic therapy carriers	Fucoidan-gold nanoparticles for photothermal-chemotherapy synergistic therapy

Ionic crosslinking method is a simple and mild preparation method that does not require the use of toxic organic solvents, and is suitable for preparing polysaccharide-based nanocarriers such as chitosan and alginate. This method utilizes the electrostatic interaction between the charged groups in polysaccharide molecules and counter ions to form stable nanoparticles. For example, chitosan (positively charged) and sodium tripolyphosphate (TPP, negatively charged) undergo an ionic crosslinking reaction in aqueous solution to rapidly form chitosan-TPP nanoparticles. This method has the advantages of simple operation and mild reaction conditions, and can also be used to load hydrophilic drugs (such as chemotherapeutic drugs and gene drugs). Relevant studies have shown that by adjusting the concentration ratio of chitosan to TPP, reaction pH and temperature, the particle size and zeta potential of nanoparticles can be effectively controlled [10].

Self-assembly method is based on the amphiphilicity of polysaccharides, which form nanocarriers (such as nanomicelles and nanocapsules) through intermolecular hydrophobic interactions, hydrogen bonds, electrostatic interactions and other forces. For marine polysaccharides with poor hydrophobicity (such as chitosan), amphiphilicity can be imparted through hydrophobic modification (such as grafting fatty acids or cholesterol), allowing them to self-assemble into nanomicelles in aqueous solution. For example, cholesterol-grafted chitosan can self-assemble into core-shell structured nanomicelles in aqueous solution. The hydrophobic core can load hydrophobic chemotherapeutic drugs (such as paclitaxel and doxorubicin), while the hydrophilic shell can improve the water solubility and stability of the carriers [11].

Emulsion-solvent evaporation method is mainly used to prepare marine polysaccharide-based nanocarriers loaded with hydrophobic drugs. In this method, hydrophobic drugs are dissolved in an

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organic solvent, then mixed with an aqueous polysaccharide solution, and an oil-in-water (O/W) emulsion is formed by ultrasonication or stirring. Subsequently, the organic solvent is evaporated to form nanoparticles. For example, the preparation of carrageenan-poly(lactic-co-glycolic acid) (PLGA) composite nanoparticles involves dissolving paclitaxel in dichloromethane, mixing it with carrageenan aqueous solution to form an emulsion, and evaporating dichloromethane to obtain carrageenan-PLGA composite nanoparticles. This carrier can effectively improve the water solubility and bioavailability of hydrophobic drugs [12].

Green synthesis method is an environmentally friendly preparation method. It utilizes the reducing property of marine polysaccharides to reduce metal ions (such as Au^{3+} and Ag^{+}) to form metal nanoparticles (such as gold nanoparticles and silver nanoparticles) without additional reducing agents. Meanwhile, marine polysaccharides can also act as stabilizers and coating agents to improve the stability and biocompatibility of metal nanoparticles. For example, fucoidan has strong reducing property and can reduce Au^{3+} to form fucoidan-gold nanoparticles in aqueous solution. These nanoparticles not only have good biocompatibility, but also can be used for synergistic photothermal therapy and chemotherapy [13].

3.2. Influencing factors of preparation process and carrier characterization technologies

The preparation process of marine polysaccharide-based nanocarriers has an important impact on their properties (particle size, zeta potential, drug loading rate, stability). The main influencing factors include the inherent properties of polysaccharides and reaction conditions. The molecular weight and degree of deacetylation (for chitosan) of polysaccharides are key factors affecting the performance of nanocarriers. Excessively high molecular weight tends to lead to increased particle size and poor dispersibility of nanoparticles; while excessively low molecular weight will reduce the stability and drug loading capacity of the carriers. For example, when the molecular weight of chitosan is in the range of 10-100 kDa, the prepared nanoparticles have uniform particle size and good stability; when the degree of deacetylation is higher than 80%, the water solubility and cationic property of chitosan will be enhanced, and the ionic crosslinking effect with TPP will also be better. Reaction conditions (pH, temperature, concentration ratio of polysaccharide to crosslinker/modifier) also significantly affect the performance of nanocarriers. The pH value can affect the charged properties of polysaccharide molecules, thereby affecting the ionic crosslinking reaction and self-assembly process [6, 7].

The performance of marine polysaccharide-based nanocarriers needs to be evaluated through a series of characterization technologies, mainly including particle size and morphology analysis, surface charge and stability analysis, drug loading and release analysis, etc. The detection purposes, common methods and core evaluation indicators of various characterization technologies are shown in Table 2:

Table 2. Detection purposes, common methods, and core indicators of characterization techniques for marine polysaccharide-based nanocarriers

Characterization Category	Common Detection Methods	Detection Purpose	Core Evaluation Indicators	Reference Standards
Particle Size and Morphology Analysis	Dynamic Light Scattering (DLS), TEM, SEM	Clarify the size, morphology and dispersibility of nanoparticles	Average particle size, PDI, morphology uniformity	PDI < 0.3 indicates uniform particle size

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Table 2. (continued)

Surface Charge and Stability Analysis	Zeta potential measurement, in vitro stability test	Evaluate the stability and in vivo behavior of nanocarriers	Zeta potential, particle size change rate	Zeta potential above ±20mV indicates good stability
Drug Loading and Release Analysis	High Performance Liquid Chromatography (HPLC)	Evaluate drug delivery and controlled release capabilities	Drug Loading (DL), Encapsulation Efficiency (EE), release curve	Adjust according to drug type and carrier type

Particle size and morphology are important physical parameters of nanocarriers, which directly affect their in vivo distribution and targeting ability. Dynamic light scattering (DLS) is a common method for determining the particle size and particle size distribution of nanoparticles, which can quickly and accurately obtain the average particle size and polydispersity index (PDI) of nanoparticles. The smaller the PDI value, the more uniform the particle size of nanoparticles [14]. Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) can be used to observe the morphology, size and dispersibility of nanoparticles. The core-shell structure and spherical morphology of nanoparticles can be clearly observed through TEM. For example, fucoidan-gold nanoparticles appear spherical under TEM observation, with uniform particle size and good dispersibility. Surface charge (zeta potential) is an important factor affecting the stability and in vivo behavior of nanocarriers. The larger the absolute value of zeta potential, the stronger the electrostatic repulsion between nanoparticles, and the better the stability [14]. Generally, marine polysaccharide-based nanocarriers have good stability when their zeta potential is above ±20 mV. In vitro stability experiments can evaluate the stability of nanocarriers in simulated body fluids (such as PBS buffer and serum). By measuring the changes in particle size and zeta potential of nanoparticles at different time points, their in vivo stability can be judged. Drug loading rate and in vitro release kinetics are key indicators for evaluating the drug delivery ability of nanocarriers. Drug loading (DL) refers to the percentage of the mass of the drug loaded in the nanocarrier to the total mass of the carrier; entrapment efficiency (EE) refers to the percentage of the mass of the drug encapsulated by the carrier to the total mass of the administered drug. High-performance liquid chromatography (HPLC) is a common method for determining drug loading rate and in vitro release amount, with the characteristics of high sensitivity and good separation effect. In vitro release kinetics experiments are usually carried out in simulated tumor microenvironment (such as pH 5.0 buffer) and normal physiological environment (pH 7.4 PBS buffer). By measuring the drug release amount at different time points and drawing the release profile, the drug release characteristics of the nanocarrier can be evaluated [14].

4. Applications of marine polysaccharide-based nanocarriers in cancer therapy

4.1. Chemotherapeutic drug delivery

Chemotherapy is currently the most widely used clinical treatment for tumors, but its limitations of insufficient targeting and obvious toxic and side effects severely restrict its therapeutic efficacy. Marine polysaccharide-based nanocarriers can optimize the delivery efficiency of chemotherapeutic drugs, increase the accumulation of drugs at tumor sites, and reverse tumor multidrug resistance. Single-drug loading is the most basic application form of such carriers, which can encapsulate various common chemotherapeutic drugs such as doxorubicin, paclitaxel and cisplatin. Folate-modified chitosan-doxorubicin nanocarriers can achieve passive targeted accumulation through the

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EPR effect and active targeting via folate groups, thereby increasing the drug concentration in breast cancer tissues. This not only enhances the anti-tumor effect, but also reduces the toxic damage caused by drugs to normal organs such as the heart and liver [15]. Paclitaxel-loaded fucoidan nanoparticles can improve the water solubility of hydrophobic drugs and effectively inhibit the proliferation and growth of lung cancer and liver cancer cells [13].

Combined drug loading is an efficient method to optimize chemotherapy efficacy. Polysaccharide carriers can simultaneously load two or more chemotherapeutic drugs, or be combined with small molecule inhibitors to achieve synergistic therapy. For example, chitosan nanoparticles co-loaded with doxorubicin and programmed death ligand 1 (PD-L1) inhibitors can directly kill cancer cells on the one hand, and block the tumor immune escape pathway to enhance the body's anti-tumor immune response on the other hand. The combined medication mode can reduce the dosage of a single drug and lower the incidence of adverse reactions [16]. In addition, carriers can simultaneously load chemotherapeutic drugs and anti-angiogenic agents to cut off the nutrient supply of tumors and further amplify the therapeutic effect.

Marine polysaccharide-based nanocarriers can reverse tumor drug resistance by inhibiting the expression of P-glycoprotein. P-glycoprotein can efflux chemotherapeutic drugs from cancer cells, reduce the intracellular drug concentration, and thereby induce drug resistance. Doxorubicin-loaded alginate nanoparticles can inhibit the expression of P-glycoprotein, reduce drug efflux, and reverse the drug resistance characteristics of breast cancer cells. Meanwhile, marine polysaccharides can also regulate the intracellular signaling pathways of cancer cells and improve the sensitivity of tumor cells to chemotherapeutic drugs [17].

4.2. Gene therapy delivery

Gene therapy is a new type of tumor treatment technology. Its technical principle is to deliver therapeutic genes such as tumor suppressor genes and small interfering RNA (siRNA) into tumor cells to inhibit tumor proliferation and induce cancer cell apoptosis. However, gene drugs such as small interfering RNA and deoxyribonucleic acid (DNA) are easily degraded by nucleases and difficult to penetrate cell membranes, which limits the clinical promotion of this technology. Marine polysaccharide-based nanocarriers can protect gene drugs from enzymatic degradation and effectively improve cell uptake rate and gene transfection efficiency. Marine polysaccharide-based nanocarriers can serve as gene delivery vectors to protect gene drugs from nuclease degradation and enhance their cell uptake efficiency and transfection efficiency [3, 17]. Positively charged chitosan can bind to negatively charged small interfering RNA through electrostatic interaction and assemble into structurally stable nanocomplexes. These complexes can enter cancer cells through receptor-mediated endocytosis and silence oncogenes such as survivin and signal transducer and activator of transcription, thereby inhibiting tumor growth [13, 17]. In terms of DNA delivery, fucoidan-modified polyethyleneimine (PEI) carriers can optimize their biocompatibility and nuclear targeting ability, improve the transfection efficiency of the p53 tumor suppressor gene, and effectively inhibit the proliferation of lung cancer cells. Chitosan-alginate composite carriers also have excellent gene delivery ability with extremely low biological toxicity [15].

Gene-chemotherapy combined therapy can integrate the advantages of the two treatment modalities and achieve synergistic anti-tumor effects. Chitosan-alginate composite nanoparticles co-loaded with doxorubicin and small interfering RNA can not only directly kill cancer cells with chemotherapeutic drugs, but also silence the MDR1 drug resistance gene and reverse tumor multidrug resistance, greatly improving the overall therapeutic effect [3].

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4.3. Synergistic immunotherapy

Immunotherapy is a major breakthrough in cancer treatment in recent years. It achieves precise cancer treatment by activating the body's immune system and enhancing the ability of immune cells to recognize and kill tumor cells. Marine polysaccharide-based nanocarriers can serve as delivery carriers for immunotherapy, loading immunotherapeutic drugs such as immune checkpoint inhibitors and tumor antigens to enhance the efficacy of immunotherapy. Immune checkpoint blockade is an important strategy for immunotherapy. It blocks immune checkpoints (such as PD-1/PD-L1) to relieve the immune escape of tumor cells and enhance the body's immune response. Marine polysaccharide-based nanocarriers can load PD-1/PD-L1 antibodies to improve their bioavailability and achieve targeted delivery of antibodies. For example, chitosan nanoparticles loaded with PD-L1 antibodies can accumulate in tumor tissues through the EPR effect, slowly release PD-L1 antibodies, block the binding of PD-L1 to PD-1, activate the killing function of T cells, and enhance the effect of tumor immunotherapy [18]. Tumor vaccine delivery activates the body's specific immune response by delivering tumor antigens, generating immune memory against tumor cells, thereby preventing and treating tumors. Marine polysaccharides (such as carrageenan) can act as vaccine adjuvants to enhance the immunogenicity of antigens, and also serve as carriers to load tumor antigens for their sustained release. For example, tumor antigen nanovaccines using carrageenan as an adjuvant can activate the maturation of dendritic cells (DCs), promote antigen presentation by DCs, activate T cell immune responses, and effectively inhibit tumor growth and metastasis [19]. In addition, fucoidan can also act as an immune adjuvant to enhance the immune effect of tumor vaccines [13].

4.4. Theranostic applications

Theranostics integrates tumor diagnosis and treatment to achieve the integration of "diagnosis-treatment-monitoring", improving the precision and effectiveness of cancer treatment. Marine polysaccharide-based nanocarriers, due to their good biocompatibility and multifunctionality, can simultaneously load therapeutic drugs and imaging agents for theranostic applications [3, 20].

Imaging-guided therapy is an important form of theranostics. Marine polysaccharide-based nanocarriers can load imaging agents (such as magnetic nanoparticles and fluorescent dyes) and therapeutic drugs, locate tumor sites through imaging technologies (such as MRI and fluorescence imaging), and simultaneously achieve tumor treatment. For example, chitosan-modified Fe_3O_4 magnetic nanoparticles can load DOX, clearly display tumor locations through MRI imaging. Meanwhile, Fe_3O_4 nanoparticles can generate heat under the action of a magnetic field, achieving synergistic photothermal therapy and chemotherapy and improving the efficacy of cancer treatment [21].

Photothermal/photodynamic therapy is a new type of cancer treatment method with the characteristics of strong targeting and low toxic and side effects. Marine polysaccharide-based nanocarriers can load photothermal agents (such as gold nanoparticles and indocyanine green ICG) or photosensitizers to achieve synergistic photothermal/photodynamic therapy and chemotherapy [22]. For example, fucoidan-ICG composite nanoparticles use ICG as both a photothermal agent and a photosensitizer. Under near-infrared light irradiation, ICG can generate heat and reactive oxygen species to kill tumor cells. Meanwhile, fucoidan can load chemotherapeutic drugs to achieve synergistic photothermal therapy and chemotherapy, significantly enhancing the effect of cancer treatment [13].

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5. Conclusion

Marine polysaccharides have good biocompatibility, biodegradability, low toxicity and structural modifiability, and the nanocarriers prepared from them have broad application prospects in the field of cancer therapy. This paper systematically summarizes the classification methods, structural characteristics and inherent properties of marine polysaccharides, sorts out four mainstream preparation processes and carrier characterization methods, analyzes the specific application forms of such carriers in chemotherapy, gene therapy, immunotherapy and theranostics, and elucidates the targeting mechanisms and in vivo metabolic rules of the carriers.

Marine polysaccharide nanocarriers can optimize drug delivery efficiency, increase drug concentration at tumor sites, and reduce the systemic toxic and side effects of drugs on the human body. Multi-modal combined therapy systems also provide diversified solutions for precise cancer treatment. Although such carriers have achieved good results in preclinical research, clinical translation still faces multiple constraints. First, industrial mass production is difficult. The high extraction cost of polysaccharides and unstable raw material sources lead to poor batch consistency of carriers, making it difficult to directly scale up laboratory preparation processes for industrial production. Second, the in vivo stability of carriers is insufficient. Nanoparticles are easily adsorbed by plasma proteins and cleared by the mononuclear phagocyte system, resulting in short in vivo circulation cycles and low tumor accumulation rates. Although polyethylene glycol modification can improve stability, it will reduce the targeting ability and drug loading performance of carriers.

Third, the clinical translation cycle is relatively long. At present, most studies remain at the cellular and animal experimental levels, lacking long-term biological toxicity and immunogenicity detection data, and there is no unified quality control standard for nanocarriers established within the industry. Fourth, the structural homogeneity of polysaccharides is poor. Differences in raw material sources and extraction processes will cause fluctuations in the glycosyl composition, degree of sulfation and molecular weight of polysaccharides, thereby affecting the stability of carrier performance.

Future related research can be promoted from four directions: first, develop multi-target precise targeting strategies to improve the selective recognition ability of carriers for cancer cells; second, construct multi-stimuli responsive intelligent carriers to achieve precise and controlled drug release within the tumor microenvironment; third, explore novel marine polysaccharides from deep-sea and extreme environments, and optimize the comprehensive performance of existing polysaccharides through chemical modification, engineering modification and other methods; fourth, build multi-modal combined therapy systems, integrate the advantages of chemotherapy, immunotherapy, photothermal therapy and photodynamic therapy, and delay the development of tumor drug resistance.

Overall, marine polysaccharide-based nanocarriers have outstanding clinical translation potential, and multiple carrier systems have demonstrated excellent characteristics of high efficiency and low toxicity in preclinical trials. Subsequent research needs to formulate unified quality control standards, improve the systematic evaluation of biological safety, optimize large-scale production processes, and promote the interdisciplinary integration of materials science, clinical medicine, marine biology and pharmaceutics. With the assistance of multi-party collaborative research, marine polysaccharide-based nanocarriers can be applied in clinical cancer treatment more quickly, providing reliable new solutions for precise tumor diagnosis and treatment.

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