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Note

Effects of *Platycodon Grandiflorum* Feeding on Serum and Liver Lipid Concentrations in Rats with Diet-Induced Hyperlipidemia

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Summary To study the effect of *Platycodon grandiflorum* (*P.g.*) feeding on serum and liver lipid concentrations, diet-induced hyperlipidemic rats were fed diets containing 5% and 10% *P.g.* powder for 3 weeks. The *P.g.* feeding markedly decreased both serum and liver lipid concentrations in hyperlipidemic rats. Especially, 5% *P.g.* diet significantly decreased the concentrations of total cholesterol and triglycerides in serum and liver as compared with those of the hyperlipidemic control group. Dietary *P.g.* also induced a reduction in low-density lipoprotein (LDL)-cholesterol as well as an increase in the concentration of high-density lipoprotein (HDL)-cholesterol in serum. Furthermore, the atherogenic index was also low in rats fed *P.g.* diet. These results indicated that dietary *P.g.* may have a beneficial effect on preventing hypercholesterolemia and hyperlipidemia.

Key Words *Platycodon grandiflorum* (*P.g.*), liver function, triglyceride, HDL-cholesterol, LDL-choleserol, cholesterol-lowering effect, triglyceride-lowering effect, hyperlipidemic rats

The root of *Platycodon grandiflorum A. DC* (Chinese drug, 'Jiegeng'; Korean name, 'Doraji'; and Japanese name, 'Kikyo') has been used as a traditional oriental medicine. In Korea, the root of *P. grandiflorum* (four years) has generally been used as a food, and employed as folk remedy for diseases of adulthood such as hyperlipidemia, hypertension and diabetes. Some studies on its chemical (*1–3*) and immunopharmacological effects (*4, 5*) have been done but little is known about its clinical/dietary effects on lipid metabolism in experimental animals. Recently, we observed that the root of *P. grandiflorum* (twenty-two years) had proved beneficial to obese patients with adult-onset diabetes mellitus (unpublished data). Thus, the

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possibility that *P. grandiflorum* (*P.g.*) might affect lipid metabolism was anticipated. As a first step, the present study was performed to investigate the effect of *P. grandiflorum* on serum and liver lipid levels in diet-induced hyperlipidemic rats.

Materials and methods

Platycodon grandiflorum. The root of *P.g.* (twenty-two years) was obtained from Korea. For the purposes of this experiment it was freeze-dried, milled and sifted through a 0.59-mm screen. The composition of the root of *P.g.* is shown in Table 1.

Animals and diets. Sprague-Dawley male rats used in this experiment were obtained from Clea Japan Inc. (Tokyo, Japan). Weight-matched (70±5 g) 4-week-old male rats were kept in a constant temperature (23±1°C) and humidity (55±5%) room with a 12-h light period (08:00–20:00 h). The rats were kept for 1 week before the beginning of the experiment for acclimatization to our laboratory conditions. During this period, the rats received commercial nonpurified diet (CE-2, Japan Clea Inc., Tokyo, Japan). This diet contained 50.2% carbohydrate, 25.2% protein, 4.4% fat, 4.4% fiber, and all necessary vitamins and minerals at the recommended levels. After the period of acclimatization, the rats were randomized into four groups (normal control, hyperlipidemic control, and 5% and 10% *P.g.* diet groups) of 6 animals each, and fed for 5 weeks.

Table 2 shows the compositions of the basal and experimental diets. Normal control group (Group 1) was fed basal diet containing 7% lard and 3% corn oil for 5 weeks. To induce hyperlipidemia, groups 2, 3, and 4 were given basal diet containing 17% lard and 3% corn oil for the first 2 weeks. After induction of

Table 1. Chemical composition of *Platycodon grandiflorum.*

Component	(weight %)
Moisture	5.8
Crude protein[1]	8.2
Crude fat	1.0
Ash	2.5
Fiber[2]	22.9
Soluble fiber	3.1
Insoluble fiber	19.8
Non fiber[3]	59.6
Fructose	2.75
Glucose	0.18
Mannose	N.D.
Sucrose	2.53
Crude saponin[4]	2.0

[1] Calculated by N×6.25. [2] Measured by the method of Prosky et al. (*16*). [3] Calculated as the difference between total and the sum of moisture, crude protein, ash, and fiber. [4] Measured by the method of Akiyama et al. (*1*). N.D., not detected.

Table 2. Composition of basal, hyperlipidemic, and experimental diets (%).

Ingredient	Group			
	Group 1 (Normal control)	Group 2 (Hyperlipidemic control)	Group 3 (5% *P.g.*)	Group 4 (10% *P.g.*)
Basal diet composition				
Sucrose	60.0	50.0	50.0	50.0
Casein	20.0	20.0	20.0	20.0
Cellulose powder	5.0	5.0	5.0	5.0
Mineral mixture[1]	3.5	3.5	3.5	3.5
Vitamin mixture[1]	1.0	1.0	1.0	1.0
DL-methionine	0.3	0.3	0.3	0.3
Choline bitartrate	0.2	0.2	0.2	0.2
Lard	7.0	17.0	17.0	17.0
Corn oil	3.0	3.0	3.0	3.0
Experimental diet composition				
Sucrose	60.0	60.0	60.0	55.0
Casein	20.0	20.0	20.0	20.0
Lipid[2]	10.0	10.0	10.0	10.0
Mineral mixture[1]	3.5	3.5	3.5	3.5
Vitamin mixture[1]	1.0	1.0	1.0	1.0
DL-methionine	0.3	0.3	0.3	0.3
Choline bitartrate	0.2	0.2	0.2	0.2
Cellulose powder	5.0	5.0	—	—
P.g. powder[3]	—	—	5.0	10.0

[1] AIN-76™. [2] 7% lard+3% corn oil. [3] *Platycodon grandiflorum* (twenty-two years).

hyperlipidemia, group 2, the hyperlipidemic control group, was fed experimental diet containing 5% cellulose powder for the last 3 weeks. To test the efficacy of *P.g.*, groups 3 and 4 were given experimental diet containing 5% and 10% *P.g.* powder, respectively, for the same period. The diets and water were given *ad libitum.* Food intake was measured everyday and weight gain was recorded weekly. At the end of the 5-week period, the animals were fasted overnight and then killed by ether anesthesia.

Blood collection and preparation. The blood was collected via cardiac puncture and immediately put on ice. Serum was separated from whole blood by centrifugation at 2,500 rpm for 15 min at 4°C. The liver was excised, blotted to remove excess blood, weighed and stored at −20°C until analyzed. The low-density lipoprotein (LDL) fraction was separated from serum by sequential ultracentrifugation, according to the method of Hatch and Lees (*6*).

Chemical assays. The activities of glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT) and lactate dehydrogenase (LDH) in rat serum were determined by the method of POP-TOOS using a commercial kit (Wako Pure Chemical Ind. Ltd., Japan). Serum concentrations of total cholester-

ol, free cholesterol, high density lipoprotein (HDL)-cholesterol, LDL-cholesterol, phospholipid, and blood glucose were also measured using standard kits (Wako Pure Chemical Ind. Ltd., Japan). Liver lipids were extracted by the method of Folch et al. (7), and the total cholesterol, triglyceride, and phospholipid concentrations in the extracts were measured by enzymatic methods using standard kits (Wako Pure Chemical Ind. Ltd., Japan).

Statistical analysis. Data are expressed as M±SE and the data were statistically analyzed by analysis of variance (ANOVA). Duncan's multiple range test was used to determine the significance of differences among the groups. Values less than 0.05 were considered significant.

Results and discussion

Weight gain and food intake

The body weight gain, food intake, and the food efficiency are shown in Table 3. Food intakes were significantly lower in rats fed *P.g.* diet (especially 10% *P.g.* diet) as compared with those of rats fed diet containing 5% cellulose powder (Group 1 and 2), suggesting that *P.g.* tastes bitter. Body weight gain, however, was significantly increased in 5% *P.g.* diet group. These results imply that the nutritive value of 5% *P.g.* diet is greater than the 10% *P.g.* diet.

Activities of GPT, GOT and LDH in serum

The activities of serum GPT, GOT and LDH are shown in Table 4. Serum GPT, GOT, and LDH activities, which indicate liver injury, were in the normal range in all groups. *P.g.* feeding resulted in an decreasing tendency of GPT and GOT levels as compared to cellulose feeding, and led to a significant decrease in LDH activity.

Concentration of serum and liver lipids

The effect of *P.g.* feeding on serum and liver lipid concentrations is summarized in Table 5. The total cholesterol and triglyceride concentrations in serum and liver were significantly decreased in the *P.g.* diet groups (Groups 3 and 4) as compared with those of the hyperlipidemic control group (Group 2). It is notable that dietary *P.g.* improved hyperlipidemia, accompanied by a significant decrease in serum and liver triglyceride concentrations.

Table 3. Body weight gain, food intake, and FER of rats fed experimental diets for 3 weeks.

Group	Weight gain (g)	Food intake (g)	FER[1]
1	113±2.4[a,2]	346±5.2[c]	0.32
2	119±5.5[b]	352±6.1[c]	0.34
3	135±2.4[c]	329±5.2[b]	0.41
4	124±3.4[b,c]	307±2.3[a]	0.41

[1] Food efficiency ratio. [2] Values are M±SE ($n=6$). Values within the same column not sharing a common superscript letter are significantly different at $p<0.05$.

Table 4. Activities of GPT, GOT, and lactate dehydrogenase (LDH) in serum of rats fed experimental diets for 3 weeks.

Group	GPT (Karmen unit/ml)	GOT (Karmen unit/ml)	LDH (Wroblewski unit/ml)
1	$45.7\pm2.1^{c,1}$	90.1 ± 2.5^{b}	$1{,}067\pm23.7^{a}$
2	35.6 ± 8.3^{b}	$81.5\pm3.3^{a,b}$	$1{,}474\pm40.6^{c}$
3	29.5 ± 5.1^{a}	$80.7\pm1.3^{a,b}$	$1{,}329\pm53.3^{b,c}$
4	24.3 ± 4.1^{a}	76.1 ± 3.0^{a}	$1{,}225\pm99.5^{b}$

[1] Values are M±SE ($n=6$). Values within the same column not sharing a common superscript letter are significantly different at $p<0.05$.

Table 5. Effects of dietary *Platycodon grandiflorum* on the serum and liver lipid concentrations in rats fed experimental diets for 3 weeks.

Parameter	Group			
	1	2	3	4
Serum lipids				
Total cholesterol (mg/dl)	$168\pm6.0^{a,1}$	262 ± 6.4^{c}	166 ± 3.8^{a}	188 ± 2.3^{b}
HDL-cholesterol (mg/dl)	52.5 ± 2.3^{a}	62.7 ± 2.5^{b}	65.9 ± 2.6^{b}	77.1 ± 1.8^{c}
LDL-cholesterol (mg/dl)	94.4 ± 2.8^{b}	137 ± 4.3^{c}	74.5 ± 3.0^{a}	95.2 ± 3.1^{b}
Free cholesterol (mg/dl)	31.8 ± 0.9^{a}	45.0 ± 0.6^{c}	37.2 ± 1.5^{b}	44.9 ± 1.7^{c}
Triglycerides (mg/dl)	174 ± 5.3^{b}	270 ± 12.0^{c}	129 ± 5.0^{a}	$187\pm4.4^{a,b}$
Phospholipids (mg/dl)	160 ± 4.7^{c}	188 ± 3.3^{d}	118 ± 5.4^{a}	139 ± 5.3^{b}
Atherogenic index[2]	2.2 ± 0.2^{b}	3.2 ± 0.3^{c}	1.5 ± 0.1^{a}	1.4 ± 0.1^{a}
Blood glucose (mg/dl)	142 ± 3.8^{a}	158 ± 5.5^{b}	141 ± 1.4^{a}	$151\pm5.5^{a,b}$
Liver lipids				
Total cholesterol (mg/g)	8.0 ± 1.7^{a}	17.8 ± 2.8^{d}	12.4 ± 3.2^{b}	14.2 ± 1.8^{c}
Free cholesterol (mg/g)	4.0 ± 0.6^{a}	4.8 ± 0.4^{b}	5.1 ± 0.4^{b}	6.1 ± 0.5^{c}
Triglycerides (mg/g)	73.5 ± 2.3^{b}	88.1 ± 2.1^{c}	46.0 ± 3.5^{a}	75.0 ± 5.4^{b}
Phospholipids (mg/g)	$23.7\pm3.5^{a,b}$	$25.1\pm4.1^{a,b}$	22.4 ± 3.0^{a}	24.2 ± 3.8^{b}

[1] Values are M±SE ($n=6$). Values within the same row not sharing a common superscript letter are significantly different at $p<0.05$. [2] (Total chol.−HDL-chol.)/HDL-chol.

Dietary *P.g.*, furthermore, significantly increased the serum HDL-cholesterol concentration (especially in 10% *P.g.* diet) while markedly reducing the LDL-cholesterol concentration compared with those of the hyperlipidemic control groups.

Serum phospholipid values in the *P.g.* diet group were significantly decreased, whereas liver phospholipid values with the *P.g.* diet were similar to those with cellulose diet. The blood glucose concentration was decreased in the 5% *P.g.* diet group but not in the 10% *P.g.* group.

The atherogenic index of the rats fed *P.g.* diet was significantly lower than that of the rats fed the cellulose diet. In this study, 5% *P.g.* diet was shown to be more

effective than 10% *P.g.* diet in reducing the cholesterol and triglyceride concentrations in serum and liver. Unfortunately, these dose-dependent differences can not be explained in the present study.

As shown in Table 1, *P.g.* contains a variety of components, but it is not clear from the present experiment which of them influence lipid metabolism. Of the them, dietary fiber (23% of *P.g.*) may be required for improvement of lipid metabolism.

Extensive studies have indicated that dietary fiber has distinct hypocholesterolemic (*8, 9*), and hypolipidemic (*10, 11*) effects, and might protect against atherosclerosis (*12*). In the experiment described here, the cholesterol- and triglyceride-reducing effects of dietary *P.g.* may be partially attributed to its dietary fiber. On the other hand, it has been reported that dietary proteins from various plants (*13*), and dietary purified saponin (*14*), or saponin-rich food such as soya-bean protein (*15*) have hypocholesterolemic effects. In this study, the possibility that some minor components such as plant protein and saponin are partially responsible for these effects cannot be excluded.

In conclusion, the present results indicated that dietary *P.g.* has a potential property in lowering cholesterol and triglyceride concentrations in serum and liver, and may be useful in preventing atherosclerosis and obesity.

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