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Review

Anticancer polysaccharides from natural resources: A review of recent research

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ABSTRACT

Taking into account the rising trend of the incidence of cancers of various organs, effective therapies are urgently needed to control human malignancies. However, almost all of the chemotherapy drugs currently on the market cause serious side effects. Fortunately, several previous studies have shown that some non-toxic biological macromolecules, including polysaccharides and polysaccharide–protein complexes, possess anti-cancer activities or can increase the efficacy of conventional chemotherapy drugs. Based on these encouraging observations, a great deal of effort has been focused on discovering anti-cancer polysaccharides and complexes for the development of effective therapeutics for various human cancers. This review focuses on the advancements in the anti-cancer efficacy of various natural polysaccharides and polysaccharide complexes in the past 5 years. Most polysaccharides were tested using model systems, while several involved clinical trials.

Contents

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1. Introduction

Cancer is a leading cause of death worldwide and a diverse group of diseases characterized by the uncontrolled proliferation of anaplastic cells which tend to invade surrounding tissues and metastasize to other tissues and organs. Cancer results from a mutation in the chromosomal DNA of a normal cell, which can be triggered by both external factors (tobacco, alcohol, chemicals, infectious agents and radiation) and internal factors (hormones, immune conditions, inherited mutations, and mutations occurring in metabolism). A report released by the World Health Organization (WHO) showed that an estimated 12.7 million people were diagnosed with cancer globally and about 7.6 million people died of it in 2008. As estimated in this report, more than 21 million new cancer cases and 13 million deaths are expected by 2030. Although cancer accounts for around 13% of all deaths in the world, more than 30% of cancer deaths can be prevented by modifying or avoiding key risk factors (World Health Organization, 2011).

The abilities to invade and metastasize are the defining characteristics of a cancer. After the transformation from a normal cell into a malignant cell *via* genetic mutation, cancerous cells proliferate rapidly, invade surrounding tissues, break off from the parent lump, migrate around the body in the blood or the lymphatic system, and set up secondary foci of cancerous growths at distant sites (Fidler, 2003). Metastasis is responsible for 90% of the deaths caused by cancer.

Polysaccharides are biopolymers comprised of monosaccharides linked together through glycosidic bonds. These structures can be linear or contain branched side chains. Polysaccharides have a general formula of $C_x(H_2O)_y$ where x is usually a large number between 200 and 2500. Considering that the repeating units in the polymer backbone are often six-carbon monosaccharides, the general formula can also be represented as $(C_6H_{10}O_5)_n$ where $40 \leq n \leq 3000$.

Polysaccharides can be classified into two groups based on their source. Natural polysaccharides are obtained from various organisms, such as algae, plants, microorganisms, and animals. In contrast, semi-synthetic polysaccharides are produced by the chemical or enzymatic modification of the parent macromolecules (Caliceti, Salmaso, & Bersani, 2010). Polysaccharides obtained from different sources and by different chemical manipulations exist in a variety of chemical compositions, molecular weights and structures. The polysaccharides possess various physicochemical properties including gelation, solubility, low osmotic effect, and surface properties depending on their composition and architecture (Chandra & Rustgi, 1998; Meyers, Chen, Lin, & Seki, 2008).

As a structurally diverse class of macromolecules, polysaccharides play diverse and important roles in many biological processes. As well as serving as stores of energy (*e.g.* starch and glycogen) and structural components (*e.g.* cellulose in plants and chitin in arthropods), polysaccharides and their derivatives participate in signal recognition and cell–cell communication and also play key roles in the immune system, fertilization, pathogenesis prevention, blood clotting, and system development (Naveen Chandra et al., 2011).

Recently, accumulated evidence has demonstrated that polysaccharides have a broad spectrum of biological effects, such as antibiotic, antioxidant, anti-mutant, anticoagulant, and immunostimulation activities (Ali, Ziada, & Blunden, 2009; Wijesekara, Pangestuti, & Kim, 2011; Yu, Yin, Yang, & Liu, 2009). The anti-cancer efficacy of polysaccharides was first recognized by Nauts et al. in 1946 when it was found that certain polysaccharides could induce complete remission in patients with cancer (Zhang, Cui, Cheung, & Wang, 2007). Numerous studies have suggested that polysaccharides can inhibit tumor growth through the following common mechanisms: (1) the prevention of tumorigenesis by oral consumption of active preparations; (2) direct anti-cancer activity, such as the induction of tumor cell apoptosis; (3) immunopotentiation activity in combination with chemotherapy; and (4) the inhibition of tumor metastasis.

This review covers anti-cancer polysaccharides derived from nature in the past 5 years. The chemical structures, anti-cancer activities and mechanisms of action are discussed.

2. Polysaccharides from fungi

2.1. Polysaccharides from mushrooms

Mushrooms have an established history of use by many countries as an edible and medical resource, especially in traditional oriental therapies of some Asian countries. Even in modern clinical practice, mushroom-derived bioactive components are still utilized. Over the last half-century, studies in Japan, China, Korea, and, more recently, the United States have increasingly demonstrated the potential of mushroom-extracted compounds in the prevention and treatment of cancer. Polysaccharides are found to be the most potent mushroom-derived substances with anti-cancer and immunomodulating properties. It is well established that mushroom-derived polysaccharides inhibit cancer growth, which commonly act as immunomodulators or as biological response modifiers (BRMs).

Polysaccharides or extracts mainly containing polysaccharides from dozens of mushrooms have shown anti-cancer activity in animal models, whereas only a few of them have been further taken to clinical assessment in humans. Of these, all are chemically α- or β-glucans or peptide-bound glucans. Five polysaccharide constituents from mushrooms have shown significant anti-cancer efficacy against several human cancers in clinical trials as BRMs, including lentinan from *Lentinus edodes*, D-fraction from *Grifola frondosa*, schizophyllan from *Schizophyllum commune*, polysaccharide-K (PSK) from *Trametes versicolor*, and polysaccharide–peptide (PSP), also from *T. versicolor* (Wasser, 2002). It was shown that β-glucans can induce biological responses by binding to a membrane receptor, complement receptor type 3 (CR3). More recently, another receptor, dectin-1, was characterized as a β-glucan receptor that mediates this activity (Zaidman, Yassin, Mahajna, & Wasser, 2005).

As for the identification of anti-cancer activity of mushroom extracts, searching for new anti-tumor substances from mushrooms has become a matter of great significance. Besides the glucans mentioned before, a wide range of anti-cancer polysaccharides or polysaccharide–protein/peptide complexes have been identified.

2.1.1. D-fraction and MD-fraction

A bioactive β-glucan fraction termed the D-fraction was isolated from both the mycelia and fruit body of *G. frondosa* by Japanese mycologists in 1984. The predominant component of D-fraction is a protein-bound polysaccharide with a molecular weight of about 1×10^6 Da. It consists of β-glucan (both β-1,6-linked glucan with β-1,3 branches and β-1,3-linked glucan with β-1,6 branches) as the main polysaccharide backbone in combination with a few uncharacterized protein units. The MD-fraction was obtained from further purification of the D-fraction and showed a superior anti-cancer effect (Mayell, 2001). The D- and MD-fractions have been shown to have outstanding anti-tumor activity and have consequently been proposed for phase I/II clinical trials in the United States and Japan.

The MD-fraction can induce cancer cell apoptosis *via* activation of the BAK-1 gene (Soares et al., 2011). The combination of IFN-α2b and the MD-fraction has been shown to have a synergistic effect that triggers DNA-PK activation and induces cancer cell arrest at the G1 cell cycle checkpoint (Louie, Rajamahanty, Won, Choudhury, & Konno, 2009; Pyo, Louie, Rajamahanty, Choudhury, & Konno, 2008). The MD-fraction has been proven to enhance the anti-tumor and anti-metastatic activity of cisplatin and decrease cisplatin-induced immunosuppression and nephrotoxicity in mice (Masuda, Inoue, Miyata, Mizuno, & Nanba, 2009). In cyclophosphamide-induced granulocytopenic mice, the MD-fraction significantly enhanced granulopoiesis and the mobilization of granulocytes by increasing granulocyte colony-stimulating factor (G-CSF) production and modulating CXCR4/SDF-1 (stromal cell-derived factor 1) expression (Ito, Masuda, Yamasaki, Yokota, & Nanba, 2009).

In addition, a heteropolysaccharide maitake Z-fraction (MZF) was isolated from *G. frondosa*. MZF significantly inhibits tumor growth by inducing cell-mediated immunity *in vivo* (Masuda, Matsumoto, et al., 2009) and enhances the anti-tumor activity of bone marrow-derived dendritic cell-based immunotherapies against murine colon cancer (Masuda, Ito, Konishi, & Nanba, 2010). GFPPS1b, a novel polysaccharide–peptide isolated from cultured mycelia of *G. frondosa* exerts anti-tumor activities by arresting cell cycle and inducing apoptosis in tumor cells.

2.1.2. Lentinan

Lentinan is a high molecular weight (5×10^5 Da) glucan extracted from the cell wall of the fruiting body of *L. edodes* with mostly β-(1 → 3)-glucose linkages in the regularly branched backbone and β-(1 → 6)-glucose side-chains. It was first isolated and studied by Chihara et al. in 1970 who demonstrated that its anti-tumor effects were greater than other mushroom polysaccharides. In 1985, lentinan injection was approved and produced as an adjuvant for the treatment of gastric cancer in Japan (Bisen, Baghel, Sanodiya, Thakur, & Prasad, 2010). The synergistic effects of lentinan with various chemical drugs or other therapies have been demonstrated in clinical trials in the following years.

Lentinan as an adjuvant has been formulated as S-1/paclitaxel/lentinan (Akazawa et al., 2010; Kataoka et al., 2009; Kubota et al., 2009; Nakagawa, Yanagawa, Matsunaga, & Noda, 2010), S-1/CDDP/lentinan (Hori et al., 2009, 2011; Takahashi et al., 2006), S-1/lentinan (Nimura et al., 2006; Yagi et al., 2010) or superfine dispersed lentinan (SDL) (Hazama et al., 2009; Isoda et al., 2009; Shimizu et al., 2009; Yamada, 2009; Yoshino, Watanabe, et al., 2010) and has been used in combination chemotherapies for advanced gastric cancer, pancreatic cancer, colorectal cancer and hepatocellular carcinoma. These combination chemotherapies have been proven to prolong the administration period and decrease the incidence rates of adverse effects of chemotherapies. Therefore, they can prolong the survival time and improve the quality of life (QOL) of cancer patients. Other combination therapies containing lentinan in the formulation, including lentinan/OK-432 (Yoshino, Yoshida, et al., 2010), lentinan/DCV vaccine (Wang, Zhou, & Xia, 2007), lentinan/TACE/RFA (Yang, Liang, Zhang, & Shen, 2008) and lentinan/thermotherapy (Li, Jia, & Chen, 2011), have also shown enhanced anti-cancer potency against various cancers without obvious adverse reactions. In addition, orally administered superfine dispersed lentinan as a complementary and alternative medicine for advanced pancreatic cancer, hepatocellular carcinoma, gastric cancer and colorectal cancer was deemed safe and effective for patients' survival and the improvement of quality of life (Hazama et al., 2009; Isoda et al., 2009; Oba, Kobayashi, Matsui, Kodera, & Sakamoto, 2009; Shimizu et al., 2009; Yoshino, Watanabe, et al., 2010).

Common chemotherapy has shown little anti-tumor efficacy for advanced oral squamous cell carcinoma (OSCC) patients. Therefore, it is necessary and urgent to develop more effective treatments for patients with advanced OSCC. Recently, the combination therapy of lentinan and S-1 has been shown to inhibit the growth of human OSCC tumor xenografts in nude mice and significantly induce apoptosis in OSCC tumor cells (Harada, Itashiki, Takenawa, & Ueyama, 2010).

2.1.3. PSK and PSP

PSK is a protein-bound β-glucan with a molecular weight of 94 kDa that is derived from mycelia of the strain *Trametes* (*Coriolus*) *versicolor* CM-101. It consists of (1 → 4)-β-glucan with (1 → 6)-β-glucopyranosidic lateral chains and 25–38% protein residues (Mantovani et al., 2008). PSK has been developed in Japan as a

non-specific immunostimulant and has been used for the treatment of gastric and colorectal cancers. Clinical trials showed that immunochemotherapies consisting of PSK and chemotherapeutic agents, including fluoropyrimidines (Sakai et al., 2008), UFT (tegafur/uracil) (Ohwada et al., 2006; Yoshitani & Takashima, 2009), S-1 (tegafur/gimeracil/oteracil) (Kono et al., 2008) or FOLFOX4 (5-FU/folinic acid/oxaliplatin) (Shibata et al., 2011), can improve long-term prognosis, reduce the risk of recurrence and increase the survival rates in patients with gastric and colorectal cancer. The immunoregulation effects of PSK are, in part, attributed to its prevention of the apoptosis of circulating T cells and the decrease of the peripheral neuropathy and bone marrow suppression induced by chemotherapy (Kono et al., 2008; Shibata et al., 2011). In addition, studies in mice have shown that PSK can also enhance the cytotoxicity of such drugs (Katoh & Ooshiro, 2007; Kinoshita et al., 2010; Umehara et al., 2009; Yamasaki et al., 2009).

The anti-cancer effect of PSK *via* immunostimulation, as well as its ability to enhance the efficacy of trastuzumab (Lu, Yang, Gad, Inatsuka, et al., 2011), was correlated with its role as a selective TLR2 agonist (Lu, Yang, Gad, Wenner, et al., 2011) and TGF-β pathway inhibitor (Ono et al., 2012). Besides its immunostimulatory effect, PSK also showed direct anti-tumor effects, as it was able to inhibit the proliferation of various tumor cell lines *via* the arrest of cell cycle and the induction of apoptosis (Hirahara, Fujioka, Fujieda, Wada, & Tanaka, 2010; Hirahara et al., 2011; Jiménez-Medina et al., 2008).

PSP is another proteoglucan derived from *T. versicolor* which has been developed in China. As they are both derived from the same species, PSP and PSK have the same polysaccharide component but with different underlying protein structures bound to the polysaccharide (Ooi & Liu, 2000).

PSP has been shown to inhibit tumor cell proliferation through the induction of apoptosis and cell cycle arrest (Hsieh, Wu, Park, & Wu, 2006). As a result of interfering with the S phase progression, PSP enhances the cytotoxicity of certain S-phase targeted-drugs, such as doxorubicin, etoposide, camptothecin and cyclophosphamide, on human cancer cells (Wan, Sit, & Louie, 2008; Wan, Sit, Yang, Jiang, & Wong, 2010) and decreases drug clearance *in vivo* (Chan & Yeung, 2006). In addition, PSP has shown a chemopreventive effect on prostate cancer *via* the targeting of prostate cancer stem cell-like populations (Luk et al., 2011).

The new formulation composed of PSP and Astragalus polysaccharide (APS) has shown significant immunomodulatory effects and can restore the immunological effects against adriamycin-induced immunosuppression, as well as anti-cancer activity involved in the regulation of apoptosis protein expression in tumor tissue. These results indicate that the new formulation has better effects than those of PSP alone (Li, Bao, et al., 2008).

2.1.4. Glucans from Agaricus blazei

An α-(1 → 4)-glucan-β-(1 → 6)-glucan-protein complex was isolated from the *A. blazei* Murrill mushroom. It showed no cytotoxicity on tumor cells *in vitro* but strong anti-tumor effect *in vivo*. Moreover, it prevented the leucopenia caused by 5-FU treatment in mice (Gonzaga et al., 2009), and a linear β-(1-3)-glucan (LMPAB) with a low molecular weight isolated from *A. blazei* Murill was also found to significantly reduce the invasion of tumor cells *in vitro*. LMPAB inhibited tumor growth and metastasis in mice models *via* modulating the immune function and expression of MMP-9 and nm23-H1 (Niu, Liu, Zhao, & Cao, 2009; Niu, Liu, Zhao, Su, & Cui, 2009). The polysaccharide fraction ABP-Ia with a molecular weight of 4.2×10^5 Da mainly consisted of glucose, mannose, and galactose in a molar ratio of 1:1:1. It showed an evident inhibitory effect on tumor cell growth by inducing cell apoptosis (Wu, Cui, Zhang, & Li, 2012).

2.1.5. Polysaccharides from Cordyceps sinensis

Two glucans, WIPS with a molecular weight of 1180 kDa and AIPS with a molecular weight of 1150 kDa, were extracted from *C. sinensis* (strain Cs-HK1). WIPS was an α-(1 → 4)-D-glucan with α-(1 → 6)-linked branches, but AIPS was a linear α-(1 → 4)-D-glucan. AIPS was shown to exhibit more significant anti-tumor and immunostimulatory effects than WIPS on melanoma tumor-bearing mice (Yan, Wang, Li, & Wu, 2011). In addition, *C. sinensis* polysaccharides were found to enhance triptolide-induced apoptosis in HL-60 cells (Shen, Shao, Ni, Xu, & Tong, 2009) and cisplatin-induced cytotoxicity and the expression of VEGF and bFGF in H157 cells (Ji et al., 2011).

2.1.6. Polysaccharide from Ganoderma atrum

The *G. atrum* polysaccharide (PSG-1) was the major active ingredient isolated from *G. atrum*. PSG-1 inhibited tumor growth in S180-bearing mice *via* the induction of apoptosis through mitochondrial pathways and immunoenhancement effects (Li, Chen, et al., 2011), and also enhanced the cyclophosphamide-induced anti-tumor effect (Li, Nie, et al., 2011).

2.1.7. Polysaccharide–protein/peptide conjugates from Ganoderma lucidum

The crude water-soluble extract of *G. lucidum* (Reishi or Ling-Zhi) has been used in traditional Chinese medicine as anti-tumor and immunomodulating agent. Recently, five polysaccharide–protein/peptide conjugates with anti-cancer or immunomodulation efficacies were obtained from *G. lucidum*. The monosaccharide compositions, molecular weights and ratios of carbohydrate to protein of these glycoconjugates are listed in Table 1.

Polysaccharide fraction 3 (F3) was the main active component of a glycoprotein isolated from the water-soluble extract of *G. lucidum* (Wang et al., 2002). F3 was found to induce macrophage-like differentiation and apoptosis in human leukemia THP-1 cells. It was suggested that F3 might induce death receptor ligands such as TNF-α and TRAIL to initiate signaling *via* receptor oligomerization, recruitment of specialized adaptor proteins and the activation of caspase cascades in THP-1 cells (Cheng et al., 2007; Hsu, Huang, Chen, Wong, & Juan, 2009). The combinations of the Ling-Zhi polysaccharide fraction 3 (LZP-F3) and cisplatin or arsenic trioxide were able to dramatically reverse the chemosensitivity of cisplatin and arsenic trioxide-resistant bladder urothelial carcinoma cell N/P(14) and N/As(0.5) in a dose-dependent manner. All of these effects were shown to be mediated by modulating the expression and activation of apoptosis-correlated proteins (Huang et al., 2010). GLIS was reported to have a significant inhibitory effect on tumor growth and dramatically enhanced both humoral and cellular immune functions in a mouse model (Zhang et al., 2010). *Gl*PS significantly inhibited tumor growth in a murine sarcoma 180 model and the adhesion ability of tumor cells to HUVECs *via* the up-regulation of serum amyloid A protein expression (Li, Wang, Wu, et al., 2008). It also showed an immunomodulation effect as it could antagonize the culture supernatant of cancer cells-induced suppression on lymphocytes (Sun, Lin, Duan, et al., 2011) and cyclophosphamide-induced immunosuppression in mice (Zhu, Chen, & Lin, 2007). Moreover, *Gl*PS promoted cancer cells to induce lymphocyte proliferation and activation, and it is thought that H-2D(b), B7-1 and B7-2 might partially be involved in this process (Sun, Lin, Li, et al., 2011). The *Gl*PP fraction was a polysaccharide–peptide conjugate with a molecular weight of 512,500 Da and its polysaccharide chain was assembled in β-glycosidic linkages. *Gl*PP was indicated to inhibit the proliferation of HUVECs by inducing cell apoptosis and decrease the expression of secreted VEGF in human lung cancer cells. These findings were suggested to be the mechanisms of *Gl*PP on anti-angiogenesis (Cao & Lin, 2006). GLPP significantly inhibited the growth of inoculated

Table 1
Polysaccharide–protein/peptide conjugates isolated from *Ganoderma lucidum*.

Name	M_w (Da)	Major monosaccharides	Other monosaccharides	Ratio of carbohydrate to protein	Reference
F3	–	Glc, Man	Fuc, GlaNAc, Xyl, Rha	84.4–15.6%	Wang et al. (2002)
GLIS	–	Glc, Gal, Man	–	11.5:1	Zhang, Tang, Zimmerman-Kordmann, Reutter, and Fan (2002)
*Gl*PS	584, 900	Fru, Glc	Gal, Man, Rha, Xyl, UA	93.61–6.49%	Zhu et al. (2007)
*Gl*PP	512, 500	Xyl, Fru, Glc	Rha, Gal	94.84–5.16%.	Cao and Lin (2006)
GLPP	6600	Glc	Man, Gal	89.4–10.6%	Pang et al. (2007)

S180, Heps, and EAC tumor cells in mice with an enhanced host immunofunction, and prevented the immunosuppression induced by cyclophosphamide treatment and ^{60}Co radiation in mice. All of these activities of GLPP were stronger than PSP (Pang et al., 2007).

2.1.8. Protein-bound polysaccharide from Phellinus linteus

The protein-bound polysaccharide isolated from the *P. linteus* mushroom (PL) could suppress SW480 tumor growth (Song et al., 2011) and melanoma cell metastasis (Han, Lee, Kang, Yoon, Lee, et al., 2006) in mice. *In vitro* assays showed that PL inhibited cancer cell adhesion and invasion, and angiogenesis through the inhibition of Wnt/β-catenin signaling and MMP-9 activity. However, the anti-proliferative effect of PL on cancer cells was contentious (Han, Lee, Kang, Yoon, Lee, et al., 2006; Song et al., 2011).

2.1.9. Proteoglycan fractions from Pleurotus abalonus and Pleurotus ostreatus

A novel polysaccharide–peptide conjugate, named LB-1b, and a polysaccharide named LA were purified and identified from the fruiting bodies of *P. abalonus*. The polysaccharide moiety of LB-1b was composed of glucose, rhamnose, glucuronic acid and galactose, and the peptide moiety was IPKERKEFQQAQHLK. LA was a polysaccharide with a molecular weight of 120 kDa composed of glucose, rhamnose, glucuronic acid, xylose, galactose and arabinose, and its backbone was α-(1 → 6)-D-Gly. Both of these were capable of inhibiting the proliferation of hepatoma HepG2 cells and breast cancer MCF7 cells. The IC_{50}s of LB-1b to HepG2 and MCF7 cells, and LA to MCF7 cells were 24 μM, 14 μM and 3.7 μM, respectively (Li et al., 2012; Wang, Ng, et al., 2011).

Three neutral water-soluble proteoglycan fractions were obtained from *P. ostreatus* mycelia. The polysaccharide-to-protein ratios of the three fractions were found to be 14.2, 26.4 and 18.3, and the molecular weights of their major components were about 66 kDa, 47 kDa and 32 kDa, respectively. These proteoglycans could inhibit tumor growth in S180-bearing mice by arresting cell cycle in pre-G0/G1 phase *in vivo*. These proteoglycan fractions also possessed an immunoregulation effect (Sarangi, Ghosh, Bhutia, Mallick, & Maiti, 2006). In addition, an α-glucan with low molecular weight isolated from *P. ostreatus* mycelia showed an anti-proliferative activity toward HT-29 cells through the apoptotic induction pathway by up-regulating Bax and cytosolic cytochrome-c (Lavi, Friesem, Geresh, Hadar, & Schwartz, 2006). The polysaccharide POPS-1 extracted from *P. ostreatus* fruiting bodies had a backbone of β-(1 → 3)-glucan with branches composed of (1 → 3)-linked Glc, (1 → 4)-linked Gal and (1 → 4)-linked Man. POPS-1 presented significant anti-proliferative activity and decreased 5-Fu-induced cytotoxicity in Hela cells (Tong et al., 2009).

2.1.10. Polyporus polysaccharide

The Polyporus polysaccharide (PPS) derived from the sclerotium of *Polyporus umbellatus* (Per) Fr was an anti-cancer component consisting of (1 → 3)-β-glucan backbone and (1 → 6)-β-glucopyranose side chains with a molecular weight of approximately 1.6×10^5 Da (Han, 1988; Haranaka et al., 1985). This polysaccharide was first commercially produced as an immunomodulator for the treatment of hepatitis in China in 1990. PPS effectively inhibited bladder carcinogenesis in rat models induced by N-butyl-N-(4-hydroxybutyl)-nitrosamine, which might be associated with the up-regulation of glutathione S-transferase pi and NAD(P)H:quinone oxidoreductase 1 (NQO1) in the bladder (Zhang, Zeng, et al., 2011). In addition, PPS can suppress the over-activation of the NF-κB signaling pathway induced by Bacillus Calmette–Guerin (BCG) in bladder cancer cells and accordingly attenuate the adverse effects of BCG therapy (Wei, Zeng, Han, & Huang, 2011).

2.1.11. Polysaccharides from Poria cocos

Heteropolysaccharides isolated from *P. cocos* mainly contained glucose, galactose, and mannose, and exhibited anti-tumor activities both *in vitro* and *in vivo* (Huang, Jin, Zhang, Cheung, & Kennedy, 2007; Ke, Lin, Chen, Ji, & Shu, 2010). (1 → 3)-β-D-Glucan extracted from *P. cocos* was water-insoluble and showed no anti-cancer activity, whereas its phosphorylated derivatives exhibited strong inhibition against S-180 tumors (Chen, Xu, Zhang, & Zeng, 2009).

2.1.12. Polysaccharides from other mushrooms

Polysaccharides with anti-cancer activities from other mushrooms, such as *Auricularia polytricha*, *Inonotus obliquus*, *Phellinus rimosus* and so on, are listed in Table 2.

2.2. Yeast beta-glucans

The combination treatment of yeast β-glucan and bevacizumab showed augmented efficacy in terms of tumor progression and long-term survival compared with bevacizumab-treated alone in cancers with membrane-bound VEGF expression (Salvador et al., 2008), accompanied with massive complement deposition and neutrophil infiltration within tumors (Zhong et al., 2009). Sulfoethyl glucan (SEG), a novel derivative prepared from the β-glucan isolated from the yeast *Saccharomyces cerevisiae*, has shown DNA-protective, anti-mutagenic, and anti-clastogenic effects. SEG also exerted cytotoxic/cytostatic enhancement effects with teniposide against mouse leukemia cells (Vlcková et al., 2006).

2.3. Polysaccharides from Penicillium jiangxiense

MPPJ4 and MPPJ5 were polysaccharide fractions isolated from *P. jiangxiense*. These two fractions showed slight cytotoxic effects on inhibiting human gastric adenocarcinoma SGC-7901 cell proliferation, but significantly induced cell apoptosis and cell cycle arrest at the S phase (Xiao, Fang, Liu, & Chen, 2008).

Table 2
Polysaccharides with anti-cancer activities from other mushrooms.

Sources	Tumor models	Effects	Reference
Agaricus brasiliensis	Ehrlich tumor-bearing mice	Decreased tumor-induced IL-10 production, changed tumor microenvironment	Pinto et al. (2009)
Astraeus hygrometricus	Daltons lymphoma-bearing mice	Inhibited tumor growth, induced cell apoptosis, activated immune system	Mallick, Maiti, Bhutia, and Maiti (2010)
Auricularia auricular-judae	S180-bearing mice	Inhibited tumor growth, induced cell apoptosis	Ma, Wang, Zhang, Zhang, and Ding (2010)
Auricularia polytricha	S180-bearing mice	Inhibited tumor growth	Song and Du (2010)
Cordyceps gunnii	K562 cells	Inhibited cell growth	Zhu et al. (2012)
Cordyceps militaris	S180-bearing mice	Inhibited tumor growth, decreased toxic effect of chemotherapy drug	Zhong et al. (2008)
Cordyceps sphecocephala	HepG2 cells, SK-N-SH cells	Induced DNA fragmentation and cell apoptosis	Oh et al. (2008)
Flammulina velutipes	BGC-823 cells, A549 cells	Inhibited cell growth	Yang et al. (2012)
Fomes fomentarius	SGC-7901 and MKN-45 cells	Inhibited cell growth	Chen, Zhao, and Li (2011)
Hypsizigus marmoreus	AGS cells	Inhibited cell growth	Bao, Choi, and You (2010)
Inonotus obliquus	B16F10-bearing mice	Prolonged the survival rate, inhibited tumor growth, promoted macrophages proliferation	Kim et al. (2006)
Isaria farinosa B05	S180-bearing mice	Inhibited cell growth	Jiang et al. (2008)
Lactarius deliciosus Gray	S180-bearing mice	Inhibited tumor growth	Ding, Hou, and Hou (2012)
Phellinus gilvus	TMK-1-bearing mice	Inhibited tumor growth and metastasis, increased cell apoptosis	Bae, Jang, and Jin (2006)
Phellinus igniarius	S180 and H22 bearing mice	Inhibited tumor growth, enhanced cell mediated immunity	Chen, Pan, et al. (2011)
Phellinus ribis	HepG2 cells, zebrafish	Inhibited cell growth, blocked new angiogenic vessel formation	Liu, Liu, et al. (2009)
Phellinus rimosus	Swiss albino mice	Radioprotective effect	Joseph, Smina, and Janardhanan (2011)
Pholiota dinghuensis Bi	BGC-823 cells	Inhibited cell growth	Gan, Ma, Jiang, Xu, and Zeng (2011)
Pleurotus geesteranus	MCF-7 cells	Inhibited cell growth	Zhang, Zhu, et. (2011)
Pleurotus tuber-regium	Sarcoma 180 tumor cells	Inhibited cell growth	Tao, Zhang, and Zhang (2009)
Rice Bran Fermented with *Lentinus edodes*	S180-bearing mice, B16/Bl6-bearing mice	Inhibited tumor growth, induced the activation of NK cells	Kim, Kim, et al. (2007)
Tricholoma matsutake	B16 cells	Inhibited cell growth	Lu et al. (2008)

3. Polysaccharides from plants

3.1. Polysaccharide from Achyranthes bidentata

The *A. bidentata* polysaccharide (ABPS) isolated from its root is a graminans-type fructan with a molecular weight of 1400 Da (Zou et al., 2011). It consists of a β-D-fructofuranosyl backbone with (2→1)- and (2→6)-linked residues with branches and an α-D-glucopyranose residue on the non-reducing end of the fructan chain (Jin et al., 2007). ABPS showed opposite effects on tumor growth depending on its dose (Jin et al., 2007). At doses of 100 mg kg^{-1} and 50 mg kg^{-1}, the inhibition rate of ABPS on Lewis lung cancer (LLC) growth in mice was 5.36% and 40.06%, respectively. The anti-cancer activity of ABPS was mediated through the induction of cell cycle arrest, while the stimulation of tumor growth by high doses of ABPS was associated with a dysfunction of NK cells and the up-regulation of IL-6 and TNF-α mRNA expression in mice spleen.

3.2. Angelan

Angelica gigas Nakai of Umbelliferae is a well-known oriental drug used for the treatment of gynecological diseases (Han et al., 1998). Angelan is a pectic polysaccharide with a molecular weight of 10 kDa that is purified from the root and cell culture of *A. gigas* Nakai. In previous studies, it has been shown that angelan could activate the immune functions of B cells and macrophages, and increase the survival of B16F10 melanoma tumor-bearing mice (Han, Lee, Kang, Yoon, Kang, et al., 2006).

Recent studies demonstrated that angelan could significantly inhibit the pulmonary metastasis of B16F10 melanoma as well as prolong the survival time of B16F10-implanted mice. The anti-cancer and anti-metastatic effects of angelan were mediated by stimulating host immunity and directly inhibiting cancer cell adhesion. Moreover, the combination treatment of angelan and doxorubicin showed that it could more effectively inhibit tumor growth and metastasis than either compound alone (Han, Lee, Kang, Yoon, Kang, et al., 2006). In addition, angelan could efficiently induce dendritic cell (DC) maturation through toll-like receptor 4 and increase the inhibitory effect of DC against B16F10 tumor growth (Kim, Yoon, et al., 2007).

3.3. Polysaccharides from Angelica sinensis (Oliv.) Diels

A. sinensis (Oliv.) Diels, also known as Chinese Danggui, is a well-known traditional Chinese medicine and has been used in gynecology for thousands of years (Sarker & Nahar, 2004). Previous studies revealed that the crude polysaccharide from *A. sinensis* possessed anti-tumor effects in tumor-bearing mice *via* the activation of the host immune response (Shang et al., 2003).

Several polysaccharide fractions were extracted and further purified from the roots of *A. sinensis* (Oliv.) Diels. Among them, a neutral polysaccharide, APS-1d, and three acidic polysaccharides, APS-2a, APS-3b and APS-3c (Table 3), were shown to inhibit

Table 3
Anti-cancer polysaccharides extracted from the roots of *Angelica sinensis* (Oliv.) Diels.

Name	M_w (Da)	Neutral monosaccharides composition	Protein content (wt%)
APS-1d	5.1×10^3	Glc, Ara	0
APS-2a	7.4×10^5	Glc, Gal, Ara, Rha	0.4
APS-3b	2.3×10^5	Glc, Gal, Ara, Rha, Man	1.4
APS-3c	1.4×10^4	Glc, Gal, Ara, Rha, Man, Xyl	7.8

tumor growth and extend the life-span of tumor-bearing mice. The mechanisms of action were attributed to enhancing host immune function and inducing cell apoptosis, which primarily involved the activation of the intrinsic mitochondrial pathway (Cao et al., 2008, 2006; Cao, Li, Wang, Fan, et al., 2010; Cao, Li, Wang, Li, et al., 2010).

Another *Angelica* polysaccharide fraction (AP) was comprised of 97% carbohydrate (about 30% of them uronic acids) and 3% protein. AP contained 5 major polysaccharide sub-fractions with molecular weights of about 670, 433.72, 167.55, 82.10 and 15.54 kDa, respectively. The subcutaneous injection of AP could effectively protect hematopoietic and gastrointestinal tissues against the cytotoxicity of cyclophosphamide in mouse models (Hui, Wu, Shin, So, & Cho, 2006).

3.4. Astragalus polysaccharide

Astragalus membranaceus has a long history of medicinal use in China and has been shown to be effective in immunoenhancement and in the treatment of diabetes, viral infections and cancers (Cassileth et al., 2009; Dang et al., 2009; McCulloch et al., 2006; Wang et al., 2009). The Astragalus polysaccharide (APS) isolated from the radix of *A. membranaceus* is an active anti-cancer component. Structural analysis indicated that the polysaccharides of Astragalus were mainly composed of α-(1 → 4)-glucan with α-(1 → 6)-linked branches (Li, Chen, Wang, Tian, & Zhang, 2009), or α-(1 → 3)-glucan with side-chains containing arabinoses and xyloses (Zhu et al., 2011). APS displayed an anti-proliferative effect on cancer cells. Up-regulation of the expressions of p53 and PTEN by regulating p53/MDM2 feedback loops was shown to be one of its anti-proliferative mechanisms (Ye, Chen, Zhou, & Liao, 2011). In addition, the treatment of APS integrated with vinorelbine and cisplatin could significantly improve the QOL of patients with advanced non-small-cell lung cancer compared with cisplatin alone (Guo, Bai, Zhao, & Wang, 2011). APS also showed a high efficacy in the treatment of leukemia. It efficiently induced erythroid differentiation by modulating the *LMO2*, *Klf1*, *Klf3*, *Runx1*, *EphB4* and *Sp1* genes, increasing γ-globin mRNA expression and fetal hemoglobin synthesis in K562 cells (Yang, Qian, Zhao, & Fu, 2010). Furthermore, APS enhanced the immune function of plasmacytoid dendritic cells (pDCs), and promoted the differentiation and maturation of pDCs in chronic myelogenous leukemia patients (Liu & Zhang, 2010).

3.5. Polysaccharides from ginseng

Panax ginseng C. A. Meyer (ginseng) has been used as an invaluable and effective traditional medicine to increase the QOL in East Asia since ancient times (Helms, 2004). It has been well documented that the polysaccharides of ginseng possess various anti-tumor activities including preventive and inhibitory effects against tumors as well as enhanced immunological functions (Choi, 2008).

Ginseng polysaccharides have been shown to inhibit tumor growth due to the induction of apoptosis and the stimulation of macrophages (Wang, Zuo, et al., 2010; Zhao & Wang, 2006). The total polysaccharides of ginseng were separated into neutral (WGPN) and acidic (WGPA) fractions. The acidic polysaccharide fraction was found to protect mice from radiation-induced damage of the small intestine (Ni et al., 2010). A homogalacturonan (HG)-rich pectin was isolated from the acidic fraction, which was capable of inhibiting cell proliferation and inducing cell cycle arrest at the G2/M phase. Temperature modification dramatically increased the anti-proliferative effect of HG-rich pectin and induced apoptosis accompanied by the activation of caspase-3 (Cheng et al., 2011). The neutral fraction (WGPN) showed an immunoenhancement effect and inhibited S180 tumor growth. In combination with 5-FU, WGPN decreased damage to the immune system caused by 5-FU in S180-bearing mice and showed a synergistic anti-cancer effect (Ni et al., 2010). A ginseng polysaccharide injection has been developed in China as a useful adjuvant for irradiation therapy and chemotherapy for cancer patients.

Panax quinquefolium (American ginseng) has been used more often as herbal dietary supplement in the United States in recent years. Polysaccharides of American ginseng inhibited the proliferation of wild-type HCT116 human colon cancer cells *via* its pro-apoptotic effects, and the p21−/−HCT116 cells were found to be more sensitive to these treatments (King & Murphy, 2010).

3.6. Modified citrus pectin (MCP)

Modified citrus pectin (MCP) is a modified polysaccharide extracted from the peel and pulp of citrus fruits *via* pH and temperature treatments. MCP is rich in β-galactose and can antagonize the β-galactoside binding protein galectin-3 on the surface of certain types of cancer cells to inhibit tumor metastasis. In its native form, citrus pectin (CP) has a limited solubility in water and is unable to interact with galectin-3. In contrast, the shorter, non-branched, water soluble and galactose-rich MCP polysaccharide fractions obtained by pH and temperature treatments have the ability to access and interact tightly with galectin-3 (Glinsky & Raz, 2009; Nangia-Makker et al., 2002).

In a mouse colon cancer liver metastases model, the expression level of galectin-3 was higher than that of normal mice. MCP was indicated to effectively inhibit liver metastasis and the tumor volume of colon cancer in the model (Liu, Huang, Yang, Lu, & Yu, 2008). MCP has shown an inhibitory effect on prostate cancer cell growth due to the inhibition of MAP kinase activation, the induction of pro-apoptotic protein expression and the cleavage of caspase-3 (Yan & Katz, 2010). Commercially available fractionated pectin powder (FPP) could induce apoptosis in both androgen-responsive (LNCaP) and androgen-independent (LNCaP C4-2) human prostate cancer cells. In contrast, CP and the pH-modified CP showed little or no apoptotic activity. In addition, base-sensitive ester linkages were shown to be required for the apoptotic activity of FPP, while heat treatment of CP led to the induction of apoptosis (Jackson et al., 2007).

Moreover, MCP has immunostimulatory properties in human blood samples, including the activation of functional NK cells against K562 leukemic cells in culture. The unsaturated oligogalacturonic acids appear to be the immunostimulatory carbohydrates in MCP (Ramachandran et al., 2011).

3.7. Polysaccharides from Solanum nigrum Linne

Polysaccharides isolated from *S. nigrum* L. (SNL-P) markedly inhibited the growth of cervical cancer transplanted into mice. The anti-cancer activity of SNL-P was mediated by increasing cell apoptosis, inducing cell cycle arrest and activating host immune responses (Li et al., 2007, 2010). It was shown that polysaccharide fractions that mainly contained galactose and arabinose had significant anti-tumor and immunomodulatory activities, whereas glucose-rich fractions hardly demonstrated this activity (Ding, Zhu, & Gao, 2012).

3.8. Polysaccharides from other plants

Polysaccharides obtained from other species of plants which presented inhibitory effects on tumor growth are summarized in Table 4.

4. Polysaccharides from algae

4.1. Fucoidan

Fucoidan is a general term for sulfated polysaccharides derived from brown seaweeds and some marine invertebrates, like sea urchins and sea cucumbers (Holtkamp, Kelly, Ulber, & Lang, 2009). Fucoidans are mainly composed of L-fucose and sulfate ester groups together with small numbers of other monosaccharides (mannose, galactose, glucose, xylose, *etc.*), uronic acids, acetyl groups and proteins. The chemical compositions and structures of fucoidans from different organisms are usually various, and methods of extraction can affect their structures (Li, Lu, Wei, & Zhao, 2008).

The anti-cancer activity of fucoidans has been reported frequently in recent years, and the potential mechanisms of action of fucoidans were investigated. Novel fucoidans derived from about 11 seaweeds were found to possess anti-tumor effects. Studies also demonstrated that fucoidans inhibit tumor growth through inducing apoptosis and cell cycle arrest, inhibiting tumor metastasis and potentiating the toxic effect of chemical drugs. The apoptosis induction activities of fucoidans were mediated by blocking the PI3K/Akt signal pathway (Hyun et al., 2009), activating the MAPK pathway (Jin, Song, Kim, Park, & Kwak, 2010), activating the caspase-8-dependent pathway (Kim, Park, Lee, & Park, 2010; Yamasaki-Miyamoto, Yamasaki, Tachibana, & Yamada, 2009) and regulating the expression of apoptosis-related genes (Park, Kim, Nam, Deuk Kim, & Hyun Choi, 2011). Besides, fucoidans exerted anti-cancer effects through immunomodulatory action (Hu et al., 2010). Fucoidans activated macrophages (Takeda et al., 2012), induced the maturation of DCs and drove their differentiation (Yang, Ma, et al., 2008), and protected DCs from 5-FU-induced cellular damage (Jeong, Ko, & Joo, 2012) to inhibit tumor growth indirectly. Fucoidans from different sources with anti-cancer activities and the mechanisms of their action are listed in Table 5. Fucoidan-vitamin C (1:0.23, w/w) inclusion body was produced by a critical-point freeze-drying method and shown to markedly repress HT-1080 cell invasion through the inhibition of MMP-2 and -9 activities and intracellular ROS generation (Saitoh, Nagai, & Miwa, 2009).

4.2. Polysaccharides from brown algae

Polysaccharides (SFPS) from *Sargassum fusiforme* showed significant anti-tumor activity both *in vitro* and *in vivo*, and improved the immune function in tumor-bearing mice (Chen, Nie, et al., 2012). WPS-2-1 with an average molecular weight of 80 kDa was purified from *Laminaria japonica*. It was composed of mannose, rhamnose and fucose. WPS-2-1 presented significant anti-tumor activity and low cytotoxicity *in vitro* (Peng, Liu, Fang, Wu, & Zhang, 2012). Two polysaccharide fractions, SP-3-1 and SP-3-2, which were purified from *Sargassum pallidum* showed significantly higher anti-tumor activity *in vitro* (Ye, Wang, Zhou, Liu, & Zeng, 2008). *Sargassum latifolium* polysaccharide E3 showed a selective cytotoxicity against lymphoblastic leukemia 1301 cells (Gamal-Eldeen, Ahmed, & Abo-Zeid, 2009).

4.3. Polysaccharides from green algae

Polysaccharides isolated from *Capsosiphon fulvescens* (Cf-PS) inhibited cell proliferation and induced apoptosis by inhibiting IGF-IR signaling and the PI3K/Akt pathway (Kwon & Nam, 2007). *Chlorella pyrenoidosa* polysaccharides CPPS Ia and IIa presented significant anti-proliferative activity against A549 cells *in vitro* (Sheng et al., 2007). Sulfated polysaccharides isolated from *Monostroma nitidum* showed direct cytotoxic effects on AGS cells (Karnjanapratum & You, 2011).

4.4. Polysaccharides from red algae

4.4.1. Polysaccharide from Champia feldmannii (Diaz-Pifferer)

A sulfated polysaccharide (Cf-PLS) was isolated from the red seaweed *C. feldmannii*. Cf-PLS did not show significant cytotoxicity *in vitro*. However, Cf-PLS inhibited the development of sarcoma 180 tumors in mice as an immunomodulator. The combination therapy with 5-FU demonstrated that the Cf-PLS could enhance the anti-cancer efficiency of 5-FU and prevent leucopenia that is induced by 5-FU (Lins et al., 2009).

4.4.2. γ-Carrageenan from Chondrus ocellatus

Carrageenans are sulfated galactans isolated from red algae. γ-Carrageenan extracted from *C. ocellatus* was degraded, and the low molecular γ-carrageenans were proven to enhance the anti-tumor activity of 5-Fu and to increase the immunocompetence that was damaged by 5-Fu (Zhou, Sheng, Yao, & Wang, 2006).

4.4.3. Polysaccharide from Gracilaria lemaneiformis

An acidic polysaccharide (GLSPs) chiefly composed of galactose was isolated from *G. lemaneiformis*. GLSPs significantly inhibited the growth of transplanted H22 hepatoma *in vivo* and displayed remarkable immunomodulatory activities (Fan et al., 2012).

4.4.4. Polysaccharides from Grateloupia longifolia

Polysaccharides isolated from *G. longifolia* (GLP) were mainly composed of galactose with an estimated molecular weight of 1000 ± 100 kDa. GLP inhibited tumor growth in sarcoma 180-bearing mice by inhibiting vascularization in tumor masses. The anti-angiogenic activity of GLP was achieved by inhibiting the proliferation and migration of vascular endothelial cells and the expression of tissue factors (Zhang et al., 2006).

4.4.5. Polysaccharides from Porphyridium cruentum

The extracellular polysaccharides (EPSs) of *P. cruentum* were highly sulfated acidic heteropolymers and consisted mainly of xylose, galactose and glucose. EPSs inhibited the growth of the implanted S180 tumor *via* immunoenhancement (Sun, Wang, & Zhou, 2012).

5. Polysaccharides from animals

5.1. Polysaccharides from Cyclina sinensis

CSPS-3 was a purified fraction obtained from the crude polysaccharides of *C. sinensis* (CSPS). It possessed a strong inhibitory effect

Table 4
Anticancer polysaccharides obtained from plants.

Sources	Tumor models	Effects	Reference
Aconitum coreanum	H22 tumor cells *in vitro* and *in vivo*	Inhibited tumor growth, induced cell cycle arrest	Liang et al. (2012)
Actinidia eriantha	S180 and H22 bearing mice	Inhibited tumor growth, improved immune responses	Xu et al. (2009)
Anemone raddeana	H22 bearing mice	Inhibited tumor growth, improved immune responses	Liu, Li, Yang, Zhang, and Cao (2012)
Asparagus officinalis	BEL-7404 and HeLa cells	Inhibited cell proliferation	Zhao et al. (2012)
Black currant	Ehrlich carcinoma in mice	Inhibited tumor growth	Takata, Yanai, Yamamoto, and Konno (2007)
Brassica napus L.	S180 and B16 bearing mice	Inhibited tumor growth, improved immunofunction and leukogenic actions	Yang, Guo, Zhang, and Wu (2007)
Boschniakia rossica	S180 bearing mice	Inhibited tumor growth, presented synergistic effects with 5-FU	Wang et al. (2012)
Buckwheat	THP-1 cells	Inhibited cell proliferation, induced cell differentiation and maturity	Wu and Lee (2011)
Cactus pear fruit	S180-bearing mice	Inhibited tumor growth, promoted apoptosis and immune responses	Liang, Liu, and Cao (2008)
Camellia oleifera Abel.	S180-bearing mice	Inhibited tumor growth	Jin (2012)
Codonopsis pilosula	H22-bearing mice	Inhibited tumor growth, activated immune system	Xu, Liu, Yuan, and Guan (2012)
Curcuma kwangsiensis	CNE-2 cells	Inhibited cell proliferation, induced cell apoptosis	Zeng et al. (2012)
Dahlia tubers γ-inulin	B16BL6, MCA205 and FsaR-bearing mice	Enhanced effect of photodynamic therapy, reduced recurrence rates of tumor	Korbelik and Cooper (2007)
Dendrobium nobile Lindl	HL-60 cells, S180 bearing mice	Inhibited tumor growth	Wang, Luo, Zha, and Feng (2010)
Dimocarpus longan Lour.	S180-bearing mice	Inhibited tumor growth, stimulated immune system	Zhong, Wang, He, and He (2010)
Gastrodia elata Bl.	PANC-1 cells	Inhibited cell proliferation	Chen, Cao, et al. (2011)
Ginkgo biloba sarcotesta	U937 cells	Inhibited cell proliferation	Wu, Mao, et al. (2011)
Gynostemma pentaphyllum Makino	HepG2 cells and Hela cells	Inhibited cell proliferation, induced cell cycle arrested	Chen, Li, et al. (2011)
Hedysarum polybotrys Hand.-Mazz	HEP-G2 and MGC-803 cells	Inhibited cell proliferation	Li, Wang, Tian, et al. (2008)
Lycium barbarum	MGC-803, BIU87, SGC-7901, SW480 and Caco-2 cells	Inhibited cell proliferation, induced cell cycle arrested	Ke et al. (2011), Mao et al. (2011)
Melia toosendan Sieb. Et Zucc	BGC-823 cells	Inhibited cell proliferation	He et al. (2011), Miao et al. (2010)
Ornithogalum caudatum Ait	K562 cells, S180 bearing mice	Inhibited tumor growth	Chen, Meng, Liu, Chen, and Zhang (2010)
Orostachys japonicus	HT-29 cells	Inhibited cell growth, induced cell apoptosis and cell cycle arrested	Ryu, Baek, Kim, Kim, and Lee (2010)
Passiflora edulis	S180-bearing mice	Inhibited tumor growth	Silva et al. (2012)
Patrinia scabra Bunge	U14-bearing mice	Inhibited tumor growth, induced cell apoptosis and cell cycle arrested	Lu et al. (2009)
Phaseolus vulgaris L.	HT-29 cells	Up-regulated SIAH1, PRKCA and MSH2 genes, down regulated CHEK1 and GADD45A genes	Campos-Vega, Guevara-Gonzalez, Guevara-Olvera, Dave Oomah, and Loarca-Piña (2010)
Prunella vulgaris L.	Lewis lung carcinoma mice model	Inhibited tumor growth, enhanced immune function	Feng, Jia, Shi, and Chen (2010)
Pulsatilla chinensis	C6-bearing mice	Inhibited tumor growth, prolong survival	Zhou et al. (2012)
Punica granatum	MCF-7 and K562 cells	Inhibited cell proliferation	Joseph, Aravind, Varghese, Mini, and Sreelekha (2012)
Safflower	S180 and LA795-bearing mice	Inhibited tumor growth, enhanced the cytotoxicity of immunocytes	Shi, Ruan, Wang, Ma, and Li (2010)
Schisandra chinensis leaf	L5178Y-bearing mice	Inhibited tumor growth, enhanced functions of immune system	Xu, Li, et al. (2012)
Sweet potato	K562 and Hca-f cells	inhibit tumor cells fissiparity	Tian and Wang (2008)
Taxus yunnanensis	Hela, HT1080 cells	Inhibited cell growth	Yin et al. (2010)
Tea leaf	H22-bearing rats	Inhibited tumor growth, decrease microvessel density in tumor, regulated immune function	Chen, Zhou, et al. (2012)
Tea plant flower	S180-bearing mice	Inhibited tumor growth, prolonged the mice survival day, regulated immune function	Han, Ling, He, and Xiong (2010)
Tea seeds	K562 cells	Inhibited cell proliferation	Wei, Mao, Cai, and Wang (2011)
Thuja occidentalis	B16F-10 bearing mice	Stimulated cell-mediated immune system, decreased pro-inflammatory cytokines, inhibited metastasis of tumor	Sunila, Hamsa, and Kuttan (2011)
Zizyphus jujuba	Melanoma cells	Inhibited cell proliferation, induced cell apoptosis	Hung, Hsu, Chang, and Chen (2012)

Table 5
Anticancer effects of fucoidans from algae.

Sources	Tumor models	Effects	Reference
Ascophyllum nodosum	U937 cells	Inhibited cell proliferation, induced DNA-fragmentation and apoptosis	Nakayasu, Soegima, Yamaguchi, and Oda (2009)
Cladosiphon okamuranus Tokida	S180-bearing mice	Inhibited tumor growth, stimulated macrophages	Takeda et al. (2012)
Eclonia cava, *Sargassum hornery*, *Costaria costata*	SK-MEL-28 cells, DLD-1 cells	inhibited cell colony formation	Ermakova et al. (2011)
Fucus evanescens	MT-4 cells	Enhanced etoposide induced cell death	Philchenkov, Zavelevich, Imbs, Zvyagintseva, and Zaporozhets (2007)
Fucus evanescens	Lewis lung carcinoma bearing mice	Antitumor and antimetastatic effects, potentiated the toxic effect of cyclophosphamide	Alekseyenko et al. (2007)
Fucus vesiculosus, *Fucus evanescens* (Sigma)	Human leukemic cells	Induced apoptosis	Jin et al. (2010)
Fucus vesiculosus (Sigma)	NY-ESO-1 expressing human cancer cells	Enhanced the cross-presentation of NY-ESO-1 to T cells, increased T-cell cytotoxicity	Hu et al. (2010)
Fucus vesiculosus (Sigma)	AGS cells	Inhibited cell growth, induced apoptotic and autophagic cell death	Park et al. (2011)
Fucus vesiculosus (Sigma)	HT-29 cells, HCT116 cells, HCT-15 cells, Lewis lung carcinoma cells, B16 cells	Induced cell apoptosis	Ale, Maruyama, Tamauchi, Mikkelsen, and Meyer (2011), Hyun et al. (2009), Kim et al. (2010)
NPO organization fucoidan laboratory	MCF-7 cells	Inhibited cell proliferation, induced cell apoptosis	Yamasaki-Miyamoto et al. (2009)
Saccharina japonica, Undaria pinnatifida	T-47D and SK-MEL-28 cells	Inhibited cell proliferation and colony formation	Vishchuk, Ermakova, and Zvyagintseva (2011)
Sargassum sp.	Lewis lung carcinoma cells, B16 cells	Inhibited cell proliferation, induced cell apoptosis and enhanced NK cell activity	Ale et al. (2011)
Undaria pinnatifida	A549 cells	Inhibited cell proliferation, induced apoptosis	Boo et al. (2011)

on the growth of tumor cells *in vitro* (Jiang, Wang, Liu, Gan, & Zeng, 2011).

5.2. Polysaccharide from Gekko swinhonis Guenther

G. swinhonis Guenther is a traditional Chinese medicine, and the dried whole body has been used as an anti-cancer drug in China for hundreds of years. A homogeneous sulfated polysaccharide–protein conjugate (GSPP) possessing anti-cancer activities was isolated from *G. swinhonis* Guenth. GSPP significantly inhibited the proliferation of the hepatocarcinoma cells Bel-7402 and SMMC-7721 by blocking cells in G2/M (Wu, Chen, & Xie, 2006) and S phases (Chen, Yao, et al., 2010), respectively. It could also induce hepatocarcinoma cell differentiation and inhibit cell migration by decreasing the secretion of IL-8, as well as calcium-mediated regulation of the actin cytoskeleton reorganization. GSPP did not inhibit the proliferation and viability of normal liver cells, and had no direct toxicity against normal cells (Chen, Yao, et al., 2010; Wu, Chen, & Han, 2011).

Dendritic cells (DCs) are the major antigen-presenting cells in the human body that present tumor-associated antigens, thereby generating tumor-specific immunity (Ma, Aymeric, Locher, Kroemer, & Zitvogel, 2011). It has been reported that the biorheological properties of DCs can be severely impaired by the SMMC-7721 microenvironment, while GSPP can partially restore the defective biorheological characteristics of DCs by modifying the tumor microenvironment and decreasing the secretion of IL-10 in DCs (Chen, Zhang, et al., 2012).

5.3. Polysaccharide from Hyriopsis cumingii

A water-soluble polysaccharide (WSP) isolated from mantles of *H. cumingii* showed an anti-proliferative effect on HepG2 cells. WSP arrested the cell cycle at the G0/G1 phase and induced cellular apoptosis (Qiu, Huang, Huang, Pan, & Zhang, 2010).

5.4. Polysaccharide from Misgurnus anguillicaudatus

A free neutral heteropolysaccharide MAP was isolated from the mucus of the loach *M. anguillicaudatus*. MAP induced tumor cell apoptosis through mitochondrial pathways (Zhang & Huang, 2006).

5.5. Polysaccharide from Ommastrephes bartrami

A sulfated derivative of the squid ink polysaccharide isolated from *O. bartrami*, named TBA-1, was shown to inhibit the invasion and migration of HepG2 cells and angiogenesis in the chick embryo chorioallantoic membrane (Chen, Wang, et al, 2010).

5.6. Polysaccharide from porcine cartilage

A short-chain polysaccharide (PS) isolated from porcine cartilage was composed of repeating disaccharide units (Liu, Song, Yang, Liu, & Zhang, 2007). It has been demonstrated that PS possesses anti-cancer and anti-metastatic activities both *in vitro* and *in vivo*. PS dramatically inhibited the growth of human breast carcinoma, hepatoma and leukemia cells, as well as transplanted tumors in mice. Its anti-tumor effect was believed to act by inducing cellular apoptosis by down-regulating the expression levels of cyclin D1 (Liu, Song, et al., 2007), up-regulating the levels of vimentin (Liu, Han, Zhang, Zhao, & Zheng, 2009) and the p21 protein, increasing the ratio of Bax/Bcl-2 (Liu, Yang, Song, Cao, & Wang, 2009), and activating caspase-9 and caspase-3 (Liu, Hu, Liu, Yao, & Zhang, 2009), with little effect on normal cells. The anti-metastatic effect of PS on MCF-7-bearing mice was mediated through the inhibition of MMP-2 and MMP-9 activity by decreasing the levels of laminin receptor 1 and $\alpha\beta 3$ integrin (Liu, Hu, et al., 2009). PS increased the annexin A2

mRNA in H22 cells and therefore was able to enhance the immunogenicity and anti-tumor activity of H22 cells as a tumor vaccine (Liu, Liu, et al., 2010).

5.7. Polysaccharides from Sepiella maindroni

A novel heteropolysaccharide SIP with a molecular weight of 1.13×10^4 Da was isolated from *S. maindroni* ink. SIP was composed of a hexasaccharide repeating unit containing fucose, *N*-acetylgalactosamine and mannose in a backbone with a single branch of glucuronic acid at the C-3 position of mannose. SIP presented a strong anti-mutagenic activity as it was able to significantly reduce the frequency of micronucleated cells in polychromatic erythrocytes and reticulocytes induced by cyclophosphamide in tumor-bearing mice (Liu, Li, et al., 2008). The SIP-SII fraction is a sulfated derivative of SIP with a sulfate content of 34.7%. SIP-SII showed a weak inhibitory effect on tumor cell growth without cytotoxicity *in vitro*, but significantly decreased MMP-2 activity and expression in SKOV3 cells and inhibited the invasion and migration of carcinoma cells (Wang et al., 2008).

5.8. Polysaccharide from Strongylocentrotus nudus eggs

A polysaccharide, SEP, with a molecular weight of 1.95×10^6 Da was isolated from the eggs of *S. nudus*. SEP was a D-glucan containing α-(1 → 4)-linked backbone (branched α-(1 → 6)-linkage) (Liu, Lin, et al., 2007). It was shown to remarkably inhibit the growth of sarcoma 180 (Liu, Lin, et al., 2007) and hepatocarcinoma H22 tumors (Wang, Wang, et al., 2011) *in vivo via* the enhancement of the host immune system function.

6. Polysaccharides from bacteria

6.1. Polysaccharide from Escherichia coli

The O-sulfated polysaccharide from capsular of *E. coli* K5 (K5PS) is a heparin-like polysaccharide without any anticoagulant activity. O-sulfated K5PS has been shown to inhibit tumor metastasis in mice models as well as tumor cell invasion and adhesion *in vitro*. The anti-metastatic effect of O-sulfated K5PS was suggested to be associated with its inhibition of the activity of heparanase (Borgenström et al., 2007).

6.2. Polysaccharide from Paenibacillus polymyxa EJS-3

A levan-type exopolysaccharide EPS-1 was isolated from the endophytic bacterium *P. polymyxa* EJS-3. It was mainly composed of a (2 → 6)-linked β-D-fructofuranosyl residue backbone with (2 → 1)-linked branches (Liu, Luo, et al., 2010). EPS-1 exhibited anti-proliferative activity against tumor cells. Acetylated, phosphorylated and benzylated modifications of EPS-1 were able to enhance its anti-proliferative activity (Liu, Luo, Ye, & Zeng, 2012).

6.3. Polysaccharide from Rhizobium sp. N613

The rhizobium exopolysaccharide (REPS), with a molecular weight of about 35 kDa, is a β-glucan with a backbone of β-(1 → 4)-linked glucose and branches of β-(1 → 6)-glucose. REPS can significantly suppress tumor formation and enhance immunofunction in mice (Zhao, Chen, Ren, Han, & Cheng, 2010). A β-glucan with a molecular weight of 10.352 kDa was obtained from microwave irradiation degradation of REPS in the presence of H_2O_2, and showed an enhanced anti-cancer activity (Wei, Lv, Chen, & Zhao, 2011).

7. Conclusions

From the foregoing review, it is obvious that the structural diversity of polysaccharides depends largely on their botanical or biological sources. The unique structure diversities and physiochemical properties can be utilized successfully in various medical applications, and many polysaccharides have shown promising potential as anti-cancer agents. The anti-cancer properties of polysaccharides have been shown to be primarily mediated through three approaches: (1) direct cytotoxicity, (2) immunoenhancement, and (3) synergistic effects in combination treatment with conventional anti-cancer drugs.

Direct cytotoxicity involves polysaccharides interfering with cancer induction, growth, and progression by inducing cellular apoptosis and cell cycle arrest, and inhibiting tumor invasion, adhesion and metastasis. Immunoenhancement describes enhancing host immunofunction, which has been considered the main or singular mechanism of some types of polysaccharides, especially β-glucans from fungi, in order to inhibit tumor progression. Synergistic studies with other chemotherapeutic drugs have shown distinct improvements in the anti-cancer potential toward cancer treatment compared with single agents, which are mediated by enhancing the sensitivity of tumor and enhancing immune response to the treatments. However, except for β-glucans from medical mushrooms such as lentinan, PSK and PSP, which have been approved for commercial production and have been used on cancer patients for decades as biological reaction moderators, most of the remaining polysaccharides were tested simply by using cancer cells or tumor-transplanted mouse models without clinical trials.

There has been tremendous interest in developing anti-cancer polysaccharide drugs over the last decade. Some *in vitro* studies results appear to be promising, but more in-depth investigation is still required, and it is essential that *in vivo* studies are performed to confirm the results obtained *in vitro*. Nevertheless, developing more efficient and economic approaches for the preparation and modification of polysaccharides and elucidating the structure–activity relationship remain significant challenges, and thus an active area of research for years to come.

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References

Akazawa, N., Taguchi, K., Imai, A., Kikuchi, H., Minato, M., & Iwaki, H. (2010). A case of advanced gastric cancer responding to S-1/paclitaxel/lentinan as neoadjuvant chemoimmunotherapy. *Gan To Kagaku Ryoho*, *37*, 1365–1367.

Ale, M. T., Maruyama, H., Tamauchi, H., Mikkelsen, J. D., & Meyer, A. S. (2011). Fucoidan from *Sargassum* sp. and *Fucus vesiculosus* reduces cell viability of lung carcinoma and melanoma cells *in vitro* and activates natural killer cells in mice *in vivo*. *International Journal of Biological Macromolecules*, *49*, 331–336.

Alekseyenko, T. V., Zhanayeva, S. Y., Venediktova, A. A., Zvyagintseva, T. N., Kuznetsova, T. A., Besednova, N. N., et al. (2007). Antitumor and antimetastatic activity of fucoidan, a sulfated polysaccharide isolated from the Okhotsk Sea *Fucus evanescens* brown alga. *Bulletin of Experimental Biology and Medicine*, *143*, 730–732.

Ali, B. H., Ziada, A., & Blunden, G. (2009). Biological effects of gum arabic: A review of some recent research. *Food and Chemical Toxicology*, *47*, 1–8.

Bae, J. S., Jang, K. H., & Jin, H. K. (2006). Effects of natural polysaccharides on the growth and peritoneal carcinomatosis of human gastric adenocarcinoma in a nude mouse model. *Cancer Letters*, *235*, 60–68.

Bao, H., Choi, W. S., & You, S. (2010). Effect of sulfated modification on the molecular characteristics and biological activities of polysaccharides from *Hypsizigus marmoreus*. *Bioscience Biotechnology and Biochemistry*, *74*, 1408–1414.

Bisen, P. S., Baghel, R. K., Sanodiya, B. S., Thakur, G. S., & Prasad, G. B. (2010). *Lentinus edodes*: A macrofungus with pharmacological activities. *Current Medicinal Chemistry*, *17*, 2419–2430.

Boo, H. J., Hyun, J. H., Kim, S. C., Kang, J. I., Kim, M. K., Kim, S. Y., et al. (2011). Fucoidan from *Undaria pinnatifida* induces apoptosis in A549 human lung carcinoma cells. *Phytotherapy Research*, http://dx.doi.org/10.1002/ptr.3489

Borgenström, M., Wärri, A., Hiilesvuo, K., Käkönen, R., Käkönen, S., Nissinen, L., et al. (2007). O-sulfated bacterial polysaccharides with low anticoagulant activity inhibit metastasis. *Seminars in Thrombosis and Hemostasis*, *33*, 547–556.

Caliceti, P., Salmaso, S., & Bersani, S. (2010). Polysaccharide-based anticancer prodrugs. In L. H. Reddy, & P. Couvreur (Eds.), *Macromolecular anticancer therapeutics* (pp. 163–219). New York, NY: Humana Press Inc.

Campos-Vega, R., Guevara-Gonzalez, R. G., Guevara-Olvera, B. L., Dave Oomah, B., & Loarca-Piña, G. (2010). Bean (*Phaseolus vulgaris* L.) polysaccharides modulate gene expression in human colon cancer cells (HT-29). *Food Research International*, *43*, 1057–1064.

Cao, Q. Z., & Lin, Z. B. (2006). *Ganoderma lucidum* polysaccharides peptide inhibits the growth of vascular endothelial cell and the induction of VEGF in human lung cancer cell. *Life Sciences*, *78*, 1457–1463.

Cao, W., Li, X. Q., Hou, Y., Fan, H. T., Zhang, X. N., & Mei, Q. B. (2008). Structural analysis and anti-tumor activity *in vivo* of polysaccharide APS-2a from *Angelica sinensis*. *Journal of Chinese Medicinal Materials*, *31*, 261–266.

Cao, W., Li, X. Q., Liu, L., Yang, T. H., Li, C., Fan, H. T., et al. (2006). Structure of an anti-tumor polysaccharide from *Angelica sinensis* (Oliv.) Diels. *Carbohydrate Polymers*, *66*, 149–159.

Cao, W., Li, X. Q., Wang, X., Fan, H. T., Zhang, X. N., Hou, Y., et al. (2010). A novel polysaccharide, isolated from *Angelica sinensis* (Oliv.) Diels induces the apoptosis of cervical cancer HeLa cells through an intrinsic apoptotic pathway. *Phytomedicine*, *17*, 598–605.

Cao, W., Li, X. Q., Wang, X., Li, T., Chen, X., Liu, S. B., et al. (2010). Characterizations and anti-tumor activities of three acidic polysaccharides from *Angelica sinensis* (Oliv.) Diels. *International Journal of Biological Macromolecules*, *46*, 115–122.

Cassileth, B. R., Rizvi, N., Deng, G., Yeung, K. S., Vickers, A., Guillen, S., et al. (2009). Safety and pharmacokinetic trial of docetaxel plus an Astragalus-based herbal formula for non-small cell lung cancer patients. *Cancer Chemotherapy and Pharmacology*, *65*, 67–71.

Chan, S. L., & Yeung, J. H. (2006). Effects of polysaccharide peptide (PSP) from *Coriolus versicolor* on the pharmacokinetics of cyclophosphamide in the rat and cytotoxicity in HepG2 cells. *Food and Chemical Toxicology*, *44*, 689–694.

Chandra, R., & Rustgi, R. (1998). Biodegradable polymers. *Progress in Polymer Science*, *23*, 1273–1335.

Chen, B. D., Zhou, W. Y., Ning, M. L., Wang, Z. Z., Zou, L. L., Zhang, H. H., et al. (2012). Evaluation of antitumour activity of tea carbohydrate polymers in hepatocellular carcinoma animals. *International Journal of Biological Macromolecules*, *50*, 1103–1108.

Chen, D., Yao, W. J., Zhang, X. L., Han, X. Q., Qu, X. Y., Ka, W. B., et al. (2010). Effects of *Gekko* sulfated polysaccharide–protein complex on human hepatoma SMMC-7721 cells: Inhibition of proliferation and migration. *Journal of Ethnopharmacology*, *127*, 702–708.

Chen, D., Zhang, X. L., Du, Y., Jia, B. B., Ka, W. B., Sun, D. G., et al. (2012). Effects of *Gekko* sulfated polysaccharide–protein complex on the defective biorheological characters of dendritic cells under tumor microenvironment. *Cell Biochemistry and Biophysics*, *62*, 193–201.

Chen, L., Pan, J. Z., Li, X., Zhou, Y., Meng, Q. L., & Wang, Q. (2011). Endo-polysaccharide of *Phellinus igniarius* exhibited anti-tumor effect through enhancement of cell mediated immunity. *International Immunopharmacology*, *11*, 255–259.

Chen, R. Z., Meng, F. L., Liu, Z. Q., Chen, R. P., & Zhang, M. (2010). Antitumor activities of different fractions of polysaccharide purified from *Ornithogalum caudatum* Ait. *Carbohydrate Polymers*, *80*, 845–851.

Chen, S. G., Wang, J. F., Xue, C. H., Li, H., Sun, B. B., Xue, Y., et al. (2010). Sulfation of a squid ink polysaccharide and its inhibitory effect on tumor cell metastasis. *Carbohydrate Polymers*, *81*, 560–566.

Chen, T., Li, B., Li, Y. Y., Zhao, C. D., Shen, J. M., & Zhang, H. X. (2011). Catalytic synthesis and antitumor activities of sulfated polysaccharide from *Gynostemma pentaphyllum* Makino. *Carbohydrate Polymers*, *83*, 554–560.

Chen, W., Zhao, Z., & Li, Y. Q. (2011). Simultaneous increase of mycelial biomass and intracellular polysaccharide from *Fomes fomentarius* and its biological function of gastric cancer intervention. *Carbohydrate Polymers*, *85*, 369–375.

Chen, X., Cao, D. X., Zhou, L., Jin, H. Y., Dong, Q., Yao, J., et al. (2011). Structure of a polysaccharide from *Gastrodia elata* Bl., and oligosaccharides prepared thereof with anti-pancreatic cancer cell growth activities. *Carbohydrate Polymers*, *86*, 1300–1305.

Chen, X. M., Nie, W. J., Yu, G. Q., Li, Y. L., Hu, Y. S., Lu, J. X., et al. (2012). Antitumor and immunomodulatory activity of polysaccharides from *Sargassum fusiforme*. *Food and Chemical Toxicology*, *50*, 695–700.

Chen, X. Y., Xu, X. J., Zhang, L. N., & Zeng, F. B. (2009). Chain conformation and anti-tumor activities of phosphorylated (1 → 3)-β-D-glucan from *Poria cocos*. *Carbohydrate Polymers*, *78*, 581–587.

Cheng, H. R., Li, S. S., Fan, Y. Y., Gao, X. G., Hao, M., Wang, J., et al. (2011). Comparative studies of the antiproliferative effects of ginseng polysaccharides on HT-29 human colon cancer cells. *Medical Oncology*, *28*, 175–181.

Cheng, K. C., Huang, H. C., Chen, J. H., Hsu, J. W., Cheng, H. C., Ou, C. H., et al. (2007). *Ganoderma lucidum* polysaccharides in human monocytic leukemia cells: From gene expression to network construction. *BMC Genomics*, *8*, 411.

Choi, K. T. (2008). Botanical characteristics, pharmacological effects and medicinal components of Korean *Panax ginseng* C A Meyer. *Acta Pharmacologica Sinica*, *29*, 1109–1118.

Dang, S. S., Jia, X. L., Song, P., Cheng, Y. A., Zhang, X., Sun, M. Z., et al. (2009). Inhibitory effect of emodin and Astragalus polysaccharide on the replication of HBV. *World Journal of Gastroenterology*, *15*, 5669–5673.

Ding, X., Hou, Y. L., & Hou, W. R. (2012). Structure feature and antitumor activity of a novel polysaccharide isolated from *Lactarius deliciosus* Gray. *Carbohydrate Polymers*, *89*, 397–402.

Ding, X., Zhu, F. S., & Gao, S. G. (2012). Purification, antitumour and immunomodulatory activity of water-extractable and alkali-extractable polysaccharides from *Solanum nigrum* L. *Food Chemistry*, *131*, 677–684.

Ermakova, S., Sokolova, R., Kim, S. M., Um, B. H., Isakov, V., & Zvyagintseva, T. (2011). Fucoidans from brown seaweeds *Sargassum hornery*, *Eclonia cava*, *Costaria costata*: Structural characteristics and anticancer activity. *Applied Biochemistry and Biotechnology*, *164*, 841–850.

Fan, Y. L., Wang, W. H., Song, W., Chen, H. S., Teng, A. G., & Liu, A. J. (2012). Partial characterization and anti-tumor activity of an acidic polysaccharide from *Gracilaria lemaneiformis*. *Carbohydrate Polymers*, *88*, 1313–1318.

Feng, L., Jia, X. B., Shi, F., & Chen, Y. (2010). Identification of two polysaccharides from *Prunella vulgaris* L. and evaluation on their anti-lung adenocarcinoma activity. *Molecules*, *15*, 5093–5103.

Fidler, I. J. (2003). The pathogenesis of cancer metastasis: The 'seed and soil' hypothesis revisited. *Nature Reviews Cancer*, *3*, 453–458.

Gamal-Eldeen, A. M., Ahmed, E. F., & Abo-Zeid, M. A. (2009). *In vitro* cancer chemopreventive properties of polysaccharide extract from the brown alga, *Sargassum latifolium*. *Food and Chemical Toxicology*, *47*, 1378–1384.

Gan, D., Ma, L. P., Jiang, C. X., Xu, R. J., & Zeng, X. X. (2011). Production, preliminary characterization and antitumor activity *in vitro* of polysaccharides from the mycelium of *Pholiota dinghuensis* Bi. *Carbohydrate Polymers*, *84*, 997–1003.

Glinsky, V. V., & Raz, A. (2009). Modified citrus pectin anti-metastatic properties: One bullet, multiple targets. *Carbohydrate Research*, *344*, 1788–1791.

Gonzaga, M. L., Bezerra, D. P., Alves, A. P., de Alencar, N. M., Mesquita Rde, O., Lima, M. W., et al. (2009). *In vivo* growth-inhibition of Sarcoma 180 by an glucan-protein complex polysaccharide obtained from *Agaricus blazei* Murill. *Journal of Natural Medicines*, *63*, 32–40.

Guo, L., Bai, S. P., Zhao, L., & Wang, X. H. (2011). Astragalus polysaccharide injection integrated with vinorelbine and cisplatin for patients with advanced non-small cell lung cancer: Effects on quality of life and survival. *Medical Oncology*, http://dx.doi.org/10.1007/s12032-011-0068-9

Han, J. (1988). Traditional Chinese medicine and the search for new antineoplastic drugs. *Journal of Ethnopharmacology*, *24*, 1–17.

Han, Q., Ling, Z. J., He, P. M., & Xiong, C. Y. (2010). Immunomodulatory and antitumor activity of polysaccharide isolated from tea plant flower. *Progress in Biochemistry and Biophysics*, *37*, 646–653.

Han, S. B., Kim, Y. H., Lee, C. W., Park, S. M., Lee, H. Y., Ahn, K. S., et al. (1998). Characteristic immunostimulation by angelan isolated from *Angelica gigas* Nakai. *Immunopharmacology*, *40*, 39–48.

Han, S. B., Lee, C. W., Kang, J. S., Yoon, Y. D., Lee, K. H., Lee, K., et al. (2006). Acidic polysaccharide from *Phellinus linteus* inhibits melanoma cell metastasis by blocking cell adhesion and invasion. *International Immunopharmacology*, *6*, 697–702.

Han, S. B., Lee, C. W., Kang, M. R., Yoon, Y. D., Kang, J. S., Lee, K. H., et al. (2006). Pectic polysaccharide isolated from *Angelica gigas* Nakai inhibits melanoma cell metastasis and growth by directly preventing cell adhesion and activating host immune functions. *Cancer Letters*, *243*, 264–273.

Harada, K., Itashiki, Y., Takenawa, T., & Ueyama, Y. (2010). Effects of lentinan alone and in combination with fluoropyrimidine anticancer agent on growth of human oral squamous cell carcinoma *in vitro* and *in vivo*. *International Journal of Oncology*, *37*, 623–631.

Haranaka, K., Satomi, N., Sakurai, A., Haranaka, R., Okada, N., & Kobayashi, M. (1985). Antitumor activities and tumor necrosis factor producibility of traditional Chinese medicines and crude drugs. *Cancer Immunology Immunotherapy*, *20*, 1–5.

Hazama, S., Watanabe, S., Ohashi, M., Yagi, M., Suzuki, M., Matsuda, K., et al. (2009). Efficacy of orally administered superfine dispersed lentinan (beta-1,3-glucan) for the treatment of advanced colorectal cancer. *Anticancer Research*, *29*, 2611–2617.

He, L., Ji, P. F., Gong, X. G., Li, W. Q., Cheng, J. W., Qian, H., et al. (2011). Physicochemical characterization, antioxidant and anticancer activities *in vitro* of a novel polysaccharide from *Melia toosendan* Sieb. Et Zucc fruit. *International Journal of Biological Macromolecules*, *49*, 422–427.

Helms, S. (2004). Cancer prevention and therapeutics: *Panax ginseng*. *Alternative Medicine Review*, *9*, 259–274.

Hirahara, N., Fujioka, M., Edamatsu, T., Fujieda, A., Sekine, F., Wada, T., et al. (2011). Protein-bound polysaccharide-K (PSK) induces apoptosis and inhibits proliferation of promyelomonocytic leukemia HL-60 cells. *Anticancer Research*, *31*, 2733–2738.

Hirahara, N., Fujioka, M., Fujieda, A., Wada, T., & Tanaka, T. (2010). Analysis of the mechanism of apoptosis induction by PSK. *Gan To Kagaku Ryoho*, *37*, 2255–2257.

Holtkamp, A. D., Kelly, S., Ulber, R., & Lang, S. (2009). Fucoidans and fucoidanases-focus on techniques for molecular structure elucidation and modification of marine polysaccharides. *Applied Microbiology and Biotechnology*, *82*, 1–11.

Hori, T., Ikehara, T., Takatsuka, S., Fukuoka, T., Tendo, M., Tezuka, K., et al. (2011). Combination chemotherapy of S-1/low-dose CDDP/lentinan for advanced gastric cancer. *Gan To Kagaku Ryoho*, *38*, 293–295.

Hori, T., Ikehara, T., Takatsuka, S., Fukuoka, T., Tendou, M., Tezuka, K., et al. (2009). A case of the local advanced gastric cancer which became a resection possible in S-1/CDDP/lentinan neoadjuvant chemotherapy. *Gan To Kagaku Ryoho*, *36*, 2309–2311.

Hsieh, T. C., Wu, P., Park, S., & Wu, J. M. (2006). Induction of cell cycle changes and modulation of apoptogenic/anti-apoptotic and extracellular signaling regulatory protein expression by water extracts of I'm-Yunity™ (PSP). *BMC Complementary and Alternative Medicine*, *6*, 30.

Hsu, J. W., Huang, H. C., Chen, S. T., Wong, C. H., & Juan, H. F. (2009). *Ganoderma lucidum* polysaccharides induce macrophage-like differentiation in human leukemia THP-1 cells via Caspase and p53 activation. *Evidence-Based Complementary and Alternative Medicine*, *2011*, 358717.

Hu, Y., Cheng, S. C., Chan, K. T., Ke, Y., Xue, B., Sin, F. W., et al. (2010). Fucoidin enhances dendritic cell-mediated T-cell cytotoxicity against NY-ESO-1 expressing human cancer cells. *Biochemical and Biophysical Research Communications*, *392*, 329–334.

Huang, C. Y., Chen, J. Y., Wu, J. E., Pu, Y. S., Liu, G. Y., Pan, M. H., et al. (2010). Ling-Zhi polysaccharides potentiate cytotoxic effects of anticancer drugs against drug-resistant urothelial carcinoma cells. *Journal of Agricultural and Food Chemistry*, *58*, 8798–8805.

Huang, Q. L., Jin, Y., Zhang, L. N., Cheung, P. C., & Kennedy, J. F. (2007). Structure, molecular size and antitumor activities of polysaccharides from *Poria cocos* mycelia produced in fermenter. *Carbohydrate Polymers*, *70*, 324–333.

Hui, M. K., Wu, W. K., Shin, V. Y., So, W. H., & Cho, C. H. (2006). Polysaccharides from the root of *Angelica sinensis* protect bone marrow and gastrointestinal tissues against the cytotoxicity of cyclophosphamide in mice. *International Journal of Medical Sciences*, *3*, 1–6.

Hung, C. F., Hsu, B. Y., Chang, S. C., & Chen, B. H. (2012). Antiproliferation of melanoma cells by polysaccharide isolated from *Zizyphus jujuba*. *Nutrition*, *28*, 98–105.

Hyun, J. H., Kim, S. C., Kang, J. I., Kim, M. K., Boo, H. J., Kwon, J. M., et al. (2009). Apoptosis inducing activity of fucoidan in HCT-15 colon carcinoma cells. *Biological & Pharmaceutical Bulletin*, *32*, 1760–1764.

Isoda, N., Eguchi, Y., Nukaya, H., Hosho, K., Suga, Y., Suga, T., et al. (2009). Clinical efficacy of superfine dispersed lentinan (beta-1,3-glucan) in patients with hepatocellular carcinoma. *Hepatogastroenterology*, *56*, 437–441.

Ito, K., Masuda, Y., Yamasaki, Y., Yokota, Y., & Nanba, H. (2009). Maitake beta-glucan enhances granulopoiesis and mobilization of granulocytes by increasing G-CSF production and modulating CXCR4/SDF-1 expression. *International Immunopharmacology*, *9*, 1189–1196.

Jackson, C. L., Dreaden, T. M., Theobald, L. K., Tran, N. M., Beal, T. L., Eid, M., et al. (2007). Pectin induces apoptosis in human prostate cancer cells: Correlation of apoptotic function with pectin structure. *Glycobiology*, *17*, 805–819.

Jeong, B. E., Ko, E. J., & Joo, H. G. (2012). Cytoprotective effects of fucoidan, an algae-derived polysaccharide on 5-fluorouracil-treated dendritic cells. *Food and Chemical Toxicology*, *50*, 1480–1484.

Ji, N. F., Yao, L. S., Li, Y., He, W., Yi, K. S., & Huang, M. (2011). Polysaccharide of *Cordyceps sinensis* enhances cisplatin cytotoxicity in non-small cell lung cancer H157 cell line. *Integrative Cancer Therapies*, *10*, 359–367.

Jiang, C. X., Wang, M. C., Liu, J., Gan, D., & Zeng, X. X. (2011). Extraction, preliminary characterization, antioxidant and anticancer activities *in vitro* of polysaccharides from *Cyclina sinensis*. *Carbohydrate Polymers*, *84*, 851–857.

Jiang, Y. H., Jiang, X. L., Wang, P., Mou, H. J., Hu, X. K., & Liu, S. Q. (2008). The antitumor and antioxidative activities of polysaccharides isolated from *Isaria farinosa* B05. *Microbiological Research*, *163*, 424–430.

Jiménez-Medina, E., Berruguilla, E., Romero, I., Algarra, I., Collado, A., Garrido, F., et al. (2008). The immunomodulator PSK induces *in vitro* cytotoxic activity in tumour cell lines via arrest of cell cycle and induction of apoptosis. *BMC Cancer*, *8*, 78.

Jin, J. O., Song, M. G., Kim, Y. N., Park, J. I., & Kwak, J. Y. (2010). The mechanism of fucoidan-induced apoptosis in leukemic cells: Involvement of ERK1/2, JNK, glutathione, and nitric oxide. *Molecular Carcinogenesis*, *49*, 771–782.

Jin, L. Q., Zheng, Z. J., Peng, Y., Li, W. X., Chen, X. M., & Lu, J. X. (2007). Opposite effects on tumor growth depending on dose of *Achyranthes bidentata* polysaccharides in C57BL/6 mice. *International Immunopharmacology*, *7*, 568–577.

Jin, X. C. (2012). Bioactivities of water-soluble polysaccharides from fruit shell of *Camellia oleifera* Abel: Antitumor and antioxidant activities. *Carbohydrate Polymers*, *87*, 2198–2201.

Joseph, J., Smina, T. P., & Janardhanan, K. K. (2011). Polysaccharide protein complex isolated from mushroom *Phellinus rimosus* (berk.) Pilat alleviates γ radiation-inuced toxicity in mice. *Cancer Biotherapy and Radiopharmaceuticals*, *26*, 299–308.

Joseph, M. M., Aravind, S. R., Varghese, S., Mini, S., & Sreelekha, T. T. (2012). Evaluation of antioxidant, antitumor and immunomodulatory properties of polysaccharide isolated from fruit rind of *Punica granatum*. *Molecular Medicine Reports*, *5*, 489–496.

Karnjanapratum, S., & You, S. G. (2011). Molecular characteristics of sulfated polysaccharides from *Monostroma nitidum* and their *in vitro* anticancer and immunomodulatory activities. *International Journal of Biological Macromolecules*, *48*, 311–318.

Kataoka, H., Shimura, T., Mizoshita, T., Kubota, E., Mori, Y., Mizushima, T., et al. (2009). Lentinan with S-1 and paclitaxel for gastric cancer chemotherapy improve patient quality of life. *Hepatogastroenterology*, *56*, 547–550.

Katoh, R., & Ooshiro, M. (2007). Enhancement of antitumor effect of tegafur/uracil (UFT) plus leucovorin by combined treatment with protein-bound polysaccharide, PSK, in mouse models. *Cellular & Molecular Immunology*, *4*, 295–299.

Ke, M., Zhang, X. J., Han, Z. H., Yu, H. Y., Lin, Y., Zhang, W. G., et al. (2011). Extraction, purification of *Lycium barbarum* polysaccharides and bioactivity of purified fraction. *Carbohydrate Polymers*, *86*, 136–141.

Ke, R. D., Lin, S. F., Chen, Y., Ji, C. R., & Shu, Q. G. (2010). Analysis of chemical composition of polysaccharides from *Poria cocos* Wolf and its anti-tumor activity by NMR spectroscopy. *Carbohydrate Polymers*, *80*, 31–34.

Kim, E. J., Park, S. Y., Lee, J. Y., & Park, J. H. (2010). Fucoidan present in brown algae induces apoptosis of human colon cancer cells. *BMC Gastroenterology*, *10*, 96.

Kim, H. Y., Kim, J. H., Yang, S. B., Hong, S. G., Lee, S. A., Hwang, S. J., et al. (2007). A polysaccharide extracted from rice bran fermented with *Lentinus edodes* enhances natural killer cell activity and exhibits anticancer effects. *Journal of Medicinal Food*, *10*, 25–31.

Kim, J. Y., Yoon, Y. D., Ahn, J. M., Kang, J. S., Park, S. K., Lee, K., et al. (2007). Angelan isolated from *Angelica gigas* Nakai induces dendritic cell maturation through toll-like receptor 4. *International Immunopharmacology*, *7*, 78–87.

Kim, Y. O., Park, H. W., Kim, J. H., Lee, J. Y., Moon, S. H., & Shin, C. S. (2006). Anti-cancer effect and structural characterization of endo-polysaccharide from cultivated mycelia of *Inonotus obliquus*. *Life Sciences*, *79*, 72–80.

King, M. L., & Murphy, L. L. (2010). Role of cyclin inhibitor protein p21 in the inhibition of HCT116 human colon cancer cell proliferation by American ginseng (*Panax quinquefolius*) and its constituents. *Phytomedicine*, *17*, 261–268.

Kinoshita, J., Fushida, S., Harada, S., Makino, I., Nakamura, K., Oyama, K., et al. (2010). PSK enhances the efficacy of docetaxel in human gastric cancer cells through inhibition of nuclear factor-κB activation and survivin expression. *International Journal of Oncology*, *36*, 593–600.

Kono, K., Kawaguchi, Y., Mizukami, Y., Mimura, K., Sugai, H., Akaike, H., et al. (2008). Protein-bound polysaccharide K partially prevents apoptosis of circulating T cells induced by anti-cancer drug S-1 in patients with gastric cancer. *Oncology*, *74*, 143–149.

Korbelik, M., & Cooper, P. D. (2007). Potentiation of photodynamic therapy of cancer by complement: The effect of γ-inulin. *British Journal of Cancer*, *96*, 67–72.

Kubota, E., Kataoka, H., Hayashi, K., Kamiya, T., Sasaki, M., Ogasawara, N., et al. (2009). Advanced stomach and pancreas cancer successfully treated with combination chemotherapy with S-1/paclitaxel/lentinan. *Hepatogastroenterology*, *56*, 106–110.

Kwon, M. J., & Nam, T. J. (2007). A polysaccharide of the marine alga *Capsosiphon fulvescens* induces apoptosis in AGS gastric cancer cells via an IGF-IR-mediated PI3K/Akt pathway. *Cell Biology International*, *31*, 768–775.

Lavi, I., Friesem, D., Geresh, S., Hadar, Y., & Schwartz, B. (2006). An aqueous polysaccharide extract from the edible mushroom *Pleurotus ostreatus* induces anti-proliferative and pro-apoptotic effects on HT-29 colon cancer cells. *Cancer Letters*, *244*, 61–70.

Li, B., Lu, F., Wei, X. J., & Zhao, R. X. (2008). Fucoidan: Structure and bioactivity. *Molecules*, *13*, 1671–1695.

Li, J., Bao, Y. X., Lam, W. K., Li, W. W., Lu, F., Zhu, X., et al. (2008). Immunoregulatory and anti-tumor effects of polysaccharopeptide and Astragalus polysaccharides on tumor-bearing mice. *Immunopharmacology and Immunotoxicology*, *30*, 771–782.

Li, J., Li, Q. W., Feng, T., Zhang, T., Li, K., Zhao, R., et al. (2007). Antitumor activity of crude polysaccharides isolated from *Solanum nigrum* Linne on U14 cervical carcinoma bearing mice. *Phytotherapy Research*, *21*, 832–840.

Li, J., Li, Q. W., Peng, Y., Zhao, R., Han, Z. S., & Gao, D. W. (2010). Protective effects of fraction 1a of polysaccharides isolated from *Solanum nigrum* Linne on thymus in tumor-bearing mice. *Journal of Ethnopharmacology*, *129*, 350–356.

Li, N., Li, L., Fang, J. C., Wong, J. H., Ng, T. B., Jiang, Y., et al. (2012). Isolation and identification of a novel polysaccharide–peptide complex with antioxidant, antiproliferative, and hypoglycemic activities from the abalone mushroom. *Bioscience Reports*, *32*, 221–228.

Li, R., Chen, W. C., Wang, W. P., Tian, W. Y., & Zhang, X. G. (2009). Extraction, characterization of Astragalus polysaccharides and its immune modulating activities in rats with gastric cancer. *Carbohydrate Polymers*, *78*, 738–742.

Li, S. G., Wang, D. G., Tian, W., Wang, X. X., Zhao, J. X., Liu, Z., et al. (2008). Characterization and anti-tumor activity of a polysaccharide from *Hedysarum polybotrys* Hand.-Mazz. *Carbohydrate Polymers*, *73*, 344–350.

Li, W. J., Chen, Y., Nie, S. P., Xie, M. Y., He, M., Zhang, S. S., et al. (2011). *Ganoderma atrum* polysaccharide induces anti-tumor activity via the mitochondrial apoptotic pathway related to activation of host immune response. *Journal of Cellular Biochemistry*, *112*, 860–871.

Li, W. J., Nie, S. P., Chen, Y., Wang, Y. X., Li, C., & Xie, M. Y. (2011). Enhancement of cyclophosphamide-induced antitumor effect by a novel polysaccharide from *Ganoderma atrum* in sarcoma 180-bearing mice. *Journal of Agricultural and Food Chemistry*, *59*, 3707–3716.

Li, X. J., Jia, Y. J., & Chen, L. (2011). Clinical observation of thermotherapy combined with thoracic injection of lentinan in treatment of cancerous hydrothorax of patients with lung cancer. *Chinese Journal of Integrative Medicine*, *31*, 1062–1065.

Li, Y. B., Wang, R., Wu, H. L., Li, Y. H., Zhong, L. J., Yu, H. M., et al. (2008). Serum amyloid A mediates the inhibitory effect of *Ganoderma lucidum* polysaccharides on tumor cell adhesion to endothelial cells. *Oncology Reports*, *20*, 549–556.

Liang, B. B., Liu, H. G., & Cao, J. T. (2008). Antitumor effect of polysaccharides from cactus pear fruit in S180-bearing mice. *Chinese Journal of Cancer*, *27*, 580–584.

Liang, M., Li, S. C., Shen, B., Cai, J. P., Li, C., Wang, Z. Y., et al. (2012). Anti-hepatocarcinoma effects of *Aconitum coreanum* polysaccharides. *Carbohydrate Polymers*, *88*, 973–976.

Lins, K. O., Bezerra, D. P., Alves, A. P., Alencar, N. M., Lima, M. W., Torres, V. M., et al. (2009). Antitumor properties of a sulfated polysaccharide from the red seaweed *Champia feldmannii* (Diaz-Pifferer). *Journal of Applied Toxicology*, *29*, 20–26.

Liu, A. J., Yang, N., Song, W., Cao, D. X., & Wang, W. J. (2009). Cartilage polysaccharide induces apoptotic cell death of L1210 cells. *Leukemia & Lymphoma*, *50*, 1017–1029.

Liu, A. J., Han, X., Zhang, G. R., Zhao, X. H., & Zheng, G. Q. (2009). Effects of cartilage polysaccharide on apoptosis of human hepatoma BEL-7402 cells and murine

H22 hepatocarcinoma. *International Journal of Food Sciences and Nutrition*, *31*, 47–58.
Liu, A. J., Hu, Y. X., Liu, C. J., Yao, X. L., & Zhang, G. R. (2009). The mechanism of inhibition of metastasis by cartilage polysaccharide in breast-cancer cells. *Biotechnology and Applied Biochemistry*, *53*, 253–263.
Liu, A. J., Liu, D. Y., Zhao, S. S., Zheng, J., Cao, D. X., & Zhang, H. (2010). Up regulation of annexin A2 on murine H22 hepatocarcinoma cells induced by cartilage polysaccharide. *Cancer Epidemiology*, *35*, 490–496.
Liu, A. J., Song, W., Yang, N., Liu, Y. J., & Zhang, G. R. (2007). Cartilage polysaccharide induces apoptosis in human leukemia K562 cells. *Cell Biology and Toxicology*, *23*, 465–476.
Liu, C. H., Li, X. D., Li, Y. H., Feng, Y., Zhou, S., & Wang, F. S. (2008). Structural characterisation and antimutagenic activity of a novel polysaccharide isolated from *Sepiella maindroni* ink. *Food Chemistry*, *110*, 807–813.
Liu, C. H., Lin, Q. X., Gao, Y., Ye, L., Xing, Y. Y., & Xi, T. (2007). Characterization and antitumor activity of a polysaccharide from *Strongylocentrotus nudus* eggs. *Carbohydrate Polymers*, *67*, 313–318.
Liu, H. Y., Huang, Z. L., Yang, G. H., Lu, W. Q., & Yu, N. R. (2008). Inhibitory effect of modified citrus pectin on liver metastases in a mouse colon cancer model. *World Journal of Gastroenterology*, *14*, 7386–7391.
Liu, J., Luo, J. G., Ye, H., & Zeng, X. X. (2012). Preparation, antioxidant and antitumor activities *in vitro* of different derivatives of levan from endophytic bacterium *Paenibacillus polymyxa* EJS-3. *Food and Chemical Toxicology*, *50*, 767–772.
Liu, J., Luo, J. G., Ye, H., Sun, Y., Lu, Z. X., & Zeng, X. X. (2010). Medium optimization and structural characterization of exopolysaccharides from endophytic bacterium *Paenibacillus polymyxa* EJS-3. *Carbohydrate Polymers*, *79*, 206–213.
Liu, L. M., & Zhang, L. S. (2010). Effect of astragalus polysaccharide on the function and maturation of plasmacytoid dendritic cells from chronic myelogenous leukemia before and after treatment. *Chinese Journal of Hematology*, *31*, 740–743.
Liu, Y., Li, Y. M., Yang, W. B., Zhang, L., & Cao, G. (2012). Anti-hepatoma activity in mice of a polysaccharide from the rhizome of *Anemone raddeana*. *International Journal of Biological Macromolecules*, *50*, 632–636.
Liu, Y. H., Liu, C. H., Tan, H. N., Zhao, T., Cao, J. C., & Wang, F. S. (2009). Sulfation of a polysaccharide obtained from *Phellinus ribis* and potential biological activities of the sulfated derivatives. *Carbohydrate Polymers*, *77*, 370–375.
Louie, B., Rajamahanty, S., Won, J., Choudhury, M., & Konno, S. (2009). Synergistic potentiation of interferon activity with maitake mushroom D-fraction on bladder cancer cells. *BJU International*, *105*, 1011–1015.
Lu, H., Yang, Y., Gad, E., Inatsuka, C., Wenner, C. A., Disis, M. L., et al. (2011). TLR2 agonist PSK activates human NK cells and enhances the anti-tumor effect of HER2-targeted monoclonal antibody therapy. *Clinical Cancer Research*, *17*, 6742–6753.
Lu, H., Yang, Y., Gad, E., Wenner, C. A., Chang, A., Larson, E. R., et al. (2011). Polysaccharide krestin is a novel TLR2 agonist that mediates inhibition of tumor growth via stimulation of CD8 T cells and NK. *Clinical Cancer Research*, *17*, 67–76.
Lu, J. H., Meng, Q. F., Ren, X. D., Chen, Y. G., Li, T. T., & Teng, L. R. (2008). Extraction and antitumor activity of polysaccharides from *Tricholoma matsutake*. *Journal of Biotechnology*, *136S*, S469.
Lu, W. Z., Geng, G. X., Li, Q. W., Li, J., Liu, F. Z., Han, Z. S., et al. (2009). Anti-tumor activity of polysaccharides isolated from *Patrinia scabra* Bunge on U14 cervical carcinoma bearing mice. *American Journal of Chinese Medicine*, *37*, 933–944.
Luk, S. U., Lee, T. K., Liu, J., Lee, D. T., Chiu, Y. T., Ma, S., et al. (2011). Chemopreventive effect of PSP through targeting of prostate cancer stem cell-like population. *PLoS One*, *6*, e19804.
Ma, Y., Aymeric, L., Locher, C., Kroemer, G., & Zitvogel, L. (2011). The dendritic cell-tumor cross-talk in cancer. *Current Opinion in Immunology*, *23*, 146–152.
Ma, Z. C., Wang, J. G., Zhang, L. N., Zhang, Y. F., & Ding, K. (2010). Evaluation of water soluble β-D-glucan from *Auricularia auricular-judaeas* potential antitumor agent. *Carbohydrate Polymers*, *80*, 977–983.
Mallick, S. K., Maiti, S., Bhutia, S. K., & Maiti, T. K. (2010). Antitumor properties of a heteroglucan isolated from *Astraeus hygrometricus* on Dalton's lymphoma bearing mouse. *Food and Chemical Toxicology*, *48*, 2115–2121.
Mantovani, M. S., Bellini, M. F., Angeli, J. P., Oliveira, R. J., Silva, A. F., & Ribeiro, L. R. (2008). Beta-glucans in promoting health: Prevention against mutation and cancer. *Mutation Research*, *658*, 154–161.
Mao, F., Xiao, B. X., Jiang, Z., Zhao, J. W., Huang, X., & Guo, J. M. (2011). Anticancer effect of *Lycium barbarum* polysaccharides on colon cancer cells involves G0/G1 phase arrest. *Medical Oncology*, *28*, 121–126.
Masuda, Y., Inoue, M., Miyata, A., Mizuno, S., & Nanba, H. (2009). Maitake β-glucan enhances therapeutic effect and reduces myelosupression and nephrotoxicity of cisplatin in mice. *International Immunopharmacology*, *9*, 620–626.
Masuda, Y., Ito, K., Konishi, M., & Nanba, H. (2010). A polysaccharide extracted from *Grifola frondosa* enhances the anti-tumor activity of bone marrow-derived dendritic cell-based immunotherapy against murine colon cancer. *Cancer Immunology Immunotherapy*, *59*, 1531–1541.
Masuda, Y., Matsumoto, A., Toida, T., Oikawa, T., Ito, K., & Nanba, H. (2009). Characterization and antitumor effect of a novel polysaccharide from *Grifola frondosa*. *Journal of Agricultural and Food Chemistry*, *57*, 10143–10149.
Mayell, M. (2001). Maitake extracts and their therapeutic potential. *Alternative Medicine Review*, *6*, 48–60.
McCulloch, M., See, C., Shu, X. J., Broffman, M., Kramer, A., Fan, W. Y., et al. (2006). Astragalus-based Chinese herbs and platinum-based chemotherapy for advanced non-small-cell lung cancer: Meta-analysis of randomized trials. *Journal of Clinical Oncology*, *24*, 419–430.
Meyers, M. A., Chen, P. Y., Lin, A. Y., & Seki, Y. (2008). Biological materials: Structure and mechanical properties. *Progress in Materials Science*, *53*, 1–206.
Miao, Y., Xiao, B. X., Jiang, Z., Guo, Y. N., Mao, F., Zhao, J. W., et al. (2010). Growth inhibition and cell-cycle arrest of human gastric cancer cells by *Lycium barbarum* polysaccharide. *Medical Oncology*, *27*, 785–790.
Nakagawa, Y., Yanagawa, K., Matsunaga, N., & Noda, S. (2010). A case of gastric cancer with para-aortic lymph node metastasis successfully treated with S-1/paclitaxel/lentinan combination therapy. *Gan To Kagaku Ryoho*, *37*, 1131–1134.
Nakayasu, S., Soegima, R., Yamaguchi, K., & Oda, T. (2009). Biological activities of fucose-containing polysaccharide ascophyllan isolated from the brown alga *Ascophyllum nodosum*. *Bioscience Biotechnology and Biochemistry*, *73*, 961–964.
Nangia-Makker, P., Hogan, V., Honjo, Y., Baccarini, S., Tait, L., Bresalier, R., et al. (2002). Inhibition of human cancer cell growth and metastasis in nude mice by oral intake of modified citrus pectin. *Journal of the National Cancer Institute*, *94*, 1854–1862.
Naveen Chandra, A., Susmitha, Y., Manjusha, O., Sreelatha, A., Manohari, V., & Visweswara Rao, C. H. (2011). Quantitative evaluation of carbohydrate levels in different natural foodstuffs by UV-visible spectrophometer. *International Journal of Research in Pharmacy and Chemistry*, *1*, 44–45.
Ni, W. H., Zhang, X., Wang, B., Chen, Y., Han, H., Fan, Y. Y., et al. (2010). Antitumor activities and immunomodulatory effects of ginseng neutral polysaccharides in combination with 5-fluorouracil. *Journal of Medicinal Food*, *13*, 270–277.
Nimura, H., Mitsumori, N., Takahashi, N., Kashimura, H., Takayama, S., Kashiwagi, H., et al. (2006). S-1 combined with lentinan in patients with unresectable or recurrent gastric cancer. *Gan To Kagaku Ryoho*, (Suppl. 1), 106–109.
Niu, Y. C., Liu, J. C., Zhao, X. M., & Cao, J. (2009). A low molecular weight polysaccharide isolated from *Agaricus blazei* Murill (LMPAB) exhibits its anti-metastatic effect by down-regulating metalloproteinase-9 and up-regulating Nm23-H1. *American Journal of Chinese Medicine*, *37*, 909–921.
Niu, Y. C., Liu, J. C., Zhao, X. M., Su, F. Q., & Cui, H. X. (2009). Immunostimulatory activities of a low molecular weight antitumoral polysaccharide isolated from *Agaricus blazei* Murill (LMPAB) in Sarcoma 180 ascitic tumor-bearing mice. *Pharmazie*, *64*, 472–476.
Oba, K., Kobayashi, M., Matsui, T., Kodera, Y., & Sakamoto, J. (2009). Individual patient based meta-analysis of lentinan for unresectable/recurrent gastric cancer. *Anticancer Research*, *29*, 2739–2745.
Oh, J. Y., Baek, Y. M., Kim, S. W., Hwang, H. J., Hwang, H. S., Lee, S. H., et al. (2008). Apoptosis of human hepatocarcinoma (HepG2) and neuroblastoma (SKN-SH) cells induced by polysaccharides–peptide complexes produced by submerged mycelial culture of an entomopathogenic fungus *Cordyceps sphecocephala*. *Journal of Microbiology and Biotechnology*, *18*, 512–519.
Ohwada, S., Ogawa, T., Makita, F., Tanahashi, Y., Ohya, T., Tomizawa, N., et al. (2006). Beneficial effects of protein-bound polysaccharide K plus tegafur/uracil in patients with stage II or III colorectal cancer: Analysis of immunological parameters. *Oncology Reports*, *15*, 861–868.
Ono, Y., Hayashida, T., Konagai, A., Okazaki, H., Miyao, K., Kawachi, S., et al. (2012). Direct inhibition of the TGF-β pathway by protein-bound polysaccharide through inactivation of Smad2 signaling. *Cancer Science*, *103*, 317–324.
Ooi, V. E., & Liu, F. (2000). Immunomodulation and anti-cancer activity of polysaccharide–proteins complexes. *Current Medicinal Chemistry*, *7*, 715–729.
Pang, X., Chen, Z., Gao, X., Liu, W., Slavin, M., Yao, W., et al. (2007). Potential of a novel polysaccharide preparation (GLPP) from Anhui-grown *Ganoderma lucidum* in tumor treatment and immunostimulation. *Journal of Food Science*, *72*, S435–S442.
Park, H. S., Kim, G. Y., Nam, T. J., Deuk Kim, N., & Hyun Choi, Y. (2011). Antiproliferative activity of fucoidan was associated with the induction of apoptosis and autophagy in AGS human gastric cancer cells. *Journal of Food Science*, *76*, T77–T83.
Peng, Z. F., Liu, M., Fang, Z. X., Wu, J. L., & Zhang, Q. Q. (2012). Composition and cytotoxicity of a novel polysaccharide from brown alga (*Laminaria japonica*). *Carbohydrate Polymers*, *89*, 1022–1026.
Philchenkov, A., Zavelevich, M., Imbs, T., Zvyagintseva, T., & Zaporozhets, T. (2007). Sensitization of human malignant lymphoid cells to etoposide by fucoidan, a brown seaweed polysaccharide. *Experimental Oncology*, *29*, 181–185.
Pinto, A. V., Martins, P. R., Romagnoli, G. G., Campanelli, A. P., Terezan, A. P., Filho, E. R., et al. (2009). Polysaccharide fraction of *Agaricus brasiliensis* avoids tumor-induced IL-10 production and changes the microenvironment of subcutaneous Ehrlich adenocarcinoma. *Cell Immunology*, *256*, 27–38.
Pyo, P., Louie, B., Rajamahanty, S., Choudhury, M., & Konno, S. (2008). Possible immunotherapeutic potentiation with D-fraction in prostate cancer cells. *Journal of Hematology & Oncology*, *1*, 25.
Qiu, S., Huang, S., Huang, J., Pan, J., & Zhang, W. (2010). Antitumor activity of the water-soluble polysaccharide from *Hyriopsis cumingii in vitro*. *Toxicology and Industrial Health*, *26*, 151–161.
Ramachandran, C., Wilk, B. J., Hotchkiss, A., Chau, H., Eliaz, I., & Melnick, S. J. (2011). Activation of human T-helper/inducer cell, T-cytotoxic cell, B-cell, and natural killer (NK)-cells and induction of natural killer cell activity against K562 chronic myeloid leukemia cells with modified citrus pectin. *BMC Complementary and Alternative Medicine*, *11*, 59.
Ryu, D. S., Baek, G. O., Kim, E. Y., Kim, K. H., & Lee, D. S. (2010). Effects of polysaccharides derived from *Orostachys japonicus* on induction of cell cycle arrest and apoptotic cell death in human colon cancer cells. *BMB Reports*, *43*, 750–755.
Saitoh, Y., Nagai, Y., & Miwa, N. (2009). Fucoidan–vitamin C complex suppresses tumor invasion through the basement membrane, with scarce injuries to normal or tumor cells, via decreases in oxidative stress and matrix metalloproteinases. *International Journal of Oncology*, *35*, 1183–1189.

Sakai, T., Yamashita, Y., Maekawa, T., Mikami, K., Hoshino, S., & Shirakusa, T. (2008). Immunochemotherapy with PSK and fluoropyrimidines improves long-term prognosis for curatively resected colorectal cancer. *Cancer Biotherapy and Radiopharmaceuticals*, *23*, 461–467.

Salvador, C., Li, B., Hansen, R., Cramer, D. E., Kong, M., & Yan, J. (2008). Yeast-derived beta-glucan augments the therapeutic efficacy mediated by anti-vascular endothelial growth factor monoclonal antibody in human carcinoma xenograft models. *Clinical Cancer Research*, *14*, 1239–1247.

Sarangi, I., Ghosh, D., Bhutia, S. K., Mallick, S. K., & Maiti, T. K. (2006). Anti-tumor and immunomodulating effects of *Pleurotus ostreatus* mycelia-derived proteoglycans. *International Immunopharmacology*, *6*, 1287–1297.

Sarker, S. D., & Nahar, L. (2004). Natural medicine: The genus Angelica. *Current Medicinal Chemistry*, *11*, 1479–1500.

Shang, P., Qian, A. R., Yang, T. H., Jia, M., Mei, Q. B., Cho, C. H., et al. (2003). Experimental study of anti-tumor effects of polysaccharides from *Angelica sinensis*. *World Journal of Gastroenterology*, *9*, 1963–1967.

Shen, Y. D., Shao, X. T., Ni, Y. D., Xu, H., & Tong, X. M. (2009). *Cordyceps sinensis* polysaccharide enhances apoptosis of HL-60 cells induced by triptolide. *Journal of Zhejiang University, Medical sciences*, *38*, 158–162.

Sheng, J. H., Yu, F., Xin, Z. H., Zhao, L. Y., Zhu, X. J., & Hu, Q. H. (2007). Preparation, identification and their antitumor activities *in vitro* of polysaccharides from *Chlorella pyrenoidosa*. *Food Chemistry*, *105*, 533–539.

Shi, X., Ruan, D., Wang, Y., Ma, L., & Li, M. (2010). Anti-tumor activity of safflower polysaccharide (SPS) and effect on cytotoxicity of CTL cells, NK cells of T739 lung cancer in mice. *China Journal of Chinese Materia Medica*, *35*, 215–218.

Shibata, M., Shimura, T., Nishina, Y., Gonda, K., Matsuo, S., Abe, H., et al. (2011). PSK decreased FOLFOX4-induced peripheral neuropathy and bone marrow suppression in patients with metastatic colorectal cancer. *Gan To Kagaku Ryoho*, *38*, 797–801.

Shimizu, K., Watanabe, S., Watanabe, S., Matsuda, K., Suga, T., Nakazawa, S., et al. (2009). Efficacy of oral administered superfine dispersed lentinan for advanced pancreatic cancer. *Hepatogastroenterology*, *56*, 240–244.

Silva, D. C., Freitas, A. L., Barros, F. C., Lins, K. O., Alves, A. P., Alencar, N. M., et al. (2012). Polysaccharide isolated from *Passiflora edulis*: Characterization and antitumor properties. *Carbohydrate Polymers*, *87*, 139–145.

Soares, R., Meireles, M., Rocha, A., Pirraco, A., Obiol, D., Alonso, E., et al. (2011). Maitake (D fraction) mushroom extract induces apoptosis in breast cancer cells by BAK-1 gene activation. *Journal of Medicinal Food*, *14*, 563–572.

Song, G. L., & Du, Q. Z. (2010). Isolation of a polysaccharide with anticancer activity from *Auricularia polytricha* using high-speed countercurrent chromatography with an aqueous two-phase system. *Journal of Chromatography A*, *1217*, 5930–5934.

Song, K. S., Li, G., Kim, J. S., Jing, K., Kim, T. D., Kim, J. P., et al. (2011). Protein-bound polysaccharide from *Phellinus linteus* inhibits tumor growth, invasion, and angiogenesis and alters Wnt/beta-catenin in SW480 human colon cancer cells. *BMC Cancer*, *11*, 307.

Sun, L. Q., Wang, L., & Zhou, Y. (2012). Immunomodulation and antitumor activities of different-molecular-weight polysaccharides from *Porphyridium cruentum*. *Carbohydrate Polymers*, *87*, 1206–1210.

Sun, L. X., Lin, Z. B., Duan, X. S., Lu, J., Ge, Z. H., Li, X. J., et al. (2011). *Ganoderma lucidum* polysaccharides antagonize the suppression on lymphocytes induced by culture supernatants of B16F10 melanoma cells. *Journal of Pharmacy and Pharmacology*, *63*, 725–735.

Sun, L. X., Lin, Z. B., Li, X. J., Li, M., Lu, J., Duan, X. S., et al. (2011). Promoting effects of *Ganoderma lucidum* polysaccharides on B16F10 cells to activate lymphocyte. *Basic & Clinical Pharmacology & Toxicology*, *108*, 149–154.

Sunila, E. S., Hamsa, T. P., & Kuttan, G. (2011). Effect of *Thuja occidentalis* and its polysaccharide on cell-mediated immune responses and cytokine levels of metastatic tumor-bearing animals. *Pharmaceutical Biology*, *49*, 1065–1073.

Takahashi, T., Fujisaki, M., Hirahata, S., Maeda, D., Tokura, H., Ohyama, T., et al. (2006). A case of advanced gastric cancer with multiple liver metastases successfully treated with TS-1/low-dose CDDP/lentinan combination chemotherapy. *Gan To Kagaku Ryoho*, *33*, 2061–2063.

Takata, R., Yanai, T., Yamamoto, R., & Konno, T. (2007). Improvement of the antitumor activity of black currant polysaccharide by an enzymatic treatment. *Bioscience Biotechnology and Biochemistry*, *71*, 1342–1344.

Takeda, K., Tomimori, K., Kimura, R., Ishikawa, C., Nowling, T. K., & Mori, N. (2012). Anti-tumor activity of fucoidan is mediated by nitric oxide released from macrophages. *International Journal of Oncology*, *40*, 251–260.

Tao, Y. Z., Zhang, Y. Y., & Zhang, L. N. (2009). Chemical modification and antitumor activities of two polysaccharide–protein complexes from *Pleurotus tuber-regium*. *International Journal of Biological Macromolecules*, *45*, 109–115.

Tian, C. Y., & Wang, G. L. (2008). Study on the anti-tumor effect of polysaccharides from sweet potato. *Journal of Biotechnology*, *136S*, S351.

Tong, H. B., Xia, F. G., Feng, K., Sun, G. R., Gao, X. X., Sun, L. W., et al. (2009). Structural characterization and *in vitro* antitumor activity of a novel polysaccharide isolated from the fruiting bodies of *Pleurotus ostreatus*. *Bioresource Technology*, *100*, 1682–1686.

Umehara, S., Fujiwara, H., Suchi, K., Okamura, S., Okamura, H., Todo, M., et al. (2009). PSK-mediated growth suppression and enhancement of 5-FU/docetaxel-induced cytotoxicity in human esophageal cancer cell lines. *Gan To Kagaku Ryoho*, *36*, 1972–1974.

Vishchuk, O. S., Ermakova, S. P., & Zvyagintseva, T. N. (2011). Sulfated polysaccharides from brown seaweeds *Saccharina japonica* and *Undaria pinnatifida*: Isolation, structural characteristics, and antitumor activity. *Carbohydrate Research*, *346*, 2769–2776.

Vlcková, V., Nadová, S., Dúhová, V., Závodná, K., Moránová, Z., Rauko, P., et al. (2006). Natural microbial polysaccharide sulphoethyl glucan as antigenotoxic and cancer preventing agent. *Neoplasma*, *53*, 524–529.

Wan, J. M., Sit, W. H., & Louie, J. C. (2008). Polysaccharopeptide enhances the anticancer activity of doxorubicin and etoposide on human breast cancer cells ZR-75-30. *International Journal of Oncology*, *32*, 689–699.

Wan, J. M., Sit, W. H., Yang, X., Jiang, P., & Wong, L. L. (2010). Polysaccharopeptides derived from *Coriolus versicolor* potentiate the S-phase specific cytotoxicity of Camptothecin (CPT) on human leukemia HL-60 cells. *Chinese Medicine*, *5*, 16.

Wang, C. R., Ng, T. B., Li, L., Fang, J. C., Jiang, Y., Wen, T. Y., et al. (2011). Isolation of a polysaccharide with antiproliferative, hypoglycemic, antioxidant and HIV-1 reverse transcriptase inhibitory activities from the fruiting bodies of the abalone mushroom *Pleurotus abalonus*. *Journal of Pharmacy and Pharmacology*, *63*, 825–832.

Wang, J., Zhou, Z. D., & Xia, D. J. (2007). Study on effect of lentinan in enhancing antitumor action of dendritic cytoma vaccine and its mechanism. *Chinese Journal of Integrative Medicine*, *27*, 60–64.

Wang, J., Zuo, G., Li, J., Guan, T., Li, C., Jiang, R., et al. (2010). Induction of tumoricidal activity in mouse peritoneal macrophages by ginseng polysaccharide. *International Journal of Biological Macromolecules*, *46*, 389–395.

Wang, J. H., Luo, J. P., Zha, X. Q., & Feng, B. J. (2010). Comparison of antitumor activities of different polysaccharide fractions from the stems of *Dendrobium nobile* Lindl. *Carbohydrate Polymers*, *79*, 114–118.

Wang, M. Y., Wang, H., Tang, Y., Kang, D., Gao, Y., Ke, M. Y., et al. (2011). Effective inhibition of a *Strongylocentrotus nudus* eggs polysaccharide against hepatocellular carcinoma is mediated via immunoregulation *in vivo*. *Immunology Letters*, *141*, 74–82.

Wang, N., Zhang, D. L., Mao, X. Q., Zou, F., Jin, H., & Ouyang, J. P. (2009). Astragalus polysaccharides decreased the expression of PTP1B through relieving ER stress induced activation of ATF6 in a rat model of type 2 diabetes. *Molecular and Cellular Endocrinology*, *307*, 89–98.

Wang, S. B., Cheng, Y. N., Wang, F. S., Sun, L. R., Liu, C. H., Chen, G. J., et al. (2008). Inhibition activity of sulfated polysaccharide of *Sepiella maindroni* ink on matrix metalloproteinase (MMP)-2. *Biomedicine & Pharmacotherapy*, *62*, 297–302.

Wang, Y. Y., Khoo, K. H., Chen, S. T., Lin, C. C., Wong, C. H., & Lin, C. H. (2002). Studies on the immuno-modulating and antitumor activities of *Ganoderma lucidum* (Reishi) polysaccharides: Functional and proteomic analyses of a fucose-containing glycoprotein fraction responsible for the activities. *Bioorganic & Medicinal Chemistry*, *10*, 1057–1062.

Wang, Z. H., Wu, B. J., Zhang, X. H., Xu, M., Chang, H. M., Lu, X., et al. (2012). Purification of a polysaccharide from *Boschniakia rossica* and its synergistic antitumor effect combined with 5-Fluorouracil. *Carbohydrate Polymers*, *89*, 31–35.

Wasser, S. P. (2002). Medicinal mushrooms as a source of antitumor and immunomodulating polysaccharides. *Applied Microbiology and Biotechnology*, *60*, 258–274.

Wei, G. Q., Lv, L. H., Chen, Y. L., & Zhao, L. Q. (2011). Preparation and anti-tumor activity of low molecular weight exopolysaccharide from *Rhizobium* sp. N613. *Microbiology China*, *38*, 743–749.

Wei, J. A., Zeng, X., Han, L., & Huang, Y. (2011). The regulatory effects of polyporus polysaccharide on the nuclear factor kappa B signal pathway of bladder cancer cells stimulated by Bacillus Calmette–Guerin. *Chinese Journal of Integrative Medicine*, *17*, 531–536.

Wei, X. L., Mao, F. F., Cai, X., & Wang, Y. F. (2011). Composition and bioactivity of polysaccharides from tea seeds obtained by water extraction. *International Journal of Biological Macromolecules*, *49*, 587–590.

Wijesekara, I., Pangestuti, R., & Kim, S. K. (2011). Biological activities and potential health benefits of sulfated polysaccharides derived from marine algae. *Carbohydrate Polymers*, *84*, 14–21.

World Health Organization. (2011). Cancer. Retrieved from http://www.who.int/mediacentre/factsheets/fs297/en/

Wu, B., Cui, J. C., Zhang, C. G., & Li, Z. H. (2012). A polysaccharide from *Agaricus blazei* inhibits proliferation and promotes apoptosis of osteosarcoma cells. *International Journal of Biological Macromolecules*, *50*, 1116–1120.

Wu, S. C., & Lee, B. H. (2011). Buckwheat polysaccharide exerts antiproliferative effects in THP-1 human leukemia cells by inducing differentiation. *Journal of Medicinal Food*, *14*, 26–33.

Wu, X. Y., Mao, G. H., Zhao, T., Zhao, J. L., Li, F., Liang, L. H., et al. (2011). Isolation, purification and *in vitro* anti-tumor activity of polysaccharide from *Ginkgo biloba* sarcotesta. *Carbohydrate Polymers*, *86*, 1073–1076.

Wu, X. Z., Chen, D., & Han, X. Q. (2011). Anti-migration effects of Gekko sulfated glycopeptide on human hepatoma SMMC-7721 cells. *Molecules*, *16*, 4958–4970.

Wu, X. Z., Chen, D., & Xie, G. R. (2006). Effects of Gekko sulfated polysaccharide on the proliferation and differentiation of hepatic cancer cell line. *Cell Biology International*, *30*, 659–664.

Xiao, J. H., Fang, N., Liu, Z. L., & Chen, D. X. (2008). Investigation on antitumor mechanism of polysaccharide from medicinal fungus *Penicillium jiangxiense*. *Journal of Chinese Medicinal Materials*, *31*, 71–76.

Xu, C., Liu, Y., Yuan, G. X., & Guan, M. (2012). The contribution of side chains to antitumor activity of a polysaccharide from *Codonopsis pilosula*. *International Journal of Biological Macromolecules*, *50*, 891–894.

Xu, C. L., Li, Y. H., Dong, M., Wu, X., Wang, X. C., & Xiao, Y. S. (2012). Inhibitory effect of *Schisandra chinensis* leaf polysaccharide against L5178Y lymphoma. *Carbohydrate Polymers*, *88*, 21–25.

Xu, H. S., Wu, Y. W., Xu, S. F., Sun, H. X., Chen, F. Y., & Yao, L. (2009). Antitumor and immunomodulatory activity of polysaccharides from the roots of *Actinidia eriantha*. *Journal of Ethnopharmacology*, *125*, 310–317.

Yagi, M., Watanabe, S., Yoshino, S., Hazama, S., Suga, T., & Nakazawa, S. (2010). Provision for adverse effect of S-1 containing chemotherapy in patients with advanced digestive cancer—Combination with superfine dispersed lentinan. *Gan To Kagaku Ryoho*, *37*, 457–462.

Yamada, J. (2009). Alleviation of seasonal allergic symptoms with superfine beta-1,3-glucan: A randomized study. *Nihon Ganka Gakkai Zasshi*, *113*, 1082–1087.

Yamasaki, A., Shoda, M., Iijima, H., Nagai, S., Wada, J., Suzuki, H., et al. (2009). A protein-bound polysaccharide, PSK, enhances tumor suppression induced by docetaxel in a gastric cancer xenograft model. *Anticancer Research*, *29*, 843–850.

Yamasaki-Miyamoto, Y., Yamasaki, M., Tachibana, H., & Yamada, K. (2009). Fucoidan induces apoptosis through activation of caspase-8 on human breast cancer MCF-7 cells. *Journal of Agricultural and Food Chemistry*, *57*, 8677–8682.

Yan, J., & Katz, A. (2010). PectaSol-C modified citrus pectin induces apoptosis and inhibition of proliferation in human and mouse androgen-dependent and -independent prostate cancer cells. *Integrative Cancer Therapies*, *9*, 197–203.

Yan, J. K., Wang, W. Q., Li, L., & Wu, J. Y. (2011). Physiochemical properties and antitumor activities of two α-glucans isolated from hot water and alkaline extracts of Cordyceps (Cs-HK1) fungal mycelia. *Carbohydrate Polymers*, *85*, 753–758.

Yang, B., Liang, M. H., Zhang, Y. X., & Shen, B. Z. (2008). Clinical application of a combination therapy of lentinan, multi-electrode RFA and TACE in HCC. *Advances in Therapy*, *25*, 787–794.

Yang, M., Qian, X. H., Zhao, D. H., & Fu, S. Z. (2010). Effects of Astragalus polysaccharide on the erythroid lineage and microarray analysis in K562 cells. *Journal of Ethnopharmacology*, *127*, 242–250.

Yang, M. X., Ma, C. H., Sun, J. T., Shao, Q. Q., Gao, W. J., Zhang, Y., et al. (2008). Fucoidan stimulation induces a functional maturation of human monocyte-derived dendritic cells. *International Immunopharmacology*, *8*, 1754–1760.

Yang, W. J., Pei, F., Shi, Y., Zhao, L. Y., Fang, Y., & Hu, Q. H. (2012). Purification, characterization and anti-proliferation activity of polysaccharides from *Flammulina velutipes*. *Carbohydrate Polymers*, *88*, 474–480.

Yang, X. P., Guo, D. Y., Zhang, J. M., & Wu, M. C. (2007). Characterization and antitumor activity of pollen polysaccharide. *International Immunopharmacology*, *7*, 427–434.

Ye, H., Wang, K. Q., Zhou, C. H., Liu, J., & Zeng, X. X. (2008). Purification, antitumor and antioxidant activities *in vitro* of polysaccharides from the brown seaweed *Sargassum pallidum*. *Food Chemistry*, *111*, 428–432.

Ye, M. N., Chen, H. F., Zhou, R. J., & Liao, M. J. (2011). Effects of Astragalus polysaccharide on proliferation and Akt phosphorylation of the basal-like breast cancer cell line. *Journal of Chinese Integrative Medicine*, *9*, 1339–1346.

Yin, Y., Yu, R. M., Yang, W., Yuan, F., Yan, C. Y., & Song, L. Y. (2010). Structural characterization and anti-tumor activity of a novel heteropolysaccharide isolated from *Taxus yunnanensis*. *Carbohydrate Polymers*, *82*, 543–548.

Yoshino, S., Watanabe, S., Imano, M., Suga, T., Nakazawa, S., Hazama, S., et al. (2010). Improvement of QOL and prognosis by treatment of superfine dispersed lentinan in patients with advanced gastric cancer. *Hepatogastroenterology*, *57*, 172–177.

Yoshino, S., Yoshida, S., Maeda, N., Maeda, Y., Maeda, K., Hazama, S., et al. (2010). Clinical evaluation of the combination treatment of intrapleural or intraperitoneal administration of lentinan and OK-432 for malignant effusion. *Gan To Kagaku Ryoho*, *37*, 2798–2800.

Yoshitani, S., & Takashima, S. (2009). Efficacy of postoperative UFT (Tegafur/Uracil) plus PSK therapies in elderly patients with resected colorectal cancer. *Cancer Biotherapy and Radiopharmaceuticals*, *24*, 35–40.

Yu, Z. H., Yin, L. H., Yang, Q., & Liu, Y. (2009). Effect of *Lentinus edodes* polysaccharide on oxidative stress, immunity activity and oral ulceration of rats stimulated by phenol. *Carbohydrate Polymers*, *75*, 115–118.

Zaidman, B. Z., Yassin, M., Mahajna, J., & Wasser, S. P. (2005). Medicinal mushroom modulators of molecular targets as cancer therapeutics. *Applied Microbiology and Biotechnology*, *67*, 453–468.

Zeng, J. H., Dai, P., Ren, L. Y., Song, B., Chen, X., Wang, X. H., et al. (2012). Apoptosis-induced anti-tumor effect of *Curcuma kwangsiensis* polysaccharides against human nasopharyngeal carcinoma cells. *Carbohydrate Polymers*, *89*, 1067–1072.

Zhang, C., Yang, F., Zhang, X. W., Wang, S. C., Li, M. H., Lin, L. P., et al. (2006). *Grateloupia longifolia* polysaccharide inhibits angiogenesis by downregulating tissue factor expression in HMEC-1 endothelial cells. *British Journal of Pharmacology*, *148*, 741–751.

Zhang, C. X., & Huang, K. X. (2006). Mechanism of apoptosis induced by a polysaccharide, from the loach *Misgurnus anguillicaudatus* (MAP) in human hepatocellular carcinoma cells. *Toxicology and Applied Pharmacology*, *210*, 236–245.

Zhang, G. W., Zeng, X., Li, C. X., Li, J. J., Huang, Y., Han, L., et al. (2011). Inhibition of urinary bladder carcinogenesis by aqueous extract of sclerotia of *Polyporus umbellatus* fries and polyporus polysaccharide. *American Journal of Chinese Medicine*, *39*, 135–144.

Zhang, J., Tang, Q., Zhou, C., Jia, W., Da Silva, L., Nguyen, L. D., et al. (2010). GLIS, a bioactive proteoglycan fraction from *Ganoderma lucidum*, displays anti-tumour activity by increasing both humoral and cellular immune response. *Life Sciences*, *87*, 628–637.

Zhang, J., Tang, Q., Zimmerman-Kordmann, M., Reutter, W., & Fan, H. (2002). Activation of B lymphocytes by GLIS, a bioactive proteoglycan from *Ganoderma lucidum*. *Life Sciences*, *71*, 623–638.

Zhang, M., Cui, S. W., Cheung, P. C., & Wang, Q. (2007). Antitumor polysaccharides from mushrooms: A review on their isolation process, structural characteristics and antitumor activity. *Trends in Food Science & Technology*, *18*, 4–19.

Zhang, M., Zhu, L., Cui, S. W., Wang, Q., Zhou, T., & Shen, H. (2011). Fractionation, partial characterization and bioactivity of water-soluble polysaccharides and polysaccharide–protein complexes from *Pleurotus geesteranus*. *International Journal of Biological Macromolecules*, *48*, 5–12.

Zhao, J. P., & Wang, Y. Y. (2006). Experimental study of the A549 cell apoptosis of human non-small cell lung cancer induced by ginseng polysaccharide *in vitro*. *Chinese Journal of Integrative Medicine*, *S1*, 95–97.

Zhao, L. Q., Chen, Y. L., Ren, S., Han, Y., & Cheng, H. B. (2010). Studies on the chemical structure and antitumor activity of an exopolysaccharide from *Rhizobium* sp. N613. *Carbohydrate Research*, *345*, 637–643.

Zhao, Q. S., Xie, B. X., Yan, J., Zhao, F. C., Xiao, J., Yao, L. Y., et al. (2012). *In vitro* antioxidant and antitumor activities of polysaccharides extracted from *Asparagus officinalis*. *Carbohydrate Polymers*, *87*, 392–396.

Zhong, K., Wang, Q., He, Y., & He, X. H. (2010). Evaluation of radicals scavenging, immunity-modulatory and antitumor activities of longan polysaccharides with ultrasonic extraction on in S180 tumor mice models. *International Journal of Biological Macromolecules*, *47*, 356–360.

Zhong, M., Wang, L. H., Ma, H., Guo, Z. F., Wang, C. C., & Liu, S. X. (2008). Effect of selenium-protein polysaccharide extracted from Se-rich *Cordyceps militaris* on tumor-bearing mice. *China Journal of Chinese Materia Medica*, *33*, 2120–2123.

Zhong, W., Hansen, R., Li, B., Cai, Y., Salvador, C., Moore, G. D., et al. (2009). Effect of yeast-derived beta-glucan in conjunction with bevacizumab for the treatment of human lung adenocarcinoma in subcutaneous and orthotopic xenograft models. *Journal of Immunotherapy*, *32*, 703–712.

Zhou, F. G., Lv, O., Zheng, Y. R., Wang, J. J., Hu, P., Wang, Z. Y., et al. (2012). Inhibitory effect of *Pulsatilla chinensis* polysaccharides on glioma. *International Journal of Biological Macromolecules*, *50*, 1322–1326.

Zhou, G. F., Sheng, W. X., Yao, W. H., & Wang, C. H. (2006). Effect of low molecular γ-carrageenan from *Chondrus ocellatus* on antitumor H-22 activity of 5-Fu. *Pharmacological Research*, *53*, 129–134.

Zhu, X. L., Chen, A. F., & Lin, Z. B. (2007). *Ganoderma lucidum* polysaccharides enhance the function of immunological effector cells in immunosuppressed mice. *Journal of Ethnopharmacology*, *111*, 219–226.

Zhu, Z. Y., Liu, N., Si, C. L., Liu, Y., Ding, L. N., Jing, C., et al. (2012). Structure and anti-tumor activity of a high-molecular-weight polysaccharide from cultured mycelium of *Cordyceps gunnii*. *Carbohydrate Polymers*, *88*, 1072–1076.

Zhu, Z. Y., Liu, R. Q., Si, C. L., Zhou, F., Wang, Y. X., Ding, L. N., et al. (2011). Structural analysis and anti-tumor activity comparison of polysaccharides from Astragalus. *Carbohydrate Polymers*, *85*, 895–902.

Zou, Y. X., Meng, J. J., Chen, W. N., Liu, J. L., Li, X., Li, W. W., et al. (2011). Modulation of phenotypic and functional maturation of murine dendritic cells (DCs) by purified *Achyranthes bidentata* polysaccharide (ABP). *International Immunopharmacology*, *11*, 1103–1108.