

Review Article

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## Beta-Glucans as a therapeutic agent: Literature Review

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### Article Info

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### Abstract

Functional foods have been used due to benefits promoted for patient's health. There are several types of functional foods. Thus, the prebiotics being a class used because of the health effects promoted on gastrointestinal tract. Among the prebiotic, beta-glucans (BG's) is highlighted due to the activity in modulation of host immune response. However, besides to modulating the immune response, BG's may exert effects on metabolic parameters such as glycaemia and cholesterolemia. Such effects occur due to the formation of a gelatinous layer in the intestine, which impairs the absorption of glucose and lipids. Thus, many studies have investigated the effects of BG consumption in patients with diabetes *mellitus* or hypercholesterolemia. According to literature, the use of these prebiotics in glycemic and lipid metabolism control was shown to be effective mainly in diabetic patients. Such results show that beyond to the known immunomodulatory effects of BG's, exist a metabolic effect that is beneficial in prevention and may be adjuvant in the treatment of metabolic diseases.

**Keywords:** Beta-glucan; Prebiotic; Metabolism; Immune response; Functional foods.

### Introduction

Functional foods can be considered as enriched, fortified or improved foods with one or more components that promote health benefits within a basic nutrition [1]. Because of this, such foods have been used due to their effects on disease prevention and health maintenance [2].

Among the types of functional foods are highlighted omega-3 fortified eggs, meats with reformulated fatty acid profile, cereals, functional beverages, probiotics and prebiotics [1]. Considering these last two classes of functional foods, there is great interest in their use due to the benefits provided to the gastrointestinal tract, such as the balance of the microbiota, immunomodulation, increased bioavailability of minerals, among others factors [3].

Among the main classes of prebiotics are galacto-oligosaccharides (GOS), fructooligosaccharides (FOS), insulin and beta-glucans (BG) [4]. BG's have been widely investigated due to their immunomodulatory activity [4], as well as to the activity on the metabolism of carbohydrates and lipids [5]. In this sense, we aimed to present the functional effects of BGs on the immune response and metabolism.

### Probiotics

Probiotics can be defined as microorganisms, mainly non-pathological bacteria, which are safe for consumption and which promoted beneficial effects on host's health when ingested in sufficient quantities [6]. Besides, the term probiotic, according to its Greek origin, means "in favor of life" [7].

According to Schrezenmeir and de Vrese [8], the effects of probiotics on health maintenance include: a decrease in the frequency and duration of diarrhea, the stimulation

of humoral and cellular immunity, and the reduction of undesirable metabolites in the colon (such as ammonia and pro-carcinogenic enzymes). In addition to these effects, the consumption of probiotics is related to reduction of infection by *Helicobacter pylori*, decrease of allergy symptoms, benefits on mineral metabolism, cancer prevention, intestinal constipation relief, cholesterol reduction and plasma triacylglycerol [8].

Among the action mechanisms of probiotics, we can highlight the pH decrease, as well as hydrogen sulfide production and increase of antimicrobial peptides in the lumen that occurs due to the metabolism of probiotic bacteria [9]. These effects create an unfavorable environment for the maintenance of pathogens [9,10]. In addition, probiotics can improve the intestinal barrier through modulation in the cytoskeleton that enhances cell interaction and stability [9]. The maintenance of the intestinal barrier preserves the epithelial cells that support the intestinal health, being observed that the rupture of this barrier favors the establishment of pathogens [10].

With respect to the immunomodulatory effects of probiotics, a possible mechanism is the stimulation of Immunoglobulin A (IgA) and relief of inflammatory responses in the intestine [11]. Besides that, some probiotics are able to interact with immune cells, or their receptors, promoting increased phagocytic activity, increasing intraepithelial lymphocyte proliferation, and modulation of Th1 and Th2 responses [6].

Thus, considering the importance of probiotics for health, studies have investigated the effects of the consumption of these microorganisms concomitantly with their energy substrates [12,13]. These substrates are called prebiotics, and are defined as non-digestible food ingredients that cause health improvement through stimulation in the growth or activity of the microbiota in the gastrointestinal tract [13].

## Prebiotics

Another definition for prebiotic includes it as a selectively fermentable ingredient that promotes specific changes in composition and activity of the intestinal microbiota and promotes benefits to the health's host [14]. The combination of probiotics and prebiotics in a commercial product, in order to promote beneficial effects to host by improving the microbiota of the gastrointestinal tract, is defined as symbiotic [15].

The consumption of prebiotics alone has shown beneficial effects on health [16,17]. Such effects include a decrease in the prevalence and duration of infectious agents and antibiotic-associated diarrhea; improvement of the bioavailability and absorption of minerals (calcium, magnesium and possibly iron); reduction of inflammation and symptoms associated with inflammatory bowel disease as well as colon cancer; besides weight loss and prevention of obesity due satiety promoting [16].

In addition, some oligosaccharides and polysaccharides promote prebiotic activity [14]. Among them, it highlighted fruit-oligosaccharides (FOS), galacto-oligosaccharides (GOS), insulin, pyrodextrins and glucans [18,19]. Glucans are the major structural components of the cell wall of fungi, grass

and some bacteria [20]. Among the glucans, beta-glucans (BG) have been highlighted as prebiotics used as modulators both of the immune response [21], as well as lipid and carbohydrate metabolism [5].

## Beta-Glucans (BG)

BG's are non-starch polysaccharides found in cell wall structure of fungi, mushrooms and yeasts [22]. Some cereals such as oats, rye and barley [23], as well as bacteria [24] also have BG in their structure. These compounds promote benefits on metabolic and immunological parameters and such actions have been demonstrated in chronic diseases such as diabetes *mellitus* [22,25], dyslipidemias [26] and infections [27,28].

The chemical structure of the BG contains a central linear bond of  $\beta$ -type (1-3), formed by units of glucose connected in the main chain, that differ according to their length and ramifications [29]. The BG's isolated from grasses have a linear structure and presents branching with  $\beta$ -bonds (1-4), and those from fungi and yeasts have  $\beta$ -bonds (1-6), which confer different biological actions of these polysaccharides [22].

The peculiarity of the actions of each type of BG varies with its conformation, molecular mass, solubility and the degree of positioning of its branches [30]. BG's with lower branching and lower polymerization (such BG's from plants with  $\beta$  (1-4) binding) are characterized as soluble, whereas insoluble ones such as BG's isolated from fungi with type bonds  $\beta$  (1-6), have higher polymerization and greater number of branches [30].

Low-weight BG's are usually inactive, while those of intermediate weight have biological actions *in vivo*, and their efficacy is low at cellular levels [27]. On the other hand, those BG with high molecular weight can activate leukocytes directly, stimulating their phagocytic, cytotoxic and antimicrobial activity [27].

The chemical structure of BG's isolated from oats presents a linear structure formed by glucose units communicated by  $\beta$  (1-3) and  $\beta$  (1-4) bonds, having short branches. The  $\beta$  (1-4) bonds correspond to 70% of the glycosidic bonds, and appear in sequence of two or three glucose units interrupted by a  $\beta$  (1-3) [31].

BGs from oats have beneficial characteristics in metabolic parameters, such as cholesterol reduction and plasma triglycerides, and possibly act in the prevention and treatment of diabetes *mellitus* by lowering glycemic levels [32]. However, studies investigate the effects of these prebiotics on the immune response [21,33,34]. Such activity is observed in both innate and adaptive immunity, benefiting the anticarcinogenic action [21,33], besides presenting chemopreventive action [33].

As a consequence of its immunomodulatory effect, oats BG supports in the prevention of bacterial infections such as *Candida albicans*, as well as from protozoa such as *Toxoplasma gondii* [35] and resistant bacteria [4,36]. In addition, BG favors phagocytosis and the production of proinflammatory cytokines by macrophages stimulating neutrophils and monocytes, thus leading to an improvement in the immune response [37].

However, the effects of BGs exceed immunomodulatory parameters, and several studies have also demonstrated their efficacy in metabolic functions, such as hypocholesterolemic and hypoglycemic effect [33,38-40].

Lo et al. [40] demonstrated that BGs from oat and fungus reduce glycaemia when consumed orally. The mechanisms that explain this effect are related to the formation of a gelatinous layer that acts as a barrier that hinders the absorption of glucose and lipids [39], decreasing glycaemia and cholesterolemia in humans and animals [26,41-43].

This gelatinous layer promotes an increase in the viscosity of the contents formed in the intestinal lumen, acting as a sieve that filters small molecules and slowing the digestion and absorption of some nutrients and the large molecules are not filtered and pass directly through the intestine [39]. There is also the hypothesis that this gelatinous layer delays the interaction of starch and its digestive enzyme causing the reduction in absorption of carbohydrates and consequently the reduction of glycaemia [44].

The effect of this selection causes a decrease in glucose uptake by enterocytes [45], decreasing blood glucose concentration [39] and increasing insulin sensitivity. Such effects may aid in treatment of metabolic disorders such as diabetes, as well as other diseases associated with these illnesses [46]. In addition, studies suggest that this viscosity formed by the BGs reduces the levels of total cholesterol, low density lipoprotein (LDL-C) and triacylglycerol, increasing the rate of high density lipoproteins (HDL-C), justifying the prevention of cardiovascular diseases [42,47,48]. Additionally, the formation of the gelatinous layer induces a sensation of satiety caused by delayed gastric emptying reducing the need for more food intake and altering energy consumption, thus causing weight loss [42,49,50].

Apparently, BG doses below 3.0 g/patient/day are not efficient in improve glycemic control in diabetic patients [42,51,52]. However, BG doses above 6.0 g/patient/day reduced glycaemia and insulin concentration in the study of Tappy et al. [41].

Regarding the lipid profile was observed that doses between 3.0 and 6.0 g/patient/day reduced serum concentrations of triglycerides, total cholesterol [42,53,54] and LDL-C [42,53]. The mechanism involved in this alteration may be associated with decreased cholesterol uptake and bile acid reabsorption in the gut. Thus, the reduction of these substances in enterohepatic circulation leads to an increase in the conversion of cholesterol to bile acids [55].

It has been reported that BG inhibits *in vitro* the uptake of long chain fatty acids into the intestinal tissue when these lipids are in high concentration [56]. Furthermore, these fibers reduced the risk of cardiovascular and metabolic diseases by mediating the inflammatory process [57,58]. The hypotheses for these mechanisms demonstrate that BG's decreases oxidation of glucose and lipids by promoting a healthy intestinal environment; preventing inflammation by altering the adipocytokines of adipose tissue and increasing the hepatic whole circulation of lipids and lipophilic compounds

[59]. Thus, these mechanisms demonstrate the inverse association between fiber intake and levels of inflammatory biomarkers in diabetic, hypertensive and obese patients [59,60]. These particularities in the action of BG's arise from their physicochemical properties (molecular weight and solubility), their predisposition to water retention, viscosity, emulsification, fermentability, and resistance to degradation by intestinal bacteria and their propensity to absorb nutrients [52].

Regarding their toxicity, when orally administered during four weeks, BGs showed no signs of toxicity, nor when administered in large quantities [61,62].

## Conclusions

A large part of the studies presented exemplify the beneficial effects of BG's on both immunological and metabolic parameters. In this way, the use of these prebiotics can be made, within the safe limits, especially in order to maintain glycemic and lipid profile within normality, besides attenuating inflammatory and infectious symptoms.

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