

Research Progress of Polysaccharides and Cancer Treatment

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Abstract. Over the past decade, scientists have already discovered several methods for cancer treatment, however, most of the treatments have various kinds of negative side effects. Researchers have focused on creating medications with few adverse effects for cancer because it is one of the most fatal diseases. Due to their anti-tumor properties and non-toxic attributes, bioactive macromolecules like polysaccharides are seen as viable options against cancer. Nowadays, there have been many studies on the mechanisms and possibilities of polysaccharides against tumors, and this paper attempts to summarize the progress and main problems achieved so far in polysaccharides against cancer. This article will start from these aspects, the idea of cancer treatment, how cancer affects the immune system, how polysaccharides are absorbed and processed, how they are used in anti-tumor therapy, and how they work are all covered in the current review. Future therapeutic research will place a high priority on polysaccharides since they have the potential to be significant therapeutic targets.

Keywords: Cancer treatment, polysaccharides, anti-tumor therapy.

1. Introduction

Cancer is a condition in which some of the body's cells grow and divide uncontrollably, spreading to other parts of the body [1]. Cancer can develop in any of the millions of cells in the human body. Normally, cells divide and grow to create new cells as the body needs them, replacing old or damaged cells. However, sometimes this process goes wrong, and damaged or abnormal cells begin to grow and divide when they shouldn't. These cells can form tumors, which are masses of tissue. Tumors can be cancerous or non-cancerous, depending on whether they are capable of spreading to other parts of the body. Cancerous tumors can invade surrounding tissues and spread to distant parts of the body to form new tumors; a process called metastasis. Blood cancers, such as leukemias, rarely form solid tumors like other types of cancer. Non-cancerous tumors do not spread to neighboring tissues, and benign tumors typically do not recur after removal.

Cancer cells differ from healthy cells in several ways, including their ability to divide and grow without receiving the usual signals that regulate cell growth. Normal cells only divide when they receive specific signals to do so, and they stop growing or die when they receive other signals. Cancer cells, on the other hand, ignore these signals and continue to grow and divide, even when they come into contact with other cells. They also have the ability to invade surrounding tissues and spread to other parts of the body. This abnormal behavior is essential for cancer cells to survive and grow. Researchers have taken advantage of these differences to develop treatments that target specific features of cancer cells. For example, some cancer therapies block the formation of blood vessels that supply tumors with the nutrients they need to grow.

Today, some treatments are well developed and can help patients become healthier and less tumor-initiated to some degree. The most common treatment is chemotherapy [2, 3], which has advantages and disadvantages. As the treatment travels through the entire human body, it is able to reach and kill cancer cells that grow in different parts of the body, although it will also kill healthy cells due to difficulty in differentiation. In contrast, cell-plant transplantation is a new technology that can aid in the treatment of tumors. Damaged blood cells are replaced with healthy ones by a bone marrow or stem cell transplant. It can be used in the treatment of diseases such as leukemia and lymphoma that damage blood cells. Bone marrow, a spongy substance found inside many bones, produces unique cells known as stem cells that can develop into numerous types of blood cells. The use of stem cells has the potential to revolutionize the field of organ transplantation and disease treatment. Stem cells

can be used to generate healthy, functioning organs for transplantation, as well as to study the underlying mechanisms of diseases that are currently incurable. However, there are a number of clinical, moral, and social concerns surrounding the use of stem cells. These concerns may vary depending on the type of stem cells used, such as adult, embryonic, or therapeutically cloned stem cells. There are also ethical considerations related to the potential use of stem cells in regenerative medicine and gene editing.

Nanosystems made of polysaccharides have received a lot of attention as potential platforms for drug delivery in the treatment of various diseases because they are biocompatible and biodegradable, making them safe to use in medical procedures [4]. There is a need for natural substances that can prevent cancer, as current treatments are often not effective enough [5]. Therefore, it is important to find anticancer drugs that are potent but have low toxicity, as many current chemotherapy drugs can harm healthy cells. The search for new anticancer drugs with fewer side effects is crucial for the successful treatment of cancer [6].

1.1. Types and Structures of Polysaccharides

Monosaccharide chains combine to form polysaccharides, which are complex biomacromolecules. It's the glycosidic bonds of these chains that hold them together. Simple sugars such as glucose, fructose, mannose and galactose are commonly found as monomeric units in polysaccharides. Polysaccharides can be classified into two general categories: Homo-polysaccharides and Hetero-polysaccharides. Homo-polysaccharides such as cellulose, starch and glycogen consist of a single monosaccharide unit. There are at least two different types of monosaccharide units that combine to form hetero polysaccharides. for example, hyaluronic acid, and give the organisms extracellular support (Table1).

Table 1. Classification of Carbohydrates.

Carbohydrates		
Simple		Complex
Monosaccharides	Disaccharides	
Glucose	maltose	starch
fructose	sucrose	glycogen
galactose	lactose	fiber

The same fundamental procedure is used to create all polysaccharides, which involves the joining of monosaccharides via glycosidic bonds. Glycosidic bonds are a type of chemical bond that links two carbon rings by an oxygen molecule. This bond is created through a process known as dehydration synthesis, where a hydroxyl group is lost from one molecule and a hydrogen is lost from the other. This reaction results in the formation of a new bond, while also releasing one oxygen molecule and two hydrogen molecules. This process is called a dehydration reaction because it involves the loss of water molecules (Figure1). The architecture and characteristics of the resulting polysaccharide are governed by the molecular structures that are being blended together. Whereas a polysaccharide used for support typically consists of a long monosaccharide chain that creates fibrous structures, the use of a polysaccharide for energy storage will allow simple access to the constituent monosaccharides.

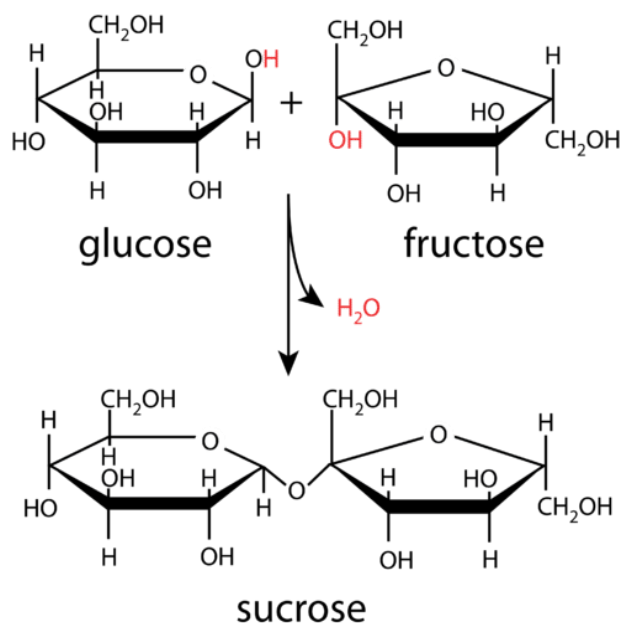


Figure 1. Hydration occurs to make monosaccharides into disaccharides.

2. Immunity and Tumor

2.1. Set up of the Immune System

The immune system is the body's defense against harmful substances, microorganisms, and other threats that can cause illness. It is made up of various cells, organs, and proteins that work together to protect the body. When the immune system is functioning properly, people are usually not aware of it. However, if the immune system is weakened or unable to fight off particularly virulent germs, people can become sick. Some germs only cause disease when they are first introduced to the human body, such as childhood illnesses like chickenpox.

The immune system is crucial for protecting the body against harmful substances and disease-causing microorganisms. It fights off pathogens like bacteria, viruses, and parasites, and removes them from the body. The immune system also helps to prevent harmful elements in the environment from causing damage and protects against diseases like cancer. Without it, the body would be unable to defend itself against these dangers.

The body's immune system is activated when it encounters substances that it doesn't recognize as its own. These substances are called antigens and can include proteins on the surfaces of bacteria, fungi, and viruses. When antigens bind to specific receptors on immune cells, this triggers a series of processes in the body. Over time, the body learns how to fight off the pathogen after initially encountering it, and can quickly recognize and defend against it if it comes into contact with it again. This is known as immune memory.

Proteins are commonly found on the surface of the body's cells, but they typically do not trigger an immune response. However, in some cases, the immune system may mistake the body's own cells for foreign invaders and attack them. This is called an autoimmune response, and it can lead to the immune system attacking healthy, uninjured cells in the body.

The immune system can be divided into two main types: innate immunity and adaptive immunity. The immune system itself consists of two subsystems: the innate (non-specific) immune system and the adaptive (specific) immune system. When pathogens or other harmful substances trigger an immune response, these two subsystems work together closely to provide protection.

The innate immune system, also known as the non-specific immune system, provides a broad line of defense against dangerous microbes and chemicals. This system is activated immediately upon exposure to a pathogen, and it does not require prior exposure or specific knowledge of the pathogen to be effective.

The adaptive immune system, on the other hand, produces antibodies that are specifically designed to combat particular pathogens that the body has encountered before. This is called the specific or acquired immune response. The adaptive immune system can adapt and evolve to new viruses and bacteria, allowing the body to fight off new infections. This system requires prior exposure to the pathogen in order to develop immunity.

2.2. Immune System and Tumor

Tumor immunity develops during the early stages of cancer development and can affect the course of the disease and the patient's prognosis. However, tumor cells and the pro-inflammatory environment around them can suppress the immune system, preventing it from attacking cancer cells. This phenomenon has been observed not only at the primary tumor site but also in nearby immune regions, such as lymph nodes and the bone marrow, indicating that there are factors that can influence immune responses throughout the body.

The immune system uses antigens to distinguish between normal and tumor cells, and immune cells gather at the tumor site in response to inflammation in the microenvironment. To avoid detection by the immune system, tumors use various mechanisms to suppress immunity in their microenvironment.

2.2.1. Mechanisms of Immunological Tumor Recognition

Immune cells are equipped with a variety of tools to combat tumors. These can include taking up and presenting tumor antigens, producing cytokines that attract other immune cells, or directly destroying tumor cells. These actions can help to neutralize the tumor and prevent its growth or spread. Some immune responses, like phagocytosis, help to identify and clear damaged or dying cells. Efferocytosis, the removal of apoptotic cells, is a specialized function performed by different types of cells, including immature macrophages and dendritic cells. There are two types of cells that can carry out the process of phagocytosis. The first are professional phagocytes, which are specialized immune cells that are specifically designed for this purpose. Examples of professional phagocytes include neutrophils, macrophages, and dendritic cells. The second type are non-professional phagocytes, which are not specifically designed for this purpose but can still carry out phagocytosis when needed. Examples of non-professional phagocytes include fibroblasts and epithelial cells.

2.2.2. Phosphatidylserines

The inner (cytosolic) cell membranes contain phospholipids called phosphatidylserines. Phosphatidylserines are released onto the cell surface of apoptotic cells. As a result, the signal for phagocytes to absorb the apoptotic cells is received. Numerous receptors can recognize phosphatidylserine [7]. According to some studies, tumor cells may have more surface phosphatidylserines [8].

2.2.3. Calreticulin

Calreticulin is a protein that is expressed on the surface of cells during stress, which signals to nearby phagocytes that the cell is in need of help [9]. When calreticulin attaches to the phagocyte's CD91 receptor, this triggers the phagocyte to take up and engulf the target cell. However, normal cells with low levels of calreticulin on their surface are not targeted for phagocytosis because they also express the CD47 protein, which sends a signal to the phagocytes that the cell is not in need of help and should be left alone [10]. This helps to prevent healthy cells from being mistakenly targeted and destroyed by the immune system. However, some cancer cells show high levels of calreticulin on their surface, which can make them more susceptible to phagocytosis. These cells often also have high levels of CD47, which helps them avoid being targeted by phagocytes [11].

3. Polysaccharides and Tumor

Due to their anti-tumor properties and non-toxic attributes, bioactive macromolecules like polysaccharides are viewed as viable options to treat cancer [12]. Numerous studies revealed that polysaccharide extraction techniques had a big impact on their functions. Additionally, the structure of polysaccharides and their anti-tumor actions are strongly connected, with molecular alteration and high bioavailability having the potential to increase anti-tumor activity. Additionally, the majority of polysaccharides exhibited anti-tumor action mostly through mechanisms that inhibited angiogenesis, apoptosis, and immune regulation,

Specifically, the anticancer activity of polysaccharides has also been significantly influenced by their acetylation. The extension of polysaccharide chains can be altered by acetyl groups, which exposes the polysaccharides to hydroxyl groups and increases their solubility in water. The anti-tumor action of polysaccharides is significantly influenced by the quantity and placement of acetyl groups. When all of the O sites in polysaccharides are acetylated, the anticancer action is noticeably reduced and disappears. Because acetyl groups can alter polysaccharide molecules' orientation and lateral order, they can alter both the spatial arrangement of sugar chains and the activity of those chains.

There are several more detailed solutions for cancer treatment by using polysaccharides.

3.1. Mechanisms of Action

The mechanisms of action for polysaccharides and their derivatives are diverse, and this is reflected in their varied effects on tumor cells. The two main modes of action for polysaccharides are indirect (immunostimulant) and direct action, which can include inhibition of tumor growth and induction of apoptosis.

3.2. Indirect Action of the Immune System

Indirect action of the immune system involves the activation of T and B lymphocytes, macrophages, and natural killer (NK) cells, and relies on stimulating the body's own defense mechanisms [13]. Research has shown that many glucans can stimulate the production of cytokines such as interferons and interleukins, which are believed to be the initial line of defense and can effectively convert cells before more developed immune responses are set in motion [14].

Studies have shown that glucans trigger an immune response by binding to receptors on immune cells [15]. The CR3 receptor, also known by its various names such as Mac-1, CD11b/CD18, is a key component of the immune system. It is a type of receptor that is found on the surface of certain immune cells, including neutrophils, macrophages, NK cells, and K+T cells. This receptor is particularly important in recognizing and binding to glucans, which are complex sugars found on the surface of bacteria and fungi. The binding of the CR3 receptor to these glucans allows the immune cells to identify and target the invading pathogens, helping to protect the body from infection. It is possible that CR3 recognizes iC3b, a protein that is often found on the surface of cancer cells. Cytotoxicity is reduced when either of these components is missing, but when both CR3 and iC3b are attached to -glucan, it stimulates phagocyte activity. Polysaccharides are complex sugars that are composed of multiple saccharide units. They have been found to enhance the ability of immune cells to recognize tumor cells as abnormal and potentially harmful to the body. This can improve the body's ability to mount a defense against the tumor cells, resulting in a more effective immune response. The use of polysaccharides in this way can help to improve the overall effectiveness of the body's defense system against tumor cells.

4. Conclusions

Overall, polysaccharides have full potential in future tumor treatment, they have well-developed functions that can work as an anti-cancer. What's more, polysaccharides are healthier and have fewer side effects. Also, they are easy to get. When treating cancer, it is typically given together with other traditional pharmaceutical medications, such as those used to treat ovarian, lung, intestine, liver, and

stomach cancers. It improves the therapeutic process and, as a result, the survival rate of patients. Numerous studies have demonstrated that the injection of polysaccharides prevents metastasis as well as oncogenesis caused chemically or by viruses.

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