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Medicinal Mushrooms as Sources of Immunomodulatory Polysaccharides: Extraction and Bioactivity

Meena Acharya¹●, Friederike Kranzbuehler²●, Alvaro Olabarria³●

¹Senior Scientist, Department of Biotechnology, Nallamala Institute of Life Sciences, Kurnool, India.

²Senior Scientist, Department of Industrial Microbiology, Hunsrueck Institute of Biochemistry, Simmern, Germany.

³Research Associate, Department of Bioprocess Engineering, Rioja Institute of Biotechnology, Logrono, Spain.

Email: ¹m.acharya@nils.ac.in, ²f.kranzbuehler@hib-s.de, ³a.olabarria@ribt.es

ORCID: ¹0000-0001-3463-1386, ²0000-0001-3525-0139, ³0000-0001-3635-9785

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ABSTRACT

Polysaccharides from medicinal mushrooms, above all beta-glucans and protein-bound glucans from shiitake, reishi, turkey tail and related species, are among the best known natural immunomodulators, and they are sold as drugs in a few countries and as supplements in many. This narrative review asks how these polymers are extracted and characterised, what the immune system appears to do with them, and how much weight the reported bioactivity can bear. It draws on published work on structure, receptor recognition, extraction technology, analytical chemistry and clinical use, and it reports no new data. Hot-water and alkaline extraction remain the workhorses, and newer ultrasound-, microwave- and enzyme-assisted methods promise gentler and faster recovery, yet every step changes the polymer that is eventually tested. Cell and animal studies show consistent activation of innate immune cells through recognised receptors, whereas clinical evidence is patchy, concentrated on a few purified products and hard to transfer to crude supplements. Poor description of the starting material, residual protein and endotoxin, and mixing of fruit body with grain-based mycelium blur many comparisons. The review concludes that immunomodulatory activity is real but conditional on the preparation, and it sets out the details a convincing report should give.

Keywords: Medicinal mushrooms; Polysaccharides; Beta-glucan; Immunomodulation; Extraction; Characterisation; Narrative review

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Article Class: Review Article

1. Introduction

Mushrooms have been eaten and used as folk remedies in East Asia for centuries, and the modern scientific interest in them rests largely on one class of molecules. Extracts of Basidiomycetes were found in

the twentieth century to slow the growth of experimental tumours in animals, and the active material turned out to be polysaccharides, not the small molecules that pharmacology had usually looked for (1). One of these, lentinan from shiitake,



was developed into an injectable product that is still used in Japan as an adjunct in the treatment of gastric cancer (2).

The polysaccharides in question are mostly beta-glucans, together with a varied group of heteroglycans and protein-bound complexes (3, 4). They are not toxic in the way a cytotoxic drug is. They are thought to work by being recognised by receptors on innate immune cells, which then change how the rest of the immune system behaves (5, 6). That is the sense in which they are called immunomodulatory: they adjust a response, and they do not simply switch it on or off.

The literature on them is large and uneven. Papers differ in species, in the part of the mushroom used, in the way polymer was extracted and in the assay chosen to show activity, and these differences make direct comparison hard (7). This review asks three linked questions. How are mushroom polysaccharides extracted and characterised? What does the immune system appear to do with them? And how much weight can the reported bioactivity bear? It is a narrative review of published work and reports no new data. The aim is to describe the field as it stands, not as its advertisements would have it.

2. Literature Review

2.1 Structural Diversity

The best-known mushroom polysaccharides are beta-glucans built on a backbone of glucose units joined through the first and third carbons, with side chains attached through the sixth. Lentinan is the classic example (8). Other fungal glucans carry different linkages, and some mushrooms also make alpha-glucans, mannans, galactans, xylans and mixed heteropolymers, so that the phrase mushroom polysaccharide covers a family and not a single substance (9, 10).

Activity is usually discussed in terms of a handful of structural features: the length of the chain, the frequency and length of the branches, the way the chain folds in solution, and the presence of attached protein or chemical substituents (4, 11). Reishi illustrates the complexity. Its polysaccharides include glucans and heteroglycans of several kinds, and the reviews treat them as a mixed bag whose individual members have rarely been tested alone (12, 13). Protein-bound preparations from turkey tail, developed in Japan and China, were among the first mushroom products to reach the clinic (14). Small differences in chain length or branching can matter more than the species name on the label.

Structure is not fixed by species. It shifts with strain, with the stage of growth, with the part of the mushroom analysed and with the way the mushroom was cultivated (7). A figure for the glucan content of a species therefore describes a particular batch more than it describes the species. This is one reason the same mushroom can look potent in one laboratory and inert in the next.

2.2 How the Immune System Reads Them

The central discovery of the past two decades was that innate immune cells carry receptors for beta-glucans. Dectin-1 was identified as a beta-glucan receptor on macrophages and related cells (5, 15), and later work added complement receptor 3 and members of the Toll-like and scavenger receptor families to the list (6, 16). Engagement of these receptors can lead to phagocytosis, to the release of signalling molecules and to the activation of dendritic cells, which in turn shape the adaptive response (4, 16).

Two complications run through this literature. The first is that the physical form of the glucan matters; particles and



soluble chains do not always trigger the same response, so a preparation tested as a solution may behave differently from one given as a suspension (6). The second is that most experiments use cells or injected material, whereas most consumers swallow a powder. How orally given glucans reach immune cells, and in what form, is still discussed in the reviews (17, 18). Some authors point to the gut microbiota as an additional route through which mushroom fibres could act (19). The wider group of fungal metabolites also includes compounds that damp inflammation, so the label immunostimulant is too simple (20, 21).

2.3 Species and Traditions

Five mushrooms recur in the clinical and nutraceutical literature (Table 1). Shiitake supplies lentinan, which is the one polysaccharide in this review that exists as a purified, injected medicine (2, 22). Reishi is used mostly as an oral supplement, and its reviews are enthusiastic about antioxidant and immune effects while admitting that human data are thin (13, 23). Maitake and *Agaricus blazei* have been studied largely in cells and animals, with a few small human reports (24, 25).

The geography of the evidence is worth noting. A large share of the clinical work on purified products comes from Japan and China, where the regulatory route for such products differs from that in Europe and North America, so that a finding from one setting does not carry automatically to another (26, 27). Trial populations, products and endpoints also differ, and the same product may be given by injection in one country and sold as a tablet in another. For that reason the reviews are cautious about pooling results across studies, and the present review does the same. Readers should treat Table 1 as a map of what has been studied, not a league table of what

works best.

Table 1. Medicinal mushrooms and the polysaccharides most often studied.

Mushroom	Polysaccharide	Main interest
Shiitake (<i>Lentinula edodes</i>)	Lentinan, a branched beta-glucan (8, 22)	Purified drug in Japan; adjunct in gastric cancer (2)
Reishi (<i>Ganoderma lucidum</i>)	Glucans and heteroglycans (12, 13)	Antioxidant and immune effects (23)
Turkey tail (<i>Trametes versicolor</i>)	Protein-bound glucans (14)	Adjunct cancer therapy (14)
Maitake (<i>Grifola frondosa</i>)	Branched beta-glucan fractions (24)	Immune enhancement in cells and animals
<i>Agaricus blazei</i>	Glucans and protein complexes (25)	Infection and cancer models (25)

Note: Qualitative summary of the cited reviews; it is not a ranking of potency.

2.4 From Mushroom to Product

Beyond medicine, mushroom polysaccharides are marketed as functional food ingredients and dietary fibre (28, 29, 30). Commercial products vary from powdered fruit bodies to extracts to dried culture of mycelium on grain. These are not interchangeable, and reviews have repeatedly asked for clearer labelling of which part of the fungus, and which extraction, a product contains (7, 28).

3. Materials and Methods

3.1 Scope

The review addresses two questions. The first concerns the chemistry and technology of obtaining polysaccharides from mushrooms: how they are extracted, purified and measured. The second concerns bioactivity: what immunological effects have been reported, in which systems, and how well the evidence is documented. It does not attempt to rank mushrooms or to recommend a product.



3.2 Literature Assembly

This is a narrative synthesis. We drew on peer-reviewed reviews and primary papers in four areas, namely structure, receptor biology, extraction and analysis, and clinical use, published up to 2022. No formal systematic search was run, no databases were screened against fixed criteria and no study was excluded by protocol. A narrative approach has real strengths when a field is broad and its questions are conceptual (31), but it lacks the reproducibility of a method such as PRISMA (32), and the selection of sources reflects our judgement. We used a quality scale for narrative reviews as a prompt for transparency (33).

3.3 Appraisal Framework

To judge how far a report can be trusted, we asked five questions of each source in turn (Table 2). Was the starting material defined? Was the extraction described? Was purity shown? Was contamination excluded? Does the assay fit the claim made? The questions are a reading aid and not a scoring system, and no numerical grade was assigned to any paper. Each can be answered from the text of the paper itself, which keeps the exercise repeatable. It is a small discipline, and it saves a good deal of confusion later.

4. Results

4.1 Extraction Routes

Most protocols follow the same broad sequence (Figure 1). The mushroom is dried and milled, extracted with hot water, precipitated with ethanol to obtain a crude polysaccharide, and then cleared of protein and pigment before fractionation by chromatography (34, 38). Hot water removes soluble glucans and heteroglycans, whereas alkaline extraction is used to release glucans that are bound within the wall and insoluble in water (34). The reviews note that the harshness of

these conditions alters chain length and can strip branches, so the polymer that is tested is not always the one that was in the mushroom. Heat, time and alkali are not neutral steps; each leaves a mark on the polymer.

Table 2. Questions used to appraise a report of mushroom polysaccharide bioactivity.

Question	Why it matters	Typical gap
Is the material defined?	Species, strain and part change the polymer (7)	Fruit body and mycelium not separated
Is the extraction described?	Conditions alter chain length (34)	Only the solvent is named
Is purity shown?	Protein and other sugars confound results (35, 36)	Total sugar reported as glucan
Is contamination excluded?	Endotoxin can mimic activity (37)	No test reported
Does the assay fit the claim?	Cells cannot stand in for patients (17)	In vitro result stated as health benefit

Note: The framework is a reading aid devised for this review, not a validated instrument.

Pre-treatment is easily overlooked. Defatting with an organic solvent removes lipids and some pigments before the aqueous step, and the temperature at which the mushroom is dried and stored can affect what the later extraction recovers (34, 39). Neither step is usually treated as a variable, although both belong to the process that makes the product.

Precipitation and clean-up bring their own compromises. Adding ethanol to the aqueous extract brings polysaccharides out of solution, but smaller fragments may stay dissolved and be discarded, so the yield describes only the part of the material that precipitates (34). Protein is then removed by enzymatic digestion or by repeated shaking with organic solvent, and each round risks taking some polysaccharide with it. A fraction described as purified



therefore reflects a series of choices made by the laboratory, not a property of the mushroom itself.

Newer approaches aim for gentler and faster recovery (Table 3). Ultrasound, microwave heating and enzymes that loosen the cell wall have all been applied to natural products, and general accounts of green extraction describe their advantages as well as their limits (39, 40, 41). The published comparisons rarely test the same mushroom under all methods, and each method has its own risk of damaging the polymer. Ultrasound can break chains if the treatment is too intense, microwave heating can overheat a sample locally, and enzymes add a further protein to be removed afterwards. Gentler does not automatically mean better, and a method that shortens the extraction time may not be the one that best preserves the structure a later bioassay is meant to test. Few papers report the intensity, duration and temperature of treatment in enough detail for another laboratory to repeat it. Any one of these steps can change the product, and few papers report all of them.

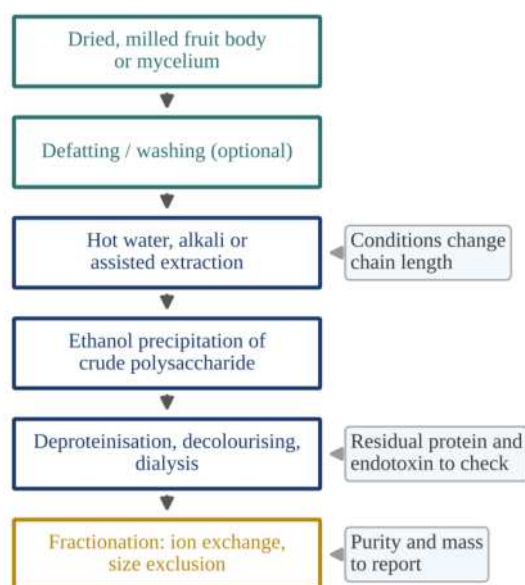


Figure 1. From fruit body to purified fraction: a typical extraction sequence (schematic, not data).

Table 3. Extraction approaches for mushroom polysaccharides.

Approach	Advantage	Concern
Hot water	Simple, widely used (34)	Slow; may leave insoluble glucans behind
Alkaline	Releases water-insoluble glucans (34)	Can alter or degrade the polymer
Ultrasound-assisted	Shorter time, milder heating (41)	Cavitation may shorten chains
Microwave-assisted	Rapid heating (39)	Local overheating; scale-up
Enzyme-assisted	Gentle, targets cell wall (40)	Enzyme cost; extra purification

Note: Advantages and concerns are those discussed in the cited reviews; their balance depends on the species and the target polymer.

4.2 Characterisation and Purity

Once a fraction is in hand, three simple colorimetric assays are in near-universal use: the phenol-sulfuric method for total carbohydrate (36), a dye-binding method for residual protein (35), and a method for uronic acids (42). They are quick and cheap, but a total carbohydrate result cannot tell glucan from other sugars, and reports that equate the two overstate the content of the active polymer. More informative work determines monosaccharide composition, linkage pattern and molecular mass distribution, usually by chromatography, mass spectrometry and nuclear magnetic resonance (9, 34).

Heteroglycans pose a different analytical problem from glucans. They are built from several sugars, commonly including galactose, mannose, fucose and xylose in proportions that differ between species, and their structures are harder to assign than that of a simple glucan (3, 10). For



this reason much of the older literature describes them only by their sugar composition and not by their linkages.

Even thorough characterisation does not make the assignment of activity to a structure simple. Many preparations are mixtures, and a biological effect may belong to a minor component. The authors of the cited reviews therefore treat structure-activity statements as hypotheses unless pure fractions of defined structure were tested (4, 43). A reader who wants to know whether a preparation would behave in their own assay needs that detail, not an adjective such as potent.

Molecular mass deserves a separate word. Estimates obtained by size-exclusion chromatography are relative to the standards used for calibration, and a polymer that folds into a helix or aggregates in solution can run differently from the standards, so values from different laboratories are not always comparable (9, 34). Because chain length is among the features most often linked to activity, this uncertainty feeds directly into any structure-activity argument.

4.3 What the Bioactivity Evidence Shows

The sequence of evidence has a familiar shape (Figure 2). In cell culture, preparations activate macrophages and other cells through the receptors described above, and the pattern is reproducible across many laboratories (6, 16). In animals, several preparations slow transplanted tumours or improve resistance to infection, although the models are far from human disease (38, 44). A result in cultured cells shows what is possible, not what is likely in a person who has swallowed a capsule.

Dose and route complicate the picture again. Injected and oral doses cannot be compared directly, and the dose at which a cell response appears in a dish has no

simple counterpart in a person (16, 17). Reviews therefore caution against reading cell data as dose advice, and they note that the few trials of oral products rarely report what the product contained (18, 43).

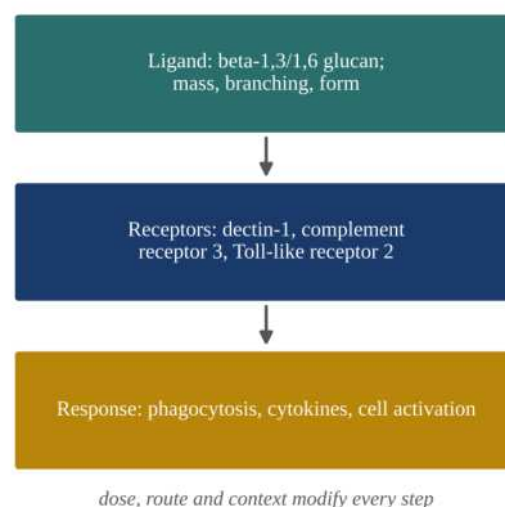


Figure 2. How a beta-glucan reaches an immune response, in three layers (schematic, not data).

Human evidence is thinner. For lentinan and the protein-bound turkey tail products, trials and meta-analyses in cancer patients, mainly in Asia, suggest a benefit as an adjunct to chemotherapy, though the designs, doses and comparators differ and the settings are specialised (2, 14). For oral beta-glucan as a supplement, reviews describe small trials of variable quality in infection and general immune function and conclude that the question of whether it behaves as a supplement or as a drug is unresolved (18, 45). The mushroom-specific work on *Agaricus blazei* is of the same kind (25).

4.4 Where the Evidence Is Weakest

Several weaknesses recur. Many studies do not state which part of the mushroom was used or whether mycelium grown on grain was included. Residual protein is often not reported. A more subtle problem is contamination with bacterial endotoxin, which is a potent immune stimulus and can be mistaken for the activity of the



polysaccharide when preparations are tested on immune cells (37). The problem is well known in nanoparticle research and is as relevant to natural polymers. Claims of purity deserve the same scrutiny as claims of potency.

A second weakness concerns how results are reported. Reviews written by enthusiasts of the field tend to collect positive findings, and the number of negative or null studies is difficult to know (26, 27). Taken with the heterogeneity of the preparations, this means that a list of beneficial findings is a poor guide to what a given product will do (Figure 3).

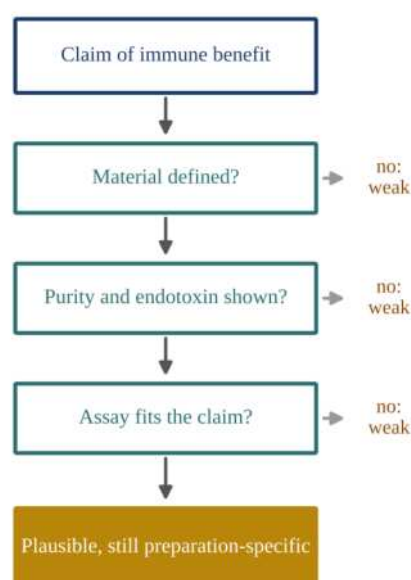


Figure 3. A decision path for reading a bioactivity claim (schematic, not data).

The choice of study material is a related difficulty. Fruit bodies, cultured mycelium and the liquid in which mycelium is grown differ in composition, and results from one cannot be assumed for another (7, 28). Where a supplement is made from mycelium grown on grain, the starch of the grain may account for much of the carbohydrate measured, which is one reason a total carbohydrate assay is a weak guide to glucan content (36).

5. Discussion

5.1 Interpretation

The main finding of this review is conditional. Mushroom polysaccharides, especially beta-glucans, are recognised by defined receptors, and the immunological effects seen in cells are reproducible. Whether those effects translate into a health benefit depends on the preparation, the dose, the route and the person. The evidence is strongest for a few purified products and weakest for the crude powders and extracts that dominate the market. Nothing here argues against studying mushroom polysaccharides; it argues for describing them properly.

The practical consequence is that extraction and characterisation are not background technicalities. They decide what substance is being tested and therefore what the result means. A protocol that is described in one line cannot be repeated, and a result that cannot be repeated cannot be built upon (7, 34).

The clinical story deserves one more caution. The best-documented benefit is that of purified products given alongside standard therapy in specific cancers, and it does not follow that a mixed powder taken by healthy people has a comparable effect (2, 27). Moving from the first to the second claim is a change of substance, dose, population and aim at once, and the evidence for each step would have to be assembled separately.

5.2 Limitations

This is a narrative review and shares the limitations of that form. Sources were selected without a fixed protocol, so selection bias is possible, and we may have missed work that would change the balance. Our emphasis on reviews inherits whatever those reviews emphasised, including the optimism of the field.



5.3 Future Work

Several steps would make the field easier to read. Authors could report the species, strain, part of the mushroom, extraction conditions, composition and endotoxin status of every preparation. Shared reference materials would allow laboratories to calibrate their assays. Human trials of defined products, with adequate comparators and clear endpoints, are needed to separate supplement from drug, and the possible role of the gut microbiota deserves study in its own right (18, 19). The same cautions apply to polysaccharides from other fungi, plants and algae.

6. Conclusion

Medicinal mushrooms do contain polysaccharides that interact with the immune system through recognised receptors, and a few of them have a clinical history. The evidence for most commercial preparations is much less secure, because the material tested is often poorly defined and because cell and animal results do not transfer simply to people. That is a modest claim, but it is the one the literature can currently carry.

For readers and researchers the lesson is practical. Ask what was extracted, from what, by which method, and how pure it was, before asking how potent it is. Reports that answer these questions are rare, and they are the ones from which the field will be built.

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9. Conflict of Interest

The authors declare no conflict of interest.

10. Author Contributions

M.A. conceived the review and wrote the sections on structure and bioactivity. F.K. wrote the sections on extraction and analytical methods. A.O. wrote the sections on bioprocess aspects and product considerations. All authors revised the manuscript and approved the final version.

11. Ethics Statement

This is a review of published literature. No human participants or animals were used and no ethical approval was required.

12. Data Availability

No new data were generated. All sources are cited in the reference list.

13. References

1. Wasser, S. P. (2002). Medicinal mushrooms as a source of antitumor and immunomodulating polysaccharides. *Applied Microbiology and Biotechnology*, 60(3), 258–274. DOI: [10.1007/s00253-002-1076-7](https://doi.org/10.1007/s00253-002-1076-7)
2. Ina, K., Kataoka, T., & Ando, T. (2013). The use of lentinan for treating gastric cancer. *Anti-Cancer Agents in Medicinal Chemistry*, 13(5), 681–688. DOI: [10.2174/1871520611313050002](https://doi.org/10.2174/1871520611313050002)
3. Ruthes, A. C., Smiderle, F. R., & Iacomini, M. (2016). Mushroom heteropolysaccharides: A review on their sources, structure and biological effects. *Carbohydrate Polymers*, 136, 358–375. DOI: [10.1016/j.carbpol.2015.08.061](https://doi.org/10.1016/j.carbpol.2015.08.061)
4. Meng, X., Liang, H., & Luo, L. (2016). Antitumor polysaccharides from mushrooms: A review on the structural characteristics, antitumor mechanisms and immunomodulating activities. *Carbohydrate Research*, 424, 30–41. DOI: [10.1016/j.carres.2016.02.008](https://doi.org/10.1016/j.carres.2016.02.008)
5. Brown, G. D., & Gordon, S. (2001). A new receptor for beta-glucans. *Nature*, 413(6851), 36–37. DOI: [10.1038/35092620](https://doi.org/10.1038/35092620)
6. Goodridge, H. S., Wolf, A. J., & Underhill, D. M. (2009). Beta-glucan recognition by the innate immune system. *Immunological Reviews*, 230(1), 38–50. DOI: [10.1111/j.1600-065X.2009.00793.x](https://doi.org/10.1111/j.1600-065X.2009.00793.x)
7. Wasser, S. P. (2011). Current findings, future trends, and unsolved problems in studies of medicinal mushrooms. *Applied Microbiology and Biotechnology*, 89(5), 1323–1332. DOI: [10.1007/s00253-011-1111-1](https://doi.org/10.1007/s00253-011-1111-1)



- [10.1007/s00253-010-3067-4](https://doi.org/10.1007/s00253-010-3067-4)
8. Zhang, Y., Li, S., Wang, X., Zhang, L., & Cheung, P. C. K. (2011). Advances in lentinan: Isolation, structure, chain conformation and bioactivities. *Food Hydrocolloids*, 25(2), 196–206. DOI: [10.1016/j.foodhyd.2010.02.001](https://doi.org/10.1016/j.foodhyd.2010.02.001)
 9. Synytsya, A., & Novák, M. (2013). Structural diversity of fungal glucans. *Carbohydrate Polymers*, 92(1), 792–809. DOI: [10.1016/j.carbpol.2012.09.077](https://doi.org/10.1016/j.carbpol.2012.09.077)
 10. Wang, Q., Wang, F., Xu, Z., & Ding, Z. (2017). Bioactive mushroom polysaccharides: A review on monosaccharide composition, biosynthesis and regulation. *Molecules*, 22(6), 955. DOI: [10.3390/molecules22060955](https://doi.org/10.3390/molecules22060955)
 11. Chen, J., & Seviour, R. (2007). Medicinal importance of fungal beta-1,3/1,6-glucans. *Mycological Research*, 111(6), 635–652. DOI: [10.1016/j.mycres.2007.02.011](https://doi.org/10.1016/j.mycres.2007.02.011)
 12. Ferreira, I. C. F. R., Heleno, S. A., Reis, F. S., Stojkovic, D., Queiroz, M. J. R. P., Vasconcelos, M. H., & Sokovic, M. (2015). Chemical features of *Ganoderma* polysaccharides with antioxidant, antitumor and antimicrobial activities. *Phytochemistry*, 114, 38–55. DOI: [10.1016/j.phytochem.2014.10.011](https://doi.org/10.1016/j.phytochem.2014.10.011)
 13. Cör, D., Knez, Ž., & Knez Hrnčič, M. (2018). Antitumour, antimicrobial, antioxidant and antiacetylcholinesterase effect of *Ganoderma lucidum* terpenoids and polysaccharides: A review. *Molecules*, 23(3), 649. DOI: [10.3390/molecules23030649](https://doi.org/10.3390/molecules23030649)
 14. Ooi, V. E. C., & Liu, F. (2000). Immunomodulation and anti-cancer activity of polysaccharide-protein complexes. *Current Medicinal Chemistry*, 7(7), 715–729. DOI: [10.2174/0929867003374705](https://doi.org/10.2174/0929867003374705)
 15. Brown, G. D., & Gordon, S. (2005). Immune recognition of fungal beta-glucans. *Cellular Microbiology*, 7(4), 471–479. DOI: [10.1111/j.1462-5822.2005.00505.x](https://doi.org/10.1111/j.1462-5822.2005.00505.x)
 16. Chan, G. C. F., Chan, W. K., & Sze, D. M. Y. (2009). The effects of beta-glucan on human immune and cancer cells. *Journal of Hematology & Oncology*, 2, 25. DOI: [10.1186/1756-8722-2-25](https://doi.org/10.1186/1756-8722-2-25)
 17. Murphy, E. J., Rezoagli, E., Major, I., Rowan, N. J., & Laffey, J. G. (2020). Beta-glucan metabolic and immunomodulatory properties and potential for clinical application. *Journal of Fungi*, 6(4), 356. DOI: [10.3390/jof6040356](https://doi.org/10.3390/jof6040356)
 18. Vetvicka, V., & Vetvickova, J. (2019). Beta glucan: Supplement or drug? From laboratory to clinical trials. *Molecules*, 24(7), 1251. DOI: [10.3390/molecules24071251](https://doi.org/10.3390/molecules24071251)
 19. Jayachandran, M., Xiao, J., & Xu, B. (2017). A critical review on health promoting benefits of edible mushrooms through gut microbiota. *International Journal of Molecular Sciences*, 18(9), 1934. DOI: [10.3390/ijms18091934](https://doi.org/10.3390/ijms18091934)
 20. Lull, C., Wichers, H. J., & Savelkoul, H. F. J. (2005). Antiinflammatory and immunomodulating properties of fungal metabolites. *Mediators of Inflammation*, 2005(2), 63–80. DOI: [10.1155/MI.2005.63](https://doi.org/10.1155/MI.2005.63)
 21. Tzianabos, A. O. (2000). Polysaccharide immunomodulators as therapeutic agents: Structural aspects and biologic function. *Clinical Microbiology Reviews*, 13(4), 523–533. DOI: [10.1128/CMR.13.4.523](https://doi.org/10.1128/CMR.13.4.523)
 22. Sheng, K., Wang, C., Chen, B., Kang, M., Wang, M., Liu, K., & Wang, M. (2021). Recent advances in polysaccharides from *Lentinus edodes* (Berk.): Isolation, structures and bioactivities. *Food Chemistry*, 358, 129883. DOI: [10.1016/j.foodchem.2021.129883](https://doi.org/10.1016/j.foodchem.2021.129883)
 23. Bishop, K. S., Kao, C. H. J., Xu, Y., Glucina, M. P., Paterson, R. R. M., & Ferguson, L. R. (2015). From 2000 years of *Ganoderma lucidum* to recent developments in nutraceuticals. *Phytochemistry*, 114, 56–65. DOI: [10.1016/j.phytochem.2015.02.015](https://doi.org/10.1016/j.phytochem.2015.02.015)
 24. Vetvicka, V., & Vetvickova, J. (2014). Immune-enhancing effects of Maitake (*Grifola frondosa*) and Shiitake (*Lentinula edodes*) extracts. *Annals of Translational Medicine*, 2(2), 14. DOI: [10.3978/j.issn.2305-5839.2014.01.05](https://doi.org/10.3978/j.issn.2305-5839.2014.01.05)
 25. Hetland, G., Johnson, E., Lyberg, T., Bernardshaw, S., Tryggestad, A. M. A., & Grinde, B. (2008). Effects of the medicinal mushroom *Agaricus blazei* Murill on immunity, infection and cancer. *Scandinavian Journal of Immunology*, 68(4), 363–370. DOI: [10.1111/j.1365-3083.2008.02156.x](https://doi.org/10.1111/j.1365-3083.2008.02156.x)
 26. Wasser, S. P. (2014). Medicinal mushroom science: Current perspectives, advances, evidences, and challenges. *Biomedical Journal*, 37(6), 345–356. DOI: [10.4103/2319-4170.138318](https://doi.org/10.4103/2319-4170.138318)
 27. Kothari, D., Patel, S., & Kim, S.-K. (2018). Anticancer and other therapeutic relevance of mushroom polysaccharides: A holistic appraisal. *Biomedicine & Pharmacotherapy*, 105, 377–394. DOI: [10.1016/j.biopha.2018.05.138](https://doi.org/10.1016/j.biopha.2018.05.138)
 28. Giavasis, I. (2014). Bioactive fungal polysaccharides as potential functional ingredients in food and nutraceuticals. *Current Opinion in Biotechnology*, 26, 162–173. DOI: [10.1016/j.copbio.2014.01.010](https://doi.org/10.1016/j.copbio.2014.01.010)
 29. Cheung, P. C. K. (2013). Mini-review on edible mushrooms as source of dietary fiber: Preparation and health benefits. *Food Science and Human Wellness*, 2(3–4), 162–166. DOI: [10.1016/j.fshw.2013.08.001](https://doi.org/10.1016/j.fshw.2013.08.001)



30. Valverde, M. E., Hernández-Pérez, T., & Paredes-López, O. (2015). Edible mushrooms: Improving human health and promoting quality life. *International Journal of Microbiology*, 2015, 376387. DOI: [10.1155/2015/376387](https://doi.org/10.1155/2015/376387)
31. Greenhalgh, T., Thorne, S., & Malterud, K. (2018). Time to challenge the spurious hierarchy of systematic over narrative reviews? *European Journal of Clinical Investigation*, 48(6), e12931. DOI: [10.1111/eci.12931](https://doi.org/10.1111/eci.12931)
32. Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & The PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine*, 6(7), e1000097. DOI: [10.1371/journal.pmed.1000097](https://doi.org/10.1371/journal.pmed.1000097)
33. Baethge, C., Goldbeck-Wood, S., & Mertens, S. (2019). SANRA—a scale for the quality assessment of narrative review articles. *Research Integrity and Peer Review*, 4, 5. DOI: [10.1186/s41073-019-0064-8](https://doi.org/10.1186/s41073-019-0064-8)
34. Ruthes, A. C., Smiderle, F. R., & Iacomini, M. (2015). D-Glucans from edible mushrooms: A review on the extraction, purification and chemical characterization approaches. *Carbohydrate Polymers*, 117, 753–761. DOI: [10.1016/j.carbpol.2014.10.051](https://doi.org/10.1016/j.carbpol.2014.10.051)
35. Bradford, M. M. (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Analytical Biochemistry*, 72(1–2), 248–254. DOI: [10.1016/0003-2697\(76\)90527-3](https://doi.org/10.1016/0003-2697(76)90527-3)
36. Dubois, M., Gilles, K. A., Hamilton, J. K., Rebers, P. A., & Smith, F. (1956). Colorimetric method for determination of sugars and related substances. *Analytical Chemistry*, 28(3), 350–356. DOI: [10.1021/ac60111a017](https://doi.org/10.1021/ac60111a017)
37. Li, Y., & Boraschi, D. (2016). Endotoxin contamination: A key element in the interpretation of nanosafety studies. *Nanomedicine*, 11(3), 269–287. DOI: [10.2217/nnm.15.196](https://doi.org/10.2217/nnm.15.196)
38. Zhang, M., Cui, S. W., Cheung, P. C. K., & Wang, Q. (2007). Antitumor polysaccharides from mushrooms: A review on their isolation process, structural characteristics and antitumor activity. *Trends in Food Science & Technology*, 18(1), 4–19. DOI: [10.1016/j.tifs.2006.07.013](https://doi.org/10.1016/j.tifs.2006.07.013)
39. Azmir, J., Zaidul, I. S. M., Rahman, M. M., Sharif, K. M., Mohamed, A., Sahena, F., ... Omar, A. K. M. (2013). Techniques for extraction of bioactive compounds from plant materials: A review. *Journal of Food Engineering*, 117(4), 426–436. DOI: [10.1016/j.jfoodeng.2013.01.014](https://doi.org/10.1016/j.jfoodeng.2013.01.014)
40. Chemat, F., Vian, M. A., & Cravotto, G. (2012). Green extraction of natural products: Concept and principles. *International Journal of Molecular Sciences*, 13(7), 8615–8627. DOI: [10.3390/ijms13078615](https://doi.org/10.3390/ijms13078615)
41. Chemat, F., Rombaut, N., Sicaire, A.-G., Meullemiestre, A., Fabiano-Tixier, A.-S., & Abert-Vian, M. (2017). Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. *Ultrasonics Sonochemistry*, 34, 540–560. DOI: [10.1016/j.ultsonch.2016.06.035](https://doi.org/10.1016/j.ultsonch.2016.06.035)
42. Blumenkrantz, N., & Asboe-Hansen, G. (1973). New method for quantitative determination of uronic acids. *Analytical Biochemistry*, 54(2), 484–489. DOI: [10.1016/0003-2697\(73\)90377-1](https://doi.org/10.1016/0003-2697(73)90377-1)
43. Zhu, F., Du, B., Bian, Z., & Xu, B. (2015). Beta-glucans from edible and medicinal mushrooms: Characteristics, physicochemical and biological activities. *Journal of Food Composition and Analysis*, 41, 165–173. DOI: [10.1016/j.jfca.2015.01.019](https://doi.org/10.1016/j.jfca.2015.01.019)
44. Ren, L., Perera, C., & Hemar, Y. (2012). Antitumor activity of mushroom polysaccharides: A review. *Food & Function*, 3(11), 1118–1130. DOI: [10.1039/C2FO10279J](https://doi.org/10.1039/C2FO10279J)
45. Vannucci, L., Krizan, J., Sima, P., Stakheev, D., Caja, F., Rajsiglova, L., ... Horak, V. (2013). Immunostimulatory properties and antitumor activities of glucans (Review). *International Journal of Oncology*, 43(2), 357–364. DOI: [10.3892/ijo.2013.1974](https://doi.org/10.3892/ijo.2013.1974)