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ORIGINAL ARTICLE

Fermentation characteristics and hypoglycemic activity of an exopolysaccharide produced by submerged culture of *Stropharia rugosoannulata* #2

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Abstract We have investigated the mycelial growth and extracellular polysaccharide (EPS) production of *Stropharia rugosoannulata* #2 under optimal culture conditions in a 5-L stirred-tank fermenter. Maximum biomass growth (16.35 g/L) was achieved after 5 days of cultivation, whereas EPS reached its maximum level (10.83 g/L) after 8 days. The morphological parameters (i.e., mean diameter, circularity, roughness, compactness) of the fungal pellets and broth viscosity were also characterized. The compactness of the pellets was determined to be significantly and positively correlated with EPS content. The hypoglycemic effect of the polysaccharide, investigated in streptozotocin-induced diabetic rats, included decreases in the plasma concentrations of glucose (37 %), total cholesterol (26 %), and triacylglycerol (24 %) and decreased aspartate aminotransferase activity (20 %). The results indicate the potential of this polysaccharide to prevent hyperglycemia in diabetic patients.

Keywords Exopolysaccharides · *Stropharia rugosoannulata* #2 · Submerged culture · Hypoglycemic effect · Mycelia

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Introduction

In recent years, submerged fermentation of medicinal mushrooms has received great interest as a promising technique for the efficient production of intracellular polysaccharides (IPS) isolated from mycelia and exopolysaccharides (EPS) and other active products. The different polysaccharides extracted from the fruiting-bodies, mycelia, or fermentation broth of medicinal mushrooms have been extensively studied and are currently being marketed as commercial drugs and health supplements due to their antitumor, antioxidant, hypolipidemic, and hypoglycemic activities and other biological activities (Chihara et al. 1970; Hwang et al. 2005; Wasser 2010; Zheng et al. 2011).

The morphology of filamentous microorganisms in submerged culture has been shown to play a critical role in industrial fermentation (Gibbs and Seviour 1996). Many investigators have characterized the mycelial pellets and found that mycelial morphology is influenced by the physicochemical conditions, including growth medium, culture pH, and temperature, among others, during mycelial cultivation (Riscaldati et al. 2000). Alternatively, the mycelial morphology markedly affects yields in terms of mycelial growth and the desired product (Sinha et al. 2001). Park et al. (2002) reported that the compactness of the pellets of *Cordyceps militaris* was the most critical parameter affecting EPS biosynthesis, and Tepwong et al. (2011) observed that the morphology of the mycelial pellets, particularly mean diameter, was highly positively correlated with ergothioneine accumulation throughout the fermentation period of *Lentinula edodes*. However, to the best of our knowledge, there is little information available on the relationship between morphological parameters and productivity of fermentation products.

The fungus *Stropharia rugosoannulata* is one of the best known mushrooms grown commercially, with a pleasant refreshing, slightly sweet taste accompanied by a delicate fragrance and a crisp texture (Balazs 1974; Szudyga 1978; Huang 1995). *S. rugosoannulata* also has a beneficial effect on hyperglycemia, coronary heart disease, solid tumor S-180, ascites cancer, among others (Shang and Wang 1999; Noriko et al. 2003; Yan et al. 2004). Although we investigated the optimal culture conditions of *S. rugosoannulata* #2 in terms of EPS production in a previous study (He et al. 2012), the possible relationship between changes in physical parameters (i.e., mycelial morphology and broth viscosity) and changes in biomass and EPS production during fermentation remain to be investigated. In the study reported here, we also studied the hypoglycemic effect of EPS in male Sprague-Dawley rats.

Materials and methods

Microorganism and growth conditions

Stropharia rugosoannulata #2 was kindly provided by Prof. Xinsheng He of the School of Life and Engineering, Southwest University of Science and Technology, Mianyang, Sichuan Province, China. It was originally isolated in a mountainous district in Sichuan Province, then authenticated and preserved at the Henan Province Microbiological Culture Collection Center (HPMCC no. 197873). Stock cultures are maintained on potato dextrose agar (PDA) slants that are incubated at 26 °C for 8 days and then stored at 4 °C, with sub-culture at 1-month intervals. For our study, the seed culture was grown in a 250-mL flask containing 50 ml of glucose–peptone medium (0.3 % peptone, 3 % glucose) at 26 °C on a rotary shaker incubator (150 revolutions/min) for 4 days. *S. rugosoannulata* #2 was initially grown on PDA medium in a petri dish and then transferred into the seed medium by punching out 5-mm discs of the agar plate culture with a self-designed cutter (Park et al. 2001).

Bioreactor fermentation

The fermentation medium was inoculated with 4 % (v/v) of the seed culture and the inoculated medium was cultivated in a 5-L stirred-tank fermenter (Infors AG, Bottmingen, Switzerland). Unless otherwise specified, fermentations were performed under the following optimized conditions (He et al. 2012): 60.0 g/L sucrose, 6.0 g/L tryptone, 5 mM KH_2PO_4, and an initial pH of 7.0 (adjusted by addition of 1.0 M NaOH or HCl), 28 °C, an agitation speed of 150 rpm, a working volume of 3 L, and a cultivation time of 13 days. All experiments were performed in triplicate to ensure the trends observed were reproducible.

Mycelial dry weight and EPS quantification

Samples collected periodically from the bioreactor were centrifuged at 9,000 *g* for 15 min, and the resulting supernatant was filtered through a membrane filter (0.45 μm, Millipore, Billerica, MA). The dry weight of mycelium was measured after repeated washing of the mycelial pellet with distilled water and drying at 70 °C overnight so as to obtain a constant weight. The resulting culture filtrate was mixed with fourfold its volume of absolute ethanol, stirred vigorously, and kept overnight at 4 °C. The precipitated EPS was centrifuged at 11,000*g* for 15 min and the supernatant discarded (Bae et al. 2000). The precipitate of pure EPS was redissolved in distilled water, and the concentration of the EPS was determined by the phenol–sulfuric acid method (Dubois et al. 1956). For a quantitative measurement of glucose, the filtrate from the membrane filtration was analyzed by high-performance liquid chromatography (Waters, Milford, MA) using a Sugar-Pak column (300×6.5 mm; Waters Co.) equipped with an evaporative light scattering detector (Alltech Associates, Deefield, IL).

Viscosity and morphology measurements

The viscosity of the culture broth (prior to removal of mycelial biomass) was measured on samples collected from the bioreactor at regular intervals using a Brookfield programmable LVD-VII+ digital viscometer (Benelux Scientific BV, Ochten, the Netherlands) fitted with a small sample adapter. The morphological properties of the samples collected were evaluated using an image analyzer (DT2000 System; China) with software linked to a light microscope (Nikon, Tokyo, Japan) through a CCD camera. Samples were fixed with an equal volume of fixative (13 mL of 40 % formaldehyde, 5 mL glacial acetic acid, 200 mL of 50 % ethanol). An aliquot (0.1 mL) of each fixed sample was transferred to a slide, air dried, and then stained with methylene blue (0.3 g of methylene blue, 30 ml of 95 % ethanol in 100 mL water). For each sample, the morphology of the pellet was characterized by measuring the area and perimeter of the pellet core and the maximum diameter of the pellet. Normally, a 40-fold magnification was used. The morphology of the pellets was characterized by their mean diameter, circularity, roughness, and compactness. The circularity was estimated as the ratio of the Fieret's minimum diameter to the Fieret's maximum diameter of the pellets or aggregates. The compactness was estimated as the ratio of the projected area of the hyphae in a clump to the projected convex area of that clump, the latter being the area after filling internal voids and concavities in the clump's external perimeter. In addition, the roughness (R) was measured using the following equation: $R = (\text{pellet/aggregate perimeter})\, 2/(4\pi \times \text{pellet area})$.

Animal experiments and induction of diabetes

Sprague–Dawley male rats (5 weeks of age) obtained from the Henan Experimental Animal Center (Zhengzhou, China) were housed in individual stainless steel cages and acclimatized with free access to food and water for at least 1 week in an air-conditioned room (23±2 °C with 55±5 % humidity) under a 12/12-h light/dark cycle. The rats were fed with a commercial pellet diet (Henan Experimental Animal Center) throughout the experimental period.

Rats were adapted for 7 days in the growth room and fasted for 12 h. Diabetes was induced by intramuscular injection of streptozotocin (Sigma Chemical Co., St. Louis, MO) dissolved in 0.1 M sodium citrate buffer (pH 4.5) at a dose of 50 mg/kg body weight (Bolkenta et al. 2000; Kim et al. 2001). Two days after injection of the diabetogenic agent (streptozotocin, STZ), fasting blood glucose was determined and rats with a blood glucose level of >300 mg/dL were included in the group of diabetics. All procedures were conducted in accordance with the "Guide for the Care and Use of Laboratory Animals" approved by Zhengzhou University of Light Industry.

Animal experimental design and analytical measurements

All animals were randomly divided into five groups of eight animals each (Table 1). The normal group consisted of normal rats which received 0.9 % NaCl solution; the control group comprised STZ-induced diabetic rats treated with 0.9 % NaCl solution; the diabetic low-treated group (L) comprised diabetic rats treated with *S. rugosoannulata* EPS at 50 mg/kg body weight; the diabetic middle-treated group (M) comprised diabetic rats treated with *S. rugosoannulata* EPS at 100 mg/kg body weight; the diabetic high-treated group (H) comprised diabetic rats treated with *S. rugosoannulata* EPS at 200 mg/kg body weight. All injections were made daily for 3 weeks using an oral zonde needle.

Table 1 Experimental groups for testing the dose-dependent hypoglycemic activity of *Stropharia rugosoannulata* extracellular polysaccharides

Group	Oral administration
Normal[a]	None
Control[b]	0.9 % NaCl
Low-treated (L)[b]	50 mg/kg day *S. rugosoannulata* EPS
Medium-treated (M)[b]	100 mg/kg day *S. rugosoannulata* EPS
Hight-treated (H)[b]	200 mg/kg day *S. rugosoannulata* EPS

EPS, Extracellular polysaccharide

[a] Group of 8 normal rats

[b] Rats in which diabetics had been induced by streptozotocin injections (50 mg/kg body weight). Each group consisted of 8 rats. The rats were administered daily doses of either saline (control) or EPS produced from the submerged mycelial culture of *S. rugosoannulata* at 50–200 mg/kg body weight daily for 3 weeks

The body weight gain and food intake were periodically measured. Blood samples of the experimental animals were collected in heparinized tubes, and plasma was separated by centrifugation at 1,100 *g* for 10 min. Each organ was isolated and weighed after washing with 0.9 % NaCl. The plasma glucose level was measured using a glucose oxidase kit (Biosino Bio-technology and Science Inc., Beijing, China). Total cholesterol and triglyceride levels were measured using a CHOD-PAP method (Biosino Bio-technology and Science Inc.) (Henry 1974). The activities of alanine aminotransferase (ALT) and asparate aminotransferase (AST) were determined by using enzyme kits (Biosino Bio-technology and Science Inc.) based on an ultraviolet rate assay (Lum and Gambino 1972). High-density lipoprotein (HDL)-cholesterol levels were determined using enzymatic test kits (Biosino Bio-technology and Science Inc.) with polyethylene glycol-modified enzymes (Okada et al. 2001). Low-density lipoprotein (LDL) cholesterol and the atherogenic index (AI) were calculated by the following equations:

$$\text{LDL cholesterol} = \text{total cholesterol} - \text{HDL cholesterol} - (\text{triglyceride}/5)$$

$$\text{AI} = (\text{total cholesterol} - \text{HDL cholesterol})/\text{HDL cholesterol}$$

Statistical analysis

Data were expressed as the mean ± standard deviation (SD). The results were analyzed for statistical significance by one-way analysis of variance (ANOVA) test using the Statistical Package of the Social Science (SPSS) ver. 11.0 (SPSS, Chicago, IL). Group means were considered to be significantly different at $P<0.05$, as determined by the technique of protective least-significant difference (LSD). The Pearson coefficient analysis was used to analyze the coefficient of determination (R^2) and evaluate the relationship between EPS content and mean diameter, roughness, circularity, and roughness of the mycelium.

Results and discussion

Fermentation results in a stirred-tank reactor

The typical time courses of mycelial growth and the yield of EPS in a 5-L stirred-tank bioreactor under optimal culture conditions for the yield of EPS are shown in Fig. 1. Maximal yield of EPS was 10.83 g/L after 8 days of

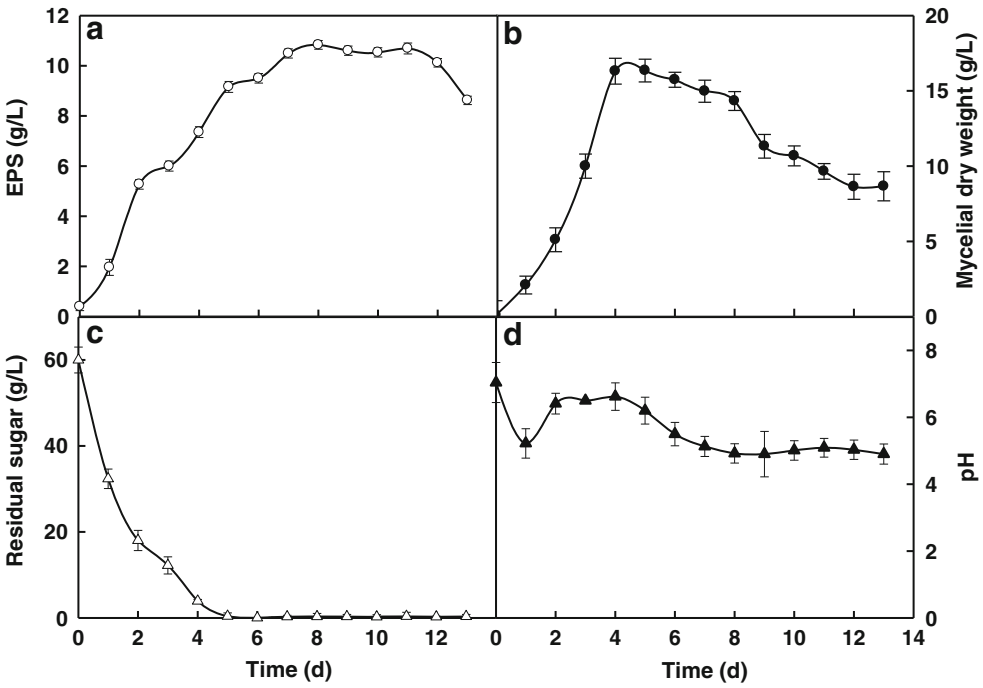

Fig 1 Time profiles of extracellular polysaccharide (EPS) (**a**), mycelial biomass (**b**), residual sugar (**c**), and pH (**d**) in submerged culture of *Stropharia rugosoannulata* #2 in a stirred-tank fermenter

fermentation (Fig. 1a), and maximum mycelial yield was 16.35 g/L after 5 days (Fig. 1b). As expected, the concentration of residual sugars decreased as the fermentation progressed, with corresponding increases in biomass and EPS production (Fig. 1c). However, no drastic change in pH value was recorded during the course of fermentation (Fig. 1d).

Characterization of broth viscosity and mycelial morphology

The apparent viscosity of the whole broth according to the length of the fermentation period is depicted in Fig. 2. After day 2, the viscosity of the fermentation broth at 300 rpm increased rapidly as the mycelial cells entered their exponential growth. This trend continued up to day 4 (55.92 mPa·S), when the mushroom culture entered its stationary phase, and the viscosity of the broth, which was proportional to the biomass concentration, declined accordingly. It should noted that mycelial biomass is also a desired product in most fermentation processes of higher fungi because many groups of bioactive intracellular polysaccharides are major constituents of mycelial biomass. Figure 3 shows the typical morphological changes that occurred during the entire fermentation period (0–13 days). The hyphae were observed to form primarily pellets during the entire culture period. Pellet diameter increased rapidly during the fermentation period, and the outer hairy regions of the pellets became fluffier over time, but as the fermentation processed, especially by day 13, the outer hairy region of the pellets had been lost. Figure 4 shows the mean diameter (Fig. 4a), circularity (Fig. 4b), roughness (Fig. 4c), and compactness (Fig. 4d) of the pellets during the cultivation of *S. rugosoannulata*. The mean diameter and compactness of the pellets increased during the first 5 and 8 days of fermentation, respectively, and then oscillated. In contrast, there were no drastic changes in circularity and roughness during the fermentation period. Further investigation of EPS accumulation in the mycelial pellets during the first 6 days of the fermentation period revealed that broth viscosity (R^2=0.950, P<0.05) was significantly positively correlated with mycelial biomass; moreover, pellet morphology, i.e., compactness (R^2=0.926, P<0.01), was significantly positively correlated with EPS content. These results clearly demonstrate that the changes in viscosity of the fermentation broth and in the morphology of the mycelia coincided with fungal biomass and EPS production, respectively. Park et al. (2002) also reported that the compactness of the pelleted form

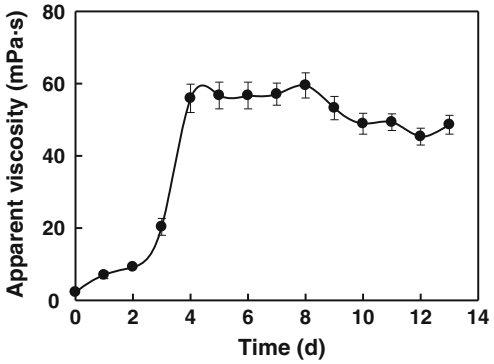

Fig 2 Time profile of the apparent viscosity of the fermentation broth of *S. rugosoannulata* #2 in a stirred-tank fermenter

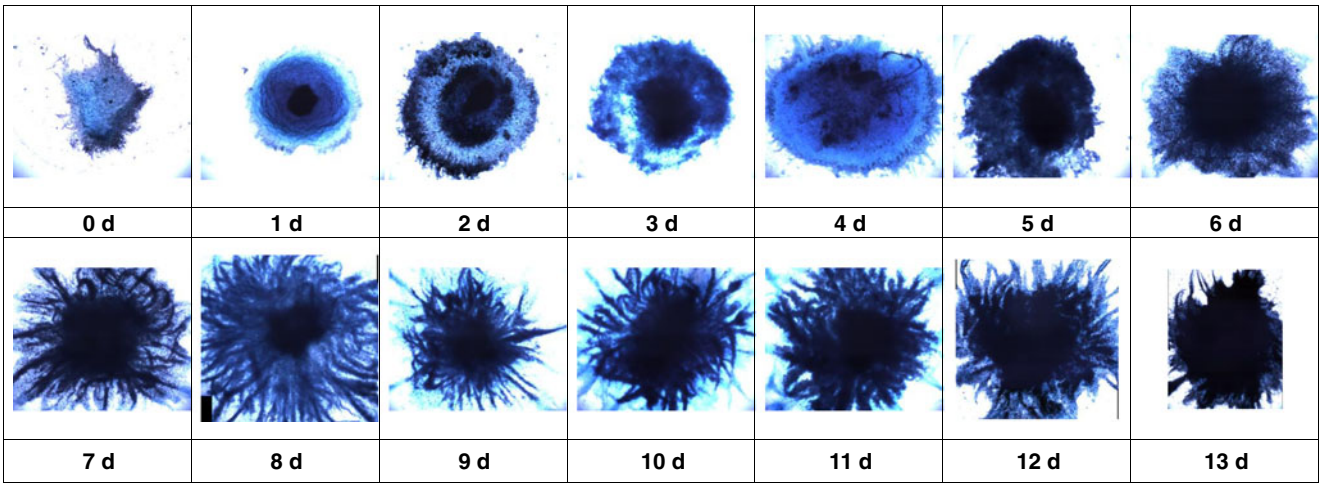

Fig 3 Morphological changes in *S. rugosoannulata* #2 in a 5-L batch reactor. Representative images were taken at 40-fold magnification. *d* Length of the fermentation period in days

of *Cordyceps militaris* was related to EPS production. It is interesting to note that the relationship between other physical parameters and metabolic products is nonlinear or incomprehensible due to the complicated fermentation process.

Hypoglycemic effect of EPS

We have already reported that EPS from *S. rugosoannulata* #2 exhibits high antitumor and antioxidative effects (He et al. 2012). In this study, the hypoglycemic effects of EPS from *S. rugosoannulata* #2 in STZ-induced diabetic rats were compared to those of saline injections in control rats. STZ-induced hyperglycemia has been described as a very useful experimental model for investigating the activity of hypoglycemic agents (Junod et al. 1969). In such models, STZ-induced diabetic rats generally lose weight and reduce their food intake; in addition, they tend to overeat, a behavior which recovers when they are given hypoglycemic treatment (Furuse et al. 1993).

The body weight gain, food intake, and food efficiency ratio after oral administration of EPS in STZ-induced diabetic rats are presented in Table 2. Diabetic rats underwent a significant weight loss, while the treatment with EPS in the treated diabetic group resulted in a remarkable improvement in their body weight. The ability of the EPS to protect the rats from body weight

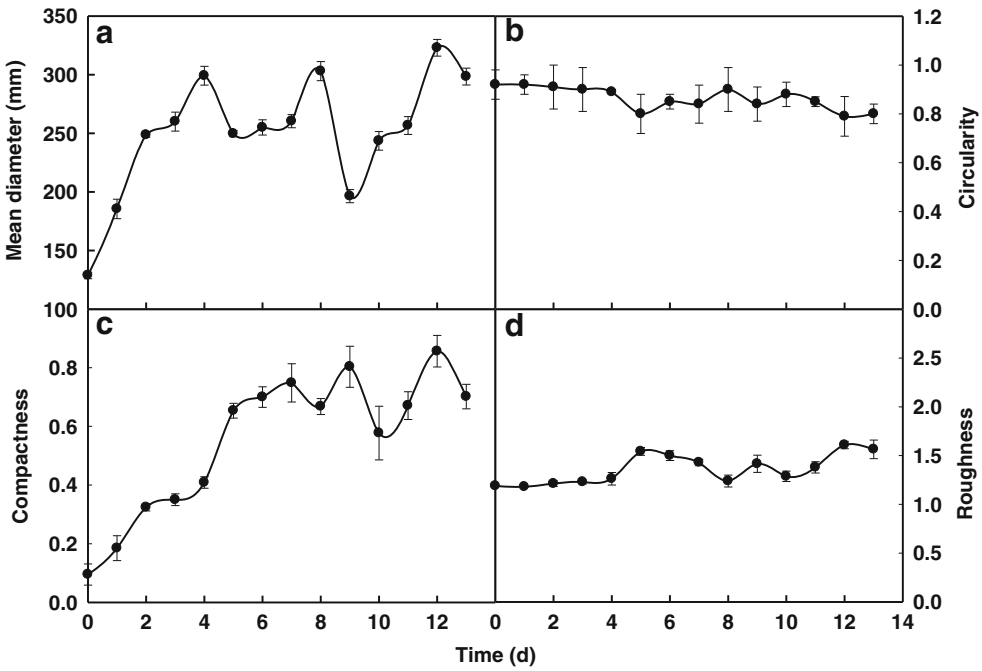

Fig 4 Mean diameter (**a**), circularity (**b**), compactness (**c**), and roughness (**d**) of *S. rugosoannulata* #2 pellets growing in a 5-L batch reactor

Table 2 Effects of *Stropharia rugosoannulata* EPS on the growth parameters and the various organs in streptozotocin-induced diabetic rats for 3 weeks

Parameter	Group[a]				
	Normal	Control	L	M	H
Growth parameters					
Body weight gain (g/day)	9.1550±0.2963 c	6.4525±0.9000 a	6.8650±0.4906 a,b	7.7425±0.8710 b	8.4050±0.6553 b,c
Food intake (g/day)	36.7075±1.2153 a	55.0625±1.8960 d	52.8175±1.5989 d	47.6925±1.7400 c	42.6325±1.6991 b
Food efficiency ratio[b]	0.2498±0.0151 d	0.1173±0.0164 a	0.1302±0.0125 a,b	0.1622±0.0144 b	0.1971±0.0126 c
Various organs					
Liver (g/100 g BW)	3.0824±0.3281 a	4.5042±0.1418 c	4.4417±0.3225 b,c	4.4043±0.2706 b,c	4.1477±0.2267 b
Kidney (g/100 g BW)	0.6165±0.0416 a	1.0186±0.0663 b	1.0765±0.0347 b	1.0742±0.2230 b	1.0295±0.0743 b
Spleen (g/100 g BW)	0.2134±0.0300 NS	0.2065±0.0263	0.1920±0.0397	0.2237±0.0325	0.2339±0.0487
Pancreas (g/100 g BW)	0.2369±0.0570 a	0.3488±0.1084 b	0.3396±0.0860 b	0.3375±0.0478 b	0.2742±0.0673 a,b

NS, Not significant

Data are presented as the mean of eight rats (n = 8 per group) ± standard error. Values followed by different lowercase letters within the same column are significantly different among the groups at $P<0.05$

[a] See Table 1

[b] Body weight (BW) gain/food intake

loss seems to be due to its hypoglycemic activity. The food intake of both experimental groups (M and H) did, however, decrease significantly compared to the control group, and the data are therefore inconsistent compared to the normal group. The cause of intake suppression may be due to the presence of a specific component in the EPS that has not yet been identified (Kiho et al. 2001). Moreover, STZ-induced diabetic rats also had a markedly lower food efficiency ratio than those in the normal group, although EPS-treated diabetic

Table 3 Effect of *S. rugosoannulata* EPS on plasma glucose, total cholesterol, triglyceride levels, plasma high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, atherogenic index, plasma alanine aminotransferase, and aspartate aminotransferase in streptozotocin-induced diabetic rats for 3 weeks

Parameter	Group[a]				
	Normal	Control	L	M	H
Plasma glucose, total cholesterol, and triglyceride levels					
Glucose (mmol/L)	7.2967±1.264 3a	34.7833±0.8837 d	28.4533±3.6187 c	25.7300±1.8237 c	22.0333±0.6658 b
Total cholesterol (mmol/L)	1.8500±0.0913 a	2.7150±0.0742 d	2.4625±0.0465 c	2.3900±0.0548 c	2.0625±0.0869 b
Triglyceride (mmol/L)	0.4575±0.0499 a	0.8625±0.0746 d	0.7975±0.0359 c,d	0.7150±0.0342 b,c	0.6375±0.0680 b
Plasma HDL cholesterol, and LDL cholesterol levels, and atherogenic index					
HDL cholesterol (mmol/L)	0.6825±0.0222 d	0.3875±0.0287 a	0.4275±0.0419 a	0.5025±0.0479 b	0.6000±0.0356 c
LDL cholesterol[b] (mmol/L)	1.0760±0.1134 a	2.1550±0.0673 e	1.8755±0.0502 d	1.7445±0.0590 c	1.3350±0.0701 b
Atherogetic Index[c]	1.7100±0.0510 a	6.0275±0.3408 e	4.5450±0.1692 d	3.8950±0.2207 c	2.4400±0.0673 b
Plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST)					
Alanine aminotransferase (IU/L)	35.4150±3.4579 a	58.4950±2.8626 c	49.3925±2.0108 b	48.2525±2.2658 b	45.3300±3.3633 b
Aspartate aminotransferase (IU/L)	96.6850±2.4504 a	133.2475±4.2493 c	116.5300±3.5965 b	114.0350±2.7041 b	110.6700±2.7200 b

HDL, High-density lipoprotein; LDL, low-density lipoprotein

Data are presented as the mean of eight rats (n = 8 per group) ± SE. Values followed by different lowercase letters within the same column are significantly different among the groups at $P<0.05$

[a] See Table 1

[b] (Total cholesterol − HDL-cholesterol) − (triglyceride/5)

[c] (Total cholesterol − HDL-cholesterol)/HDL-cholesterol

rats did undergo a significant increase in their food efficiency ratio that corresponded with an increase administration of EPS doses.

The weight of the various organs of the experimental animals are shown in Table 2. The weight of liver decreased slightly but significantly (ANOVA test) due to the administration of EPS at 200 mg/kg body weight ($P<0.05$). In contrast, the EPS treatment had no impact on the weights of the kidney, spleen, and pancreas.

The influence of EPS on the blood glucose level in STZ-induced diabetic rats over a 3-week period is shown in Table 3. The reduction in blood glucose level was dose-dependent, and maximum reduction (37 %) was achieved when the EPS was administered at the dose of 200 mg/kg body weight. In the STZ-induced hyperglycemia model, diabetes arises from irreversible destruction of the pancreatic β-cells by STZ (Warram et al. 1990)—i.e., the STZ treatment causes degranulation or reduction of insulin secretion by the pancreas through selective destruction of β-cells in the pancreatic islets (Benwahhoud et al. 2001). Although the mechanism by which EPS accomplishes its blood glucose-lowering effect is open to debate, two possible explanations are that it may act by preserving a functional portion of the pancreatic β-cells that initially survived exposure to STZ toxicity or it may behave as an insulin-like factor (Hwang et al. 2008). Thus, EPS could increase glucose utilization in diabetic rats by promoting insulin secretion in the pancreas or by exhibiting some insulin-like activities. The findings of Gray and Flatt (1998) with a water-soluble extract of *Agaricus campestris* may support the above suppositions. Hwang et al. (2008) found the EPS obtained from *Laetiporus sulphureus* var. *miniatus* enhanced both β-cell proliferation and insulin secretion. A number of possible mechanisms to explain the insulin-like activities of natural compounds have been suggested. These agents are able to enhance insulin secretion by binding to sulfonylurea receptors on the β-cell, with subsequent closure of K^+-ATP channels, membrane depolarization, and Ca^{2+} influx (Gray et al. 2000).

A maximum reduction of total cholesterol and triacylglycerol of 24 and 26 %, respectively, was obtained at a dose of 200 mg/kg body weight (Table 3). The decrease in total cholesterol and triacylglycerol levels in the diabetic rats by EPS reinforces its hypoglycemic potential. In general, the high plasma level of triacylglycerol and total cholesterol observed in diabetic animals may be due to impaired liver function caused by the damage inflicted by STZ, which acts either directly or indirectly by enhancing the plasma glucose level (Van Horn 1996).

Table 3 also shows the effect of EPS on the LDL-cholesterol and HDL-cholesterol levels and on the atherogenic index in STZ-induced diabetic rats. At the rate of 200 mg/kg body weight, EPS substantially increased the HDL-cholesterol by 53.8 % and lowered the LDL cholesterol and atherogenic index by 38.0 and 59.5 %, respectively, as compared to the control group. Generally, ALT and AST levels are increased when the liver functions abnormally, which can be used as markers to evaluate the extent of liver damage (Bursch and Schulte-Hermann 1986). The influence of EPS on plasma ALT and AST levels is shown in Table 3: ALT and AST levels decreased with increasing concentration of EPS, with the maximum reductions (22.5 and 16.9 %, respectively, as compared to the control group) achieved at the dose of 200 mg/kg body weight. This decrease signifies that *S. rugosoannulata* EPS might play a corrective role in liver function by promoting insulin synthesis, thereby reducing the blood glucose level. This in turn, would reduce the level of triacylglycerol and total cholesterol in the blood plasma of diabetic animals. Although the exact mechanism of *S. rugosoannulata* extracellular polysaccharide is not fully understood, our results suggest that a combination of mechanisms might be involved in producing the hypoglycemic effect.

Conclusions

Our findings establish that pellet morphology and viscosity are associated with the production of EPS and mycelial biomass, respectively. The compactness of the pellet formation of *S. rugosoannulata* #2 in submerged culture was highly correlated with EPS production. Moreover, we show that the EPS of *S. rugosoannulata* #2 has hypoglycemic capacity, indicating its potential as an active ingredient in hypoglycemic drugs.

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