Proceedings of the 5th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/96/2025.21556

Research on the Antitumor Effects of β-Glucan in the Gut

Siyuan Gu[1,a,*]

[1]*School of Food and Health, Beijing Technology and Business University, No. 11 and 33 Fucheng Road, Haidian District, Beijing, China*
a. gusiyuankobe24@qq.com
**corresponding author*

Abstract: Intestinal tumors pose a significant threat to human health, and existing treatments have limitations, making the exploration of new therapeutic approaches highly important. β-Glucan, a naturally occurring bioactive polysaccharide, has garnered significant interest in anti-tumor research. This paper, using literature review and case analysis methods, systematically elaborates on its mechanisms of action in combating intestinal tumors. β-Glucan is widely sourced, structurally diverse, and possesses various physiological functions, such as immune regulation and anti-inflammatory effects. Its anti-tumor mechanisms primarily include: Immune modulation – activating immune cells, it can trigger the apoptosis of tumor cells, restrain the proliferation of tumors, and prevent tumor metastasis. Modulating gut microbiota - encouraging the growth of beneficial bacteria while inhibiting harmful ones; its metabolic byproducts can also inhibit tumor growth. Clinical studies have shown that β-glucan, when used alone, exhibits immune-regulatory and potential tumor-suppressive effects. Moreover, it can work synergistically with chemotherapeutic drugs to boost effectiveness, providing a new approach for the prevention as well as treatment of tumors in the intestine.

Keywords: β-glucan, intestinal tumors, immune regulation, gut microbiota, colon cancer

1. Introduction

Intestinal tumors severely threaten global human health, with both incidence and mortality rates continuously rising. Currently, treatments for intestinal tumors mainly include surgery, chemotherapy, and radiotherapy. However, these treatments often have significant limitations, such as severe side effects and high recurrence rates. Therefore, finding a safe and effective method for the prevention and treatment of intestinal tumors holds important clinical significance and social value. β-glucan, a bioactive polysaccharide found in nature, has attracted considerable interest in antitumor research in recent years.

β-Glucan is a type of polysaccharide made up of β-glucose units linked by β-glycosidic bonds. The glycosidic bonds in most β-glucan molecules are primarily β-1,3-glycosidic bonds or β-1,6-glycosidic bonds. In contrast, cellulose, which is commonly known, contains β-1,4-glycosidic bonds. In the scientific exploration of tumor immunotherapy, β-glucan, as a natural bioactive regulator, has been widely applied. In recent years, a number of studies have definitively verified[1] that β-glucan is capable of playing an immunomodulatory role. It has presented positive findings in suppressing tumor cell growth and inducing antitumor immune reactions[2-5]. A thorough investigation into the mechanisms by which β-glucan functions in intestinal antitumor effects is crucial for creating

DOI: 10.54254/2753-8818/96/2025.21556

innovative approaches for the prevention and treatment of intestinal tumors.This study aims to systematically explain the mechanisms of β-glucan in intestinal antitumor effects and demonstrate them through actual research examples. The research methodology includes literature review, extensively collecting relevant domestic and international research data, and providing a comprehensive analysis and summary of β-glucan's structural characteristics, sources, extraction methods, mechanisms of action, and research examples. Additionally, case analysis is used to conduct in-depth studies of specific research instances to validate the actual effects of β-glucan in intestinal antitumor applications.

2. Sources of β-Glucan and Intestinal Tumors

2.1. Sources and Structure of β-Glucan

β-Glucan is found in a variety of plants and fungi, including mushrooms, yeast, and algae. It is a well-known and thoroughly documented bioactive polysaccharide. As a non-starch polysaccharide, it is composed of β-D-glucose monomer units, which are linked by β(1→3), (1→4), or (1→6) glycosidic bonds, forming either branched or non-branched structural configurations [6]. Previous studies have identified sources for extracting β-glucan, including Cordyceps sinensis, Hericium erinaceus, Bamboo fungus, and oats. The structure of β-glucan can vary depending on its source. For example, yeast-derived β-glucan primarily features a β-1,3-glucan backbone with some β-1,6-glucan branches. Oat-derived β-glucan mainly connects β-1,3- and β-1,4-glycosidic bonds. It is this structural diversity that grants β-glucan different physicochemical properties and biological activities.

2.2. Causes of Intestinal Tumor Development

The occurrence of intestinal tumors is closely related to genetic factors, environmental influences, physiological changes, injuries, and chronic pathological states. Genetic factors play a significant role in the development of intestinal tumors, particularly in individuals with familial adenomatous polyposis or those carrying APC gene mutations, who have a higher risk of developing intestinal tumors. Environmental factors also have a significant impact. Long-term dietary habits high in fat, protein, and insufficient fiber intake has the potential to disturb the balance of the gut microbiota., thereby increasing the likelihood of intestinal tumors.

Moreover, unhealthy lifestyle habits like smoking, drinking too much alcohol, and not being physically active are risk factors for the development of intestinal tumors.From a physiological perspective, a weakened immune surveillance function, along with the accumulation of cellular mutations with age, creates favorable conditions for the formation of intestinal tumors. Traumas and persistent inflammatory states, like non - treated intestinal polyps, ulcerative colitis, or Crohn's disease, are capable of triggering abnormal tissue growth. As time passes, this abnormal growth might progress into malignant tumors.

For instance, studies have shown that defects in core protein glycosaminoglycan genes, leading to their targeted inactivation, can trigger intestinal tumors. In this process, the expression levels of p21, p27, ITF/Muc2, and E-cadherin decrease, while β-catenin signaling is upregulated. The formation of intestinal tumors is a result of the interplay and synergistic regulation between genetic and dietary factors [7].

DOI: 10.54254/2753-8818/96/2025.21556

2.3. Physiological Functions of β-Glucan

2.3.1. Immunomodulatory Effects

β - Glucan has the ability to attach to specific receptors on the surface of immune cells. Take Dectin - 1 receptors as an example. These receptors exist on macrophages, dendritic cells, and other immune cells, and when β - Glucan binds to them, it activates these immune cells. Additionally, β-glucan stimulates immune cells to secrete various cytokines and immunomodulatory substances, such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and others, which help enhance the body's immune response.

Furthermore, β-glucans from different sources exhibit distinct mechanisms and effects in immunoregulation. β-Glucan produced by Schizophyllum commune activates the immune response in the small intestine, indirectly mediating immunomodulatory activity [8]. Water-soluble β-glucan from the edible mushroom Entoloma lividoalbum stimulates macrophages, spleen cells, and thymic cells, acting as an immune stimulant [9].

At the same time, the (1→3)(1→6)-β-D-glucan extract obtained from the pathogenic Pythium insidiosum directly triggers a substantial and specific Th17 cell immune reaction, while also raising the concentration of immunoglobulin G (IgG)[10]. Dietary yeast-derived β-glucans enhance immunity by raising immunoglobulin levels and stimulating alkaline phosphatase (ALP) activity [11]. In vitro experiments have shown that β-D-glucan extracts not only significantly promote the proliferation of splenic lymphocytes but also greatly increase the generation of cytokines, including IL-2, IL-6, IL-10, TNF-α, and IL-17A[12-13].

2.3.2. Anti-inflammatory Effects

A large number of research findings have indicated that β - glucan holds the possibility of reducing intestinal inflammation. In animal models of inflammatory bowel disease (IBD), administration of β-glucan results in reduced inflammatory damage to the intestinal mucosa, improved intestinal barrier function, reduced infiltration of inflammatory cells, and lower levels of inflammatory factors. The mechanism may involve the regulation of gut microbiota balance and enhancement of mucosal immunity. For instance, β-glucan derived from yeast can alleviate DSS-induced mucosal inflammation and alterations in the intestinal barrier. It alleviates intestinal inflammation in multiple ways. Firstly, it curbs the expression of inflammatory mediators and enhances the expression of tight junction proteins related to intestinal permeability, as documented in [14]. Additionally, high molecular weight β - glucan has the capacity to directly stimulate leukocytes and regulate the generation of pro - inflammatory cytokines and chemokines. In contrast, low molecular weight β-glucan stimulates leukocytes by activating nuclear transcription factors [15].

2.4. Current Progress in Intestinal Cancer Treatment

For resectable rectal cancer, traditional surgical methods such as open surgery are more invasive. In recent years, laparoscopic surgery and robot-assisted surgery have become increasingly popular, offering advantages such as smaller incisions, quicker recovery, and fewer complications, thereby better preserving the patient's anal function and quality of life. For colorectal cancer (CRC), the only chemotherapy drug that effectively increased the 12-month survival rate for CRC patients after being discovered decades ago was the anti-metabolite drug 5-fluorouracil (5-FU). With the advancement of medical science, a combination of multiple chemotherapy drugs has been incorporated into standard clinical treatment protocols. Currently, a combination treatment regimen consisting of irinotecan, oxaliplatin, and capecitabine is widely used in CRC treatment, appearing in first-line treatment, second-line treatment, and sequential therapies [16].

DOI: 10.54254/2753-8818/96/2025.21556

Moreover, in the field of immunotherapy, the combination of immunotherapy with chemotherapy and targeted therapy not only enhances treatment efficacy but also shows some effect in patients with microsatellite stable (MSS) tumors, opening new treatment paths for late-stage cancer patients who previously had no effective treatment. The rapid, durable, and effective responses induced by immune checkpoint inhibitors will undoubtedly become a hot research direction in future cancer treatments. With the continuous progress of research into the signaling pathways of cytotoxic T lymphocyte - associated antigen 4 (CTLA - 4) and programmed cell death receptor 1 / programmed cell death ligand 1 (PD - 1/PD - L1), immunosuppressive drugs are expected to assume an ever - more vital role in the treatment of cancer [17-18].

3. Mechanisms of β-Glucan's Antitumor Effects

3.1. Immunoregulation

The immunomodulatory function of β-glucan relies on its complex conformational changes [19]. It can bind to pattern recognition receptors (PRRs) on the cell surface, thereby regulating innate immune cells and exerting antitumor effects [20-22]. β-Glucan has the ability to trigger particular receptors or proteins like Dectin - 1, Toll - like receptors (TLRs), complement receptor 3 (CR3), scavenger receptors (SRs), and lactosylceramide (LacCer). This activation leads to the promotion of cytokine secretion and the activation of other immune cells that play a role in anti - tumor responses[23-26]. Additionally, upon β - glucan's entry into the bloodstream, it attaches to endogenous plasma anti - β - glucan antibodies (ABA). During this attachment process, the complement system gets activated. As a result, the complement protein iC3b binds to ABA, giving rise to the β - glucan–ABA–iC3b complex. This complex is then capable of interacting with immune effector cells, which activates certain aspects of the innate immune function, such as phagocytosis mediated by CR3. The activation and formation of this complex contribute to the direct killing of tumor cells that the antibody targets. [27-28].

Furthermore, β-glucan can induce tumor cell apoptosis to exert its antitumor effects. It activates apoptosis signaling pathways within tumor cells, promoting programmed cell death. Simultaneously, β-glucan can inhibit tumor cell proliferation and metastasis by interfering with tumor cell metabolic processes, influencing the expression of tumor cell adhesion molecules, and reducing the invasive ability of tumor cells, thus preventing their spread in the body. In addition, β-glucan can indirectly exert antitumor effects by enhancing the body's immune function. Activated immune cells can recognize and kill tumor cells.

β-glucan can also regulate the immune cell and cytokine networks in the tumor microenvironment, creating an immune environment that is unfavorable to tumor growth and metastasis. For example, β-glucan inhibits the activity of lectins. The inhibition mechanism involves the internalization of lectins by macrophages induced by the Dectin-1 receptor. In RAW 264.7 macrophages, particulate β-glucan is more efficient at inducing TNFα production than certain water-soluble β-glucans [29]. It sourced from Saccharomyces cerevisiae (BBG) has the capacity to engage with CR3 and TLR2 present on the surface of macrophage - like RAW264.7 cells, consequently triggering the activation of these cells. Once activated, these cells generate substantial quantities of TNF - α and monocyte chemoattractant protein - 1 (MCP - 1). Moreover, research findings indicate that BBG is able to activate nuclear factor kappa B p65 (NF - κB p65), c - Jun N - terminal kinase (JNK), and extracellular signal - regulated kinases (ERK). This strongly illustrates the stimulatory impacts of BBG on RAW264.7 cells[30].

DOI: 10.54254/2753-8818/96/2025.21556

3.2. Effects on Gut Microbiota

β-Glucan possesses prebiotic properties, as it can precisely support the growth and proliferation of beneficial gut bacteria, while effectively suppressing the growth of harmful bacteria. A large number of studies have demonstrated that in the presence of β - glucan, probiotic bacteria like Bifidobacterium and Lactobacillus exhibit enhanced activity in the intestinal tract. As these beneficial bacteria conduct metabolic processes within the gut environment, they generate short - chain fatty acids (SCFAs).

SCFAs play a significant role in gut health. On one hand, they provide energy to intestinal epithelial cells, ensuring their normal function; on the other hand, they assume a vital function in the regulation of the gut immune system and have the capacity to suppress the proliferation of tumor cells. Furthermore, β-glucan can strengthen the intestinal barrier function by regulating the structure and function of the gut microbiota, reducing the irritation and damage caused by harmful substances in the gut, and fundamentally lowering the risk of intestinal tumor development, thus safeguarding gut health comprehensively. Studies have shown that continuous intake of β-glucan for 8 to 12 weeks can increase the concentration of butyrate in feces. Butyrate, a fermentation product of β-glucan and a type of SCFA, is considered an important substance in reducing colon cancer incidence and plays a key role in the prevention and treatment of colon cancer.

3.3. Clinical Applications

In some clinical studies, β-glucan has demonstrated certain immunomodulatory effects and potential antitumor properties. For some early-stage cancer patients, particularly those whose physical condition is not suitable for immediate surgery, radiotherapy, or chemotherapy, the administration of β-glucan supplements has been observed to enhance the activity of immune cells in the body. For example, the phagocytic ability of macrophages is enhanced, and the cytotoxic activity of natural killer (NK) cells against tumor cells is also increased. To some extent, this may help control the growth and spread of tumor cells.

Research indicates that in the treatment of colon cancer, β-glucan possesses unique anticancer effects. On one hand, it stimulates the immune system, enhancing immune cells' ability to recognize and attack tumor cells; on the other hand, it also exhibits direct cytotoxicity. With these dual effects, it can effectively reduce the tumor volume in xenograft models of colon cancer.

Moreover, β-glucan can synergize with chemotherapy drugs and other immune stimulants, further enhancing treatment efficacy. Currently, researchers have proposed an innovative treatment strategy: using β-glucan to precisely deliver chemotherapy drug-loaded nanoparticles to the colon cancer site. This method allows the chemotherapy drugs to be more concentrated in the tumor tissue, increasing the drug's targeting ability and thereby improving the overall treatment outcome for colon cancer, offering new hope for colon cancer patients [31].

4. Conclusion

This study focuses on the mechanism of action of β-glucan in intestinal antitumor effects. By extensively collecting relevant research data from both domestic and international sources and thoroughly analyzing specific research examples, this paper systematically elaborates on the important value of β-glucan in this field. As a natural bioactive polysaccharide with a complex structure and broad sources, β-glucan's unique structure determines its diverse physicochemical properties and biological activities.

The development of intestinal tumors is closely related to various factors, including genetics, environment, physiology, and chronic pathological conditions. Although various treatment methods are currently available, they still have limitations. Regarding the mechanism of action, β-glucan

DOI: 10.54254/2753-8818/96/2025.21556

mainly exerts its intestinal antitumor effects through immune regulation and modulation of the gut microbiota.

In terms of immune regulation, it can bind to specific receptors on the cell surface, activate immune cells, induce cytokine secretion, activate the complement system, directly kill tumor cells, induce tumor cell apoptosis, inhibit tumor cell proliferation and metastasis, and regulate the immune network in the tumor microenvironment. When it comes to modulating gut microbiota, β - glucan shows prebiotic characteristics. It spurs the growth and multiplication of beneficial bacteria and restrains the development of harmful bacteria. Its metabolic products, short-chain fatty acids (SCFAs), not only offer energy to the epithelial cells of the intestine but also participate in immune regulation, inhibit tumor cell growth, enhance the function of the intestinal barrier, and reduce the risk of tumor development.

From a clinical application perspective, β-glucan alone has immunomodulatory effects and potential tumor-suppressive effects on early-stage cancer patients. It can enhance immune cell activity. In colon cancer treatment, it stimulates the immune system, exhibits direct cytotoxicity, and can synergize with chemotherapy drugs and other immune stimulants, further enhancing the therapeutic effect. Additionally, innovative targeted drug delivery strategies have made the treatment of colon cancer more diverse and promising.

References

[1] *Wani S M, Gani A, Mir S A, et al. β-Glucan: A dual regulator of apoptosis and cell proliferation[J]. International journal of biological macromolecules, 2021, 182: 1229-1237.*

[2] *Ding C, Shrestha R, Zhu X, Geller AE, Wu S, Woeste MR, et al. Inducing trained immunity in pro-metastatic macrophages to control tumor metastasis. Nat Immunol. (2023) 24:239–54.*

[3] *Liu N, Zou S, Xie C, Meng Y, Xu X. Effect of the β-glucan from Lentinus edodes on colitis-associated colorectal cancer and gut microbiota. Carbohydr polymers. (2023) 316:121069.*

[4] *da Silva TP, Geraldelli D, Martins KO, Braga AJL, Rosa AP, Ferneda JMA, et al. Antioxidant, anti-inflammatory and beneficial metabolic effects of botryosphaeran [(1→3)(1→6)-β-d-glucan] are responsible for its anti-tumour activity in experimental non-obese and obese rats bearing Walker-256 tumours. Cell Biochem Funct. (2022) 40:213–27.*

[5] *Khan AA, Gani A, Khanday FA, Masoodi FA. Biological and pharmaceutical activities of mushroom β-glucan discussed as a potential functional food ingredient. Bioactive Carbohydrates Dietary Fibre. (2018) 16:1–13.*

[6] *Ahmad A, Kaleem M. β-Glucan as a Food Ingredient[M]//Biopolymers for food design. Academic Press, 2018: 351-381.*

[7] *Bi X, Tong C, Dockendorff A, et al. Genetic deficiency of decorin causes intestinal tumor formation through disruption of intestinal cell maturation[J]. Carcinogenesis, 2008, 29(7): 1435-1440.*

[8] *Aoki S, Iwai A, Kawata K, et al. Oral administration of the β-glucan produced by Aureobasidium pullulans ameliorates development of atherosclerosis in apolipoprotein E deficient mice[J]. Journal of functional foods, 2015, 18: 22-27.*

[9] *Maity P, Sen I K, Maji P K, et al. Structural, immunological, and antioxidant studies of β-glucan from edible mushroom Entoloma lividoalbum[J]. Carbohydrate polymers, 2015, 123: 350-358.*

[10] *Chethan G E, Garkhal J, Sircar S, et al. Immunomodulatory potential of β-glucan as supportive treatment in porcine rotavirus enteritis[J]. Veterinary immunology and immunopathology, 2017, 191: 36-43.*

[11] *Tao M A, Yan T U, Zhang N F, et al. Effects of dietary yeast β-glucan on nutrient digestibility and serum profiles in pre-ruminant Holstein calves[J]. Journal of Integrative Agriculture, 2015, 14(4): 749-757.*

[12] *Jellmayer J A, Ferreira L S, Manente F A, et al. Dectin-1 expression by macrophages and related antifungal mechanisms in a murine model of Sporothrix schenckii sensu stricto systemic infection[J]. Microbial pathogenesis, 2017, 110: 78-84.*

[13] *Tondolo J S M, Ledur P C, Loreto É S, et al. Extraction, characterization and biological activity of a (1, 3)(1, 6)-β-d-glucan from the pathogenic oomycete Pythium insidiosum[J]. Carbohydrate polymers, 2017, 157: 719-727.*

[14] *Han F, Fan H, Yao M, et al. Oral administration of yeast β-glucan ameliorates inflammation and intestinal barrier in dextran sodium sulfate-induced acute colitis[J]. Journal of Functional Foods, 2017, 35: 115-126.*

[15] *Brown G D, Gordon S. Fungal β-glucans and mammalian immunity[J]. Immunity, 2003, 19(3): 311-315.*

[16] *M. McQuade R, Stojanovska V, C. Bornstein J, et al. Colorectal cancer chemotherapy: the evolution of treatment and new approaches[J]. Current medicinal chemistry, 2017, 24(15): 1537-1557.*

DOI: 10.54254/2753-8818/96/2025.21556

[17] Ciardiello D, Vitiello P P, Cardone C, et al. Immunotherapy of colorectal cancer: Challenges for therapeutic efficacy[J]. Cancer treatment reviews, 2019, 76: 22-32.
[18] Hermel D J, Sigal D. The emerging role of checkpoint inhibition in microsatellite stable colorectal cancer[J]. Journal of personalized medicine, 2019, 9(1): 5.
[19] Bohn JA, BeMiller JN. (1→3)-β-d-Glucans as biological response modifiers: a review of structure-functional activity relationships. Carbohydr Polymers. (1995) 28:3–14.
[20] Vetvicka V, Dvorak B, Vetvickova J, Richter J, Krizan J, Sima P, et al. Orally administered marine (1–>3)-beta-D-glucan Phycarine stimulates both humoral and cellular immunity. Int J Biol macromolecules. (2007) 40:291–8.
[21] Song K, Xu L, Zhang W, Cai Y, Jang B, Oh J, et al. Laminarin promotes anti-cancer immunity by the maturation of dendritic cells. Oncotarget. (2017) 8:38554–67.
[22] Lee DH, Kim HW. Innate immunity induced by fungal β-glucans via dectin-1 signaling pathway. Int J medicinal mushrooms. (2014) 16:1–16.
[23] Javmen A, Nemeikaitė-Čėnienė A, Bratchikov M, Grigiškis S, Grigas F, Jonauskienė I, et al. β-glucan from saccharomyces cerevisiae induces IFN-γ Production in vivo in BALB/c mice. In Vivo (Athens Greece). (2015) 29:359–63.
[24] Brown GD, Gordon S. Immune recognition of fungal beta-glucans. Cell Microbiol. (2005) 7:471–9.
[25] Brown GD, Gordon S. Immune recognition. A New receptor beta-glucans. Nature. (2001) 413:36–7.
[26] Noorbakhsh Varnosfaderani SM, Ebrahimzadeh F, Akbari Oryani M, Khalili S, Almasi F, Mosaddeghi Heris R, et al. Potential promising anticancer applications of β-glucans: a review. Bioscience Rep. (2024) 44:BSR20231686.
[27] Bedirli A, Kerem M, Pasaoglu H, et al. Beta-glucan attenuates inflammatory cytokine release and prevents acute lung injury in an experimental model of sepsis[J]. Shock, 2007, 27(4): 397-401.
[28] Chan A S H, Jonas A B, Qiu X, et al. Imprime PGG-mediated anti-cancer immune activation requires immune complex formation[J]. PLoS One, 2016, 11(11): e0165909.
[29] Brown G D, Gordon S. Fungal β-glucans and mammalian immunity[J]. Immunity, 2003, 19(3): 311-315.
[30] Zheng X, Zou S, Xu H, et al. The linear structure of β-glucan from baker's yeast and its activation of macrophage-like RAW264. 7 cells[J]. Carbohydrate polymers, 2016, 148: 61-68.
[31] Chen J, Zhang X D, Jiang Z. The application of fungal beta-glucans for the treatment of colon cancer[J]. Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents), 2013, 13(5): 725-730.