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Review

# Biological activities and pharmaceutical applications of polysaccharide from natural resources: A review

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ABSTRACT

Pharmacotherapy using natural substances can be currently regarded as a very promising future alternative to conventional therapy. As biological macromolecules, polysaccharide together with protein and polynucleotide, are extremely important biomacromoleules which play important roles in the growth and development of living organism. Polysaccharide is important component of higher plants, membrane of the animal cell and the cell wall of microbes. It is also closely related to the physiological functions. Recently, increasing attention has been paid on polysaccharides as an important class of bioactive natural products. Numerous researches have demonstrated the bioactivities of natural polysaccharides, which lead to the application of polysaccharides in the treatment of disease. In this paper, the various aspects of the investigation results of the bioactivities of polysaccharides were summarized, including its diversity pharmacological applications, such as immunoregulatory, anti-tumor, anti-virus, antioxidation, and hypoglycemic activity, and their application of polysaccharides in the treatment of disease are also discussed. We hope this review can offer some theoretical basis and inspiration for the mechanism study of the bioactivity of polysaccharides.

## 1. Introduction

Polysaccharide is a kind of natural macromolecular polymer, which is usually composed of more than 10 monosaccharides through glycosidic linkages in linear or branched chains, with a molecular weight of tens of thousands or even millions (Xie, Jin et al., 2016). It is widely exist in the plants, microorganism, algae, and animals. Similar to that of proteins and polynucleotides, polysaccharide is essential macromolecular in the life activities, and plays important roles in cell–cell communication, cell adhesion, and molecular recognition in the immune system (Dwek, 1996).

In recent years, polysaccharides isolated from natural resources, eg plant, animal, fungi, seaweed have attracted increasing attention due to their wide variety of pharmacological activities, such as antitumor, immunomodulation, anti-oxidation, and anti-inflammatory effects (Cho et al., 2015; Li, Li, Li et al., 2012; Li, Li, Fang et al., 2012; Xie et al., 2010). Specifically, arabinogalactan, galactomannan and pectic polysaccharides derived from higher plant, β-glucans and glycoproteins derived from mushroom, sulfated polysaccharides derived from seaweed have been all proved to possess antioxidant and immunomodulatory activities (Di et al., 2017; Petera et al., 2015; Schepetkin & Quinn, 2006; Wang, Liu et al., 2013; Wang, Wang et al., 2013). The (1 → 6)-α-D-glucan from *Dimocarpus longan* is believed to have excellent antitumor activities (Zhu et al., 2013), and (1 → 3)-β-D-glucan is known as good immunoregulator (Bohn & BeMiller, 1995). Recently, studies have shown that the mannoglucan and sulfated polysaccharides extract from *Bullacta exarata* possess a broad range of biological activities, including hepato-protective, antioxidant, anticancer, antihypertension, and hypocholesterolemic effects (Liu et al., 2013; Zhang, Luo, Bi, & Zhou, 2012; Zhang, Wu et al., 2012). Pharmacological studies have found that polysaccharides isolated from *Cordyceps sinensis* exhibit immunomodulatory, antitumor, hypoglycaemic, and anti-fibrosis activities (Nie, Cui, Xie, Phillips, & Phillips, 2013). Modern pharmacological studies demonstrated that *Sargassum pallidum* polysaccharides possessed wide-ranging beneficial health-promoting properties, such as antioxidant, anticancer, hypolipidemic, and immunomodulatory activities (Li, Li, Li et al., 2012; Li, Li, Fang et al., 2012; Ye, Wang, Zhou, Liu, & Zeng, 2008; Zhang, Luo et al., 2012). Owing to their safety and nontoxic properties, some of bioactive polysaccharides have been widely used in biochemical and medical practical applications (Huang, Wang, Zhou, Yang, & Wang, 2015; Yang & Zhang, 2009). *Astragalus* polysaccharide, *ginseng* polysaccharide, lentinan, fucoidan, *coriolus versicolor* polysaccharide and pachman are already polysaccharide drugs in domestic and foreign market.

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Bioactive polysaccharide has been a hot spot in each scientific field both at home and abroad (Zhang & Kang, 2017). In general, the application of polysaccharides can be divided into two categories: one is the use of polysaccharide easy to form gel, with high osmotic pressure, high viscosity and water absorption and other unique physical and chemical properties to prepare pharmaceutical materials, drug release agent and plasma substitutes; the other is the biological activities of polysaccharides, their antigenicity, anti-tumor and other biological function to prepare vaccines or new drugs. This article attempts to review the current development in the area of the bioactive polysaccharides isolated from natural sources and their application in fields of pharmacology and biological medicine, the various aspects of bioactivities of polysaccharides, such as immunoregulatory, anti-tumor, anti-virus, anti-inflammatory, antioxidation, hypoglycemic activity, and the effects of polysaccharides on the intestinal mucosal immune system are summarized, and their pharmacological application of polysaccharides in the treatment of disease are also discussed.

## 2. Overview of biological activities of polysaccharides

### 2.1. Antitumor activity

Cancer, one of the most serious diseases, is the leading cause high morbidity and mortality worldwide, accounting for more than 8.2 million deaths in recent years (Li, Gao et al., 2017; Li, Wang et al., 2017). Malignant tumor is a serious disease that is currently harmful to human health. Chemotherapy is one of the main methods used in systemic therapy with side effects. Recent accumulating evidences have demonstrated that polysaccharides isolated from botanical sources have also attracted a great deal of attention because of their anticancer activities (Fan et al., 2017; Xie et al., 2013; Yu et al., 2015; Zong, Cao, & Wang, 2012). In the search for novel compounds with antitumor properties, marine resources have become particular interest given their unique bioactivities (Li et al., 2014; Shao, Pei, Fang, & Sun, 2014; Shao, Chen, & Sun, 2014). Studies demonstrated that fucoidans exerted anti-cancer effects through mediated different signal pathway to regulating cell apoptosis, inhibiting tumor metastasis and potentiating the toxic effect of chemical drugs (Hyun, Kim, Kang, Kim, Boo, & Kwon, 2009; Jin, Song, Kim, Park, & Kwak, 2010; Kim, Park, Lee, & Park, 2010). Polysaccharides from Laminaria japonica showed significant anti-tumor activity against A375 and BGC823 cells and low cytotoxicity to vascular smooth muscle cells (Peng, Liu, Fang, Wu, & Zhang, 2012). Polysaccharides isolated from *Capsosiphon fulvescens* can inhibit the proliferation of AGS gastric cancer cells and induce apoptosis by inhibiting IGF-IR signaling and the PI3K/Akt pathway in AGS cells (Kwon & Nam, 2007). An acidic polysaccharide was isolated from *Gracilaria lemaneiformis* significantly inhibited the growth of transplanted H22 hepatoma *in vivo* (Fan, Wang et al., 2012). Polysaccharides isolated from *Grateloupia longifolia* were mainly composed of galactose and has antitumor properties by inhibiting vascularization in tumor masses (Zhang et al., 2006). Pectin is a family of complex polysaccharides, is a significant source of dietary fibre, have been shown to inhibitory activity towards several cancer cell lines (Maxwell et al., 2016). The antitumor activity of polysaccharides is affected by the size of the molecules, their form, degree of branching, and solubility in water (Ji et al., 2017; Shao, Chen et al., 2014; Shao, Pei et al., 2014). The anticancer properties of fucoidans are suggested to be defined by their chemical structure and notably related to their molecular weight (Yang et al., 2008). The anticancer activity of fucoidans depends on a combination of the several factors, such as an amount of sulfate groups, monosaccharide residues ratio, and type of sugar residues binding (Ermakova et al., 2011). Generally, the greater the molecular weight and the higher the water solubility of the polysaccharides, the greater is its antitumor activity (Ren, Perera, & Hemar, 2012).

The anti-tumor effects of polysaccharides mainly through three aspects, the mechanism has been summarized in Table 1. Inducting the apoptosis of tumor cells is considered useful in tumor growth and therapy as well as in the prevention of cancer (Tavakkol-Afshari, Brook, & Mousavi, 2008). Animal polysaccharides, which have significant antitumor effects, can exert antitumor effects mainly by inhibiting the growth of tumor cells, inducing apoptosis and enhancing immunity. However, plant polysaccharides and microbial polysaccharide mainly affect a variety of tumor cell through inhibiting tumor growth, inducing apoptosis, enhancing immune function and synergistic chemotherapy drugs and other ways. Lentinan is a typical T cell activator that enhances the immune function of T cells, macrophages, natural killer cells and other immune cells and enhances the phagocytosis of immune cells to play an anti-tumor effect (Zhang, Li, Wang, Zhang, & Cheung, 2011). A polysaccharide from the root of *Sanguisorba officinalis* L. can play its antitumor effect by restoring the immunity of mice that are inhibited by tumor cells (Cai et al., 2012). Polysaccharopeptide (PSP) derives from the medicinal mushroom *Coriolus versicolor* has arrested the Molt 4 leukemic cells in the S-phase and finally cause apoptosis (Lee, Yang, & Wan, 2006). *Ganoderma lucidum* (*G. lucidum*) polysaccharide can inhibit the growth of human breast malignant carcinoma cells MT-1, reduce the expression of Erk, through the Erk signaling pathway to inhibit tumor cell proliferation (Xie et al., 2006). *G. lucidum* polysaccharide can activate macrophage cell, enhance the phagocytosis of macrophages in a dose-dependent manner, and inhibit the growth of human breast cancer cells MDA-MB-231 (Zhao, Dong, Chen, & Hu, 2010). The sulfated polysaccharide p-KG03 which is purified from the marine microalgae *Gyrodinium impudium* can induce nitric oxide (NO) production and stimulate the production of cytokines via the JNK dependent pathway in macrophages to prevent tumor cell growth both *in vitro* and *in vivo* (Bae, Yim, Lee, & Pyo, 2006). Wu, Sun, and Wang (2017) isolated a polysaccharide (SpaTA) from *Sparganii Rhizoma*, it showed that SpaTA can induce apoptosis in ZR-75-1 breast cancer cells through ERα mediated apoptosis pathway. *Lycium barbarum* polysaccharides (LBP) shows antitumor activities against various types of cancer cells and inhibit tumor growth in nude mice through induction of apoptosis and cell cycle arrest (Ke et al., 2011; Xie, Tang, Jin, Li, & Xie, 2016). Ke et al. (2011) reported that LBP could inhibit the growth of human bladder carcinoma cell line BIU87 and induce BIU87 apoptosis. The MD-fraction from *Grifola frondosa* has been proven to induce cancer cell apoptosis via activation of the BAK-1 gene (Soares et al., 2011). *Angelica sinensis* polysaccharides kill tumor cells by inducing apoptosis (Cao et al., 2010). *Astragalus* polysaccharide can increase the number of splenic lymphocytes of gastric cancer rats, increase the activity of IL-2 and NK cells, increase the levels of LgA, LgG and LgM in blood, and stimulate the immune activity of gastric cancer rats (Li, Chen, Wang, Tian, & Zhang, 2009). PC-3 human prostate cancer cells, HeLa human cervical cancer cells and A549 human lung cancer cells were significantly inhibited by the polysaccharides extracted from sporophyll of Korean brown seaweed *Undaria pinnatifida* (Synytsya et al., 2010). Therefore, inhibition of tumor cells and kill tumor cells represent promising strategies for developing novel drugs to effectively restrain the progression of cancer (Wei et al., 2012). Based on these encouraging observations, a great deal of effort has been focused on discovering anticancer polysaccharides and complexes for the development of effective therapeutics for various human cancers.

### 2.2. Immunoregulatory activity

Immunostimulation is regarded as one of the important body's defense strategies for preventing and fighting infections, inflammatory diseases, and cancer. Natural herbs extracts are widely used in daily life as medicine or health care products (Zhu et al., 2016). In recent years, natural resources extracts have attracted extensive attention. Especially polysaccharides have attracted impressive attention and play diverse and important roles in many biological processes due to their structural diversity, low toxicity and distinct biological activities, especially the regulation of immune system (Schepetkin & Quinn, 2006). Nowadays,