Review Article www.ijcps.com

International Journal of
Chemical and Pharmaceutical Sciences
2012, Mar., Vol.3 (1)

ISSN: 0976-9390
IJCPS

Beta-Glucans: A New Source For Human Welfare

[1]Menaga D,[1] Dhandapani R, [2]Rajakumar S and [1]Ayyasamy PM

[1]Department of Microbiology, Periyar University, Salem, Tamil Nadu, India.

[2]Department of Marine Biotechnology, Bharathidasan University, Tiruchirappalli, India

*Corresponding Author: E-mail: pmayyasamy@gmail.com

ABSTRACT

Beta -glucans are now recognized as potent immunological activators, and they are used clinically in world wide. β-glucans consist of a backbone of glucose residues linked by β-(1/3) - glycosidic bonds, often with attached side-chain glucose residues joined by β - (1/6) linkages. β-glucans are commonly called as biological response modifiers and they are mostly present in cereals, grains, fungi, mushrooms, bacteria, sea breams and algae. The literature points out that β-glucans are effective in treating diseases like cancer, microbial infections, hypercholesterolaemia and diabetes. Based on extensive research, this review explains the mechanisms, effects and their role against different types of infections. Now a day the attention was focused on the future research on clinical applications. Several researchers have worked on β-glucans but the main mechanisms of the receptors and pathways are not clear. It should be studied clearly to help the patient's to get recovered from chemotherapy and radiotherapy.

Keywords: Drug interaction, Cytochrome P-450 monooxygenase, malathion, drug-drug interaction and drug-herb interactions.

1. INTRODUCTION

Betaglucans are polysaccharides of D - glucose monomers linked by β-glycosidic bonds. They were a diverse group of molecules which can vary with respect to molecular mass, solubility, viscosity and 3-D configuration. They are known as "biological response modifiers" because of their ability to activate the immune system. Some forms of β-glucans are used in food products as texturing agents and soluble fiber supplements.

1, 3- β-D glucans are widely distributed in living organisms such as plant, fungi, yeast, and in some bacteria. About half the mass of fungal cell wall contain β-(1, 3) or (1, 4) glucans [1, 2]. In addition to structural and as storage material, more specialized functions are also involved [3]. Non-cellulosic β-glucans are recognized as potent immunological stimulators in human cell. These characteristic features make them potential in treating several diseases in China and Japan.

Plant 1,3 β-D glucans play an important role in cell division and defense responses against various kinds of stresses like microbial attacks and mechanical stresses [3]. In microorganisms, cell wall β-glucans are apparently shielded by mannan layers, but β-glucans become exposed after heat treatment and hence can induce immune responses in humans [5]. Brown *et al* [6] reported that β-glucans are not synthesized by human so the compounds are recognized by immune system as non-self molecules inducing both by innate and adaptive immune responses. Researchers have identified that β-glucans are one of the most effective immune enhancing substances, but still in infancy level.

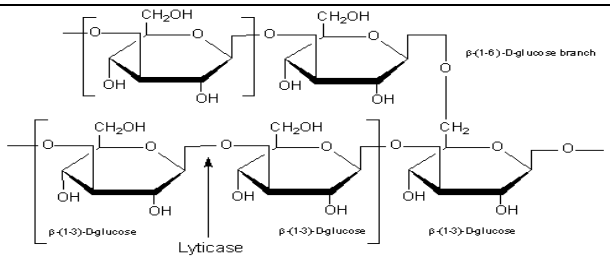
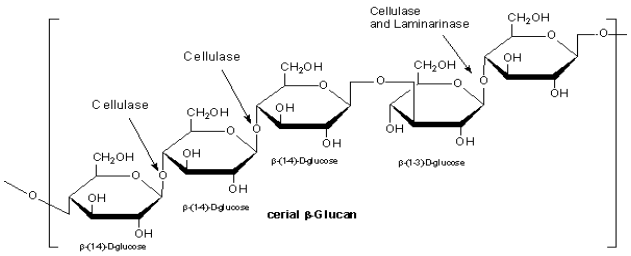
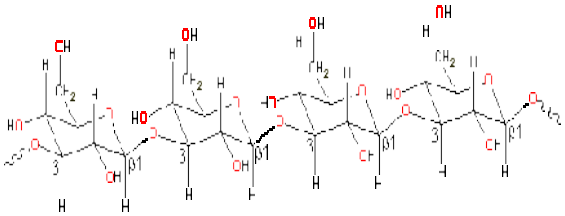
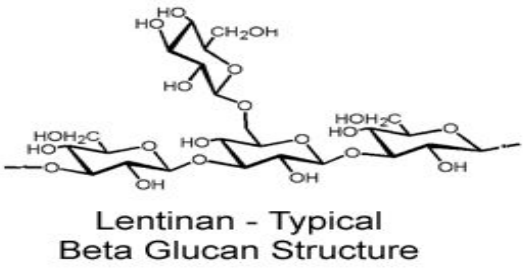
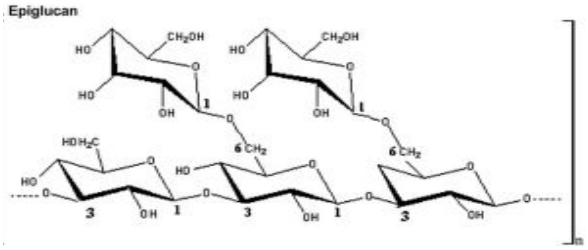
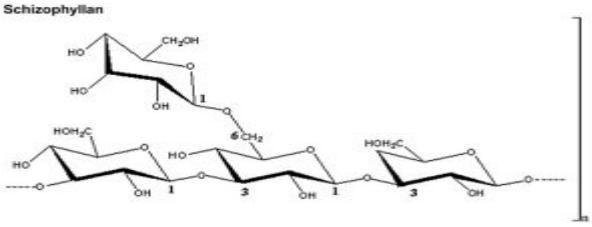
2. SOURCES IN NATURE

Most common source of supplemented β-glucans is derived from cell wall of baker's yeast (*Sacchromyces cerevisiae*). They also occur in plant cellulose, the bran of cereal grains, cell wall of fungi, mushrooms, bacteria, sea breams and algae. β 1, 3 and 1, 4 - glucans are extracted from the bran of the some grains such as oats and barley, rye and wheat. The β (1, 3) glucans from yeast cell wall are insoluble, whereas from grains are both soluble and insoluble. β-glucans are also extracted from some types sea weed and various species of mushrooms such reishi, shiitake, maitake, Lz-8, schizophyllan and lentinan (Table 1).

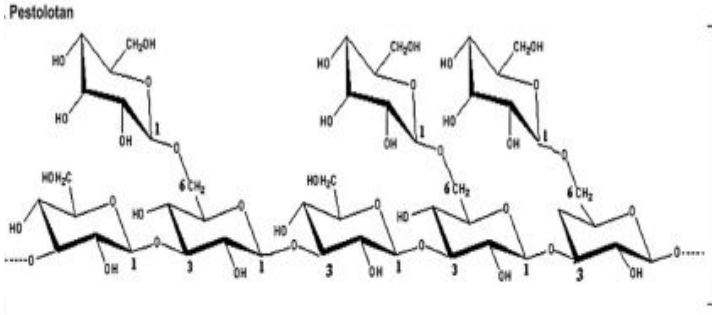
3. β-GLUCANS CHEMISTRY AND STRUCTURE

Glucans comprise upto 60% dry weight of fungal cell wall; β-glucans include glucose polymers with variable degrees of branching and it exist as triple helix, single helix or random coils [7].

Table 1: Various types of beta glucan and their structures

Source	Structure
Saccharomyces Cerevisiae	
Cereal	
Alcaligenes Faecalis	
Lentinula edode	
Epicoccum nigrum	
Schizophyllum Commune	

Pestalotia sp. 815



Bradirhizobium japanicum

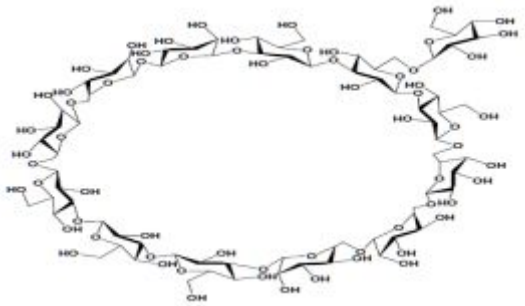


Table 2: Structure of various beta glucans sources (118).

Beta Glucan Type	Structure	Description
Bacterial		Linear β1,3-glucan (Curdlan)
Fungal		Short β1,6 branched β1,3-glucan (i.e. Schizophyllan)
Yeast		Long β1,6 branched β1,3-glucan (Beta Glucan, Betafectin™)
Cereal		Linear β1,3/ β1, 4-glucan (i.e. oats, barley, rye)

β-glucans are chains of D-glucose polysaccharides showing six carbon numbering and β orientation. Curdlan and Zekovic *et al* [8] reported that due to wide variety in degree of branching and polymerization, molecular weights of 1, 3 β-glucans range from 103 to 106 Da. Usually, relatively high molecular weight glucans appear to be more effective anti-tumor activity than those of low molecular weight [94], (Table 2).

A variety of β-glucans having different structures originated from various sources and by different extraction [8]. β-glucans from microorganisms generally have β-D (1,3) glucans linked an hydro D-glucose units as a backbone and periodic β-D (1,6) linked side chains but some glucans consists of linear linkage without branching . Mushroom polysaccharides are present mostly as linear and branched glucans with different types of glycosidic linkages, such as (1, 3) (1, 6) β-glucans and (1, 3) α glucans. *Auricularia auricula-judae* β-glucan (AAG) composed of a main chain of (1, 4)-linked D-glucopyranosyl with branching points at O-6 of (1, 6)-linked D-glucopyranosyl residues. The content of glucuronic acid is about 19% and the distribution of glucuronic acid was not periodic in the polysaccharide [93].

The cell wall of yeast and fungi β-glucans consists of (1, 3) β-linked glycopyranosyl residue with small numbers of (1, 6) β-linked branches. The oats and barley cell wall contain unbranched β-glucans with (1, 3) (1, 4) β-linked glycopyranosal residues, where β-glucans from bacteria are unbranched (1, 3) β-linked glycopyranosal residues [10, 11]. Cui *et al* 2000 reported that (1, 3), (1, 4) β-D-glucans are cell wall polysaccharides located in cereal endosperm and aleurone cells [12]. Cereals β-glucans are linear homoglucans of D-gluco-pyranose arranged as blocks of consecutive (1, 4) linked β-D glucose residue separated by single (1, 3) linkages [13, 14]. These polysaccharides are polymers of β-D glucopyranose [15] where about 30% of glucose residues are c(O) 3 linked and 70% are c[o] 4 linked. Extracellular β-D glucans were highly branched and have complex structure. High degree of branching and an adequate size of side chains seem to be correlated to the biological activities of β-D glucans [17]. The molecular features of β-glucans are construed by the analysis of the oligomers obtained by digestion of polymers with a specific (1,3)(1,4) β-D glucan hydrolase that releases 3,O-β-D cellobiosyl D-glucose and 3,O- β-D cellotrisyl-D- glucose accounting for 90-95% of total oligosaccharides,

and longer oligosaccharides accounting for 5-10%. In β-glucan chain, the non-random arrangement of individual (1, 3) (1, 4) β-linkages, the cellostriosyl, cellotetraosyl and longer cello-oligomers are arranged in independent and random fashion [18]. A new colorimetric method is introduced for determining β-1,3-1,6-glucan quantification based on the cogo red dye compared with the total β-1,3-glucan content, measured by a fluorimetric method [124].

4. EFFECTS OF **β**-GLUCANS ON IMMUNE SYSTEM

β-glucans activate monocytes, macrophages, neutrophils, NK cells, and also indirectly T and B lymphocytes via cytokines [19, 20]. Hashimoti *et al* [21] proposed scleroglucan (SSG) can activate peyer's patch cells, thus enhancing antigen-specific and non-specific production of IgA at several muscosal sites. In vivo administration of (1, 3) β-D glucans to murine macrophages which induces the production of cytokines such as IL-1 and TNFα, activates and differentiates lymphocytes as well as proliferation of granulocytes, enhancing cytotoxicity and in vivo activity [17]. Dectin l has been identified as the major β-immunomodulatory glucan receptor of mammalian macrophages [21], which mediates leukocyte activation and cytokine production. β-glucans are able to modulate the innate immune response although the effects depend on the molecular weight and degree of branching [11]. In mammals, β-glucans stimulate the proliferation of mouse monocytes, macrophages [22] and activate the production of cytokines such as IL-6, IL-8 (23) and TNF α [23]. It can enhance the innate immune response against tumor [24] and several infective agents such as bacteria, viruses and fungi [25]. Some fungal β-glucans protect us from attack by pathogenic microbes and from harmful effects of environmental toxins and carcinogens by stimulating our immune system [26, 27]. Some β-glucans including lentinan, Yeast whole β-glucan particules (WGP), betafectin (PPG) and SSG are also effective against bacterial infections. Lentinan reduced *M tuberculosis* infections by increasing macrophage levels in vivo in a rat model and in vitro examination showed these macrophages had increased killing ability toward *M tuberculosis* [28, 29]. Certain β-glucans including zymosan, grifolan (GRN) and lentinan appear to activate phagocytes, thus leading to elimination of pathogens by phagocytosis [30].

The antinfective action of soluble (1, 3) β-glucans is thought to be mainly derived from enhanced macrophage and neutrophil function [30]. Ca^{2+} is important in mediating leukocyte responses [31] demonstrated that stimulation of (1,3) β-glucan receptors with unopsonized zymosan activates Ca^{2+} influx resulting in increase in intracellular Ca^{2+} levels in rat NR8383 AMS. Soluble (1, 3) β-glucans are less effective than particulate β-glucans which indirectly activates Ca^{2+} influx. β-glucan receptor activity has been reported on a variety of leukocytes including monocytes, macrophages, neutrophils and langerhans cells [71]. Oat β-glucans modulate the intestinal immune response, activates the central immune transcription factor NK-kB and increase cytokine secretion. Water soluble α (1, 6) glucan obtained from *Pleurotus florida* shows macrophage activation through release of nitric oxide. β-glucan particles induce the production of TNFα and interlukin- β through the stimulation of human monocyte β-glucan receptor. Glucans have been demonstrated to stimulate innate immunity [33] and to play a vital role in the recognition and response to fungal pathogens by the innate immune system [11].

Fungal β-glucans are used clinically for their stimulatory effect on the immune system; particularly on macrophages [33, 34] studied the effect of dietary β-glucans on growth performance, neutrophils and macrophage functions, haptoglobin production and resistance to *Streptococcus suis* challenge in weaning pigs. NF-kB activation induces transcription of genes encoding for inflammatory proteins like cytokines and chemokines and induces free radical production [35]. Some of the β-glucans can induce the release of TNF-α from macrophages both in vitro and in vivo conditions (16). (1, 6)- β -D-glucan, protoplast fused polyssacharide from *Pleurotus florida* and *Volvariella volvacea* strains was a, stimulates the macrophages, splenocytes and thymocytes [95].

5. BIOLOGICAL EFFECTS OF **β**-GLUCAN

β-glucans in cereals improve blood glucose regulation, reduce serum cholesterol levels and relieve constipation. The structural features such as tri/ tetra saccharide ratio varies with the order of 4.2-4.5 for wheat, 2.8 -3.3 for barley and 2.0-2.4 for oat [36]. β-glucans, the major fibre constituents of barley have been implicated in lowering plasma cholesterol, improving lipid metabolism and reducing glycaemic index [37, 38, 39]. Watkins *et al* 2004 proposed β-glucans to regulate cholesterol homeostasis could in order to improve the treatment of hypercholesterolemia, a leading cause of heart disease [40]. β-glucans are effective in reducing mild LDL elevations but not in high level cases[41]. Theuwissen *et al* 2007showed that β-glucans can reduce IL- β to enhance cholesterol [42]. In mouse, ligation and puncture induced polymicrobial sepsis, glucan phosphate inhibiting

the activities of IL-1β and TNF-α, inhibition increased the level of IL-1β and TNF-α in serum.

Oral administration of β-glucans to piglets showed decrease susceptibility of ETEC, thus β-glucans could be an alternative for antibiotics for prevention of postweaning infections with *E.coli*. β-D glucans from cell walls of *Phytophthora capsicii* and *P. parasitica* consists of (1, 3) (1, 6) β-D glucans exhibited a prominent activity against the allogenic solid sarcoma 180 on CD1 mice. It can also exhibit antiviral activity on tobacco leaves inoculated with TMV [43].

The effects of β-glucans have tested in several invertebrate species like molluscs, crayfish, earthworm and shrimp. In molluscs, it increase nitric oxide and in crayfish, enhance the prophenoloxidase and peptidase activity, in earthworm it activate the prophenoloxidase activation pathway and in the shrimp increased the resistance against vibriosis [45]. Intra-venous administration of a soluble (1, 3) - β-glucan to mice infected with *Staphylococcus aureus* prolonged survival time [46]. β-glucans also known to have antimutagenic activity, effect of carboxymethylglucan (CMG) derivatives on the frequency of micronuclei in bone marrow polychromatic erythrocytes (PCG) of mice irradiated by using CO°60 were studied.

Yeasts β-glucans were used as adjuvant in a *Vibrio species* vaccine for turbot (*Scophthalmus maximus*) [47]. β-glucans stimulate the non-specific defence mechanisms in plants [48], invertebrate [49] and vertebrates [50]. Some β-glucans having antitumor or anti HIV and anti HSV activities could interact with the mannose rich polymer chain found in tumor cells or viruses [51]. Sulfated β-glucans derived from mushrooms have the potential to be developed as an anti HSV agent [52]. Mushrooms contain biologically active β-glucans with antitumor and immunostimulating properties [53]. β-glucans protect against myelotoxic injury from radiation and chemotherapy [54].

6. IMMUNOMODULATORY ACTIVITY OF **β**-GLUCANS

Raa [60] and Vetvicka *et al* [61] proposed β-glucans, polymers of β-glucans extracted from the cell wall of bacteria, fungi or yeast are known as immunostimulators. β-glucans are believed to have various immunomodulatory properties. Plant and microbial β-glucans are natural polysaccharides exhibiting positive effects on human and animal health such as immune stimulation, anti-inflammatory, anti-microbial, anti-tumoral, hepatoprotective, cholesterol lowering as well as antifibrotic, antidiabetic and hypoglycemic activity [55]. Several fungal β-glucans appear to be effective immunomodulators and they appear to impact positively on cancers and several bacterial infections [11] (Table 3). Studies in vitro and in vivo reveal that the immunostimulating activity of β-glucan depends on structure, molecular weight and number of branches [11]. β-glucans are effective immunomodulators capable of enhancing resistance of a variety of infection in preclinical animal models [50] and animal subjects [56].

Table 3: Various, commonly used, **β**-glucans from different sources (Modified Ref [118]**)**

Name	Sources
Glomerellan	*Glomerella cingulata*
GRN (grifolan)	*Grifola frondosa* (Maitake mushroom)
LNT (Lentinan)	Lentinus (*Lentinula edode*)
Pneumocytis carinii	*Pneumocytis carinii*
PSG (polysaccharide from *Ganoderma lucidum*)	*G. lucidum*
SPG (Sonifilan/ schizophyllan)	*Schizophyllum commune*
SR (Scleroglucan)	*Sclerotium rolfsii or S. glucanicum*
SSG (*Sclerotinia sclerotiorum* glucan)	*S. sclerotiorum* (ascomycotina)
CSBG (*Candida spp.* β-glucan)	*Candida albicans*
Glucan phosphate (GluP)	*Saccharomyces cerevisiae*
PGG (betafectin)	*Saccharomyces cerevisiae*
Saccharomyces cerevisiae	*Saccharomyces cerevisiae*
WGP-glucan (whole glucan particle)	*Saccharomyces cerevisiae* (baker's yeast)
Zymocel	*Saccharomyces cerevisiae*
Zymozan	*Saccharomyces cerevisiae*
Curdlan	*Alcaligenes faecalis*
LAM (Laminarin/ Laminaran)	*Laminaria species* (e.g. digitata)
Krestin PSK	*Trametes versicolor*
Pestolotan	*Pestalotia sp. 815*
Epiglucan	*Epicoccum nigrum*

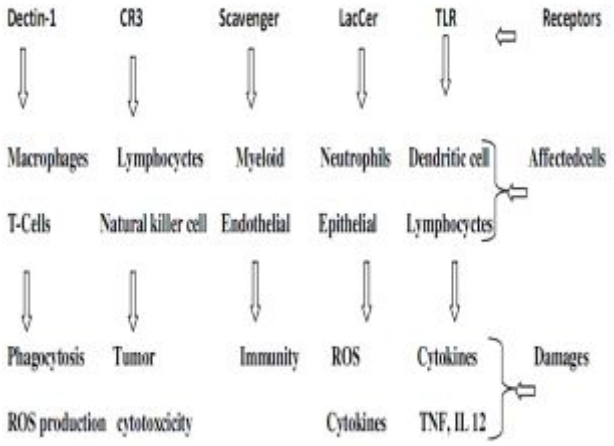
Pleurotus species β-glucans shows great immunomodulation property, stimulation of phagocytic activity [57], antioxidant, anti-inflammatory and analgestic properties [58], antitumor activity [59]. Barley and yeast β-glucans

can be phagocytosed by macrophages in intestine and conveyed to spleen, lymphnode and bonemarrow. Large molecule β-glucans can be degraded into small soluble β-glucans in bone marrow, which bind to several receptors like dectin-1 and complement receptor 3 and induce immunomodulatory cytokines [60]. Liu *et al* 2005 [63] proposed a new method to extract β-D glucans which was composed of induced autolysis, water and organic solvent treatment, homogenization and protease hydrolysis. β-glucans activate the innate immune system, enhancing the defence barriers and thus providing protection against severe or lethal infection. β-glucans can be used as adjuvants in immunizations [64]. Recently, Babineau *et al* [65] reported that β-glucans of *Agaricus blazei* had no genotoxic effects on testing with HepG2 cell line, but it protected against DNA damage caused by inducers.

7. CLINICAL APPLICATIONS

7.1. Importance of **β**-glucans in the treatment of infectious diseases

Table **4 :** Beta glucans receptors and their nature



Alpha-Beta Technologies conducted a series of human clinical trials in 1990's to evaluate the impact of β-glucan therapy for controlling infections in high-risk surgical patients .A subsequent human clinical trial [66] studied the impact of β-glucan for reducing the incidence of infection with high-risk surgical patients. Cell wall β-glucans were identified as the active component [67], having various effects on the immune system such as anti-tumor activity as well as anti-infective activities that include protection against fungal, bacterial, viral, parasitic and protozoan infections [68, 69, 70, 22, 71]. Schizophyllan (SPG), lentinan, zymosan, and bacterial curdlan all appear effective against several viral agents [72]. SPG controls chronic hepatitis B infections, by modulating both cellular and humoral immune responses [73]. Zymosan from *S. cerevisiae* enhanced the immune response in humans administered the human immunodeficiency virus (HIV) vaccine by stimulating cell-mediated immunity through activation of the complement system and interferon gamma [74] and also decreased viral nucleic acid levels in swine influenza virus infected pigs [75]. Lentinan showed increased CD4 cell numbers in HIV patients suffering no accompanying opportunistic infections [76]. Beta-glucans like lentinan, WGP, PPG, and SSG, are effective against bacterial infections. Lentinan reduced *Mycobacterium tuberculosis* infections by increasing macrophage levels in vivo and in vitro conditions [28, 29]. PPG and WGP have effectively treated mice against *Bacillus anthrax* infections [77]. SSG was tested against *Streptococcus pneumoniae* types 4 and 6B in mice infected experimentally intraperitoneally, it protect the animal against both strains (Table 4).

Liang *et al* [78] proposed that PGG from *Saccharomyces cerevisiae* is effective treatment for *Staphylococcus aureus* infections. PGG act as preventive wound infections, and was more effective in combination with the antibiotic cefazolin than alone [53]. [18, 19] reported that zymosan act by stimulating hepatic macrophages (Kupffer cells) and increasing their sensitivity to LPS, leading to increased TNF-α induced hepatic lesion . All species from the Rhizobiaceae family examined so far have been shown to synthesize cyclic L-glucans [80]. Intramuscular administration of soluble (1, 3) β-glucans to rat challenged with *E.coli* or *S.aureus* reduced bacterial levels in the blood and enhanced survival [78].

Taylor *et al* [81] reported that β-glucans are major components of walls of pathogenic fungi and probably act as important induces of immune responses against them by binding to the dectin-1 receptor. Zymosan β-glucan can protect host cells against *Candida albicans* and *P.carinii* infections [91, 92]. β-glucans can activate phagocytic cells including macrophages, neutrophils and DC to enhance the host's innate response to fungal infections [82]. Cell wall β-glucans of *Pseudomonas carinii* bind to dectin-1 and lac receptors on alveolar epithelial cells to promote innate immune responses.

7.2. **β**-glucan role in the treatment of cholesterol and diabetes

β-glucans from fungi such as *Agaricus blazei* and *Grifola frondosa* have a hypocholesterolemia effect [83]. β-glucans are effective hypoglycemic and hypocholesterolemic agents in human diets [84, 85]. Oat β-D glucan was shown to reduce serum cholesterol level and

attenuate post brandial blood glucose and insulin response in a viscosity related fushion [86, 87]. Oat β-glucans increase bile acid excretion by inhibiting bile acid reabsorption [88].

(1, 3)(1, 4) mixed linkage β-D glucans are polysaccharides which exhibit health benefits such as lowering of blood cholesterol. β-glucans showed anti-hyperglycemic, antihyperitriglyceridemic, anti-hypercholesterolmic and anti arteriosclerotic activity in diabetic rats. It reduces the risk of cardiovascular disease by lowering serum cholesterol and the mediating effect on stabilizing blood glucose and insulin levels in diabetes [89, 90]. Cardiovascular disease related to elevated blood cholesterol levels is still the most common cause of death in humans in western countries. Yeast β-glucans appear to be effective in lowering blood cholesterol but the mechanism is still unclear. Several fungal β-glucan reduce blood glucose level after eating, possibly by delaying stomach emphying so that dietary glucose is absorbed more gradually [121].

7.3. **β**-glucan role in treatment of blood pressure, radiation exposure, septic shock and surgery

In animal experiments, therapy with β-glucans enhances recovery after radiation exposure and results in improvements in bone marrow, spleen and WBC. Intravenous administration of β-glucan to mice exposed to gamma radiation exhibited an enchanced recovery of blood leukocyte, platelet and red blood cells. β-glucan could reverse the myelo-suppression produced with chemotherapeutic drugs such as fluorouracil, carboplatinum or cyclophosphamide [122].

Administration of soluble β-glucan reduces the production of pro-inflammatory cytokines, mainly tumor necrosis factor alpha which reduced mortality [95]. Yeast β-glucan reduces septic shock by killing bacteria in blood. Kaiser *et al* 1998 reported that preventive dosing of yeast glucan prior to infection with *S.aureus* prevented sepsis in guinea pig [96]. β-glucan protects against oxidative organ injury. In pre or post surgical, β-glucan treated mice reduced the production of nuclear factor –kappa B and Interleukin-6, which increased long term survival approximately 40% [31].

8. IMPORTANCE OF **β**-GLUCANS IN CANCER TREATMENT

Lucas and his collaborators first demonstrated the antitumor activity of the higher Basidiomycetes in 1957. Before 50 years, antitumor activity was first demonstrated by animal experiments, remarkable effects of certain fungal β-glucans on the range of tumors [25]. Seven human trials have tried and the datas are still preliminary and controversial. Currently lentinan, PSK and schizophyllan are approved in Japan for human use in cancer treatment. β -glucans appear to beneficially influence both tumor promotion and progression [97].

β-glucan in conjuction with interferon gamma in mouse model inhibited tumors and liver metastasis. In mouse administration of cyclophosphamide with 1, 3 β-glucan from yeast resulted in reduced mortality. In humans advanced gastric or colo-rectal cancer, administration of β-glucans from shiitake mushrooms with chemotheraphy resulted in prolonged survival times. Orally delivered glucan found to increase proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer [123].

Intralesional administration of β-glucans resulted in rapid tumor shrinkage delivered yeast β-glucan with monoclonal antibody therapy increased neuroblastoma tumor regression and long term survival in mice [98, 59]. Harada *et al* [99] reported that some β-glucans amelicrate chemotheraphy and radiation treatment by increasing patient tolerance and speed recovery from toxic effects. The carboxymethylated-sulfated derivative of *Poria coccos,* CS-PCS3-II exhibited significantly higher inhibition ratio to Sarcoma 180 tumor in BALB/c mice than PCS3-II [100].

β-glucans like lentinan and schizophyllan are not effective by oral administration, while SSG from fungus *Sclerotinia sclerotiorum* possess immunomodulating and antitumor activites in mice at high doses (80mg/kg) [101]. β-glucans from *Pleurotus tuber-regium* have different molecular weight, CMHAE- β-glucans have high water solubility and high in vivo and in vitro antitumor activity than the native HAE- β-glucans. In vivo administration of β-D glucan enhanced immunoreactivity unregulated the immunological surveillance and the resistance of host against tumor cells [102].

Falch *et al* [103] reported that two other mushroom β-glucans, schizophyllan and lentinan lost their antitumor activity when their high-order structures were lost as indicated by a decrease in the values of the molecular parameters such as μL, q and Cα as well as α following destruction of the helical compounds. Beneficial effects of β-1, 3 glucans from the cell wall of fungi, such as shiitake, lentinan and SSG on human and animal health antitumor activity [30]. The oral administration of gamma-irradiated β-glucan

significantly increased the proliferation and cytokine (IFN-g and IL-2) release of spleen and Peyer's patch cells compared with non-irradiated β–glucans [104].

Zymosan from yeast β-glucan activate macrophages and stimulate the secretion of inflammatory products, such as tumor necrosis factor α (TNF-α). Lentinan β-D-glucan, as an antitumor polysaccharide has been isolated from fruiting body of *Lentinus edodes* [105]. Antitumor activities may be related to the triple helical structure of the β-glucan backbone chain, schizophyllan [106]. The triple helical structure of the β-glucans has exhibited the inhibition of growth of implanted sarcoma 180 ascites in mice [107].

Han *et al* [108] evaluated the inhibitory effects against lung metastasis and promotion of splenocytes by using water extracts from various mushrooms including *Armillaria mellea, Grifola frondosa, Garnoderma frondosa, Codyceps militaris, Hericium erinaceus, Coriolus versicolor, Agaricus Blazei* with *Lycium Chinense Miller* (known as M8). Oral administration of M8 resulted in a dose-dependent tendency to inhibit lung metastasis after intravenous injection of colon26-L5 cells and significant increase of T cell and B cell mitogenic stimuli and also it showed marked augmentation of mitogenstimulated proliferation of splenocytes. Schizophyllan, one of the β-glucan known to have immunomodulating potential and antitumor activity that has been used clinically as an immunopotentiator against some types of cancer, chiefly leukocytopenia [52].

9. INDUSTRIAL ORIENTED APPLICATIONS OF GLUCANS

Glucans are widely used in many fields of industry as coagulation agents, as immunomodulators in pharmacology and medicine and as cosmetical ingredients. Due to high viscosity of the β-glucans, they are used as thickening agents in sources, salad dressings and in icecream formulation [109]. Oatrim a product containing oat β-glucans and amylodextrins, as well as hydrolyzed oat flow have been proposed as fat mimetics [110]. β-glucans have been used in various reduced fat and soluble fiber enriched foods, mostly in breakfast cereals and snack foods [111].

The addition of cereal β-glucans of food increase the nutritional value of food and improves the quality parameters, in particular the stability during ware housing [62]. β-glucans are used in the manufacture of low fat ice creams and yoghurts [112]. β-glucan incorporation into low fat cheese has beneficial effects on their gelatin and rhelogical characteristics. Addition of β-glucan solution to milk modifies curd and increasing curd yields [113].

Potential use of β-glucans as hydrocolloids in food industry has been proposed based on their rheological characteristics. Fresh cereal β-glucan solutions exhibit a typical visco elastic flow behavior but under certain conditions can form molecular aggregates and network structure [114] that can be controlled by their molecular features.

Sulfated β-glucans shows anticoagulant activity of less than 1% upto 135% [77] and have an anti-thrombotic effect, reducing hemorrhagic risks. β-glucans are therefore used as anticoagulant agents [115]. β-glucans are not desirable for brewing and malting industries [116] or animal feed, especially the broiler industry [117]. Since it causes fillering problems in brewing and forms a viscous solution, also in feed industry especially for monogastric animals. β-glucans are not hydrolyzed in the human digestive tract and hence contribute to no caloric value [54].

10. CONCLUSIONS

β –glucans are appeared to be beneficial to humans for treating different diseases occurred from impaired immune systems and microbial infectious disease and cancer. β –glucans are in helping the patient's recovery from chemotherapy and radiotherapy. Fortunately, in the last fifteen years research in reputed laboratories is focused on β –glucans, it has reached a phase where the basic mechanisms of β –glucans effects are known and the relationship between structure and activity is clearly outlined.

11. REFERENCES

1. Seviour RJ, Stasinopoulos SJ and Auer DPF. Production of pullulan and other exopolysaccharides by filamentous fungi. Critical Reviews in Biotechnology. 1992; 12: 279-298.
2. Klis FM, de Groot P and Hellingwerf K. Molecular organization of the cell wall of Candida albicans. Medical Mycology, 2001; 39: 1-8.
3. Stone BA and Clarke AE. Chemistry and biology of (1, 3) β -glucans. Melbourne, Australia: La Trobe University Press. 1992.
4. Gantner BN, Simmons RM and Underhill DM. Dectin-1 mediates macrophage recognition of Candida albicans yeast but not filaments. The EMBO Journal, 2005; 24: 1277-1286.
5. Brown GD and Gordon S. Immune recognition of fungal β -glucans. Cellular Microbiology, 2005; 7: 471-479.

6. Williams DL. Overview of (1, 3)-beta-D-glucan immunobiology, Mediators Inflamm. 1997; 6: 47-250.
7. Zekovic DB, Kwiatkowski S, Vrvic MM, Jakovljevic D and Moran CA. Natural and modified (1/3) - β -D-glucans in health promotion and disease alleviation. Critical Reviews in Biotechnology, 2005; 25: 205-230.
8. Bohn JA and BeMiller JN. (1, 3)- β -Glucans as biological response modifiers: a review of structure-functional activity relationships. Carbohydr. Polym., 1995; 28: 3–14.
9. Estrada A, Yun CH, Van Kessel A, Li B, Hauta S and Laarveld B. Immunomodulatory activities of oat beta-glucan in vitro and in vivo. Microbiol Immunol., 1997; 41: 991–8.
10. Brown GD and Gordon S. Fungal beta-glucans and mammalian immunity. Immunity, 2003; 19: 311–5.
11. Cui W, Wood PJ, Blackwell B and Nikiforuk J. Physicochemical properties and structural characterization by two-dimensional NMR spectroscopy of wheat β -D-glucans – Comparison with other cereal β -D-glucans. Carbohydrate Polymers, 2000; 41(3) : 249–258.
12. Dais P and Perlin AS. High-field, C-N.M.R. spectroscopy of β -D-glucans, amylopectin, and glycogen. Carbohydrate Research, 1982; 100(1): 103–116.
13. Bacic A and Stone BA. Chemistry and organisation of aleurone cell wall components from wheat and barley. Australian Journal of Plant Physiology, 1981; 8: 475–495.
14. Preece IA and Mackenzie KG. Non-starchy polysaccharides of cereal grains. I. Distribution of water-soluble gum-like material in cereals. Journal of the Institute of Brewing, 1952; 58: 457–464.
15. Adachi Y, Okazaki M, Ohno N and Yadomae T. Enhancement of cytokine production by macrophages stimulated with (1-3)- β -Dglucan Grifolan (GRN), isolated from *Grifola fromdosa*. Biological Pharmacy Bulletin, 1994; 17: 1554–1560.
16. Saito K, Nishijima M and Miyazaki K. Chem. Pharm. Bull., 1990; 38 (6), 1745–1747.
17. Buliga GS, Brandt DA and Fincher GB. The sequence statistics and solution conformation of a barley (1, 3, 1, 4) - β -D-glucan. Carbohydrate Research, 1986; 157(1): 139–156.
18. Sherwood ER, Williams DL, Mc Namer R, Jones E, Browder IW and Di Luzio N. Enhancement of IL-1 and IL-2 production by soluble glucan. Int. J. Immunopharmacol., 1987; 9: 261–267.
19. Lowe EP, Wei D, Rice PJ, Li C, Kalbfleisch J, Browder IW and Williams DL. Human vascular endothelial cells express pattern recognition receptors for fungal glucans which stimulate nuclear factor kB activation and interleukin 8 production. Am. Surg., 2002; 68: 508–517.
20. Brown GD, Herre J, Williams DL, Willment JA, Marshall ASJ and Gordon S. Dectin-1 mediate the biological effects of β glucans. **J** Exp Med., 2003; 197: 1119– 24.
21. Patchen ML and Lotzova E. Modulation of murine hemopoiesis by glucan. Exp Hematol., 1980; 8: 409-22.
22. Young SH, Ye J, Frazer DG, Shi X and Castranova V. Molecular mechanism of tumor necrosis factor-alpha production in 1/3-beta-glucan (zymosan)-activated macrophages. **J** Biol Chem., 2001; 276: 20781-7.
23. Ross GD, Vetvicka V, Yan J, Xia Y, Vetvickova J. Therapeutic intervention with complement and beta-glucan in cancer. Immunopharmacology, 1999; 42: 61-74.
24. Tzianabos AO. Polysaccharide immunomodulators as therapeutic agents: structural aspects and biologic function. Clin Microbiol Rev., 2000; 13: 523-33.
25. McIntosh M, Stone BA and Stanisich VA. Curdlan and other bacterial (1/3) - β-D-glucans. Applied Microbiology and Biotechnology, 2005; 68: 163–173.
26. Brown GD and Gordon S. Immune recognition. A new receptor for β -glucans. Nature, 2001; 413: 36–37.
27. Markova N, Kussovski V, Drandarska I, Nikolaeva S, Georgieva N and Radoucheva T. Protective activity of Lentinan in experimental tuberculosis. International Immunopharmacology, 2003; 3: 1557–1562.
28. Markova N, Michailova L, Kussovski V, Jourdanova M and Radoucheva T. Intranasal application of lentinan enhances bactericidal activity of rat alveolar macrophages against *Mycobacterium tuberculosis*. Pharmazie, 2005; 60: 42–48.
29. Bleicher P and Mackin W. Betafectinw PGG-glucan: a novel carbohydrate immunomodulator with anti-infective

properties. J. Biotechnol. Healthcare, 1995; 2: 207–222.

30. Surenjav U, Zhang L, Xu X, Zhang X and Zeng F. Effects of molecular structure on antitumor activities of (1,3) - β-Dglucans from different *Lentinus Edodes*. Carbohydrate Polymers, 2006; 63: 97–104.
31. Williams DL, Ha T, Li C, Kalbfleisch JH, Laffan JJ and Ferguson DA. Inhibiting early activation of tissue nuclear factor-kB and nuclear factor interleukin 6 with (1, 3)- β-D-glucan increases long-term survival in polymicrobial sepsis. Surgery, 1999; 126: 54– 65.
32. Fruehauf JP, Bonnard GD and Herberman RB. The effect of lentinan on production of interleukin-1 by human monocytes. Immunopharmacol., 1983; 5: 65–74.
33. Dritz SS, Shi J, Kielian TL, Goodband RD, Nelssen JL, Tokach MD, Chengappa MM, Smith JE and Blecha F. Influence of dietary β -glucan on growth performance, nonspecific immunity and resistance to *Streptococcus suis* infection in weanling pigs. J. Anim. Sci. 1995; 73: 3341–3350.
34. Karin M, Delhase M. The I kappa B kinase (IKK) and NF-kappa B: key elements of proinflammatory signalling. Semin Immunol 2000; 12:85–98.
35. Cui W and Wood PJ. In Hydrocolloids, Part 1; Nishinari, K., Ed.; Elsevier: Amsterdam, 2000; 159–168.
36. Behall KM, Scholfield DJ and Hallfrisch J. Lipids significantly reduced by diets containing barley in moderately hypercholesterolemic men. Journal of the American College of Nutrition, 2004; 23: 55–62.
37. Behall KM, Scholfield DJ and Hallfrisch J. Comparison of hormone and glucose responses of overweight women to barley and oats. Journal of the American College of Nutrition, 2005; 24: 182–188.
38. Behall KM, Scholfield DJ and Hallfrisch J. Barley β -glucan reduces plasma glucose and insulin responses compared with resistant starch in men. Nutrition Research, 2006; 26: 644–650.
39. Watkins LO. Epidemiology and burden of cardiovascular disease. Clin Cardiol., 2004; 27: III2–III26.
40. Theuwissen E and Mensink RP. Simultaneous intake of beta-glucan and plant stanol esters affects lipid metabolism in slightly hypercholesterolemic subjects. **J** Nutr., 2007; 137: 583–588.
41. Williams DL, Li C and Ha TModulation of the phosphoinositide 3-kinase pathway alters innate resistance to polymicrobial sepsis. **J** Immunol., 2004; 172: 449–456.
42. Rouhier P, Bruneteau M, and Michel G. Carbohydr. Res., 1995;14 (2): 247–254.
43. Ooi VEC and Liu F. Immunomodulation and anti-cancer activity of polysaccharide–protein complexes. Current Medicinal Chemistry, 2000; 7: 715–729.
44. Campa-Cordova AI, Hernandez-Saavedra NY, De Philippis R and Ascencio F. Generation of superoxide anion and SOD activity in haemocytes and muscle of American white shrimp (*Litopenaeus vannamei*) as a response to beta-glucan and sulphated polysaccharide. Fish Shellfish Immunol., 2002; 12: 353-66.
45. DiLuzio NR, Williams DL, McNamee RB, Edwards BF and Kitahama A. Comparative tumor-inhibitory and antibacterial activity of soluble and particulate glucan. Int. J. Cancer 1979; 24: 773–779.
46. Figueras A, Santare Am, MM, Novoa B. In vitro immunostimulation of turbot (*Scophthalmus maximus*) leucocytes with β -glucans and/or Photobacterium damsela bacterin. Fish Pathol., 1997; 32(3): 153-157.
47. Darvill AG and Albersheim P. Phytoalexins and their elicitor's ± a defence against microbial infections in plants. Ann. Rev. Plant. Physiol., 1984; 35: 243-275.
48. Unestam T and SoÈderhall K. Soluble fragments from fungal cell walls elicit defence reactions in crayfish. Nature, 1977; 267: 45-46.
49. DiLuzio NR. Immunopharmacology of glucan: a broad spectrum enhancer of host defense mechanisms. Trends Pharmacol. Sci., 1983; 4: 344– 347.
50. Shieh MT, WuDunn D, Montgomery RI, Esko JD and Spear PG. J. Cell. Biol., 1992; 116: 1273–1281.
51. Yarchoan RH, Mitsuya H, Myers CE and Broder S. NewEngl. J. Med. 1989; 321: 726–738.
52. Borchers AT, Stern JS, Hackman RM, Keen CL and Gershwin ME. Mushrooms, tumors, and immunity. Proceedings of the Society for Experimental Biology and Medicine, 1999; 221: 281–293.

53. Patchen ML, MacVittie TJ, Solberg BD and Souza LM. Survival enhancement and hemopoietic regeneration following radiation exposure: therapeutic approach using glucan and granulocyte colony-stimulating factor. Exp Hematol., 1990; 18:1042–1048.

54. Morgan K. Cereal β -glucans. In G. O. Phillips, & P. A. Williams (Eds.). Cambridge, UK:Woodhead Publishing Limited. Handbook of hydrocolloids 2000; 287–307.

55. Cisneros RL, Gibson FC and Tzianabos AO. Passive transfer of poly-_1-6. β -glucotriosyl-(1, 3)- β -glucopyranose glucan protection against lethal infection in an animal model of intra-abdominal sepsis**.** Infect. Immun., 1996; 64: 2201–2205.

56. Paulik S, Mojisova JD urove A, Benisek Z and Huska M. The immunomodulatory effect of the soluble fungal glucan *(Pleurotus ostreatus*) on delayed hypersensitivity and phagocytic ability of blood leucocytes in mice. Journal of Veterinary and Medical Biology*,* 1996; 43: 129–135.

57. Bobek P and Galbavy S. Effect of pleuran (β -glucan from *Pleurotus ostreatus*) on the antioxidant status of the organism and on dimethylhydrazine-induced precancerous lesions in rat colon. British Journal of Biomedical Sciences*,* 2001; 58: 164–168.

58. Tao Y, Zhang L and Cheung PCK. Physicochemical properties and antitumor activities of water-soluble native and sulfated hyperbranched mushroom polysaccharides. Carbohydrate Research*,* 2006; 341: 2261–2269.

59. Hong F, Yan J and Baran JT. Mechanism by which orally administered beta-1, 3-glucans enhance the tumoricidal activity of antitumor monoclonal antibodies in murine tumor models. **J** Immunol., 2004; 173: 797–806.

60. Raa J. The use of immunostimulatory substances in fish and shellfish farming. Rev. Fischer. Sci., 1996; 4: 229–288.

61. Vetvicka V, Terayama K, Mandeville R, Brousseau P, Kournikakis B and Ostroff G. Orally administered yeast beta-1, 3-glucan prophylactically protects against anthrax infection and cancer in mice. J. Am. Nutriceutical Assoc., 2002; 5: 1–5.

62. Liu S, Buring JE, Sesso HD, Rimm EB, Willett WC and Manson JE. A prospective study of dietary fiber intake andrisk of cardiovascular disease among women. Journal of the American College of Cardiology, 2005; 70: 613–619.

63. Mohagheghpour N, Dawson M, Hobbs P, Judd A, Winant R, Dousman L, Waldeck N, Hokoma L, Tuse D, Kos F, Benike C and Engleman E. Glucans as immunological adjuvans**.** Immunobiol. Protein Pept., 1995; VIII: 13–22.

64. Angeli JPF *et al.,.* Evaluation of the anti genotoxicity of polyssacharides and beta glucans from *Agaricus blazei* a model study with the single cell gel electrophoresis HepG2. 2009.

65. Babineau TJ, Hackford A, Kenler A, Bistrian B, Forse RA, Fairchild PG, Heard S, Keroack M, Caushaj P and Benotti P. A phase II multicenter, double-blind, randomized, placebo-controlled study of the three dosages of an immunomodulator _PGG-glucan. in high-risk surgical patients. Arch. Surg., 1994; 129: 1204–1210.

66. Di Luzio NR and Riggi SJ. The effects of laminarin, sulfated glucan and oligosaccharides of glucan on reticuloendothelial activity. J. Reticuloendothel. Soc., 1970; 8: 465–473.

67. Cook JA, Holbrook TW and Dougherty WJ. Protective effect of glucan against visceral leishmaniasis in hamsters**.** Infect. Immun., 1982; 37: 1261–1269.

68. Itoh W. Augmentation of protective immune responses against viral infection by oral administration of schizophyllan. Mediators Inflamm., 1997; 6: 267–269.

69. Kokoshis PL, Williams DL, Cook JA and Di Luzio N.R. Increased resistance to *Staphylococcus aureus* infection and enhancement in serum lysozyme activity by glucan. Science, 1978; 199: 1340– 1342.

70. Williams DL. Overview of (1, 3)-beta-D-glucan immunobiology. Mediators Inflamm., 1997; 6: 247–250.

71. Mayell M. Maitake extracts and their therapeutic potential. Alternative Medicine Review, 2001; 6: 48–60.

72. Kakumu S, Ishikawa T, Wakita T, Yoshioka K, Ito Y and Shinagawa T. Effect of sizofiran, a polysaccharide, on interferon gamma, antibody production and lymphocyte proliferation specific for hepatitis B virus antigen in patients with chronic hepatitis B. International Journal of Immunopharmacology, 1991; 13: 969–975.

73. Ara Y, Saito T, Takagi T, Hagiwara E, Miyagi Y, Sugiyama M, Kawamoto S, Ishii N, Yoshida T, Hanashi D, Koshino T, Okada H and Okuda K. Zymosan enhances the immune response to DNA vaccine for human immunodeficiency virus type-1 through the activation of complement system. Immunology, 2001; 103: 98–105.

74. Jung K, Ha Y, Ha SK, Han DU, Kim DW, Moon WK and Chae C. Antiviral effect of *Saccharomyces cerevisiae* β -glucan to swine influenza virus by increased production of interferon-gamma and nitric oxide. Journal of Veterinary Medicine Series **B** Infectious Diseases and Veterinary Public Health, 2004; 51: 72–76.

75. Gordon M, Bihari B, Goosby E, Gorter R, Greco M, Guralnik M, Mimura T, Rudinicki V, Wong R and Kaneko Y. A placebocontrolled trial of the immune modulator, lentinan, in HIV-positive patients: a phase I/II trial. Journal of Medicine, 1998; 29: 305–330.

76. Kournikakis B, Mandeville R, Brousseau P and Ostroff G. Anthrax-protective effects of yeast β 1,3 glucans. Medscape General Medicine, 2003; 5: 1.

77. Liang J, Melican D, Cafro L, Palace G, Fisette L, Armstrong R and Patchen ML. Enhanced clearance of a multiple antibiotic resistant *Staphylococcus aureus* in rats treated with PGG-glucan is associated with increased leukocyte counts and increased neutrophil oxidative burst activity. International Journal of Immunopharmacology, 1998; 20: 595–614.

78. Yamaguchi M, Matsuura M, Kobayashi K, Sasaki H, Yajima T and Kuwata T. Lactoferrin protects against development of hepatitis caused by sensitization of Kupffer cells by lipopolysaccharide. Clinical and Diagnostic Laboratory Immunology, 2001; 8: 1234–1239.

79. Breedveld MW and Miller KJ. Cyclic L-glucans of members of the family Rhizobiaceae. Microbiol. Rev., 1994; 58: 145-161.

80. Taylor PR, Tsoni SV, Willment JA, Dennehy KM, Rosas M,Findon H, Haynes K, Steele C, Botto M, Gordon S and Brown GD. Dectin-1 is required for β -glucan recognition and control of fungal infection. Nature Immunology, 2007; 8: 31–38.

81. Herre J, Gordon S and Brown GD. Dectin-1 and its role in the recognition of beta-glucans by macrophages. Mol Immunol., 2004; 40: 869-76.

82. Kim YW, Kim KH, Choi HJ and Lee DS. Anti-diabetic activity of betaglucans and their enzymatically hydrolyzed oligosaccharides from *Agaricus blazei*. Biotechnol Lett., 2005; 27: 483–487.

83. Wood PJ, Braaten JT, Scott FW, Riedel KD and Wolynetz MS. Effect of dose and modification of viscous properties of oat gum on blood glucose and insulin following an oral glucose load. British Journal of Nutrition, 1994a; 72: 731–743.

84. Newman RK, Newman CW and Graham H. The hypocholesterolemic function of barley b-glucans. Cereal Foods World, 1989; 34: 883–886.

85. Braaten JT, Wood PJ, Scott FW, Wolynetz MS, Lowe MK, Bradley-White P and Collins MW. The effect of oat gum on serum cholesterol levels of hypercholesterolemic subjects. European Journal of Clinical Nutrition, 1994; 48: 465–474.

86. Wood PJ. Oats as a functional food for health—the role of β glucan. Canadian Chemistry News, Nov/Dec, 1997; 17–19.

87. Anderson JW. Cholesterol-lowering effects of soluble fiber in human. In Kritchevsky, & Bonfield (Eds.), Dietary Fiber in health and disease St Paul, MN: Eagan Press, 1995; 126–145.

88. Hecker KD, Meier ML, Newman RK and Newman CW. Barley β-glucan is effective as a hypocholesterolaemic ingredient in foods. **J** Sci Food Ag., 1998; 77: 179–183.

89. Pomeroy S, Tupper R, Cehun Aders M and Nestel P. Oat β- glucan lowers total and LDL-cholesterol. Aust **J** Nutr Diet, 2001; 58: 51.

90. Viriyakosal S, Fierer J, Brown GD and Kirkland TN. Innate immunity to the pathogenic fungus *Coccidioides posadasii* is dependent on toll - like receptor 2 and dectin-1**.** Infection and immunity, 2005; 73: 1553-1560.

91. Hobson RP, Munro CA, Bates S, Mac Callum DM, Cutler JE, Brown GD, Odds FC and Gow NA. Loss of cell wall mannosylphosphate in *Candida albicans* does not influence macrophage recognition. Journal of biological chemistry, 2004; 279: 39628-39635.

92. Ma Z, Wang J and Zhang L. Structure and chain conformation of beta-glucan isolated from *Auricularia auricula-judae*. Biopolymers, 2008; 89: 614–622.

93. Mizuno T. Development of antitumor polysaccharides from mushroom fungi. Thai Food: Finding Ingredients in Japan, 1996; 167: 69–87.

94. Das *et al*., A (1, 6)-beta-glucan from a somatic hybrid of *Pleurotus florida* and *Volvariella volvacea*: isolation, characterization, and study of immunoenhancing properties. Carbohydrate research, 2010; 345: 974–978.

95. Soltes L, Alfoldi J and Sandula J. HPLC and 13C-NMR study of carboxymethyl- β - (1, 6)-D-gluco- β -(1, 3)-D-glucan derived from *Saccharomyces cerevisiae*. J. Appl. Polym. Sci., 1993; 48: 1313–1319.

96. Kaiser AB and Kernodle DS. Synergism between poly-(1, 6) - β - D-glucopyranosyl-(1-3)- β -D-glucopyranose glucan and cefazolin in prophylaxis of Staphylococcal wound infection in a guinea pig model. Antimicrobial Agents and Chemotherapy, 1998; 42: 2449–2451.

97. Nilsson A, Granfeldt Y, Ostman E, Preston T and Bjorck I. Effects of GI and content of indigestible carbohydrates of cereal-based evening meals on glucose tolerance at a subsequent standardized breakfast. Eur **J** Clin Nutr., 2006; 60: 1092–1099.

98. Lin H, De Stanchina E, Zhou XK, She YH, Hoang D, Cheung SW, Cassileth BR and Cunningham-Rundles S. Maitake betaglucan enhances umbilical cord blood stem cell transplantation in the NOD/SCID mouse. Exp Biol Med. (Maywood), 2009; 234: 342–353.

99. Harada T, Masada M, Fujimori K and Maeda I. Production of a film, resilient gel-forming polysaccharide by a mutant of *Alcaligenes faecalis* var myxogenes IOC3. Agricultural and Biological Chemistry, 1966; 30: 196–198.

100. Chen *et al*., Immunopotentiation and anti-tumor activity of carboxymethylated-sulfated β-(1, 3)-D-glucan from *Poria cocos,* International Immunopharmacology, 2009; 10: 398–405.

101. Suzuki I, Hashimoto K, Ohno N, Tanaka H and Yadomae T. Immunomodulation by orally administered β -glucan in mice. Int. J. Immunopharmacol., 1989; 11: 761–769.

102. Kogan G. (1, 3) (1, 6) -β-D-glucans of yeasts and fungi and their biological activity. Studies in natural products (Part D), Amsterdam: Elsevier, 2000; 107–152.

103. Falch, B. H., Espevik, T., Ryan, L., & Stokke, B. T. (2000). The cytokine stimulating activity of (1, 3) - β -D-glucans is dependent on the triple helix conformation. Carbohydrate Research, 329, 587–596.

104. Nak-YunSung , Eui-HongByun , Sun-KyuKwon , Beom-SeokSong , Jong-ilChoi , Jae-HunKim , Myung-WooByun , Young-Choon Yoo , Mee-Ree Kim , Ju-Woon Lee. Immune-enhancing activities of low molecular weight β -glucan depolymerized by gamma irradiation. Radiation Physics and Chemistry, 2009; 78: 433–436.

105. Chihara G, Hamuro J, Maeda YY, Arai Y and Fukuoka F. Fractionation and purification of the polysaccharides with marked antitumor activity, especially Lentinan, from *Lentinus edodes* (Berk.) Sing. (An edible mushroom). Cancer Research, 1970; 30: 2776–2781.

106. Chihara G. Immunopharmacology of Lentinan, a polysaccharides isolated from *Lentinus edodes*. Its application as a host defense potentiator. International Journal of Oriental Medicine, 1992; 17: 57–77.

107. Kulicke WM, Lettau AI and Thielking H. Correlation between immunological activity, molar mass, and molecular structure of different (1, 3) - β-D-glucan. Carbohydrate Research, 1997; 297: 135–143.

108. Han RS, Cho CK, Lee YW and Yoo HS. Antimetastatic and Immunomodulating Effect of Water Extracts From Various Mushroom. **J** Acupunct Meridian Stud., 2009; 2(3): 218–227.

109. Wood PJ. Oat β -glucan: structure, location and properties. In F. H. Webster (Ed.), Oats: Chemistry and technology, 1986; 121–152.

110. Inglett GE. USDA's oatrim replaces fat in many food products. Food Technology, 1990; 44: 100.

111. Cui SW. Polysaccharides gums from agricultural products: Processing, structure and functionality. Lancaster, USA: Technomic Publishing Company Inc., 2001.

112. Brennan CS, Tudorica CM and Kuri V. Soluble and insoluble dietary fibres (non-starch polysaccharides) and their effects on food structure and nutrition. Food Industry Journal, 2002; 5: 261–272.

113. Tudorica CM, Jones E, Kuri V and Brennan CS. The effects of refined barley - β glucan on the physico-structural properties of low-fat dairy products: curd yield, microstructure, texture and rheology.

Journal of Science of Food and Agriculture, 2004; 84: 1159–1169.

114. Lazaridou A and Biliaderis CG. Cryogelation of cereal β -glucans: Structure and molecular size effects. Food Hydrocolloids, 2004; 18: 933–947.

115. Chang CF, Su MS, Chen HY and Liao IC. Dietary beta-1, 3-glucan effectively improves immunity and survival of Penaeus monodon challenged with white spot syndrome virus. Fish Shellfish Immunol., 2003; 15: 297-310.

116. Bamforth CW. Barley β -glucans. Their role in malting and brewing. Brewers Digest, June, 1982; 22–27.

117. Bhatty RS. Nonmalting uses of barley. In: MacGregor AW, Bhatty RS. (Eds.), Barley: Chemistry and Technology. AACC, St. Paul, MN, 1993; 355–417.

118. Julia JV *et al.,* Dietary modulation of immune function by β-glucans. Physiology **&** Behavior, 2008; 94: 276–284.

119. Jiezhong Chen, Robert Seviour, Medicinal Importance of Fungal β -(1/3), (1/6)-glucans, Mycological Research, 2007; 111: 635 – 652.

120. Daniel Man-Yuen and Godfrey Chi-Fung Chan, Supplements for immune enhancement in hematologic malignancies, American Society of Hematology, 2009; 313-319.

121. Li W, Wang Q, Cui SW, Huang X and Kakuda Y. Food Hydrocolloids, 2006; 20: 361–368.

122. Vaikousi H, Biliaderis CG and Izydorczyk MS. Solution flow behavior and gelling properties of water-soluble barley (1-3, 1-4) -β -glucans varying in molecular size. Journal of Cereal Science, 2004; 39: 119–137.

123. Wood PJ. Cereal β -glucans in diet and health. Journal of Cereal Science, 2007; 46: 230–238.

124. Jorg, Hendrik, Ekkehard, Reimund, Hans-Josef A and Helga M. A new colorimetric method to quantify β -1, 3-1, 6-glucans in comparison with total β -1, 3-glucans in edible mushrooms. Food Chemistry, 2011; 127: 791–796.