NOTE**Effects of Brewer's Yeast Cell Wall on Serum Lipid Levels in Rats Fed a High Cholesterol and Fat Diet****Yoshitaka HITOMI, Michiko YOSHIDA, Tomohiko NAKAMURA and Yoshiharu SHIRASU***Applied Bioresearch Center, Research and Development Department, Kirin Brewery Co., Ltd.**(Miyahara Machi 3, Takasaki, Gunma 370-1295, JAPAN)*

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Abstract: We examined whether brewer's yeast cell wall (BYC) is able to reduce serum lipid levels in rats fed a high cholesterol and fat (HCF) diet. Male Sprague-Dawley rats were fed a standard diet, an HCF diet or an HCF diet containing 2.5% or 5.0% BYC for 14 days. The addition of 5.0% BYC to the HCF diet significantly reduced the increment of serum total cholesterol levels. On the basis of the results obtained, BYC may be utilized as a cholesterol-lowering foodstuff.

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Key words: brewer's, yeast cell wall, dietary fiber, serum cholesterol, foodstuff

The cell wall of yeast is composed mainly of polysaccharides and their complexes with proteins. The principal building units of cell wall polysaccharides in yeast are glucose and mannose, with galactose, xylose, *N*-acetyl-D-glucosamine and uronic acids as the minor components. The proteins in yeast exist in the form of covalent complexes with mannans (1). Brewer's yeast cell wall (BYC) is considered to be an improved foodstuff component consisting mainly of water-insoluble dietary fibers such as β -glucan and α -mannan (1). In addition, mannoprotein in BYC is considered to be a resistant protein (1). It is well known some dietary fibers reduce blood cholesterol and/or triglyceride levels in experimental animals or humans (2). In this study, we investigated the effect of BYC on serum lipid levels in rats fed a high cholesterol and fat (HCF) diet.

BYC was produced from brewer's yeast slurry provided by Kirin Brewery, Shiga Factory (Shiga, Japan). The manufacturing method of BYC was previously reported by Nakamura *et al.* (1). The chemical composition of BYC is shown in **Table 1**. Casein, cornstarch, sucrose, mineral mixture (AIN-93G), vitamin mixture

(AIN-93) and lard were purchased from Oriental Yeast (Tokyo, Japan). Soybean oil and L-cystine were purchased from Nacalai Tesque (Kyoto, Japan). Choline bitartrate, tert-butylhydroquinone, cholesterol and cholic acid were purchased from Wako Pure Chemical Industries (Osaka, Japan).

Four-week-old male rats of the Sprague-Dawley strain were purchased from Charles River Japan (Yokohama, Japan). The rats were housed in stainless steel cages in a room with controlled temperature ($22 \pm 1^\circ\text{C}$) and ambient humidity (45-55%). Lighting was maintained on a 12-h light-dark cycle (lights on from 8:00 a.m. to 8:00 p.m.). The rats were acclimatized by feeding a commercial laboratory chow (CRF-1 powder, Charles River Japan, Yokohama, Japan) for eight days. The rats were allowed free access to their respective diets and water throughout the experimental period. The study was approved by the Ethics Committee of Kirin Brewery Co., Ltd.

After the acclimation period, the rats were individually housed and divided into four groups ($n=8$) on the basis of their body weights ($155 \pm 2.78\text{g}$, $155 \pm 2.61\text{g}$, $156 \pm 2.61\text{g}$ and $155 \pm 1.82\text{g}$, respectively). Each group was fed a standard (STD) diet, a high cholesterol and fat (HCF) diet, an HCF diet containing 2.5% BYC

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Table 1 Composition of Brewer's Yeast Cell Wall.

Component	Composition (%)
Water	1.4
Protein	8.6
Lipid	1.4
Ash	1.2
Dietary fiber ¹	84.8
Nitrogen-free extract ²	2.6

¹ Measured by the Prosky Method (AOAC).

² Calculated as follows: %NFE = 100 - (water + protein + lipid + ash + dietary fiber).

(BYC2.5) or an HCF diet containing 5.0% BYC (BYC5.0) (**Table 2**) for 14 days. The STD diet and the HCF diet did not contain any dietary fibers. Blood samples were collected from the tail veins on days 0, 7, 14 at 3:00 p.m. after six hours of starvation. Serum total cholesterol, HDL-cholesterol and triglyceride levels were measured using commercial kits (Cholesterol E-test, HDL-cholesterol E-test and Triglyceride E-test, Wako Pure Chemical Industries, Osaka, Japan). At the end of the experimental period, the rats were sacrificed. All data were analyzed by one-way ANOVA. Fisher's test of least significant difference was used to determine whether mean values were significantly different at p value of <0.05 .

Table 2 Composition of the Experimental Diets.

Ingredient	STD ³	HCF ⁴	BYC2.5 ⁵ BYC5.0	
			(g/kg diet)	
Cornstarch	579.5	173.5	151.0	128.6
Casein	200.0	200.0	19.78	19.57
Sucrose	100.0	400.0	400.0	400.0
Soybean Oil	70.0	70.0	69.7	69.3
Mineral mixture ¹	35.0	35.0	35.0	35.0
Vitamin mixture ²	10.0	10.0	10.0	10.0
L-Cystine	3.0	3.0	3.0	3.0
Choline bitartrate	2.5	2.5	2.5	2.5
Tert-butylhydroquinone	0.014	0.014	0.014	0.014
Cholesterol		5.0	5.0	5.0
Cholic acid		1.0	1.0	1.0
Lard		100.0	100.0	100.0
BYC			25.0	50.0

¹ Based on the AIN-93G mineral mixture protocol.

² Based on the AIN-93 vitamin mixture protocol.

³ Standard.

⁴ High cholesterol and fat.

⁵ Brewer's yeast cell wall.

Body weight gain and food intake are shown in **Table 3**. The body weight gain did not differ among four groups, however the rats fed a STD diet consumed more diets than rats fed other diets. **Figure 1** shows the time-dependent changes of serum total cholesterol level (a), serum HDL-cholesterol level (b) and serum triglyceride level (c). Serum total cholesterol levels of rats fed the HCF diet were significantly higher than those of rats fed the STD diet on day 7 and 14. The addition of 2.5% BYC to the HCF diet did not affect the serum cholesterol levels, however the addition of 5.0% BYC to the HCF diet significantly reduced serum cholesterol levels on day 14. Since serum HDL-cholesterol levels did not differ between the HCF diet group and BYC5.0 diet group, the reduction of the serum total cholesterol level must be due to LDL+VLDL fraction. Serum triglyceride levels of rats fed the BYC2.5 or BYC5.0 diet were also slightly lower than those of rats fed the HCF diet, but the difference was not significant.

Yeast has been used for food since ancient times and for the production of many kinds of fermented food such as beer, bread and wine. Dried yeast has recently been widely used for producing healthy and nutritious food, and is included in the Japanese Pharmacopoeia (1). Many studies on health-promoting effects of yeast have been carried out, and in those studies the blood-cholesterol-lowering effect has been reported (3,4). Furthermore, those studies have shown that some yeast fractions (3,4), including the cell wall fraction and β -glucans from the yeast cell wall (5), reduced blood cholesterol in rats (3,4) and humans (5). In this study,

Table 3 Comparison of the Body Weight Gain and Food Intake.¹

Group	Body weight gain	Food intake
	(g/14d)	(g/14d)
STD ²	122 $\pm$ 6.26	321 $\pm$ 11.4 ^b
HCF ³	129 $\pm$ 3.80	282 $\pm$ 4.93 ^a
BYC2.5 ⁴	123 $\pm$ 6.03	272 $\pm$ 7.65 ^a
BYC5.0	118 $\pm$ 4.31	271 $\pm$ 5.01 ^a

¹ Values are means $\pm$ SEM (n=8). Within a column, values with different superscripts are significantly different ($p<0.05$). Statistical comparisons were made with Fisher's least significant difference test.

² Standard.

³ High cholesterol and fat.

⁴ Brewer's yeast cell wall.

Fig. 1 Effect of Brewer's Yeast Cell Wall on Serum Total-Cholesterol (a), HDL-Cholesterol (b) and Triglyceride (c) Levels. Data are means $\pm$ SEM (n=8). Values not sharing a common letter at the same time point are significantly different ($p < 0.05$). Statistical comparisons were made with Fisher's least significant difference test. STD, standard diet; HCF, high cholesterol and fat; BYC2.5, HCF diet containing 2.5% brewer's yeast cell wall; BYC5.0, HCF diet containing 5.0% brewer's yeast cell wall.

we found the serum-cholesterol-lowering effect of BYC produced by the newly improved method (1). Previously, Nakamura *et al.* reported that BYC alleviated constipation in experimental model rats (1) and BYC added to yogurt improved defecation frequency in healthy female volunteers (6), because of the high content of

dietary fibers in BYC. Therefore, BYC may be utilized in the design of functional food that possesses not only defecation-frequency-improving effect but also cholesterol-lowering effect.

In generally, the mechanism of blood cholesterol-lowering effect of dietary fiber is not fully understood,

however the following mechanisms were proposed. First, dietary fibers inhibit dietary cholesterol absorption in the gastrointestinal tract (2,7). Second, dietary fibers bind to bile acids and inhibit the re-absorption of the bile acid in the intestine, thereby reducing the hepatic bile acid pool and subsequently reducing blood cholesterol levels (7). Third, dietary fibers are fermented in the large intestine by microorganisms to produce short-chain fatty acids (SCFAs), such as acetate, propionate and butyrate, and the SCFAs mediate the blood cholesterol-lowering effect (7-9). Hara *et al.* showed that ingestion of SCFAs lowered plasma cholesterol levels (8) and reduced cholesterol synthesis in the liver and the intestine (9). The mechanisms by which BYC reduce the increment of serum cholesterol levels are still unknown. However, Nakamura *et al.* reported that dietary BYC increases intestinal SCFAs in rats (1) and healthy volunteers (6); therefore, the increased SCFAs might participate in the reduction of serum cholesterol levels.

In this study, we found that BYC reduced the increment of serum total cholesterol levels in rats fed a high cholesterol and fat diet. We must investigate further by which mechanisms BYC exhibits the serum-cholesterol-lowering effect, and whether BYC is effective or not in humans.

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