



The Potential of β -Glucan from *Saccharomyces cerevisiae* Cell Wall as Anti Cholesterol

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Abstract | Hypercholesterolemia may cause diabetes in animals and often happens to beloved pets such as Labrador retrievers, Terrier cairns, and Beagles. Treatments for hypercholesterolemia commonly causes side effects. β -glucan is a biologically-derived polysaccharide from sources like extracted *Saccharomyces cerevisiae*. *Saccharomyces cerevisiae* is a valid natural/herbal alternative in reducing cholesterol levels. The safety of β -glucan from *S. cerevisiae* is clear, as it has been considered Generally Recognized As Safe (GRAS) by the Food and Drug Administration (FDA). Extracted *Saccharomyces cerevisiae* may produce up to 85% β -glucan. β -glucan may be developed for treatment of hypercholesterolemia as it has no side effects.

Keywords | β -glucan, *Saccharomyces cerevisiae*, anti-cholesterol

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INTRODUCTION

Cholesterol is an important component as it functions as a precursor for steroid hormone synthesis, bile acid, and vitamin D in humans and in animals (Mumpuni et al., 2011). The presence of cholesterol in the body helps in building cell walls and phospholipid synthesis, a cell membrane component (Fitriarini et al., 2012).

Excess cholesterol with high serum levels for prolonged period of time can cause cholesterol plaque build-up in arteries, thickening and hardening of blood vessel walls which cause obstructions in the blood stream (Damayanti, 2013). Hypercholesterolemia in animals may trigger the development of diabetes (Manens et al., 2012).

Biological compounds are known to produce a reduction in cholesterol level without causing dangerous side effects, one of them being β -glucan (Ardhani et al., 2017; Golomb

et al., 2010; Talati et al., 2009). Microorganism-based materials may be used as an alternative when plant-derived materials that are very reliant on environmental factors and unsupportive weather factors are unavailable. In addition, microorganisms are also easier to control and require less land area, making it more preferable. Microorganisms can also be grown in modified media, its productivity increased, and the extraction process is easier.

β -Glucan is a food fiber with a high molecular weight and viscosity so that it has positive effects in lipid and carbohydrate metabolism (Nazare et al., 2007). β -Glucan acts as an anti-cholesterol by preventing destruction of Low Density Lipoprotein cholesterol through oxidative processes, as an antioxidant by bonding with free radicals (Lee et al., 2001; Miura et al., 2003; Józefowski et al., 2012; Utama et al., 2020).

β -glucan may be produced from several sources such as ce-

reals, algae, bacteria, molds, and currently often produced from the yeast *S. cerevisiae*. *S. cerevisiae* is a known producer of β -glucan. β -Glucan extracted from *S. cerevisiae* has a higher purity compared to β -glucan extracted from molds as they contain more mycelia, unlike β -glucan derived from *S. cerevisiae*, because *S. cerevisiae* contain protein (Young., 2004).

S. cerevisiae also produces the enzyme zymase that is able to break down polysaccharide bonds, sucrose, and fructose into glucose. *S. cerevisiae* has a cell wall structure containing glucose and functions as glycoprotein (Febriyanti et al., 2016; Siwicki et al., 2015). The articles aimed to elaborating the data of the potential of β -glucan from *S. cerevisiae* as an anti-cholesterol.

β -GLUCAN FROM *S. CEREVISIAE* CELL WALLS

β -glucan is a polysaccharide containing D-glucose monomers that bond with β -glycosidic bonds, and according to the Food Drug and Administration (FDA) of United States of America, it is categorized under GRAS (Generally Recognized As Safe), safe for human consumption without toxicity or side effects (Zhu et al., 2016; Ardhani et al., 2017; Leonid., 1998). β -glucan are generally formed by D-glucose molecule chains in positions (1,3) and mostly have branches in positions (1,4) or (1,6) (Appeldoorn et al., 2002).

S. cerevisiae is a form of yeast that plays a big role in fermentation of food products. FDA approved this yeast as GRAS, and has authorized it safe for consumption without side effects. Many researchers are interested in *S. cerevisiae* and its biological potentials, including as a producer of β -glucan (Pengkumsri et al., 2016), (Leentjens et al., 2014).

The safety of *S. cerevisiae* has made it a subject of numerous studies aiming to develop its potential, including as a source of β -glucan. (Liu et al., 2017). β -glucan extracted from *S. cerevisiae* has better yield compared to those extracted from molds, which contain higher number of mycelia compared to β -glucans (Kustiyawati et al., 2016).

The structure of the *S. cerevisiae* cell wall is mostly comprised of glucan polysaccharides with β -1,3-glucan and β -1,6-glucan bonds (Zeković et al., 2005). Its other components include mannoprotein located in the outer cell wall and which binds to β -(1,6)-glucan (Stone., 2009).

β -glucan is the main component of the *S. cerevisiae* cell wall (Figure 1) (Kusmiati et al., 2016). The dry weight of *S. cerevisiae* cell wall is about 10% – 25% of its total cell biomass, wherein that dry weight of the cell wall contains 35% – 40% mannoprotein, 5% - 10% β -1,6 glucan, more than half

or 50% - 55% is made up of β -1,3 glucan, 2% - 14% lipid, and 1% - 2% chitin (Kapteyn et al., 1996), (Appeldoorn et al., 2002). The type of β -glucan in the *S. cerevisiae* cell wall is β -(1,3)-glucan with β -(1,6)-glucan branches. The β -(1,3)-glucan and chitin complex is the main constituent of the inner cell wall, β -(1,6)-glucan connects the inner and outer cell wall components that bound with mannoprotein on the outer surface of the cell wall (Stone., 2009). β -glucan from *S. cerevisiae* consists of the main chain β -(1,3) with β branches bonded in positions O-6 (Figure 2). β -(1,3;1,6)-glucan isolated from *S. cerevisiae* is not water-soluble, as it has low branching values, and is bonded with chitin and several other polysaccharides, making it insoluble in high-temperature alkaline solutions (Synytsya., 2013). The average polymerization of β -(1,3)-glucan yeast is about 1.500 degrees with a molecular mass of 240 kDa, whereas the average polymerization of β -(1,6)-glucan is about 150 degrees with a molecular mass of 24 kDa (Nie et al., 2018).

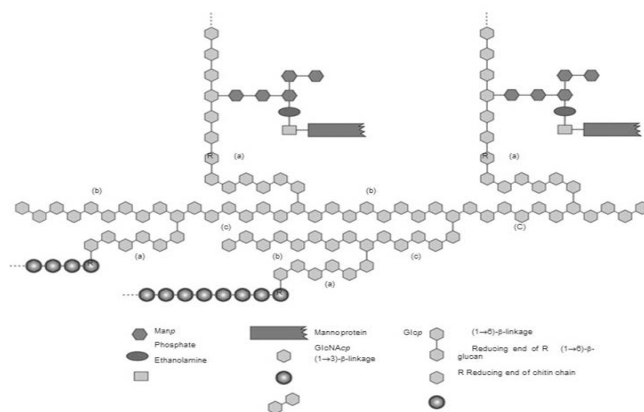


Figure 1: *Saccharomyces cerevisiae* Cell Wall Model
Source: (Stone., 2009)

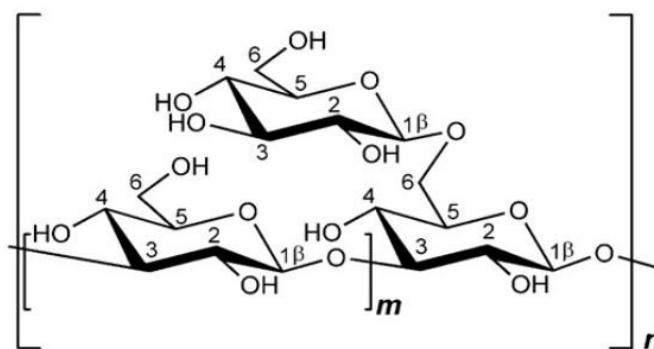


Figure 2: β -(1,3;1,6)-glucan structure
Source: (Synytsya., 2013)

β -glucan from *S. cerevisiae* or plant cell walls has a high molecular weight and branches containing more than 250,000 glucose (Robinson, 1995). β -1,3-glucan has a polymerization degree of about 1500 with a molecular weight of 240,000 and fiber length of 660nm (Lipke and Ovalle, 1998). Administration of β -glucan from *S. cerevisiae* ex

Table 1: The production of β -glucan from *Saccharomyces cerevisiae*

Source	Production Process	Production Time	Amount of β -glucan	Sources
<i>S. cerevisiae</i> strains HII31		72 hour	41.69 %	(Pengkumsri et al., 2016)
<i>S. cerevisiae</i> strains TISTR5003			36.31 %	
<i>S. cerevisiae</i> strains TISTR5024			38.48 %	
<i>S. cerevisiae</i> strains TISTR5051			39.42%	
<i>S. cerevisiae</i> strains TISTR5059	NaOH/HCl extraction		41.24%	
<i>S. cerevisiae</i> strains TISTR5191			38.58%	
<i>S. cerevisiae</i> strains TISTR5197			38.07%	
<i>S. cerevisiae</i> strains TISTR5278			40.07%	
<i>S. cerevisiae</i> strains TISTR5328			38.53%	
<i>S. cerevisiae</i> strains TISTR5623			40.60%	
<i>Saccharomyces cerevisiae</i>	0.25 M KOH and 1.2 M KCl extraction	ND	85%	(Odabasi et al., 2006)
<i>Saccharomyces cerevisiae</i>	NaOH 0.75 M	72 hour	56.48%	(Kusmiati et al., 2007)
<i>Saccharomyces cerevisiae</i>			85-90%	(Andriani, 2007)

traction has a larger effect in the body's immune system compared to β -glucan sourced from wheat (Novak et al., 2008; Vetvicka et al., 2010), (Vetvicka et al., 2006).

Mechanism of β -glucan formation on the cell walls of yeast is through glucose metabolism. Glucose is converted into glucose-6-phosphate, which then produces glucose-1-phosphate because of the enzyme phosphoglucomutase, and is then converted back into uridine diphosphate glucose (UDP-glucose). This UDP-glucose is a component that makes up the yeast cell wall, including β -glucan (Appeldoorn et al., 2002; Diez, 2016). β -glucan in the *S. cerevisiae* cell wall (Figure 1) works as supporting framework for the cell wall to strengthen the cell's structure, also as a food reserve for the cell (Nguyen et al., 1998). Various studies have shown that *S. cerevisiae* is one of many yeasts with potential to produce β -glucan (Table 1).

Another study (Odabasi et al., 2006) reported that *S. cerevisiae* that is extracted contains a supernatant β -glucan up to 2.336 pg/ml. β -glucan with structure β -(1,3)-glucan and β -(1,6)-glucan from *S. cerevisiae*, may produce immunomodulators with positive effects on an animal's immune system (Yalçın et al., 2012; Ortuño et al., 2002)

β -GLUCAN AS AN ANTI-CHOLESTEROL

β -glucan acts as anti-hypercholesterol through mechanisms of reducing cholesterol absorption in the intestines by binding, disturbing enterohepatic circulations, causing an increase in bile acid production from cholesterol, therefore reducing cholesterol levels in the liver and its food fiber components increase excretion of bile acid or neutral lipids, through increased catabolism of Low Density Lipoprotein, and reduces fat absorption (Ferdiansyah., 2018; Mursito et al., 2011). β -glucan regulate 7-alpha-hydroxylase activity, which in turn regulates excretion of bile acid and reduce fat absorption (Yang et al., 2003; Andersson et al., 2002). In other mechanisms, β -glucan form a gel layer in the gastrointestinal tract especially in the small intestine; as in lower concentrations, β -glucan may dissolve water and has high viscosity (Nazare et al., 2007). This increased viscosity delays gastric emptying and reduce glucose and lipid absorption in the small intestine (Lund et al., 1989; Wurscht et al., 1997; Babicek et al., 2007). High viscosity of the intestine may reduce reabsorption of bile acid, increasing excretion of bile acid, causing increased bile acid synthesis and increased Low Density Lipoprotein absorption in the liver (El-Arab et al., 2009).

Table 2: Results of In Vivo Studies of β -glucan as an Anti-cholesterol

Strain	Result	Sources
<i>S. cerevisiae</i>	By consuming 15 grams of β -glucan every day for 7 weeks, may reduce cholesterol levels up to 8% in obese and hypercholesterolemia patients	(Nicolosi et al., 1999)
<i>S. cerevisiae</i>	β -glucan extracted from <i>S. cerevisiae</i> may reduce total cholesterol level up to nearly normal levels with dosages 10 mg 33.71% and 32.79%. Whereas for triglyceride levels with dosages 30 mg β -glucan 19.45% and 10 mg β -glucan 64.43% in blood plasma with reasonable decrease	(Kusmiati et al., 2016)
<i>S. cerevisiae</i>	Consumption of β -glucan from <i>S. cerevisiae</i> isolated from bread yeast for 21 days with a dose of 1 mg/kgBW/day may reduce cholesterol levels in mice blood up 67%.	(Andriani., 2007)

Reduction of cholesterol may also happen as a secondary mechanism from fermentation of β -glucan by large intestinal microflora. Fermentation of β -glucan results in the formation of Short-Chain Fatty Acids (SCFA), mainly acetate, propionate, and butyrate. Propionates are proven to significantly inhibit cholesterol synthesis in the human body by inhibiting HMG-Coenzyme A reductase enzyme activity (Chaiyasut et al., 2018; Ide et al., 1977). Inhibition of the enzymes hydroxylase and reductase which converts HMG-Coenzyme A into mevalonate, will inhibit cholesterol production. This is due to the process of cholesterol production in the liver starting from formation of HMG (Hydroxymethylglutaryl)-Coenzyme A, mevalonate, squalene, lanosterol, until cholesterol is formed (Amaral et al., 1992; Robbins et al., 1995).

Low Density Lipoprotein is the main cholesterol in blood, LDL cholesterol may be oxidized by free radicals (reactive oxygen). In order to prevent LDL cholesterol build-up on blood vessel walls, cholesterol must avoid oxidative processes in the body. Concentrations of cholesterol may be reduced up to 13% and LDL cholesterol plasma level up to 14% in hypercholesterolemia patients undergoing β -glucan therapy (Kirby et al., 1981). High LDL cholesterol content is also a risk factor for coronary heart disease.

Feeding mice with high-fiber diets and added β -glucan from barley significantly increased plasma glucose concentration and reduced cholesterol levels when compared to mice fed low-fiber diets such as corn, flour, and rice (41). High-fiber feed can bind bile acid, free fatty acid, and cholesterol, reducing absorption and increasing fecal excretion (Chau et al., 2005; Cho et al., 2007). Feeding β -glucan on mice may reduce total cholesterol, triglyceride, and malondialdehyde levels up to 42% (Kusmiati et al., 2016). β -glucan from yeast may reduce cholesterol levels in mice and may elicit monocyte and macrophage response (Vetvicka et al., 2009).

By consuming 3 grams/day β -glucan as a part of a low-saturated-fat diet in addition to a healthy life style, it may reduce blood cholesterol (Othman et al., 2011). Male rats from the Wistar breed given feed containing 10% β -glu-

can showed hypocholesterolemic activities (Yoshida et al., 2004). β -glucan produced from extraction of *S. cerevisiae* showed positive activity as a hypocholesterolemic effective in reducing total cholesterol, triglyceride, and repairing lipid metabolism disturbances (Waszkiewicz et al., 2009). β -Glucan exhibited a Biological Defence Mechanism (BDM) with potential to activate the body's immune system through macrophages (Andriani., 2007). β -glucan has an easily-absorbed metabolic property (El khoury et al., 2012) and a great biological activity by reducing cholesterol levels up to 8% in patients with diabetes and obesity by consuming 15 grams/day β -glucan for seven weeks. β -glucan inside the body elicits a positive response, not causing any dangerous side effects for the body's health (Babicek et al., 2007).

CONCLUSIONS

S. cerevisiae is a yeast categorized under GRAS by the FDA, therefore its role in the health sector may be optimized as a producer of β -glucan. Production of β -glucan from *S. cerevisiae* is predicted to increase in the future, considering the plentiful β -glucan contents in cell walls of *S. cerevisiae* and its safety. The safety results of in vivo trials has pushed β -glucan from *S. cerevisiae* to become the subject of numerous studies in optimizing its role as an anti-cholesterol.

Development of β -glucan from *S. cerevisiae* as an anti-cholesterol is met with various challenges such as β -glucan production from *S. cerevisiae* is still prone to contamination, lowering its purity. Even so, with the continuing advancements of technology, it is entirely possible to create and develop a technology to extract β -glucan from *S. cerevisiae* that will produce a heavier molecular weight β -glucan and one that is safer from contamination.

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