

A review on the production, structure, bioactivities and applications of Tremella polysaccharides

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International Journal of
Immunopathology and Pharmacology
Volume 35: 1–14
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DOI: 10.1177/20587384211000541
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Abstract

Tremella polysaccharide is known to be structurally unique and biologically active natural products, abundant and versatile in activities and applications in food industry, daily chemical industry and medicine industry. In order to improve the industrialisation of Tremella polysaccharide, the limitations of preparation and structure-activity relationship of Tremella polysaccharide were reviewed in this paper. The research progress of Tremella polysaccharide in the past 20 years was summarized from the sources, preparation methods, molecular structure, activity and application, and the research trend in the future was also prospected. The application prospect of Tremella polysaccharide in against multiple sub-health states was worth expecting.

Keywords

application prospect, bioactive mechanism, structure-activity relationship, Tremella polysaccharide

Date received: 31 December 2020; accepted: 9 February 2021

Introduction

Tremella (*Tremella fuciformis* Berk) is the fruiting body of basidiomycete fungus tremella, also known as snow ear, white fungus. It has been used for thousands of years in China for its excellent traditional therapeutic effects on skin care, immune enhancement, and disease prevention. Tremella polysaccharide is an important active substance which exists in the fruiting body, mycelium and fermentation broth of *Tremella fuciformis*. Tremella polysaccharide is composed of xylose, mannose and glucuronic acid linked by an α -1,3-glycosidic bond, with side chains composed of galactose, arabinose and small amounts of fucose.

In the past decades, many studies have demonstrated Tremella polysaccharide potent effects on moisturising, gelatinous, anti-inflammatory, promoting wound healing, anti-oxidation, anti-aging and anti-radiation. As a new drug, Tremella

polysaccharide has incomparable safety compared with synthetic drugs.¹ It has been clinically used for antineoplastic agents as a safe and nontoxic natural active product. In the cosmetics industry, Tremella polysaccharide can be used as a moisturising

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additive. Compared with the traditional moisturizer hyaluronic acid, the cost is reduced by 86% under the same effect.²

Although Tremella polysaccharide has many advantages, its industrialisation is not smooth. There are three main reasons. First of all, the polysaccharides extracted from edible Tremella is of unstable quality, and the polysaccharides prepared by fermentation is of high cost, thus affecting the application of Tremella polysaccharide. Secondly, studies on the activity of tremella polysaccharide are mostly carried out in cell models and animal models, lacking in in vivo experiments and clinical data. Finally, as biological macromolecules, Tremella polysaccharide have complex tertiary and quaternary structures, and their active centres and structure-activity relationships are not well understood.

In this paper, the research of Tremella polysaccharide is summarized, which provides a new idea for the industrial production and application of Tremella polysaccharide.

Preparation of Tremella polysaccharide

Effects of strains on the yield of Tremella polysaccharide

Different *Tremella fuciformis* have different morphology and yield potential. Molecular imprinting³ and high-throughput sequencing⁴ could be used to identify and distinguish strains of tremella with high polysaccharide yield potential. However, the yield of Tremella polysaccharide could not be improved by means of gene function analysis and modification yet. Studies have shown that the dimorphism of fungus⁵⁻⁷ appears during the fermentation of *Tremella fuciformis*, and the yield of Tremella polysaccharide is related to the cell morphology. The number of elongated yeast cells in the fermentation broth is directly related to the yield of Tremella polysaccharides,⁸⁻¹⁰ but the mechanism of its effect is still unclear.

Effects of culture conditions on the yield of Tremella polysaccharide

The cultivation process of *Tremella fuciformis* is easily affected by temperature, light, water and other factors, which leads to the instability of the polysaccharide quality.¹¹ In contrast, it is easier to

control these sensitive factors by submerged fermentation. By controlling fermentation conditions, the yield of Tremella polysaccharide was significantly affected.

Glucose and galactose were the suitable carbon sources for the fermentation of Tremella polysaccharide, and ammonium nitrate and sodium glutamate were the suitable nitrogen sources.¹² The favorable pH level for Tremella extracellular polysaccharide production (4.48 g/L) was found to be 6.0.¹³ Acidic Tremella polysaccharide is an important active component, and the optimum pH of the enrichment of acidic Tremella polysaccharide (74.8%) was about 7.0.¹⁴ Controlling pH at different stages of fermentation was beneficial to maintain the maximum production rate. Phased fermentation can also be used to supplement nutrients. Baets'¹⁵ research showed that the yield of Tremella polysaccharide was increased by 2.2 times in a fed-batch fermentation in a starch-free medium. During the three-stage cultivation of Tremella, Zhu et al.¹⁶ used orbital and reciprocating cycles to perform shake flask fermentation. The yield of Tremella polysaccharide was increased by 2.6 times compared to single-stage fermentation. When the fermentation process was controlled by stages, the electronic nose and electronic tongue could monitor the fermentation degree by collecting the fermentation tail gas and fermentation liquid.¹⁷ In addition, increasing the viscosity of fermentation broth, reducing nitrogen content and increasing inorganic salt content can also promote the accumulation of Tremella polysaccharide.^{18,19}

Effect of extraction method on the yield of Tremella polysaccharide

Tremella polysaccharide includes fruit body polysaccharide, extracellular polysaccharide, intracellular polysaccharide and cell wall polysaccharide. The most common method to extract Tremella polysaccharides is ethanol precipitation, but this method takes a long time for extract and has a high loss rate of polysaccharides. Moreover, the extracted crude polysaccharides still contain a lot of impurities such as pigment, protein and nucleic acid, which need to be further separated and purified. Therefore, there is a need to find a new extraction method to replace ethanol precipitation. The advantages and disadvantages of the methods available for extracting polysaccharides are listed in Table 1.

Table 1. Comparison among the extraction methods.

Extraction methods	Advantages	Disadvantages	Extraction rate/%	References
Alcohol precipitation	The most common method	Slow process and low yield	20.52	Duan and Wang ²⁰
Alkali extraction	Suitable for acidic polysaccharides extraction	Damage the structure of polysaccharides	10.49	Wu ²¹
Acid extraction	Suitable for cationic polysaccharides extraction	Damage the structure of polysaccharides	–	Nguyen et al. ²²
Ultrasonic-assisted extraction	High extraction rate; extract intracellular polysaccharides	Not suitable for mass production	36.38	Chen et al. ²³
Enzymatic hydrolysis	High extraction rate; extract intracellular polysaccharides	High cost and specific	15.36	Bao ²⁴
Aqueous two-phase system for extraction	Mild operating conditions and high recovery	Higher prices for dual polymer systems	16.2	Zhang and Wang ²⁵
Membrane Filtration	Strong selectivity; No other reagents are introduced	Need the molecular weight of polysaccharides in advance, Small sample throughput	–	Gao et al. ²⁶ and Liu et al. ²⁷

The principle of extracting Tremella polysaccharide is to obtain the maximum extraction rate and ensure that the active structure of polysaccharide is not destroyed, so it is very important to select the appropriate extraction method.²⁸ The yield, physicochemical properties and biological activity of polysaccharides were significantly affected by different extraction processes.^{29–31} When two or more extraction methods were used, the extraction rate of Tremella polysaccharide was 3–4 times that of the single extraction method. In our previous study, repeated freezing and thawing combined with double aqueous phase method was used to extract Tremella polysaccharide from the fermentation broth. This method could remove most proteins and pigments while extracting Tremella polysaccharide, and the extraction rate of polysaccharide could reach above 80%.³²

Primary structure and physicochemical properties of Tremella polysaccharide

Effects of preparation on the structure of Tremella polysaccharide

As shown in Table 2, The molecular weight of Tremella polysaccharides is in the range of 8×10^3 – 6×10^6 Da, which is composed of fucose, galactose, xylose, mannose, glucose and glucuronic acid.^{33,34} Source of polysaccharides and extraction methods will have an impact on the structure of Tremella

polysaccharides. In conclusion, the molecular weight of polysaccharides from Tremella fruit bodies is much higher than that from submerged fermentation. The monosaccharide composition of Tremella polysaccharide will change with the different strains, but it is not limited to the mannose main chain structure that previously thought. The monosaccharide composition of Tremella fuciformis polysaccharide obtained from the same strain was similar, but the molar ratio was slightly different.

The relationship between structure and physicochemical properties

Many studies have proved that the differences in the primary structure of Tremella polysaccharides will greatly affect its physicochemical properties.³⁹

The polysaccharides obtained from nine kinds of Tremella fuciformis showed obvious pseudoplasticity in dilute solution (5%). Moreover, when the concentration of Na^+ and K^+ in the solution increases, the ionic bridge between the molecular chains of Tremella polysaccharide will occur, resulting in the increase of solution viscosity.⁴⁰ While, the larger the molecular weight of Tremella polysaccharide, the stronger the inter-molecular hydrogen bond interaction force, the better the viscosity of its aqueous solution, which shows a lubricating taste in food and a better skin sensation in cosmetics. The structure of Tremella polysaccharide is stable, temperature and storage time have no significant effect on its electrical conductivity, pH

Table 2. Comparison of Tremella polysaccharide structure analysis.

Strains	Polysaccharide component	Culture condition	Relative Mw	Composition and molar ratio	Extraction method	Biological activities
Tongjiang Tremella TJ001 ¹⁷	Mycelium polysaccharide IPS1 Mycelium polysaccharide IPS2 Exopolysaccharide EPS1 Exopolysaccharide EPS2	Glucose 20g/L, beef extract 4g/L, KH_2PO_4 0.46g/L, K_2HPO_4 1g/L, MgSO_4 1g/L, 25°C, 150 r/min, aeration rate 5vvm, fermentation for 7 days.	736114.5, 207136.2Da 782,672.1, 481,025.1Da 554,098.3, 254,250.4Da 420,602.4Da	Mannose, galactose, glucose, rhamnose = 93.7:47.3:37.4:1 Mannose, rhamnose, glucuronic acid, glucose = 45.8:6.4:18.9:32.2 Mannose, galactose, glucose, rhamnose = 93.7:47.3:37.1:1 Mannose, galactose, xylose, rhamnose, glucuronic acid = 2.4:2.7:6.4:1:33.7	Hot water extraction and alcohol precipitation	Antioxidant activity, antitumor activity, antidepressant activity
Yeast spore T19 ³⁵	Exopolysaccharide	6% glucose, 0.4% yeast extract, 0.05% KH_2PO_4 , 0.05% K_2HPO_4 and 0.05% MgSO_4 , pH 7.0, at 30°C for 5 days.	–	Glucuronic acid, xylose, mannose = 0.8:1.2:1, in addition to containing some fucose and O-acetyl.	Hot water extraction	–
Yeast spore T7 ³⁵	Exopolysaccharide	–	–	Glucuronic acid, xylose, mannose = 1.3:1:3.5, in addition to containing some fucose and O-acetyl.	Hot water extraction	–
Fermentation of Tremella fuciformis spores ³⁶	Exopolysaccharide TF-A Exopolysaccharide TF-B Exopolysaccharide TF-C Exopolysaccharide TF-D	– – – –	62,830Da 63,710Da 58,962Da 51,454Da	D-glucose, D-xylose, D-mannose = 5:5:3 D-glucose, D-xylose, D-mannose = 2:2:5:8 D-glucose, L-rhamnose = 1:15 D-glucose, D-xylose, D-mannose, D-galactose = 3:2.5:6:1	Alkali extraction	hydroxyl free radicals scavenging, superoxide anion free radicals elimination and red cells hemolysis inhibition
Tremella fruit body ³⁷	TL04	–	2033 kDa	Composed of (1→2)- and (1→4)-linked-mannose and (1→3)-linked-glucans	Hot water extraction and alcohol precipitation	Intracellular lactate dehydrogenase (LDH) release, ROS accumulation and caspase-3 activity determination and neuroprotection
PTF-M38 (from the mycelial form) ³⁸	Cell wall polysaccharides	Glucose, 20 g/L; $(\text{NH}_4)_2\text{SO}_4$, 1.32 g/L; $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, 0.25 g/L; $\text{KH}_2\text{PO}_4 \cdot 3\text{H}_2\text{O}$, 0.5 g/L; vitamin B ₁ , 0.2 mg/L;	1240 Da	Xylose, mannose, glucose, galactose = 1:1.47:0.48:0.34	Alkali-extracted	–
PTF-Y3 (from the yeast form)	Cell wall polysaccharides	$\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$, 2 mg/L; and $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, 0.5 g/L, 25°C for 3~5 days.	1080 Da	Xylose, mannose, glucose = 1:1.65:4.06	Alkali-extracted	–
PTF-Y8 (from the yeast form)	Cell wall polysaccharides	–	1190 Da	Xylose, mannose, glucose = 1:1.21:0.44	Alkali-extracted	–

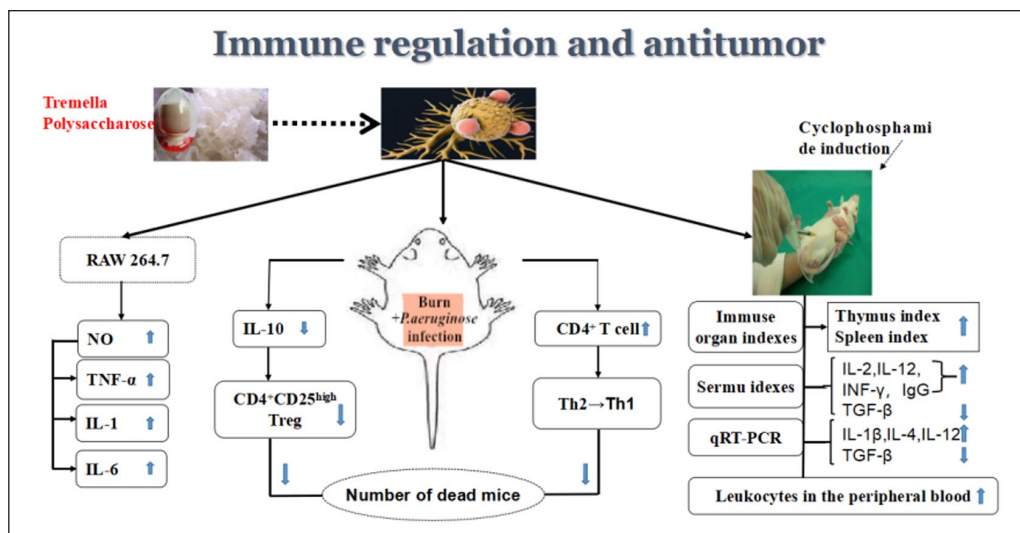


Figure 1. Mechanism of Tremella polysaccharide-induced immune augmentation in previous studies.

and other physical and chemical properties.⁴¹ Because it contains carboxyl and ammonium, it is easy to hydrolyze in acid-base condition. Under neutral conditions, the aqueous solution of Tremella polysaccharide forms weak gel structure. In addition, Tremella polysaccharide also crosslinks with protein, which makes the hydrogen bond between proteins stronger, so as to increase the viscosity of solution and improve the rheological property and food digestibility.^{42,43}

The structure of Tremella polysaccharide also had a great influence on its activity. Low molecular weight Tremella polysaccharide (1000 Da–10,000 Da) can penetrate multiple cell membrane barriers to reach the target organs for pharmacological effects. For example, low molecular weight Tremella polysaccharides show better immune activity in mice inhibited by cyclophosphamide.⁴⁴ In addition, the type and number of functional groups in Tremella polysaccharide will significantly affect its activity. The number of hydroxyl groups in Tremella fuciformis is related to its solubility. The more hydrophilic groups such as hydroxyl groups and acetyl group on branch,⁴⁵ the better the solubility and the better the effect as an injection or moisturizer.⁴⁶ The antioxidative properties of Tremella polysaccharides are related to the joint action of various groups. Acetyl groups can inhibit the free radical chain reaction, have a good scavenging effect on hydroxyl radicals, and have iron reducing ability and lipid peroxidation inhibitory activity.⁴⁷ Sulfate as an electron-withdrawing group can reduce the potential in vitro by scavenging DPPH free

radicals.⁴⁸ The carboxyl group in the polysaccharide has strong electron tolerance and good scavenging activity for superoxide.⁴⁹ The active group of Tremella polysaccharide is involved in the expression of various genes in the cell, and it is closely related to various activities such as immunity, hypoglycemia, and anti-aging.⁵⁰

In conclusion, the structure of Tremella polysaccharide is closely related to its physical and chemical properties, which is concern with the application in food industry, cosmetics industry and pharmaceutical industry. Therefore, it is very important to improve the yield and ensure the stability of product structure for promote the industrialisation process of Tremella polysaccharide.

Biological activity mechanism of Tremella polysaccharide

Immune regulation and antitumor activity

Recently, Tremella polysaccharide has received considerable attention for its anti-cancer activity. Ukai et al.⁵¹ firstly study on the immune activity of Tremella polysaccharide, he found that it has an inhibitory effect on mice with Sarcoma180. The next few decades, the mechanism of the immune function of Tremella polysaccharide has been studied. As shown in Figure 1, Tremella polysaccharides play an important role in enhancing immune function by activating macrophages, T-lymphocytes, and B-lymphocytes, regulating non-specific immunity, humoral immunity and cellular immunity.

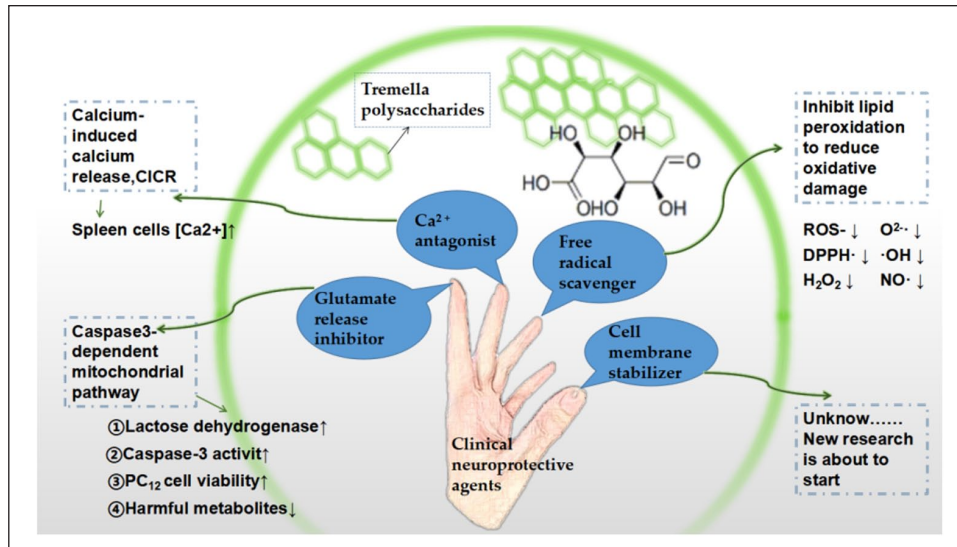


Figure 2. Neuroprotective mechanisms of Tremella polysaccharide in previous studies.

In Deng et al.'s research,⁵² Tremella mycelium polysaccharide (MCP) induced RAW264.7 macrophage proliferation, NO production and secretion of tumor necrosis factor- α , interleukin (IL)-1 and IL-6, so as to achieve the effect of immune stimulation. Tremella Polysaccharides attenuated sepsis through inhibiting abnormal CD4⁺CD25 high regulatory T cells in mice.^{53,54} When Tremella polysaccharides are used to treat mice suffering from burns and *Pseudomonas aeruginosa* infection, Tremella polysaccharides can inhibit the proliferation of CD4⁺CD25^(high) Treg CD4⁺T lymphocytes by reducing IL-10 and IL-4 and increasing the secretion of IFN- γ . In vitro experiments In Tremella polysaccharides, CD4⁺CD25^(high) Treg-mediated changes in CD4⁺T cell proliferation-induced differentiation of regulatory T cells were significantly reversed. Tremella polysaccharides had a significant effect for enhancing immunity in cyclophosphamide-induced immunosuppression.⁴⁴ When high-concentration Tremella polysaccharide (80 mg/kg) is used in immunosuppressed mice, it can significantly increase the thymus and spleen indexes and reduce the pathological characteristics of immunosuppression, such as: sinus and liver plate disorder, hepatocyte infiltration and steatosis, the spleen was broken and died, splenic sinus extension, spleen D lymphocytes decreased. In addition, it can also increase serum IL-2, IL-12, IN F- γ and IgG levels, reduce serum TGF- β levels, and significantly promoted the mRNA expression of IL-1 β , IL-4 and IL-12 in the liver and spleen, and inhibited the mRNA expression of TGF- β . Immunomodulatory

effect studies also indicated that⁵⁵ Tremella polysaccharide can significantly increase the number of leukocytes in mice inhibited by cyclophosphamide, and the smaller the molecular weight of Tremella polysaccharide, the better the effect on mice.

Tremella polysaccharides have inhibitory effects on a variety of cancer cells, including S180 (sarcoma),⁵⁶ A549 (lung cancer),⁵⁷ PC-3 (human prostate cancer)⁵⁸ and HepG-2 (liver cancer).⁵⁹ Tremella polysaccharides can induce cancer cell apoptosis by down-regulating the expression of anti-apoptotic genes bcl-2 and survivin, which is related to its immune mechanism⁶⁰

Neuroprotective effect

Nerve injury is a complex biochemical process, which may be caused by free radical reactions, glutamate accumulate excitotoxicity, insufficient blood supply, oxidative stress, mitochondrial dysfunction, inflammatory reactions, protein degradation, etc. Neuroprotective agents currently in clinical use are widely used in the treatment of stroke, Parkinson's disease, coronary heart disease and other diseases. The neuroprotective agents that have been approved for marketing in China mainly achieve protective functions through four mechanisms: calcium ion antagonism, free radical scavenging, stabilisation of cell membranes and inhibition of glutamate release. As shown in Figure 2, the protective effect of Tremella polysaccharide on neurons is also base on these four mechanisms.

Tremella polysaccharides have no neurotoxicity, can inhibit nerve damage through various ways, and have the potential to become neuroprotective agents. The purified polysaccharide isolated from *Tremella fuciformis* (TL04) has neuroprotective effect on glutamate-induced DPC₁₂ cell damage.³⁷ TL04 treatment can improve cell viability and inhibit the accumulation of reactive oxygen species, release of lactose dehydrogenase and caspase-3 activity and improve mitochondrial abnormalities caused by glutamate. The presence of Ac-DEVD-CHO (a caspase-3 inhibitor) significantly enhances the efficacy of TL04 in improving the viability of PC₁₂ cells exposed to glutamate. The neuroprotective effect of cells is mainly achieved through the caspase-dependent mitochondrial pathway. Tremella polysaccharides have a neurotrophic effect on PC₁₂ cells.^{61,62} Tremella polysaccharide aqueous solution (0.01–1 µg/mL) will promote neuron growth of PC₁₂ cells in a dose-dependent manner. Oral treatment for 14 days can significantly improve the intelligence and memory impairment in rats. Tremella polysaccharide can increase the concentration of free calcium ions in splenocytes in a dose-dependent manner within a certain dose range, which may be related to neuroprotective ability.⁶³ According to Ma's research,⁶⁴ Tremella polysaccharides improve the learning and memory ability of mice by reducing the pathological changes of ischemic brain tissue, reducing the formation of harmful metabolites, improving the tolerance of ischemia and hypoxia, and reducing the damage of brain neurons.

Antioxidant and anti-inflammatory effects

Recently, a variety of low-toxic or non-toxic natural antioxidants are used to prevent cancer, fight aging, and reduce inflammation. Fungal polysaccharides are an important component of natural antioxidants. Tremella polysaccharides have high antioxidant capacity, including free radical scavenging ability (OH, DPPH, O₂⁻, ABTS) and iron reducing ability (FRAP).^{65–69}

Tremella polysaccharides exhibits antioxidative stress and anti-inflammatory properties in LPS-treated macrophages by inhibiting the miR-155 and NFκB pathways, suggesting that TFPS may be a potential therapeutic agent for the treatment of inflammation-related diseases.⁷⁰ Tremella polysaccharide can regulate the expression of Sirtuin protein in cancer cells and participate in fatty acid

oxidation, aging, inflammation and other life processes.⁷¹ Tremella polysaccharide protects human skin fibroblasts induced by hydrogen peroxide by up-regulating SIRT1 expression,⁷² also, inhibition of lipopolysaccharide-induced human lung cancer cell apoptosis and autophagy by activating SIRT1 expression.⁵⁷ Purification of polysaccharide TAPA1 and its acetylated derivative TAPA1-ac, deacetylated derivative TAPA1-deac, and sulfated fraction TAPA1-s from *Tremella fuciformis* as samples, using H₂O₂ induced PC₁₂ oxidative damage model to evaluate antioxidant Effect and repair of oxidative damage. It was found that the effect was related to different substituents, and positively related to the content of acetyl groups and the degree of substitution (DS).⁴⁷ Furthermore, Tremella polysaccharide has been reported to protect cardiomyocytes from oxidative damage in a mouse model of D-galactose-induced aging.⁷³

Skin protection

Skin health is closely related to skin moisture content. When the skin is dehydrated, the intracellular metabolism is disturbed and the stability of the cell membrane is destroyed, causing the skin to lose its elasticity, wrinkles and even rashes. Tremella polysaccharide can be used as a natural moisturizer to relieve skin dehydration, repair the skin barrier and maintain skin health.⁷⁴

The desorption kinetic simulation method was used to study the moisture content stability and characteristics of Tremella polysaccharides obtained under different drying conditions, and the results showed that the Tremella polysaccharides obtained by each drying method had good moisturising and hygroscopic ability.⁷⁵ Tremella polysaccharides can reduce the photo-damage of skin caused by ultraviolet rays. After smearing Tremella polysaccharides, the moisture content and collagen content in the skin of animals exposed to ultraviolet rays are significantly higher than those in the control group. In addition, histopathological studies have shown that oral Tremella polysaccharides can promote the regeneration of endogenous collagen and maintain the I/III collagen ratio to protect the skin structure from damage caused by ultraviolet rays.⁷⁶ In the isolated pig skin wound healing model, Tremella polysaccharides are also considered to significantly promote wound healing.⁷⁷ Apart from the above, Tremella polysaccharides are extremely cost effective

compared to traditional humectants hyaluronic acid. The moisturising effect of products added with 0.05% Tremella polysaccharides is already better than products with 0.02% hyaluronic acid, but the cost is only 14% of the latter.²

Treatment of chronic diseases

Hyperglycemia, hyperlipidemia, and obesity are the number one health crisis for the modern elderly population. Kim used Tremella polysaccharides to treat diabetic mice, and analyzed proteomic analysis of mice before and after treatment, and found that 84 genes related to obesity, insulin resistance and complications of diabetes were significantly down-regulated, indicating that Tremella polysaccharide may be used in the treatment of obesity and diabetes aspects work.⁷⁸ Tremella polysaccharides can control mild type 1 diabetes (blood glucose <130 mg/dL), by lowering blood cholesterol, triglycerides, glutamate-pyruvate transaminase, urea content and increasing high-density lipoprotein cholesterol.⁷⁹ In Elisashvili's study, blood glucose and triglycerides were significantly reduced in a dose-dependent manner after continuously feeding hyperglycemic mice with Tremella polysaccharides for 15 days.⁸⁰ The regulation effect of Tremella polysaccharides on blood glucose and blood lipids is related to the activity of glucose metabolising enzymes.^{81,82}

Jeong⁸³ found that Tremella fuciformis polysaccharide can reduce the mRNA expression of PPAR γ , C/EBP α and leptin in cells in a dose-dependent manner, thereby inhibiting the differentiation of 3T3-L1 adipocytes. This indicates the potential value of Tremella polysaccharide as an anti-obesity prebiotic. Obesity can have an adverse effect on immunity, inflammation and platelet biomarkers,⁸⁴ which means that the immunoregulatory effect and antioxidant capacity of Tremella polysaccharides play a role in anti-obesity.

Other functions

There are still some bioactivities that have been initially explored, yet to be studied thoroughly. Studies have shown that Tremella polysaccharide has the ability to resist radiation and inhibit alcoholic liver damage. Before exposure to gamma radiation, mice that received Tremella polysaccharide administration had significantly higher numbers of nucleated

cells in the bone marrow and a significantly lower rate of chromosomal aberrations.⁸⁵ Tremella fuciformis fruit body extract may achieve protective effects on liver injury in mice by reducing the levels of malondialdehyde (MDA), glutathione (GSH) and triglycerides in liver tissue.⁸⁶

Applications

Tremella polysaccharide is a full-functioning active substance, and any of its activities are not independent, but complementary to other activities. For example, Tremella polysaccharides can participate in various physiological activities such as type II diabetes, cardiovascular disease, metabolic syndrome, inflammation and aging by regulating the expression of SIRT1 protein,⁷¹ which is in line with the guidelines of eastern medicine to maintain the dynamic balance of the human body through conditioning. Tremella polysaccharides are non-toxic and harmless natural ingredients that can be used for long-term contact with the human body by smearing or oral administration. It means that Tremella polysaccharides are suitable for the daily health needs of sub-healthy people and can be widely used in food, medicine and daily chemical products.

Food Industry

In the food industry, Tremella polysaccharides can be used as an excellent emulsifier, thickener and food fortifier to develop healthy foods and reduce the use of industrial additives due to their good uniformity and viscosity.⁸⁷ Tremella polysaccharide dilute solution (>5%) will show pseudoplasticity. When monovalent cations (Na⁺, K⁺) are added to the solution, the viscosity of the solution will increase.⁴¹ This property can synergize with the gelling agent in food to enhance the gelation effect.⁸⁸ For example, using the gel properties of Tremella polysaccharide and lotus seed starch to develop Tremella lotus seed cake with unique flavor,⁸⁹ and Tremella polysaccharide and gelatin are compounded to develop fudge with health care function.⁹⁰ Besides, the addition of Tremella polysaccharides to fresh meat can enhance the elasticity and water retention effect of myofibrillar protein,⁹¹ and the addition of bread can keep the bread moist taste, thereby extending the shelf life of bread.⁹² In protein-rich foods such as sausages and yoghurt, Tremella polysaccharides cause proteins to cross-link to achieve a binder effect. When Tremella

polysaccharide was mixed with whey protein isolate, the stability of the original protein solution was improved and the digestibility of whey protein isolate was decreased. Compared with before, the compound can exist in the gastric juice for a longer time and produce a lasting sense of satiety, which has certain enlightenment significance for the development of healthy weight loss products.⁴³

Daily chemical industry

Tremella polysaccharides have natural moisturising, skin repairing, antioxidant and antibacterial properties, catering to the needs of modern society for green cosmetic materials. Therefore, it is widely used in lotions, toiletries, make-up, contact lenses and other products. It can play a role in moisturising, anti-wrinkle, increasing gloss and elasticity, improving skin quality and inhibiting inflammation.^{93–96}

Medical treatment and health care

The application of Tremella polysaccharide in medicine is the most concerned. Some Tremella polysaccharide medicine have been approved for clinical treatment. Tremella Polysaccharide Enteric Capsule was approved by the China Food and Drug Administration (SFDA) in 2002 for the treatment of leukopenia cancer patients caused by chemotherapy and radiation therapy. It is also used to treat chronic persistent hepatitis and chronic active hepatitis adjuvant.⁹⁷ Tremella polysaccharides contain acidic groups, which makes the polysaccharide negatively charged in an aqueous solution and can be assembled into a nanostructure with chitosan.⁹⁸ This property makes Tremella polysaccharides promising for sustained drug release. The gel dressing prepared by mixing Tremella polysaccharide with chitosan and polyethylene glycol can achieve the purpose of long-lasting, mild, and promote wound healing.⁹⁹ Tremella polysaccharides are transplanted onto PLA nerve catheters, which can quickly promote the connection of peripheral nerves in a large gap in a short time and promote nerve regeneration for a long time.¹⁰⁰ Therefore, it can treat peripheral nerve injury caused by trauma and be applied to the field of regenerative medicine.

Tremella polysaccharides are absorbed by the body through external application, oral administration and injection. Oral Tremella polysaccharides enter the bloodstream through the gastrointestinal

tract and clear the wounds of gastrointestinal ulcers.¹⁰¹ The majority of Tremella polysaccharides in the blood are distributed in the liver and kidney,¹⁰² and participate in the regulation of liver ATP, liver glycogen and muscle glycogen to achieve anti-fatigue effect.¹⁰³ The body distribution of the injected Tremella polysaccharide is the same as the oral polysaccharide, and the absorption rate of the Tremella polysaccharide iron complex reaches 72%.¹⁰⁴ It also has a good utilisation effect during transdermal absorption,¹⁰⁵ and has the potential to prepare medical dressings combined with moisturising, antibacterial and anti-inflammatory effects.⁹⁹

Tremella polysaccharide as a functional factor to develop health products, has the role of enhancing immunity and regulating intestinal flora. Health products containing Tremella polysaccharides such as beauty oral liquid, slimming capsules and auxiliary hypoglycemic tablets have a good market.

Conclusion and perspectives

In conclusion, Tremella polysaccharides have good application prospects in food industry, cosmetics industry and pharmaceutical industry. The unique physical and chemical properties of Tremella polysaccharide (shear thinning, weak gelation, emulsification) make it have good stability in liquid products, which is very suitable for the preparation of industrial products. The viscosity of Tremella polysaccharide can make it closely bonded with protein and other components, and increase the elasticity and lubrication of the product. In addition, Tremella polysaccharide has a variety of molecular structures and abundant biological activities, which endows its industrial products with special functions. It's both advantage and great challenge that complex molecular and various activities of Tremella polysaccharides. The preparation process of Tremella polysaccharides can control the structure of polysaccharides (Tables 1 and 2), which affects the variety of activities. This research contributes to the industrial production of Tremella polysaccharides. Alao, the article lists the activities and its mechanism which is beneficial to human health and with special concern. Over the past 20 years, Tremella polysaccharides have made remarkable progress in the research of immunity, antioxidant, hypoglycemic and other activities. But the following research still faces challenges that need to be solved urgently:

Determine the differences in structure and activity of Tremella polysaccharides obtained by fermentation of different strains.

Researchers are encouraged to use gene editing to transform Tremella fuciformis and improve the ability to produce polysaccharides.¹⁰⁶

To explore the degradation and metabolic changes of Tremella polysaccharides and its metabolites in the digestive tract and the circulation in the body.

Tremella polysaccharides have potential as anti-obesity prebiotics after entering the gastrointestinal tract. Explore the effects of molecular weight and degree of polymerisation on anti-obesity and intestinal flora.

To study the additive and synergistic properties of Tremella polysaccharide combined with anti-obesity and anti-diabetic drugs.

To explore the effect of molecular weight and viscosity on the absorption rate of Tremella polysaccharides percutaneously.

In summary, Tremella polysaccharide is a safe natural active ingredient, which can be used in the prevention, treatment and rehabilitation of diseases. Moreover, the relatively low cost can bring greater application space. It is very meaningful to further study the physical and chemical properties and biological activities of Tremella polysaccharides.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Open Project Program of State Key Laboratory of Dairy Biotechnology (No. SKLDB2013-09).

Ethics approval

Human and animal experiments are not involved in this paper.

Informed consent

All authors agreed to publish the paper. This paper has not been published in any journal in any form.

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