Chapter 14
Bioactivities

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Abstract Polysaccharides and proteins are representative natural biomacromolecules existing in animals, plants, and microorganisms. They are attracting a great attention of scholars worldwide due to their various healthy functions, such as immunomodulation, anti-tumor, anti-oxidative, hypoglycemic, and hypolipidemic activities. Besides the strong bioactivity, these natural polysaccharides and proteins are non-toxic and show no side effects. In recent decades, a large number of bioactive polysaccharides and proteins with different structure and bioactivity from natural resources have been extracted, purified, and characterized. The aim of this chapter is to summarize the bioactivities, active mechanisms, structure features, structure–activity relationships of natural polysaccharides, proteins, and their derivatives. Moreover, this chapter also presented the applications of some active natural biopolymers in foods and medicines.

Keywords Polysaccharide · Protein · Bioactivity · Structure–activity relationship

1 Introduction

The food hydrocolloid is an edible soft matter system, which determines the texture and flavor characteristics of food products (Van der Sman and Van der Goot 2009). In food processing, various food materials such as polysaccharides, proteins, lipids, emulsifiers, sugars, minerals, and water are often mixed and fabricated. Among these ingredients, polysaccharides and proteins are the most used materials, which not only acting as "building blocks" for designing food hydrocolloids, but also providing interface-stabilizing properties via the interaction with other molecules (Wijaya et al. 2017).

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Y. Fang et al. (eds.), *Food Hydrocolloids*,
https://doi.org/10.1007/978-981-16-0320-4_14

Polysaccharide is defined as carbohydrate polymers consisting of different monosaccharide linked by glycosidic bonds (Xie et al. 2016). Protein is a macromolecular compound, which is formed by the binding of peptide chains composed of amino acids. In recent decades, many natural polysaccharides and proteins have been extracted and purified from plants, animals, and microorganisms. In addition to the properties of food hydrocolloids, these natural macromolecules also possess many bioactivities, such as anti-tumor, immunomodulation, anti-oxidative, hypoglycemic, and hypolipidemic (Cho et al. 2015). Therefore, this chapter mainly introduces the bioactivities of natural hydrocolloids, including anti-tumor, immunomodulation, anti-oxidation, antimicrobial, hypoglycemic, and hypolipidemic effects. Moreover, the applications of these natural biomacromolecules in functional foods and medicines are presented in this chapter.

2 Bioactivities

In recent years, natural polysaccharides and proteins extracted from different materials have attracted increasing attention because of their wide bioactivities, such as anti-oxidation, immunomodulation, anti-tumor, antimicrobial, hypoglycemic, and hypolipidemic effects. Moreover, more and more evidence indicated that most of these bioactivities of polysaccharides and proteins are related to the immune system.

2.1 Anti-Tumor

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. According to the report released by the World Health Organization (WHO) 2018, cancer is one of the main causes of human death worldwide. Although there are many different types of antineoplastic drugs in clinic, these drugs not only have limited efficacy, but also have strong side effects. Since *Lentinan* was first recognized to have anti-tumor efficacy (Chihara et al. 1969), more and more studies on natural polysaccharides used in cancer treatment have been carried out in vitro and in vivo.

Up to date, a series of human carcinoma cell lines have been employed to investigate the anticancer activity of polysaccharides, such as the lung cancer cell line (A549 cell), the cervical carcinoma cell line (Hela cell), the gastric carcinoma cell line (BGC-823 cell), the breast carcinoma cell line (MCF-7 cell), the colon cancer cell line (HCT116 cell and HT29 cell), and the liver cancer cell line (HepG2 cell). In addition, some mouse-derived cancer cell lines were also used to evaluate the activity of polysaccharides. It has been suggested that the anti-tumor mechanisms of polysaccharides were possibly attributed to their inhibition of tumor cell proliferation, initiation of tumor cell apoptosis, and activation of immune system to kill tumor cells (Zong et al. 2012).

It has been reported that polysaccharides from *Dendrobium* (Yu et al. 2018), *Astragalus* (Zhai et al. 2018), *Lentinus edodes* (Ya 2017), *Ganoderma lucidum* (Mohan et al. 2017), and *Portulaca Oleracea L.* (Zhao et al. 2016) exhibited good inhibitory effects on HeLa cells proliferation. These anti-proliferation effects might be related to the increase in autophagic activity of HeLa cells via regulating the expression of some key proteins in mitochondria-mediated signaling pathway, such as beclin1, LC3, and p62 (Zhai et al. 2018). Polysaccharides extracted from *Houttuynia cordata* (Han et al. 2018), *Tremella* (Shi et al. 2018), *Sargassum integerrimum* (Liu et al. 2016), *Pleurotus nebrodensis* (Cui et al. 2016), *Auricularia polytricha* (Yu et al. 2014) exhibited strong activity to resist the proliferation of human A549 cells. Lin et al. (2018) reported that *Hedyotis diffusa* polysaccharides could induce the apoptosis of A549 cells via regulating caspase-3-dependent mitochondrial pathway. Wu et al. (2017) found that polysaccharide from *Glehnia littoralis* could inhibit A549 cell proliferation and migration via decreasing the expression of PCNA, leading to cell cycle arrested in S and G2/M phase. Luo et al. (2016) also found that *coix* polysaccharides had the function to inhibit the migration and invasion of A549 cells via down-regulating the expression of S100A4. S100A4, a member of the S100 family, is a sort of calcium binding protein with EF double helix domain. The S100A4 expresses in kinds of tumor and stem cells of human rather than normal somatocytes.

HepG2 is an immortalized cell line consisting of human liver carcinoma cells. It has been reported that polysaccharides extracted from *Phormidium versicolor* (Belhaj et al. 2018), *Ganoderma lucidum* (Yang et al. 2017), *Lentinus edodes* (Zhao et al. 2017), *Antrodia camphorata* (Li et al. 2009a, b), *Grifola frondosa* (Wang et al. 2013) showed strong ability to prevent the proliferation of HepG2 cells. Li et al. (2013a) reported that polysaccharide from *Phellinus linteus* could induce S-phase arrest in HepG2 cells via decreasing calreticulin expression and activating the P27kip1-cyclin A/D1/E-CDK2 pathway. Shen et al. (2014) found that polysaccharide from *Ganoderma lucidum mycelia* could induce HepG2 cells apoptosis via regulating the expression of miRNAs. Some algae polysaccharides have been proved to possess broad-spectrum antineoplastic effects. For instance, polysaccharides from *Sargassum plagiophyllum* and *Sargassum pallidum* showed strong inhibitory effects on the proliferation of HepG2 cells, A549 cells, and MGC-803 cells in vitro (Ye et al. 2008; Suresh et al. 2013).

β-glucans, a type of the most abundant polysaccharides in the cell wall of bacteria and fungus, are glucose polymers linked by 1→3 linear β-glycosidic bond (Chan et al. 2009). Over the last half-century, fungi-derived β-glucans have received great attention because of the potential medical and edible value all over the world. Lentinan is a representative β-glucan. It has been widely proved to have therapeutic effect on many kinds of tumors. In clinical trials, compared to chemotherapy alone, the addition of lentinan to standard chemotherapy could relieve the pain and prolong survival in patients with gastric cancer (Oba et al. 2009), pancreatic cancer (Shimizu et al. 1999), colorectal cancer (Hazama et al. 2009), liver cancer (Ina et al. 2016), breast Cancer (Taguchi 1983). A large number of cell and animal experiments have also proved these anti-tumor effects. For instance, lentinan has ability to inhibit proliferation and differentiation of cancer cells, such as human autologous tumor cell line (K562 cell) (Tani et al. 1993), human gastric cancer cell line (BGC823 cell) (Zhao et al. 2013), human pancreatic cancer cell line (BXPC-3 cell) (Qian et al. 2018), human cervical cancer cell line (Hela cell) (Qian et al. 2018), human breast cancer cell line (MCF-7 cell) (Yi et al. 2018), non-small cell lung cancer (Wang et al. 2020), human bladder cancer cell line (T24) (Bao et al. 2015), liver cancer cell line (H22 cell) (Yamamoto et al. 1989). Animal experiments demonstrated that lentinan could inhibit colitis-associated cancer (CAC) development via regulating TLR4/NF-kappaB signaling-mediated inflammatory responses in model mice (Liu et al. 2018).

β-glucans have also been reported to kill cancer cells directly. The anticancer mechanisms of these polysaccharides are mainly dependent on the ability of enhancement of host immune system, increase in the antioxidant capacity of host, up-regulation of phase I and phase II enzymes in metabolic transformation, and the detoxification of mutagenic compounds (Vannucci et al. 2013). Masuda et al. (2013) reported that both oral administration and intraperitoneal injection of β-glucans from *Grifola frondosa* could inhibit tumor growth via regulating the systemic immune response. Moreover, the possible mechanism was revealed that the *Grifola frondosa* β-glucans can induce systemic tumor-antigen specific T cell response via dectin-1-dependent activation of DCs, enhance the infiltration of the activated T cells into the tumor, and decrease number of tumor-caused immunosuppressive cells such as myeloid-derived suppressor cells and regulatory T cells, thus leading to the anti-tumor activity. Yeast β-glucans, extracted from by-product yeast of beer production, have been known to exhibit anti-tumor activities by potentiating host immunity (Suphantharika et al. 2003).

In recent years, a large number of anticancer peptides have been identified from plant-derived proteins. For instance, corn peptides can induce the apoptosis of HepG2 cells by increasing caspase-3 expression (Díaz-Gómez et al. 2018). The lunasin peptide from soybean has the ability to resist skin cancer (Hernandez-Ledesma et al. 2009). The potato protein was found to suppress the proliferation of mouse melanoma B16 cells (Sun et al. 2013). Kannan et al. have extracted a pentapeptide (Glu-Gly-Arg-Pro-Arg) from rice bran and proved that it had the ability against the proliferation of colon cancer cells (Kannan et al. 2010). It has been reported that peptides derived from fish proteins have the inhibitory effect on MCF-7 cells in a dose-dependent manner (Hsu et al. 2011). Nongonierma and FitzGerald (2016) also found that milk protein-derived peptides exhibited anti-proliferative activity to tumor cells.

2.2 Immunoregulation

The immune system is a complex network of cells, tissues, and organs that work together to protect the body from harmful substances and organisms and defend against disease. However, when the immune system is disorder, autoimmune

Table 14.1 Immunomodulatory effects of some polysaccharides on macrophages

Source	Mice type	Cell type	Effects on immune cells	References
Ganoderma atrum	–	RAW264.7	Phagocytosis ↑, NO ↑, TNF-α↑, IL-1β ↑	Yu et al. (2013)
Dendrobium officinale	–	RAW264.7	Phagocytosis ↑, NO ↑	Xia et al. (2012)
Astragalus membranaceus	H22 tumor-bearing mice	H22	IL-2↑, IL-12↑ TNF-α ↑, IL-10↓	Yang et al. (2013)
Mushroom sclerotia	Male BALB/c mice and athymic BALB/c nude mice	–	IL-13↑, IL-17↑, IFN-γ↑	Wong et al. (2011)
Grifola frondosa	–	HepG-2	NO ↑, TNF-α↑, IL-1β ↑	Mao et al. (2015)
Inonotus obliquus	–	SGC-7901	TNF-α↑,	Fan et al. (2012a, b)
Porphyra haitanensis	A BALB/c murine	RAW264.7 DC Tregs	Phagocytosis ↑, TNF-α ↑, NO↑, IL-10↑, IL-6↑	Liu et al. (2017a, b)
Dictyophora indusiata	–	RAW 264.7	TNF-α↑, NO↑,(IL)-6↑	Liao et al. (2015)
Ganoderma lucidum	–	CD	–	Lai et al. (2010)
Prunella vulgaris	–	RAW 264.7	NO↑, TNF-α↑, (IL)-6↑	Li et al. (2015)
Longan pulp	–	Splenic cells	Proliferation↑	Yi et al. (2012)
Cordyceps sinensis	–	RAW 264.7	TNF-α↑, (IL)-6↑, IL-10↑, IL-1α↑	Wu et al. (2014)
Panax Ginseng	–	DC	Proliferation↑, IL-12 ↑, TNF-α↑	Kim et al. (2010)
Laminaria japonica	–	RAW264.7	NO↑, TNF-α↑, IL-1β↑, IL-6↑, IL-10 ↑	Fang et al. (2015)

diseases, inflammatory diseases, and cancer will happen in the body. Many natural polysaccharides have exhibited the ability to affect the immune system via modulating the immune functions including ROS production, cytokine/chemokine production, cell proliferation, and so on (Table 14.1). Therefore, polysaccharide is considered as a potential immunomodulator with great development prospects (Schepetkin and Quinn 2006). Figure 14.1 shows the possible signaling pathways involved in macrophage activation by polysaccharides (Schepetkin and Quinn 2006). It is known that the anti-tumor activity of polysaccharide is partly related to the enhancement of immune system.

The host defense mechanism consists of innate immunity and adaptive immunity, where the innate immunity is the first line of defense mediated the initial protection against infections. It is known that the innate immune system mainly contains macrophages, monocytes, granulocytes, and humoral elements. Among these

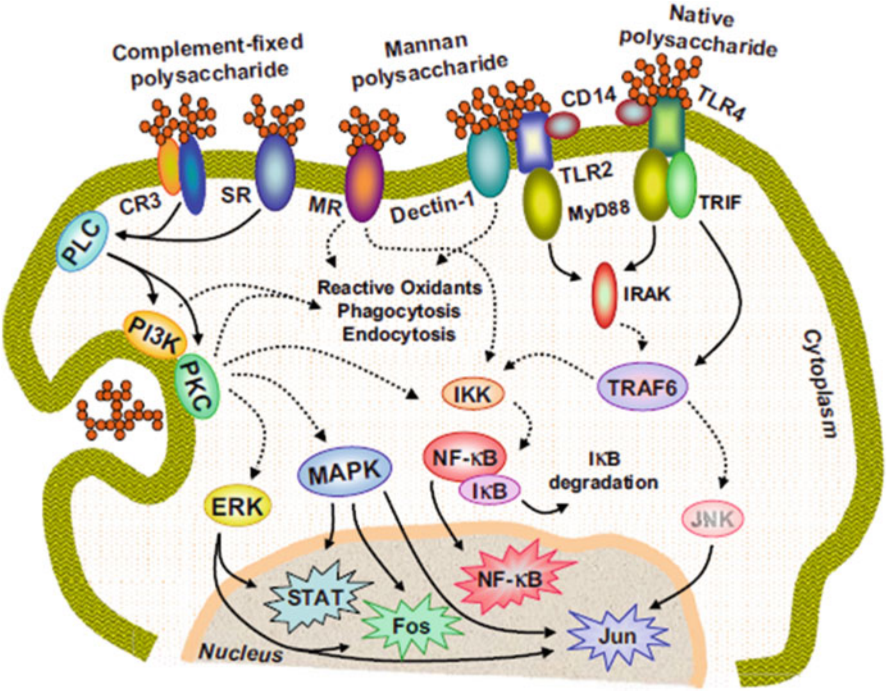

Fig. 14.1 Schematic model of potential signaling pathways involved in macrophage activation by polysaccharides. Reproduction with permission from (Schepetkin and Quinn 2006), Copyright 2006 Elsevier

components, macrophages are reported to exhibit various biological functions, such as chemotaxis, surveillance, phagocytosis, and destruction of targeted organisms, indicating the macrophages activation might be a hopeful strategy to resist diseases (José et al. 2007). It has been reported that *Juniperus scopolorum* polysaccharides could increase macrophage cytotoxic activity against tumor cells and microorganisms, activate phagocytic activity, and enhance the secretion of cytokines and chemokines, such as tumor necrosis factor (TNF-α), interleukin (IL)-1, IL-6, IL-8, IL-12, interferon gamma (IFN-γ), and IFN-2 (Chen et al. 2010a, b; Schepetkin et al. 2005). Polysaccharide from *Lycium barbarum* could activate macrophages via regulating the transcription factors AP-1 and NF-κB to induce TNF-α production and up-regulating the expression of MHC class II costimulatory molecules, resulting in the enhancement of innate immunity (Chen et al. 2008). Those phenomenons indicated that macrophage activation is required for the activation of innate immune system (Plüddemann et al. 2011). For these events, the pattern recognition receptors (PRRs) are required for these cells to recognize stimulators, triggering the activation of signaling pathways and the synthesis of pro-inflammatory cytokines (Kumar et al. 2011). Toll-like receptors (TLRs), the important PRRs, are existed on plasma membrane (Kawai and Akira 2010). It has been reported that macrophage activation induced by polysaccharides involves TLRs mediated recognition (Li et al. 2011). Figueiredo et al. (2012) have evidenced that TLR2 and TLR4 were the receptors involved in the recognition of *fungal* polysaccharides. Ferwerda et al. (2008) reported that the *saccharomyces cerevisiae* cell wall polysaccharide (Zymosan) has function to induce macrophages to release cytokines by the recognition of TLR2, TLR4, and Dectin-1. Nuclear factor κB (NF-κB) and mitogen-activated protein kinases (MAPK) are the key proteins in the downstream signaling pathway of TLR, which play important role in the host defenses via regulating the expression of multiple inflammatory and immune genes (DiDonato et al. 2012). With respect to MAPKs, mammalian cells expressed three representative MAPK pathways, containing C-Jun-N-terminal kinase (JNK), extracellular signal regulated kinase (ERK1/2), and p38. In recent years, the immunostimulatory activity mechanisms of polysaccharides have been widely studied. Results suggested that the regulation of intracellular signaling pathways is essential for the activation of macrophages (Diao et al. 2014; Zhang et al. 2014; Maeda et al. 2012). Extracellular polysaccharide LBP32 from *Bacillus sp.* strain was reported to inhibit LPS-induced production of pro-inflammatory cytokines via attenuating the phosphorylation of P38 and JNK, but not ERK1/2 (Diao et al. 2014). *Lycium barbarum* polysaccharide (LBPF4-OL) was found to have the ability to promote the secretion of TNF-α and IL-1β via inhibiting JNK and ERK1/2 MAPK phosphorylation and increasing the phosphorylation of p38-MAPK (Zhang et al. 2014). The sulfated polysaccharide SP1 from *Caulerpa lentillifera* had the function to activate macrophages and enhance NO production via regulating NF-κB and P38 MAPK signaling pathways (Maeda et al. 2012). These results demonstrated that various polysaccharides can exert their biological activities through regulating different signaling pathways. The inflammatory response has been reported to be highly dependent on MAPK signaling pathways via activating its downstream cytosolic proteins and nuclear transcriptional factors (Arthur and Ley 2013). NF-κB is a ubiquitous transcription factor, which plays a critical role in the host defenses via regulating the expression of multiple inflammatory and immune genes (DiDonato et al. 2012). In unstimulated cells, NF-κB locates in cytoplasm and combines with inhibitory proteins to form an inactive trimer (p50-p65-IκB). When cells are stimulated, IκBs will be phosphorylated by IκB kinase, leading to IκB degradation and translocation of NF-κB to the nucleus for binding to its cognate DNA in the regulation region of a variety of genes (He et al. 2013). It has been reported that the ability of some polysaccharides to activate macrophages is dependent on their level to the activation of NF-κB pathway (Zhang et al. 2011; Yu et al. 2013).

Lymphocyte is considered as a mediator of innate and adaptive immunity. Shriner et al. (2010) reported that *pneumococcal polysaccharid*e could stimulate the proliferation of IL-7-driven B lymphocytes, regulate their cytokine production, and restore impaired T cell by immune response. Among the specialized cell subsets of the innate immune system, DCs are the critical sensors via expressing various pattern recognition receptors (Steinman and Banchereau 2007). In particular, TLRs and cytosolic sensors for DNA and RNA recognition expressed by DCs use endogenous host elements carrying microbial components (such as the alarmin HMGB1), pathogen associated molecular patterns, and/or nucleic acids to stimulate intrinsic apoptotic pathways to generate protective immune responses (Peng et al. 2005; Poeck et al. 2008; Besch et al. 2009). During this process, polysaccharide was found to regulate the immunity via inducing DC maturation. For example, *Astragalus* polysaccharides could induce the differentiation of DCs to CD11c^{high}CD45RB^{low} DCs by shifting of Th2 to Th1, resulting in the enhancement of T lymphocyte immune function in vitro (Liu et al. 2011a). *Achyranthes bidentata* polysaccharide was reported to enhance DC maturation and function, supplying extra IL-12 and MHC class II molecules to up-regulating antigen presentation, activating CD4+ T cell, and thus leading to an enhancement of DC-CD4+ T cell (Zou et al. 2011). Meng et al. (2011) reported that polysaccharides from *Ganoderma lucidum* could promote effective activation of murine DCs in the immune response via up-regulating the expression of CD86, CD40, and MHC II and down-regulation of acid phosphatases.

In the past decades, the structure–activity relationships of immunomodulatory polysaccharides have been studied, indicating the interaction of immunostimulatory polysaccharides with cell receptors may trigger signaling pathways and thereby result in the induction of gene transcription (Ferreira et al. 2015a, b). A *Houttuynia cordata* pectic polysaccharide (HCP-2) with a linear chain of 1,4-linked α-D-galacturonic acid residues has been reported to increase the secretion of MIP-1α, MIP-1β, TNF-α, IL-1β, and RANTES in human peripheral blood mononuclear cells via regulating TLR-4 mediated signaling (Cheng et al. 2014). Bose et al. (2014) reported that 1,3-linked β-D-glucans could activate innate immune functions via regulating Dectin-1 and CR3 mediated signaling pathways. SR has been shown to be the pattern recognition receptor of fucoidan. Guo et al. (2009) found that a 1,3-linked glucan from spores could be recognized by dectin-1 on macrophages and thereby possess the biological activities. These results suggested that what is polysaccharide's pattern recognition receptor might be determined by the structure of polysaccharide. Lo et al. (2007) suggested that galactose, mannose, xylose, and arabinose played an important role in the stimulation of macrophages, but not glucose. The residues of 1,4-lined β-D-Rha*p* and 1,5-lined α-L-Araf were reported to be important for lymphocytes activation (Yang et al. 2012). The 1,4-linked mannose and glucose was reported to be the important elements for macrophages activation by a purified *Laminaria japonica* polysaccharide LJP-31 (Fang et al. 2015).

In recent years, some immunomodulatory peptides have been prepared from food proteins (Agyei and Danquah 2012). Otani et al. (2003) reported that phosphopeptides from casein could stimulate gastrointestinal tracts of mice to release immunoglobulin A. Pan et al. (2013a) revealed that peptide from milk protein exhibits immunomodulatory property in ICR mice. After modification with dicarbonyl methylglyoxyl, ovalbumin has the ability to stimulate immune cells to release tumor necrosis factor (TNF) alpha (Fan et al. 2003). The immunogenic ovalbumin peptides have been employed to enhance the immune response of different cancer patients (Vidovic et al. 2002; Goldberg et al. 2003). Some fish protein-derived immune peptides have also been identified in recent years (Yang et al. 2009; Hou et al. 2016). Sheu et al. (2004) have separated an immunomodulatory protein from the Jew's Ear mushroom *Auricularia polytricha*. Some peptides extracted from macroalgae were also reported to exhibit immunomodulatory activity via regulating the nuclear factor kappa B (NF-κB) pathway (Ahn et al. 2011).

2.3 Anti-Oxidation

Oxidative damage of biomolecules triggers not only physiological process of aging, but also causes various physiological functional disorders, leading to serious health problem ultimately (Harman 1993). In theory, antioxidants might have a positive effect on our health because they have ability to clear free radicals from human body. As is well known, free radicals can attack macromolecules such as proteins, membrane lipids, and DNA, leading to many health problems (i.e., cancer, neurodegenerative diseases, and diabetes mellitus) via damaging cells and tissues (Lim et al. 2014). Reactive nitrogen species (RNS) and reactive oxygen species (ROS) are free radicals that are formed during the normal metabolism of cells, which can be removed by cellular anti-oxidative defense systems, such as glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD). Under normal physiological conditions, the generation and elimination of RNS and ROS are balanced. Once this balance is broken, either by the overproduction of ROS and RNS, or by the damage in anti-oxidative system, oxidative stress will occur (Klaus et al. 2011; Sun et al. 2010). In food industries, some synthetic commercial antioxidants such as tertbutylhydroquinone (TBHQ), butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), and propyl gallate (PG) have been extensively used to reduce the oxidation and peroxidation damage. However, these antioxidants have potential hazards to human health (Nagaoka et al. 2010). Therefore, screening antioxidants from natural resources is always a hot topic (Peña-Ramos and Xiong 2002). Natural polysaccharides have attracted extensive attention and are proposed to be the potential resource of novel antioxidants due to their low toxicity and excellent anti-oxidation. Algal polysaccharides have been demonstrated as a scavenger of free radicals for the prevention of oxidative damage in vivo (Cristina Diaz et al. 2017).

In general, the polysaccharide eliminates free radicals through four aspect, including: (1) Hydrogen atoms on the structure of polysaccharides react with free radicals to form water, and the single electrons generated by the reaction can be further reduced. (2) Polysaccharides capture free radicals produced in lipid reactions or chelate with metal ions, which are important factors for the formation of free radicals. (3) Polysaccharides enhance the activity of some antioxidant enzymes. (4) Polysaccharides indirectly achieve antioxidant effect by regulating immunity. As shown in Table 14.2, β-glucan extracted from mushrooms and yeast have been reported to be the potential antioxidants. Three polysaccharides isolated from *Ganoderma lucidum* (GLP-H, GLP-V, and GLP-F) were found to possess the stronger radical scavenging activities (Fan et al. 2012a, b). *Astragalus*

Table 14.2 Antioxidants activity of β-glucan

Source	Antioxidant activity	References
Jinqian mushroom	ABT radical scavenging activity was 63.96% at 5 mg/mL DPPH scavenging ratio was 89.84% at 5 mg/mL Iron chelating effect was 14.06% at 5 mg/mL Hydroxyl radical scavenging activity was 24.30% at 5 mg/mL	Liu et al. (2014a, b)
Polyporus dermoporus	Hydroxyl radicals inhibition was 96% at 267 μg/mL Lipid peroxidation inhibition was 42.9% at 67 μg/mL Superoxide inhibition was 83.3% at 67 μg/mL	Dore et al. (2014)
Saccharomyces cerevisiae	Decreasing the formation of RBARS in LPS stimulated human blood platelets Decreasing the formation of O_2 in LPS stimulated human blood platelets	Saluk et al. (2013)
Geastrum saccatum mushroom	Inhibition of the formation of hydroxyl radicals in a dose-dependent manner	Guerra Dore et al. (2007)
Pleurotus ostreatus	The antioxidant enzymes activity, ferric reducing activity, and ascorbate concentration in human red blood cells hemolysates were markedly increased	Pietrzycka et al. (2006)
Lentinus edodes	Inhibition of lipid peroxidation, as well as a strong hydroxyl radical scavenging activity and superoxide radical scavenging activity	Feng et al. (2010)
Yeast	The level of glutathione was replenished and myeloperoxidase activity was suppressed in a rat model of sepsis	Sener et al. (2005)

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polysaccharides were reported to inhibit the generation of ROS via suppressing the NF-κB signal pathway (Xue et al. 2015). When the mice were orally administrated with extracellular polysaccharides of *Morchella esculenta*, the activity of SOD and GSH-Px were elevated in the blood, heart, liver, spleen, and kidney of mice (Meng 2010).

It has been reported that some compounds such as proteins, peptides, pigments, polyphenols, and flavones could bind to polysaccharides. Compared to the polysaccharides, these complexes have stronger antioxidant activity. For instance, the antioxidant effects of tea polysaccharides (TPS)-protein conjugates are dose-dependent on the protein content (Nie et al. 2008). In addition, the in vivo and in vitro antioxidant activities of crude tea polysaccharides were found to be better than that of tea polysaccharide fraction, which can be interpreted by the relatively higher proportion of tea pigments, vitamins, tea polyphenols, and other antioxidant components in the cruder fractions (Zhou et al. 2007). Moreover, Zhang et al. (2016a, b, c) suggested that the antioxidant activity of polysaccharides from *Ganoderma atrum* (PSG) was depended on the content of phenolic compounds/ proteins.

It is a fact that the antioxidant activity of polysaccharides is closely correlated with their structural parameters, such as solubility, degree of substitution, degree of branching, molecular weight, monosaccharide composition, solution conformation, and functional groups. Jing et al. (2009) reported that phosphorylated modification could enhance the ability of fucoidan to scavenge hydroxyl and superoxide radicals. The possible mechanism might be that the phosphate is a polyelectrolyte group and could activate the hydrogen atom of the anomeric carbon.

The acetylated modification was reported to enhance the ability of mushroom *Inonotus obliquus* polysaccharides to inhibit lipid peroxidation via affecting the conformation of polysaccharides (Ma et al. 2012). The carboxymethylated modification can increase the water solubility and antioxidant activity of β-(1,3)-glucan from the sclerotium of *Poria coco* via changing the flexibility of polysaccharides chain (Wang and Zhang 2006). Molecular weight was an important factor that can influence the antioxidant ability of polysaccharides. Yan et al. (2009) used an acidic solution to hydrolyze the exopolysaccharide from *Cordyceps sinensis*, giving a degraded exopolysaccharide. Results showed that the degraded products had much higher antioxidant activity than that of original polysaccharide.

2.4 Antimicrobial

β-glucans are ubiquitously found in both bacterial and fungal cell walls and have been implicated in the initiation of antimicrobial immune response. It has been proved that the (1→3)-β-D glucan with (1→6)-β-D branches could act as antimicrobial agent in vivo (Ferreira et al. 2015a, b). Hetland et al. (2000) obtained a soluble branched β-(1,3)-glucan (SSG) from the culture broth of the fungus *Sclerotinia sclerotiorum* IFO9395. Results exhibited that the oral administration of SSG could help the mice to resist the infection of Streptococcus pneumonia sero type 4 and 6B. Faccin et al. (2007) reported that β-glucan from the fruiting body of *Agaricus brasiliensis* mushrooms exhibited an antiviral activity against poliovirus typ1 in HEp-2 cells. Peter et al. found that oral administration of β-glucan (glucan phosphate, scleroglucan, and laminarin) at a dose of 1 mg/kg/day could enhance the survival of mice infected with *S. aureus* or *Candida albicans.* In Sharma's study (Sharma et al. 2015), it was found that both extracellular polysaccharide (EPS) and intracellular polysaccharides (IPS) extracted from *Cordyceps* species exhibited obvious antimicrobial activities against all pathogenic microorganism tested. Moreover, IPS showed stronger antimicrobial activity than that of EPS. The polysaccharides extracted from *Ganoderma* species have also been proved to exhibit spectral antimicrobial activity (Table 14.3). It has been found that the acidic polysaccharide CS-F2 from green tea had a selective anti-adhesive activity against some pathogenic bacteria and strongly inhibited the growth of gastric and skin pathogenic bacteria.

More and more evidences exhibited that some proteins and their derived peptides from plants, mammals, insects, and bacteria also have antimicrobial activity against eukaryotes, fungi, bacteria, and viruses (Zhu et al. 2019). The first antimicrobial peptide was found from the moth *Hyalophora cecropia* in 1981 (Steiner et al. 1981). A lectin-like peptide from red lentil seeds exhibited antimicrobial activity against

Table 14.3 The antimicrobial activity of polysaccharides

Specie	Microorganisms used	Type of assay	References
Ganoderma lucidum	*Bacillus subtilis*, *Bacillus cereus*, *Erwinia carotovora*, *Escherichia coli*, *Penicillium digitatum*, *Botrytis cinerea*	In vitro	Bai et al. (2008)
Ganoderma applanatum	*Acrobacter aerogenes*, *Acitenobacter aerogenes*, *Arthrobacter citreus*, *Bacillus brevis*, *B. subtilis*, *Corynebacterium insidiosum*, *Clostridium pasteurianum*, *Escherichia coli*, *Micrococcus roseus, Mycobacterium phlei*, *Proteus vulgaris*, Sarcina lutea St	In vitro	Bhattacharyya et al. (2006)
Ganoderma formosanum	*Listeria monocytogenes*	In vivo	Wang et al. (2011)
Glucans	*Staphylococcus aureus* or *Candida albicans*	In vitro	Rice et al. (2005)
Schizophyllum	*Salmonella enterica serovar*	In vivo	Chen et al. (2008)
Oat	Herpes simplex virus 1	In vivo	Murphy et al. (2009)

Mycosphaerella arachidicola (Wang and Ng 2007). The defensin PDC1 peptide, a fermentation product of corn using *Pichia pastori*s and *Escherichia coli* as the mixed strain, has an ability to inhibit the growth of *Fusarium graminearum* (Kant et al. 2009). Using *Bacillus subtilis* sck-2 to ferment soybean paste, a peptide was obtained and exhibited antibacterial activity against *Bacillus cereus* (Yeo et al. 2012). These antimicrobial peptides can be considered as the good candidates for food antisepsis.

2.5 *Hypoglycemic*

Diabetes mellitus (DM) is a group of metabolic disorders characterized by high blood sugar levels over a prolonged period. Symptoms of high blood sugar mainly include frequent urination, increased thirst, and increased hunger. If not treated in time, diabetes will cause many complications. Acute complications include hyperosmolar hyperglycemic state, diabetic ketoacidosis, or death. Serious long-term complications include cardiovascular disease, chronic kidney disease, foot ulcers, stroke, and damage to the eyes. According to the International Diabetes Federation (IDF) in 2017, an estimated 425 million individuals are living with DM. At present, the main treatment of diabetes is oral hypoglycemic drugs and insulin injection. However, long-term use of these drugs could lead to insulin resistance and other side effects. Thus, it is quite necessary to develop helpful, innoxious, and inexpensive drugs for DM patients. As the non-toxic biological

Table 14.4 The anti-diabetic effects of polysaccharides

Source	Model	Effects and mechanisms	References
Opuntia dillenii	STZ mice	Protecting the liver from peroxidation damage, maintaining tissue function, improving the sensitivity and response of target cells in diabetic mice to insulin	Zhao et al. (2011)
Tremella aurantia	KK-Ay mice	Reducing levels of insulin, total cholesterol and triglyceride in the mice blood, decreasing the level of plasma lipoperoxide	Kiho et al. (2001)
Phellinus linteus	NOD mice	Inhibiting the development of autoimmune diabetes by regulating cytokine expression	Kim et al. (2010)
Morus alba fruit	T2DM mice	Repairing of damaged pancreatic tissues of diabetic rats.	Jiao et al. (2017)
Lycium barbarum	T2DM mice	Increasing insulinogenic index	Cai et al. (2011)
Pleurotus ostreatus	STZ mice	Reducing the risk of oxidative damage by increasing catalase (CAT), glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) activities and decreasing malonaldehyde (MDA) level	Zhang et al. (2016a, b, c)
Portulaca oleracea L.	Alloxan-induced diabetic mice	Controlling blood glucose, and modulating the metabolism of glucose and blood lipid in diabetes mellitus mice	Li et al. (2009a, b)
Corn silk	T2DM	Regulating the levels of serum lipid profile, decreasing the levels of glycated serum protein, non-esterified fatty acid	Pan et al. (2017)
Hedysarum polybotrys	Alloxan-induced diabetic mice	Increasing insulin secretion, inhibiting lipid peroxidation, promoting the sensitivity to insulin, suppressing gluconeogenesis, and reducing the biosynthesis fatty acid, cholesterol, and cell cytokines related to insulin resistance	Hu et al. (2010)
Taxus cuspidata	STZ mice	Increasing the body weight of diabetic mice, and reversing the decrease of SOD and the increase of thiobarbituric acid reactive substances (TBARS) in kidney and liver of diabetic mice	Zhang et al. (2012)
Ganoderma lucidum	T2DM	Down-regulation of the hepatic glucose regulated enzyme mRNA levels via AMPK activation, improvement of insulin resistance and decrease of epididymal fat/BW ratio	Xiao et al. (2016)

macromolecules, natural polysaccharides were observed to have positive effects to treat DM (Huie and Di 2004; Zhou et al. 2007). Table 14.4 presents the anti-diabetic effects of different polysaccharides.

A polysaccharide (CSP-1) from *Cordyceps sinensis* consists of glucose, mannose, and galactose in a molar ratio of 1:0.6:0.75, and exhibited a significant drop in blood glucose level in both normal and streptozotocin (STZ)-diabetic animals. These results could be related to the increase in blood insulin level via the release of insulin from the residual pancreatic cells and/or CSP-1-induced the reduction of insulin metabolism in body (Li et al. 2006a, b). Another two purified polysaccharides (CS-F30 and CS-F10) from *Cordyceps sinensis mycelia* was also proved to have hypoglycemic effects on mice (Kiho et al. 1996, 1999). Compared to CSP-1, these two polysaccharides have different monosaccharide composition. In recent years, the hypoglycemic effect of tea polysaccharides (TPS) has also attracted much attention. Chen et al. (2010a, b) reported that the oral administration of TPS at 150 mg/kg/day can significantly reduce the blood glucose level in non-obese diabetic (NOD) mice. From TPS, two water-soluble polysaccharide fractions of TFP-1 and TFP-2 were obtained. The average molecular weight was determined to be 15.9×10^4 and 1.12×10^4 Da, respectively. Results showed that continuous administration of TFP-2 could dose-dependently decrease the blood glucose level in alloxan-induced diabetic mice by inhibiting α-amylase and α-glucosidase (Han et al. 2011a, b). Zhou et al. (2007) isolated a crude tea polysaccharides (CTP) and a tea polysaccharide fraction (TPF) from green tea. It was found that CTP and TPF have hypoglycemic effects on alloxan-induced diabetic mice. The hypoglycemic action of polysaccharides from oolong tea and black tea has also been investigated. Results exhibited that these tea polysaccharides could alleviate the diabetic mice and improve diabetes symptoms, indicating tea polysaccharides have good effects on the prevention of hyperglycemia (Nie et al. 2011).

Food-derived peptides have been reported to have antagonistic effects against glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) in type 2 diabetes via inhibiting the activity of Dipeptidyl peptidase IV (DPP-IV) (Matteucci and Giampietro 2009). So far, this active peptide has been isolated from corn, milk, soybean, rice, and other foods (Zhu et al. 2019; Mochida et al. 2010; Hira et al. 2009; Sanjukta and Rai 2016). The dipeptides and tripeptides isolated from whey proteins have been used as competitive inhibitors to interact with DPP-IV substrates (Gunnarsson et al. 2006). Recently, more attention have been paid on the application of marine bioactive peptides to treat type 2 diabetes. The peptides from *Porphyra dioica* were observed to have the inhibitory effect on DPP-IV (Stack et al. 2017). Three polypeptides (ILAP, LLAP, and MAGVDHI) with similar bioactivity were also isolated from macroalga *Palmaria palmata* (Harnedy et al. 2015).

2.6 Hypolipidemic

Hyperlipidemia is a lipid metabolic disorder characterized by the enhancement of blood total cholesterol (TC), low-density lipoprotein (LDL), very low-density lipoprotein-cholesterol (VLDL-C) and triglyceride (TG), with a concomitant decrease in the level of high-density lipoprotein-cholesterol (HDL-C) in the plasma. With the improvement of people's living standard and the change of dietary structure, the incidence of hyperlipidemia is increasing year by year (Chan et al. 2009). Hyperlipidemia is one of the main risk factors for inducting cardiovascular diseases, such as hypertension, atherosclerosis, and coronary heart disease (Rosenson et al. 2002).

In a meanwhile, lipid accumulation in liver (steatosis) can result in oxidative stress and inflammation, leading to the damage of liver (Esposito et al. 2002). Thus, how to reduce lipid level is one of most important clinical problems. At the present time, statins, nicotinic acid, and its derivatives are the most common lipid-lowering prescribed drugs. Although these drugs help in lowing lipids, their side effects are also enormous, such as headache, muscle pain, and nausea. Moreover, the long-term use of these drugs can increase the risk of type 2 diabetes (Hsu et al. 2015). In recent decades, more and more evidences exhibited that natural polysaccharides had the function to low lipids. For instance, *Enteromorpha prolifera* polysaccharides exhibited a high hypolipidemic action in high fat rats via decreasing the plasma LDL-C, TC, and TG levels and increasing HDL-C level (Teng et al. 2013). *Ganoderma lucidum* β-glucan was also reported to decrease the TC, TG, and LDL-C levels in the serum of diabetic mice, whereas the HDL-C level was increased (Li et al. 2011). Recently, significant in vivo studies testing, the efficacy of cereal β-glucans using animal and human subjects has led to health claims for this material in many industrialized countries. The soluble dietary fibers (i.e., β-glucan from cereal grains) are well accepted to be the polysaccharides with the ability to lower lipids (Pomeroy et al. 2001). Therefore, adding β-glucan-rich fiber products in the daily diet is now considered as an effective approach to lower lipids. Extensive efforts have been made to establish the relationship between the structure of cereal β-glucans and reduction of LDL-C levels (Lazaridou and Biliaderis 2004; Li et al. 2006a, b). Cereal β-glucans are linear homopolysaccharides formed by the linkage of β-D-glucopyranosyl units via (1→4)-β-linkage and separated by single (1→3)-β-linkages. They are the main component of water-soluble dietary fibers from cereals. The physiological activity of soluble β-glucan from cereal is closely related to its unique structure of (1→3)(1→4)-β-D-glucan. It was concluded that the LDL-C lowering effect and the ability to control blood glucose of cereal β-glucan may depend on its viscosity in solution, which is controlled by the M_W, structure, and concentration in the intestine (Wood 2007).

It has been reported that β-glucan can bind to the bile acid in intestinal lumen. This combination would reduce the circulation of bile acid liver and further stimulate the production of more bile acids from cholesterol. Moreover, β-glucan could be fermented in the large bowel by colonic bacteria, and producing the short-chain fatty acids. The short-chain fatty acids could be absorbed by portal vein, and inhibit hepatic cholesterol synthesis via regulating the activity of HMG-CoA reductase (a rate-limiting enzyme required for cholesterol biosynthesis), or increasing catabolism of LDL-cholesterol. Another phenomenon was observed that β-glucan reduced the concentration of postprandial serum insulin by delaying gastric emptying, leading to the inhibition of hepatic cholesterol production. It was also reported that β-glucan could interfere with the absorption of dietary fat via increasing intestinal viscosity (Bell et al. 1999).

2.7 Other Activities

Besides the healthy benefits mentioned above, some other bioactivities of polysaccharides and protein-related compounds have been studied in recent years, including antidiarrheal, anti-fatigue, anti-tussive, anti-analgesia, anti-allergic, and anti-dyszoospermia activities. Baek et al. (2010) evaluated the anti-diarrhea effect of *ginseng* polysaccharides in vitro using the model of rotavirus infection. Results showed that two pectic ginseng polysaccharides dose-dependently rescued the cell viability from rotavirus infection. Moreover, the prevention of polysaccharide on rotavirus was attributed to the inhibitory effects of rotaviral attachment to cells. In recent years, the anti-fatigue effect of polysaccharides extracted from different materials is gradually accepted by people (Jing et al. 2009). Pimentel et al. (2019) demonstrated that macroalgae-derived peptides and enzymes have protective effects on skin via eliminating free radicals and promoting moisture.

3 Structure Features

Chemical structure is the basis of polysaccharides and to exert their biological activity, including monosaccharide composition, monosaccharide arranging order, anomeric carbon configuration, glycoside bond types, branches, substituted groups, and the spatial conformation. It has been reported that most bioactive polysaccharides are mainly composed of glucose, fucose, galactose, arabinose, mannose, xylose, ribose, glucuronic acid, and galacturonic acid. According to the published literatures, the fungal derived polysaccharides have been found to be α-mannan, β-glucans and hetero-β-glucans, α-mannan-β-glucan complexes, heteroglycans, glycopeptides or glycoprotein and proteoglycan. The polysaccharides extracted from plants mainly include glucans, glucomannans, heteroglycans, arabinans, arabinogalactan, pectins, rhamnogalacturonan, and their sulfated or acetylated forms. Animal polysaccharides are mainly composed of glycosaminoglycan and sulfated glycosaminoglycan.

Although it is quite difficult to determine the structural variability of polysaccharides from different resources, a series of analytical methods have been established to achieve this. The high performance liquid chromatography (HPLC) is often performed to determine the molecular weight of polysaccharides. The infrared spectroscopy (IR), ultraviolet spectroscopy (UV), gas chromatography-mass spectrometry, NMR spectroscopy, periodate oxidation, partial acid hydrolysis, methylation, and periodate oxidation-Smith degradation are the common methods to analyze structural features of polysaccharides (Yang et al. 2009).

The chemical structure of natural polysaccharides is very complex. Table 14.5 showed the structure features of some polysaccharides extracted from different species. In most cases, one material could contain a variety of polysaccharides with different structures. Moreover, the same species growing in different places

Table 14.5 Structure features of polysaccharides from various sources. Reproduction with permission from (Nie et al. 2018), Copyright 2018 Elsevier

Source	Mw (Da)	Monosaccharide composition	Backbone	References
Pleurotus florida	180,000	Glucose	(1→6)-linked-β-D-Glc*p* (1→3,6)-linked-β-D-Glc*p*	Maji et al. (2012)
Auricularia polytricha	120,000	Glucose	1,3-β-glucan 1,3-α-glucan 1,4-α-glucan	Song and Du (2012)
Cistanche Deserticola Y. Ma	10,000	Glucose	1,4-linked-α-D-glucan	Dong et al. (2007)
Cordyceps sinensis	–	Glucose, Mannose, Galactose	(1→4)-linked-α-D-Glc*p*	Nie et al. (2011)
Ganoderma lucidum	83,000	Rhamnose, Galactose, Glucose	1,4-linked-α-D-Glc*p* 1,6-linked-β-D-Glc*p*	Bao et al. (2002a, b)
Ganoderma lucidum	200,000	Glucose, Mannose	1,3-,1,4-, 1,6-linked-β-D-Glc*p* 1,6-linked-β-D-Man*p*	Bao et al. (2002a, b)
Ophiopogon japonicus	35,200	Arabinose, Glucose, Galactose	1,4-linked-Glc*p* 1,6-linked-Glc*p* 1,4,6-linked-Glc*p*	Chen et al. (2011)
Lentinus squarrosulus (Mont.) Singer	196,000	Galactose, Glucose, Fucose	(1→4)-linked-α-D-Glc*p* (1→6)-linked-β-D-Glc*p* (1→4,6)-linked-D-Glc*p* (1→3,6)-linked-D-Glc*p*	Bhunia et al. (2010)
Dendrobium huoshanense	73,000	Glucose, Galactose, Xylose	1,4-linked-β-D-Glc*p* 1,6-linked-β-D-Glc*p* 1,4,6-linked-β-D-Glc*p*	Pan et al. (2013b)
Radix Astragali	1334,000	Rhamnose, Glucose Arabinose, Galactose, Galactose acid	1,4-linked-α-Glc*p* 1,4-linked-α-GalAp6Me1,2,4-linked-Rha*p* 1,3,6-linked-β-Gal*p*	Yin et al. (2012)

could contain different polysaccharides. It is also reported that the polysaccharides in different organs of the same species is also different in the structures. It has been observed that polysaccharides extracted from the spores of *Ganoderma lucidum* possessed a backbone of (1–3)-β-linked glucans (Bao et al. 2001). However, the backbone of fruit bodies polysaccharides was composed of 1,3-linked glucose, 1,6-linked glucose, 1,6-linked mannose, 1,4-linked glucose, and 1,6-linked galactose (Bao et al. 2002a, b).

For the preparation of natural polysaccharides, the extraction methods and extraction parameters are also critical factors affecting polysaccharide's structures and properties. For instance, Palacios et al. compared the effects of different extraction methods on the structure of polysaccharides from *Pleurotus ostreatus* mushroom. Results showed that the polysaccharides extracted by cold-water mainly consisted of 1–3-α-linked and 1–6-α-linked galactose. The polysaccharide extracted by hot-water was mainly composed of 1–4-α-linked glucose. However, the fraction extracted by hot-aqueous NaOH was mainly composed of 1–3-β-linked and 1–6-β-linked glucose (Palacios et al. 2012).

In addition to the natural factors, chemical modification can also change the polysaccharide's structure, leading to the variation of physicochemical properties and bioactivities (Fiorito et al. 2018). According to the published literatures, the acetylation, carboxymethylation, sulfation, phosphorylation, alkylation, and selenization have been employed to modify the structure of polysaccharides (Prashanth and Tharanathan 2007). Moreover, some modified polysaccharides have been developed into drug delivery systems (Shah et al. 2011).

In addition to the natural factors, polysaccharide derivatives also contribute to the structural diversity, which can also be classified as a semisynthetic polysaccharide. It has been reported that the effective chemical modification of this natural structure could improve the bioactivities and some key parameters, including solubility, bioavailability, and pharmacokinetics (Fiorito et al. 2018). Chemical modification can control the final structure of polysaccharides, and thus determining the specific biological functions. In addition, the chemical modification of polysaccharide structure mainly utilizes the polysaccharide's reactive groups, such as hydroxyl, carboxyl, and amino groups, to chemically introduce new functional groups. Chemical modification of polysaccharide includes sulfation, carboxymethylation, acetylation, alkylation, phosphorylation, and selenization. Some semisynthetic polysaccharides have been developed into various drug delivery systems.

In recent years, a large number of studies have been carried out on the structure–activity relationship of polysaccharides. Results exhibited that the activity of polysaccharides was mainly related to the molecular weight, chemical structure, and physical properties (Jin et al. 2012). The (1,3)-β-D-glucan from *Poria cocos* sclerotium is a water-insoluble polysaccharide and exhibited low bioactivity. After carboxymethylation, both the water solubility and bioactivity were enhanced (Wang et al. 2009). Di et al. (2017) reported that sulfated polysaccharides from *Gracilaria rubra* exerted immunologic activity by promoting the proliferation of RAW264.7 cells. Moreover, the activity was improved with the decrease of polysaccharide molecular weight. Chen et al. (2015) demonstrated that sulfated polysaccharide from *Ganoderma atrum* has the strongest immunological activity when the molecular weight was intermediate (4.0×10^{-6} Da). Zhang et al. (2005) found that the physicochemical property and steric conformation of polysaccharides from *Poria cocos* mycelia were changed by the introduction of sulfate groups, leading to the changes in the bioactivity of polysaccharides. Similarly, sulfated modification changed the structure and conformation of polysaccharides from *Hypsizygus marmoreus*, enhancing the ability of anticancer and immunity (Bao et al. 2010). The substitution degree of substituent groups also has a great influence on the biological activity of polysaccharides. For instance, chitosan with different substitution degree of sulfuric acid group exhibited different strength of immunoregulation ability (Yang et al. 2018). Liu et al. (2017a, b) investigated the structure–activity relationship of selenium-containing polysaccharide. Results showed that the anti-diabetic activity was improved with the increase of selenium content of *Catathelasma ventricosum* polysaccharide with triple helical structure. However, when the tri-helical structure was damaged, the anti-diabetic effect was decreased. With respect to the structure–activity relationship of proteins, it has been reported that the bioactivity of proteins was highly related to its structure characteristics, such as amino acid composition, amino acid sequence, molecular weight, and hydrophobicity (Silva et al. 2017).

4 Application

Because natural polysaccharides have wide biological activities and low toxicity, some of them have been successfully applied in fields of drugs and foods (Table 14.6). In the field of drugs, some polysaccharides such as Lentinan, *Astragalus* polysaccharide, Ginseng polysaccharide, Poria polysaccharide, and Chondroitin have been developed into injections, tablets, and capsules. In the field of foods, some polysaccharides have been used as the additives to endow new nutritional and healthy functions of foods. For instance, *Lycium barbarum* polysaccharides (LBPs) have been processed into different forms of functional foods, such as Goji beverage, Goji wine, Goji tea, Goji oral liquid, Goji tablet, Goji capsule, and Goji granules. Among these healthy foods, the Goji capsule and Goji oral liquid were popular in the public. Long-term use of Goji capsule and Goji oral liquid can enhance the immunity, improve sleep, protect liver, and reduce fatigue (Wu et al. 2018).

Proteins are the important components in foods. Since soybean protein isolate was produced in large-scale in 1958, the application of food protein becomes more and more pluralistic. In the field of traditional foods, the soybean protein, milk protein, egg protein, meat protein, and nut protein have been applied in beverage food, baby food, baked food, pastry, and meat products. In the field of non-traditional foods, the protein has been used as a main component to prepare reproduced foods and simulated foods, such as soybean protein beef, plant protein chicken, vegetarian ham, vegetarian sausage, and imitation meat hamburger. Moreover, food protein widely applied in cosmetics and biomedicine.

5 Conclusions and Future Prospects

In recent decades, the research of bioactive polysaccharides has made some important progress and has been widely used in pharmaceutical, biochemical cosmetic, and functional food industries. However, due to the limitations of existing experimental methods and the complexity of their structure, research about polysaccharides is still far behind than that of proteins and nucleic acids. Although the functional properties of polysaccharides have been widely studied, the mechanism of their actions is still unknown. One of the main reasons is that the structural

Table 14.6 Practical Applications of Polysaccharides

Applications areas	Polysaccharides	Practical applications	Bioactivities	References
Clinical drugs and medicines	*Astragalus polysaccharide*	Astragalus polysaccharide injection	Immunomodulation; Antioxidant; Anti-hypertensive	Xu (2012) Zhang et al. (2016a, b, c)
	Ginseng polysaccharide	Ginseng polysaccharide injection	Anti-tumor immunity	Xu (2015)
	Lentinan polysaccharide	Lentinan injection; Lentinan capsules	Immunomodulation; Anti-tumor	Wang (2012) Wang et al. (2013)
	Poria polysaccharide	Poria polysaccharide oral solution	Anti-gastric cancer	Yang et al. (2017) Hou and Luo (2017)
	Chondroitin sulfate	Chondroitin sulfate tablets; chondroitin sulfate capsules	Anti-arthritis; Anti-angiocardiopathy	Gacci et al. (2015) Liu et al. (2014a, b)
	Fucoidan	Active pharmaceutical ingredient; Antivirus drugs	Hypolipidemic; Antivirus	Wu and Yang (2010) Mandal et al. (2007)
	Ganoderma atrum polysaccharide	Hypoglycemic drugs	Hypoglycemic	Zhu et al. (2013)
	Heparin	Anticoagulant drugs	Anticoagulant	Bai and Ahsan (2009) Dong and Fang (2001)
Food industry	*Exopolysaccharides*	Fermented dairy products	Anti-ulcer; Immunomodulation; Anti-tumor	Yang et al. (2010)
	Soybean soluble polysaccharide	Yogurt; Milk beverage	Anti-hypertensive; Reduce weight; Hypoglycemic	Ron et al. (2010) Nakamura et al. (2006)
	Red ginseng polysaccharide	Noodles, bread, or cake making	Immunomodulation; Anti-tumor	Yu et al. (2012)
	Carrageenan	Desserts (ice cream and puddings)	Antivirus	Prajapati et al. (2014)
Cosmetics industry	*Hyaluronic acid*	Sodium hyaluronate injection	Moisture absorption and moisture retention	Zhang et al. (2008)
	Aloe polysaccharides	Aloe Vera gel	Anti-aging; Versatile skin care	Takahashi et al. (2009)
	Marine algae polysaccharides	Marine algae deep moisturizing cream	Anti-radiation; Whitening and moisturizing	Moore (2002)

diversity and heterogeneity of natural polysaccharides hamper the research and product development. Moreover, the polysaccharides extracted from the same raw material by different preparation methods often have different compositions. Therefore, the preparation process of polysaccharides needs to be standardized. To reveal the structure–activity relationship is always the focus of polysaccharides research, which will disclose the structural basis for polysaccharides to perform their healthy functions. This is not only necessary to screen and design high-active polysaccharides, but also have important theoretical guiding significance to study the medicinal mechanism of polysaccharides. In addition, because polysaccharides have a wide range of biological activities, they will have broad application prospects in functional foods in the future. Therefore, it is also necessary to strengthen the research on the activity development and mechanism of polysaccharides.

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