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The pharmacological effect of polysaccharides from *Lentinus edodes* on the oxidative status and expression of VCAM-1mRNA of thoracic aorta endothelial cell in high-fat-diet rats

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ABSTRACT

The aim of this study was to investigate the pharmacological effect of polysaccharides from *Lentinus edodes* on serum oxidative status and expression of VCAM-1mRNA of thoracic aorta endothelial cell in high-fat-diet rats. Forty male rats received two different diets during 40 days: standard chow (SC) and high-fat-diet (HF). The result indicates that the administration of polysaccharides from *L. edodes* significantly reduced serum total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-c) and enhanced serum antioxidant enzyme activity and thymus and liver index in high-fat rats. In addition, the administration of polysaccharides from *L. edodes* significantly decreased the increased expression level of VCAM-1mRNA in group (V) ($P < 0.05$). In conclusion, our data suggest that the administration of polysaccharides from *L. edodes* could decrease the increased oxidation stress induced by high-fat-diet and decrease expression of VCAM-1mRNA of thoracic aorta endothelial cell in rats.

1. Introduction

Long-valued for their culinary and medicinal properties, specialty mushrooms have been enjoyed locally and in small quantities by Native American and ethnic populations, and widely used for centuries by Asian cultures. The *Lentinus edodes* is one of several marketed specialty mushrooms including oyster, enoki, wine cap, maitake and pompom. Behind the common button and oyster mushrooms, the *L. edodes* is the third most widely produced mushroom in the world and the *L. edodes* is a large, umbrella-shaped mushroom that is dark brown and is prized both for its culinary and medicinal properties (Zheng & Shetty, 2000). It is a rich source of proteins, fats, carbohydrates, fiber, vitamins and minerals (Hatvani & Mécs, 2001). *Lentinus edodes* is revered in Asian medicine for its health-promoting effects, including antiviral, antifungal, antioxidant, and antitumor effects boosts the immune system, lowers cholesterol, works as an anticoagulant and is helpful in cancer treatment (Watanabe, Yamaguchi, Urabe, & Asada, 2003).

Hyperlipidaemia is considered a risk factor involved in the development of cardiovascular disease (Frishman, 1998; Stone, 2004; Zhao et al., 2007). The search for new drugs capable of reducing and regulating serum cholesterol and triglyceride levels has gained momentum over the years, resulting in numerous reports on significant activities of natural agents (Jahromi & Ray, 1993). Plant products are frequently considered to be less toxic and more free from side effects than synthetic agents. These properties have led to the discovery of new therapeutic agents including antioxidants, hypoglycemics, and hypolipidemics. One (1→3)-β-D-glucan, named Lentinan as an antitumor polysaccharide, has been isolated from the fruiting body of *L. edodes* by Chihara et al. (Maeda & Chihara, 1973; Maeda, Chihara, & Ishimura, 1974). It is well established that polysaccharides from *L. edodes* exhibit strong antioxidant activity and can reduce oxidative stress in rats. The Lentinan helps product T-cells to destroy bacteria and viruses, and it has anti-cancer, antitumor effects. It contains other nutrients helpful in strengthening the immune system and fighting disease-causing organisms. The Lentinan works to prevent heart disease by lowering blood pressure and cholesterol levels, helping pull fat from the system and working as an anticoagulant (Wang, Xia, Xia, Xiang, & Pan, 2005).

The aim of the present study was to evaluate the pharmacological influence of the polysaccharides from *L. edodes* on serum lipid levels in rats fed high-fat-diets. The lipid profile was taken as the major marker of hypercholesterolemia. Accordingly, serum total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-c) and high density lipoprotein cholesterol (HDL-c) were among the parameters investigated. In addition, to have a measure

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of the pharmacological effects of the plant extract, thymus, liver index and serum antioxidant activity of the treated rats, the serum superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activities, total antioxidant capacity (TAOC), serum NO_2^- levels and the plasma endothelin (ET) levels were measured relative to plant-untreated control rats. At last, pharmacological effect of the Lentinan on VCAM-1mRNA of thoracic aorta endothelial cell in high-fat-diet rats is also evaluated.

2. Materials and methods

2.1. Materials

Lentinus edodes was purchased from local medical market.

2.2. Preparation of polysaccharides from Lentinus edodes

Powdered *L. edodes* (100 g) were homogenized and extracted three times in a blender with 2 L of distilled water for 3 h at room temperature and then at 100 °C for 3 h by consulting Zha's method (2007). The whole extract was filtered and centrifuged at 12,000 rpm for 30 min at 4 °C. The supernatant was concentrated to 80 ml and precipitated by the addition of ethanol in 1:4 ratio (v/v) at room temperature (RT). After overnight precipitate, the sample was centrifuged as described above, and the precipitation was dissolved in 100 ml of distilled water. This process was repeated three times. The precipitate was then washed with sevage reagent (isoamyl alcohol and chloroform in 1:4 ratio) (Staub, 1965) and freeze dried, giving the crude polysaccharide from *L. edodes*.

2.3. Monosaccharide composition

The polysaccharides were hydrolyzed with 1 M TFA at 100 °C for 8 h, followed by evaporation to dryness and successive reduction with $NaBH_4$ and acetylation with Ac_2O–NaOAc at 120 °C for 1 h. The Ac_2O was destroyed with ice-water, and the resulting alditol acetates extracted with $CHCl_3$ (Whiton, Lau, Morgan, Gilbart, & Fox, 1985) and analyzed by GC–MS, as described above.

2.4. Animals group and treatment

Forty male rats, weighing 200–240 g and averaging 12 weeks old, were obtained from experimental animals breeding center associated to our institute. The rats were fed a standard diet and had free access to water. The rats were maintained on a 12:12 h light/dark photoperiod. Animals were randomly divided into six groups. Each experimental group was composed of eight animals and treated as follows:

Group I (normal control): Rats were fed a standard diet and administered the same volume of normal saline vehicle (2 ml) daily for 40 days. Group II (untreated negative control): Rats were fed a high-fat-diet and administered the same volume of normal saline vehicle (2 ml) daily for 40 days. Group III–V (polysaccharides-treated): Rats were fed a high-fat-diet and orally administered with polysaccharides (100, 200, 300 mg/kg body weight) in normal saline vehicle (2 ml) daily for 40 days.

All rats had free access to tap water during the experiment.

Twenty-four hours later after the last drug administration, the animals were killed by decapitation (after 24 and 72 h, respectively) and blood was collected in vials and was allowed to clot to separate serum. It is then centrifuged at 4000 rpm for 10 min to obtain clear serum. An aliquot of the whole blood was used for analysis of plasma endothelin level. The remaining freshly withdrawn blood was immediately centrifuged at 900*g* for 15 min. After careful removal of the plasma, serum was used to analyze biochemical parameters, including NO_2^-, total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c) levels and superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) activities.

Thoracic aorta was excised from the animal, washed thrice with 0.9% NaCl to remove blood, then weighed and stored at −80 °C for later RNA extraction and analysis.

2.5. Diets

The five diets contained the same quantity of protein (18%) to avoid any confounding of results. Protein content was sufficient to allow a normal growth. Mice in control group were fed with a normal laboratory diet containing 7% of total energy as fat, 18% as protein and 75% as carbohydrates. Mice in experimental groups were fed with HF diet containing 75% of total energy as fat, 18% as protein and 7% as carbohydrates.

2.6. Biochemical analysis

2.6.1. Evaluation of pharmacological function (e.g. thymus or spleen index) of polysaccharides from Lentinus edodes was performed as follows

Thymus and spleen were excised for the determination of thymus and spleen index.

$$\text{thymus or spleen index}(\%) = [\text{thymus or spleen weight}(\text{g}) / \text{body weight}(\text{g})] \times 100\%.$$

2.6.2. Nitrite/nitrate determination

The sera obtained were centrifuged at 1500*g* through 0.22-Am Millipore filters to remove opalescence. The sera were kept frozen until nitrite analysis. Determination of NO production concentrations by the enzymatic batch Griess assay in sera samples was performed using Griess reagent as described by Guevara et al. (1998) and by Moshage et al. (Moshage, Kok, Huizenga, & Jansen, 1995). In brief, 100 μl samples of sera were incubated for 45 min at 37 °C with nitrate reductase (25 mU/sample) in the presence of h-NADPH (final concentration 80 μM) in 20 mM Tris buffer, pH 7.6. The total volume of the reaction mixture was 300 μl. After the enzymatic conversion, nitrite concentration in the sera was measured using Griess reagent. Each serum sample was treated with equal volume of the Griess reagent (0.1% *N*-(1-naphthyl)-ethylenediamine dichydrochloride and 1% sulfanilamide in 5% phosphoric acid). After 10 min incubation at room temperature, the absorbance at 550 nm was measured. The concentration of nitrite was calculated from a $NaNO_2$ standard curve.

2.6.3. Determination of plasma endothelin level

Plasma endothelin level was measured by radioimmunoassay. All operation followed the manufacturers' instructions.

2.6.4. Antioxidant enzymes and lipid–peroxidation

Catalase cytochemistry was performed according to Graham and Karnovsky (1966), with some modifications: Catalase activity was determined in the cytosolic fraction (100,000*g* supernatant). Catalase activity was measured by the decrease in absorbance at 240 nm using 50 mM H_2O_2 as substrate. SOD activity was determined by the degree of inhibition of cytochrome *c* reduction by superoxide anion radical, measuring the absorbance at 550 nm as described in McCord and Fridovich (1969). The activity of this enzyme is given in SOD units (1 unit = 50% of the inhibition of cytochrome *c* reduction); assay conditions were 87 mM KH_2PO_4/K_2HPO_4, pH 7.8, 50 mM hypoxanthine, 10 mM cytochrome *c* and

1.8 mU/ml xanthine oxidase. GPx activity was measured by the NADPH consumption at 340 nm during the formation of reduced glutathione by commercial glutathione reductase. Either using 0.8 mM H_2O_2 (Se-dependent GPx) or 3 mM cumene hydroperoxide (sum of Se-dependent and Se-independent activities and referred as total-GPx) as substrate (Greenwald, 1985).

Serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c) levels were measured by enzyme methods according to reagent kits' explanation.

2.6.5. Analysis of effect of on VCAM-1mRNA

Total cellular RNA was isolated from the frozen thoracic aorta using TRIZOL reagent (Superscript Kit, GIBCO-BRL, Grand Island, NY) according to Cui et al's method (2005) and Peng et al. (2007). One hundred milligrams of thoracic aorta in iced Tris buffer (5 mmol/l pH 7.4) containing 1 ml Trizol was homogenized for 30 s in a Polytron homogenizer. The homogenates were then centrifuged for 10 min at 100*g* to remove particulate matter and unbroken cells. Total RNA was solubilized in RNase-free H_2O, and quantified in duplicate by measuring the optical density (OD) at 260 nm. Two milligrams of RNA with OD_{260}/OD_{280} ratio of 1.8–2.0 was reverse transcribed with reverse transcription polymerase in a total volume of 20 mL. One microliter of complementary DNA (cDNA) was then amplified by PCR. Primer pairs were designed by Applied Biosystems. The primer pairs were β-actin (385 bp). PCR products were VCAM-1 (650 bp). β-Actin was used as internal control. The PCR product was analyzed on 2% agarose gel and semi-quantified using Kodak Digital Science 1D 2.0 imaging software. The results are expressed by density ratios to β-actin (VCAM-1/β-actin).

3. Result

3.1. Analysis of monosaccharide composition

GC–MS analysis of the polysaccharides from *L. edodes* that had been hydrolyzed and derived showed that the polysaccharides were composed of five kinds of monosaccharides, namely arabinose, xylose, mannose, glucose, galactose, in molar ratios of 11:5:23:47:13. This result was in good agreement with standard saccharides (arabinose, xylose, mannose, glucose, galactose) and Li et al's work (2005). The results indicated that glucose was the predominant monosaccharide.

3.2. Pharmacological effect of polysaccharides from Lentinus edodes on thymus and spleen index

Evaluation of pharmacological function (e.g. thymus or spleen index) of polysaccharides from *L. edodes* was shown in Table 1. It can be found that the thymus and spleen index was significantly lower ($P < 0.01$) in untreated HF control rats (Group II) compared to normal control group. When rats were treated with polysaccharides (100, 200 and 300 mg/kg BW) for 40 days, the thymus and spleen index was significantly increased ($P < 0.05$; $P < 0.01$) (Table 1) in comparison with the untreated HF control.

Table 1
Pharmacological effect of polysaccharides from *Lentinus edodes* on thymus and spleen index

	Thymus index	Spleen index
I	1.34 ± 0.11	2.52 ± 0.13
II	0.77 ± 0.07[b]	1.45 ± 0.22[b]
III	0.96 ± 0.07[d]	1.67 ± 0.08[c]
IV	1.12 ± 0.11[d]	1.78 ± 0.17[d]
V	1.25 ± 0.09[d]	2.44 ± 0.09[d]

[b] $P < 0.01$ compared with normal control (I).
[c] $P < 0.05$.
[d] $P < 0.01$, compared with untreated HF group (II).

3.3. Pharmacological effect of polysaccharides from Lentinus edodes on serum NO_2^- levels

NO_2^- levels were measured by a microplate assay using Griess reagent. The NO_2^- levels of untreated HF control rats (Group II) were significantly higher than those of the normal control rats ($P < 0.01$). When rats were treated with polysaccharides (100, 200 and 300 mg/kg BW) for 40 days, the levels of NO_2^- were significantly decreased ($P < 0.05$; $P < 0.01$) (Fig. 1) in comparison with the untreated HF control.

3.4. Pharmacological effect of polysaccharides from Lentinus edodes on the plasma endothelin (ET) levels

As shown in Fig. 2, it can be found that the plasma endothelin levels was significantly increased in untreated HF control rats (Group II) compared to normal control group. Polysaccharides treatment (100, 200 and 300 mg/kg BW) decreased the plasma endothelin levels, but the difference was not significant ($P > 0.05$) compared to untreated HF control group. (Fig. 2).

3.5. Pharmacological effect of polysaccharides from Lentinus edodes on serum lipid metabolic parameters

The TG, TC, LDL-c levels of untreated HF control rats were significantly higher ($P < 0.01$), while level of HDL-c was significantly lower than those of the normal control rats ($P < 0.01$). When rats fed with high-fat-diet were treated with varying doses of (100, 200 and 300 mg/kg BW) polysaccharides for 40 days, the levels of TG, TC, LDL-c were significantly decreased in comparison with untreated HF control group ($P < 0.05$; $P < 0.01$) (Fig. 3 and 4). But the level of HDL-c only slightly changed ($P > 0.05$) (Fig. 3) in comparison with untreated HF control group. The data indicated that effect of polysaccharides from *L. edodes* on lipid metabolic parameters showed a dose-dependent pattern.

3.6. Pharmacological effect of polysaccharides from Lentinus edodes on serum antioxidant enzyme activities

Antioxidant enzymes, such as SOD, CAT, GPx and TAOC were significantly decreased in untreated HF control rats ($P < 0.01$) (Group II). Varying doses of polysaccharides (100, 200 and 300 mg/kg BW) treatment significantly blocked the decrease in antioxidant enzyme activities (SOD, GPx and TAOC) of rats fed with

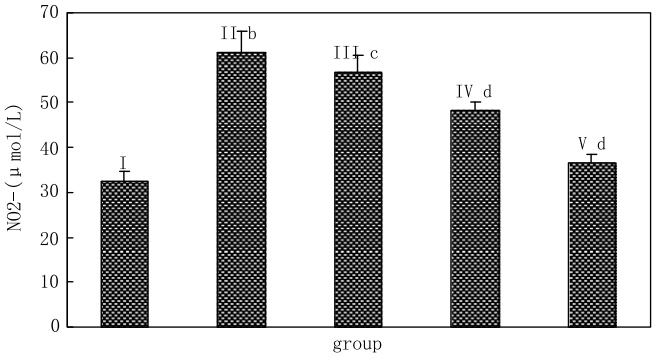

Fig. 1. Effects of polysaccharides from *Lentinus edodes* on serum NO_2^- levels. [b-] $P < 0.01$ compared with normal control (I); [c] $P < 0.05$; [d] $P < 0.01$, compared with untreated HF group (II).

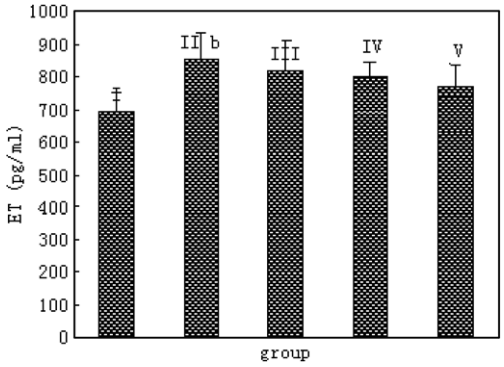

Fig. 2. Effects of polysaccharides from *Lentinus edodes* on the plasma endothelin (ET) (pg/ml) levels. $^{b}P < 0.01$ compared with normal control (I); $^{c}P < 0.05$; $^{d}P < 0.01$, compared with untreated HF group (II).

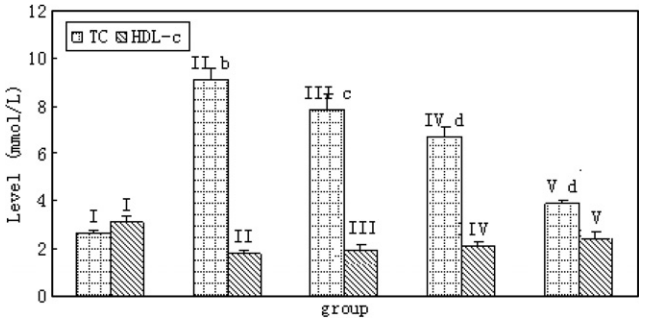

Fig. 3. Effect of polysaccharides from *Lentinus edodes* on serum level of TC and HDL-c. $^{b}P < 0.01$ compared with normal control (I); $^{c}P < 0.05$; $^{d}P < 0.01$, compared with untreated HF group (II).

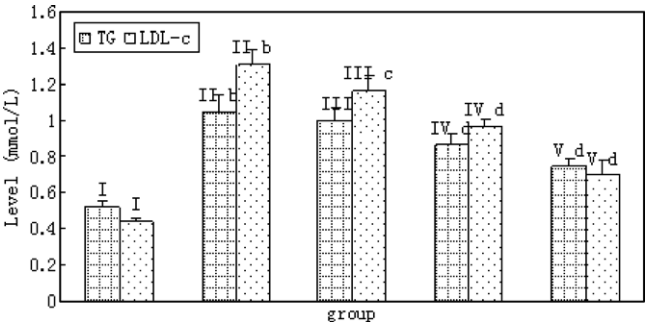

Fig. 4. Effect of polysaccharides from *Lentinus edodes* on serum level of TG and LDL-c. $^{b}P < 0.01$ compared with normal control (I); $^{c}P < 0.05$; $^{d}P < 0.01$, compared with untreated HF group (II).

high-fat-diet in a dose-dependent pattern ($P < 0.05$; $P < 0.01$) (Table 2). However, the polysaccharides treatment (100, 200 mg/kg BW) had no notable effect on CAT ($P > 0.05$) (Table 2).

Table 2
Effect of polysaccharides from *Lentinus edodes* on serum SOD, GPx, TAOC, and CAT activity

	SOD (NU/ml)	GPx (U/ml)	CAT (U/ml)	TAOC (U/ml)
I	21.74 ± 1.95	13.24 ± 1.11	5.62 ± 0.23	7.67 ± 0.57
II	15.67 ± 1.14[b]	8.45 ± 0.74[b]	3.06 ± 0.12[b]	4.59 ± 0.32[b]
III	18.06 ± 2.07[d]	9.67 ± 0.83[c]	3.47 ± 0.64	5.05 ± 0.38[c]
IV	19.78 ± 2.86[d]	10.98 ± 0.93[d]	3.67 ± 0.58	6.11 ± 0.54[d]
V	20.85 ± 3.84[d]	12.53 ± 1.09[d]	4.71 ± 0.52[d]	7.33 ± 0.66[d]

[b] $P < 0.01$ compared with normal control (I).
[c] $P < 0.05$.
[d] $P < 0.01$, compared with untreated HF group (II).

3.7. Pharmacological effect of polysaccharides from Lentinus edodes on expression level of VCAM-1mRNA of thoracic aorta endothelial cell in rats

The relative value of VCAM-1mRNA expression of untreated HF control rats was significantly higher in comparison with that of the normal control rats ($P < 0.01$). When untreated HF control rats were treated with (300 mg/kg BW) polysaccharides from *L. edodes* for 40 days, the VCAM-1mRNA expression was significantly decreased in comparison with the untreated HF control ($P < 0.01$) (Fig. 5). However, the data indicated that effect of low and middle dose of polysaccharides on VCAM-1mRNA expression of thoracic aorta endothelial cell in rats showed a slight decrease ($P > 0.05$) in comparison with the normal control.

4. Discussion

In the past, dietary recommendations were focused on reducing the consumption of foods and nutrients deemed bad for health, e.g. saturated fat, dietary cholesterol and salt. In more recent years, increasing emphasis has been given to encouraging the consumption of foods and nutrients deemed good for health, e.g. vegetables, fruits, legumes, fish, dietary fiber, and polyunsaturated fatty acids (Kromhout, 2001).

Obesity is associated with coronary heart disease, hypertension, chronic pulmonary diseases, diabetes mellitus, osteoarthritis, hypercholesterolemia, some cancers and increased all-cause mortality. Therefore, diet is an important risk determinant of these degenerative diseases. A large amount of studies show that consumption of high-fat-diet was closely associated with some diseases, e.g. coronary heart disease, cerebrovascular disease, diabetes (Alissa, Bahjri, Al-ama, Ahmed, & Ferns, 2006; Tsuchiya et al., 2003). A major risk factor for these diseases is total or low-density lipoprotein (LDL) cholesterol. Experimental research has shown that oxidized LDL rather than native LDL is the culprit in the development of atherosclerosis and its clinical complications, such as coronary heart disease (Koertge et al., 2003). Recently evidence was obtained that the diet rich in antioxidant may prevent ventricular fibrillation and reduced the risk factors of cardiovascular and cerebrovascular diseases (Huang, Zhang, Cheung, & Tan, 2006; Kosaraju, D'ath, & Lawrence, 2006; Matsui et al., 2005; Peluffo & Radi, 2007). These results make clear that diet is an important determinant of coronary heart disease.

Lentinus edodes is the second most popular and the third widely cultivated edible mushroom in the world (Chang, 1996). Several important compounds including bioactive polysaccharides (lentinan), dietary fiber, ergosterol, vitamin B1, B2 and C and minerals

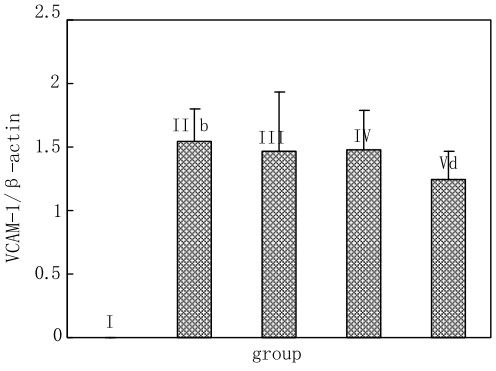

Fig. 5. Effect of polysaccharides from *Lentinus edodes* on expression of VCAM-1mRNA. $^{b}P < 0.01$ compared with normal control (I); $^{d}P < 0.01$, compared with untreated HF group (II).

have been isolated from the fruiting body, mycelia, and culture medium of this mushroom. Recent numerous studies have shown its pharmacological attributes including antitumor, antimicrobial, liver function improving and cholesterol lowering activity (Fukushoma, Ohashi, Fujiwara, Sonoyama, & Nakano, 2001; Mizuno, Sakai, & Chihara, 1995; Takehara, Kuida, & Mori, 1979; Wang & Luo, 2007). Lentinan, a (1-3)-beta-β-glucan extracted from the mushroom *L. edodes*, is a potent immunostimulatory drug, and licensed in Japan for antitumor therapy. The immunomodulatory effects of lentinan range from enhanced host resistance to bacterial, fungal, viral or parasitic infections to antitumor effects (Chihara et al, 1987; Kaneko & Chihara, 1992; Liu et al., 2007). Antioxidant activity of β-glucan has been reported (Jaehrig et al., 2008; Sener, Toklu, & Cetinel, 2007). Recent investigations have shown that the Lentinan possesses antioxidant activity (Lin, Xu, & Lian, 2006).

The intake of a particular type of dietary fat affects in a direct way the fatty acids and antioxidants profiles of the body and in an indirect way the susceptibility of the organism to undergo oxidation (Huertas, Battino, Lenaz, & Mataix, 1991; Mataix, Quiles, Huertas, Battino, & Mañas, 1998; Ramirez-Tortosa et al., 2004; Ochoa-Herrera, Huertas, Quiles, & Mataix, 2001; Quiles, Huertas, Mañas, Battino, & Mataix, 1999; Quiles et al., 2002). NO, a small molecule and a strong free radical, influences many aspects of pulmonary function in healthy subjects and patients. It is synthesized from the amino acid L-arginine by nitric oxide synthase (NOS) of which three forms exist. After production, NO can be exhaled, metabolized to nitrite and nitrate, or interact with superoxide to form peroxynitrite (Rutgers et al., 1999). Determination of NO itself is difficult because of its radical nature and very short half-life. Therefore, determination of the stable end products of the NO radical in the plasma such as nitrite and nitrate is the most frequently used method to measure the production of the NO radical (Moshage et al., 1995). High-fat-diet causes a series of the unconventionality of glucose, lipid and insulin metabolism (Muurling et al., 2002). This is in agreement with our work. Consumption of high-fat-diet can enhance the level of serum NO_2^- and lipid peroxidation. Although the diets were of short duration and the concentrations of serum lipids and lipoproteins are unlikely to have reached their final values, the results were in accordance with the meta-analyses by (Lee, Thurnham, & Chopra, 2000), suggesting that diets enriched in high-fat increase HDL cholesterol, lower the ratio of LDL to HDL and lower serum triacylglycerols, total serum cholesterol compared with normal control, the polysaccharides-treatment group. It is well known that antioxidant would be important in curing type II diabetes and hypertension (Nascimento, Costa-e-Forti, Peter, & Fonteles, 2003). Endothelin (ET) is a peptide of 21 amino acids in chain with two disulfide bonds with three distinct isoforms: ET-1, ET-2 and ET-3 (Yanagisawa et al., 1988). Endothelin causes isolated contraction of pulmonary veins, vascular smooth muscle mitogenesis, myocardial cell hypertrophy, positive inotropic and chronotropic effects, bronchoconstriction, mucous secretion, cellular proliferation, and inflammatory reactions (Levin, 1995). A large amount of studies have proven that endothelin is involved in pathological and physiological proceedings of hepatic cirrhosis by changing liver hemodynamics (Kojima et al., 2001; Minagawa, Okamura, Shigemasa, Minami, & Okamoto, 2007). We found that polysaccharides from *L. edodes* were able to decrease the level of serum NO_2^-, TC, TG, LDL-c in animals fed high-fat-diet, as well as enhanced the level of serum HDL-c. The present studies also discovered that polysaccharides from *L. edodes* might not only improve oxidative injury induced by free radicals and increase antioxidant enzyme activity, but also decreased the plasma endothelin (ET) levels. The experimental results revealed that polysaccharides from *L. edodes* had no obvious pharmacological effect on expression level of VCAM-1mRNA of thoracic aorta endothelial cell in rats in low and middle dose, but it had obvious pharmacological effect on expression level of VCAM-1mRNA of thoracic aorta endothelial cell in rats in high dose. From these results, polysaccharides from *L. edodes* could increase antioxidant enzyme activity, improve blood lipid levels in rats and inhibit the oxidative injury induced by accumulating free radicals caused by high-fat-diet to a certain extent.

It is generally accepted that the majority of the pleiotropic effects of long-term high-fat diet (HF diet) are accompanied with changes in gene expression profiles. Several genes which encode enzymes or signal mediators involved in lipid and glucose metabolism have been shown to respond to long-term HF diet (Murase et al., 2001; Yu et al., 2000). Therefore, it can be assumed that pharmacological-modulation effect of polysaccharides from *L. edodes* on high-fat-diet rats' oxidative status might be at least partly performed by stimulating expression of genes encoding antioxidant enzymes.

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