

# EFFECTS OF RED GINSENG ON PLATELET FUNCTION AND LIPID METABOLISM OR OVERWEIGHTED NONINSULIN - DEPENDENT.

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## ABSTRACTS

### Backgrounds

Diabetes mellitus is associated with accelerated atherosclerosis and predispose to specific microvascular problems. This study was performed to evaluate the usefulness of red ginseng as adjunctive therapeutic agent of NIDDM especially in preventing chronic diabetic complications.

### Materials and Methods

We treated 50 patients with NIDDM for 5 month with 2 regimens : 1)oralhypoglycemic drug therapy only(the control group), 2)oral hypoglycemic group). The patients were recruited at Korea university hospital from June, 1992 to October, 1992 and the following inclusion criteria were used : 1)age above 35 years 2)initial body weight within or above ideal body weight 3)fasting blood glucose level greater than 140mg, dl 4)no previous history of diabetes mellitus or no history of blood glucose control for recent 3 months or more. The patients were seen every 2 weeks for remaining 3 months. At every visit FBS and PP2hr blood glucose were measured with blood pressure and body weight. Lipid profiles were checked every 4 weeks and platelet function test was performed with aggregometer after administration of ADP, epineprine and collagen every 4 weeks. Free fatty acid were also analyzed every 8 weeks and glycosylated hemoglobin was measured every 12 weeks.

### Results

The results were as follows :

1. The mean values for fasting and PP2hr blood glucose decreased significantly in the control group than in the ginseng group.
2. The weight gain was less in the ginseng group than in the control group.  
The levels of systolic blood pressure decreased significantly in the ginseng group than in the control group.
3. There was no significant differences of lipid profiles in both groups.
4. The platelet hyperaggregation was improved more significantly in the ginseng group than in the control group.

### Conclusions

In patients with NIDDM who were receiving oral hypoglycemic drug therapy, the addition of red ginseng improved platelet function and blood pressure, but induced less weight gain. The data suggests that red ginseng may be useful as a

therapeutic adjunct especially in preventing chronic complications of NIDDM.

## INTRODUCTION

The incidence rate of diabetes mellitus in Korea is increasing and at present the prevalence rate of diabetes mellitus is 3.1%. Diabetes mellitus is associated with accelerated atherosclerosis and predispose to certain specific microvascular abnormalities including retinopathy, nephropathy and neuropathy. It double the risk for stroke, increase the risk for heart attacks 2 to 3 fold, and for peripheral vascular problems, particularly in the feet, 50 fold. Many clinical trials to prevent or reduce the diabetic complications were done or are in progress. We studied the usefulness of red ginseng as an adjunctive therapeutic agent in preventing chronic complications of NIDDM.

## MATERIALS AND METHODS

We treated 50 patients with NIDDM for 5 month and divide into two groups according to the treatment which composed two regimen, first, oral hypoglycemic drug therapy only(the control group), and second, oral hypoglycemic drug therapy and 4.5g administration of red ginseng(the ginseng group). The patients were recruited at Korea university hospital from June, 1992 to October, 1992 and the following inclusion criteria were used : 1)age above 35 years 2)initial body weight within or above ideal body weight 3)fasting blood glucose level greater than 140mg, dl 4)no previous history of diabetes mellitus or no history of blood glucose control for recent 3 months or more. The patients were seen every 2 weeks for remaining 3 months. At every visit fasting blood glucose and postprandial blood glucose were measured with blood pressure and body weight. Lipid profiles were checked every 4 weeks and platelet function test was performed with aggregometer after administration of ADP, epineprine and collagen every 4 weeks. Free fatty acid were also analyzed every 8 weeks and glycosylated hemoglobin was measured every 12 weeks.

Statistical analysis was performed using the paired t-test and P value below 0.05 was considered significant.

## RESULTS

### Patients Characteristics

Table 1 shows the baseline clinical and biochemical findings in the ginseng group and the control group. Fifteen patients

**Table 1.** Base - line clinical and biochemical findings in ginseng group and control group.

ginseng group									
No	SEX	AGE(year)	FBS(mg. dl)	PP2h(mg. dl)	T - Chol(mg. dl)	HDL Chol(mg. dl)	TG(mg. dl)	FFA(uEq. L)	HbA1c(%)
1	F	57	180	226	212	53	148	758	6.5
2	M	53	180	211	258	41	234	428	6.8
3	M	41	202	351	203	38	259	971	9
4	M	57	245	462	218	35		739	8.3
5	F	53	184	231	201	44	185	833	8.5
6	M	44	158	235	191	29	429	368	5.4
7	F	42	276	369	188	51	110	414	11.9
8	M	35	166	228	231	48	115	280	11.2
9	M	54	152	313	188	36	156	879	10.8
10	M	58	174	268	224	39	207	656	6.3
11	M	38	191	253	197	34	117	910	6.7
12	F	36	177	364	187	38	142	363	10.4
13	M	36	178	177	120	40	161	656	6.5
14	F	54	166	376	221	58	130	375	10
15	M	55	143	281	186	46	159	655	6.5
MEAN		47.5	184.8	289.7	201.7	42.0	182.3	619.0	8.3
SD		8.8	34.6	79.4	30.4	7.9	83.8	230.1	2.1

control group									
No	SEX	AGE(year)	FBS(mg. dl)	PP2h(mg. dl)	T - Chol(mg. dl)	HDL Chol(mg. dl)	TG(mg. dl)	FFA(uEq. L)	HbA1c(%)
1	M	53	241	411	247	64	121	332	9.3
2	F	50	227	397	258	55	144	778	11.8
3	M	40	150	310	276	39	327	513	7.1
4	M	58	191	279	196	18	297	965	7.6
5	M	62	271	440	316	54	271	849	10.3
6	M	66	171	290	251	66	96	1110	6.3
7	M	48	222	468	242	47	112	545	7.8
8	F	55	258	413	190	39	433	506	9.2
9	F	46	230	294	196	37	221	613	10.3
10	F	53	146	227	251	45	847	801	6.6
11	M	58	141	219	186	38	135	494	8.2
12	F	60	230	332	192	46	147	586	8.8
13	M	42	143	313	218	38	262	1072	9.3
14	M	55	169	229	156	32	205	452	10.3
15	M	43	184	368	177	32	105	1258	8.8
MEAN		52.6	198.3	332.7	223.5	43.3	197.3	724.9	8.8
SD		7.7	44.2	80.1	43.7	12.7	102.3	276.9	1.5

in the ginseng group and fifteen patients in the control group were studied for 20 weeks of follow - up. There were no differences in age, FBS and PP2hr blood glucose levels, total cholesterol, HDL - cholesterol, triglyceride, free fatty acid and HbA1c between both groups.

**Blood Pressure**

Mean systolic blood pressure was significantly lower in the ginseng group than in the control group during follow - up period and mean diastolic pressure was slightly decreased in ginseng group(Fig. 1,2). There were six ginseng patients and six controls whose systolic blood pressure and diastolic pre-

ssure were above 140 mmHg and 90 mmHg, respectively. In this hypertensive group, there were slightly decreased tendency of systolic and diastolic pressure in the ginseng group than in the control group, but these changes were not statistically significant(Fig. 3,4).

**Body Weight, Blood Glucose and HbA1c**

The mean % of gain in body weight was 3% during 5 months in the control group and 0.3% in the ginseng group. The mean change of body weight was significantly lower in the ginseng group than in the control group(Fig. 5). The percent changes of FBS and PP2hr during 20 weeks of follow - up in both groups

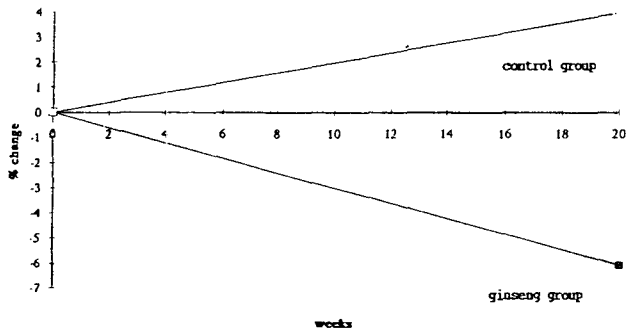


Fig 1. % Changes of systolic pressure after 20 weeks of follow - up in ginseng group and control group.  $p < 0.05$

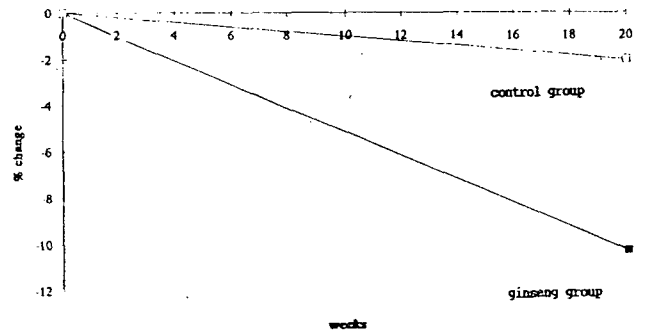


Fig 4. % Changes of diastolic pressure after 20 weeks of follow - up in hypertensive patients.

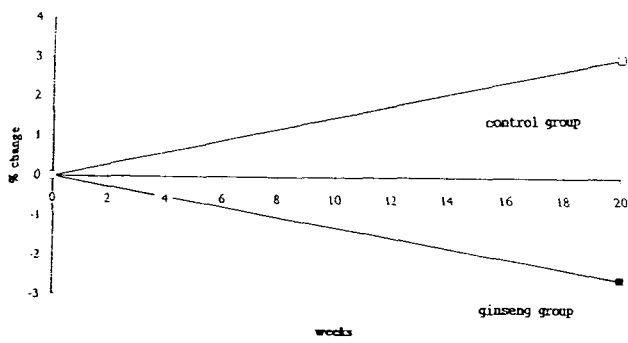


Fig 2. % Changes of diastolic pressure after 20 weeks of follow - up in ginseng group and control group.

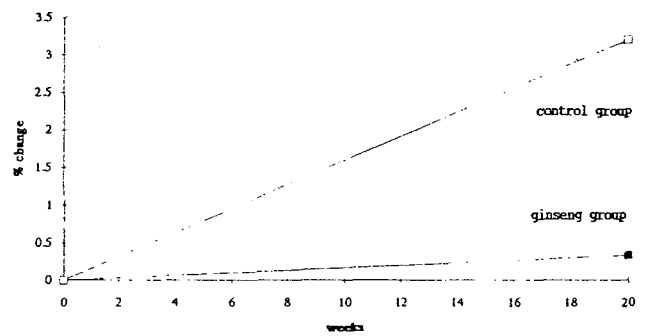


Fig 5. % Changes of body weight after 20 weeks of follow - up in ginseng group and control group.  $p < 0.05$

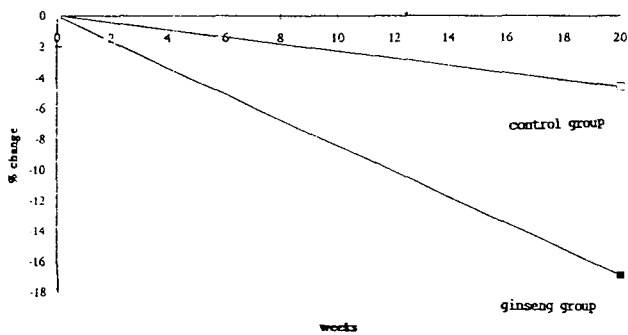


Fig 3. % Changes of systolic pressure after 20 weeks of follow - up in hypertensive patients.

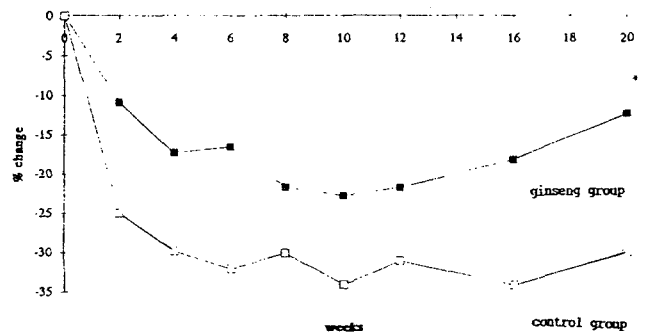


Fig 6. % Changes of FBS during 20 weeks of follow - up in ginseng group and control group. \*  $p < 0.05$

are shown in Fig. 6,7. The levels of FBS were significantly lower in the control group than the ginseng group at sixteen weeks and twenty weeks, and the levels of PP2hr blood sugar were significantly lower in the control group at sixteen weeks. There was no difference in mean HbA1c levels between control group and ginseng group(Fig. 8).

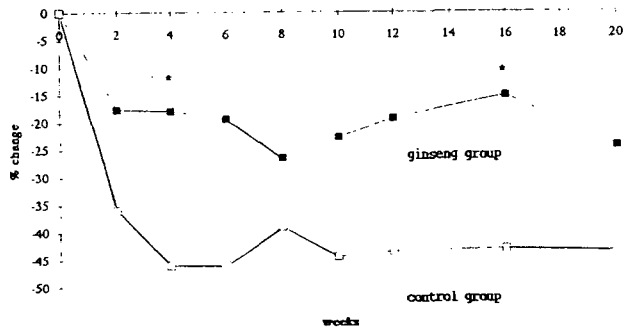


Fig 7. % Changes of PP2h during 20 weeks of follow - up in ginseng group and control group. \*  $p < 0.05$

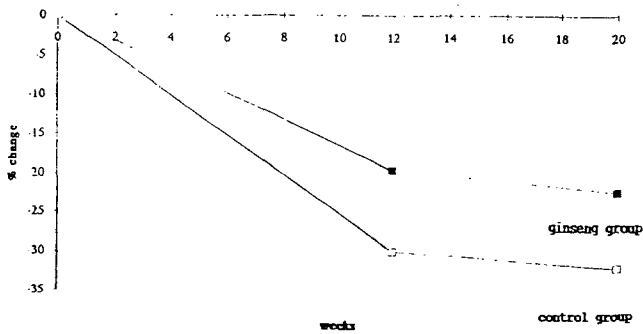


Fig 8. % changes of HbA1c during 20 weeks of follow - up in ginseng group and control group.

### Lipid Profiles

In lipid profiles, there were no differences in total cholesterol and HDL - cholesterol and on triglyceride and free fatty acid between the control group and the ginseng group during treatment(Fig. 9,10,11,12). The percent changes of total cholesterol in five ginseng and seven control hypercholesterolemic patients whose total cholesterol levels were above 220 mg/dl at baseline are shown in figure 13. There were no differences between two groups. Figure 14 shows the percent changes of triglyceride in four ginseng and seven control hypertriglyceridemic patients whose triglyceride levels were above 200 mg/dl at baseline. There were no differences between two groups. And the percent changes of free fatty acid in ten ginseng and thirteen control patients with high free fatty acid, whose serum free fatty acid levels were above 480 Eq/L at basal measurement are shown in figure 15. There was also no difference between the ginseng group and the control group.

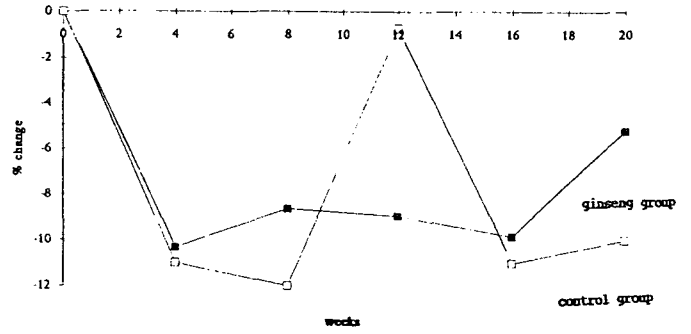


Fig 9. % changes of total cholesterol during 20 weeks of follow - up in ginseng group and control group.

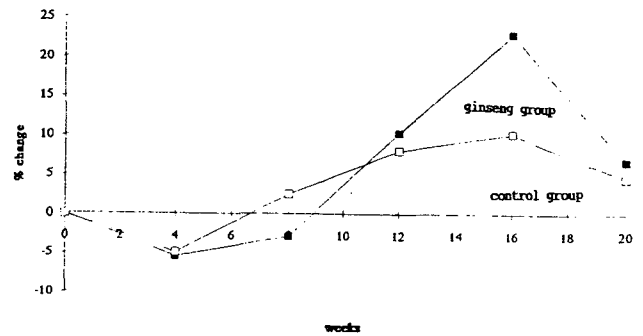


Fig 10. % changes of HDL cholesterol during 20 weeks of follow - up in ginseng group and control group.

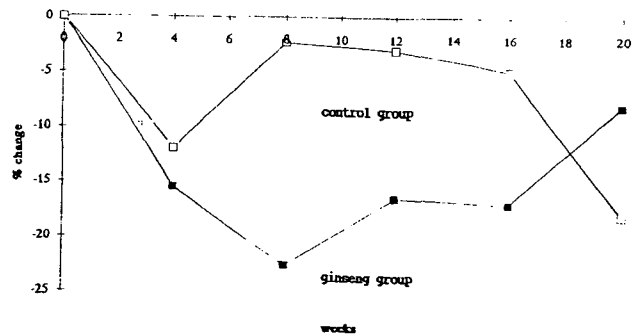


Fig 11. % changes of triglyceride during 20 weeks of follow - up in ginseng group and control group.

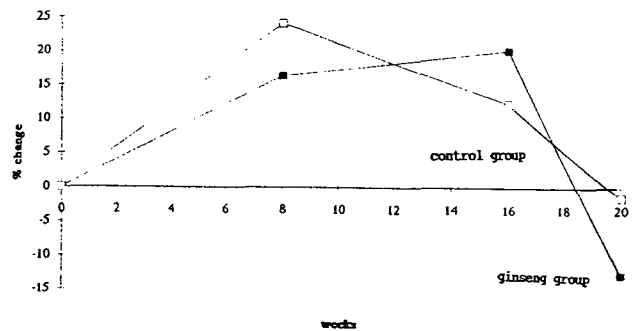


Fig 12. % changes of FFA during 20 weeks of follow - up in ginseng group and control group.

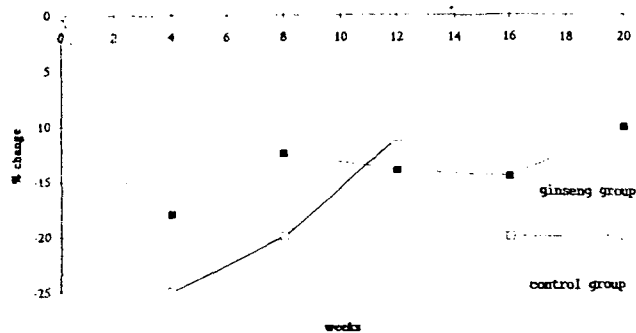


Fig 13. % changes of total cholesterol during 20 weeks of follow - up in hypercholesterolemic patients.

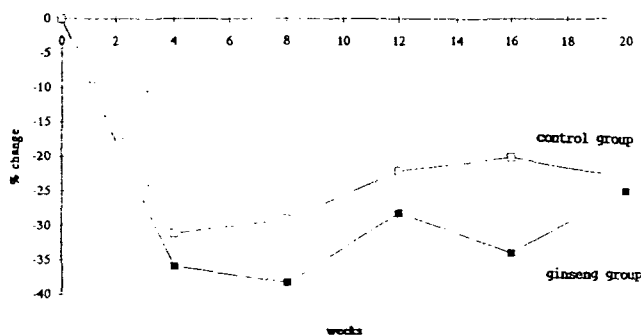


Fig 14. % changes of triglyceride during 20 weeks of follow - up in hypercholesterolemic patients.

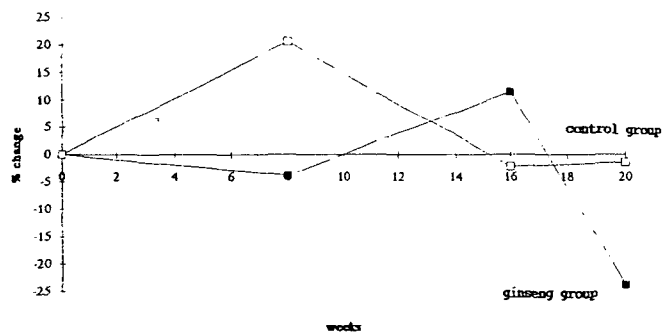


Fig 15. % changes of FFA during 20 weeks of follow - up in high FFA patients.

### Platelet Aggregation

After 20 weeks treatment, the change of mean threshold concentration of ADP to initiate second phase aggregation was increased significantly in the ginseng group than the control group (Table 2). The mean threshold concentration during follow-up period revealed an increased tendency in both groups (Fig. 16,17,18), and especially the mean thresholds of ADP ( $p=0.014$ ) and epinephrine ( $p=0.043$ ) at 20 weeks were increased more significantly in the ginseng group than in the control group (Table 3,4). The mean periods of returning of mean threshold concentration of agonists to normal are shorter

**Table 2.** The changes of mean threshold concentrations of agonist - induced platelet aggregation in NIDDM

Week	ADP(uM)					
	0	4	8	12	16	20
control group	1.8	1.8	2.1	2.4	2.5	2.4
ginseng group	2.3	2.7	2.7	3.2	3.1	3.6
p - value	0.131	0.085	0.031	0.092	0.195	0.009

Week	Epinephrine(uM)					
	0	4	8	12	16	20
control group	3.3	3.1	3.4	6.2	3.6	7.2
ginseng group	2.8	3.4	7.6	5.1	8.1	8.4
p - value	0.912	0.732	0.247	0.742	0.147	0.778

Week	Collagen(uM)					
	0	4	8	12	16	20
control group	1.3	1.3	1.4	1.6	1.7	1.7
ginseng group	1.2	1.2	1.4	1.5	1.7	1.7
p - value	0.733	0.733	1	0.431	0.559	0.559

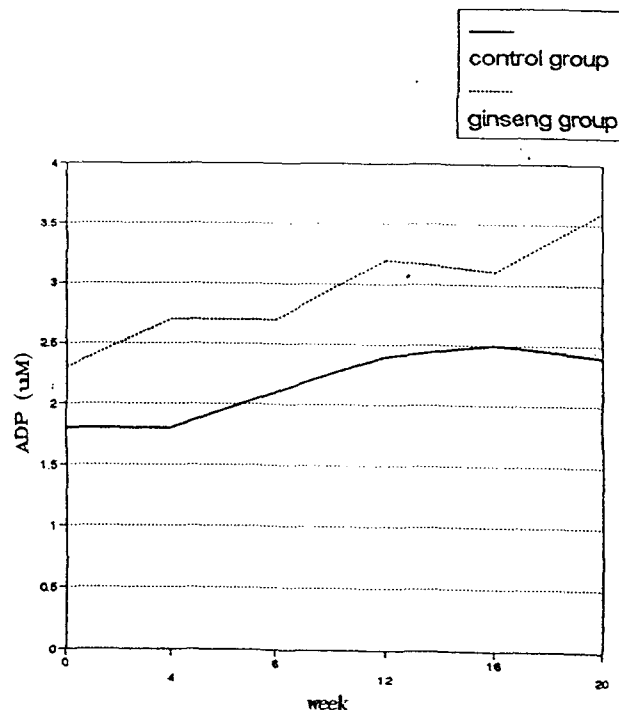


Fig 16. The changes of mean threshold concentration of ADP in NIDDM.

in the ginseng group than in the control group, but this result was not statistically significant (Table 5). There was no difference in platelet count between both groups at basal state and during follow-up period (Table 6).

**Table 3.** The changes of mean threshold concentrations of agonists among control group and ginseng group in NIDDM  
(unit : ADP uM, epinephrine uM, collagen ug/mL)

control group						
week	ADP	p - value	Epinephrine	p - value	Collagen	p - value
0	1.8		3.3		1.3	
4	1.8	1	3.1	0.794	1.3	1
8	2.1	0.51	3.4	0.952	1.4	0.733
12	2.4	0.246	6.2	0.361	1.6	0.066
16	2.5	0.198	3.6	0.764	1.7	0.022
20	2.4	0.246	7.3	0.206	1.7	0.022

ginseng group						
week	ADP	p - value	Epinephrine	p - value	Collagen	p - value
0	2.3		2.8		1.2	
4	2.7	0.799	3.4	0.627	1.2	1
8	2.7	0.799	7.6	0.187	1.4	0.495
12	3.2	0.186	5.1	0.094	1.5	0.164
16	3.1	0.251	8.1	0.092	1.7	0.001
20	3.6	0.014	5.7	0.043	1.7	0.001

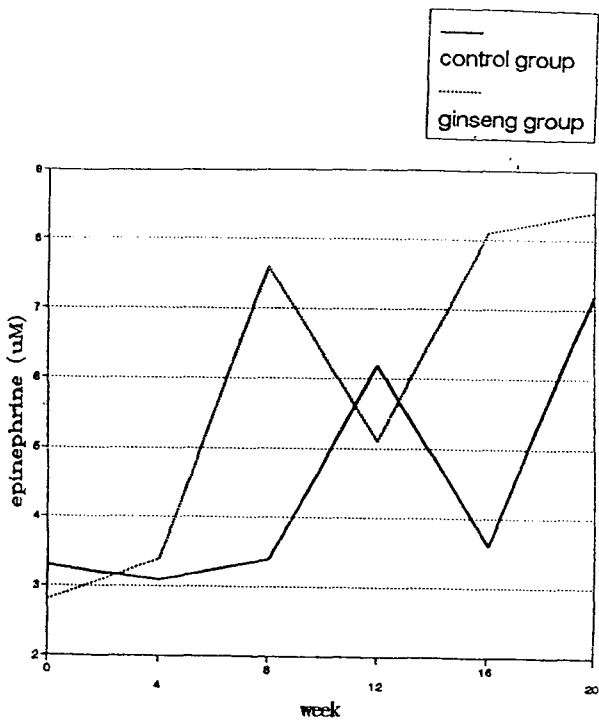


Fig 17. The changes of mean threshold concentration of epinephrine in NIDDM.

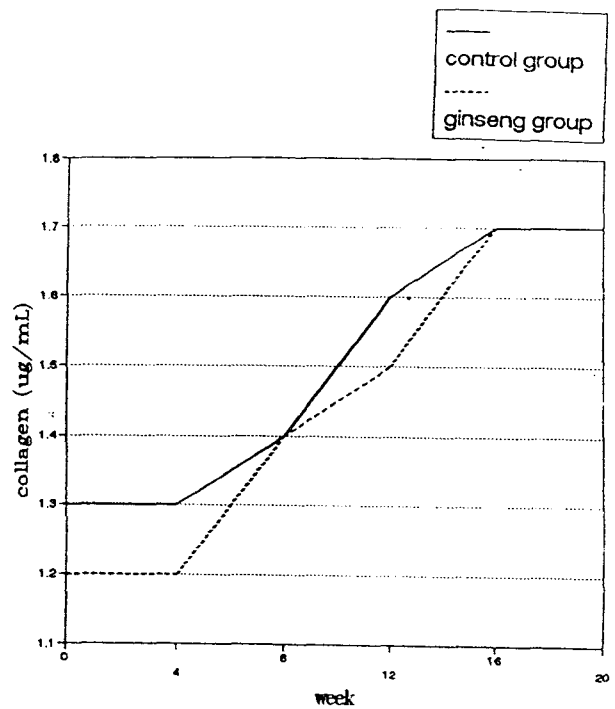


Fig 18. The changes of mean threshold concentration of collagen in NIDDM.

**Table 4.** The mean recovery time to normal threshold concentrations of agonists in NIDDM

	ADP(weeks)	Epinephrine(weeks)	collagen(weeks)
control group	18.9	19.5	14.5
ginseng group	16.7	16.7	14.2
p - value	0.28	0.354	0.444

**Table 5.** The changes of platelet count

	control group	ginseng group	p - value
basal	241000	286000	0.051
20 weeks	212000	245000	0.111
p - value	0.071	0.113	

## DISCUSSION

Many studies have been attempted to illustrate the effects of red ginseng on blood pressure, body weight, blood glucose, lipid metabolism, and platelet function in humans and experimental animals. But inconsistent results were reported. These studies have been hampered by confounding factors such as the heterogeneity of experimental animals, the variable amounts of administered red ginseng, the variable physiologic states of humans or experimental animals.

The effect of red ginseng on blood pressure is variable according to the amount of administered ginseng or the physiologic states of animal or humans. Son<sup>11</sup> et al reported that red ginseng had the transient lowering effect of blood pressure and large dose of ginseng reduced blood pressure in longterm study. It seems that ginseng has transient blood pressure lowering effects<sup>21</sup>. In this study, red ginseng showed a favorable influence on blood pressure, especially systolic. This is noteworthy considering the data from epidemiologic studies in diabetic patients showing higher incidence of hypertension.

Many reports about the effect on body weight of red ginseng are available and generally red ginseng has the effect of weight gain of red ginseng in rats. Strokin<sup>51</sup> reported that there were significant increases of body weight in ginseng - treated poliomyelitis patients. Some others reported<sup>5, 61</sup> that red ginseng prevented reduction of body weight in surgically stressful rats, and ginseng has the effect of weight gaining after recovery of stress. But our study showed there was no change of body weight in the ginseng group during 5 months of treatment. This finding may be also meaningful to diabetic patients, because one of undesirable side effects of sulfonylurea(oral hypoglycemic agent) is weight gain, which deteriorates blood glucose control in diabetic patients.

There are many studies about the effects of red ginseng on glucose metabolism. The action of red ginseng on blood glucose is also variable but in general red ginseng usually has a glucose lowering action in hyperglycemic states. Kono<sup>71</sup> et al

and some authors<sup>8-101</sup> reported mild hypoglycemic effect of ginseng. The component of ginseng extracted by methanol and water had hypoglycemic effect and reduced the mortality of alloxan - treated diabetic rat, but it could not inhibit the diabetogenic effect of alloxan. The blood glucose lowering effect in hyperglycemic animal treated by alloxan or 2, 4 - nitrophenol may be caused by anti - epinephrine effect of ginseng. Some reports showed that the amounts of glycogen stored in liver and muscle were increased in ginseng - treated rabbit. However, Jung<sup>111</sup> reported that ginseng had a hyperglycemic effect in rats treated with morphine and epinephrine. There was another study<sup>121</sup> which showed the blood glucose lowering effect of ginseng in humans.

Our studies showed the tendency of more favorable metabolic control in control group compared to the ginseng group. This finding means that red ginseng has little effect on glucose metabolism in diabetic patients or the patients taking red ginseng maintained less strict diet control or exercise for blood glucose control.

There are also many reports about the lipid lowering effect of red ginseng in humans. However, in our study no significant differences were observed in fasting levels of total cholesterol, TG, HDL - cholesterol and free fatty acid in both groups. Yamamoto<sup>131</sup> et al reported that ginsenoside increased HDL - cholesterol and decreased the LDL - cholesterol, and ginseng accelerated cholesterol synthesis in experimental rat liver. Longterm treatment of hyperlipidemic patients with red ginseng increased HDL - cholesterol and significantly decreased the fasting levels of total cholesterol, triglyceride and free fatty acid. Yokozawa<sup>141</sup> reported that ginseng increased the cholesterol synthesis in liver and decreased serum triglyceride. He showed that ginseng had the lowering effect of free fatty acid and triglyceride in old humans and combined treatment of diet and ginseng is more effective in lowering cholesterol than diet alone.

There are many reports about the antiplatelet action of ginseng but the precise mechanism is not proven until now. Teng<sup>151</sup> et al reported that diethyl ether layer of panax ginseng has more potent antiplatelet action than the butanol layer from which ginsenosides were isolated, and panaxynol component of diethyl ether layer has the principal antiplatelet action. Its mechanism of action is mainly the inhibition of thromboxane formation. In this study platelet hyperaggregation was improved more significantly in the ginseng treated group than in the control group.

In conclusion, red ginseng has beneficial effects on body weight, blood pressure and platelet function whereas no adverse effects on lipid metabolism in NIDDM patients is detected.

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