A review on β-glucan as a Prophetic medicine for health benefit

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Abstract

β-glucan is a type of fiber (can be soluble or insoluble) which is classified as a naturally occurring polysaccharide. It is found in the cell walls of whole grains, seaweeds, mushrooms and yeast. B-glucan is used as medicine and health supplement due to its health benefits as it can stimulate the immune system by modulating humoral and cellular immunity and thereby can help to fight infections caused by bacteria, virus, fungus and parasite. β-glucan also exhibits lipid lowering, hypocholesterolemic and anticoagulant properties. Recently, it has been found that β-glucan is anti-cytotoxic, antimutagenic and anti-tumorogenic. β-glucan is helpful in the diseases like chronic kidney diseases and cardiovascular diseases. These properties of β-glucan make it a promising candidate as a prophetic medicine for promotion of health. In the time of Prophet Muhammad (Peace be upon Him), prophetic medicine was developed. Prophetic medicine is the group of saying and act of prophet (Peace be upon Him) and focused on herbal lore, hygiene, dietary practices, exercise regimens. The present article discusses the evidence supporting the potential uses of β-glucan for health promotion and scope of it to be a prophetic medicine.

Keywords: β-glucan, Lipid lowering agent, hyperlipidemia, Prophetic medicine, Nutraceuticals

Introduction

Foods especially which have been used amongst the ancient society, have become a major interest for the scientist now a days. Therefore investigation has been started for finding the scientific values of the traditional medicinal plant. The evaluation of various properties of the functional foods which have some biologically active molecules is an important part of this kind of investigation. In recent years, whole grains or whole grains products such as beta-glucan have become a major field of research due to their numerous helpful propertiesl for promoting health.

Numerous epidemiological studies indicate that consumption of dietary fiber such as β-glucan can promote health as well as can be used to treat different types of disease (Wiebke & Michael, 2017). Recently, beta-glucan is turning into a licensed drug from non-specific immunomodulator due to its established uses in various disease conditions.

Polysaccharides including glucans have been described as biologically active molecules (Tzianabos, 2000; Ooi et al., 2000; Falch et al., 2000; Han et al., 1999). Certain glucose polymers, such as (1→3), (1→6)- β-glucans were recently proposed as potent immunomodulationg agents (Vaclav et al., 2018; Barsanti et al., 2011; Chan et al., 2009; Brown et al., 2005).

Glucan can be extracted from the cell walls of yeast, oat, barly, seaweeds, algae and bacteria. The foremost source of medical glucans turns out to be fungal cell walls which consist either of polysaccharides such as chitin, cellulose, (1→3), (1→6)- β-glucans and (1→3)-α-glucans or polysaccharide-protein complexes (Yap et al., 2001).

The β-glucans are the most studied polysaccharides and principally obtained from the fruit body of various types of mash rooms.

But as a health promoting factor, oat β-glucan mainly studied by the researcher. For this reason now-a-days oat β-glucan mainly termed as β-glucan. (Daou et al., 2012)

According to some scientific studies it is reported that beta-glucan can produce antitumor, immunomodulating, cardiovascular, antihypercholesterolemia, antiviral, antibacterial, antiparasitic, antifungal and antidiabetic effects (Vetvicka and Vetvickova, 2018; Novak and Vetvicka, 2017; Meng et al., 2016; Vetvicka and Vetvickova, 2015; Sima et al., 2015; Richter et al., 2014; Chen et al., 2013; Chang et al., 2012; Daou et al., 2012; Wasser, 2011; Shomori et al.,

2009; Novak and Vetvicka, 2008; Vaclav et al., 2007; Bedirli et al., 2007). It is also found in some research that beta- glucan have potential effect on chronic kidney disease and cardiovascular diseases (Mohammad et al., 2016; Chen and Raymond, 2017; Daou et al., 2012, Queenan et al., 2007). The receptors of beta-glucan in various cells and the mechanism of action of it have recently been unfolded via in vitro and in vivo animal experiments (Vaclav et al., 2018; Chan, 2007). Therefore, β-glucan may be the best type of soluble fiber for improving health condition though further investigation is needed. As beta-glucan comes mainly from oat or barley or mushroom, it can be considered as a prophetic medicine like honey, black seeds, olive etc. The aim of the current review is to assess all the possible therapeutic properties of beta-glucan.

Beta-glucan: Sources and Properties

There are lots of sources from where beta-glucan can be obtained and isolated.

B-glucan can be obtained from various species of mushrooms such as Reishi, Shiitake and Maitake (Selitrennikoff, 2001; Grun, 2001; Wasser and Weis, 1999).

It can also be obtained from some types of seaweed (Novak and Vetvicka, 2008; Teas, 1983, Black et al., 1951) and cereals (Daou et al., 2012; Basic et al., 2009, Cho, 2001).

In cereals, the content of β-glucan varies with environmental conditions during endosperm development and is regulated by (1 → 3, 1 → 4)-β-glucan endohydrolase to facilitate endosperm cell-wall degradation during germination (Stuart and Fincher, 1987). Among cereals, the highest content (g per 100 g dry weight) of β-glucan has been reported for barley: 2-20 g (water soluble fraction is 65%) and for oats: 3-8 g (water soluble fraction is 82%). Some other cereals also contain β-glucan but in much lower amounts: sorghum 1.1-6.2 g, rye 1.3-2.7 g, maize 0.8-1.7 g, triticale 0.3-1.2 g, wheat 0.5-1.0 g, durum wheat 0.5-0.6 g and rice 0.13 g (Basic et al., 2009).

Table 1: Sources of Beta-glucan.

Source Of B-Glucans	**B-Glucans Structure**
Saccharomyces cerevisiae	B-1,3-glucan
Lentinus edodes	β-1,3;1,6-glucan
Yeast	β-1,3;1,6-glucan
Schizophyllan commune	β-1,3;1,6-glucan

Seaweed	β-1,3;1,6-glucan
Grifola frondosa	β-1,3;1,6-glucan with xylose and mannose
Coriolus versicolor	Protein bound β-1,3;1,6-glucan
Cereals	B-D-glucopyranose units linked through β-1,3;1,4
Ganoderma lucidum	β-1,3;1,6-glucan
Agaricus blazei	Protein bound β-1,6-glucan
Pleurotus ostreatus	β-1,3-glucan with galactose and mannose
Coprinus comatus	β-1,3-glucan

The glucans are D-glucose based polysaccharides. They can be α-D-glucans, β-D-glucans and mixed α,β-D-glucans with their glucose anomeric structure. Glucans can be homoglucans or heteroglucans. Homoglucans are those having only glucose molecules in their structure, when they have any other molecule besides glucose molecule are called heteroglucans (Synytsya et al., 2013).

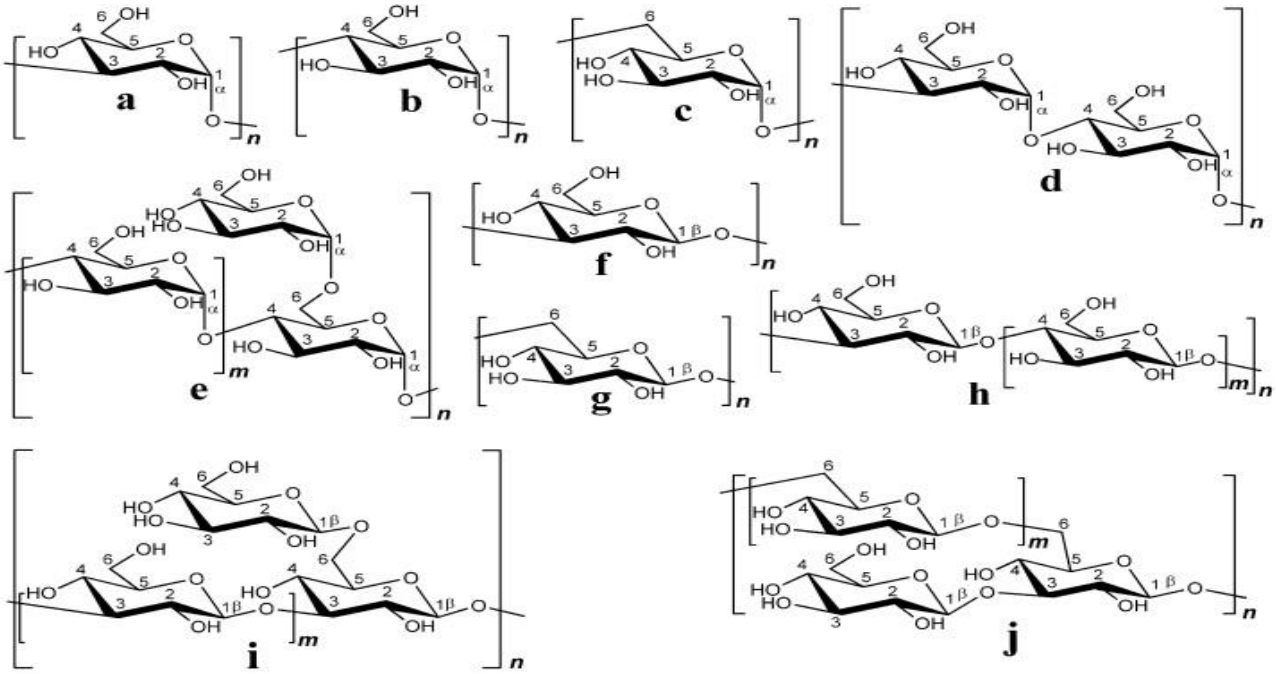

Figure-1 : Structure of Fungal glucans: (a) (1→3)-α-D-glucan; (b) (1→4)-α-D-glucan; (c) (1→6)-α-D-glucan; (d) mixed linkage (1→3), (1→4)-α-D-glucan; (e) branched (1→4), (1→6)-

α-D-glucan; (f) (1→3)-β-D-glucan; (g) (1→6)-β-D-glucan; (h) mixed- linkage (1→3), (1→4)-β-D-glucan; (i) branched (1→3), (1→6)-β-D-glucan; (j) branched (1→6), (1→3)-β-D-glucan.

The β-glucans consist of linear unbranched polysaccharides of β-D-glucose. The basic β-D-glucan is a repeating β-D-glucose units joined together in linear chains by β-bonds. These can be extend either from carbon 1 of one saccharide ring to carbon 3 of the next (β1→3) (Figure- 2) or from carbon 1 to carbon 4 (β→4) or from carbon 1 to carbon 6 (β1→6) (Tzianabos, 2000). The β-D-glucans may have up to 250,000 glucose units (Luca et al., 2013).

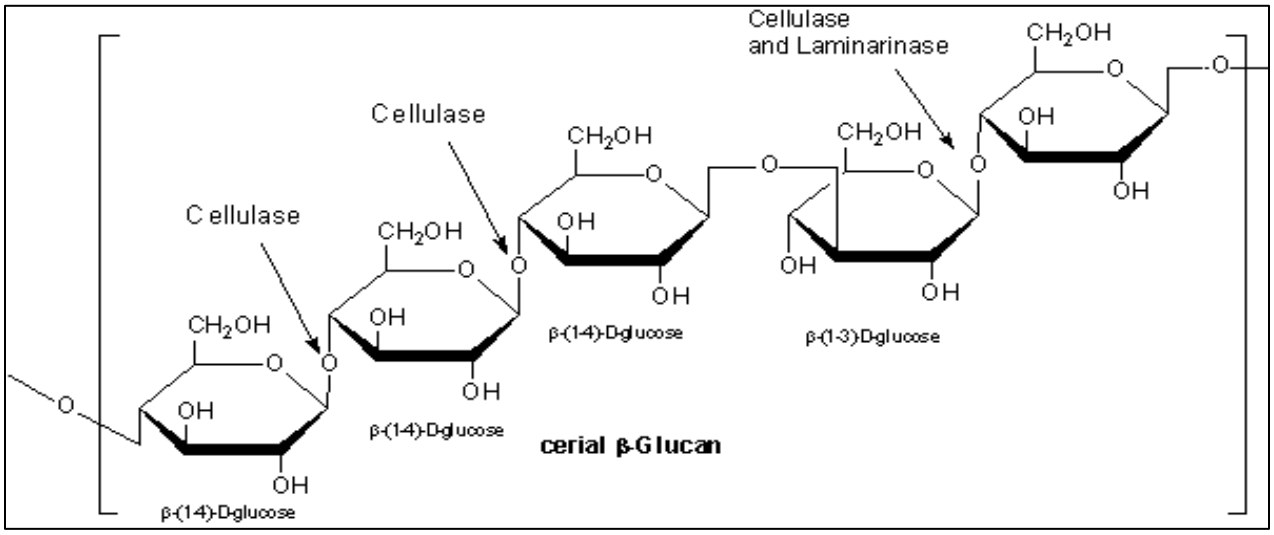

Figure-2: Cereal β-glucan.

Immunostimulatory and wound healing properties of glucans

In the initial studies, it has been found that β-D-glucans increase the resistance of mammalian cells against some pathogens including bacteria, virus, fungus and protozoa (Kaneko et al., 1992). A study compared the effects of soluble oat glucan versus Pleurotan, an insoluble β-D-glucan isolated from the mushroom *Pleurotus ostreatus.* They were administered as a food supplement for athletes. β-D-glucan which is from mushroom significantly reduces the incidence of upper respiratory tract infection whereas Pleurotan increases the number of circulating natural killer cells as well as a preventive effect on the reduction of natural killer cell activity (Majtan J, 2013). In many studies, it has been found that (1→3)-β-D-glucan activates innate immunity with

effects on adaptive immunity inducing humoral and cell-mediated immune responses. They also increase antimicrobial activity of mononuclear cells and neutrophils and enhance the functional activity of macrophages (Chanput et al., 2012; Murphy et al., 2008, Novak & Vetvicka, 2008). The overall effect of β-glucan on Immunity is summarized in the schematic diagram (Figure-3):

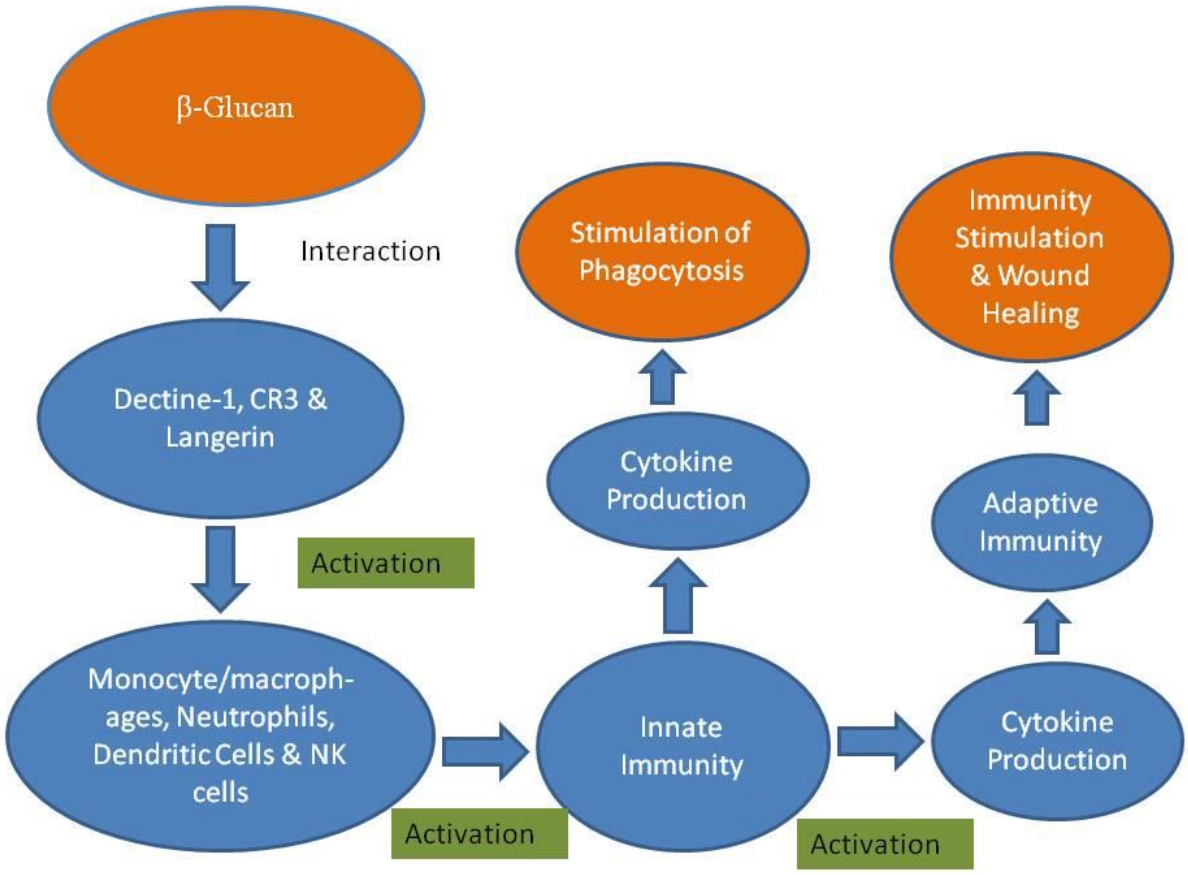

Figure-3: Immunostimulation & Wound Healing Properties of β-glucan. B-glucan interacts with dectin-1, complement receptor type 3 and langerin. These interaction individually activate either or combinely neutrophile, macrophages and natural killer cells. And thus results in stimulation of immunity and wound healing. For the immunostimulating effect of β-glucan, it can be good alternative for antibiotic agents.

Lipid Lowering Properties

Over the past several decades, it has been believed that β-glucan can reduce cholesterol level by its lipid lowering activities but not fully understood.

According to some scientific research, β-glucan has strong cholesterol and triglyceride lowering properties leading to reduced cardiovascular disease. Adding β-glucan in diet reduced LDL (Low density lipoprotein) and total cholesterol without changing HDL (High Density lipoprotein) and triglycerides (Whitehead et al., 2017; AbuMweis et al., 2010).

The main mechanism for β-glucan's lipid lowering effect is thought to be dependent on its ability to entrap whole micelles containing bile acid in the intestinal contents with the luminal membrane transporters on the intestinal epithelium, thereby the absorption or reabsorption of cholesterol decreases (Ellegard et al., 2007; Theuwissen and Mensink, 2008). As a result, hepatic conversion of cholesterol into bile acid increases and hepatic pools of free cholesterol decreases. Along with an increasing synthesis of endogenous cholesterol, the activities of 7α-hydroxylase and HMGCoA reductase increase to compensate for the loses of bile acid and cholesterol from liver. Furthermore, hepatic LDL-cholesterol receptors become unregulated which lead to decreased serum LDL-cholesterol concentration (Jeon and Blacklow 2005; Ellegard et al., 2007). Foretz et al., 2018 described that the energy sensor AMP-activated protein kinase i.e. AMPK phosphorylate and inhibited Acetyl CoA carboxylase (ACC) which results in the inhibition of de novo lipogenesis and stimulation of Fatty acid oxidation (FAO). Finally lowers the Triglycerides content [Figure-4 (a)]. Hypothetical mechanism of Lipid lowering activities of β-glucan is demonstrated in the Figure-4 (b):

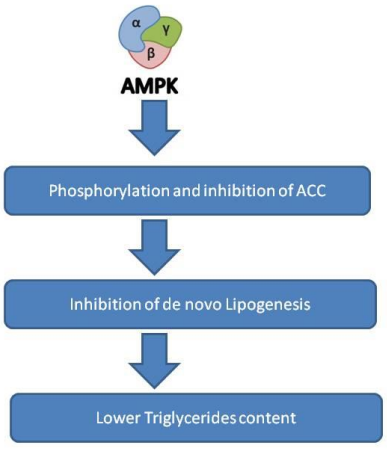

Figure-4 (a): Function of AMPK in lipid lowering.

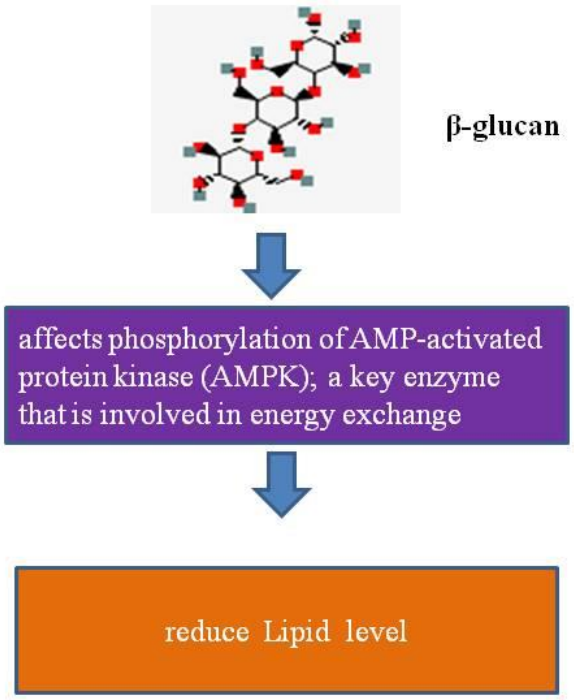

Figure-4 (b): Lipid lowering properties of β-glucan.

Antidiabetic Properties

Fibers are beneficial for the lowering of blood glucose level. B-glucan being a soluble fiber modifies the properties of chime in stomach affecting gastric emptying, gut motility and nutrient absorption with viscous characteristics of it (Behall et al., 2006). It is found that oat β-glucan intake is beneficial in type-2 diabetes (Charles, 2005).

Wood and others (1994, 2000, and 2007) suggested that the reductions in glucose and insulin responses after a meal are mainly due to the viscosity caused by oats. They studied mixtures of oat beta-glucans with different viscosity and there was a highly significant linear relationship between the viscosity and the glucose and insulin responses.

Tapola and others (2005), in their study "glycemic responses of oat bran products in type-2 diabetic patients," also concluded the same when they studied volunteers with type-2 diabetes

fed on oat bran flour, oat bran crisp, and a glucose load providing 12.5 g glycemic carbohydrate and 25 g glucose load alone, and 25 g glucose load with 30 g oat bran flour. In both series oat bran products rapidly lowered postprandial glucose concentrations than after the 12.5 g or 25 g glucose load during the 1st hour, but the glucose concentration was greater at 120 min after the oat bran products ingestion than after the glucose load. This decrease of glucose absorption will decrease insulin release and thereby attenuate pancreatic insulin response. Therefore, oat β-glucan has a greater effect at lowering peak glucose absorption concurrently with an attenuated insulin response, which has a high significance in control and prevention of type-2 diabetes (Hooda and others 2010). It was noted that the area under the plasma glucose curve (AUC) for the postprandial period after ingestion of the oat bran crisp was larger than the AUC after the oat bran flour. This means oat bran flour lowered more rapidly the postprandial glucose response than oat bran crisp. As explanation, the β-glucan content of oat bran flour is higher than oat bran crisp and the authors concluded that oat bran flour being high in β-glucan had a low-glycemic response and acted as an active ingredient, decreasing the postprandial glycemic response of an oral glucose load in subjects with type2-diabetes (Tapola and others 2005). Another test was carried on healthy volunteers who were given 4 different test meals: without added cereal fibers and enriched with 10 g cereal fibers (wheat bran, oat bran, and a combination of 5 g of each). The postprandial glucose and insulin responses were similar as previously (Juvonen and others 2011).

The effect on glucose metabolism of long-term intake of oat beta-glucan has also been investigated. An intake of oat beta-glucan (3 g in muesli) taken for breakfast for 4 wk in men with type 2-diabetes led to a decreased cholesterol level and lower postprandial glucose peaks but no effects on fasting plasma glucose, insulin, and HbA1c were observed (Kabir and others 2002). Researchers have shown that obesity is one of the causes of type 2-diabetes. In the United States of America obesity affects approximately 9 million children over 6 y of age. This dramatic rise in childhood obesity has led to a predicted risk of between 30%–40% for children born in 2000 who will be diagnosed with noninsulindependent diabetes mellitus (NIDDM or Type 2-diabetes) during their lifetime (Koplan and others 2005).Dietary fiber intake helps to decrease the prevalence of obesity. Howarth and others (2001) have reported that an increase in either soluble or insoluble fiber could play a key role in obesity control. Fiber intake increases postmeal satiety and decreases subsequent hunger. Then, the consumption of an additional 14 g/d fiber for

>2 d is associated with a 10% decrease in energy intake and body weight loss of 1.9 kg over 3 mo, and obese individuals may even exhibit a greater suppression of energy intake. Slavin (2005) also reported strong epidemiologic support that dietary fiber intake prevents obesity and that fiber intake is inversely associated with body weight and body fat. The amount of fiber intake by adults that may help to decrease the prevalence of obesity should be >25 g/d (Howarth 2001).

Anti-cancer properties

Several in vitro studies demonstrated that β-glucan has anti-mutagenic effect. B-glucan obtained from barley has protective effect against damage caused by methyl methanesulfonate (MMS), in the CHO-K1 cell line. In this study, β-glucan extracted from *Saccharomyces cerevisiae* was found to have an effect on the cell lines CHO-K1 and CHO-xrs5 in which these cell lines were found protected against damage caused by MMS (Oliveira et al., 2006). This β-glucan was also found to have a protective effect against genotoxicity and cytotoxicity when administered with drugs such as cyclophosphamide, adriamycin and cisplatin. This protective effect may be due to the entrapment of free radicals produced during the biotransformation of these drugs (Tohamy et al., 2003). Along with protective effect, β-glucan has potential anti-oxidant effect as it prevents damage by H_2O_2 and other reactive oxygen species (Krizkova et al., 2006; Slamenova et al., 2003; Angeli et al., 2006).

Some studies have demonstrated that fungal β-glucans can act as chemopreventive agents as they can inhibit isozymes of cytochrome P450 family which are involved in the activation of carcinogens such as benzo [a]pyrene (Hashimoto et al., 2002).

Some studies demonstrate that β-glucans have no direct cytotoxic effects (Chan et al., 2009). One study, it was said that β-glucan only stimulates the proliferation of monocytic lineage leukemic cells in vitro and facilitate the maturation of dendritic cells derived from leukemic cells (Chan et al., 2008).

B-glucan as an anti-oxidant and immunomodulatory agent is much more therapeutically accepted than cytotoxic agent (Sener et al., 2006). B-glucan is believed to increase anticancer activities of monoclonal antibodies in cancer therapy (Cheung et al., 2002).

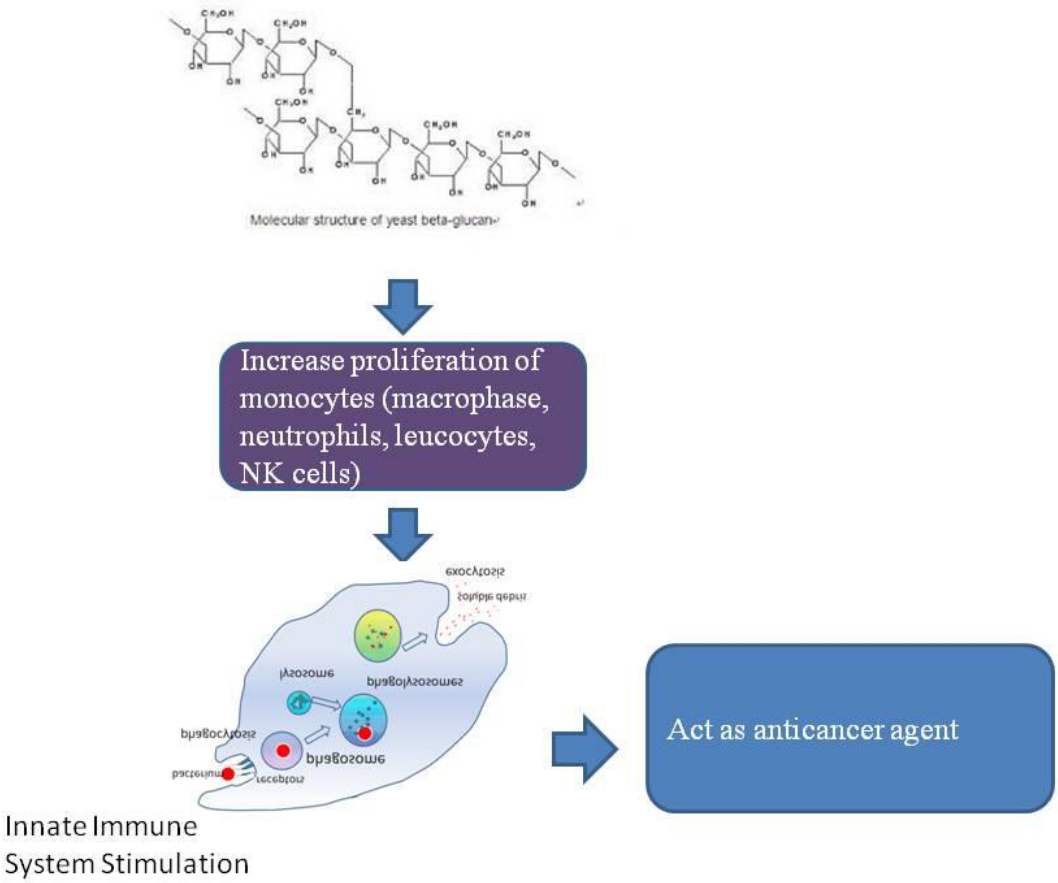

Figure-5: β-glucan as anticancer agent.

Effect on Chronic kidney disease

Some animal studies reported that β-glucan intake has positive effect on kidney function but this effect was not assessed in humans (Rouhani et al., 2016; Esrefoglu et al., 2016). But as β-glucan lower the cholesterol level in the human body, it is be helpful for patients of chronic kidney disease who has gone through hemodialysis. A study has been conducted on it (Liang et al., 2015). On this study, it is concluded that β-glucan improve the inflammatory and malnutrition condition in hemodialysis patient. However, further researches have been suggested to study thoroughly about the effect on overall chronic kidney disease. Another research have demonstrated that β-glucan have positive effect on renal ischemia and reperfusion injury (Esrefoglu et al., 2016). According to that study the mechanism is shown in figure-6.

In where, it is described that as antioxidant agent, β-qglucan reduce the level of IL-6 and IL-8 which are primarily responsible for ischemia.

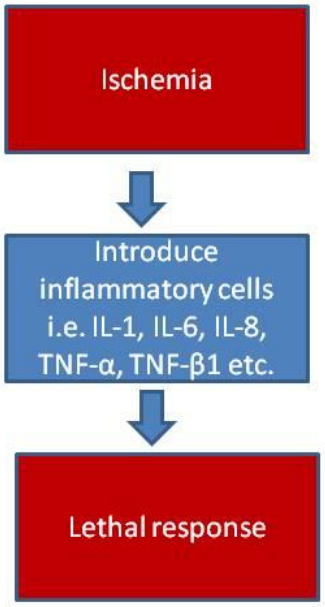

Figure-6 (a): Production of Inflammatory cells by Ischemia followed by reperfusion

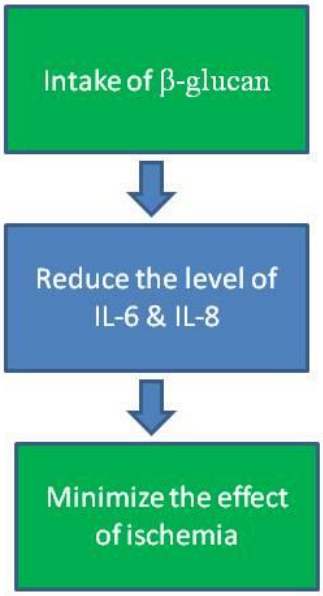

Figure-6 (b): Effect of β-glucan on renal ischemia

Further investigations are required for getting complete data on the effect of β-glucan on chronic kidney disease.

Effect on Cardiovascular diseases

B-glucan reduce the total cholesterol along with LDL cholesterol as a result the occurrences of heart disease reduced by 20% (Medscape news, 2000). It also reduces hypertension (Maki et al., 2007). In many researches, it has been studied experimentally that β-glucan effectively can reduce blood LDL as well as cholesterol and ApoB level. These three factors combinely results in a positive effect on cardiovascular disease as well as hypertension (Hoang et al., 2016).

The brief mechanism of action of β-glucan in reduction of cardiovascular disease is shown below:

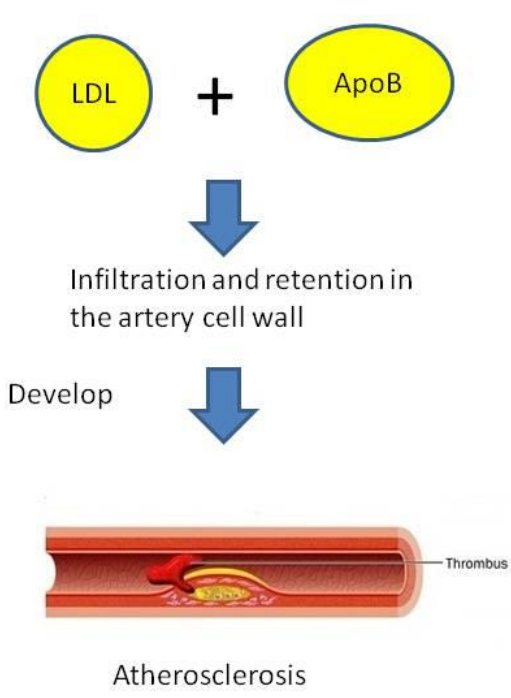

Figure-7 (a): development of Atherosclerosis by LDL and ApoB

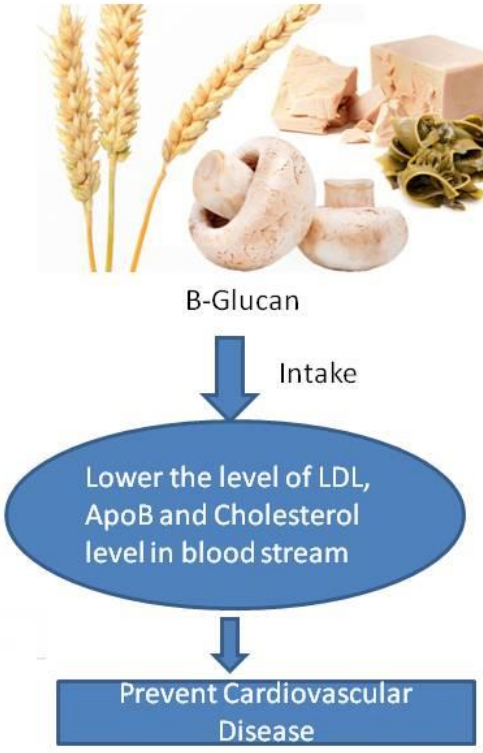

Figure-7 (b): Prevention of Cardiovascular disease by β-glucan

Low Density Lipoprotein (LDL) and Apolipoprotein (ApoB) directly stimulates the atherosclerosis in the coronary artery. Their infiltration and retention in the artery wall results in the inflammation and injury in the artery cell wall and further internalization of Apolipoprotein by macrophages promotes foam cell (hallmark of the fatty steak phase of atherosclerosis) formation. The inflammation of macrophage subsequently results in the formation of stable fibrous barrier i.e. plaque formation in the artery wall (Linton et al., 2019). Intake of β-glucan reduces the LDL cholesterol and ApoB level in the blood thus prevents the incidence of cardiovascular disease.

Conclusion and Potentiality

B-glucan has so many biological activities regardless of its origin. B-glucan have immunostimulating, lipoid lowering, antitumor effect as well as it is very useful in cardiovascular and chronic kidney diseases.

These findings make it as very good candidate as a prophetic medicine. As there is a less amount of data for human trial for all the possible properties of β-glucan, it is very much needful to do much more investigation in human to get more accurate data for future use of β-glucan. It may then be considered as an alternative for chemotherapy as well as antibiotic, antidiabetic and antihypertensive agents.

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