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Preparation and immunological activity of polysaccharides and their derivatives

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ABSTRACT

Polysaccharide is a kind of natural macromolecule polymer, which is widely existed in animals, plants and microorganisms, has a variety of biological activities, such as anti-tumor, anti-virus, anti-oxidation and immune regulation. Polysaccharides can affect macrophages, cells and other immune cells to improve the body's immune function, and have no toxic and side effects on normal cells, which make the polysaccharides receive widespread attention. In recent years, studies have shown that structural modification of polysaccharides can improve the immunological activity of polysaccharides. The common chemical modifications are sulfation, carboxymethylation, acetylation, phosphorylation, and so on. The chemical modification of polysaccharides and the immunomodulation of polysaccharides and polysaccharide derivatives were analyzed and discussed.

1. Introduction

Polysaccharides (PS), also known as polysaccharides, are compounds of more than 10 monosaccharides linked by glycosidic bonds, also known as polysaccharides, and are a class of macromolecular substances with a wide range of biological activities. Usually polysaccharides in the number of monosaccharides in more than 100, the molecular weight of up to tens of thousands or even millions. At present, up to thousands of polysaccharide compounds are isolated from natural products, which can be classified into plant polysaccharides, animal polysaccharides and microbial polysaccharides according to different sources. According to the modern chemical technology, the polysaccharide is chemically modified to obtain a series of bioactive polysaccharide derivatives. The commonly used methods include sulfation, carboxymethylation, acetylation, phosphorylation and the like. Studies have shown that some polysaccharides Immune activity after chemical modification has been significantly improved.

Polysaccharides and their derivatives can enhance the body immunity, aroused people's attention and attention day by day. Therefore, the research on polysaccharide and its derivatives in immunomodulation has broad application prospects. Herein, the immunomodulation of polysaccharides and their derivatives and the preparation of their derivatives were analyzed and discussed.

2. Preparation of polysaccharide derivatives

Studies have shown that polysaccharides have many biological activities such as anti-virus, anti-tumor, immune enhancement and anti-oxidation [1]. However, the biological activity of polysaccharides is related to its structure, so proper modification of polysaccharide structure becomes the focus of polysaccharide research One of them is also an important way to discover and develop polysaccharides. Structural modification of polysaccharide refers to the use of physical, chemical and other methods of molecular structure appropriate modification, resulting in changes in physical and chemical properties or even produces new activity of polysaccharide derivatives [2].

Common chemical modification methods are sulfation, carboxymethylation, acetylation, phosphorylation, *etc.*, of which sulfation and carboxymethylation in the production of more widely used.

2.1. The sulfated modification of polysaccharides

Sulfation of polysaccharides is one of the most studied methods in the chemical modification of polysaccharides. The principle is to add sulfate groups to the glycosyl groups of polysaccharides to change the structure of polysaccharides so as to increase their biological activity. It showed that sulfated polysaccharides could increase the phagocytosis of macrophages [3], promote macrophages to secrete NO, IL-6 and other interleukins, enhance immunomodulatory capacity [4]. Nagasawa method, Wolfrom method (chlorosulfonic acid-pyridine method) and sulfur trioxide-pyridine method are common methods for sulfating polysaccharides (Fig. 1). Different methods are used for different types

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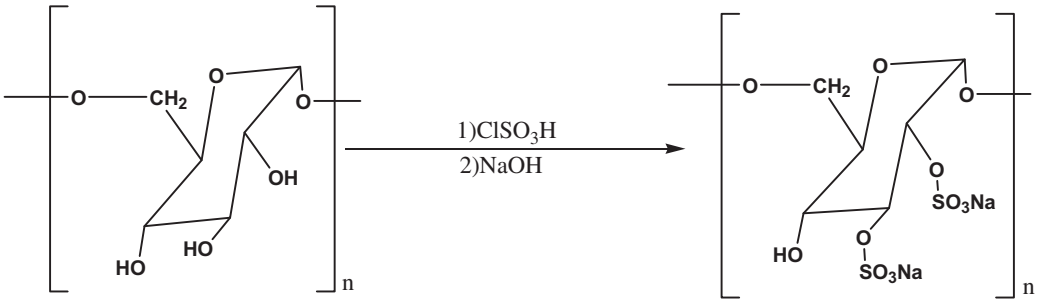

Fig. 1. The sulfation of polysaccharide with chlorosulfonic acid-pyridine.

of polysaccharides. Furan-type polysaccharides are commonly used by Nagasawa method, while pyran-type polysaccharides are often used by Wolfrom method [5].

2.2. The carboxymethylation modification of polysaccharides

Carboxymethylation of polysaccharides is the introduction of carboxymethyl to polysaccharide molecules (Fig. 2). The common method is to react polysaccharides with chloroacetic acid under basic conditions to obtain carboxymethylated polysaccharides. Studies have shown that most of the biologically active polysaccharides are water-soluble, and carboxylation can often increase the water-solubility of polysaccharides, and the degree of carboxymethyl substitution affects the biological activity of polysaccharides. It showed that the carboxymethylation could significantly enhance the ability to induce the mature of DCs when the carboxymethyl substitution degree was 0.5 to 0.6, which contributed to the function of immune regulation [6].

2.3. The acetylation of polysaccharides

Acetylation of polysaccharides (Fig. 3) makes more hydroxyl be exposed, thereby this can increase the solubility of polysaccharides in water, and is more conducive to the development of biological activity [7]. Acetylation commonly uses acetic acid and acetic anhydride as acylating agent, the reaction is often carried out in organic solvents such as formamide [8]. In recent years, it has shown that the acetylation of polysaccharides can improve the antioxidant, anti-tumor, immune regulation and other biological activities. It was found that the antioxidative and immunomodulatory activities of black *Ganoderma lucidum* polysaccharide were enhanced after acetylation modification [9].

2.4. The phosphorylation modification of polysaccharides

The hydroxyl groups on the polysaccharides are replaced by phosphate group, known as phosphorylation of polysaccharides. Phosphoric acid and its anhydride, phosphorus pentoxide (P_2O_5), phosphorus oxychloride ($POCl_3$), phosphate are commonly used for the phosphorylation of polysaccharides [10]. The polysaccharide phosphorylation was the first reported with phosphoric acid as phosphorylation agent under the catalytic condition of sulfuric acid. Because the glycoside bonds are easily hydrolyzed under strong acidic condition, the degradation of polysaccharide is serious, so this method is rarely used. Phosphorus pentaoxide is a commonly used phosphorylation agent. Taking into account the solubility of phosphorus pentoxide, the phosphorylation reaction of polysaccharide is carried out with methanesulfonic acid as a solvent under low temperature. Because the whole reaction is carried out in a strong acid environment, the degradation of polysaccharide is more serious, and the application of this method is restricted. Phosphorus oxychloride is a highly reactive phosphorylating agent that provides a high phosphorus content product. Phosphorus oxychloride as polysaccharide phosphorylation reagent will still lead to product degradation with the increase of hydrogen ion concentration in the reaction process even under the anhydrous condition. Therefore, alkaline reagents such as pyridine and triethylamine are often added to neutralize the hydrochloric acid produced during the reaction to inhibit the degradation of polysaccharide. The introduction of phosphate group will increase the immunosuppressive activity of polysaccharides. This advantage makes polysaccharide phosphorylation have great significance. It showed that dextran phosphorylation could significantly promote mouse spleen lymphocyte mitosis, enhance the expression of B lymphocytes and dendritic cells on the surface of CD86 and CD69, but also could promote IL-10 secretion [11]. The immunomodulatory activity of phosphorylated polysaccharides was related to the absorption of calcium ions [12].

2.5. The selenium modification of polysaccharides

Selenium is an essential element of life activity and plays an important role in cancer prevention, anti-aging and immune regulation. The biological activity of selenium polysaccharide is generally higher than polysaccharides and selenium. So, selenium modification of polysaccharides causes more and more attention [13]. At present, artificial synthesis of selenium polysaccharides mainly has three ways. First, the use of simple selenium or sodium selenate under mild conditions, such as

Fig. 2. The carboxymethylation of polysaccharide.