Chapter 16

Yeasts as Potential Source for Prebiotic β-Glucan: Role in Human Nutrition and Health

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Abstract

Yeasts are a potential source for prebiotic β-glucans. This polysaccharide is characterized by D-glucose monomers linked by β-glycosidic bonds. There are significant structural differences in β-glucans depending on the source and method in which they are obtaining. This polymer is a healthier food and feed additive. Numerous beneficial effects have been attributed to this polymer, in particular immunomodulatory action. Different studies confirm safe use and applicability of β-glucans in medicine for the treatment of diseases (cancer, infections, respiratory diseases) and reduction in glucose and cholesterol levels. Many advances in the processes to obtain β-glucans have been presented, including extraction, purification, and chemical modification, aiming the biological properties and yield. One limitation of their use is the cost, so a strategic discussion of the use of yeast biomass was performed for the production of β-glucans. An extensive and systematic review was undertaken to contribute to the science and technology to obtain β-glucans and their use in different applications.

Keywords: β-glucans, chemical properties, extraction, purification, immunostimulating properties

1. Introduction

One of the important biopolymers present in some cereals and fungi is the β-glucan. This polysaccharide plays an important role in the immune system, skin protection, among others. In addition to their cholesterol-lowering and potential cancer-preventing properties, β-glucans may be useful in controlling blood glucose levels. The β-D-glucans from yeast and some plants have been shown to have antitumor and antibacterial activity when injected or ingested by animals in experimentation [1–7].

Cereal grains, such as barley, oats, and rye, and fungi, such as *Aspergillus*, *Saccharomyces*, and *mushrooms*, contain β-D-glucans [8, 9]. The concentration of β-glucan in oats ranges from 1.9 to 8.0% [10, 11]. In barley grains, these values can reach 3.5–4.8% [12]. These variations are associated with genotype of grain and location and the environmental conditions in which the culture was grown and may result in variation in the quality of β-glucan. This problem is reduced if the source is from microorganisms, which are cultured in defined conditions, and they are not dependent from the location or the environmental conditions.

2. Chemical structure of β-glucans

Glucans are glucose polymers, classified according to their interchain linkage as being either α- or β-linked. β-glucans are a heterogeneous group of non-starch polysaccharides, consisting of D-glucose monomers linked by β-glycosidic bonds [13]. The central skeleton of the β-glucans is formed by linear monomers of D-glucose connected at position β-(1-3), with side chains attached to β-(1-6) or β-(1-4)-D-glucopyranosyl unit linkage (**Figure 1**). In yeast, the skeleton is branching at β-(1-6) and in plants and bacteria at β-(1-4) unit linkage [14–16]. In mushrooms, molecules with binding β-(1-6) and others with connections β-(1-6) and β-(1-4), whether or not linked to protein, were reported [17]. Significant structural differences in β-glucans are characterized by the glycosidic linkage ratios depending on both the source and method of isolation. In the cereal β-glucans, for example, the trisaccharide-to-tetrasaccharide ratios follow the order of wheat (4.2–4.5), barley (2.8–3.3), and oat (2.0–2.4) [18].

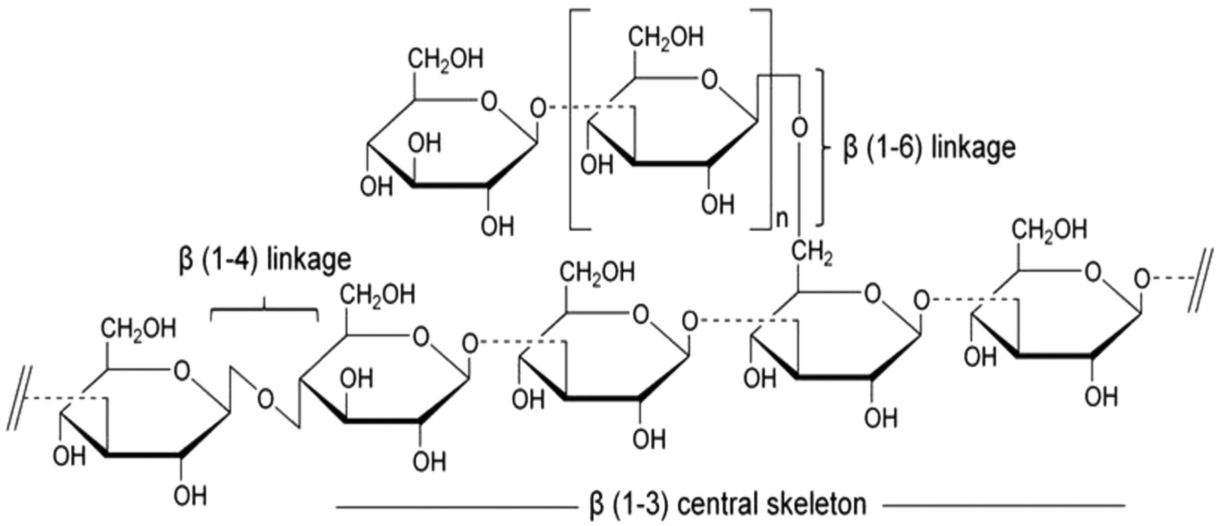

Figure 1. Polymer of β (1-3)-D-glycopyranosyl units with branching at β (1-6) and β (1-4)-D-glycopyranosyl units.

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3. Biological properties and applications of β-glucans

In the last decades, the β-glucans have received special attention for its biological activity. Numerous beneficial effects have been attributed to this polymer, in particular due to its immunomodulatory potential. However, beyond the modulatory action of the immune system, several other activities related to β-glucans have been evaluated and proven, as their antitumoral, anti-inflammatory, antimutagenic, and antioxidant action, their hypoglycemic and hypocholesterolemic capacity, and also their protective effect against infections [19]. The β-glucans have a long scientific history, encompassing hundreds of studies. However, this molecule is not properly explored even in therapy, as an additive in food or feed, probably due to its relatively expensive price—about U$ 36/kg (brand Macrogard; Biorigin, Quatá, São Paulo, Brazil). Research involving the biological activity of this polymer originated in the 1940s, with the renowned scientist Pillemer and his colleagues, who obtained a crude-insoluble extract of the cell wall of the *Saccharomyces cerevisiae*, called zymosan, consisting of proteins, chitin, β-glucan, mannans, and lipids. According to the authors, this extract was able to stimulate the immune response in a non-specific manner [20]. Clinical studies in humans involving the β-glucans began in the 1970s, even before the evidence of their mode of action on the immune system, with reports of curing different types of cancer, including breast cancer, melanoma, and adenosquamous carcinoma of the lung after the application of extracts of β-glucans [21].

3.1. Immune system and immunomodulatory activity of β-glucans

The immune system operates seeking to protect the organism from infections that can be caused by various agents, including bacteria, viruses, fungi, and parasites. The cells and molecules of the immune system are highly specialized in the defense against infection. Individuals with a compromised immune defense system due to various factors, such as age, chronic infection, or malnutrition, are subject to several problems, including arthritis, reduced healing capacity, reduced proliferation of bone marrow cells with consequent low defense cell counts, anemia, and increased incidence of all types of microbial infections. Studies also show that one of the main elements of the process of aging is a decrease in the functional effectiveness of the immune system [22]. Among the immunologically competent cells, macrophages play a major role in the initiation and maintenance of immune response both innate and adaptive [15]. In addition to the functions of phagocytosis and the release of lysosomal enzymes, macrophages are also responsible for the release of a number of cytokines and inflammatory mediators can stimulate the immune system in general [22].

The β-glucan belongs to the class of substances BRMs, or a variety of different substances known as Biological Response Modifiers. being able to trigger a series of events in the immune response [23], increasing the immune defense of the host by activating the functions of cells of the immune system [20]. This polymer is currently considered as one of the most potent stimulators of the immune response, effective both orally or intravenously, completely non-toxic and safe [15]. The response of β-glucan in vertebrates begins with its recognition by receptors present on the cell surface of various immune cells, such as macrophages, neutrophils, dendritic cells, and natural killer cells (NK), and receptors have also been described presently as non-immune cells, endothelial cells, fibroblasts, alveolar epithelial, and Langerhans cells [20]. The various receptors present on the cell membranes of immune cells related to the recognition of β-glucan in vertebrates are dectin-1, complement receptor 3 (CR3), lactosylceramide receptor, Toll-like receptor 2 (TLR-2), and scavenger receptors [24, 25]. The dectin-1 is a type II transmembrane protein with receptor extracellular domain CDR which is responsible for carbohydrate recognition, and a cytoplasmic tail with immunoreceptor ITAM (tyrosine-based activating motif) involved in superoxide production by macrophages in response to the immunosystem defense. The dectin-1 can mediate diverse cellular responses, including phagocytosis and endocytosis. This protein may also induce the production of cytokines and inflammatory chemokines, such as tumor necrosis factor (TNF-α), macrophage inflammatory protein-2 (MIP-2), and interleukin-12 (IL-12) [16]. The receptor CR3 stimulates cytokine secretion by NK cells, especially in the presence of pathogens. This receptor acts as a cell adhesion molecule since it has a binding site for carbohydrates located on the terminal carbon, and thus a receptor for the phagocyte β-glucan [15].

3.2. Medical application: cancer

Anticarcinogenic substances are able to reduce, delay, or even prevent the development of malignancies [26]. Different studies have shown anticarcinogenic action of β-glucans and their derivatives [1, 2, 4]. At the end of 1970s, a study on mice with subcutaneous tumor implantation revealed that extracts containing high concentrations of β-glucan significantly reduced growth of mammary carcinomas and melanomas in animals treated and verified an increase in survival of these animals [27]. Kogan et al. [6] observed increased inhibition in the occurrence of lung metastases up to 94% in animals that received oral administration of β-glucan during treatment with cyclophosphamide for Lewis lung carcinoma. Several surveys show the effectiveness of antitumor action of β-glucans in chemotherapy and the improvement in the survival of patients with different types of cancer. A study involving women with malignant breast tumors confirmed the activation and proliferation of monocytes in peripheral blood of patients upon oral administration of β-glucan. According to the researchers, clinical improvement in the survival of patients with no evidence of any recurrent side effects was demonstrated [4]. The effective immune response against tumor cells mediated by β-glucans is based on the activation and expansion of several immune functions, among them the activation of cytotoxic T cells specifically attack cancer cells [28]. The CD4+ T lymphocytes play a role as modulators of immune cells to produce multiple cytokines. The latter are mediators essential for the generation of an effective immune response involving CD8+ T cells, which are necessary for the defense against tumor cells [1]. The effects of β-glucan in lymphocyte activation involving the antitumor immune response have been reported in experimental animal and human models. A study of 30 patients with advanced prostate cancer, who were treated by oral administration of a soluble fraction of β-glucan (carboxymethyl glucan), revealed that after administration there was a significant increase in CD3+, CD4+, and CD8+ in peripheral blood of patients and consequent stimulation of the immune system [2].

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3.3. β-glucans applied in other diseases

Since β-glucans affect immune function stimulating various immune cell activations, studies were performed to demonstrate the effective application of this immunomodulatory compound in treatment of diseases. Patients with severe periodontitis have failed for the recruitment and activation of macrophages [29]. β-glucans induce macrophage activation and establishment of Th1, and their use may be responsible for the inhibition of tissue destruction in periodontal disease. The use of β-glucan in dental treatment has been systematically evaluated in recent years. Studies with animals showed a significantly reduced periodontal bone loss after oral administration of β-(1-3),(1-6) glucan [30]. Acar et al. [31] investigated the effects of non-surgical periodontal therapy (NPT) with an adjunctive use of systemic β-glucan on clinical, microbiological, and gingival parameters. Their findings showed that β-glucan might increase the concentration of TGF-β1, thereby augmenting periodontal healing potential. Proposals for treating allergic diseases using β-glucans have also been reported. A new therapeutic strategy for allergic diseases using β-glucan was proposed, with beneficial action in restoring the function of type 2 T-helper cells. Through the application of subcutaneous injections in child patients, β-glucan was demonstrated to be able to modulate allergic sensitization in patients, greatly improving their quality of life [32]. Furthermore, the antibacterial, antiviral, and antifungal properties of β-glucan and its derivatives are also reported. Different studies have shown the protective effect of β-glucan to *Staphylococcus aureus* [33], *Pneumocystis carinii*, *Leishmania donovani,* and *Influenza virus* [22]. The protective effect of β-glucan from *S. cerevisiae* against DNA damage and cytotoxicity in wild-type (k1) and repair-deficient xrs5 CHO cells were evaluated by Oliveira et al. [34].

3.4. Food and feed applications of β-glucans

The search for higher human living standards and greater longevity has generated the need for the development of nutritional alternatives that result in improved general health which means more enjoyment of life, less diseases and less time, and money required for medical needs. In this context, special foods enriched with molecules with health benefits are been developed. Some studies dealing with the enormous benefits of β-glucan as a nutritional supplement [31, 35–37]. Used as adjunctive to the positive effects of antioxidants, lipid balance enhancers, antibiotics, and other therapeutics, the β-glucans are currently considered a true antiaging supplement. These properties are associated with several studies which have shown biological activity of β-glucan, describing its action modulating the immune system and antitumor action [1, 3].

3.4.1. β-glucan in the human diet

In recent years, there has been increasing interest in the effect of the use of β-glucan as a dietary supplement. Different studies seek to prove the use of this polysaccharide in the diet has several health benefits. The beneficial effects of consistent intake of β-glucan and its action in reducing cholesterol levels in the blood have been systematically studied. A study of 20 hypercholesterolemic patients, who received daily dietary supplement containing 5.8 g of β-glucan for 4 weeks, reported a 9% decrease in cholesterol level in the intervention group, while there was no difference in the placebo (maltodextrin) group [7]. Nicolosi et al. [38] observed a significant reduction in total and LDL cholesterol in hypercholesterolemic obese patients after 8 weeks of intake of orange juice supplemented with β-glucan. The action of β-glucan on cholesterol reduction can be explained in terms of the reduction in bile reabsorption or the increase in viscosity in the small intestine. However, a more likely explanation relates to the size of the molecule and its subsequent absorption by the intestine. According to Kim et al. [37], molecules of small size, which are consequently less viscous, are less effective in lowering cholesterol. Studies with β-glucan of low molecular size (370,000–1,000,000) reported this polysaccharide ineffective in reducing the cholesterol level [39], whereas Braaten et al. [7] reported a significant reduction in cholesterol levels in the blood of patients who included β-glucan of molecular size above 1.2 million in their diet. β-glucans become a great special food in a diet designed to adjunct in diabetic patients. The action of this polymer in lowering blood glucose level is also reported in the literature. Research has demonstrated the antidiabetic effect of IL-1 cytokine, which increases insulin production, resulting in the lowering of blood glucose levels [40, 41]. Since the β-glucan acts on the activation of macrophages, and these are considered the major source of IL-1 in the human body, this polymer becomes useful in diets designed for diabetic patients. According to Regand et al. [42], the physiological activity of β-glucan in reducing glycemic responses has been mostly attributed to its effect in increasing viscosity in the upper digestive tract. The introduction of β-glucan in the diet may decrease the incidence of colds, respiratory diseases, in addition to alleviating the symptoms caused by these diseases, since this polymer increases the body’s potential to defend against invading pathogens [31]. A study with seventy-five marathon runners showed that daily administration of β-glucan can prevent upper respiratory tract (URTI) symptoms and improve overall health and mood following a competitive marathon [36]. More recently, a study of 162 healthy participants with recurring infections who received a diet supplemented with β-(1-3),(1-6) glucan showed a reduction in the number of symptomatic common cold infections by 25% and the mean symptom score was 15% lower compared to the control group [35].

3.4.2. β-glucan additives in animal feed

β-glucan has been prominent among the ingredients used as supplements in animal feed in order to reduce the risk of chronic diseases both in mammals and in fish and birds [43], since they are able to absorb mycotoxins, thus decreasing their toxic effect and mediating their removal from the body [44]. Different food supplements containing β-glucan are available for commercial use for animals. Among them, Bio-Mos® is used in the prevention of infectious diseases of various origins and MTB100® in the elimination of the mycotoxins and inhibition of their toxic effect, both manufactured by Alltech Inc. (Nicholasville, KY). Animals treated with foods supplemented with β-glucan exhibit greater resistance to pathogenic microorganisms, and bacteria or viruses requiring lower dosages of antibiotics or antivirals to deal with infections [5].

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4. Production of purified β-glucan

4.1. β-glucan extraction and purification by yeast cells

Many processes and raw materials of obtaining β-glucans have been described, but the challenge is finding the best extraction leading to high purity with the great immunostimulant and antitumor action, periodontal therapy, among others. After the discovery of the benefits of β-glucan for animals and humans, various processes of purification and isolation of this polysaccharide have been developed [44]. The research for new methods of obtaining β-glucan is being conducted prioritizing a non-aggressive extraction, which preserves the most of the original structure of the macromolecule. Currently, β-glucan used as additive in feed is produced by the cultivation of *S. cerevisiae* or as residue from the fuel ethanol or beer industry. In this respect, just the Brazilian production of sugar cane in the 2012/2013 harvest was 589 million tons of cane and 23.64 billion liters in ethanol was produced [45–47] with expectation of growing. The trading of β-glucan could be increased, since the yeast extraction from the fuel ethanol distilleries up to 5% per day or 7.5 kg powder yeast per m^3 ethanol/day would be possible, which could reach at least 177,300 ton of yeast/day, only in the Brazilian fuel ethanol industry.

4.1.1. Lysis of yeast cell

The basic process of β-glucan extraction involves the lysis of cells (chemical, biochemical, mechanical, or by autohydrolysis), separation of cell wall (centrifugation or filtration), extraction, and purification (precipitation and centrifugation). The yeast cells are normally processed to produce β-glucan, mannan, and yeast extract. One important aspect of the technology to produce β-glucan and other valuable products from yeasts is the method of cell wall lysis. Yeast autolysis is used in the industrial processes due to the low cost, fractionation efficiency, and quality of products obtained. Firstly, the fresh yeast cells are autolysed, and the cell wall is separated by centrifugation.

The yeast cell wall has a thickness of 100–200 nm, and the wall is not only for protection and structural function but is also metabolically important [48]. The thickness and structure of the wall could vary depending on several factors like the strain, the industrial process of yeasts, and culture conditions. The concentration of β-glucans also depends on these parameters since the wall is used for the β-glucan extraction. The outer layer of mannoproteins retains the periplasmic proteins conferring resistance to the cells of yeasts and acts as a barrier to external attack of enzymes and some other molecules [49]. The layer of glucan is more internal and linked with chitin in adjacent layers to the plasma membrane and confers rigidity and the cell shape [50].

Autolysis is an irreversible process caused by intracellular enzymes of yeast under stress conditions, such as temperature, pH, yeast concentrations unsuitable for the survival of the cells. This process is based mainly on heat treatment and causes lysis of the cells from activation of a group of intracellular enzymes that breaks the wall [51]. According to Nagodawithana [51], lysis occurs primarily because of the enzymes β-(1-3) glucanase and protease. Enzymes β-(1-6) glucanases and mannanases participate in solubilizing the matrix of the cell wall, and over forty enzymes have been identified in *S. cerevisiae* containing a major role in the autolytic process. Probably due to metabolic differences between different strains of *S. cerevisiae*, several studies disagree on the physicochemical conditions more appropriate for the autolysis of the cells vary from 45 to 55°C in 3–7 days of treatment [52]. The optimization of autolysis of *Saccharomyces cerevisiae* from a brewery was studied aiming at the maximum ribonucleic acid extraction and yeast extract production [52]. The best conditions for yeast autolysis were 55.2°C, pH = 5.1 and 9.8% NaCl in 24 h of processing. In these conditions, the RNA extraction yield was 89.7%, resulting in 51.3% of dehydrated yeast extract with 57.9% protein, and 48.7% cellular wall with 21.7% protein. The thermal shock at 60°C per 15 min prior to autolysis provided an increase in this yield of 89.7–91.4%. The optimized autolysis including NaCl plasmolysis was efficient, economic, and fast, thus usable for industrial purposes. Currently, yeast residues are exported as yeast flour for feed at low prices by the countries which are producers of fuel ethanol and beer. The improvement of the technology of fractionation and purification in other products like β-glucan, RNA, mannan, mannoprotein, and others is strategic since more valuable products can be produced. This is in accordance with the concept of biorefinery, that is, co-production of biofuels, bioenergy, and marketable chemicals from renewable biomass [53].

Thereafter, the β-glucan is extracted from autolysed yeast cells by hot alkaline hydrolysis (NaOH) and purified by citric acid precipitation. Another combination of alkali and inorganic acid to extract β-(1-3) glucan was performed by Sandula et al., [54], followed the method described by Machová et al., [55] to obtain water-insoluble β-(1-3) glucan from *S. cerevisiae*. In this method, 6% NaOH solution at 60°C was also used; however, the extraction was done by 4% phosphoric acid at room temperature [56]. The effects of drying were evaluated in three different processes (lyophilization, spray drying, and solvent precipitation) on the physical properties and immunoregulatory effect of β-glucan of *Saccharomyces*.

4.2. Chemical modification of β-1,3 glucan

The research of modification of β-1,3 glucan has been performed aiming to improve biological properties. Others steps to obtain modified glucan like methylation, permethylation, carboxymethylation, sulfoethylation, and ultrasonication Depending on the application or use of this molecule. Carboxymethylation of the glucans was made with glucan or chitin–glucan complex suspended in a mixture with 30% NaOH and isopropanol, and stirred at 10°C for 1 h. The degree of substitution of the carboxymethylated glucan was 0.56 or 0.91 for glucan and 0.43 for chitin–glucan complex, depending on the amount of monochloroacetic acid used [57]. The procedure of sulfoethylation of the glucans was performed using sodium β-chloroethylsulfonate in isopropanol solution [58], and permethylation of baker's yeast glucan was carried out according to Ciucanu & Kerek [59] using powdered NaOH. The immunomodulatory activity was detected in fibrillar (non-soluble) and partially hydrolyzed baker's yeast glucan as well as its soluble derivatives prepared by carboxymethylation and sulfoethylation. All these glucans showed anti-infective activity against *Klebsiella pneumoniae* after intravenous or subcutaneous prophylactic application to mice [60].

The evolution of β-(1,3) glucan use in the pharmaceutical and medical areas, as well as food and feed, depends on the development of more economical and efficient methods of extraction, purification, and chemical modification of this interesting molecule. Although their biological properties are amply evidenced, more studies are needed about its application, making this knowledge more available to benefit the health of human and animal.

5. Conclusion

β-(1-3) glucan is a promising healthier food and feed additive whose special properties certified ranging from the activation of the immune system, replacement of antibiotics in animal production, particularly for fish and pork, and various therapies: antitumor, allergic and respiratory diseases, periodontitis and peritonitis. This polymer has also proven to be available as food ingredient for the control of cholesterol and diabetes in special foods. Despite having started their studies for some decades, this molecule remains expensive and not widely available, with the technology dominated by a few producers.

The extraction methods using alkali and acid, with previous pre-treatments, and the step of purification and chemical modification, are needed to obtain β-glucan according to specific biological properties. The solubility, molecular size, level of protein, and degree of methylation are essential parameters to be considered for these properties. This work also highlighted some technological aspects of economic obtaining of β-glucan from yeast.

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References

[1] Magnani, M., Castro-Gómez, R.J.H., Mori, M.P., Kuasne, H., Gregório, E.P., Libos Jr., F. & Cólus, I.M.S. (2011a). Protective effect of carboxymethyl-glucan (CM-G) against

DNA damage in patients with advanced prostate cancer. *Genetics and Molecular Biology*, *34*(1), 131–135.

[2] Magnani, M., Castro-Gómez, R.J.H., Aoki, M.N., Gregório, E.P. & Libos Jr, F. Morimoto, H.K., Reiche, E.M.V. & Watanabe, M.A.E. (2011b). Analysis of peripheral T cells and the CC chemokine receptor (CCR5) delta32 polymorphism in prostate cancer patients treated with carboxymethyl-glucan (CM-G). *Natural Product Research: Formerly Natural Product Letters*, *26*(10), 945–951.

[3] Murakawa, K., Fukunaga, K., Tanouch, M., Hosokawa, M., Hossan, Z. & Takahashi, K. (2007). Therapy of myeloma in vivo using marine phospholipid in combination with *Agaricus blazei* Murill as an immune respond activator. *Journal of Oleo Science*, *56*(4), 179–188.

[4] Demir, G., Klein, H.O., Mandel-Molinas, N. & Tuzuner, N. (2007). β-glucan induces proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer. *International Immunopharm*, *7*, 113–116.

[5] Xiao, Z., Trincado, C.A. & Murtaugh, M.P. (2004). β-Glucan enhancement of T cell IFN-gamma response in swine. *Veterinary Immunology and Immunopathology*, *102*(3), 315–320.

[6] Kogan, G., Šandula, J., Korolenko, T.A., Falameeva, O.V., Poteryaeva, O.N., Zhanaeva, S.Ya., Levina, O.A., Filatova, T.G. & Kaledin, V.I. (2002). Increased efficiency of Lewis lung carcinoma chemotherapy with a macrophage stimulator—yeast carboxymethyl glucan. *International Immunopharmacol*, *2*, 775–781.

[7] Braaten, J.T., Wood, P.J., Scott, F.W., Wolynetz, M.S., Lowe, M.K., Bradley-White, P. & Collins, M.W. (1994). Oat beta-glucan reduces blood cholesterol concentration in hypercholesterolemic subjects. *European Journal of Clinical Nutrition*, *48*, 465–74.

[8] Genc, H., Ozdemir, M. & Demirbas, A. (2001). Analysis of mixed-linked (1→3), (1→4)-β-D-glucans in cereal grain from Turkey. *Food Chemistry*, *73*, 221–224.

[9] Hegsted, M., Windhauser, M.M. & Lester, S.B. (1993). Stabilized rice bran and oat bran lower cholesterol *in* humans. *Nutrition Research, 13*(4), 387–398.

[10] Saastamoinem, M.; Plaami, S. & Kumpulainen, J. (1989). Pentosans and β glucan content of Finnish winter varieties as compared with rye six other countries. *Journal of Cereal Science, 10*, 199–207.

[11] Sayar, S.; Jannink, J.; White, P.J. (2005). *In Vitro* bile acid binding of flours from oat lines varying in percentage and molecular weight distribution of *β*-glucan. *J. Agric. Food Chem., 53*: 8797–8803.

[12] Engstrom, D.F., Mathison G.W. & Goonewardene, L.A. (1992). Effect of β-glucan, starch, and fibre content and steam vs. dry rolling of barley grain on its degradability and utilization by steers. *Animal Feed Science and Technology*, *37*(2), 33–46.

[13] El Khoury, D., Cuda, C., Luhovyy, B.L. & Anderson, G.H. (2012). Beta glucan: health benefits in obesity and metabolic syndrome. *Journal of Nutrition and Metabolism*, *2012*: 28. doi:10.1155/2012/851362.

[14] Magnani, M. & Castro-Gómez, R.J.H. (2008). β-glucan from *Saccharomyces cerevisiae*: constitution, bioactivity and obtaining. *Semina: Ciencias Agrarias*, *29*(3), 631–650.

[15] Chan, G.C., Chan, W.K. Sze, D.M. (2009). The effects of β-glucan on human immune and cancer cells. *Journal of Hematology & Oncology*, *2*, 25–36.

[16] Stone, B.A. & Clarke, A.E. (1992). Chemistry and biology of (1,3)-D-glucans. *La Trobe University*, Victoria, Australia Press.

[17] Camelini, C.M., Mendonça, M., Dias, P.F. & Maraschin, M. (2005). β-glucans from mushrooms. *Biotecnologia Ciencia e Desenvolvimento*, *35*, 36–47.

[18] Li, W., Cui, S.W. & Kakuda, Y. (2005). Extraction, fractionation, structural and physical characterization of wheat β-D-glucans. *Carbohydrate Polymers, 63*, 408–416.

[19] Jantova, S., Bakos, D., Birosova, L. & Matejov, P. (2015). Biological properties of a novel coladerm-beta glucan membrane. In vitro assessment using human fibroblasts. *Biomed Papers of Medical Faculty of the University Palacky Olomouc, Czech Repub*, 159(1):67–76. doi: 10.5507/bp.2012.115.

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

[21] Mansell, P.W.A., Ichinose, I.I., Reed, R.J., Krements, E.T., McNamee, R.B. & Di Luzio, N.R. (1975). Macrophage-mediated destruction of human malignant cells in vive. *Journal of the National Cancer Institute*, *54*, 571–580.

[22] Akramienė, D., Kondrotas, A., Didžiapetrienė, J. & Kėvelaitis, E. (2007). Effects of β-glucans on the immune system. *Medicina (Kaunas)*, *43(8)*, 597–606.

[23] Bohn, J.A. & BeMiller, J.M. (1995). (1-3)-β-D-glucans as biological response modifiers: a review of structure-functional activity relationships. *Carbohydrate Polymers, 28 (1)*, 3–14.

[24] Kwiatkowski, S., Kwiatkowski, S.E. Yeast (*Saccharomyces cerevisiae*) Glucan Polysaccharides—Occurrence, Separation and Application in Food, Feed and Health Industries. (2012). In: D.N. Karunaratne (Ed.), *The Complex World of Polysaccharides*, (47–70), In Tech, Rijeka, Croatia. http://dx.doi.org/10.5772/48100.

[25] Battle, J., Ha, T., Li, C., Della Beffa, V., Rice, P., Kalbfleisch, J., Browder, W. & Williams, D. (1998). Ligand binding to the (1-3)-β-D-glucan receptor stimulates NFkB activation, but not apoptosis in U937 cells. *Biochemical and Biophysical Research Communications*, *249(2)*, 499–504.

[26] Kuroda, Y. & Hara, Y. (1999). Antimutagenic and anticarcinogenic activity of tea polyphenols. *Mutation Research*, *436*(1), 69–97.

[27] Di Luzio, N.R. (1983). Immunopharmacology of glucan: a broad spectrum enhancer of host defense mechanisms. *Trends in Pharmacological Sciences*, *4*, 344–347.

[28] Manners, D.J., Mason, A.J. & Patterson, J.C. (1973). The structure of a 1,3 β-glucan from yeast cell walls. *Biochemistry Journal, 135*, 19–30.

[29] Chaple, C.C., Srivastrava, M. & Hunter, N. (1998). Failure of macrophage activation in destructive periodontal disease. *The Journal of Pathology*, *186*, 281–286.

[30] Hartland, R.P., Vermeulen, C.A., Sietsma, J.H., Wessels, J.G.H. & Klis, F.M. (1994). The linkage of (1-3)-β-glucan to chitin during cell wall assembly in *Saccharomyces cerevisiae. Yeast (Chichester*, *England)*, *10*(12), 1591–1599.

[31] Acar, N.N., Noyan, U., Kuru, L., Kadir, T. & Kuru, B. (2012). Adjunctive Systemic Use of Beta-Glucan in the Nonsurgical Treatment of Chronic Periodontitis. In N. Budeneli (Ed.), *Pathogenesis and Treatment of Periodontitis*, (pp. 167–182). Shanghai: In Tech China.

[32] Sarinho, E., Medeiros, D., Schor, D., Silva, A.R., Sales, V., Motta, M.E., Costa, A., Azoubel, A. & Rizzo, J.A. (2009). Production of interleukin-10 in asthmatic children after beta-1-3-glucan. *Allergol Immunopathol*, *37*, 188–192.

[33] Di Luzio, N.R. & Williams, D.L. (1978). Protective effect of glucan against systemic *Staphylococcus aureus* septicemia in normal and leukemic mice. *Infection and Immunity*, *20*, 804–810.

[34] Oliveira, R.J., Matuo, R., da Silva, A.F., Matiazi, H.J., Mantovani, M.S. & Ribeiro, L.R. (2007). Protective effect of β-glucan extracted from *Saccharomyces cerevisiae* against DNA damage and cytotoxicity in wild-type (k1) and repair-deficient xrs5 CHO cells. *Toxicology In Vitro: An International Journal Published in Association with BIBRA*, *21*, 41–52.

[35] Auinger, A., Riede, L., Bothe, G., Busch, R. & Gruenwald, J. (2013). Yeast (1,3)-(1,6)-beta-glucan helps to maintain the body's defense against pathogens: a double-blind, randomized, placebo controlled, multicentric study in healthy subjects. *European Journal of Nutrition*, *52*(8), 1913–1918.

[36] Talbott, S. & Talbott, J. (2009). Effect of Beta 1,3/1,6 Glucan on upper respiratory tract infection symptoms and mood state in marathon athletes. *Journal of Sports Science and Medicine*, *8*, 509–515.

[37] Kim, S.Y., Song, H.J., Lee, Y.Y., Cho, K. & Roh, Y.K. (2006). Biomedical Issues of Dietary fiber –Glucan. *Journal of Korean Medical Science*, *21*, 781–789.

[38] Nicolosi, R., Bell, S.J., Bistrian, B.R., Greenberg, I., Forse, R.A. & Blackburn, G.L. (1999). Plasma lipid changes after supplementation with β-glucan fiber from yeast. *American Journal of Clinical Nutrition*, *70*(2), 208–212.

[39] Beer, M.U., Arrigoni, E. & Amado, R. (1995). Effects of oat gum on blood cholesterol levels in healthy young men. *European Journal of Clinical Nutrition*, *49*, 517–22.

[40] Lang, C.H. & Dobrescu, C. (1989). Interleukin-l induced increases in glucose utilization are insulin mediated. *Life Sciences 45*(22), 27–34.

[41] Robertsen, B., Engstad, R.E. & Jorgensen, J.B. (1994). Beta-glucans as Immunostimulants in fish. *Modulators of Fish Immune Responses*, *1*, Fair Haven, NJ, USA.

[42] Regand, A., Tosh, S.M., Wolever, T.M.S. & Wood, P.J. (2009). Physicochemical properties of β-glucan in differently processed oat foods influence glycemic response. *Journal of Agricultural and Food Chemistry*, *57*, 8831–8838.

[43] Kogan, G. & Kocher, A. (2007). Role of yeast cell wall polysaccharides in pig nutrition and health protection. *Livestock Science*, *109*, 161–165.

[44] Li, J., Li, D.F., Xing, J.J., Cheng, Z.B. & Lai, C.H. (2006). Effects of β-glucan extracted from *Saccharomyces cerevisiae* on growth performance, and immunological and somatotropic responses of pigs challenged with *Escherichia coli* lipopolysaccharide. *Journal of Animal Science*, *84*, 2374–2381.

[45] MAPA—Brazilian Department of Agriculture, Livestock and Supply (2013). http://www.agricultura.gov.br/vegetal/safras-estoques. Access in the site: April 23, 2014.

[46] CONAB Brazilian National Company of Supply. (2013). Site: http://www.conab.gov.br/OlalaCMS/uploads/arquivos/13_04_09_10_30_34_boletim_cana_portugues_abril_2013_4o_lev.pdf. Access in the site: Access in: April, 2014.

[47] Aguiar, C. (2011). STAB congress of sugar and ethanol. *Management practices and Sustainability*. Access site: http://www.stab.org.br/12sba/5.CLEBERAGUIAR.SAOMANOEL.26.10.11hrs.pdf

[48] Dzienzak, J.D. (1987). Yeast and Yeast derivatives applications. *Food Technology*, *41*(2), 122–125.

[49] Kopecká, M., Phaff, H.J. & Fleet, G.H. (1974). Demonstration of a fibrillar component in the cell wall of the yeast *Saccharomyces cerevisiae* and its chemical nature. *The Journal of Cell Biology*, *62*(1), 66–76.

[50] Kapteyn, J.C., Ram, A.F., Gross, E.M., Kollar, R., Montijn, R.C., Van Den Ende, H., Llobel, A.A., Cabib, E. & Klis, F.M. (1997). Altered extent of cross-linking of β 1,6-glucosylated mannoproteins to chitin in *Saccharomyces cerevisiae* mutants with reduced cell wall β 1,3 glucan content. *Journal of Bacteriology*, 179(20), 6279–6284.

[51] Nagodawithana, T. (1992). Yeast-derived flavors and flavor enhancers and their probable mode of action. *Food Technology*, 46, 138–144.

[52] Oliveira, A.M. & Oliva-Neto, P. (2011). Improvement in RNA extraction from *S. cerevisie* by optimization in the autolysis and NH3 hydrolysis. *Brazilian Archives of Biology and Technology*, 54, 1007–1018.

[53] Cherubini, F. & Ulgiati, S. (2010), Crop residues as raw materials for biorefinery systems—A LCA case study. *Applied Energy*, *87*, 47–57.

[54] Sandula, J., Kogan, G., Kacuráková, M. & Machová, E. (1999). Microbial (1-3)-β-D-glucan their preparation, physico-chemical characterization and immunomodulatory activity. *Carbohydrate Polymer*, *38*, 247–253.

[55] Machová, E., Kogan, G. Alfóldi, J., Soltes, L. & Sandula, J.(1995). Enzymatic and ultrasonic depolymerization of carboxymethylated β(1-3)-D-glucans derived from *S. cerevisiae*. *Journal of Applied Polymer Science*, *55*, 699–704.

[56] Torronen, R., Kansanen, L., Uusitupa, M., Hanninen, O., Myllymaki, O., Harkonen, H. & Malkki, Y. (1992). Effects of an oat bran concentrate on serum lipids in free-living men with mild to moderate hypercholesterolaemia. *European Journal of Clinical Nutrition*, *46*, 621–627.

[57] Jamas, S., Easson, D.D. & Ostroff, G.R. (1997). Glucan preparation. *US Patent 5622939*.

[58] Pastýr, J., Sandula, J., Master, L., Trnovec, T. & Benes, G. (1997). Preparation of water-soluble sulfoderivatives of microbial β(1-3)-D-glucans. Slovak Patent no. 278783.

[59] Ciucanu, I. & Kerek, F. (1984). A simple and rapid method for the permethylation of carbohydrates. *Carbohydr Res.*, *131*, 209–217.

[60] Kogan, G., Master, C., Sandula, J., Navarová, J. & Trnovec, T. (1989). Recent results on the structure and immunomodulating activities of yeast glucan. In V. Crescenzi, I.C.M. Dea, S. Pruletti, S.S. Stivala, I.W. Sutherland (Eds). *Biochemical and Biotechnological Advances in Industrial Polysaccharides.* Elsevier. New York.