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Fermented *Kochujang* Supplement Shows Anti-obesity Effects by Controlling Lipid Metabolism in C57BL/6J Mice Fed High Fat Diet

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Abstract The aim of the present study was to assess the anti-obesity effects of fermented *kochujang* supplement in C57BL/6J mice. Thirty mice were divided into 3 groups; normal diet control group (ND), high fat diet control group (HD), and high fat diet plus *kochujang* supplemented group (HDK). Results were as follows: 1. Fermented *kochujang* supplement in high fat diet decreased body weight and epidydimal and back fat weight compared to non-supplement in HD group. 2. Lipid content and blood glucose level were lower in HDK group than HD group. 3. Fermented *kochujang* supplement increased mRNA level of lipolytic genes such as acyl-CoA synthetase (ACS), carnitine palmitoyltransferase-1 (CPT-1), and uncoupling proteins-1 (UCP-1) expression, whereas decreased mRNA level of adipogenic genes such as acetyl CoA carboxylase (ACC) expression. These findings suggest that fermented *kochujang* supplement in high fat diet normalized body weight, epididymal and back fat weight, lipid content, and blood glucose levels through controlling lipid metabolism and provides basic information on the control of obesity.

Keywords: *kochujang*, body weight, lipid content, blood glucose, gene expression

Introduction

Kochujang (red pepper paste) is one of the Korea's most representative fermented foods with *doenjang* (soybean paste) and *ganjang* (soy sauce). It was introduced to Korea is estimated to be the late 1700's. The traditional *kochujang* is usually prepared by mixing powdered red peppers, powdered *meju* (fermented soybean powder), salt, malt-digested rice syrup, and rice flour, and the mixture is fermented for more than 6 months in an open place with direct sunlight. During the fermentation, free sugars, free amino acids, alcohols, and organic acids are produced by various microorganisms in the *meju*. These products affect the taste and color of *kochujang*. Therefore, *kochujang* has unique taste, which is a combination of a sweet taste from a starch hydrolyzate, a hot taste of red pepper, a savory taste from the soybean protein hydrolyzate and nucleic acids, and a salty taste from salt (1). The bright red *kochujang* also enhances the appearance of food. Vegetables or seafood, mixed with *kochujang* are well-balanced in terms of nutrition. It contains cabohydrate, protein, and vitamin B_1, B_2, C, and folic acid from red peppers (2). *Kochujang* has been used as a sauce and dressing for meat and vegetables, and is also added to stew and soup as a seasoning. Current researches are concentrated on biological and physiological functions of *kochujang*. Recently, several studies have indicated that traditional *kochujang* exhibits antimutagenic activity (3), antiobesity effect (4), and antitumor effect (5).

Obesity and diabetes are worldwide epidemics and cause a major public health problem (6,7). Especially, obesity is caused by an excessive increase in white adipose tissue (8). Differentiated adipocyte stores fatty acids in the form of triglycerides (TGs) in their cytoplasm, with an involvement of various enzymes such as acetyl CoA carboxylase (ACC), strearoyl CoA desaturase-1 (SCD-1), and fatty acid synthase (FAS) (9). Excessive energy intake for a long period, TGs can be accumulated in non-adipose tissues, including liver and muscle which can lead to pathological consequences such as the development of fatty liver, hyperlipidemia, diabetes, and arteriosclerosis (10). Therefore, to maintain lipid homeostasis, the body operates a fatty acid (FA)-oxidation system which allows the FA to break down into CO_2 and ketone body. These final metabolites are released into blood. In this lipolytic process, many enzymes are involved such as acyl-CoA synthetase (ACS), carnitine palmitoyltransferase-1 (CPT-1), uncoupling proteins (UCPs), and their gene expression is known to be modulated by a nuclear orphan receptor known as peroxisome proliferators activated receptor-α (PPAR-α) (11). Lipid homeostasis is maintained by the fine-tuning of lipogenesis and lipolysis, which are regulated by cooperative action of various enzymes in the metabolic organs such as adipose tissues, liver, and muscle (12).

Many attempts have been made to correct the metabolic disparity of the obesity condition. However, administration of various regents such as appetite suppressor, gastro-intestinal lipid uptake inhibiter, and fibrates cause undesirable side effects such as a dry mouth, anorexia, constipation, insomnia, dizziness, and nausea. In recent years, the importance of biologically active substances contained in foods has been noticed, and many physiological effects of foods have been reported (13).

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Fermented foods are those whose production involves the action of microorganisms or enzymes which cause desirable biochemical changes and significant modification to the food (14). *Kochujang* is a popular traditional fermented food in Korea and exhibits several physiological functions. However, there have been few studies investigating the effect of *kochujang* on obesity and its underlying mechanisms. If a fermented food has an anti-obesity activity, it would be more useful than pharmacological agents since it hardly has any side effects. The purpose of this study was to determine the decreasing effects of fermented *kochujang* supplement on body weight, lipid, and glucose levels in C57BL/6J mice, strain with a propensity for high fat diet-induced obesity. To elucidate the molecular mechanisms of that effect, we carried out experiments aimed at analyzing biochemical parameters and gene expression associated with adipogenesis and lipolysis using reverse transcription-polymerase chain reaction (RT-PCR).

Materials and Methods

Preparation of *kochujang* The *kochujang* was prepared according to the traditional method. As the first stage of *kochujang* preparation, *meju* was prepared as follows. Soybeans were soaked in water for 15 hr, drained for 30 min, steam-cooked using steam pressure at 1.2-1.3 kg_f/cm^2, pounded into pulp, and then fermented for 3 months in an open place. The lumps are powdered and used to make *kochujang*. *Kochujang* was prepared by mixing glutinous rice 18%, *meju* power 6%, melt-digested syrup 4%, salt 10.5%, red pepper powder 17.5%, and water 44%. The mixture was allowed to ferment for more than 6 months in an open place with abundant sunlight. The *kochujang* was supplied by Department of Food Science & Technology, Chonbuk National University, Korea in a state of vaccum freeze drying.

Animals and diets Male C57BL/6J mice, 4 weeks old, were maintained on a chow diet (Research Diets; New Brunswick, NJ, USA) for 1 week, and then aged 5 weeks mice randomly divided into 3 groups: normal diet control group (ND), high fat diet control group (HD), and high fat diet plus *kochujang* supplemented group (HDK): normal diet control group which was fed based on the AIN-93 modified diet (Research Diets) with 4% fat (10% fat calories) content, high fat diet group which was fed based on the AIN-93 modified high fat diet with 24% fat (45% fat calories) content, and high fat diet plus *kochujang* group which was fed based on AIN-93 modified high fat diet containing 22% *kochujang*. The composition of experimental diets is shown in Table 1.

The animals were housed in a temperature-controlled environment with a 12-hr light/dark cycle. They were allowed free to access to food and water for the 12-week study. The food consumption and body weight were measured daily and weekly. At approximately 16 weeks of age, the animals were anesthetized and sacrificed by cardiac puncture.

Serum and tissue sample Blood samples were collected from each mouse by cardiac puncture and then incubated in an ice water bath for 1 hr. Serum was separated by centrifugation at 1,100×g for 15 min at 4°C and kept at −80°C until use. Epididymal and back fat tissues were isolated, rinsed with a phosphate-buffered saline (PBS) solution, dried with a paper towel, weighed quickly, frozen in liquid nitrogen, and stored at −80°C until assayed.

Table 1. Composition of experimental diet (AIN-93 modified diet for rodents)

Ingredient (g)	I	II	III
	Normal diet[1)]	High fat diet[2)]	High fat diet+ *kochujang*
Casein, lactic	200	200	188.95
L-Cystine	3	3	2.83
Corn starch	315	72.8	-
Maltodextrin	35	100	77.3
Sucrose	350	172.8	42.54
Cellulose	50	50	45
Soybean oil	25	25	24.65
Lard	20	177.5	241.61
Mineral mix	10	10	9
Dicalcium phosphate	13	13	11.7
Calcium carbonate	5.5	5.5	4.95
Potassium citrate	16.5	16.5	14.85
Vitamin mix	10	10	9
Choline bitarate	2	2	1.8
FD&C Yellow dye #5	0.05	-	-
FD&C Blue dye #1	-	0.05	-
Kochujang[3)]	-	-	187
Total	1055.05	858.15	861.18
kcal	4057	4057	4053.2
kcal/g	3.8	4.7	4.5

[1)]AIN-93 modified diet with 4% fat (10% fat calories) content.
[2)]AIN-93 modified high fat diet with 24% fat (45% fat calories) content.
[3)]AIN-93 modified high fat diet containing 22% *kochujang*.

Analysis of lipids Levels of total cholesterol and high-density lipoprotein (HDL)-cholesterol fraction in the serum were measured by enzyme method using a commercial kit (Asan Pharmaceutical Co., Seoul, Korea). Levels of triglyceride in the serum were determined using a commercial kit (Asan Phamaceutical Co.). Liver lipids were extracted from liver tissues according to method described by Folch *et al.* (15). Levels of triglyceride in the liver were determined using a commercial kit (Asan Phamaceutical Co.).

Analysis of blood glucose concentration Blood samples were collected from the tail vein of mice at 8, 10, 12, 14, 16 week of age. The fasting blood glucose was measured in the morning after 8 hr overnight fast using a commercial kit (Dongbang International Co., Seoul, Korea).

Determination of mRNA levels in liver and adipose tissues Total RNA was extracted with Trizol reagent and concentration of RNA was determined using a spectrophotometer, and RT-PCR was carried out using a one-step

RT-PCR kit (ABgene, NY, Rochester, USA) for cDNA synthesis on an RT-PCR machine (MWG-Biotech, High Point, NC, USA). β-Actin cDNA was also prepared as a control. Upon completion of the reaction, cDNA products were analyzed by 1.5% agarose gel electrophoresis. By this method we confirmed the expressions on of acyl-CoA synthetase (ACS), carnitine palmitoyl transferase-1 (CPT-1), acetyl CoA carboxylase (ACC), uncoupling proteins-1 (UCP-1). The relative intensity of all mRNAs was analyzed by using the Alpha Ease FC software (Alpha Innotech Corporation, San Leandro, CA, USA). The primer sequences used for detection of ACS, ACC, CPT-1 in the liver and CPT-1 in abdominal fat were as follows. forward: 5'TGA AGC CAT CAC GTA CAT AGT CAA C3' and reverse: 5'TCG ACT GTA CTT TGT GGA AGA TCA G3' for ACS, forward: 5'CCA CCT ATG TGT ACG ACT TCC C3' and reverse 5'GCC CAC CTC GTT ACA ACC AG3' for ACC, forward 5'AAA GAT CAA TCG GAC CCT AGA CA3' and reverse 5'CAG CGA GTA GCG CAT AGT CA3' for CPT-1, forward 5'CTC AGG ATT GGC CTC TAC GACTC3' and reverse 5'TTG GTG TAC ATG GAC ATC GCA3' for UCP-1. PCR was initiated with denaturation for 3 min at 95°C followed by 40 cycles of denaturation (1 min, 95°C), annealing (1 min, 50-60°C) chain extension (2 min, 72°C) and then 7 min of final extension at 72°C after amplification.

Statistical analysis Data from individual experiment are expressed as the mean±standard deviation. All statistical analysis was performed using SAS software (SAS Institute, Cary, NC, USA). The data were analyzed by ANOVA and Duncan's multiple range test. Statistical significance is define as $p<0.05$.

Results and Discussion

Body weight and food intake in mice Body weight and food intake during the experimental period are shown in Table 2. This data showed that final body weight was significantly increased in HD group compared to ND group ($p<0.05$). Fermented *kochujang* supplement in HD group resulted in a significant decrease in the final body weight compared to HD group ($p<0.05$). The final body weight of HDK group was almost similar to that of ND group. Body weight gain was also significantly smaller in HDK group than in HD group ($p<0.05$). Moreover, although HDK group was the highest in energy intake, this group was the lowest in body weight gain among the groups ($p<0.05$). HD group was the lowest in food intake, but weight gain of this group was the highest among the groups. These results supported Choo's findings, that *kochujang* induced a 13% reduction in body weight of SD-rats due to the significant increase in energy expenditure (4).

Red pepper, one of the main ingredients of *kochujang*, has been shown to increase energy expenditure and has an antiobesity effect in male SD-rats (16). Capsaicin [*N*-((4-hydroxy-3-methoxyphenyl)-methyl)-8-methyl-6-nonamide], a pungent principle of red pepper, has been reported to decreased the adipose tissue weight and serum triacylglycerol content by enhancing energy metabolism (17). This effect might be due to an increase of thermogenesis in brown adipose tissues through the stimulation of the sympthetic nervous system (18). A study has also indicated that body weight gain was lower in fermented *kochujang* supplement group than in hot pepper powder supplement group (4). In addition, Rhee *et al.* (16) have reported that reduction of body weight by supplement of fermented *kochujang* is more effective than non-fermented *kochujang*. These findings suggest that primary factor of *kochujang*, for decreasing body weight seems to be produced during fermentation process.

Table 2. Body weight and food intake in mice fed experimental diets for 12 weeks[1)]

Groups	ND	High fat diet	
		HD	HDK
Initial weigh (g)	20.35±1.00	20.83±1.15	21.65±1.73
Final weight (g)	27.41±1.39[b]	31.55±2.56[a]	27.36±2.58[b]
Weight gain (g/day)	0.08±0.02[b]	0.12±0.03[a]	0.06±0.03[b]
Food intake (g/day)	1.60±0.03[b]	1.38±0.00[a]	1.69±0.10[b]
Energy intake (kcal/day)	6.08±0.10[b]	6.48±0.00[b]	7.62±0.47[a]
Feed efficiency ratio[2)]	0.049±0.014[b]	0.086±0.025[a]	0.037±0.021[b]

[1)]Mean±SD of 10 mice / group; values with different superscripts are significantly different by ANOVA with Duncan's multiple range test at $p<0.05$; ND, normal diet; HD, high fat diet; HDK, high fat diet plus *kochujang*.
[2)]Calculated as weight gain (day)/dietary intake (day).

Genistein, an isoflavone present in soybean, has estrogenic activity and is used as a natural substitute for estrogen replacement therapy in postmenopausal women (19). Genistein is also shown to decrease fat pad weight in female mice. The amount of genistein is increased in fermented soy foods compared with non-fermented soy foods, which has been attributed to cleavage of the β-glycosyl bond of genistin by microorganisms during fermentation (20).

In this study, fermented *kochujang* supplement in high fat diet significantly decreased body weight that was almost similar to that of normal diet control group. These results indicate a possibility that not only ingredient of *kochujang* but also produced some elements during fermentation are involved in reduction of body weight.

Adipose tissue mass in mice As presented in Fig. 1, epididymal fat weight was significantly decreased in HDK group than HD group ($p<0.05$). Back fat weight was also decreased significantly in HDK group than HD group ($p<0.05$). These data showed that fermented *kochujang* supplement reduces adipose tissue mass.

Adipose tissue, as a simple site of deposition and storage of energy, is now known to be an active player in the regulation of whole body metabolism. Kuriyama *et al.* (21) have reported that accumulation of intra-abdominal visceral fat is closely associated with increased incidence of metabolic complication in obesity. In more recent years, several proteins (tumor necrosis factor α, interleukin-6, resistin, and adiponectin) secreted by the adipocytes have been shown to affect insulin sensitivity and glucose metabolism (22).

Soy is a biological active plant composed of soy proteins and several bioactive components such as isoflavones

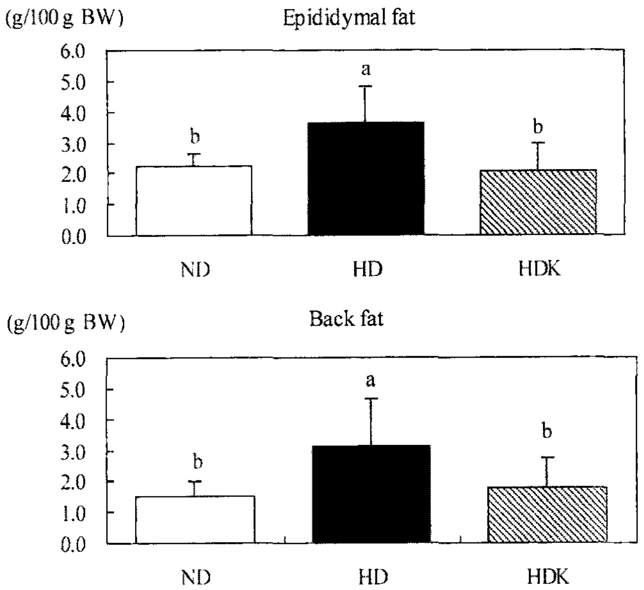

Fig. 1. Adipose tissue mass of mice fed experimental diets for 12 weeks. Mean±SD of 10 mice/group; values with different superscripts are significantly different by ANOVA with Duncan's multiple range test at $p<0.05$. ND, normal diet; HD, high fat diet; HDK, high fat diet plus *kochujang*.

peptides, globulins, saponins, phytic acid, and protease inhibitors (23). Sites *et al.* (24) have reported that supplement of soy proteins reduces the gain in total abdominal fat and subcutaneous abdominal fat compared with a daily isocaloric casein placebo in postmenopausal women. In mice, genistein is shown to decrease parametrial and inguinal adipose tissue weight, adipocyte circumference, and lipoprotein lipase messenger RNA (19). The effects of isoflavones on adipocytes may occur via regulation of genes controlling lipid accumulation, or through repression of adipocyte differentiation (25). Reduction of white adipose tissues has significant meaning on obesity and diabetes.

In this study, we found that fermented *kochujang* supplement significantly decreased total epididymal fat and back fat. These results suggest that fermented *kochujang* contains anti-obesity substances that suppress body fat accumulation.

Lipid concentration in serum and liver Cinical atherosclerotic disease is positively associated with total and low-density lipoprotein (LDL)-cholesterol and inversely associated with HDL-cholesterol (26). An atherogenic lipid profile is observed in 50-75% of patients with diabetes and is predominately characterized by elevated levels of triglycerides and apolipoprotein B, including decreased levels of HDL-cholesterol (27). Several measures of adiposity are correlated with a low concentration of HDL-cholesterol which in turn is associated with increased risk of cardiovascular disease (28).

Our data showed that HDL-cholesterol in serum was significantly higher in HD group and HDK group than ND group ($p<0.05$). Total cholesterol in serum was significantly lower in HDK group than HD group ($p<0.05$). The level of triglyceride in serum and liver from HDK group was the lowest among the groups ($p<0.05$). Total cholesterol in liver of HDK group was the lowest among the groups ($p<0.05$) (Table 3).

Table 3. Lipid concentrations in serum and liver (mg/dL)[1)]

Groups	ND	High fat diet	
		HD	HDK
Serum			
HDL-cholesterol	80.71 ± 5.00^{b}	$100.00\pm10.01^{a2)}$	101.19 ± 5.95^{a}
Total cholesterol	178.02 ± 13.19^{b}	197.80 ± 16.01^{a}	171.10 ± 4.88^{b}
Triglyceride	104.51 ± 2.25^{b}	126.61 ± 9.23^{a}	103.43 ± 12.66^{b}
Liver			
Triglyceride	84.13 ± 17.34^{a}	71.00 ± 7.52^{ab}	57.06 ± 7.37^{b}
Total cholesterol	4.69±0.96	4.38±1.47	3.95±1.12

[1)]Mean±S.D of 10 mice/group; values with different superscripts are significantly different by ANOVA with Duncan's multiple range test at $p<0.05$; ND, normal diet; HD, high fat diet; HDK, high fat diet plus *kochujang*.

In this study, fermented *kochujang* supplement in high fat diet reduced total cholesterol and triglyceride in serum and liver. The reduction of total cholesterol or low density lipoproteins found in plasma is shown to lower the risk of coronary heart disease.

A recent study has reported that soy protein reduce total and non-HDL cholesterol in plasma without significant effect on HDL-cholesterol and triglycerides in normal and hypercholesterolemic human subjects (29). Soy protein consumption prevents triglyceride accumulation in the liver and reduces deleterious effects of lipotoxicity (30). The mechanism by which soy protein prevents triglyceride accumulation is a reduction of hepatic fatty acid and triglyceride biosynthesis while fatty acid oxidation is stimulated through the activation of the transcription factor peroxisome proliferator-activated receptor (PPAR-α) (31). Our results indicate the possibility that soy protein, main ingredient of *kochujang* is involved in reduction of lipid concentration in the serum and liver.

Blood glucose concentration Long diabetes duration, poor glycemic control, hypertension, and dyslipidemia can lead to development of diabetic vascular complications (32). Levels of serum lipid are usually elevated in diabetes mellitus, and such an elevation represents a risk factor for coronary heart disease (33). This abnormal high level of serum lipids is mainly due to the uninhibited action of lipolytic hormones on the fat depots. Pushparaj *et al.* (34) have observed earlier that hypercholesterolemina and hypertriglycermina occur in STZ-induced diabetic rats. In this study, during the 12-week experiment period, blood concentration was monitored once a week (Fig. 2). After 6 weeks of the study blood glucose concentration of HDK group began to significantly decrease compared to that of HD group ($p<0.05$) After 8, 10, 12 weeks of the study, blood glucose concentrations of HDK group were significantly lower than those of HD group ($p<0.05$). Numerous studies with experimental animals and humans have documented hypolipidemic effects of soy proteins. In ovariectomized monkeys, a diet containing soy proteins with isoflavones improves insulin sensitivity and glucose effectiveness

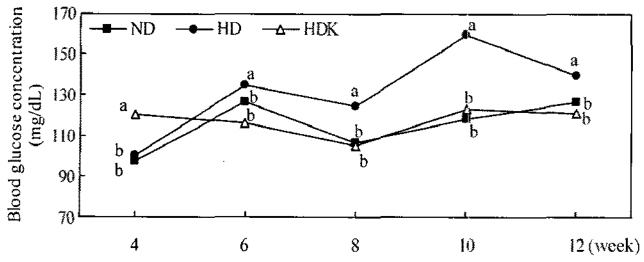

Fig. 2. Blood glucose concentration after fasting for 8 hr. Mean±SD of 10 mice/group; values with different superscripts are significantly different by ANOVA with Duncan's multiple range test at $p<0.05$; ND, normal diet; HD, high fat diet; HDK, high fat diet plus *kochujang*.

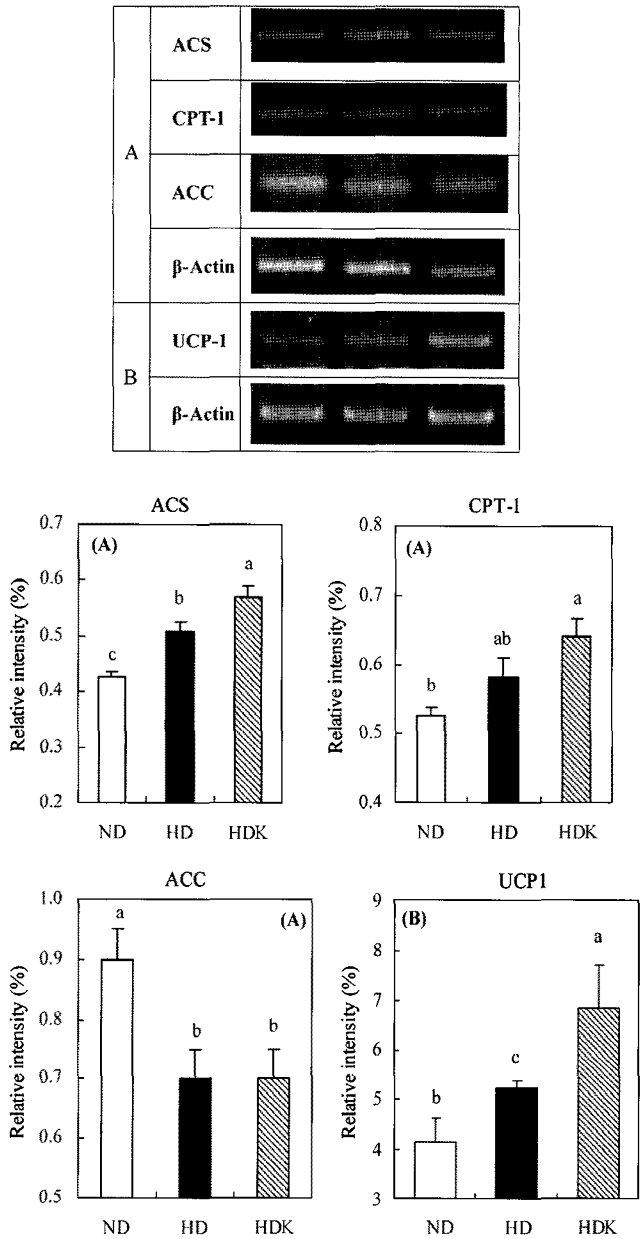

Fig. 3. Hepatic gene expressions (A) and adipose tissue gene expression (B). Values with different superscripts are significantly different by ANOVA with Duncan's multiple range test at $p<0.05$; ND, normal diet; HD, high fat diet; HDK, high fat diet plus *Kochujang*.

compared with a diet containing casein/lacto albumin protein (35). In rats, plasma insulin concentrations during glucose tolerance test are lower in soybean-fed animals (36).

In this study, fermented *kochujang* supplement in high fat diet group significantly decreased blood glucose levels compared to those of HD group. Blood glucose levels of HDK group were normalized. These data suggest that fermented *kochujang* supplement effectively prevents high-fat diet-induced diabetes. Moreover, it would have positive effects on hyperlipidemia caused by diabetes mellitus.

mRNA Expression of ACC, ACS, CPT-1 on the liver

Acecyl CoA carboxylase (ACC) enriched in lipogenic tissue, catalyzes formation of malonyl CoA from acetyl CoA, a rate-limiting enzyme in fatty acid synthesis (37). Prolonged comsumption of high-carbohydrate or fat-free diets causes an increase in enzyme synthesis, thus increasing fatty acid synthesis, conversely, a high-fat diet or fasting causes a reduction in fatty acid synthesis by decreasing the synthesis of acetyl CoA carboxylase (37). In this study, Fig. 3A showed that hepatic ACC mRNA level in HD group significantly was decreased compared to that in ND group ($p<0.05$). These data support that high-fat diet or fasting causes a reduction in fatty acid synthesis by decreasing the synthesis of acetyl CoA carboxylase (38).

Long chain fatty acyl-CoA synthetase (ACS) catalyzes the first step in intracellular lipid metabolism: The conversion of fatty acid to acyl-CoA thioesters (38). The reaction catalyzed by ACS activates free fatty acid for use in the synthesis of phospholipid or for β-oxidation. Therefore, changes in expression levels of ACS may modulate the metabolic flux of acyl-CoA in tissues that use fatty acids for the generation or storage of energy (39). Figure 3A showed that hepatic ACS mRNA levels of the HDK group is the highest among the groups. And in sequence HD group is higher than ND group ($p<0.05$). These results suggest that fermented *kochujang* supplement in high fat diet group increases β-oxidation by up-regulation of hepatic ACS expression.

Carnitine palmitoyltransferase-1 (CPT-1) is located in the outer mitochondrial membrane and catalyzes the conversion of fatty acyl-CoA to acyl carnitine (40). The activity of CPT-1 is inhibited by malonyl CoA (40). ACC catalyzes the formation of malonyl CoA from cystolic acetyl CoA (41). The primary rate controlling step in the beta-oxidation of fatty acids is catalyzed by CPT-1 (39). In this study, hepatic CPT-1 mRNA level of the HDK group is the highest among the groups (Fig. 3A). Masashi *et al.* (42) have reported that soya protein significantly increased CPT-1 mRNA levels in skeletal muscle. In this study, Fig. 3A showed that fermented *kochujang* supplement significantly increased hepatic lipolysis enzyme expression such as ACS, and CPT-1, whereas significantly decreased lipogenic enzyme expression such as ACC. These results suggest that fermented *kochujang* supplementation decrease body fat weight by suppression of adipogenic enzyme such as ACC, and overexpression of lipolytic enzyme such as ACS, CPT-1.

mRNA Expression of UCP-1 on the white adipose tissue To elucidate the molecular mechanisms of fermented *kochujang* supplement on anti-obesity effects, RC-PCR was carried out in adipose tissue genes involved in thermogenesis such as UCP. As presented in Fig. 3B, fermented *kochujang* supplement significantly increased mRNA expression UCP-1 in epididymal tissue. UCP form a subfamily within the mitochondrial anion carrier protein family. UCP-1 has an important role in controlling non-shivering thermogenesis and its mRNA expression is generally lower in obese than in normal weight rodents (43). Himms-Hagen *et al.* (44) reported that the UCP-1 mRNA level in white adipose tissue significant overexpression was found in β-adrenergic agonist injected group. The β-adrenergic agonists are known to promote energy expenditure by inducing UCP expression in a variety of tissues, brown adipose tissue, white adipose tissues and skeletal muscle (45). Capsaicin possessed potent body fat suppressive effects mediated by β-adrenergic stimulation in brown adipose tissue (46). In this study fermented *kochujang* supplement significantly increased UCP-1 expression compared to non-supplemented group (Fig. 3B). This result suggest that fermented *kochujang* supplement has anti obesity effects by overexpression of thermogenesis gene UCP-1.

In summary, our results showed that fermented *kochujang* supplement in high fat diet exhibits preventive effects on obesity of mice by reducing fat deposition and levels of cholesterol, triglyceride, and blood glucose increased by high fat diet. The preventive role of *kochujang* in obesity seems to be mediated by down-regulating expression lipogenic enzyme while up-regulation of lipolysis enzyme and thermogenesis gene UCP-1. These findings provide valuable information on fermented *kochujang* in public health.

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