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Bioactive fungal polysaccharides as potential functional ingredients in food and nutraceuticals

Ioannis Giavasis

Fungal bioactive polysaccharides deriving mainly from the *Basidiomycetes* family (and some from the *Ascomycetes*) and medicinal mushrooms have been well known and widely used in far Asia as part of traditional diet and medicine, and in the last decades have been the core of intense research for the understanding and the utilization of their medicinal properties in naturally produced pharmaceuticals. In fact, some of these biopolymers (mainly β-glucans or heteropolysaccharides) have already made their way to the market as antitumor, immunostimulating or prophylactic drugs. The fact that many of these biopolymers are produced by edible mushrooms makes them also very good candidates for the formulation of novel functional foods and nutraceuticals without any serious safety concerns, in order to make use of their immunomodulating, anticancer, antimicrobial, hypocholesterolemic, hypoglycemic and health-promoting properties. This article summarizes the most important properties and applications of bioactive fungal polysaccharides and discusses the latest developments on the utilization of these biopolymers in human nutrition.

Addresses
Technological Educational Institute (TEI) of Thessaly, Department of Food Technology, Lab of Food Microbiology and Biotechnology, End of N. Temponera Street, 43100 Karditsa, Greece

Corresponding author: Giavasis, Ioannis (igiavasis@teilar.gr)

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Introduction

Fungal polysaccharides comprise a large group of biopolymers which are either part of the cell wall or may form intracellular inclusions and serve as energy reserve, or are excreted extracellularly providing a mechanism for cell protection or attachment to other surfaces. Many of them derive from edible mushrooms, such as the Maitake or Shiitake or Oyster mushroom, or GRAS (Generally Recognized as Safe) organisms, such as bakers' yeast [1,2••,3], which offers a comparative advantage in relation to their use in food, in contrast to biopolymers from non-edible or non-food grade fungi where safety issues may arise. Although many fungi are known for their health-promoting properties and have been widely consumed in far Asia for centuries, their exact pharmaceutical properties and applications, and the mechanisms of their biological activity have been studied only in the last decades, revealing the crucial role of several fungal polysaccharides in anticancer therapy, stimulation of the immune system, as well as their prophylactic activity against chemo/radiotherapy, antimicrobial activity, and their potential for regulating and preventing hyperglycemia and hypercholesterolemia [1,2••,3,4••]. These stunning properties, along with the absence of toxicity, render these biopolymers ideal compounds for the development of novel functional foods or nutraceuticals, as consumers' consciousness and demand for healthy food rises.

Although the biological activities of several fungal polysaccharides have been reported repeatedly in the last years and efforts have been made to elucidate their structure–function relationships, only a few fungal polysaccharides have been commercialized so far, partly due to high production or purification costs, low or erratic polysaccharide yields, and unstable chemical characteristics (i.e. composition, molecular weight, degree of branching) [1,5,6,7,8•]. Such problems are encountered mainly during the production of these biopolymers from mushroom fruit bodies, however, they can be ameliorated to some extend by the use of fungal mycelium grown in submerged cultures under controlled process conditions [1,9–12]. The utilization of the pharmaceutical properties of fungal polysaccharides in a food matrix represents an additional challenge, since food processing and interactions with other food components may influence the efficacy of these biopolymers in food products [2••]. Additionally, although several clinical studies point to the immunostimulating and therapeutic effects of pure polysaccharide solutions on humans [13,14,15,16••], it is fully elucidated whether this bioactivity remains intact after addition of the biopolymers in processed food, as in the case of many β-glucans of plant origin [16••,17].

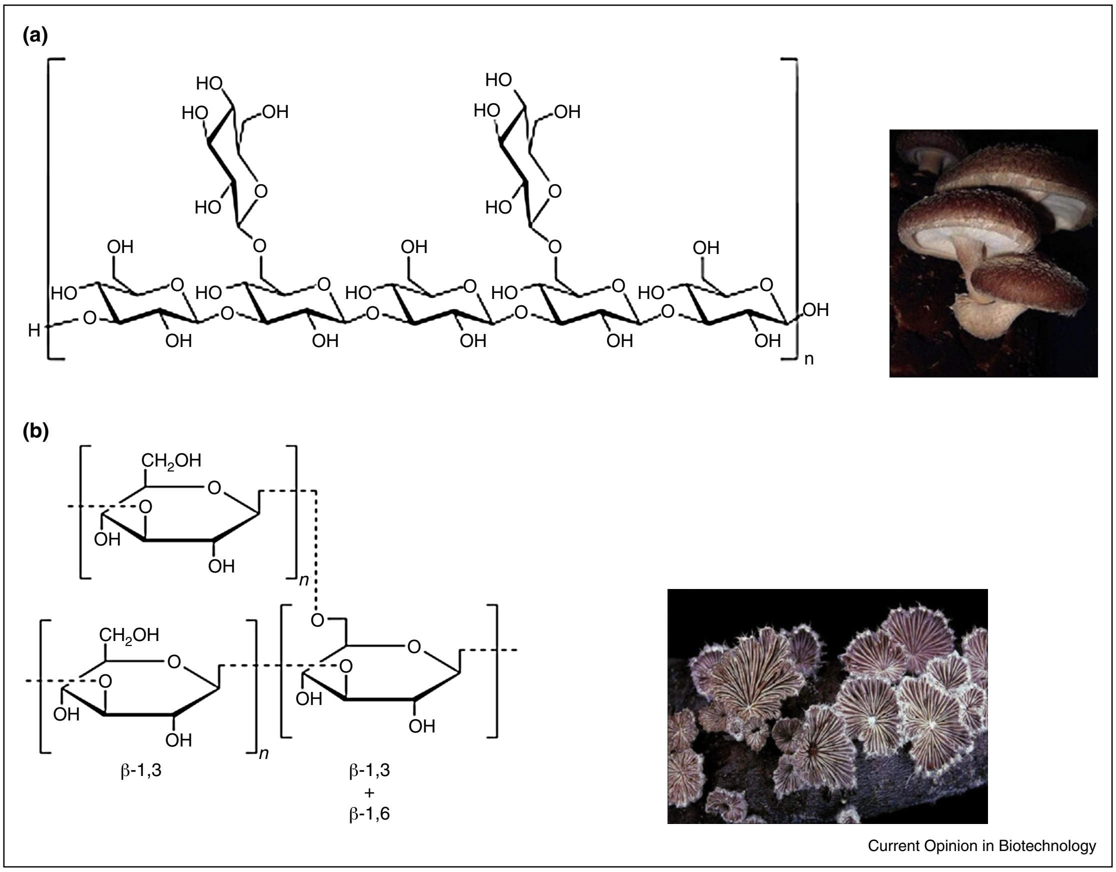
Types and sources of bioactive fungal polysaccharides

One of the most common and well-studied medicinal fungal polysaccharides is lentinan, a glucan elaborated by the edible mushroom *Lentinus* (or *Lentinula*) *edodes*, also known as the Shiitake mushroom. It is composed of a main chain of β-(1,3)-D-glucose residues to which β-(1,6)-D-glucose side groups are attached (one branch to every third main chain unit), and an average molecular weight of about 500,000 Da [2••,3,4••,18••,19]. A similar polysaccharide, schizophyllan (also called sizofiran), is produced by the edible mushroom *Schizophyllum commune*. It usually has a molecular weight of 100,000–200,000 Da and acquires a triple helical conformation. These are probably two of the most well studied immunomodulating microbial β-(1,3)-D-glucans, and both have been commercialized as novel therapeutics in cancer treatment, while *Lentinus elodes* is the most common edible mushroom in Japan [2••,3,4••,18••,19]. The chemical structure of lentinan and schizophyllan and the fruit bodies of the producer mushrooms are depicted in Figure 1.

Ganoderma lucidum is another well-studied medicinal mushroom of the *Basiodiomycetes* family which has been used in traditional East Asian medicine as a dry powder or as a hot water extract (a type of bitter mushroom tea). It produces ganoderan, a typical β-(1,3) bioactive glucan branched at C-6 with β-(1,6) glucose units, with a varying molecular weight and degree of branching, especially when isolated from the water-soluble fraction of the fruit body, while the glucan isolated from filtrates of liquid-cultured mycelia which has a MW of 1.2–4.4 × 10^6 Da [2••,19,20]. Notably, as occurs with other mushroom biopolymers, the fruit bodies of *G. lucidum* also produce several more heteroglucans and proteoglucans with immunostimulating activity [2••,21].

Another edible and medicinal mushroom, *Agaricus blazei*, originating from Brazil, is the source of several antitumor polysaccharides contained in its fruit body [1,2••,3,4••]. These include a β-(1,6);β-(1,3) glucan, an acidic β-(1,6);α-(1,3) glucan, and an acidic β-(1,6);α-(1,4) glucan. By contrast to most mushroom glucans, the above glucans have a main chain of β-(1,6) glycopyranose, instead of the more common β-(1,3) linked main chain [1,2••,3,4••]. The fruit body also contains an antitumor water-soluble proteoglucan of 380,000 Da with a α-(1,4) glucan main chain and β-(1,6) glucopyranoside branches at a ratio of 4:1 [4••,22], as well as two immunostimulating heteroglucans containing glucose, galactose and mannose, one consisting of glucose and ribose and a xyloglucan [1,4••,23]. In submerged cultures in bioreactors *A. blazei* can also synthesize an extracellular proteoglucan with mannose, glucose, galactose and ribose groups and a very high molecular weight (1000,000–10000,000 Da) which exhibits significant antitumor properties [23,24].

Figure 1



Chemical structures (left) and fruiting bodies (right) of (a) lentinan from *L. edodes* and (b) schizophyllan from *Schizophyllum commune*.

Other immunostimulating biopolymers from Basidiomycetes include grifolan, a gel-forming β-(1,3)-D-glucan with β-(1,6) glucosidic bonds at every third glucopyranosyl residue, found in the edible fungus *Grifola frondosa* and krestin, a proteoglucan with a β-(1,3)-D-glucan chain produced by the edible mushroom *Coriolous versicolor* (also known as *Trametes versicolor*), which has been commercialized in Asia as an effective immunostimulative drug [1,25–28].
The popular culinary oyster mushroom *Pleurotus ostreatus* and other species of this gender synthesize bioactive β-glucans, such as pleuran, an insoluble β-(1,3/1,6)-D-glucan [29,30], which is another potential candidate for the development of nutraceuticals [1,31]. Another type of edible medicinal mushroom is the *Tremella* group of mushrooms (*T. mesenterica, T, fuciformis, T. auriantica, T. cinnabarina*) which are jelly mushrooms with an unusually high polysaccharide content (60–70% of the fruiting body, as opposed to 10–30% in other mushrooms) [32,33]. *Tremella* acidic polysaccharide is a glucuronoxylomannan composed of a linear backbone of α-1,3-linked D-rhamnose, to which xylose and glucuronic acid side chains are attached [32,33].

Apart from mushrooms polysaccharides, other food-grade fungal biopolymers have been used or proposed for use in functional food and nutraceuticals. For instance, pullulan, a common food additive which is elaborated by submerged cultures of *Aureobasidium* (or *Pullularia*) *pullulans*. It is a soluble homopolysaccharide consisted of maltotriose units with alternating α-(1,4) and α-(1,6) linkages and has an average molecular weight of 360,000–480,000 Da, depending on process conditions and the strain used, although industrial food grade pullulan of 100,000 Da is also available [2••,34,35]. Pullulan is only partly degraded by human amylases and has been used as a dietary fiber or prebiotic substance [2••].

Scleroglucan is another extracellular glucan excreted by mycelia of *Sclerotium glucanicum* or *S. rolfsii* [1,2••,36,37]. It has a β-(1,3) linked backbone, to which single D-glucosyl side group are linked via β-(1,6) linkage to every third or fourth unit of glucosyl backbone, forming a high molecular weight glucan of approximately 1000,000 Da. Although scleroglucan is known and used mostly as a viscosifier for enhanced oil recovery, it also possesses antitumor and antiviral activity [2••,10,36].

Saccharomyces cerevisiae, the common food grade brewer's and baker's yeast is also known for the production of immnopotentiating glucans found in the cell wall. The highly branched glucans are insoluble in water, but after enzymatic hydrolysis, chemical oxidation or derivatization (sulphation of the biopolymer) soluble glucans with a low content of glucosyl branches can be produced, which facilitates their use in foods or pharmaceuticals. Figure 2 illustrates the chemical structure of soluble (slightly branched) and insoluble (highly branched) yeast glucans. BYG is the general term for commercialized Brewer's yeast glucan, which may also contain peptide moieties [1,38,39•]. PGG (also known as Betafectin) is a similar bioactive glucan from baker's yeast composed of (1,6)-β-D-glucopyranosyl-(1,3)-β-D-glucopyranose groups with a Degree of branching of 0,5 (one branch in every two molecules of the main chain) [1,40]. *S. cerevisiae* is also the industrial producer of zymosan, an immunomodulating cell wall proteoglucan with long (1,3)-glucosyl and (1,6)-glucosyl groups, as well as mannan, protein and nucleic acid groups [2••,41].

Medicinal properties of fungal polysaccharides

Immunostimulating and antitumor effects

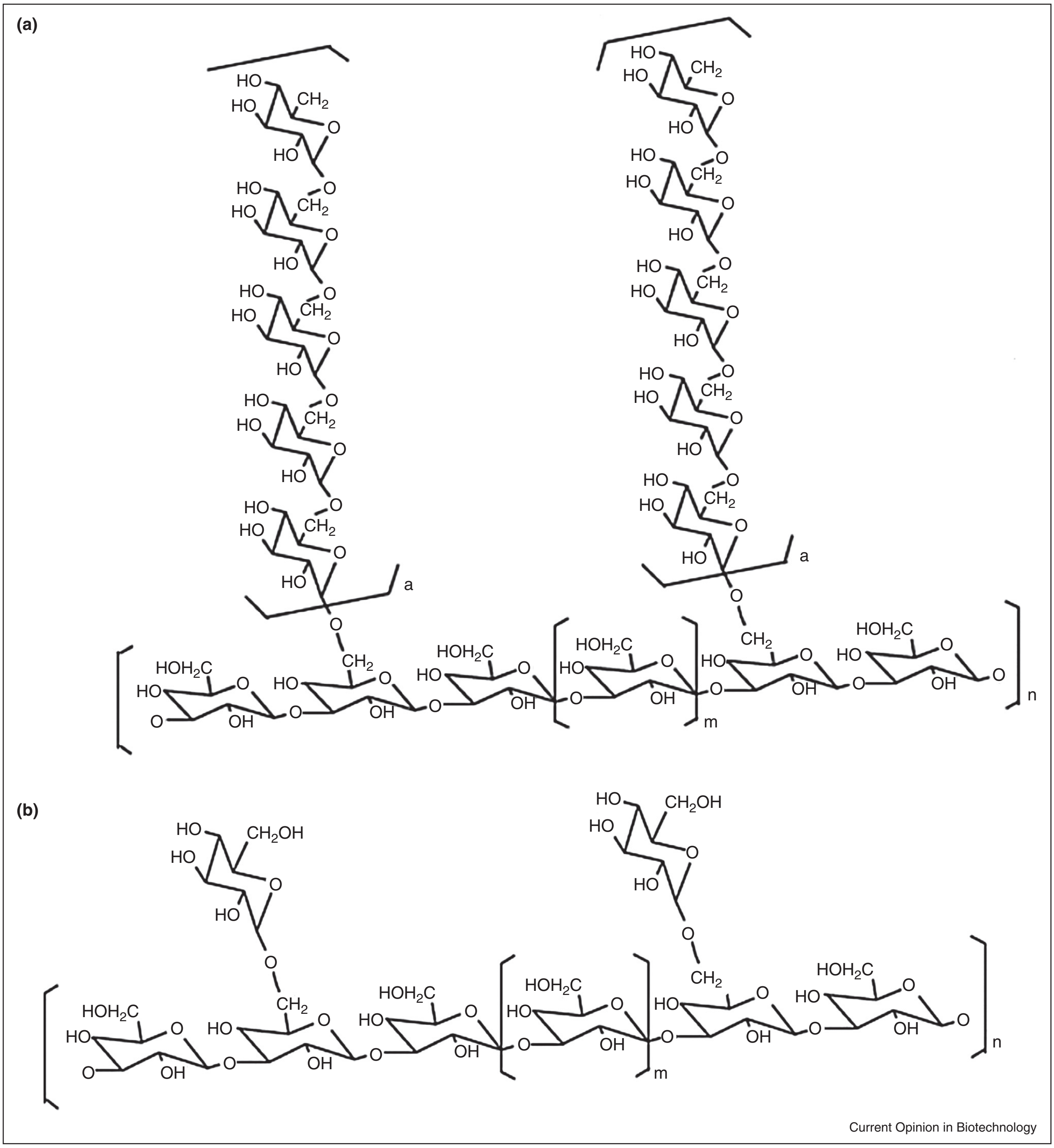
There are numerous research and review articles that describe the multiple therapeutic effects of fungal polysaccharides, and the detailed description of these biological properties goes beyond the scope of this article. However, a summary of the main medicinal properties of these biopolymers and a general description of their mode of action is necessary for understanding their potential for use in functional foods and nutraceuticals.

Bioactive fungal polysaccharides are often described as 'Biological Response Modifiers' (BRM's), due to their ability to trigger a usually non-specific reaction of the immune system against tumor cells, viral and bacterial infections, inflammations, and also to provoke an increased synthesis of hormones and cells of the host immune system. In addition, several applications describe their ability to lower cholesterol and blood sugar levels, acting as non-digestible dietary fibers, or to act as antioxidants and free-radical scavengers, as well as hepatoprotective and detoxifying molecules [1,2••,3,4••,41].

These properties depend to a great extend on structural and physicochemical characteristics of the biopolymers, such as molecular weight (usually a medium or large molecular weight is linked to higher immunomodulating activity, although low molecular weight bioactive polymers also exist, and are generally more soluble and easier to disperse in a food matrix). Also, the presence of double or triple helix or a random coil, the degree of branching and of course the type and composition of sugar or non-sugar components (especially protein complexes, or sulphate groups) greatly affect the medicinal properties of these macromolecules [1,2••,3,4••,41,42]. Lastly, the isolation process followed for these biopolymers (water or alkali extraction from fruit bodies, filtration of liquid-cultured mycelia and alcohol precipitation of the polysaccharide) may have an impact on their size, composition and functionality [1,2••].

More specifically, lentinan and schizophyllan have been effective in the treatment of gastric, breast, lung, cervical

Figure 2



Insoluble **(a)** and soluble **(b)** yeast β-glucan. In both cases, a main chain of β-(1,3)-glucose exists. In the case of soluble glucan (b), single glucose molecules are attached to this backbone via β-(1,6) glycosidic bonds, while in the case of insoluble glucan large side chains of β-(1,3)-glucose exist, which are bound to the main chain via β-(1,6)-linkages, leading to a high degree of branching.

or colorectal cancer in combination with conventional antineoplastic drugs, although they do not exhibit a direct cytotoxicity against cancer cells. They also contributed in the prevention of metastasis and reduced the side-effects of chemotherapy and radiotherapy, while they increased mitosis in bone marrow cells after suppression by anticancer drugs [1,2••,42,43]. Both these two glucans, as well as the structurally similar scleroglucan have exhibited no toxicity to humans even at high dosages, and are more effective when administered in the early stages of cancer treatment. A common characteristic among these glucans is that the highest immunostimulatory activity (e.g. stimulation of secretion of tumor necrosis factor-TNF-α by human monocytes and activation of macrophages, or platelet hemopoietic activity) has been correlated with high molecular weight and a triple helix conformation [1,6,7,44••,45]. However, other results suggest that in the case of scleroglucan a random coil conformation may activate human blood monocytes better than an ordered helix [46]. Lentinan and schizophyllan are poorly absorbed in the intestine, so in most clinical or animal trials they are injected intrapleurally, intraperitoneally, or intravenously. Scleroglucan, in comparison, can also be administered orally, which is a significant advantage, especially with regard to its use as a bioactive component in nutraceuticals [10,47].

Along with lentinan and schizophyllan, antitumor glucans from *G. frondosa* and *Trametes versicolor* have been used in different clinical trials and led to an increase of survival rate and time in patients of different types of cancer, when used in combination with chemotherapy and/or surgery [48].

Ganoderan, the biopolymer produced by *G. lucidum*, has also been used as adjuvant therapy in combination with anticancer drugs. It was able to prolong the survival of Lewis carcinoma bearing mice and to increase the effectiveness of cytotoxic drugs and immunomodulators in patient with prostate cancer [49•,50,51]. *G. lucidum* polysaccharides have also shown prophylactic activity towards chemically injured macrophages [52]. In other studies, it was found that *G. lucidum* polysaccharides and proteoglucans significantly increase tumor necrosis factor-a (TNF-a) and interferon-g (IFN-g) excretion in a dose-dependent and time-dependent manner, while they can accelerate the recovery of splenic and lymphokine natural killer cells in immunosuppressed mice, as well as stimulate the expression of macrophages and T-cell immunity [19,53•]. Nonetheless, one has to bear in mind that when crude extracts of fruit bodies of *G. lucidum* are used, the immunomodulatory activity may also derive from non-polysaccharide molecules, such as ganoderic acid and terpenoids which are also found in fruit bodies or mycelia and spores of the fungus, and possess cytotoxic properties [48].

The glucans and proteoglucans from *Agaricus blazei* have been reported to be very effective in the treatment of different types of sarcomas and carcinomas in mice, or in increasing the excretion of interferone (IFN-γ) in serum. It is also known for the suppression of several allergic reactions and has been proposed as an antiallergic immunomodulator [1,4••,54].

The insoluble glucans synthesized by *S. cerevisiae* have shown strong mitogenic activity and caused enhanced production of cytokines and monocyte and neutrophil phagocytosis [2••]. Interestingly, chemically derivatized soluble glucans from *S. cerevisiae* (e.g. glucan sulphate, carboxymethyl glucan) exhibit similar or better antitumor properties in comparison to the native insoluble glucans [2••,55].

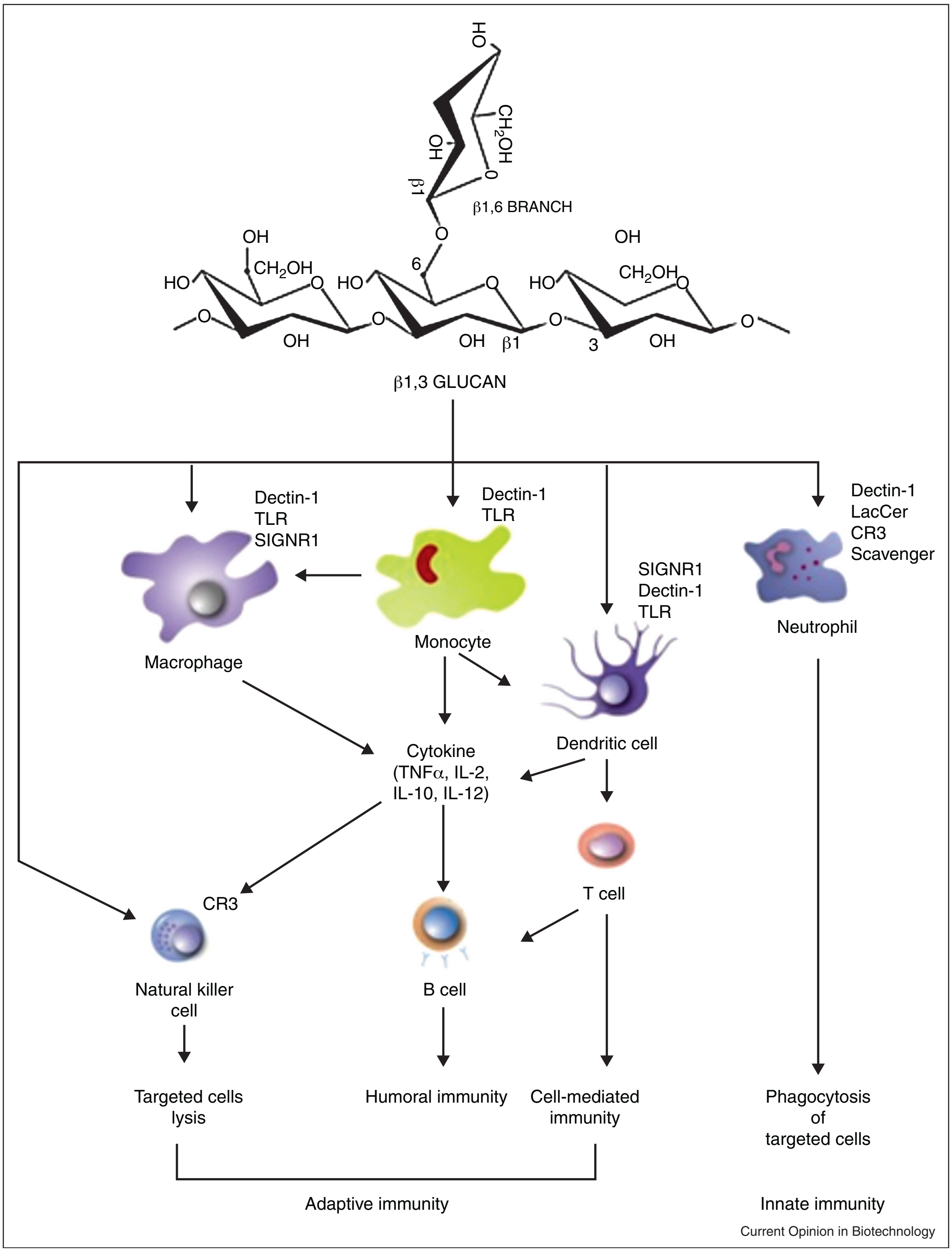
In other studies with water or methanolic extracts of glucans from the edible *P. ostreatus*, an induction of apoptosis in human prostate cancer was observed, and a suppression of proliferation of human breast cancer and colon cancer cells [56]. Also, β-glucans from fruit body extracts of *Pleurotus tuber-regium* were shown to possess antiproliferative activity against several human cancer cell lines [30].

For most of the above fungal glucans the immunostimulating and antitumor activity is the result of a combination of mechanisms which involve a mitogenic activity of soluble glucan molecules a specific stimulation of natural killer (NK) cells, T-cells, dendritic cells, neutrophiles and monocytes, an increased expression of immunoglobulins and cytokines (e.g. interleukins) and an enhancement of phagocytosis [2••,3,4••,6,47]. Although these immune responses are complex, a simplified illustration of the mode of action of many fungal glucans is shown in Figure 3.

Antimicrobial effects

Several fungal biopolymers are known to be active against bacterial and viral infections *in vitro* or *in vivo*, due to the stimulation of phagocytosis of microbes by neutrophils and macrophages. Lentinan for instance, is active against tuberculosis and *Listeria monocytogenes* infection, as well as *Salmonella enteritis* and *Staphylococcus aureus* [2••,57]. It has also been reported to reduce the total viable count and the population of *Escherichia coli* in the intestine of piglets [58]. The insoluble glucan from baker's yeast as well as SSG glucan from *Sclerotinia sclerotiorum* were also effective in controlling *Mycobacterium tuberculosis in vitro*, while PGG glucan could restrict the growth of methicillin-resistant *S. aureus* in inoculated rats [59,60]. Also, in another study with fruit body extracts from different *Agaricus* species, a significant antibacterial activity was observed against *S. aureus*, *Bacillus subtilis*, and *B. cereus*, although it was not confirmed that this result was solely due to the polysaccharide content of these extracts [61]. In addition, fungal glucans such as scleroglucan and ganoderan have antiviral activity, against rubella virus and herpes virus, respectively [62,21]. Schizophyllan is capable of stimulating the immune responses of patients with hepatitis B virus, while lentinan has showed high antiviral activity against influenza virus and polio virus [1,63]. Interestingly, lentinan and an acidic proteoglucan from *G. lucidum*, as well as glucans from *G. frondosa* and *T. versicolor* have been as used anti-HIV drugs, provoking an increased host resistance to HIV virus, and limiting the

Figure 3



Summary of immunostimulating mechanisms of fungal β-glucans: β-glucans can bind to several membrane receptors on the immune cells (such as Dectin, TLR). Subsequently, multiple signaling pathways are activated which may involve, macrophages, monocytes dendritic cells, natural killer cells, B cells, T cells and neutrophils. β-Glucans also stimulate the release of cytokines, such as tumor necrosis factor(TNF)-α and several interleukins (ILs). This immunomodulation may be either an innate or adaptive immune response.Adapted from [47].

toxicity of conventional anti-HIV drugs, a common drug used against AIDS virus [1,48,64,65•]. This antiviral activity of fungal glucans is believed to be mediated by the increased release of interferon-gamma and enhanced proliferation of peripheral blood mononuclear cells (PBMC) [1,48,64,65•].

Hypocholesterolaemic, hypoglycaemic and prebiotic effects

Since most of the fungal polysaccharides described above are non-digestible in the human intestinal tract, they can serve as sources of dietary fiber, reducing the rate of glucose release and cholesterol accumulation in the blood [1,2••].

Fungal glucans from *Lentinus edodes*, *G. lucidum*, *S. commune*, *Sclerotium rolfsii*, *Grifola frondosa*, *Agaricus blazei*, *Cordiceps miltaris*, *Cordiceps sinensis*, *P. ostreatus* and *S. cerevisiae* glucans have proved to reduce blood serum cholesterol and have hypolipidemic as well as hypoglycemic effects in animal and human studies [1,2••,39•,48,66,67•]. Interestingly, several mushroom biopolymers have proved to act synergistically in reducing hyperlipidemia and hyperglycemia [66]. Hypolipidemic effects are mediated by the interruption of the enterohepatic circulation of bile acids, which results in increased excretion in the feces, while the regulation in blood glucose levels is usually due to the attachment of the indigestible biopolymers to the intestinal surface which slows down glucose absorption [1,2••,66].

Lentinan is used as a useful hypocholesterolaemic agent for humans, as it reduces the levels of lipoproteins (both HDL and LDL) in blood. [66]. Also, the administration of glucan-rich water extracts from *P. ostreatus* have decreased the incidence of atherogenic plaques in animal studies [68]. However, one has to bear in mind that when mushroom water/alcohol extracts are used, substances other than polysaccharides, such as Plovatin/lovastin/mevinolin from *Pleurotus* species may be responsible for blocking the synthesis of cholesterol [66]. To give an example of recommended dosage and application in human diet, the National Mushroom Development and Extension Centre (Bangladesh) recommends a daily comnsumption of 5–10 g of dried *Pleurotus* mushroom for healthy individuals and 20 g for patients with diabetes, hypertension, cardiovascular complications, or cancers [56]. *S. serevisiae* glucans are reported to be capable of lowering total cholesterol and increasing the HDL fraction in obese men when 15 g fiber/day are consumed [39•].

Although native pullulan is not particularly bioactive, its chemical derivatization in order to obtain charged molecules may infer anticholesterol activity, since a charged pullulan can have bile acid binding and anticholesterolaemic capacity [1,2••]. Also, the use of pullulan as prebiotic has been suggested, as it was shown to promote the growth of Bifidobacteria [1,2••]. Soluble and insoluble glucans from *S. cerevisiae* have exhibited significant hypolipidemic activity, where the most decisive factor was the high molecular weight and large particle size. In carboxymethylated yeast glucans, although solubility was increased, hypolipidemic activity was restricted, due to the concomitant decrease of molecular weight during chemical derivatization [39•,66].

Several edible mushroom polysaccharides have exhibited hypoglycemic effect, via the decrease of glucose absorption, or the modulation of carbohydrate metabolism and insulin synthesis. Among these, *G. frondosa* glucans have shown some of the most explicit antidiabetic and antiobesity properties [66]. In addition, a glucuronoxylomannan of *Tremella mesenterica* has been reported to regulate glycemic responses in normal and diabetic rats. It appeared that ingestion of the biopolymer significantly decreased serum concentration of fructosamines, and it has been proposed that it can be used as an orally administered hypoglycemic agent, or an active component in functional foods for diabetic people [32].

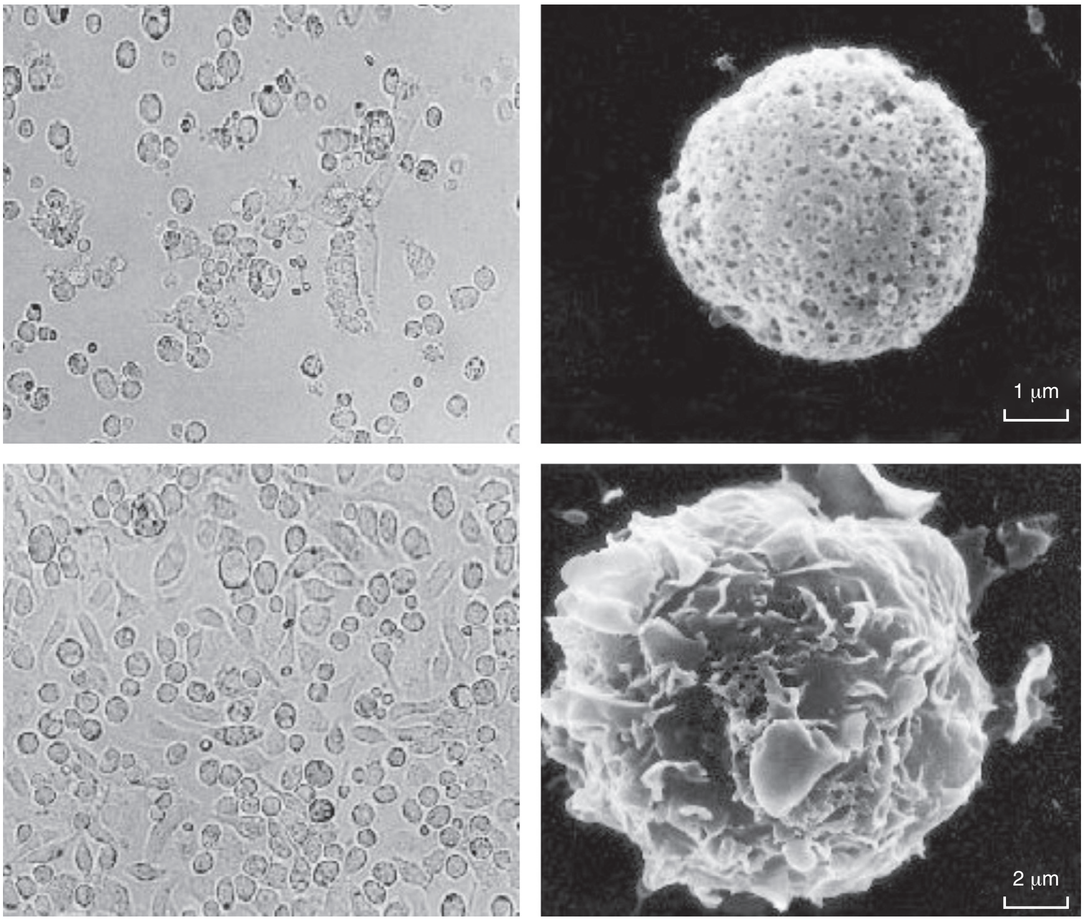
Antioxidant effects

Significant antioxidant properties have been reported for polysaccharides extracted from *T. versicolor* and *L. edodes* and *Agaricus* mushrooms. These biopolymers had chelating properties which could inhibit lipid oxidation. This effect was correlated with the presence of a β-glucan and a phenolic (mainly tyrosine and ferrulic acid) moiety bound to the main β-glucan main chain by covalent bonds [2••,69••]. Also, the methanolic extracts of *G. lucidum* and *G. tsugae* glucans and proteoglucans have been reported to possess antioxidant properties, as they can scavenge reactive oxygen species which have been implicated in oncogenesis, as well as lipid oxidation in food [66]. Also, a *G. lucidum* polysaccharide was able to decrease the production of oxygen-free radicals and could antagonize the respiratory burst induced by peripheral mononuclear cells in murine peritoneal macrophages, thus playing an important role in antiageing [69••,70]. Induced necrosis of macrophages by t-butyl hydroperoxide (*tBOOH*) has been largely prevented by the application of *G. lucidum* peptidoglucan, which protected the mitochondria, endoplasmic reticulum and macrophage microvilli from oxidative damage and malfunction, as illustrated in Figure 4 [70].

Application of medicinal fungal polysaccharides in food and nutraceuticals

'Mushroom nutraceuticals' is nowadays a relatively common term which refers to a refined polysaccharide, or a partially refined fruit body extract, or the dried biomass from mycelium or the fruiting body of a mushroom, which is consumed in the form of capsules, tablets, powder, syrops, solutions as a dietary supplement with some therapeutic properties. Several companies in Asia and

Figure 4



Mice macrophages treated with t-butyl hydroperoxide (*tBOOH*) to induce cell death (top) and macrophages treated with (*tBOOH*) + *G. lucidum* peptidoglucan (bottom). The photos on the left show the density of macrophage cells in both cases. The photos on the right show the presence (bottom right) or absence/destruction of microvilli (top right) in treated macrophages. The protective effect of the peptidoglucan against reactive oxygen species results in higher survival of macrophages (right) and prevention of loss of microvilli (left).
Adapted from [70].

elsewhere produce such products, the regular intake of which is believed to modulate immune response in humans and boost human health [66]. Such products are not yet established in the West markets, so there is a potential for new product development in this area, as long as issues of production economics, quality standardization, and stable availability are resolved. In this respect, biopolymers from controlled fermentation processes can be advantageous [1,2••,71••].

Although there is a large amount of literature describing the medicinal properties of fungal biopolymers and their potential or commercial use in novel pharmaceuticals in purified form, their application in food as functional food components has not been studied extensively, and studies of their bioactivity when incorporated into foods are very limited. It is interesting that food processing or interactions of bioactive polymers with food components, may hinder their bioactivity [2••]. Ganoderan, for instance, is degradable by pectinases and dextranases, thus its bioactivity in food containing these enzymes is not certain. Also, when lentinan and other biopolymers interacted with carrageenans their antitumor activity was reduced [2••,72]. This underlines the need for *in vivo* studies to be carried out using realistic food matrices, rather than pure/crude polysaccharide solutions, before a health claim is consolidated for the (functional) foods where they are added. Another issue of concern regarding the food applications of fungal polysaccharides is the appropriate dose for expression of bioactivity in order for a food to be declared 'functional' and without expressing any kind of toxicity [71••].

Nevertheless, several studies have brought about promising results on the use of therapeutic fungal polysaccharides in food and nutraceuticals. Glucans from *L. edodes* were successfully used as a partial replacement of wheat flour in baked foods, in order to produce a low calorie, fiber-rich functional food [73]. At concentrations up to 2% these glucans improved pasting parameters, batter viscosity and elasticity, without impairing the air holding capacity or hardness of the products [73]. In similar studies, when *L. edodes* β-glucans were added into noodles as a partial wheat flour replacement they assigned antioxidant and hypocholesterolemic effects and improved quality characteristics [74•].

Pullulan can be used as a dietary fiber and a source of prebiotic oligosaccharides, due to partial degradation by amylases and the stimulation of growth of Bifidobacteria [34]. When added to food it can also replace starch in bakeries, improve food texture, viscosity and moisture retention, however its food applications beyond Japan are limited [2••]. Scleroglucan would be a versatile functional ingredient in food, since, apart from its medicinal properties, it also serves as a stabilizer-texturizer in desserts and sauces, it is stable at low pH and high temperatures, it can form edible films and contributes to the formulation of low calorie foods, since it is not digestible. Several Japanese patents have been issued recently regarding such applications of scleroglucan [2••,10,36].

Ganoderma glucans have been reported to act as free radical scavengers in food and prevent lipid peroxidation, while stimulating interferone synthesis in human blood cells after consumption [69••]. In other studies, *Agaricus* water-soluble glucans, and especially those from *A. bisporus*, as well as glucans from *Auricularia auricula*, *Flammulina velutipes*, *G. lucidum* and *L. edodes* had notable antioxidant capacity and free radical scavenging potential, thus they were proposed as novel natural antioxidants in food applications. Again, although such functional products have not been commercialized yet, many patents exist regarding food-related applications (e.g. as functional edible film coatings, water-soluble capsules for inclusion of pickling liquids, among others) and it is believed that there is a great potential for future applications [27].

BYG glucan has emulsifying, viscosifying and water holding capacity in food applications, and along with its medicinal properties, it may act as fat replacer and source of dietary fiber. Firm BYG-gels are also formed after heating and subsequent cooling of ≥5–10% solutions [2••]. These properties can be useful in food applications of spent brewer's yeast glucans which have shown significant hypolipidemic capacity [39•].

In some recent publications the use of dried mushrooms or mushroom polysaccharides as the basis for the formulation of functional snack food has been described. For example, oyster mushroom powder has been incorporated in an Indian snack (papad) to improve its nutritive value and fiber content [75], while *Agaricus* extracts were utilized for producing snacks with high antioxidant potential and free radical scavenging capacity [76]. Other snack foods enriched with a powder from extracts of chestnut mushroom (*Agrocybe aegerita*) as a partial starch replacement (by up to 15%) exhibited a low glycemic response after consumption, which was correlated to the dietary fiber content [77•]. *Agaricus brasiliensis* is another mushroom which has been suggested as the basis for functional foods, as it was established that it can be used safely as an immunostimulant and for ameliorating obesity or diabetes [78].

Lastly, Japanese researchers managed to produce a functional cheese-like food containing *S. commune*. The novelty in their approach was that the fungus was added as a live starter culture, which was able to ferment and coagulate milk, thanks to its lactate dehydrogenase and proteolytic and milk-clotting enzymes (it had higher activity of proteases, but significantly lower clotting activity compared to rennin). The final product contained 0.58% β-glucan, which had a significant antithrombotic function [79].

Conclusions

Medicinal polysaccharides for fungi and especially those from edible mushrooms and food grade edible yeasts are exceptional target molecules for potential and existing applications in pharmaceuticals, as well as nutraceuticals and functional foods. Their multiple therapeutic properties have been extensively studied, and it seems there is a great potential for exploiting these biopolymers in formulating food that will fortify human health. However, the industrial manufacture of (more) biopolymer-based nutraceuticals and functional foods, has several prerequisitives that need to be addressed, such as the economically viable production of polysaccharides of stable and standardized quality, composition, purity and homogeneity, the understanding of molecular interactions of bioactive polysaccharides with other food components and the impact of food processing upon their functionality. Also, more human (clinical) studies on the efficacy of such food products will be needed to establish a health claim. If these concerns are answered, a bright future awaits these novel products.

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