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Effects of *Cordyceps militaris* Cultivated on Rice on Lipid Metabolism in Rats Fed High Fat-cholesterol Diets

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Abstract

Dongchunghacho rice, produced by cultivating Dongchunghacho fungus on rice, could be an effective functional food because it offers added value to rice and thus increases rice consumption. However, the physiological effect of Dongchunghacho rice has not been reported yet although there is increasing consumers demand. Therefore, we investigated the effect of Dongchunghacho rice (unpolished rice cultivated with *Cordyceps militaris*) on lipid metabolism in hyperlipidemic rats. Forty of 8 wk-old male Sprague-Dawley rats were divided into four groups after a 1 week of adaptation period and fed either a normal diet (66% polished rice diet, NC), high fat (12 g/100 g)-high cholesterol (1 g/100 g) diet with 53% polished rice (HC), or high fat-high cholesterol diets supplemented with 30% of the total rice as either unpolished rice (UR) or Dongchunghacho rice (DR). After 4 weeks, rats fed the Dongchunghacho rice diet with high fat and cholesterol had dramatically lower plasma LDL cholesterol concentrations and atherogenic indexes and higher plasma HDL cholesterol levels compared with the rats consuming polished rice or unpolished rice with high fat and cholesterol diet. Dongchunghacho rice led to less total lipid and total cholesterol accumulation in liver. However, these significant reductions in plasma or hepatic lipid profiles were not closely correlated with fecal total lipid or total cholesterol excretion. The plasma concentration of total cholesterol and triglycerides were not affected by Dongchunghacho rice. This hypolipidemic effect of Dongchunghacho rice seemed to be unrelated to unpolished rice itself, because the plasma and hepatic lipid profiles of UR group were not different from that of the HC group. These results suggest that unpolished rice containing cultivated *Cordyceps militaris* can improve plasma and hepatic lipid profiles in rats fed with high fat-high cholesterol diet.

Key words: Dongchunghacho rice, unpolished rice, *Cordyceps militaris*, high fat-cholesterol diet, cholesterol

INTRODUCTION

Hypercholesterolemia is regarded as a major risk factor for cardiovascular diseases, such as atherosclerosis, myocardial infarction, heart attacks, and cerebrovascular diseases, which are leading causes of death in advanced countries (1). Moreover, it has been well documented that lowering circulating cholesterol levels can reduce the risk of these diseases (2). To prevent such diseases, there is an enormous interest in healthy dietary habits and functional food made from natural substances capable of lowering plasma cholesterol (3).

Cordyceps militaris, a species of parasitic fungus on the larvae of *Lepidoptera*, has received considerable attention as a traditional oriental medicine (4). *Cordyceps militaris* strain is a broad host range entomopathogenic fungal species recognized as a potential candidate for biological control of pine moth populations (5). The entomogenous fungal species invade and proliferate within insect larvae, causing a systematic infection that eventually kills the hosts (6). Studies suggest that *C. militaris* may be a potential anti-hyperlipidemia agent. Koh found that supplementing the diet with 3% mycelium of *C. militaris* decreased serum cholesterol and triglycerides in rats (7,8). It was also observed that submerged mycelial culture of *C. militaris* led to a significant reduction of plasma total cholesterol and triglycerides in rats by Yang et al. (4).

Recently Dongchunghacho rice, produced by cultivating *C. militaris* or *Paecilomyces tenuipes* (normally called 'Dongchunghacho' fungus in Korea) on the rice has emerged on the market and it could be a effective functional food because it offers added value to rice and thus increases rice consumption. However, the physio-

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logical effect of Dongchunghacho rice has not yet been reported, although consumer demand for it is increasing.

In the present study we investigated the effect of the unpolished rice cultivated with *C. militaris* on lipid metabolism in rats fed a high-fat and high-cholesterol diet.

MATERIALS AND METHODS

Entomopathogenic fungi

The wild entomopathogenic fungi, *Cordyceps militaris*, were collected at Whawang Mountain, Changryung, Korea. The spores were isolated on PDA (potato dextrose agar) medium form the fruiting body of *C. militaris*, and the hyphal body cultured on the PDA was subcultured in PD medium in a shaking incubator at 12 rpm for 7 days at 25±1°C.

Induction of mycelium and spore on rice

Unpolished rice was purchased from a local supermarket and was used as the substrate for Dongchunghacho rice production under solid state cultivation. Unpolished rice was soaked in water for 40 h. After that, excessive water was removed with a sieve and the soaked rice, divided into 100 g in autoclavable bags, were autoclaved for 16 min at 121°C. After cooling, the substrate was inoculated with 1 mL of *C. militaris* (10^8 spores/mL) and cultivated at 24°C for 10 days in a dark incubator and then 30 days further under a photoperiod of 24H to induce mycelium and spore formation on the rice (Fig. 1). The Dongchunghacho rice was then lyophilized for further experimentation. Unpolished rice was prepared by the same method as Dongchunghacho rice except for inoculation with *C. militaris*.

Animal and diets

Eight-week-old male Sprague Dawley rats (n=40) were purchased from Samtako Inc. (Osan, Korea) and were bred in the Department of Sericultural and Entomological Biology, Miryang University. The animals were housed and cared for in accordance with the *Guide for Care and Use of Laboratory Animals* (Department of Health, Education and Welfare, 1985). They were allowed free access to water and fed a commercially prepared pelleted diet for 1 week for adjustment. The rats were divided in 4 groups and fed one of the following for 4 wk: normal diet containing 65.949% polished rice as the carbohydrate (NC); high-fat and high-cholesterol control diet (12 g lard+1 g cholesterol/100 g diet) with 52.949% polished rice as the carbohydrate (HC); high fat-high cholesterol diet supplemented with 30% of the rice as either unpolished rice (UR) or 30% Dongchunghacho rice (DR). The composition of the diets is shown in Table 1. Animals were monitored daily for

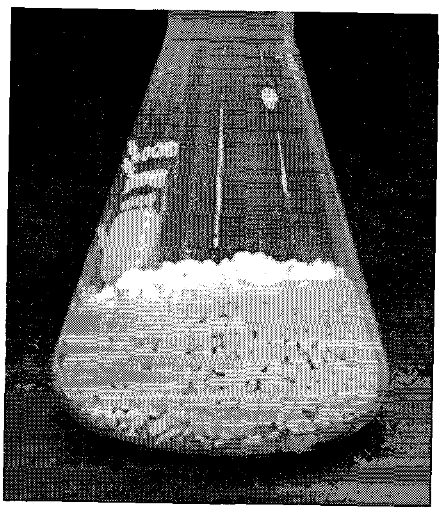

Fig. 1. Image of unpolished rice cultivated with *Cordyceps militaris*.

Table 1. Composition of the experimental diet (g/100 g diet)

Ingredients	Groups[1]			
	NC	HC	UR	DR
Casein	20	20	20	20
Polished rice	65.949	52.949	37.0643	37.0643
Unpolished rice	-	-	15.8847	-
Dongchunghacho rice	-	-	-	15.8847
Corn oil	5	5	5	5
Lard	0	12	12	12
Cholesterol	0	1	1	1
Cellulose	4	4	4	4
Vitamin mixture[2]	1	1	1	1
Mineral mixture[3]	3.5	3.5	3.5	3.5
Choline bitartarate	0.25	0.25	0.25	0.25
DL-Methionine	0.3	0.3	0.3	0.3
Butylated hydroxy toluene	0.001	0.001	0.001	0.001
Total	100	100	100	100

[1]NC, normal control diet provided 65.949% of polished rice as carbohydrate; HC, high-fat and high-cholesterol control diet (12 g lard+1 g cholesterol/100 g diet) provided with 52.949% polished rice as carbohydrate; UR, high fat-high cholesterol diet supplemented with 30% unpolished rice; DR, high fat-high cholesterol diet supplemented with 30% Dongchunghacho rice of total polished rice.

[2]AIN 76 vitamin mixture contained (in g/kg of mixture): thiamine HCl 0.6; riboflavin 0.6; pyridoxine HCl 0.7; niacin 3; d-calcium pantothenate 1.6; folic acid 0.2; d-biotin 0.02; cyanocobalamin (vitamin B_{12}) 0.001; dry vitamin A palmitate (500,000 U/d) 0.8; dry vitamin E acetate (500 U/d) 10; vitamin D_3 trituration (400,000 U/g) 0.25; menadione sodium bisulfite complex 0.15; sucrose finely powdered 981.08.

[3]AIN 76 mineral mixture contained (in g/kg of mixture): calcium phosphate, dibasic 500; sodium chloride 74; potassium citrate, monohydrate 220; potassium sulfate 52; magnesium oxide 24; manganous carbonate (43~48% Mn) 3.5; ferric citrate (16~17% Fe) 6; zinc carbonate (70% ZnO) 1.6; cupric carbonate (53~55% Cu) 0.3; potassium iodate 0.01; sodium selenite 0.01; chromium potassium sulfate 0.55; sucrose, finely powdered 118.03.

general health, and body weights were recorded every week for the duration of the study. Feces were collected during the final 3 days, and were used to determine fecal lipid profiles. At the end of the experimental period, the rats were anesthetized with ethyl ether and blood was collected from the abdominal artery into heparinized sterile tubes. Plasma was obtained from the blood samples by centrifugation (1500 rpm for 30 min) and stored at -80°C until further analysis. The livers were removed and washed with ice-cold saline and then stored at 80°C before analysis.

Plasma AST, ALT activities, protein and lipid profiles

Plasma aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, total bilirubin, uric acid, creatinine, albumin and lipid profiles (total lipids, total cholesterol, HDL-cholesterol and triglycerides) were measured by enzymatic colorimetric methods with a commercial kit (Bio Clinical System Co., Korea) and a photometric autoanalyzer (SEAC, CH-100 plus, Italy). Plasma LDL cholesterol level was calculated using the formula developed by Friedewald et al. (9). The atherogenic index (AI) was calculated as follows: AI= (total cholesterol−HDL cholesterol)/HDL cholesterol.

Liver and fecal lipid profiles

Hepatic and fecal lipids were extracted according to the procedure developed by Folch et al. (10). Liver or fecal lipid extract was prepared by extracting 1~2 g liver or feces with a chloroform/methanol mixtures (2:1 v/v). The total lipids in the liver and feces were then quantified gravimetrically by evaporating the solvent. Dried lipids were dissolved in 1 mL of ethanol for cholesterol and triglycerides measurement after Triton X-100 treatment. Hepatic cholesterol and triglycerides were analyzed with the same enzymatic kit as used in the plasma analysis.

Statistical analysis

Data were analyzed using SPSS for Windows (Version 10). Values were expressed as mean±standard error (SE). The data was evaluated by one-way ANOVA and the differences between the means assessed using Duncan's multiple range test. The differences were considered significant at $p<0.05$.

RESULTS

As shown in Table 2, the daily body weight gain of the UR and DR group (2.3±0.3 and 2.3±0.3) was slightly higher than the NC and HC group (2.1±0.2 and 2.0±0.2) without significance. Food intake did not appear to be influenced by Dongchunghacho rice or unpolished rice. Also, the organ weights were not found to differ among the groups.

The plasma lipid profiles are summarized in Table 3. Plasma total cholesterol and triglycerides were not sig-

Table 2. Effect of Dongchunghacho rice supplementation on weight gains, food intake and relative organ weights of rats fed a high-fat and high-cholesterol diet

	Groups[1)]			
	NC	HC	UR	DR
Body weight gain (g/day)	2.1±0.2[2)ns3)]	2.0±0.2	2.3±0.3	2.3±0.3
Food intakes (g/day)	16.7±0.1[ns]	16.3±0.1	15.8±0.3	15.9±0.4
Organ weight (g/100 g BW)				
Liver	2.5±0.1[ns]	3.3±0.2	2.4±0.1	2.8±0.3
Spleen	0.20±0.02[ns]	0.20±0.01	0.25±0.04	0.22±0.01
Kidney	0.62±0.03[ns]	0.76±0.13	0.49±0.02	0.59±0.03

[1)]Groups are the same as in Table 1.
[2)]Values are the mean±SEM for 10 animals in each group.
[3)]Not significant.

Table 3. Effect of Dongchunghacho rice supplementation on lipid profiles in plasma in male SD rats fed a high-fat and high-cholesterol diet

	Groups[1)]			
	NC	HC	UR	DR
Total cholesterol (mg/dL)	77.6±5.0[2)ns3)]	99.8±9.1	96.2±7.2	80.5±8.3
Triglycerides (mg/dL)	57.5±12.6[ns]	56.4±7.0	40.3±5.2	45.3±7.2
LDL cholesterol (mg/dL)	37.6±3.4[a4)]	66.3±7.9[b]	68.4±7.9[b]	38.7±4.1[a]
HDL cholesterol (mg/dL)	28.5±2.8[bc]	22.2±3.2[ab]	19.7±1.7[a]	30.6±2.2[c]
HDL-C/Total-C	36.5±1.7[b]	22.4±2.8[a]	21.2±3.2[a]	39.3±1.1[b]

[1)]Groups are the same as in Table 1.
[2)]Values are the mean±SEM for 10 animals in each group.
[3)]Not significant
[4)]Values within a row with different superscripts are significantly different at $p<0.05$ by ANOVA and Duncan's multiple range test.

nificantly affected by Dongchunghacho rice supplementation, however, LDL cholesterol was significantly lower in the DR group compared to HC and UR groups. HDL cholesterol and the ratio of HDL cholesterol to total cholesterol was significantly higher in DR group, which were almost same the values as the normal control. On the other hand, atherogenic values were significantly lower in the DR group compared to the HC and UR groups (Fig. 2).

The effects of Dongchunghacho rice on the hepatic and fecal lipid profiles are summarized in Table 4. Hepatic total lipid and total cholesterol were significantly lower in the DR group than in HC and UR groups. Hepatic triglyceride concentrations were lower in the DR group compared to the UR group. However, the significantly lower plasma and hepatic lipid profiles were not closely correlated with fecal total lipid or total cholesterol excretion except fecal triglycerides levels, which were significantly lower in the DR group than in the HC group.

The plasma AST and ALT activities, and plasma protein concentrations are detailed in Table 5. No significant differences were observed in plasma AST and ALT activities, total protein, total bilirubin, uric acid, creatinine and albumin levels among the groups.

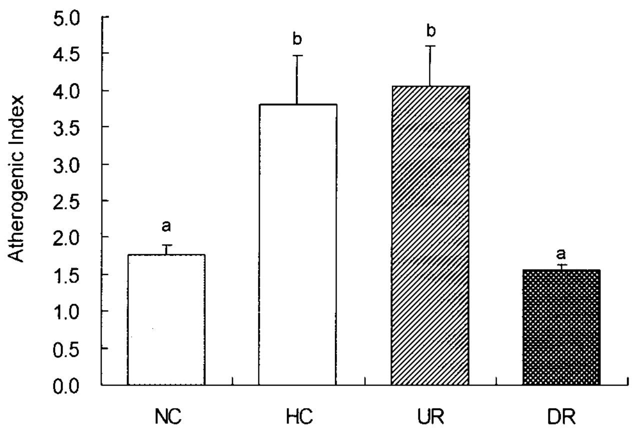

Fig. 2. Effect of Dongchunghacho rice on atherogenic index in SD male rat. Each bar represents mean±SEM for 10 animals in each group. Bars with different superscripts are significantly different at the $p<0.05$ level by ANOVA and Duncan's multiple range test. Abbreviations are the same as in Table 1.

Table 4. Effects of Dongchunghacho rice supplementation on lipid profiles in liver and feces in male SD rats fed a high-fat and high-cholesterol diet

	Groups[1)]			
	NC	HC	UR	DR
Liver lipid profiles				
Total lipid (mg/g wet wt)	13.4±1.5[2)a3)]	60.2±14.9[b]	59.2±5.0[b]	27.7±4.5[a]
Total cholesterol (mg/g wet wt)	1.3±0.2[a]	8.8±2.6[c]	9.8±0.7[c]	6.0±0.6[b]
Triglycerides (mg/g wet wt)	2.9±0.8[a]	8.5±1.1[bc]	13.6±1.4[c]	7.1±1.5[ab]
Fecal lipid profiles				
Total lipid (mg/g dry wt)	11.6±1.5[a]	40.9±6.6[b]	43.4±6.5[b]	36.7±8.6[b]
Total cholesterol (mg/g dry wt)	3.8±1.0[a]	29.0±2.0[b]	30.0±0.9[b]	23.0±2.4[b]
Triglycerides (mg/g dry wt)	0.41±0.02[a]	1.0±0.1[a]	1.5±0.3[ab]	1.9±0.5[b]

1)Groups are the same as in Table 1.
2)Values are the mean±SEM for 10 animals in each group.
3)Values within a row with different superscripts are significantly different at $p<0.05$ by ANOVA and Duncan's multiple range test.

Table 5. Effect of Dongchunghacho rice supplementation on plasma AST, ALT, and protein profiles in male SD rats fed a high-fat and high-cholesterol diet

	Groups[1)]			
	NC	HC	UR	DR
AST (U/L)	59.4±3.6[2)ns3)]	51.7±3.3	55.6±4.8	60.4±5.1
ALT (U/L)	24.8±2.9[ns]	20.8±2.0	21.8±2.1	16.8±5.2
Total protein (g/dL)	7.40±0.24[ns]	7.80±0.17	7.58±0.20	7.41±0.38
Total bilirubin (mg/dL)	0.38±0.02[ns]	0.37±0.01	0.35±0.01	0.37±0.03
Uric acid (mg/dL)	3.86±0.56[ns]	3.77±0.48	3.92±0.38	3.90±0.77
Creatinine (mg/dL)	0.49±0.04[ns]	0.50±0.06	0.48±0.02	0.43±0.01
Albumin (g/dL)	3.08±0.05[ns]	2.85±0.10	2.76±0.07	3.03±0.11

1)Groups are the same as in Table 1.
2)Values are the mean±SEM for 10 animals in each group.
3)Not significant.

DISCUSSION

Dongchunghacho rice used in this study was a cultivated product of unpolished rice on which *Cordyceps militaris* had been grown. Unpolished rice, also known as brown rice, contains much more dietary fiber than polished rice. It is possible that the higher contents of dietary fiber in unpolished rice could also exert effects on cholesterol metabolism. However, in this study, equal amounts of unpolished rice eaten with a high fat-cholesterol diet did not significantly affect the lipid profile compared with rats fed high fat-cholesterol diet alone, although their higher dietary fiber contents were higher (0.27 g/100 g diet in UR vs. 0.16 g/100 g diet in HC) (11). These results are consistent with a study of Miyoshi et al. (12) in which they found that plasma cholesterol was not significantly affected by polished rice diet vs. brown rice diet for 14 days in young men. On the other hand, rats consuming Dongchunghacho rice diet with high fat and cholesterol had dramatically lower plasma LDL cholesterol concentration and atherogenic index and higher plasma HDL cholesterol levels compared with the rats consuming polished rice or unpolished rice with high fat and cholesterol diet. To our knowledge, this is the first finding of a beneficial effect of Dongchunghacho rice on prevention of hyperlipidemia. Dongchunghacho rice supplementation also significantly reduced hepatic cholesterol in hypercholesterolemic rats, suggesting that the hepatic biosynthesis of cholesterol had been suppressed. The hypolipidemic effect of Dongchunghacho rice could be ascribed to mycelia and spores of *C. militaris* cultivated on unpolished rice. The hypolipidemic effect of mycelium or fruiting body of *C. militaris* has already been reported in rats (4,7,8). Although the mechanism by which Dongchunghacho rice improves plasma lipid profiles in hypercholesterolemic rats is not understood, the hypolipidemic effect of the mycelium and spore of *C. militaris* could be due to a reduced activity of the liver enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme of cholesterol biosynthesis (13). In relation to our results, red yeast rice, a fermented rice product on which red yeast (*Monascus purpureus*), has been found to have the ability to lower blood-lipid levels in animal models and in humans (14-16) and is used in China as well as in many other countries including the United States (17). Several studies reported that *Monascus* yeast naturally produced a substance that inhibits cholesterol synthesis, which named monacolin K, as well as a family of 8 monacolin-related substances with the ability to inhibit HMG-CoA reductase (18). In addition to the inhibitors of HMG-CoA reductase, red yeast rice has been found to contain sterols (β-sitosterol, campesterol, stigmasterol, and sapogenin), isoflavones and isoflavone glycosides, and monounsaturated fatty acid (15).

It is also possible that increased plasma HDL cholesterol by Dongchunghacho rice supplementation results from cholesterol or cholesterol esters being transported from peripheral tissues or cells to the liver where cholesterol is metabolized into bile acids. This pathway plays a very important role in reducing the cholesterol level in blood and peripheral tissues, and in inhibiting the atheroslerotic plaque formation in the aorta (19). Further studies should be conducted to elucidate the exact mechanism underlying the plasma and hepatic lipid-lowering effects of unpolished rice cultivated with *C. militaris* and the possible hypolipidemic compound(s) contained in Dongchunghacho rice, similar to monacolin K in red yeast rice. In addition to the hypolipidemic activities, other bioactivities of Dongchunghacho rice should be investigated further, because studies have reported that *C. militaris* itself may have anti-proliferation effect on tumor cells as well as prolonging the life or mice bearing ascites tumor (20), has cytotoxic and anti-genotoxic effects on the human cancer cell lines (21), and has hypoglycemic effects in rat (22).

Our results suggest Dongchunghacho rice has potential health benefits as a modulator of physiological functions, e.g., various atherogenic lipid profiles in hypercholesterolemia. The developed method of cultivation provides a novel functional food supplement that may also act as a prophylactic against hypercholesterolemia and provide health benefits in terms of counteracting hyperlipidemia and its related complications. In addition, it will also provide an economic opportunity for farmers to have access to specialized crops with the potential for greater income from smaller sized farms by distributing the mass production technique of Dongchunghacho rice production to farm houses, and to develop Dongchunghacho rice as an export product.

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REFERENCES

1. Wald NJ, Law MR. 1995. Serum cholesterol and ischemic heart disease. *Atherosclerosis* 118: S1-S5.
2. Barter PJ, Rye KA. 1996. Molecular mechanisms of reverse cholesterol transport. *Curr Opin Lipidol* 7: 82-87.
3. Heber D. 2001. Herbs and atherosclerosis. *Curr Atheroscler Rep* 3: 93-96.

4. Yang BK, Ha JY, Jeong SC, Das S, Yun JW, Lee YS, Choi JW, Song CH. 2000. Production of exo-polymers by submerged mycelial culture of *Cordyceps militaris* and its hypolipidemic effect. *J Microbiol Biotechnol* 10: 784-788.
5. Alicja S. 1998. Towards an integrated management of *Dendrolimus pini* L. Proceedings, USDA forest service general technical report NE-247, Banska Stiavnica, Slovak Republic. p 129.
6. Clarkson JM, Charnley AK. 1996. New insights into the mechanisms of fungal pathogenesis in insects. *Trends Microbiol* 4: 197-203.
7. Koh JB. 2001. Effect of fruiting body *Cordyceps militaris* on growth, lipid and protein metabolism, and enzyme activities in male rats. *Korean J Nutr* 34: 741-747.
8. Koh JB. 2002. The effect of *Cordyceps militaris* on lipid metabolism, protein levels and enzyme activities in rats fed a high fat diet. *Korean J Nutr* 35: 414-420.
9. Friedewald WT, Levy RI, Fredrickson DS. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 18: 499-502.
10. Folch J, Lees M, Sloan-Stanley GH. 1956. A simple method for isolation and purification of total lipids from animal tissues. *J Biol Chem* 226: 497-509.
11. The Korean Nutrition Association. 2000. Recommended dietary allowance for Koreans. 7th revision. p 276-277.
12. Miyoshi H, Okuda T, Okuda K, Koishi H. 1987. Effects of brown rice on apparent digestibility and balance of nutrients in young men on low protein diets. *J Nutr Sci Vitaminol* 33: 207-218.
13. Endo A. 1992. The discovery and development of HMG-CoA reductase inhibitors. *J Lipid Res* 33: 1569-1582.
14. Zhao SP, Liu L, Cheng YC, Li YL. 2003. Effect of xuezhikang, a cholestin extract, on reflecting postprandial triglyceridemia after a high-fat meal in patients with coronary heart disease. *Atherosclerosis* 168: 375-380.
15. Heber D, Yip I, Ashley JM, Elashoff DA, Elashoff RM, Go VL. 1999. Cholesterol-lowering effects of a proprietary Chinese red-yeast-rice dietary supplement. *Am J Clin Nutr* 69: 231-236.
16. Wei W, Li C, Wang Y, Su H, Zhu J, Kritchevsky D. 2003. Hypolipidemic and anti-atherogenic effects of long-term Cholestin (*Monascus purpureus*-fermented rice, red yeast rice) in cholesterol fed rabbits. *J Nutr Biochem* 14: 314-318.
17. Journoud M, Jones PJ. 2004. Red yeast rice: a new hypolipidemic drug. *Life Sci* 74: 2675-2683.
18. Endo A. 1979. Monacolin K, a new hypocholesterolemic agent produced by a Monascus species. *J Antibiot* 32: 852-854.
19. Stein O, Stein Y. 1999. Atheroprotective mechanisms of HDL. *Atherosclerosis* 144: 285-301.
20. Lee H, Yang M, Park T. 2003. Inhibitory effect of *Cordyceps militaris* water extracts on Sarcoma-180 cell-induced ascities tumor in ICR mice. *Korean J Nutr* 36: 1022-1029.
21. Kim MN, Cui CB, Lee SK, Han SS. 2001. Cytotoxicity and antigenotoxic effects of *Cordyceps militaris* extracts. *J Korean Soc Food Sci Nutr* 30: 921-927.
22. Kwon YM, Cho SU, Kim JH, Lee JH, Lee YA, Lee SJ, Lee MW. 2001. Hypoglycemic effect of *Cordyceps militaris*. *Kor J Pharmacogn* 32: 327-329.

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