

Recent advances in microbial polysaccharides as biotherapeutics

Opinion

Microorganisms are known to produce several biopolymers. Certain species of bacteria, fungi are known to produce polysaccharides during their metabolic processes. The microbial origin polysaccharides have captivated significant attention due to their unique biological properties, which make them appropriate for innumerable applications.¹ The microbial polysaccharides (MIPs) such as cellulose, pullulan, sodium alginate, chitosan, chitin, xanthan, dextran, curdlan, pectin, etc. are commonly known.² The microbial-origin polysaccharides are advantageous as compared to those derived from plants and animals.

This includes high production efficiency and less susceptibility to natural environmental influences. Additionally, they have diverse biological properties, such as antibacterial, antioxidative, anti-tumor, and immunomodulatory functions. These properties ultimately signify their immense potential for applications in the food, cosmetics, and textile sectors.³ Being non-toxic, biodegradable, biocompatible, and cost-effective, there is a mounting interest in the safety and efficacy of MIPs in the biomedical field too. The recent studies of the antitumor properties of polysaccharides have gathered much attention for MIPs.⁴

An increasing number of studies have revealed the potential benefits of MIPs in the treatment of deadened diseases such as cancer. The disease is now recognized as a significant threat to public health. The scientific community is concerned about the increasing incidence of cancer worldwide. Cancer cells multiply uncontrollably and spread throughout the body. Recently, the American Cancer Society (ACS) released its Global Cancer Statistics, which evaluated 20 million new cancer cases and 9.7 million deaths in year 2022.⁵ The increased mortality rate is due to the delayed diagnosis and the lack of treatment options for advanced cancer stages.

The use of surgery and radiation therapy to remove malignant tumors is not the key solution, as some metastasis cells always survive, resulting in recurring tumors. The current treatment methods, such as chemotherapy and immunotherapy, prevent re-initiating tumor growth but cause severe toxicity to healthy cells, which results in death. Scientific communities are thus looking forward to developing more precise biomaterials for treatment in order to precisely tune the functionality of malignant cells. Recent advances in polysaccharide applications have validated the utility of MIPs in cancer treatment because they participate in a variety of cellular events such as immune reactions, cell adhesion, and signal transduction.⁶

Some natural polysaccharides, such as lentinan and schizophyllan, are reported to be effective antitumor agents.⁷ The activity of conventional chemotherapeutic drugs could be enhanced by polysaccharide-protein conjugate.⁸ Additionally, many studies have proven the immunosuppressive activity of MIPs against tumor growth.⁹ The studies by Zhang et al. and Ren et al. established that polysaccharides derived from the fungus mushroom have been broadly studied for their potent antitumor and pharmaceutical activity

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properties. This includes *Ganoderma lucidum* which proved to have potent in vitro immune activation as well as antitumor activity on breast cancer cells.^{10,11} The other one is *Lentinus edodes*, which unveiled a noticeable antitumor property against transplanted sarcoma.¹²

Additionally, polysaccharides from algae also have a diversity of pharmacological activities including antitumor activity.¹³ The mechanistic action of polysaccharides includes the activation of effector cells, such as macrophages, T and B lymphocytes, cytotoxic T lymphocytes, and natural killer cells to express cytokines (TNF- α , IFN- γ , and IL-1 β , cytokines) which invariably own the antiproliferative activity, causing the apoptosis and differentiation in tumor cells and also secrete products like reactive nitrogen, oxygen intermediates, and interleukins.¹⁴ The efficacy of microbial peptides varies with their molecular weight (M.W.) as well as the composition of sugar. Low M.W. and hydrophobic glucans are less efficient as compared to high M.W. and hydrophilic glucans.

Likewise, polysaccharides, which possess β -(1 \rightarrow 3) bonds in the parent backbone and branching in β -(1 \rightarrow 6) owns promising antitumor activity.¹⁵ Concurrently MIPs have an important role as drug delivery systems. The functional groups such as hydroxyl (OH), amino ($-\text{NH}_2$), carboxylic ($-\text{COOH}$) and aldehyde make them suitable for augmenting cancer treatment strategy. The polysaccharides are chemically modified by conjugation with chemical structures such as carboxy-methyl glycol, PEG resulting in the synthesis of nanostructures, self-assembled micelles, polymeric microspheres that result in better delivery at cancer sites. RNA interference therapies and cancer chemotherapeutics efficiently increase when they become integrated or co-integrated with MIPs -based nanocarriers.

The limitation of RNA interference therapies is due to the off-target site toxicity, rapid renal clearance, and degradation of siRNA by endogenous nucleases. The MIPs possess efficient binding and protection capabilities to siRNA, which could result in maintaining the stability under various physiological conditions, increasing intracellular uptake, and sustaining the release of siRNA and drugs. MIPs can also act as ligands for cell surface receptors, which could frequently involve the design of nano-assembly to deliver chemotherapeutics. However, surface charge is a critical feature of MIPs that influences the fate of engineered nanomaterials.

Cationic polysaccharides promote cancer cell endocytic uptake, whereas anionic polysaccharides increase bioavailability while decreasing glomerular capillary wall secretion. The spatial conformation of MIPs confirms their hydrophilicity and bio-adhesion properties, which can be applied to bio-nanomaterials or pharmaceutical formulations. The ease of tailoring, inherent bioactivity, distinct mucoadhesiveness, ability to absorb hydrophobic drugs, and abundant availability of MIPs make them effective green biological materials for overcoming the significant limitations of cancer chemotherapies.^{2,16}

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Conflicts of interest

Author declares that there is no conflict of interest.

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