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# Effect of *Fomitopsis pinicola* extract on blood glucose and lipid metabolism in diabetic rats

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**Abstract**−This study was performed to investigate the effects of *Fomitopsis pinicola* extract on blood glucose and lipid metabolism in diabetic rats. The blood glucose concentration was similar to that of the control at 30 min, but after 60 min of glucose administration the blood glucose concentration rapidly decreased, and after 120 min was 100.7±4.0 mg/dL, representing an approximate 50% decrease compared to the control. In the case of the diabetic rats induced by streptozotocin, the concentration of blood glucose was decreased from 362.0±16.7 to 204.5±11.4 mg/dL after 20 days of administration. HDL- and LDL-cholesterol concentrations were 39.0±4.3 mg/L and 13.2±3.4 mg/dL, respectively, representing an approximate increase of 73% and approximate decrease of 76%, respectively, compared to the control. The activities of aspartate aminotransferase and alanine transaminase were increased. On the other hand, activities of amylase, alkaline phosphatase, lactate dehydrogenase, glutamic oxaloacetic transaminase, and glutamic pyruvic transaminase were decreased compared to that of the control. No difference was evident between test and control rats with respect to white blood cell, red blood cell, hemocyte, hemoglobin, hematocrit, and platelet counts. These results indicate that *F. pinicola* extract is useful as a preventative and treatment agent for damage of liver and kidney cells.

Key words: *F. pinicola*, Blood Glucose, Lipid Metabolism, Cholesterol

## INTRODUCTION

Mushroom production has substantially increased in recent years. Many mushroom varieties are a nutritious food source, and have been consumed by people for millennia. Compared with vegetables, mushrooms are high in protein and have a good balance of vitamins and minerals. They contain little fat and digestible carbohydrates, making them suitable for low-calorie diets [1,2]. Moreover, they can be cultivated with higher biological efficiency than animal proteins. Besides being a non-animal protein source, several types of mushrooms possess tonic and medicinal qualities, and have significant pharmacological attributes [3]. Especially, mushroom extract including polysaccharide has been reported to have possible pharmacological applications that include antitumor, antiviral, antifungal, antiparasitic, and antihistaminic activities [4].

*Fomitopsis*, which belongs to the Basidiomycota fungal class, has been widely cultivated and studied in Japan as well as being traditionally used as a health food source for plant growth regulation and in the treatment of diabetes [5]. Lanstane triterpenoids and lanstane triterpene glycosides isolated from the fruiting bodies of *Fomitopsis pinicola* have been examined for their anti-inflammatory activity mediated by action against cyclooxygenase-1 and -2 [6]. Hwang et al. investigated the effects of extracts of *F. pinicola* on the dental caries pathogens [7]. Recently, we researched the optimal growth conditions for *F. pinicola* liquid cultures including temperature, pH, and carbon, nitrogen, and mineral sources, in order to effectively produce exopolysaccharide and elicit mycelial growth using an air lift bioreactor. Our results agreed with a model developed from experimental data and simulated results [8]. Our previous research also investigated the biological activities of *F. pinicola* extracts including the scavenging rates of 1,1-diphenyl-2-picrylhydrazyl radical, superoxide anion, and linoleic acid, nitric oxide production, and phenolic content *in vitro*, and the effects of *F. pinicola* extracts on glutathione production, and the activities glutathione peroxidase, catalase, alcohol dehydrogenase, and acetaldehyde dehydrogenase *in vivo*. In addition, the antitumor activities of a series of *F. pinicola* extracts obtained by using hot water and methanol were examined [9].

In this study, we investigated the effect of *F. pinicola* extract on the serum glucose levels in rats who received a large amount of glucose and in rats induced for diabetes using N-methylnitrosocarbamoyl-$\alpha$-glucosamine. We also investigated the concentration of triglyceride, HDL-cholesterol, and LDL-cholesterol, and the extracts' influence on liver and kidney blood-borne toxicity.

## MATERIALS AND METHODS

### 1. Sample and Animals

To investigate the biological activity of *F. pinicola* extract, fruit

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body cultivated on an industrial medium was used. White male Sprague-Dawley rats weighing 100 g were raised in the same conditions for 8 weeks to acclimate to the 20 °C temperature and 50% humidity conditions of the lab environment. Rats received solid feed (Samyang Foods, Pusan, Korea) for 2 weeks prior to supplementation of the diet of the test group of rats with sample.

**2. Preparation of *F. pinicola* Extract**

Approximately 500 g of *F. pinicola* was extracted with 1,000 mL of hot water using a Graham condenser apparatus for 4 h or for 24 h for diabetic study. Each extract was filtered by passage through a 0.5 μm pore size filter. The filtrate was evaporated and the residue was used as the sample.

**3. Glucose Tolerance Test**

Thirty minutes following the oral administration of 0.5 ml of *F. pinicola* extract into each rat, 3.0 mL of glucose solution (1 g glucose/mL) was administered, and blood was withdrawn from the tail 30, 60, 90, and 120 min later. The serum glucose concentration of each blood sample was measured with a Glucotrend 2 blood glucose meter (Roche Diagnostic GmbH, Mannheim, Germany). Control rats received 0.5 mL of tap water instead of glucose.

**4. Glucose Concentration in Diabetic Rats**

Rats were intravenously injected with streptozocin (STZ, N-methylnitrosocarbamoyl-α-glucosamine, Wako Pure Chemical, Osaka, Japan) at a concentration of (60 mg/kg body weight, kg). Two days after STZ introduction, blood was sampled at 16:00-17:00 h. One day later, 0.5 mL of *F. pinicola* extract or tap water (control) was administered. Blood was withdrawn and blood glucose determined as described above.

**5. Blood Analyses**

The concentrations of HDL- and LDL-cholesterol and triglyceride, and the activities of amylase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) from blood were determined by using an ADVIA Model 1650 chemistry analyzer (Bayer Diagnostics) and Hitachi Model 7180 chemistry analyzer (Hitachi, Tokyo, Japan).

**6. Blood Chemistry Tests**

After oral administration of 1.0 mL of *F. pinicola* extract into Sprague/Dawley rats for 3 weeks, 1.0 mL of blood was collected from the abdominal vein. After separation of serum, components of blood used to ascertain liver toxicity and hemocyte status [total protein, albumin, glutamic oxaloacetic transaminase (GOT), and glutamate pyruvate transaminase (GPT)] and kidney toxicity [white blood cell, red blood cell, hemoglobin, hematocrit, and platelet counts] were measured by standard protocols. GOT and GPT activities were measured with an automatic blood analyzer equipped with a diagnostic test kit and reagent.

**7. Statistics**

Mean data values are presented with their deviation (mean±SD).

## RESULTS AND DISCUSSION

The search for natural substances that are capable of lowering blood cholesterol is ongoing in the field of nutrition, and many dietary factors, which include plant proteins, unsaturated fatty acids, calcium and flavonoids, have been reported for their hypolipidemic potential [10]. Edible mushrooms are the ideal dietetic materials for the prevention of atherosclerosis due to their high content of fiber, proteins, microelements and their low fat content [11,12]. Recently, a variety of mushroom extract has been investigated in an attempt to apply to anti-diabetic agents [13-15]. Despite the many reports on the medicinal properties of mushrooms, little is known of blood glucose and lipid metabolism of *F. pinicola* extract containing polysaccharide in diabetic rats.

In this study, we extended these observations by investigating the effects of *F. pinicola* extract on the glucose levels in rats administered a large amount of glucose and in diabetic rats, and the physiological influence of the extract including liver and kidney toxicity. To investigate the effects of *F. pinicola* extract on serum glucose levels during the 180 min following the administration of glucose, oral glucose tolerance testing was performed. The results are shown in Fig. 1. The blood glucose concentration was similar to that of

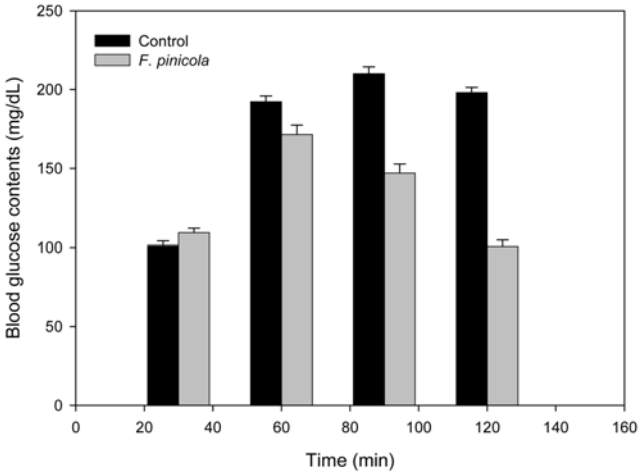


**Fig. 1. Effect of *F. pinicola* on serum glucose levels over 120 min in the rats administered a large amount of glucose. Control: administered with water before glucose-administration. *F. pinicola*: administered with hot-water extract of *F. pinicola* before glucose-administration.**

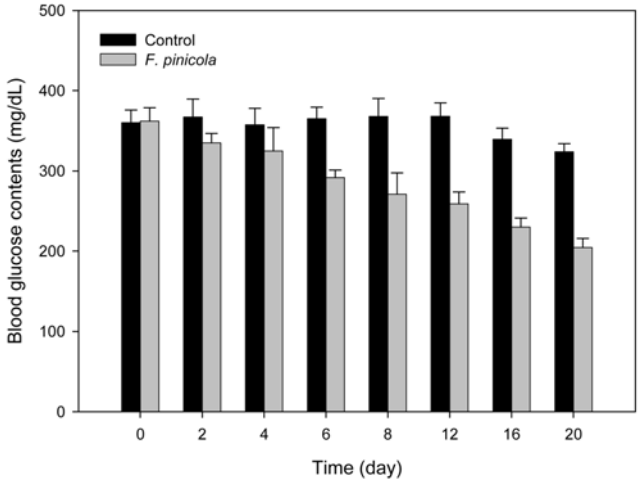


**Fig. 2. Effect of *F. pinicola* on the serum glucose levels over 20 days in the diabetic rats. Control: administered with water after induced diabetes by STZ. *F. pinicola*: administered with hot-water extract (2.5 g/kg body wt/day) of *F. pinicola* after induced diabetes by STZ.**

control at 30 min. However, after 60 min, glucose assimilation produced a rapid decrease in blood glucose concentration. This decrease was especially pronounced in the presence of *F. pinicola* extract; blood glucose concentrations at 60 min and 120 min were 17.5±5.9 mg/dL and 100.7±4.0 mg/dL, respectively. The latter represented an approximately 50% decrease compared to the control rats. To investigate the effects of *F. pinicola* extract on the serum glucose levels in diabetic rats, blood glucose concentrations were measured over 20 days. A time-dependent decrease was evident when *F. pinicola* extract was used, from 362.0±16.7 mg/dL at day 0 to 204.5±11.4 mg/dL at day 20, representing a decrease of approximately 77% compared to control (Fig. 2).

Hypercholesterolemia is regarded as a major risk factor of cardiovascular diseases such as atherosclerosis, myocardial infarction, heart attack, and cerebrovascular disease, which are leading causes of death in advanced countries. Lessening circulating cholesterol levels can reduce the risk of these diseases. Hypercholesterolemia is related to increased levels of oxidative stress and lipid metabolism, with LDL generation being identified as a major contributor to the vascular damage induced by high cholesterol levels [5]. Table 1 summarizes the data on the concentration of triglyceride, HDL-cholesterol, and LDL-cholesterol in diabetic rats over 20 days. When *F. pinicola* extract was administered, the triglyceride concentrations in blood were decreased compared to that of the control. Generally, LDL-cholesterol is a main carrier of blood cholesterol and is linearly related to the levels of serum cholesterol. Circulating HDL cholesterol is regarded as 'good cholesterol', which carries cholesterol from peripheral cells to the liver for metabolic conversion into bile acids. This pathway is crucial for maintaining cholesterol homeostasis between blood and peripheral tissues. HDL-cholesterol protects against coronary heart disease [6]. When *F. pinicola* extract was used, HDL- and LDL-cholesterol concentrations were 39.0±4.3 mg/L and 13.2±3.4 mg/dL, respectively, representing an approximate increase of 73% and approximate decrease of 76%, respectively, compared to the control. These desirable results lend credence to the view that *F. pinicola* extract may be useful in therapeutic strategies aimed at treating and preventing atherosclerosis.

**Table 1. Serum contents of triglyceride, HDL-cholesterol, and LDL-cholesterol in serum of diabetic rats**

| Samples | Triglyceride (mg/dL) | HDL-cholesterol (mg/dL) | LDL-cholesterol (mg/dL) |
|---|---|---|---|
| Normal | 52.3±3.7 | 20.1±4.5 | 24.1±5.3 |
| Control | 75.5±4.8$^{+}$ | 22.5±3.9 | 17.3±3.0 |
| *F. pinicola* | 60.0±5.9 | 39.0±3.3 | 13.2±2.4 |

Normal: not administered STZ and extract, Control: administered water after induction of diabetes by STZ, *F. pinicola*: administered with hot-water extract (2.5 g/kg body wt/day) of *F. pinicola* after induction of diabetes by STZ

Table 2 shows activities of amylase, AST, ALT, ALP, and LDH in the serum of diabetic rats. When *F. pinicola* extract was administered, the activities of AST and ALT were increased compared to control, while amylase, ALP, and LDH activities were decreased.

To evaluate liver function, the concentrations of total protein, albumin, creatinine, and blood urea nitrogen, and the activities of GOT and GPT in blood were measured. The results are shown in Table 3. The concentrations of total protein, albumin, creatinine, and blood urea nitrogen were similar to that of the control. Generally, increased activities of GOT and GPT are evident in liver injury. Presently,

**Table 2. Activities of amylase, AST, ALT, ALP, and LDH in serum of diabetic rats**

| Samples | Amylase (U/L) | AST (U/L) | ALT (U/L) | ALP (U/L) | LDH (U/L) |
|---|---|---|---|---|---|
| Normal | 1,720.5±77.7 | 119.1±8.5 | 33.8±2.4 | 100.5±4.4 | 2,737.6±390.4 |
| Control | 1,464.3±61.3 | 165.6±14.4 | 78.3±4.8 | 397.3±32.3 | 3,251.6±409.0 |
| *F. pinicola* | 1,157.3±63.3 | 185.8±14.4 | 91.0±6.7 | 368.3±45.6 | 3,133.6±295.3 |

Normal: not administered STZ and extract, Control: administered water after induction of diabetes by STZ, *F. pinicola*: administered with hot-water extract (2.5 g/kg body wt/day) of *F. pinicola* after induction of diabetes by STZ

**Table 3. Effect of *F. pinicola* extract on the concentrations of total protein, albumin, creatinine, and blood urea nitrogen, and on the activities of serum GOT and GPT**

| | Total protein (g/L) | Albumin (g/L) | Creatinine (mg/dL) | Blood urea nitrogen (mg/dL) | GOT (U/L) | GPT (U/L) |
|---|---|---|---|---|---|---|
| Control | 6.10±1.0 | 3.86±0.2 | 0.60±0.1 | 16.62±2 | 92.60±7.7 | 38.40±3.2 |
| *F. pinicola* | 6.06±1.2 | 3.78±0.4 | 0.62±0.1 | 14.92±3 | 80.20±8.3 | 28.40±2.9 |

Normal: not administered STZ and extract, Control: administered water after induction of diabetes by STZ, *F. pinicola*: administered with hot-water extract (2.5 g/kg body wt/day) of *F. pinicola* after induction of diabetes by STZ

**Table 4. Effect of *F. pinicola* extract on white blood cell, red blood cell, hemoglobin, hematocrit, and platelet concentrations in rat hemocytes**

| | WBC ($\times 10^3$ cells/μL) | RBC ($\times 10^6$ cells/ μL) | Hemoglobin (g/dL) | Hematocrit (%) | Platelets ($\times 10^3$ cells/μL) |
|---|---|---|---|---|---|
| Control | 9.20±1.7 | 7.76±1.2 | 14.48±2.4 | 42.60±9.2 | 1003.00±11.6 |
| *F. pinicola* | 8.43±2.1 | 7.88±1.5 | 15.05±2.7 | 44.70±8.1 | 973.00±14.2 |

Normal: not administered STZ and extract, Control: administered water after induction of diabetes by STZ, *F. pinicola*: administered with hot-water extract (2.5 g/kg body wt/day) of *F. pinicola* after induction of diabetes by STZ

GOT and GPT activities were decreased compared to that of the control. These results indicate that *F. pinicola* extract is useful as a preventative and treatment agent against damage of liver cells. To investigate kidney toxicity upon the administration of *F. pinicola* extract, white blood cell, red blood cell, hemocyte, hemoglobin, hematocrit, and platelet contents of hemocytes were measured. When *F. pinicola* extract was administered, these parameters were similar to those of the control (Table 4), indicating that the potential benefits of *F. pinicola* extract appear not to be accompanied by liver damage.

## CONCLUSION

The blood glucose concentrations were decreased with the increase of time when *F. pinicola* extract was administered. Especially, after 20 days of administration, it was about a 77% decrease compared to that of the control. The HDL cholesterol concentration was about a 73% increase and the LDL-cholesterol concentration was about 76% decrease compared to that of the control. These results indicate the therapeutic potential of the increase of HDL cholesterol concentration and the decrease of LDL-cholesterol using *F. pinicola* extract in the serum may be exploited for the prevention and treatment of atherosclerosis. From these results, we found that *F. pinicola* extracts decreased significant serum glucose and lipid in blood. However, further studies are necessary to elucidate the relationship between serum glucose and lipid in blood and the pharmacological activity of the *F. pinicola* extract.

## ACKNOWLEDGMENTS

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