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Bioactive polysaccharides from natural sources: A review on the antitumor and immunomodulating activities

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ABSTRACT

Polysaccharides are a structurally diverse group of biological macromolecules of well-known occurrence in nature. The mushroom, plant and other polysaccharides draw a lot of attention due to their several difficult biological properties, such as, anticancer, antiviral, immunomodulating, antimicrobial, anticoagulant, antidiabetic, antioxidant, and antitumor activities. Several bioactive glucans and heteroglycans were isolated from different mushroom, plant and bacterial cell wall. Polysaccharides have highest ability for carrying biological information comparison with other biopolymers such as proteins and nucleic acids due to the structural variability. It is the focus of this review to bring together the available knowledge of the structure, and function of the different polysaccharides of the mushroom, plant and bacterial cell wall.

1. Introduction

The great bulk of the carbohydrates in nature are present as polysaccharides, which have relatively large molecular weights (Maity et al., 2014a, 2015; Xu et al., 2016). Polysaccharides have been produced as the first biopolymer on Earth (Tolstoguzov, 2004). These biopolymers are complex carbohydrates and made up of monosaccharides joined together by glycosidic linkages (Maity et al., 2014b; Nandi et al., 2014; Shakhmatov et al., 2016). Their structures may be linear or they may contain various degrees of branching (Bhanja et al., 2013; Manna et al., 2017; Patra et al., 2012a). The high structural diversity reflects the functional diversity of these molecules (Maity et al., 2017; Meng et al., 2014; Wang et al., 2016). There is a clear correlation between allowed conformations and linking pattern (Li et al., 2018). For example, the chains in amylose tend to adopt single coiled helical (D.E.C. Cambridge, 2013) conformations while some (1→3)-, (1→6)-β-D-glucan chains adopt triple helical (Giese et al., 2013) conformation.

Polysaccharides exist in an enormous structural diversity as they are produced by a vast variety of species; including microbes, algae, plants, and animals (Denman and Morris, 2015; Ji et al., 2003; Ghorai et al., 2009; Kanagasabapathy et al., 2011; Li et al., 2017a; Wu et al., 2006). They are able to offer the highest capacity for carrying biological information because they have the greatest potential for structural variability (Liu et al., 2014; Popov et al., 2007). Polysaccharide related technologies have played a leading role in the development of a wide range of products that include foods, pharmaceuticals, textiles, papers and biodegradable packaging materials (Licht et al., 2010; Wu et al., 2016a,b). The medicinal properties of mushrooms and plants have been confirmed through an intensive research conducted worldwide (Fan et al., 2012; Jiang et al., 2015; Oliveira et al., 2019). Different type of antioxidant, antitumor and immunomodulating polysaccharides were isolated from edible mushrooms, bacterial cell wall, and plants ((Bhanja et al., 2012; Feng et al., 2016; Mandal et al., 2015; Patra et al., 2012b; Patra et al., 2013; Smiderle et al., 2008; Siu et al., 2016). These polysaccharides do not directly attack to the cancer cells. They generate their antitumor effect indirectly, through stimulation of various defensive

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immune systems (Wu et al., 2016; Zhang et al., 2017). Due to different biological activities, mushroom and plant polysaccharides are suitable for application in many distinct areas, such as food industry, biomedicine, cosmetology, agriculture, environmental protection and waste water management (Hwang et al., 2017; Wani et al., 2010; Zhao et al., 2006). This review summarized the different type of polysaccharides isolated from different mushroom, plant, and other sources and their bioactivities.

2. Mushroom polysaccharides

For millennia, mushrooms have been valued by human kind as an edible and medical resource (Vetvicka et al., 2019). Mushrooms contain biologically active polysaccharides in fruit bodies, cultured mycelium and culture broth. Mushrooms are potential source of different polysaccharides like chitin, hemicelluloses, glucans and heteroglycans (Wang et al., 2014). Immunomodulating mushroom polysaccharides are present mostly as glucans with different types of glycosidic linkages, such as (1 → 6)-β-D-glucan, (1 → 3)-, (1 → 6)-β-D-glucans, (1 → 3)-α-D-glucans (Jesus et al., 2018; Maity et al., 2015; Samanta et al., 2013; Wang et al., 2007). Some other immunostimulating heteropolysaccharides and protein-glucan complexes have been also found in mushrooms (Bhunia et al., 2010; Mandal et al., 2011; Patra et al., 2012a; Oliveira et al., 2019). It appears that the most active forms of β-glucans contain β-(1 → 3, 1 → 6) linkages. β-D-(1 → 3,1 → 6)-linked glucans have the ability of enhancing and stimulating the immune system (Bhanja et al., 2012) of humans and thus called biological response modifiers (BRMs). Another broadly reported activity of mushroom polysaccharide is antioxidative and radical scavenging (Fan et al., 2011; Kozarski et al., 2012). Molecules in medicinal mushrooms, most responsible to up-regulate the immune response, are a specific type of polysaccharide known as β-glucan. β-glucans have the ability to stimulate macrophage, NK cells, T cells and produce cytokines (Zhang et al., 2015; Ooi and Liu, 2000). Moreover, several immunostimulatory polysaccharides have also been reported to affect macrophage proliferation and differentiation (Xu et al., 2012). A water soluble β-glucan was isolated from edible mushroom Entoloma lividoalbum act as an immunostimulating agent via macrophage, splenocyte, and thymocyte stimulation and also shows antioxidant activities (Maity et al., 2015). This polysaccharide contains (1 → 3,6)-β-D-Glc*p*, (1 → 3)-β-D-Glc*p*, (1 → 6)- β-D-Glc*p*, and terminal β-D-Glc*p* moieties in a molar ratio of nearly 1:1:3:1. A water soluble heteroglycan of average molecular weight $\sim 1.45 \times 10^5$ Da was isolated from the aqueous extract of an ectomycorrhizal edible mushroom, *Russula albonigra* (Krombh.) Fr (Nandi et al., 2013). Structural analysis revealed that it was composed of terminal 2-*O*-methyl-Fuc*p*, terminal Man*p*, (1 → 2)-Fuc*p*, (1 → 3)-Glc*p*, (1 → 3,4)-Glc*p*, (1 → 6)-Gal*p*, and (1 → 2,6)-Gal*p* residues in a relative proportion of approximately 1:1:1:1:1:1:1. This heteroglycan showed macrophage activation by NO production as well as splenocytes and thymocytes proliferation. A novel polysaccharide named as NTHSP-A1 was isolated from *Hohenbuehelia serotina* mushroom and composed of arabinose, mannose, glucose and galactose in a molar ratio of 4:16:28:11 (Li et al., 2017). This polysaccharide was shows strong antioxidant properties. A β-D-glucan was obtained from the edible mushroom *Pholiota nameko* by hot aqueous extraction (Abreu et al., 2019). This β-glucan showed shear thinning behavior and also presented gel-like behavior and thermal stability under a simulated pasteurization process. This β-D-glucan also significantly inhibited the inflammatory pain in different doses. A novel polysaccharide was isolated from *Lentinus giganteus* and show antitumor activity (Tian et al., 2016). It has been established that β-(1,3)-glucans are very attractive materials not only as a food additive and a preventive therapeutic but also as a carrier for drug delivery (Ranade and Cannon, 2011; Sakurai et al., 2005). A immunostimulatory α-(1–6)-D-glucan was isolated from the cultured Armillariella tabescens mushroom (Luo et al., 2008). A novel water soluble polysaccharide was isolated from edible mushrooms Auricularia *polytricha* and consisted of arabinose, mannose, glucose and galactose in a molar ratio of 1:1.33:1.06:1.23 with an average molecular weight of 21,242 Da (Chen and Xue, 2018). It showed the stronger reducing power and stronger scavenging activity against hydroxyl radicals, superoxide radicals and DPPH radicals in a concentration dependent manner. A new polysaccharide (MIPW50-1) with a molecular weight of 28.5 kDa was isolated from edible mushroos *Morchella importuna* fruiting bodies (Wen et al., 2019). It was composed of N-acetylglucosamine, galactose, glucose, andmannose with molar ratios of 1.00:14.95:1.53:10.51. It has able of stimulating macrophage function, rising phagocytosis of RAW264.7 cells as well as promoting secretion of NO, TNF-α and IL-6. Schizophyllan was a β-(1 → 3), β-(1 → 6) glucan and isolated from the mushroom *schizophyllum commune* (Zhang et al., 2013). Schizophyllan has great significance in the medicinal industries (Reyes et al., 2009). It is also used in number of diseases, including AIDS, and to enhance the effect of vaccines and antitumor therapies (Daba and Ezeronye, 2003: Leathers et al., 2006). Agarican, the polysaccharide isolated from *Agaricus blazei* mushroom was used to prevent various diseases including chronic hepatitis, allergies, and asthma (Ahn et al., 2004; Biedron et al., 2012; Grinde et al., 2006; Kawamura et al., 2005). Seven polysaccharide fractions obtained from *A. blazei* fruit bodies were demonstrated to have antitumor activity (Fujimiya et al., 1998; Mizuno, 2002). 1,3-β-D-glucan derived from the fruiting body of *Antrodia camphorate* shows anticancer effects on human pancreatic cancer cells (Lee et al., 2014). *Grifola frondosa* (also known as Maitake) is a traditional medicinal mushroom used in enhancing the immune system. Maitake also protects cells with its antioxidant properties (Fulleroton and Samadi, 2000). Grifron-D from Grifola frondosa was inhibiting hepatitis B virus (Gu et al., 2006). Krestin (PSK) is a unique protein bound polysaccharide, obtained from turkey tail mushroom *Trametes versicolor* (Cui and Chisti, 2003). The medicinal mushroom *Trametes versicolor* has a wide range of biological activities including antiviral, antitumor, and immunomodulatory effects (Jimenez-Medina et al., 2008; Rai et al., 2005). It prevents liver cancer and is also useful for treating hepatitis B (Iguchi et al., 2001). It was found that the polysaccharides isolated from *Trametes versicolor* to use improve the bone properties in diabetic rats (Chen et al., 2015). A polysaccharopeptide (PSP) has also been isolated from a strain of *Coriolus versicolor* in China and become widely used in clinical treatments as an anti-cancer and immunomodulatory agent (Cui et al., 2007; Sun and Zhu, 1999). PSP is also called biological response modifier that stimulates T-cell activation, macrophage and induces IFN-γ and IL-2 production (Collins and Ng, 1997; Lee et al., 2006). Four different antioxidative and immunomodulating polysaccharides were isolated from the medicinal mushrooms *Agaricus bisporus*, *Agaricus brasiliensis*, *Ganoderma lucidum* and *Phellinus linteus* (Kozarski et al., 2011; Ruthes et al., 2012; Tian et al., 2012; Wang et al., 2015). Smiderle et al. (2011, 2013) were isolated (1 → 6)-β-D-glucans from Agaricus bisporus and Agaricus brasiliensis show immunostimulatory activity on human THP-1 derived macrophages. A inflammatory pain inhibition fucomannogalactan and glucan was isolated from medicinal mushroom *Amanita muscaria* (Ruthes et al., 2013). Polysaccharide isolated from culinary mushroom *Pleurotus pulmonarius* exhibits antioxidant, anti-cholinesterase, and anti-inflammatory effects (Nguyen et al., 2016). A water soluble carboxymethylated β-glucan, isolated from the sclerotia of PTR, was reported to reduce the proliferation of MCF-7 cells via cell-cycle arrest and the induction of apoptosis (Deng et al., 2000; Zhang et al., 2006). A antioxidanatic heteroglycan was isolated from *Phellinus linteus* mycelia (Yan et al., 2016). β-glucan possesses several beneficial properties, including the ability to eliminate free radicals in a way similar to antioxidants (Kofuji et al., 2012; Maity et al., 2017). A triple-helical polysaccharide was isolated from *Dictyophora indusiata* shows anti-tumor activity (Deng et al., 2013). Chen et al. (2008) isolated a heteropolysaccharide from the fruiting bodies of *Ganoderma atrum* which shows antioxidant activity. A heteropolysaccharides was isolated from *Tricholoma matsutake* and shows antioxidant and antitumor activities (You et al., 2013). Lentinula edodes (shiitake mushroom) is one of the most widely cultivated edible mushrooms and is highly valued for its medical applications (Chihara, 1992; Xu et al., 2014). Lentinan is a (1 → 3)-, (1 → 6) β-D-glucan (Gordon et al., 1998). Lentinan showed prominent antitumor activity not only against allogenic tumors, but also against various synergic and autochthonous tumors (Hobbs, 2000; Xu et al., 2012). It stimulates the production of white blood cells in the human cell line U937 (Sia and Candlish, 1999; Wasser and Weis, 1999). Mushroom and plant polysaccharides are also referred to as biological response modifiers (BRMs) (Novak and Vetvicka, 2009; Xu et al., 2012a, b,c). A possible pathway of the biological action of β-D-Glucan has been presented in Fig. 1 (Mizuno, 2002). Several mushroom polysaccharides are widely used and commercialized worldwide as anti cancer agents for therapeutic purposes (Cui and Chisti, 2003; Mizuno, 2002). Different parts of the mushroom are being used for the treatment of blood sugar, high blood pressure, as a preventive of ageing as well as for the beauty treatment (Wu et al., 2016a,b).

3. Hybrid mushrooms polysaccharides

Quality traits within the gene pool of any particular edible mushroom species are limited. Development of new hybrid strains are therefore needed in order to introduce important qualitative and quantitative traits like high bio-efficacy, high temperature tolerance, enhanced shelf life and shorter cropping periods within a gene pool. Production of new hybrid mushroom strains through para-sexual mating is now well established. Protoplast fusion is an important approach for inter-specific and inter-generic somatic hybridization for strain improvement among edible mushrooms (Peberdy and Fox, 1999). There are number of reports on production of hybrid mushroom through inter-generic protoplast fusion. Several hybrid fruit bodies e.g. PC H8, PC H11, PC H17 and PC H18 were prepared through protoplast fusion between two edible strains *Pleurotus florida* and *Calocybe indica* (Chakraborty and Sikdar, 2010). Protoplast fusion of *Pleurotus florida* and *Volvariella volvacea* produced two new fruit bodies PfloVv1aFB and PfloVv5FB (Chakraborty and Sikdar, 2008). Intergeneric protoplast fusion between the strains of *Pleurotus florida* and *Lentinula edodes* produced nine new hybrid strains named as *pfle* were found to produce fruit bodies (Mallik and Sikdar, 2014). Twelve inter-generic somatic hybrids named as *pfls* were produced through PEG-mediated protoplast fusion between *Pleurotus florida* and *Lentinus squarrosulus* using double selection method (Mallik and Sikdar, 2015). Hybridity of the fusant lines was set up on the basis of their colony morphology, mycelia growth rate and hypal traits, while the fruit body generating lines were demonstrated on the basis of nature of sporophores, isozymes, random amplified polymorphic DNA markers (Chakraborty and Sikdar, 2010). A few biologically active glucans and heteroglycans have been isolated and reported from hybrid mushrooms. Dey et al. (2013) isolate a heteroglycan from somatic hybrid mushroom of *Pleurotus florida* and *Calocybe indica* var. APK2, shows immunoactivation properties. A β-glucan was isolated from asomatic hybrid (*PfloVv5FB*) of *Pleurotus florida* and *Volvariella volvacea* mushrooms (Maity et al., 2013a). Two water soluble immunoenhancing hetero polysaccharides (PS-I and PS-II) were isolated from

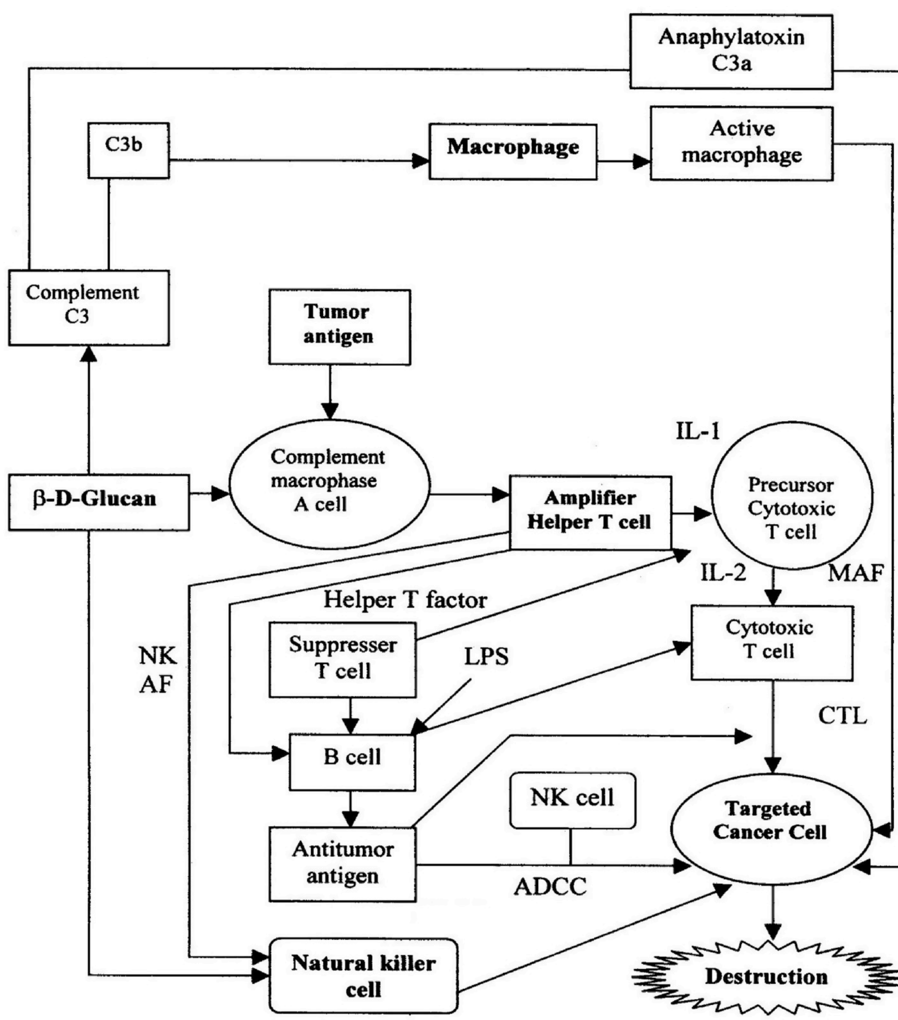

Fig. 1. Possible immune mechanism: β-D-glucan as biological response modifier (BRM) to target cancer cells (Mizuno, 2002).

the fruit bodies of *pfle 1p* (Maity et al., 2013b, 2014c). Recently a immunoenhancing (1 → 6), (1 → 3)-β-D-glucan was isolated from hybrid mushroom strains *pfle 1r* (Maji et al., 2012). A α,β-D-glucan from alkaline extract of a somatic hybrid mushroom (*PCH9FB*) of *P. florida* and *C. indica var.* APK2 exhibit significant immunoenhancing properties which could stimulate the macrophages, splenocytes and thymocytes and also shows antioxidant properties (Maity et al., 2011a). Another heteroglycan from aqueous extract of a hybrid mushroom *PCH9FB* (obtained by hybrid mushroom *P. florida* and *C. indica var.* APK2) has been also found to be antioxidant and immunostimulating in nature (Maity et al., 2011b). Three polysaccharide fractions (PS-I, PS-II, and PS-III) were isolated from the aqueous extract of a hybrid mushroom obtained through backcross mating of a somatic hybrid mushroom PfloVv12 (Sterile line) with *Volvariella volvacea*. Two different glucans (water-soluble PS-I, water-insoluble PS-II) were isolated from the alkaline extract of the fruit bodies of hybrid mushroom PfloVv12 (Sterile line) with *Volvariella volvacea* and exibit immunoenhancing and antioxidant properties (Sarkar et al., 2012). A (1 → 6)-β-glucan was isolated from a somatic hybrid (Pflo Vv5 FB) of *Pleurotus florida* and *Volvariella volvacea* and shows immunoenhancing properties (Das et al., 2010). A immunoenhancing water soluble heteroglycan, isolated from the alkaline extract of the fruit bodies of the somatic hybrid mushroom (PfloVv1aFB), raised through protoplast fusion between the strains of *Pleorutus florida* and *Volverilla volvacea* (Bhunia et al., 2012). A water soluble polysaccharide isolated from the hot aqueous extract of the fruit bodies of the somatic hybrid mushroom (PfloVv1aFB), raised through protoplast fusion between the strains of *Pleurotus florida* and *Volvariella volvacea* was found to consist of D-glucose, D-galactose, and D-mannose in a molar ratio of nearly 4:1:1 and showed macrophage, splenocyte, and thymocyte activation (Patra et al., 2011).

4. Plant polysaccharides

Now a day Plant polysaccharides isolated from different vegetables and its plant have been drawn the attention of chemist and immunobiologists on account of their due to its diversity (Sun et al., 2015). They exhibit antitumor, immunostimulatory, anti-complementary, anti-inflammatory, antioxidant anti-coagulant, and fibrinogenic activities (Chanda and Dave, 2009; Li et al., 2014; Zou et al., 2014). Now day's plant polysaccharides are very attractive source of additive for the food and drug industries because of their use in complementary medicinal supplement (Liu et al., 2018). Plant polysaccharides showed both antigenotoxic and anti-tumor promoting activities (Popov et al., 2011). A sulfated polysaccharide was isolated from the green seaweed *Monostroma angicava* and shows anticoagulant property (Li et al., 2017b). An immunoenhancing polysaccharides isolated from the hot aqueous extract of mature pods (fruits) *Moringa oleifera* (sajina) was found to contain only D-glucose as a monosaccharide unit (Mondal et al., 2004). A water soluble polysaccharide was isolated from the aqueous extract of pods of Moringa oleifera. The polysaccharide contains D-galactose, 6-O-Me-D-galactose, D-galacturonic acid, L-arabinose, and L-rhamnose in a molar ratio of 1:1:1:1:1 (Roy et al., 2007). A water soluble heteropolysaccharide was isolated from the aqueous extract of the stem of *Lagenaria siceraria* (Lau) and found to be constituted of D-methyl galacturonate, 2-O-methyl-D-xylose, and D-xylose in a ratio of 1:1:1 (Ghosh et al., 2008). A water soluble polysaccharide, isolated from fruiting bodies of Lagenaria siceraria, is composed of methyl-α-D-galacturonate, 3-O-acetyl methyl-α-D-galacturonate, and β-D-galactose in a ratio of nearly 1:1:1. This polysaccharide showed cytotoxic activity in vitro against human breast adenocarcinoma cell line (MCF-7) (Ghosh et al., 2009). A water soluble heteropolysaccharide was isolated from hot water extract of the stems of *Amaranthus tricolor* Linn (Amaranthus gangeticus L.) (Sarkar et al., 2009).. A heteropolysaccharide isolated from the gum (Katira) of *Cochlospermum religiosum* was found to consist of D-galactose, D-galacturonic acid and L-rhamnose in a molar ratio 2:1:3 (Ojha et al., 2008). An immunoenhancing polysaccharide isolated from the aqueous extract of the leaves of *Catharanthus rosea* was found to consist of 6-*O*-methyl-glucose, arabinose, rhamnose, and methyl galacturonate sugar units. This polysaccharide showed optimum activation of macrophages at 100 μg/mL and both splenocyte and thymocyte at 50 μg/mL, respectively (Patra et al., 2010). A polysaccharide was isolated from the aqueous extract of the unripe (green) tomatoes (*Lycopersicon esculentum*) consists of D-galactose, D-methyl galacturonate, D-arabinose, L-arabinose, and L-rhamnose (Chandra et al., 2009). A water-soluble polysaccharide was isolated from hot aqueous extracts of fruits of *Psidium guajava* (Guava). The polysaccharide was found to contain 2-O-methyl-L-arabinose, 2-O-acetyl-D-galactose, and D-methyl galacturonate in a molar ratio of approximately 1:1:1 (Mandal et al., 2009). A water soluble new arabinoxylan, isolated through hot water extraction from the green leaves of *Litsea glutinosa* (Lauraceae) was found to contain xylose and arabinose in a molar ratio of nearly 1:3 (Das et al., 2013). These polysaccharide shows splenocyte and thymocyte proliferation were at 25 μg/mL and 50 μg/mL, respectively and also enhanced production of NO was observed at 100 μg/mL. A water soluble gluco-arabinan (PS-II) was isolated from the alkaline extract of the endosperm of *Caesalpinia bonduc* (Mandal et al., 2013). This gluco-arabinan showed the maximum splenocyte proliferation indexes at 12.5 μg/mL whereas thymocyte proliferation indexes showed maximum effect at 25 μg/mL and the macrophage activation at 200 μg/mL. Arabinoxylan isolated from rice bran was used in sensitize human leukemic cells to death receptor (Ghoneum and Gollapudi, 2003) and also used in human breast cancer (Ghoneum and Gollapudi, 2008). Several plant polysaccharides isolated from *Aloe barbadensis*, fruit juice of *Morinda citrifolia* (noni) (Hirazumi and Furusawa, 1999), *Morus alba*, *Chlamydomonas Mexicana*, and *Poria cocos* (Shuxiu et al., 1995) show immunomodulatory and antitumor activity. Dendrobium officinale and many other Dendrobium plants have been used as herbal medicines and nutraceutical products since ancient time in China (Bao et al., 2001; Li et al., 1990; Li et al., 2004; Li et al., 2011; Li et al., 2012; Zha et al., 2007). Several polysaccharides were isolated different plant such as *Chuanminshen violaceum* (Fana et al., 2017), *Sophorae tonkinensis* Radix (Cai et al., 2018), and *Mesona chinensis* (Huanga et al., 2018) shows antioxidant activities. *Bupleurum chinense* is a natural Chinese medicine and widely used in pharmacological research (Tong et al., 2014, 2017). The polysaccharides were isolated from four different *Dendrobium* species possess different hypoglycemic and antioxidant activities (Pan et al., 2014). A health benefits (1 → 6)-α-D-glucan was identified from longan, and shows anticancer activity (Zhu et al., 2013). A polysaccharide from the root of *Sanguisorba officinalis* L. can play its antitumor effect by restoring the immunity of mice that are inhibited by tumor cells (Cai et al., 2012). The water soluble tea polysaccharides (Deng and Yu, 2002) are exhibit different type of bioactivities, such as, reducing blood sugar levels, immunological, and anticancer activities (Marcel and ChiCho, 2004; Wang et al., 2001).

5. Dietary fibers

Dietary fibers are edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in human small intestine with partial or complete fermentation in the large intestine (Lunn and Buttriss, 2007). The major components of dietary fiber are cellulose, hemicelluloses, chitins, pectin, hydrocolloids, β-glucans, lignin (polymer of aromatic molecules) etc (Peerajit et al., 2012). Some sources of soluble fibers are oats, peas, beans, apples, citrus fruits, carrots, barley and psyllium (Mei et al., 2010; Stacewicz- Sapuntzakis et al., 2001). Mostly soluble fiber can slow the absorption of sugar which can help to improve blood sugar levels. Sources of insoluble fiber include whole wheat, corn bran, flax seed lignans and vegetables such as carrots, celery, green beans potato skins and tomato peel (Alvarado et al., 2001; Lan et al., 2012). Dietary fibers facilitate mineral absorption and inhibit the growth of pathogenic bacteria in colon and they are useful for prevention of cancers (Gmeiner et al., 2000). Fiber found in whole grain products is helpful in the treatment of constipation and inhibition of cancer at colon and rectum (Abdul-Hamid and Luan, 2000). Most dietary fibers come from plant processing by-products including red grape pomace (Pérez-Jiménez and Sáyago-Ayerdi, 2009), apple pulp (Bravo et al., 1992), cocoa fiber (Lecumberri et al., 2007), and carrot peel (Chantaro et al., 2008). Short chain fructo oligosaccharide (Campbell et al., 1997) along with other dietary fibers occurs naturally in different tuber crop vegetables like onion (*Allium cepa*), khamalu (*Dioscorea alata*) and garlic (*Allium sativum*) etc (Patra et al., 2013). Soluble dietary fiber (SDF) was isolated from *Canna edulis* Ker by-product and used as dietary supplement and additive in the food industry (Zhang and Wang, 2013). The main constituent in the *C. edulis* by-product composed of cellulose, glucose converts to other single sugars, which form a series of compounds in the SDF. It has been reported that dietary fibers also retard the rate of starch digestion, which may have important health benefits (Chen et al., 2017). Xylo-oligosaccharides (hemicellulose) were isolated from the wastewater of a viscose fiber mill (Zhang et al., 2016). It was confirmed that the hemicellulose was mainly 4-*O*-methylglucuronoxylan with a small amount of glucomannan and xyloglucan. The water insoluble polysaccharides of the dietary fiber complex from oat grain and oat bran were isolated after enzymatic treatment for starch and protein digestion. The analysis of the alkali insoluble residue indicates the presence of cellulose (Heims and Steinhart, 1991). Corn fiber gum is a hemicellulose (arabinoxylan) enriched fraction obtained by the extraction of corn bran/fiber using a mild alkaline hydrogen peroxide process (Yadav et al., 2012). Coffee silverskin dietary fiber (DF) was obtained by alkaline hydrogen peroxide (AHP) extraction procedure from Coffee silverskin (Behrouzian et al., 2016). Coffee silverskin was used as a source of insoluble dietary fiber especially cellulose in food formulations. 15% polysaccharides are found of the coffee brew and have a significant nutritional contribution as dietary fibre (Díaz-Rubio and Saura-Calixto, 2007). Galactomannan and arabinogalactan type II are the main nondigestible polysaccharides of coffee brews, contributing to coffee brew dietary fibre (Gniechwitz et al., 2007; Nunes and Coimbra, 2002). Soluble dietary fiber (SDF) from the peel of papaya (*Carica papaya* Linn.) was isolated through alkaline extraction (a-SDF) and ultrasound-assisted alkaline extraction (u-SDF) processes (Zhang et al., 2017). A monosaccharide analysis indicated that the primary sugars in a-SDF and u-SDF were neutral sugars and pectic saccharides, respectively. Papaya peel is a potential inexpensive source of natural dietary fiber and a potential functional food ingredient. Its antitumor activities have also recently been recognized (Yogiraj et al., 2014).

6. Pectic polysaccharides

Pectic polysaccharides are extracted from the cell wall with hot water or dilute acid or calcium chelators (like EDTA) (White et al., 2010). They are the easiest constituents to remove from the cell wall. They are also a diverse group of polysaccharides and rich in galacturonic acid (Mohare et al., 2013). The pectic polysaccharides serve a variety of functions including determining wall porosity, providing a charged wall surface for cell-cell adhesion, cell-cell recognition, pathogen recognition drug delivery, gene delivery, and others due to its biocompatibility, good biodegrability and low-toxicity (Munarin et al., 2012; Ridley, ONeil, & Mohnen, 2001). Pectin is one of the main structural components of plant cell walls (Caffal and Mohnen, 2009). It is an essentially linear polysaccharide and composed of a backbone of α-(1 → 4)-linked galacturonic acid or its ester units. Most plants, apples, citrus fruits (oranges, lemons, and grapefruits), murta (*Ugni molinae Turcz*), myrtle (*Myrtus communis* L.), jambo (*Syzygium jambos* L.) and sugar beets are very rich in pectins and their by-products are the most important sources of pectin industry (Chen et al., 2014; Chidouh et al., 2014; Taboada et al., 2010; Tamiello et al., 2018; Wang and Lü, 2014). Pectins are naturally occurring biopolymers that possess increasing applications in the pharmaceuticals, foods, and biotechnology industry (Popov et al., 2005; Popov et al., 2011). The most important use of pectin is its ability to form gels (Chan et al., 2017; Funami et al., 2007). These are widely used as food additives with gelling and stabilizing properties in jams, jellies, milks and confectionery products (Barbieri et al., 2018). It can reduce cholesterol levels in blood and exhibit anti-inflammatory activities (Attele et al., 1999; Srivastava and Malviya, 2011). A new type of sugar beet pulp pectin (SBPP), has recently established much attention in chemist (Fissore et al., 2013). Arabinan rich pectic polysaccharide was isolated from aqueous extract of buriti fruit pulp (Mauritia flexuosa) (Cantu-Jungles et al., 2015). Ovodova et al. (2009) isolated an anti-inflammatory pectic polysaccharide from celery stalks. High antioxidant pectic-polysaccharide was extracted from mangosteen (Garcinia mangostana) rind (Gan and Latiff, 2011). A water soluble pectic polysaccharide isolated from the hot water extract of the pods of green bean (*Phaseolus vulgaris* L.) was found to consist of methyl ester of D-galacturonic acid, D-galactose, and L-arabinose in a molar ratio of nearly 2:2:1. This molecule showed splenocyte, thymocyte activation as well as antioxidant properties (Patra et al., 2012b). A immunoenhancing water soluble pectic polysaccharide (Patra et al., 2013) was isolated from immature onion stick (*Allium cepa*), that contained D-galactose, 6-O-Me-D-galactose, 3-O-acetyl-D-methyl galacturonate and D-methyl galacturonate in a molar ratio of nearly 1:1:1:1. The pectic polysaccharide showed in vitro splenocyte, thymocyte as well as macrophage activations. Zhang et al. (2018) isolated a RG-I enriched pectic polysaccharides from mandarin citrus peel. A pectic polysaccharide (CPP1b) was at isolated from *Codonopsis pilosula* and sugar analysis revealed that CPP1b was composed of rhamnose (Rha), arabinose (Ara), galactose (Gal) and galacturonic acid (GalA) with a molar ratio of 0.25:0.12:0.13:2.51 (Yang et al., 2013). CPP1b was exhibited cytotoxicity to human lung adenocarcinoma A549 cells in a dose and time dependent manner. RG-I type pectin from *Panax ginseng* shows immunological activity (Zhang et al., 2012). A pectic polysaccharide was isolated from the fruit pulp of *Spondias cytherea* and that act as a peritoneal macrophage activation (Iacomini et al., 2005). A bioactive pectic heteropolysaccharides was found in elder flowers (Sambuci flos) (Ho et al., 2016). A pectic heteropolysaccharide was isolated from Siberian fir (Abies sibirica Ledeb.) (Makarova et al., 2013). A particular pectic polysaccharide (FPLP) was extracted and purified from the fruits of *Ficus pumila* Linn and shows hypoglycemic effect (Wu et al., 2017). A pectic heteropolysaccharide was extracted from *Ligusticum chuanxiong* and used in antioxidant defense in aged mice (Huang et al., 2017). A water-soluble pectic polysaccharide (MP-A40) was isolated and purified from *Mosla chinensis* Maxim.cv. Jiangxiangru and comprised of 68.63% galacturonic acid and 13.05% neutral sugar (Li et al., 2014). In addition, arabinose, galactose, rhamnose, mannose and glucose composed the neutral sugar in a relative ratio of 4.94, 3.07, 2.13, 1.62 and 1.29% of the dry weight of MP-A40, respectively. It was inhibiting the growth of human leukemic cell line K562 and stimulates nitric oxide production from RAW 264.7 macrophages both in dose-dependent manners. A water soluble pectic polysaccharide isolated from the aqueous extract of the green fruits of *Momordica charantia* (Karela) contains D-galactose and D-methyl galacturonate in a molar ratio of nearly 1:4. It showed splenocyte, thymocyte as well as macrophage activations. Moreover, it exhibited potent antioxidant activities (Panda et al., 2015). The pulp of gabiroba (*Campomanesia xanthocarpa Berg*) fruits was submitted to a hot water extraction, giving rise to pectin and composed mainly of arabinose (54.5%), galacturonic acid (33.5%), galactose (7.6%), and rhamnose (1.6%) (Barbieri et al., 2019). This pectin shows rheological behavior. A water soluble arabinoxylan was isolated from the green stem of *Andrographis paniculata* and contained D-xylose, 2-methoxy D-xylose and L-arabinose in molar ratio of 3:1:1 (Maity et al., 2019). In vitro antioxidant assay, arabinoxylan was found to possess ferrous ion chelating activity ($EC_{50} = 283$ μg/ml), superoxide radical scavenging activity ($EC_{50} = 470$ μg/ml), and hydroxide radical scavenging activity ($EC_{50} = 193$ μg/ml). A immunobiological arabinan-rich active pectic polysaccharides was isolated from the cell walls of *Prunus dulcis* and arabinan glycosidic linkage composed of T-Ara*f*: (1 → 5)-Ara*f*: (1 → 3, 5)-Ara*f*: (1 → 2,3,5)-Ara*f* in the relative proportions of approximately 3:2:1:1 (Dourado et al., 2006). Highly branched arabinan-rich pectic polysaccharides, containing 84% of arabinose, was extracted from wood greenery of *Abies sibirica* L. It had a strongest stimulating effect on germination and growth rate of seeds, germs and roots of *Triticum aestivum, Avena sativa*, and *Secale cereale* (Shakhmatov et al., 2014). A pectic polysaccharide DNP-W5 was obtained from the stems of *Dendrobium nobile* Lindl showed immunostimulating activities (Wang et al., 2010). It contained mannose, glucose, galactose, xylose, rhamnose and galacturonic acid in molar ratios of 3.1:8.1:8.2:0.6:4.2:3.9.

7. Exopolysaccharides (EPS)

Extracellular polysaccharides or exopolysaccharides (EPS) are found in microorganisms, as well as algae, plants and animals (Li and Shah, 2016; Sutherland, 2005; Wang et al., 2015). A biological active exopolysaccharide (KNPS) of a molecular mass $\sim 1.8 \times 10^5$ Da was isolated from the culture medium of *Klebsiella pneumoniae* PB12 (Mandal et al., 2015). Sugar analysis showed that the KNPS composed of arabinose, galactose, 3-O-methyl-galctose and glucose in a molar ratioof nearly 4:3:1:1. KNPS enhanced malondialdehyde (MDA), reactive oxygen species (ROS), and have the potential to alter the ratio of oxidized glutathione (GSSG) and reduced glutathione (GSH) levels in the cellular system. A water soluble heteropolysaccharide was isolated from extracellular polymeric substances (EPS) produced by a novel metal tolerant bacterium, Acinetobacter junii BB1A and sugar analysis showed that the it was composed of mannose, galactose and arabinose in a molar ratio of nearly 3:1:1 (Sen et al., 2014). This polysaccharide showed significant in vitro splenocyte, thymocyte, and macrophage activations with optimum dose of 100 μg/mL for macrophage and 25 μg/mL both forthe splenocyte and thymocyte. A strain *Agrobacterium* HX1126 was used to production of a new exopolysaccharide, named PGHX (Liu et al., 2016). PGHX composed mainly of galactose, with lower amounts of arabinose and aminogalactose and also shows the gel forming property. Different exopolysaccharides were isolated from *Pseudomonas aeruginosa*, and used for biofilm development (Ryder et al., 2007; Yadav et al., 2012). The potential benefits of bacterial polysaccharides are enormous and help for the development of novel antibacterial drugs like vaccines and several commercial applications (Rehm, 2009; Ullrich, 2009). Bacterial EPS are important because they are used in bioadsorbents, heavy metal removal and drug delivery agents (Arena et al., 2006; Wang et al., 2008). It has also exposed different biological activities like anticancer and immunostimulating properties (Jiang et al., 2011). Xanthan gum is the chief bacterial polysaccharide generally used by the food industry. Bacterial EPS are important because they are used in bioadsorbents, heavy metal removal and drug delivery agents (Jiang et al., 2011). A bioactive exo-β-D-glucosaminidase was isolated from a Koji Mold, *Aspergillus oryzae* IAM2660 (Zhang et al., 2000). Water soluble exo-polysaccharide was isolated from *Syncephalastrum racemosum*, which act as a strong inducer of plant defence reactions (Valepyn et al., 2014). A exopolysaccharide was extracted from Lachnum shows promoting effect on wound healing (He et al., 2014). Exopolysaccharide isolated from *pleurotus eryngii* SI-02 shows antioxidant activity (Sun et al., 2013). A immunoenhancing exopolysaccharides produced by submerged mycelial culture of *Collybia maculata* TG-1 (Lim et al., 2005). Antioxidant and DNA damage protecting activity of exopolysaccharides was isolated from the endophytic bacterium Bacillus cereus SZ1 (Zheng et al., 2016). A exopolysaccharide produced by Enterobacter cloacae Z0206 and shows biological activities (Jin et al., 2010). Du et al. (2016) was reported that the anti-hypoxia activity of an exopolysaccharide isolated from fermentation broth of *Lachnum sp*. A antitumor and immunomodulatory exopolysaccharide fraction was isolated from cultivated *Cordyceps sinensis* (Chinese caterpillar fungus) which used in tumour-bearing mice (Zhang et al., 2005). A anti-ageing extracellular polysaccharide was extracted from a strain of Lachnum sp. (Ye et al., 2012). *Zymomonas mobilis* produces a mixture of two Bacterial cell surface exopolysaccharides (EPS), an [α-(1 → 6)-D-Man*p*] mannose homopolymer and a galactose containing polysaccharide: [→2)-β-D-Gal*f*-(1 → 3)-β-D-Galp-(1→]n and used in the industry in bio-ethanol production process (Pallach et al., 2018). A water soluble exopolysaccharide REPS2-A was isolated from *R. mucilaginosa* CICC 33013 (Ma et al., 2018). REPS2-A was composed of galactose, arabinose, glucose, and mannose at a molar ratio of 63.1:0.2:18.3:18.3, respectively, with a molecular weight of 7.125×10^6 Da. REPS2-A also exhibited excellent free radical scavenging (DPPH, ABTS, and reducing power) and antitumor activities. A new type of exopolysaccharide (EPS) was isolated by *Bacillus sp*. S-1 from Sichuan Pickles and the major component mainly consisted of galactose, glucose, and mannose with average molecular weight of 1.765×10^4 Da (Hu et al., 2019). These EPSs showed potent antioxidant activity by quenching capacities on superoxide, hydroxyl, and DPPH radicals in a dose-dependent way.

8. Conclusion

Polysaccharides belong to a structurally diverse class of macromolecules. The sources of the polysaccharides are higher photosynthetic plants, fungi, algae, bacteria and so on. Mushrooms, plants and other polysaccharides have a wide range of effects including antitumor, lowering blood pressure, immunomodulatory, antimicrobial, antidiabetic, antioxidant, and anticancer. So, this polysaccharide will be important for their application in food and medicinal fields. There has been great interest in developing anticancer polysaccharide drugs over the last decade. Lentinan, Schizophyllan, Krestin, Agarican, and Grifron-D have been commercialized and used as anticancer drugs. Hence, the macrofungal polysaccharides are applied as multipurpose medicines in future.

Declaration of competing interest

The authors declare no Conflict of Interest.

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Appendix A. Supplementary data

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