Transactions on Cancer (2025)
Clausius Scientific Press, Canada

DOI: 10.23977/tranc.2025.060104
ISSN 2523-6482 Vol. 6 Num. 1

Progress on the extraction of polysaccharides from Lentinus edodes and their anti-tumor mechanisms

Yanzhe Liu[#], Jingyang Tang[#], Lan He, Danting Luo, Xin Xiong

Hunan Agricultural University, Changsha, Hunan, China
[#]These authors contributed equally to this work

Keywords: Lentinus Edodes, Polysaccharide, Anti-Tumor, Extraction Technology, Medicinal Food

Abstract: Lentinus edodes, as a precious Lentinus edodes species with medicinal and food origins, not only has a delicious taste, but also contains a variety of pharmacological active ingredients. Among them, polysaccharide (Lentinan) is a typical β-(1-3)-D-glucan, which has multiple pharmacological effects, such as hypoglycemic, antiviral, immunomodulatory and antitumor effects. Despite the long history of clinical application of polysaccharides, the molecular mechanism of their antitumor effects remains controversial. The traditional view is that polysaccharides exert indirect antitumor effects mainly by activating the immune system and relying on T lymphocytes, rather than directly killing tumor cells. In view of this, this thesis reviews the extraction technology of polysaccharides, their antitumor effects and their intrinsic molecular mechanisms, with the aim of providing a solid theoretical and experimental foundation for the broadening of the scope of the clinical application of polysaccharides, the enhancement of their medicinal value, and the development of novel therapeutic agents for oncology.

1. Introduction

With the change of human living environment, air quality, dietary habits, life pressure and many other external factors induce cancerous transformation of tumors. Cancer, as one of the most harmful diseases, is a great threat to human life and health, so it is urgent to seek an efficient and harmless anti-tumor pathway. In recent years, the field of Chinese herbal medicine has gradually entered the public's field of vision, with its long history and rich bioactivity deeply rooted in people's hearts. Lentinus edodes, as a typical Chinese herbal medicine with homology of medicine and food, is widely cultivated, with high yield and good medicinal properties, which fits the needs of natural drug development [1]. Among them, polysaccharide (Lentinan) is a typical β-(1-3)-D-glucan, which has a variety of pharmacological effects, such as cholesterol-lowering, antibacterial, immunomodulatory and antitumor [2]. Currently, Lentinus edodes polysaccharides can activate T cells [3], NK cells and other immune cells through intracellular signaling pathway, enhance immunity to prevent the proliferation and differentiation of cancer cells, and also indirectly affect the tumor microenvironment and inhibit tumor angiogenesis to play an anti-tumor role [4]. Although polysaccharides have great potential for anti-tumor activity, there are still problems such as low extraction rate and unclear biological activity. In this paper, we will review the latest

extraction process of polysaccharides and its anti-tumor molecular mechanism in the light of the latest research, which will provide some help for the subsequent research.

2. Composition and pharmacological value of polysaccharide

Polysaccharide is a natural polymer compound with significant biological activity extracted from the Lentinus edodes fruiting bodies, which is mainly composed of β-(1-3)-D-glucan [5], with a complex and unique chemical structure. The composition of polysaccharides is dominated by glucose, which is connected to the main chain by β-(1-3) glycosidic bonds, and part of the main chain also has side chains connected by β-(1-6) glycosidic bonds [6], forming polysaccharide chains with a branching structure. This special structure makes polysaccharides show unique physicochemical properties and biological activities in solution. Studies have shown that polysaccharides possess a variety of pharmacological activities such as antitumor, anti-inflammatory, antiviral, and immunomodulatory [7]. Lentinus edodes polysaccharide has a remarkable performance in antitumor, which can inhibit the proliferation of tumor cells and induce apoptosis through multiple pathways, and also can improve the body's own immunity and activate the body cells to produce interferon, tumor necrosis factor, etc., thus inhibiting the growth of tumor cells [8]. In addition, polysaccharides can also act as immunomodulators, activating macrophages, T cells, NK cells and other immune cells to produce cytokines and antibodies, thus enhancing the body's immunity [9]. polysaccharides not only have the effect of flavoring and health care in food, but also have a wide range of applications in medicine and other fields.

3. Lentinus edodes polysaccharide extraction process

3.1 Aqueous extraction

As a kind of polar macromolecule substance, aqueous extraction is one of the most common polysaccharide extraction methods in the laboratory at present, with fast rate, simple operation and low cost. Water extraction method through the raw materials and extraction solvent (usually water) contact, the use of polysaccharides in water with high solubility characteristics, so that polysaccharides from the raw materials dissolved out. Studies have shown that factors such as water extraction temperature, time, and material-liquid ratio affect the extraction rate of Lentinus edodes polysaccharides, and in the extraction of polysaccharides with distilled water leaching yielded 0.98%, warm water leaching yielded 1.05%, and boiling water leaching yielded 1.18% [10]. In the extraction experiment of Chen et al [11], the polysaccharide extraction rate of 5.86% was measured by controlling the extraction temperature of 90℃ and time of 4h. Although the aqueous extraction method has lower requirements for polysaccharide extraction, many non-polysaccharide hydrophilic species will be extracted during the extraction process, which has relatively low purity, takes too long, and the high extraction temperature will also lead to the destruction of polysaccharide substances in the Lentinus edodes, resulting in a further decrease in the extraction rate.

3.2 Supercritical fluid extraction technology

In recent years, supercritical fluid extraction technology has received more and more attention in Lentinus edodes polysaccharide extraction because of its high efficiency and environmental protection. Supercritical fluid extraction technology utilizes the strong solubility of CO_2 in the supercritical state, which is able to extract polysaccharide components in Lentinus edodess rapidly and efficiently. By precisely controlling the parameters such as temperature and pressure during the extraction process, the polysaccharides can be selectively extracted to avoid the interference of

other impurities, thus improving the purity of the product [12]. In addition, CO_2, as an extractant, is non-toxic, odorless, non-flammable and non-explosive, environmentally friendly and easy to recycle. Zhao Zijian et al. [13] used an isothermal variable pressure process to extract Poria cocos polysaccharide using CO2 supercritical fluid, and obtained the yield of Poria cocos polysaccharide was 5.276% at a temperature of 35 ℃, a pressure of 20 Mpa, an entrainer dosage of 0.4 mL/g, and an extraction time of 4.0 h. The extraction time of Poria cocos polysaccharide was 5.0% and the yield of Poria cocos polysaccharide was 4.0%. However, the supercritical fluid extraction technique also has some limitations. The equipment required for this technique is costly, requires high-precision temperature and pressure control systems as well as specialized operation and maintenance personnel, and the extraction process is relatively complex and requires strict control of various parameters, such as temperature, pressure, and extraction time, which makes it difficult to operate [14].

4. Mechanism of anti-tumor effects of Lentinus edodes polysaccharides

4.1 Direct anti-tumor effect

Direct antitumor effect is an important aspect of Lentinus edodes polysaccharide in the field of antitumor, which is mainly reflected in the direct killing and inhibition of tumor cells [15]. This mechanism of action not only slows down the growth of tumor cells, but also inhibits the malignancy of tumors. The rapid proliferation of cancer cells is one of the important features of their malignant behavior and the basis for the continuous growth and spread of tumors. Studies have shown that Lentinus edodes polysaccharides can inhibit the proliferation of cancer cells and effectively slow down the proliferation of cancer cells by interfering with their DNA synthesis and cell cycle regulation [16]. It was found that Lentinus edodes polysaccharides could further activate the mitochondria-mediated apoptosis signaling pathway by down-regulating the expression of thioredoxin reductase and inducing the overproduction of reactive oxygen species (ROS), thus increasing the sensitivity of PC3 cells to X-ray-induced apoptosis to play an antiprostate cancer role [17]. In addition, polysaccharides have the effect of inducing apoptosis in tumor cells. Apoptosis is a programmed cell death process, which plays an important role in maintaining cellular homeostasis in the body and removing damaged or abnormal cells [18]. In summary, the direct anticancer action mechanism of Lentinus edodes polysaccharides involves multiple aspects such as inhibiting cancer cell proliferation and inducing cancer cell apoptosis. These mechanisms of action synergize with each other and together constitute the important role of polysaccharides in the field of anticancer.

4.2 Indirect anti-tumor effects

As a kind of natural active polysaccharide, polysaccharide has been widely noticed in the research of antitumor field in recent years, especially its indirect antitumor action mechanism [19], which has brought a new dawn for tumor treatment. As an immunomodulator, polysaccharide mainly exerts antitumor effects by regulating the body's immune system, rather than directly killing tumor cells [20]. Studies have shown that polysaccharides can significantly activate macrophages [21], which play an important immunomodulatory role in the organism. They can not only directly phagocytose and digest tumor cells, but also secrete a variety of cytokines, such as interleukin-2, tumor necrosis factor, and granulocyte colony-stimulating factor [22], which are able to further activate other immune cells and form a powerful anti-tumor immune network. In addition, Lentinus edodes polysaccharides can promote the proliferation and differentiation of T lymphocytes [23], which are an important part of the body's immune system, and they are able to specifically recognize and attack tumor cells. By regulating the function of T lymphocytes, polysaccharides can

enhance the body's immune response to tumor cells, thus inhibiting the growth and spread of tumors [24]. Lentinus edodes polysaccharides can also regulate the function of immune cells such as natural killer (NK) cells, which have a powerful nonspecific killing ability and can directly attack and kill tumor cells [25]. By enhancing the activity of NK cells, polysaccharides further enhance the body's defense against tumor cells Fig1.

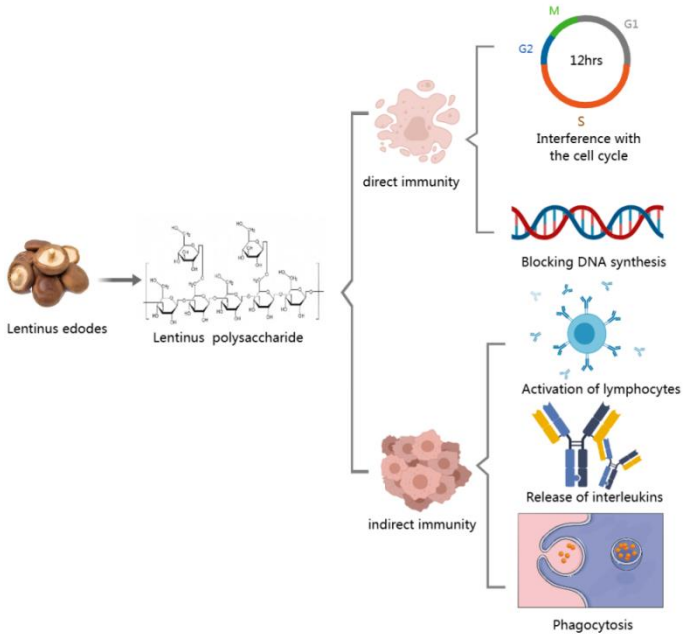

Fig.1. Antitumor mechanism of Lentinus edodes polysaccharide

5. Conclusion

As an important biologically active substance, polysaccharide has significant antitumor efficacy and great research potential. With the continuous optimization of Lentinus edodes polysaccharide extraction process, the traditional methods such as aqueous extraction, enzymatic digestion, acid-base method and other process enhancement, the extraction rate of Lentinus edodes polysaccharides has been improved to a certain extent. The emergence of new extraction methods also brings significant innovation for polysaccharide extraction, supercritical fluid extraction, microwave-assisted extraction method, etc. Through the improvement of the process, the polysaccharide extraction rate, purity and quality have been greatly improved. However, there are still problems such as high production cost, poor equipment conditions, and high operating difficulty, so it is urgent to seek an efficient, simple, and low-cost extraction method. As a kind of traditional Chinese medicine anti-tumor substance, Lentinus edodes polysaccharide has great potential because of its mild and non-toxic properties. Lentinus edodes polysaccharide can activate immune cells through signal transduction and further stimulate the production of immune factors, which can intervene in the proliferation and growth of tumor cells in two ways, from stimulating the production of immune cells, such as T cells and NK cells, to activating the tumor-killing factor. At the same time, polysaccharides can also improve the body's immunity and resist the attack of foreign germs on the body. In recent years, researchers have also improved the anti-tumor efficacy of polysaccharides by preparing complexes such as iron, which intervenes in the production of tumor cells through non-immune pathways. The valuable biological activity of polysaccharides opens up unlimited possibilities for their future development, and researchers can enhance their efficacy by preparing polysaccharides with other substances. At the same time, the clinical

application of Lentinus edodes polysaccharides can be developed, and the molecular mechanism of Lentinus edodes polysaccharides' intervention on tumor cells can be better understood, and it is hoped that this article can provide certain help for the development of antitumor drugs.

References

[1] Ma Chuangui et al, Studies on polysaccharide activity and application in edible mushrooms. Edible Mushrooms, 2024. 46(04): p. 1-5+9.

[2] Gao Qiming, Inhibitory effect of mushroom polysaccharides on Marek's disease virus infection in chicks, 2024, Shandong Agricultural University.

[3] Lin, Y., et al., Effects of montelukast on M2-related cytokine and chemokine in M2 macrophages. journal of Microbiology, Immunology and Infection, 2018 . 51(1): p. 18-26.

[4] Liu, Yali & Che, Huilian, Advances in the study of β-glucan to enhance intestinal immune function. Journal of Food Safety and Quality Testing, 2023. 14(19): p. 172-178.

[5] Hui Xu, Antitumor activity of mushroom polysaccharides and its potential mechanism, 2016, Wuhan University.

[6] Zhao, F., et al., The dose-dependent mechanism behind the protective effect of lentinan against acute alcoholic liver injury via proliferating intestinal probiotics. food & function, 2024.

[7] Peng, F.M. et al. Progress in the study of Paeonia lactiflora polysaccharides. Modern Chinese traditional medicine: 2023. pp. 1-10.

[8] Guangda, Z., et al., Lentinan progress in inflammatory diseases and tumor diseases. European journal of medical research, 2024. 29(1): p. 8-8.

[9] Liu, Z. et al. Progress of Chinese medicine in interfering with JAK/STAT signaling pathway to prevent sepsis. Chinese Pharmacy, 2024. 35(21): p. 2697-2702.

[10] Zhao Banping, Shen Yeshou, Ge Shengfang, Hu Jiaju, Separation and purification of polysaccharides from Danshi and their hypoglycemic effect. Journal of Anhui University (Natural Science Edition), 1999(02): pp. 92-95.

[11] Chen, J., et al., Effect of Extraction Methods on Polysaccharide of Clitocybe maxima Stipe. Advance journal of food science and technology, 2013. 5(3): p . 370-373.

[12] Zhao N et al. Advances in structural characterization and quality evaluation of Chinese herbal polysaccharides. Chinese herbal medicine, 2024. 55(21): p . 7491-7506.

[13] Zhao ZJ et al. Optimization of carbon dioxide supercritical fluid extraction of Poria cocos polysaccharides by orthogonal experiments. Shizhen Guomao Guomao, 2008(07): pp. 1628-1629.

[14] Wang, S. M., Application of supercritical fluid extraction technology in chemical production. Polyester Industry, 2024. 37(06): pp. 89-91.

[15].Elnahas, M.O., W.A. Elkhateeb and G.M. Daba, Nutritive profile, pharmaceutical potentials, and structural analysis of multifunctional bioactive fungal polysaccharides-A review. International journal of biological macromolecules, 2024. 266(P1): p. 130893-130905.

[16] Wenhan, F., et al., Safety and efficacy of lentinan nasal drops in patients infected with the variant of COVID-19: a randomized, placebo-controlled trial. Frontiers in Pharmacology, 2023. 14: p. 1292479-1292490.

[17] Zou, Y., et al., Enhancing Radiotherapy Sensitivity in Prostate Cancer with Lentinan-Functionalized Selenium Nanoparticles: Mechanistic Insights and Therapeutic Potential. Pharmaceutics, 2024. 16(9): p. 1230-1245.

[18] Liu, X., et al., The RIP3 activator C8 regulates the autophagy flux mediated by p62 and promotes the immunogenic form of cell death in human gastric cancer cells. Bioorganic Chemistry, 2024. 153: p. 107937-107956.

[19] Chu, Z., et al., Network pharmacology combined with molecular docking and molecular dynamic simulation to reveal the potential mechanism of lentinan ameliorating hyperlipidemia. Food Bioscience, 2024. 60: p. 104306-104319.

[20] Ishtiaq, A., et al., Therapeutic values and nutraceutical properties of Lentinus edodes (Lentinula edodes): A review. Trends in Food Science & Technology, 2023. 134: p. 123-135.

[21] Ziyi, G., et al., Lentinan regulates the immune efficacy of macrophage for lung metastasis in triple negative breast. Journal of Functional Foods, 2023. 105.

[22] Han, T., et al., Air bag-embedded MIL-101(Fe) metal-organic frameworks for an amplified tumor microenvironment activation loop through strategic delivery of iron ions and lentinan. Theranostics, 2024. 14(15): p. 5883-5902.

[23] Jiao, L., et al., The effect of lentinan on dexamethasone-induced immunosuppression in mice. International journal of biological macromolecules, 2024. 264(P2): p. 130621-130635.

[24] Xie, Z., et al., The Mechanisms of Polysaccharides from Tonic Chinese Herbal Medicine on the Enhancement Immune Function: A Review. Molecules, 2023. 28(21).

[25] Baindara, P., D. Roy and S.M. Mandal, CycP: A Novel Self-Assembled Vesicle-Forming Cyclic Antimicrobial Peptide to Control Drug-Resistant S. aureus. Bioengineering, 2024. 11(8): p. 855-876.