REVIEW ARTICLE

Beta Glucans: The 21st Century's Multifunctional Key to Drug Delivery

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ABSTRACT

β-Glucans are naturally occurring polysaccharides composed of β-D-glucose units, increasingly recognized for their multifunctional roles in human health and industrial biotechnology. Their physicochemical parameters, including molecular weight, branching, solubility, and viscosity, critically determine biological activity, rendering them superior to α-glucans in nutraceutical, pharmaceutical, and cosmeceutical applications. The motivation for this review arises from the need to integrate fragmented knowledge into a unified framework that connects structural attributes with therapeutic and industrial outcomes. This review consolidates evidence from biochemical, biophysical, and molecular studies, emphasizing β-glucan interactions with immune receptors, including Complement Receptor 3, Lactosylceramide, Scavenger Receptors, and Dectin-1, which mediate antifungal defense, immune regulation, and the control of inflammation. The scope further extends to their expanding applications in the food, beverage, healthcare, cosmetics, animal feed, agriculture, vaccine adjuvant, and biotechnology sectors. Importantly, emerging molecular docking studies highlight their ability to function as immune checkpoint modulators, opening novel opportunities in cancer immunotherapy. Key findings highlight β-glucans as versatile, sustainable agents that bridge nutrition, medicine, and industry. The uniqueness of this work lies in its holistic synthesis of structure–function relationships and translational relevance, positioning β-glucans as pivotal 21st-century biomolecules for advancing drug delivery and global innovation.

Keywords: β-Glucans; Polysaccharide; Nutraceutical; Cosmeceuticals; Immune pathway; Receptors

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INTRODUCTION

Glucans are diverse glucose molecules linked by glycosidic bonds, forming ring-shaped structures categorized into two types: Alpha (α-) and Beta (β-). Alpha (α-) Glucans consist of D-glucose molecules connected by alpha-glycosidic bonds. In contrast, beta (β-) Glucans are high molecular weight polysaccharides made of β-D-glucose units, linked through β-glycosidic bonds, and are found in prokaryotes and eukaryotes, including algae, bacteria, mushrooms, cereals, yeast, and fungi. They can differ in length, branching, and solubility. β-Glucans have more nutraceutical significance than α-Glucans[1]. β-Glucans are biologically active molecules with broad therapeutic benefits and expanding commercial applications as immunomodulators, nutraceuticals, cosmeceuticals, and in agriculture. β-Glucans are biologically active molecules with broad therapeutic benefits and expanding commercial applications as immunomodulators, nutraceuticals, cosmeceuticals, and in agriculture. Recent advances in fungal biotechnology, including synthetic biology, CRISPR-based genome editing, AI/ML-driven modeling, and omics integration, are accelerating the discovery of novel metabolites, including β-Glucans and sustainable biomanufacturing applications at the forefront of industrial, medical, and environmental biotechnology[2].

According to the Precedence Statistics report, the global β-Glucans market reached US$501 million in 2023 and is projected to grow to US$734 million by 2028, with a compound annual growth rate (CAGR) of 7.64%. This upward market trend underscores the growing interest in yeast-derived β-Glucans, supporting their potential application in next-generation glucan-enriched therapeutics, including nutraceutical supplements, burn wound dressings, and skin health formulations[1]. Consumer demand for β-Glucans is driven by increasing awareness of their health benefits, including lowering cholesterol, supporting the immune system, and potential anti-cancer properties[3]. Furthermore, molecular docking studies have revealed that β-Glucans exhibit potential as immune checkpoint modulators. β-Glucans exhibited a significantly stronger affinity for PD-L1(binding energy: −9.8 kcal/mol), compared to the standard chemotherapeutic agent 5-fluorouracil (binding energy: −4.3 kcal/mol). This suggests that β-Glucans have the potential to disrupt PD-1/PD-L1

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signaling, potentially restoring T-cell activity and promoting anti-tumor immunity, particularly for melanoma, where immunotherapeutic interventions are urgently needed[4,5]. The physicochemical properties of β-Glucans depend on the bonds and interactions, molecular weight, solubility, and viscosity. β-Glucans are mainly composed of β-D-glucose polysaccharides, although some D-glucose side chains branch off the backbone, are linked to different positions on the main chain, or are attached to proteins[6]. The mechanism of action of β-Glucans also varies depending on their source and structure, but generally involves interactions with the immune system. They activate innate immune pathways through receptors such as CR3 (Complement Receptor 3), LC (Lactosylceramide), SCR (Selected Scavenger Receptors), and bGR (Dectin-1), triggering immune responses that provide health benefits[7].

This review highlights the impact of physicochemical parameters on β-Glucan's behavior, mechanism of action, and applications in various industries, including food, pharmaceuticals, cosmetics, agriculture, biotechnology, and vaccine adjuvants. Therefore, β-Glucans have potential as nutraceuticals, pharmaceuticals, cosmeceuticals, and more, contributing to drug delivery, health and wellness across different fields.

Physicochemical Parameters and their Impact on the β-Glucan’s Behaviour

Various physicochemical parameters like molecular weight, solubility, temperature and thermal stability, pH and ionic strength, viscosity, rheological properties, structure, and their impact on the behavior of β-Glucans are as follows:

Molecular Weight

The molecular weight (Mw) of β-glucans was reported to be in the range of 209–487 × 10^3,65–3100 × 10^3, 31–2700 × 10^3,21–1100 × 10^3 g/mol in the case of wheat, oat, barley, and rye, respectively, which is controlled by the degree of branching, self-association, aggregation, and chain length. It also affects their solubility, viscosity, and pseudo-plastic behavior[8.]

Solubility

β-Glucans are hydrophilic, i.e., Water-soluble dietary fiber, which can store water in both insoluble and soluble forms because of a high concentration of hydroxyl groups in the molecule. β-Glucan’s rheological, nutritional, and sensory applications depend on its solubility profile[9].

Temperature and Thermal Stability

β-Glucans should be stored in airtight storage bottles for several weeks, with stability at ambient conditions, whereas increasing the storage temperature causes their degradation. The thermal stability of β-Glucans is a critical attribute influencing their suitability for high-temperature applications, ensuring product quality, functionality, and nutritional efficacy across various industries[9,10].

pH and Ionic Strength

The optimum pH range for β-Glucans is 5.5–7.0. The pH and ionic strength impact the solubility and stability of β-Glucans. For example, high ionic strength solutions can cause β-Glucans to aggregate, while acidic pH can lead to hydrolysis of β-Glucans[11].

Viscosity

β-Glucans are viscous, soluble dietary fiber components[12,13]. Viscosity is a significant factor in the applicability of β-Glucans as a thickening agent in drinks, dairy products, and salad dressings in the food industry. In contrast, highly viscous β-Glucans may have an antinutritional impact on food preparations.5. β-Glucans with reduced viscosity are required to provide stability against phase separation in beverage products without compromising other sensory characteristics[14].

Rheological Properties

The rheological properties of β-Glucans, together with their elasticity and viscosity, are critical factors determining their functionality, processing suitability, and performance in

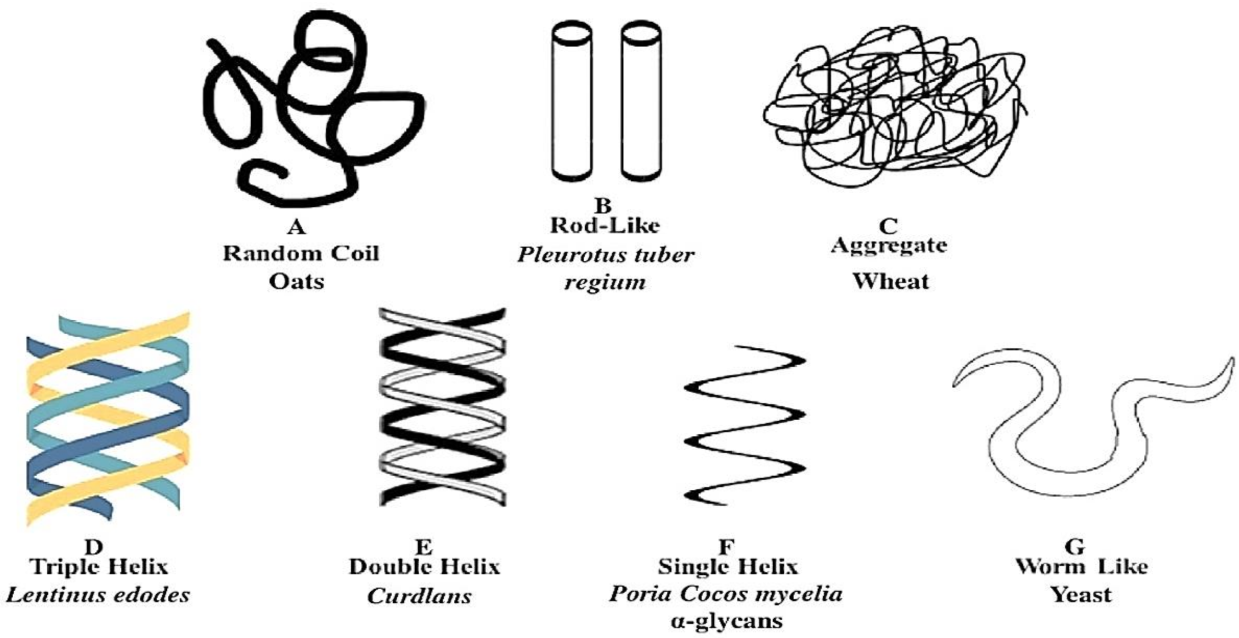

Figure 1: Structural Confirmations of β-Glucans: (A) Random coils (Oat); (B) Rod-like (*Pleurotus tuber regium);* (C) Aggregate (Wheat); (D) Triple helix (*Lentinus edodes*); (E) Double helix (*Curdlans*); (F) Single helix (*Poria Cocos mycelia*); (G) Worm-like (Yeast)

various applications, extending from food products to pharmaceutical formulations[15].

Structure

β-Glucans can reside in various structural conformations like random coils, rod-like shapes, aggregates, helices (single, double, or triple), or worm-like forms, depending on factors such as origin, extraction, and modification processes utilized (Fig.1)[9,16].

Overall, understanding the physicochemical properties of β-Glucans is important for their optimal utilization in various applications, including food, pharmaceuticals, etc.

The structural diversity of β-Glucans is based on factors like molecular weight, glycosidic linkages, degree of branching, and solubility. Most of the β-Glucans from cereals include β-D-(1→3) and β-D-(1→4) glycosidic linkages[17]. The linear β-D-(1→3) backbones of Yeast β-Glucans (for example *Saccharomyces cerevisiae*) are combined with straight chains of 30 residues and are joined by lengthy branches with β-D-(1→6) linkages. β-Glucans from fungi are composed of straight β-D-(1→3) Glucans linked by short-branched chains at the β-D-(1→6) position. β-Glucans from Seaweeds, like those present in *luminaria* and *brown kelp,* are species-dependent and could include the straight chain backbone or straight chain β-D-(1→3) residues together with high levels of β-D-(1→6) branches. β-Glucans from Bacteria, like those from *Agrobacterium biobaris,* show unbranched and straight β-D-(1→3)-Glucans support (Fig. 2)[8,18].

Mechanism of Action of β-Glucans

The mechanism of action of β-Glucans is complex and multifaceted, depending on their source and structure, which involves interactions with the immune system and other biological systems in the body[3]. Here are some of the ways that β-Glucans are thought to work.

Binding to Immune Cells

The binding of β-Glucans to immune cells plays a decisive role in regulating the immune response by initiating immune reactions and encouraging immune cell activities. β-Glucans interact with specific receptors on immune cells, activating immune responses, essential for immune system function[19]. Research studies indicate that β-Glucans can enhance antitumor dendritic cells, increase CD8+ T cells, and promote cytokine production, thereby improving resistance to intestinal inflammation and delaying colorectal cancer development[20]. Furthermore, research on chickens and healthy adult volunteers has demonstrated that β-Glucan supplementation positively impacts immune activity by increasing gene expression related to immunity and enhancing phagocytosis activity in immune cells[21]. Overall, β-Glucans binding to immune cells influences immune responses, stimulating immune cell functions and promoting immune system regulation.

Enhancing Phagocytosis

β-Glucans can improve immune cells' phagocytic activity, such as macrophages, which can better engulf and eliminate invading pathogens, like bacteria or fungi[22].

Modulating Immune Responses

β-Glucans act as a modulator of biological responses by promoting cytokine secretion, maturation of dendritic cells, and regulation of adaptive immune responses through Glucan receptors. Studies conducted on mouse macrophages, fish, and aquatic organisms support the notion that β-Glucans induce a trained immune phenotype in innate immune cells, defending against fungal and bacterial infections by promoting the expression of interferon-β and interleukin-6 and attenuating viral-induced pathological damage[7]. Furthermore, β-Glucans bind to specific receptors on immune cells, stimulating the release of cytokines and chemokines, which consequently activate immunocompetent cells like monocytes, macrophages, and neutrophils, enhancing bactericidal activity, phagocytosis, and cytotoxic killing activities[23]. This modulation of immune responses by β-Glucans is crucial for maintaining immune and metabolic homeostasis, protecting against pathogens, and improving disease resistance in various organisms[24].

Receptors of β-Glucans

Recent studies have concentrated on the intercommunication of β-Glucans with their receptors in the immune system on the cell surface, such as CR3, LC, SCR, and bGR (Fig. 3)[25,26]. These receptors trigger immune cells such as dendritic cells, monocytes, macrophages, natural killer cells, and neutrophils, leading to diverse immune responses upon β-Glucan recognition[25].

CR3 (Complement Receptor 3)

CR3 is a glycoprotein dimer of two subunits: a CD18 beta chain and one of three alpha chains (CD11a, b, or c), which are joined non-covalently. This glycoprotein functions as a transmembrane glycoprotein and a contributor to the beta integrin family. The plasma membrane of phagocytic cells, such as natural killer cells, monocytes, neutrophils, and, to a limited extent, macrophages, contains CR3 protein. CR3 has added significance in β-Glucan-mediated reactions in humans, while in pigs, it plays a fundamental role in β-Glucan signaling in neutrophils[26]. Phagocytosis, cytotoxic responses, and cellular adhesion are three of CR3's primary roles, depending on proteins in a resting or activated state[27].

LC (Lactosylceramide)

LC is a Glycosphingolipid involved in β-Glucans recognition and cellular responses in various cells, including immune cells, participating in cell signaling pathways regulating immune responses.25.This receptor has a variety of roles, including triggering the inflammatory protein MIP-2 in macrophages, activating nuclear factor-kB (NF-kB), reducing neutrophil oxidative stress, and performing some antimicrobial actions. However, the precise mechanism by which these receptors function is not yet known[28,29].

SCR (Selected Scavenger Receptors)

SCRs, also known as Pattern Recognition Receptors (PRRs), are utilized to identify microbes by their distinctive proteins, lipids, and carbohydrates as part of the innate immune system[29]. SCR does not recognize host products. They recognize and bind β-Glucans found on macrophages and dendritic cells and are associated with phagocytosis and clearance of pathogens[30].

bGR (Dectin-1)

β-Glucan Receptor (bGR) is a crucial receptor for β-Glucans, performing a significant role in antifungal innate immunity[31]. It is a type II transmembrane protein which may bind to the β-D-(1→3) and β-D-(1→6) Glucans. Its primary function is to identify yeast and fungal infections. This receptor has an immunoreceptor tyrosine-based activation motif (ITAM) in its tail, performing several roles, such as promoting the release of arachidonic acid, which is crucial for producing some chemicals during acute inflammation. Additionally, it collaborates with toll-like receptor 2 to cause macrophages to respond in a pro-inflammatory manner when mycobacterial infections are present[27].

While β-Glucans may not be absorbed directly into the bloodstream in their full molecular form, they still exert systemic effects through a combination of receptor-mediated immune activation in the gut, cytokine signaling, immune cell migration, and microbiome modulation. These processes enable β-Glucans to influence immune responses and inflammation throughout the body, even though their activity begins primarily in the gastrointestinal tract[23].

Applications of β-Glucans

β-Glucans have broad applications in various sectors due to their inimitable properties and potential health benefits (Table 1) and (Fig. 4).

Beverages and Food

β-Glucans offer versatility in beverages and food applications, providing functional benefits such as texture enhancement, nutritional enrichment, and health promotion. Their inclusion in various food products allows manufacturers to catch consumer demands for healthier and more functional options[32].

Thickening and Stabilizing Agent

β-Glucans are used as a hydrocolloid, which substantially increases the viscosity of a liquid without altering its other properties. β-Glucans modify the food texture, helping as a stabilizing agent in sauces, soups, puddings, ice cream, frozen items, salad dressings, and cheese spreads[33]. It is also a fat alternative in non-fat yogurt production without altering its taste[34].

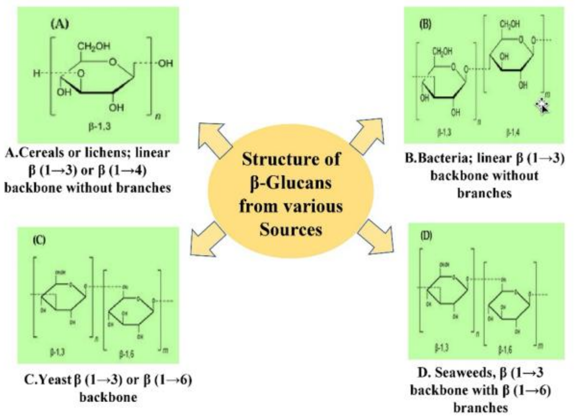

Figure 2: Chemical compositions of β-Glucans: (A) Cereals or Lichens (Linear); (B) Bacteria (Branched); (C) Yeast (Branched); (D) Seaweed (Branched)

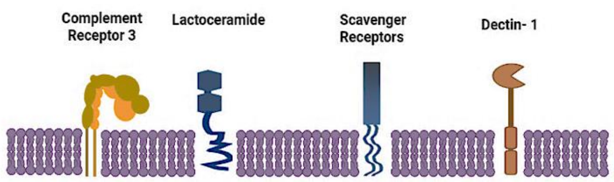

Figure 3: Receptors of β-Glucans: CR3 (Complement Receptor 3); LC (Lactosylceramide); SCR (Selected Scavenger Receptors); bGR (Dectin-1)

Viability Enhancer

β-Glucans are utilized as a texturizer and prebiotic. It enhances probiotic viability and improves the food product's sensory properties and texture through the modulation of volatile organic compounds[35,36].

Pharmaceuticals/Healthcare Applications

β-Glucans have been studied extensively for their potential pharmaceutical applications.

Anti-inflammatory Property

β-Glucans exhibit anti-inflammatory properties by modulating immune responses, potentially dampening excessive inflammation while promoting healing and immune defense without suppressing inflammation[37]. In male Sprague-Dawley rats, eight weeks old, oral administration of β-Glucans derived from fungi reported the anti-inflammatory action by inhibiting the production of interleukin 1β, i.e., pro-inflammatory cytokines, stimulating distinct immune receptors (like Dectin-1) on macrophages, dendritic cells, and other immune cells. This activation leads to a balanced immune response, enhancing immune surveillance, supporting wound healing, and modulating production of pro- and anti-inflammatory cytokines, such as IL-1, IL-6, and TNF-α. Its anti-inflammatory properties are also important to prevent and treat neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease[38,39].

Anti-cancer Property

β-Glucans are well-known natural immunomodulators with considerable anti-cancer characteristics, including an anti-tumor property. It can stimulate the immune system and enhance its activity against invading pathogens and cancer cells. β-Glucans interact with glucan receptors and either directly stop the growth of cancer cells or trigger natural killer or neutrophil cells to attack and destroy cancer cells. In humans, they can stimulate the growth of peripheral blood mononuclear cells and speed up the functional maturation of dendritic cells produced from monocytes by significantly increasing IL-10 and IL-12 production[40,41]. The β-D-(1→3) Glucans improved the mice's immune activity by reducing the tumor progression in S180 and decreasing the ratio of $CD4^+/CD8^+$ T cells in tumor-bearing mice[42].

Anti-infectious Properties

β-Glucans have been demonstrated for their antimicrobial properties by improving resistance against infections primarily by activating the immune system's phagocytic cells, like neutrophils and macrophages. It participates actively through phagocytosis[43]. It is observed to exhibit antiviral, antibacterial, and antifungal properties.

Antiviral Properties

β-Glucans can defend against numerous viral infections by modifying immune reactions. They may also have a role in reducing COVID-19-related morbidity and death globally[44]. It can minimize the frequency of flu-like illnesses in children and diminish the frequency of lower respiratory tract infections.

β-Glucans obtained from various bioactive compounds like ganodermadiol, ganodermic acid, and lucidol have been isolated from mushroom fruiting bodies responsible for medicinal properties and shown activity against herpes, influenza, and HIV[45].

β-Glucans from schizophyllan, lentinan, and zymosan also show antiviral effects. Lentinan also has inhibitory effects against measles, mumps, polio, rotavirus, viral encephalitis, and herpes simplex virus (HSV). β-Glucans administration exhibited a considerable growth in the helper T cells[38].

Antibacterial Properties

β-Glucans are observed to prevent or reduce bacterial infection against the gram-positive bacteria *Staphylococcus aureus*[46] Lentinan β-Glucans were found to have a repressive effect on tuberculosis growth through macrophage stimulation. Diverse fish species showed increased resistance to pathogenic *Aeromonas* and *Vibrio* bacteria when β-Glucans were added to their diet[38].

Antifungal Properties

β-Glucans are also reported to have powerful antifungal properties. Widespread use of antibiotic therapy may lead to opportunistic microscopic fungal infections. It has been reported that β-Glucans from edible mushrooms prevent the growth of microscopic fungi from the genera *Mycosphaerella, Fusarium,* and *Physalospora* by promoting cell phagocytosis. It improves the host immune system's non-specific cellular response against fungal infections[47]. β-Glucans found in macrofungi also protect against mycoses. Toll-like receptors on phagocytic cells and the Dectin-1 receptor of immune cells are also important for preventing fungal infections[48,49].

Anti-coagulant Property

The sulfated β-Glucans have been reported for their anticoagulant properties, possibly developed from the sulfated polysaccharide OCSH4 extracted from the green alga *Cladophora oligoclada*. The location of the sulfate groups was the key determinant of the anticoagulant action. The β-Glucan's anticoagulant effect was estimated at around 1/10 of heparin, a natural anticoagulant, suitable as a potential heparin alternative. Experimental evidence indicated that *in vivo* and *in vitro* studies on Male Sprague–Dawley rats involved partial thromboplastin time (APTT), activated thrombin time, and fibrinogen levels. The signal for clotting time was at 15 mg/kg *in vivo* and more than 200s at 100 µg/mL *in vitro*[50,51].

Anti-cholesterol Property

β-Glucans have cholesterol-lowering ability. Many individual randomized-controlled trials in mice and subsequent meta-analyses of consumption of enough oat products could reduce host cholesterol, consequently modifying the risk of cardiovascular disease[52]. Oat β-Glucans alter the gut microbiota and specifically influence bacterial species, affecting the host's bile acid metabolism and the synthesis of short-chain fatty acids[53].

Cholesterol-regulating mechanisms of β-Glucans involve Reverse Cholesterol Transport (RCT) and Trans-Intestinal Cholesterol Excretion (TICE). In the RCT, cholesterol is directly transferred from the tissues to the liver and excreted into the bile and feces. β-Glucans' ability to serve as dietary fiber and elevate the food viscosity in the small intestine are additional factors contributing to their hypocholesterolemic effect. It also influences the structure, composition, and production of micelles. Elevated intestinal lumen viscosity decreases cholesterol, bile acid binding, and fat absorption, and increases their excretion in the feces. A decrease in the concentration of bile acids leads the body to utilize more stored cholesterol for bile acid production in the liver. Additionally, the bile acid synthesis is facilitated by an increase in 7α-hydroxylase activity to compensate for lowered bile acid levels. Subsequently, the liver cholesterol level and blood LDL cholesterol concentration decrease[54,55].

Radioprotective Property

β-Glucans also exhibit radioprotective properties. Its immunostimulatory action boosts the immune system, which could help patients recover more quickly from radiation therapy. It was observed that the leukocyte and lymphocyte counts were increased in female mice after receiving a single dose of β-Glucans. Furthermore, β-Glucan's enhanced immunological activity leads to increased natural killer cell activity, which helps prevent radiation-related secondary infections[56,57].

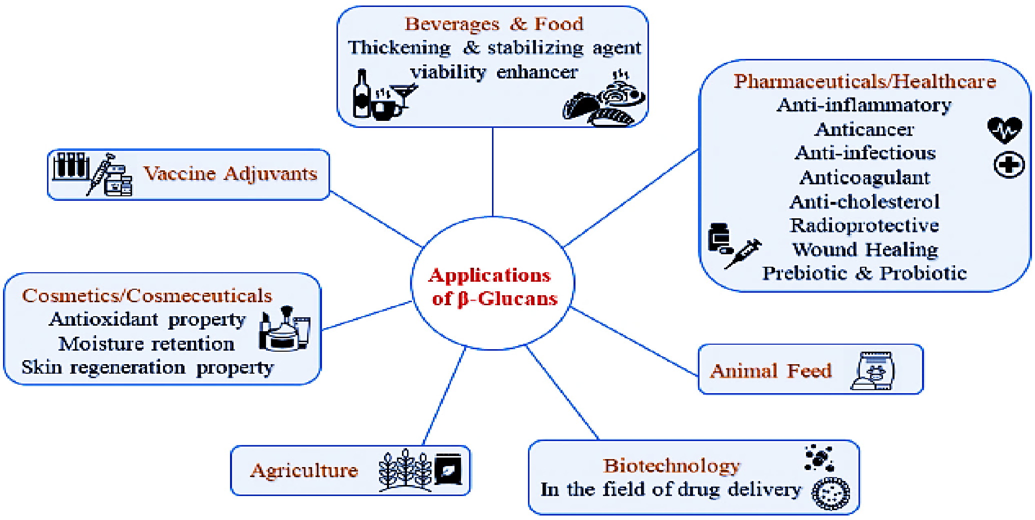

Figure 4: Applications of β-Glucans

Table 1: Applications and role of β-Glucans

S. No.	Applications	Role /Mechanism of β-Glucans	References
1	Beverages and Food		
1.1	Thickening and stabilizing agent	β-Glucans are used as a hydrocolloid, which substantially increases the viscosity of a liquid without changing its other properties, modifies the food texture, and acts as a stabilizing agent in various food products. It is also a fat substitute in non-fat yogurt without altering its taste.	33,34
1.2	Viability enhancer	β-Glucans are utilized as a texturizer and prebiotic that enhances probiotic viability and improves the sensory properties and texture of food products through the modulation of volatile organic compounds.	35,36
2	Pharmaceuticals/Healthcare applications		
2.1	Anti-inflammatory Property	There are two suggested mechanisms. 1. Inhibiting the production of interleukin 1β, pro-inflammatory cytokines. 2. β-Glucans modulate immune responses, promoting healing and immune defense without suppressing inflammation.	37,61
2.2	Anti-Cancer / Anti-Tumor Property	β-Glucans can stimulate the immune system after interacting with glucan receptors, stopping the growth of cancer cells or triggering natural killer or neutrophil cells to attack and destroy cancer cells.	40,41
2.3	Anti-infectious properties		
2.3.1	Antiviral Properties	β-Glucans administration exhibited a considerable rise in the concentration of helper T cells (Th).	38
2.3.2	Antibacterial Properties	β-Glucans have a preventive effect against bacteria through macrophage stimulation.	46
2.3.3	Antifungal Properties	β-Glucans promote cell phagocytosis, which improves the host immune system's non-specific cellular response against fungal infections.	48
2.4	Anti-coagulant property	The sulfated β-Glucans were reported for their anticoagulant action by activated thrombin time, partial thromboplastin time (APTT), and fibrinogen level.	50
2.5	Anti-cholesterol property	Cholesterol-regulating mechanisms of β-Glucans involve Reverse Cholesterol Transport (RCT) and Trans-Intestinal Cholesterol Excretion (TICE).	54,55
2.6	Radioprotective property	β-Glucan's enhanced immunological activity leads to increased natural killer cell activity, which helps prevent radiation-related secondary infections.	56,57
2.7	Wound healing property	β-Glucans promote macrophage infiltration for re-epithelialization, collagen deposition, tissue granulation, and defense against wound proteases.	58
2.8	Prebiotic and probiotic properties	β-Glucans have the potential to promote the growth of health-beneficial probiotic microorganisms and inhibit the development of pathogenic microorganisms.	40,62,63
3	Cosmetics/Cosmeceutical applications		
3.1	Antioxidant property	β-Glucans decrease lipid oxidation and lower lipid levels, due to their chelating properties, neutralize free radicals, and induce a respiratory burst that causes the creation of Reactive Oxygen Species (ROS).	68
3.2	Moisture retention and Skin regeneration property	β-Glucans enhance skin moisture retention through their film-forming properties, hydrophilic nature, skin repair, and regeneration. Furthermore, support anti-inflammatory and antioxidant effects, and immune modulation.	70
4	Animal feed	β-Glucans improve the growth performance of animals by increasing animal productivity regarding daily feed and body weight gain conversion ratio while lowering mortality.	32,72
5	Agriculture	β-Glucans lead to the accumulation of various antioxidant defense enzymes, reactive oxygen species (ROS), Ca^{2+}-influx, pathogenesis-related proteins (PR-proteins), as well as the mitogen-activated protein kinase (MAPK) pathway that aids the plant in developing adaptations to counteract climate change and maintain sustainability.	75,77
6	Biotechnology/ In the field of drug delivery		
6.1	Encapsulation within gels	The β-D-(1→3) Glucans are frequently utilized to create gels in curdlan to encapsulate drugs, including indomethacin, prednisolone, and salbutamol sulfate, in the presence of hydrogen bond disruptors such as urea, thiocyanates, and dimethyl sulfoxide.	81
6.2	Microparticles	β-Glucans microspheres can deliver Proteins, DNA, siRNA, and other types of payloads, including Immune cells like macrophages and dendritic cells.	80

Table 1: Applications and role of β-Glucans

S. No.	Applications	Role /Mechanism of β-Glucans	References
6.3	Nanoparticles	β-Glucans from Carboxymethyl curdlan (CM-curdlan) are used by silver nanoparticles to lower nitrate. Natural hyperbranched β-Glucans (Se-HBP) strongly absorb hydroxyl groups from the selenium surface, stabilizing water-dispersible selenium nanoparticles due to HBP ligation.	82
7	Vaccine adjuvants	β-Glucans are used as vaccine adjuvants because they can activate various immunological pathways to form antibodies and improve the immunogenicity of vaccinations against coccidioidomycosis, influenza, hepatitis B, and systemic aspergillosis.	83,85

Wound Healing Property

β-Glucans promote wound healing through macrophage infiltration, promoting re-epithelialization, collagen deposition, tissue granulation, and defense against wound proteases. Wild-type mice (C57BL/6) were punched in their lumbar skin and treated with barley β-Glucans solution for two weeks, resulting in improved wound healing[58]. A β-Glucans dressing could be an appropriate wound-healing solution[59,60].

Prebiotic and Probiotic Properties

β-Glucans have prebiotic properties, showing a valuable impact on the microflora of the gastrointestinal tract by stimulating the growth and activity of the desired natural intestinal microbiota and inhibiting the growth of pathogens. It helps the proper functioning of the gastrointestinal tract by preventing inflammation and colon cancer. Colon microflora ferments soluble β-Glucans from grain sources, leading to many valuable health benefits by increasing short-chain fatty acids (SCFA) production[40] Another study suggests that β-Glucans derived from barley are potential prebiotic resources in baked food and beer manufacturing[33,61].

Supplementing with oat β-Glucans reduces the activation of pattern recognition receptors (PRRs) and the infiltration of monocyte-derived macrophages. It also alters the composition of the intestinal microbiota by encouraging protective bacterial species to lower the translocation of TLR4 ligands. Additionally, it supports the growth of health-promoting probiotic microorganisms and inhibits the development of pathogenic microbes[62,63].

Cosmetics/Cosmeceutical Applications

β-Glucans are utilized in the cosmetics industry due to their film-forming, moisturizing, and anti-aging properties. Skin's Langerhans cells slow down with age. β-Glucans help to stimulate the Langerhans cells and repair damage from environmental trauma after sun exposure. They thoroughly penetrate the skin's epidermis and dermis, improving skin hydration and reducing fine age lines and wrinkles, acne, cellulite, crow's feet, dermatitis, eczema, psoriasis, and other skin disorders, resulting in an overall improvement in skin texture, with a revitalizing effect that helps to maintain healthy skin. It also boosts collagen formation after utilising it in all-purpose protective lotions, ointments, powders, and suspensions[49,64,65].

Antioxidant Property

β-Glucans have better antioxidant activity than several synthetic polymers, usually used in cosmetics[40,66]. Their antioxidant activity depends on their structure and molecular size, which depends on the sources and extraction techniques[38,67].

β-Glucans extracted from *Pleurotus-genus* fungi have antioxidant actions like reducing, transition metal chelating, and free radical scavenging properties for iron ions and potent reducing activities against the superoxide anion radical and the radical 2, 2-diphenyl-1-picrylhydrazyl (DPPH). β-Glucan's chelating abilities decrease lipid oxidation and considerably lower lipid levels. Malondialdehyde, a marker of the lipid peroxidation process, was produced in laboratory animal liver cells after the administration of β-Glucans. They can neutralize free radicals and a respiratory burst that causes the creation of reactive oxygen species[68].

Moisture Retention and Skin Regeneration Property

β-Glucans protect against reduced skin humidity. It was reported that β-Glucans application improved the skin moisture content remarkably by 5-6%[64,69].

β-Glucans have active involvement in collagen-producing cell regeneration and revitalizing the immune cells. It enhances skin texture by promoting anti-wrinkle and anti-aging, skin moisture retention, hydrophilic nature, skin repair, regeneration support, anti-inflammatory and antioxidant effects, and immune modulation. It has an anti-ultraviolet effect[69] and is used in the treatment of burn injuries[41]. Those combined actions increase skin hydration and boost a healthier skin barrier[70]. The dorsal side of mice was injured using a 5-mm biopsy punch, and wounds were treated with β-Glucans-based hydrogel for 2 weeks. β-Glucans were responsible for fighting infections at the wound site and promoting the migration and proliferation of fibroblasts and keratinocytes. They were prepared as a three-dimensional hydrogel membrane with high water content, providing a soothing and cooling effect that reduced pain, and were analyzed for their cutaneous wound healing mechanism[71].

Animal Feed

β-Glucans are served as a dietary supplement in animal feed to improve the growth performance of animals. It increases animal productivity, concerning the daily feed and body weight gain conversion ratio, while lowering mortality. It also reduces the need for antibiotics in the animal population by reducing bacterial infections, improving gut health, boosting antibody titers after immunization, and enhancing their immune system. It has shown encouraging results as a potential anticancer drug for livestock. β-Glucans pellets fed to rainbow trout (*Oncorhynchus mykiss*) at a dose of 0.5 g/100 g of pellets (0.5%) per day increased the number of cells that secrete a certain type of antibody and a particular type of Ig in serum[32,72,73]. β-Glucans dietary supplementation improved carcass length, nutrient digestibility, growth performance, and pork quality of finishing pigs[74].

Agriculture

β-Glucans can activate the functional plant innate immune system by initiating one or more downward signaling cascades in plants. The barley β-Glucans respond to a non-adapted isolate of the *Blumeria graminis* f. sp. *tritici* by accumulation of various antioxidant defense enzymes, ROS, Ca^{2+}-influx, pathogenesis-related proteins (PR-proteins), as well as the mitogen-activated protein kinase (MAPK) pathway that aids the plant in developing adaptations to counteract climate change and maintain sustainability[75-77].

Biotechnology/ In the Field of Drug Delivery

β-Glucans have potential applications in the biotechnology industry for biomaterials and drug delivery systems development. They can act as scaffolds for tissue engineering and carriers for drugs and other therapeutic molecules. It can encapsulate various compounds by utilizing several polysaccharides[78,79]. The β-Glucans are useful for drug delivery as complexes, gels, microparticles, or nanoparticles.

Encapsulation within Gels

The β-D-(1→3) Glucans are frequently used to create curdlan gels. In curdlan gels, drugs like indomethacin, prednisolone, and salbutamol sulfate have been encapsulated. The creation of protein delivery systems also utilizes curdlan gels, which can produce aqueous gels in the presence of hydrogen bond disruptors such as urea, thiocyanates, and dimethyl sulfoxide[80]. *Pleurotus ostreatus* extracts can also serve as an innovative emulsifier for physical protection against oxygen-sensitive lipophilic functional ingredients by microencapsulation[81].

Microparticles

β-Glucans microspheres, which range in size from 2-4 µm, are porous, hollow microparticles derived from the cell walls of *Saccharomyces cerevisiae* (Baker's yeast). They mostly contain β-D-(1→3) Glucans and very little chitin. Immune cells such as macrophages and dendritic cells can take up the microspheres' β-Glucans and have a specific target. β-Glucan microspheres can deliver proteins, DNA, siRNA, and other types of payloads[80].

Nanoparticles

β-Glucans have been employed in nanoparticle synthesis as a stabilizing and reducing agent for drug delivery. They can be used for photothermal cancer therapy using their surface interactions with gold nanorods. β-D-(1→3) and β-D-(1→6) Glucans were isolated from the edible Pleurotus florida mushroom and used to prepare and stabilize gold nanoparticles, thereby decreasing the toxicity of chloroauric acid.

Carboxymethyl curdlan (CM-curdlan) is used by silver nanoparticles to lower nitrate. These silver nanoparticles were stable and similar in dimensions to those produced using the traditional method. Natural hyperbranched β-Glucans (Se-HBP) strongly absorb hydroxyl groups from the selenium surface, stabilizing water-dispersible selenium nanoparticles. Se-HBP's increased water stability for a minimum of 30 days was observed because of the HBP ligation[82].

Vaccine Adjuvants

β-Glucans can function as vaccine adjuvants. Oral β-Glucans with β-D-(1→3) and β-D-(1→6) bonds are used as vaccine adjuvants because they can activate several immunological pathways to form antibodies and improve the immunogenicity of vaccines against coccidioidomycosis, influenza, hepatitis B, SARS-CoV-2, and systemic aspergillosis[83,84].

Overall, β-Glucans have diverse applications, and their unique properties make them an attractive and promising ingredient in various industries.

CONCLUSION

β-Glucans are naturally occurring molecules with significant therapeutic potential, particularly as metabolic and immune modulators. Many clinical trials of β-Glucans reflect the enthusiasm for their therapeutic potential as well as applications in other fields.

Understanding the Physicochemical parameters and their impact on the behavior of β-Glucans in eukaryotes is important for developing strategies to manipulate β-Glucans for numerous applications, including the development of new drugs and biomaterials, and products for multiple industries, together with food, pharmaceuticals, agriculture, biotechnology, and cosmetics. As not much information is available on it, the domain is open for exploration, integrating physicochemical parameters, mechanism of action studies, and receptor identification. Artificial intelligence (AI) and omics technologies provide a comprehensive framework for understanding the complex interactions between β-Glucans and eukaryotic systems. This interdisciplinary approach has the potential to drive innovation in healthcare, cosmetics, biotechnology, and other domains, leading to the development of diagnostics and novel therapies for a wide range of diseases.

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