STUDIES ON THE SAFETY OF KOREAN GINSENG INGESTED AS FOOD SUBSTANCE

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INTRODUCTION

Ginseng has been widely used as a miraculous herbal medicine for many centuries. Records of pharmacological use and effectivness of Korean ginseng appear as long as 2,000 years ago in early Chinese medical books such as *Shengnong bencao jing*[1] and *Shanghan lun.*[2]

With the development of modern complex societies, many kinds of stresses and air pollution have begun to have a deleterious effect on human health. As a result, increasing number of people have turned to ginseng to counter this trend. To meet this varied demand, ginseng products have been greatly diversified.

As the people of the Far East have used ginseng for thousands of years, they have known of its singular safety and lack of adverse side-effects. Westerners, however, do not have this history of usage and seek modern scientific proof that ginseng is indeed safe.

It is for these people, who would like to be assured that ginseng may safely be ingested, that we have carried out this study on the safety of ginseng.

MATERIALS AND METHODS

1. Preparation of Red Ginseng Feed

Red ginseng roots were powdered and passed through an 80-mesh screen. 0.625g, 1.25g, or 2.5g of the ginseng powder was mixed with 1 kg of commercially available laboratory animal feed and formed into pellets as shown in Table 1.

Control animals were fed the same diet without the red ginseng powder also as shown in Table 1.

Table 1. Proximate analysis of feed.

Crude protein	22.0%	Ca	0.6%
Crude fat	3.0%	P	0.4%
Crude fiber	6.0%	TDN	73.0%
Crude ash	9.0%		

2. Method of Feeding

Sprague-Dawley rats (male, 60-100g), fed a normal diet, were used as experimental animals. Six groups of 48 animals were established with each group being fed the experimental feed for 1, 2, 3, 4, 5 or 6 months. These groups were further divided into 4 subgroups, each consisting of 12 animals. One subgroup was given normal feed and established as control, subgroup 1 was fed 0.625g/kg diet, subgroup 2 was fed 1.25g/kg diet and subgroup 3 was fed 2.5g/kg pellets.

Additionally, 12 4-month old rats were fed the same diet as subgroups 1 (0.625g/kg) for 6

months to test the effect of red ginseng on mature rats.

3. Data Collection

1) Weight Determination

Each subgroup was weighed once a week during the entire period of the experiment.

2) Organ Weight

The animals to be sacrificed were not fed for the last 24 hours, anesthetized with sodium thiopental and the liver, spleen, heart, small intestines, brain, kidney, and the lungs removed. These organs were washed with saline, blotted dry with filter paper, and weighed.

3) Blood Analysis and Blood Count

A portion of blood removed from the heart was stabilized with EDTA in a test tube and used for blood count and hemoglobin level determination using a Coulter-counter (ZBI).

The rest of the sample was used for measuring total cholesterol, triglyceride, phospholipid, free fatty acid, free cholesterol, HDL-cholesterol, S-GPT, S-GOT, total protein, alkaline phosphatase, and total lipid levels in the blood. Commercially available kits were used in these determinations.

4) F_1, F_2 Generations

Rats (60-80g, male and female) were fed red ginseng enriched diet for 2 months and mated to obtain F_1 progeny. After weaning (4-5 weeks after birth), 12 males and 12 females were selected as test animals and the rest were mated to obtain F_2 offsprings. These F_2 progeny were then used as test subjects and experimented on as discussed above.

5) Histopathological Investigations

A portion of the organs removed from both the control and test groups were fixed in 5% formalin solution. A 2 mm piece of tissue was prepared for microscopy by immobilizing in paraffin wax and then cutting into 5-7 um thickness. These tissue sections were simultaneously stained with hematoxylin-eosin and looked at with light microscope.

RESULTS

1. Weight Determination and Growth Rate

As shown in Table 2, each test group showed a light difference in body weight change during the test period but no significant differences were observed. The 1, 3, 5 and 6 month-fed groups showed similar increase in both the test and the control animals while subgroup 3 among the 2 month-fed group had a lower increase in weight than the control. Subgroup 2 in the 4-month-fed group showed a greater increase in weight than the control, but this was not statistically significant.

The overall weights of the 6 months-fed group, shown in Figure 1, showed very little difference between the 4 subgroups.

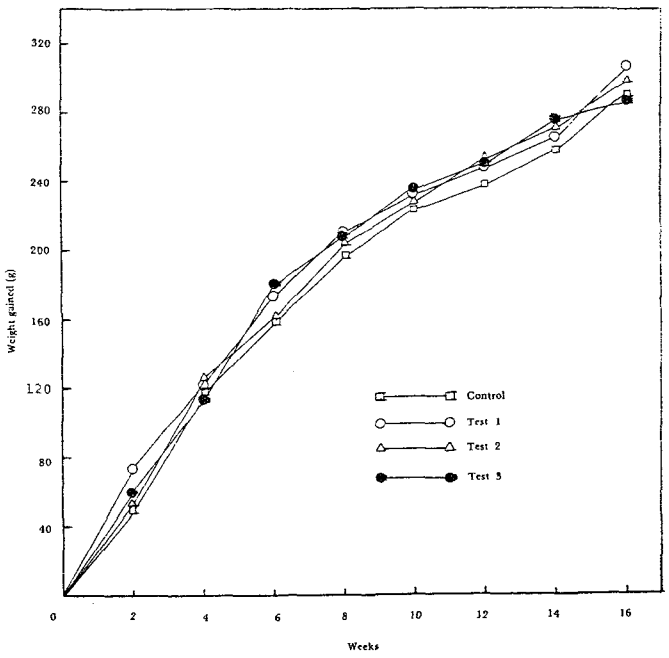

Fig. 1. Growth rate of rats fed diets containing various amount of ginseng powder for 16 weeks.

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 2. Weight gain of rats fed diet containing various amount of ginseng powder for 1 - 6 months.

(g)

Group	Month	1	2	3	4	5	6
Control	initial	82.3 ± 8.5	64.0 ± 3.3	70.2 ± 2.2	68.3 ± 8.3	63.3 ± 4.7	114.2 ± 8.8
	final	218.0 ± 27.2	324.5 ± 19.6	363.3 ± 26.6	362.4 ± 43.1	402.6 ± 27.0	402.2 ± 32.5
	increased	135.7 ± 20.3	260.5 ± 16.3	293.1 ± 24.4	294.4 ± 34.8	339.3 ± 29.0	288.0 ± 23.7
Test 1	initial	81.7 ± 7.7	62.2 ± 2.5	65.2 ± 4.0	69.0 ± 5.2	72.0 ± 5.4	114.8 ± 4.7
	final	260.0 ± 25.2	329.4 ± 16.3	346.3 ± 18.2	380.1 ± 33.0	414.9 ± 46.9	411.5 ± 34.7
	increased	134.3 ± 17.5	267.2 ± 13.8	281.1 ± 14.2	311.1 ± 27.8	342.9 ± 41.5	296.7 ± 30.0
Test 2	initial	79.5 ± 4.3	62.3 ± 1.8	62.8 ± 1.6	63.8 ± 5.1	72.8 ± 12.5	112.2 ± 11.6
	final	210.6 ± 21.9	339.2 ± 20.6	360.0 ± 24.5	401.2 ± 26.4	399.4 ± 39.1	412.0 ± 29.4
	increased	131.1 ± 17.6	276.9 ± 18.8	297.2 ± 22.9	☆337.4 ± 21.3	326.6 ± 26.6	299.8 ± 17.8
Test 3	initial	73.6 ± 9.5	63.0 ± 2.7	63.2 ± 5.6	73.8 ± 6.1	65.6 ± 2.3	104.0 ± 4.5
	final	217.5 ± 19.9	282.9 ± 20.1	345.0 ± 23.0	38.0 ± 40.2	394.4 ± 38.6	406.2 ± 23.9
	increased	143.9 ± 10.4	☆☆219.9 ± 17.4	281.8 ± 17.4	306.2 ± 34.1	328.8 ± 36.7	302.2 ± 19.4

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

☆ $P < 0.05$
☆☆ $P < 0.01$

2. Organ Weights

Tables 3-8 show the organ weights of the test animals during the experimental period. No significant differences were observed.

3. Blood Analysis and Blood Count

1) Alkaline Phosphatase

The level of alkaline phosphatase activity

Table 3. Heart weights of rats fed diets containing ginseng powder for 1 - 10 months.

(g)

Dietary level	Month 1	2	3	4	5	6	10
Control	0.8 ± 0.1	1.2 ± 0.2	1.4 ± 0.1	1.2 ± 0.1	1.1 ± 0.1	1.3 ± 0.2	1.5 ± 0.2
Test 1	0.8 ± 0.1	1.2 ± 0.1	1.3 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	1.3 ± 0.1	1.5 ± 0.2
Test 2	0.8 ± 0.1	1.3 ± 0.1	1.3 ± 0.1	1.3 ± 0.1	1.2 ± 0.0	1.3 ± 0.1	
Test 3	0.8 ± 0.1	1.2 ± 0.1	1.3 ± 0.1	1.2 ± 0.2	1.2 ± 0.1	1.3 ± 0.1	

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 4. Liver weights of rats fed diets containing ginseng powder for 1 - 10 months.

(g)

Month / Dietary level	1	2	3	4	5	6	10
Control	6.6± 0.8	8.0± 0.7	9.1 ±0.7	8.9± 0.6	8.7± 0.6	8.8± 0.9	10.0 ±1
Test 1	6.5± 0.7	8.0± 0.6	8.9± 0.8	8.7± 0.7	8.5± 0.6	8.9± 0.8	10.3± 1
Test 2	6.4± 0.5	8.1± 0.5	9.0± 0.9	8.9± 0.7	8.5± 0.6	8.8± 0.7	
Test 3	6.5± 0.6	8.2± 0.5	9.0± 0.9	8.7± 0.7	8.6± 0.7	8.8± 0.9	

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 5. Kidney weights of rats fed diets containing ginseng powder for 1 - 10 months.

(g)

Month / Dietary level	1	2	3	4	5	6	10
Control	1.7± 0.1	2.3± 0.2	2.5± 0.2	2.4± 0.3	2.5± 0.3	2.7± 0.3	3.2± 0.3
Test 1	1.7± 0.2	2.3± 0.1	2.4± 0.1	2.4± 0.2	2.4± 0.2	2.6± 0.4	3.2± 0.4
Test 2	1.6± 0.1	2.3± 0.1	2.4± 0.2	2.4± 0.2	2.4± 0.2	2.6± 0.3	
Test 3	1.7± 0.1	2.3± 0.2	2.4± 0.2	2.3± 0.3	2.4± 0.1	2.6± 0.3	

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 6. Lung weights of rats fed diets containing ginseng powder for 1 - 10 months.

(g)

Month / Dietary level	1	2	3	4	5	6	10
Control	1.2 ± 0.1	1.8 ± 0.2	2.0 ± 0.1	2.2 ± 0.1	2.2 ± 0. 2	2.5 ± 0.2	2.7 ± 0.3
Test 1	1.2 ± 0.1	1.8 ± 0.2	2.0 ± 0.2	2.1 ± 0.3	2.2 ± 0.1	2.5 ± 0.3	2.9 ± 0.2
Test 3	1.1 ± 0.2	1.8 ± 0.2	1.9 ± 0.2	2.3 ± 0.2	2.1 ± 0.2	2.5 ± 0.4	
Test 4	1.1 ± 0.1	1.8 ± 0.1	2.0 ± 0.3	2.3 ± 0.2	2.1 ± 0.2	2.5 ± 0.3	

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 7. Spleen weights of rats fed diets containing ginseng powder for 1 - 10 months.

(g)

Month / Dietary level	1	2	3	4	5	6	10
Control	0.4 ± 0.1	0.8 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	0.7 ± 0.1	0.9 ± 0.1	0.9 ± 0.2
Test 1	0.4 ± 0.1	0.8 ± 0.1	1.0 ± 0.2	0.9 ± 0.2	0.8 ± 0.1	1.0 ± 0.1	0.8 ± 0.2
Test 2	0.5 ± 0.1	0.9 ± 0.1	1.0 ± 0.1	0.9 ± 0.2	0.8 ± 0.1	0.9 ± 0.1	
Test 3	0.5 ± 0.1	0.8 ± 0.1	1.0 ± 0.2	0.8 ± 0.1	0.7 ± 0.2	0.9 ± 0.1	

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 8. Brain weights of rats fed diets containing ginseng powder for 1 - 10 months.

(g)

Month / Dietary level	1	2	3	4	5	6	10
Control	1.8 ± 0.1	2.1 ± 0.1	2.1 ± 0.1	2.1 ± 0.1	1.9 ± 0.1	2.1 ± 0.1	2.0 ± 0.1
Test 1	1.8 ± 0.0	2.0 ± 0.1	2.1 ± 0.1	2.2 ± 0.1	2.0 ± 0.1	2.1 ± 0.1	2.1 ± 0.1
Test 2	1.8 ± 0.1	2.1 ± 0.1	2.1 ± 0.1	2.1 ± 0.1	2.0 ± 0.1	2.1 ± 0.1	
Test 3	1.8 ± 0.1	2.1 ± 0.1	2.1 ± 0.1	2.0 ± 0.1	2.0 ± 0.1	2.1 ± 0.1	

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

in the test animals after feeding with red ginseng enriched diet is shown in Figure 2. The results after 1 month of feeding showed an increase of 26% for subgroup 1, 23% for subgroup 2 and 36% for subgroup 3 over the control levels. The amount on increase was not related to be concentration of ginseng in the feed. From the 2nd month, the levels in the test groups were similar to those obtained for control groups. Subgroup 3 alone had a 25% higher level of activity than the controls.

Alkaline phosphatase activity increased during the maturation period (0-2 months after birth) and decreased thereafter during the experimental period. The alkaline phosphatase content in both the control and the test groups were similar after the first 2 months.

2) Triglyceride

As shown in Figure 3, the triglyceride level in serum was nearly constant during the entire experimental period. However, subgroup 3 showed a lower level than the control group at 1,2, 3, 4, and 5 months, and had 49.1% lower level at 4 months and 28% lower level at 5 months.

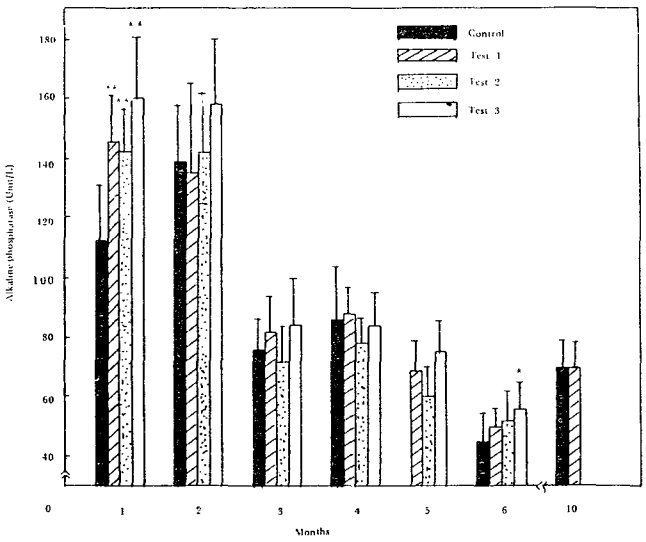

Fig. 2. Serum alkaline phosphatase of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$
F :

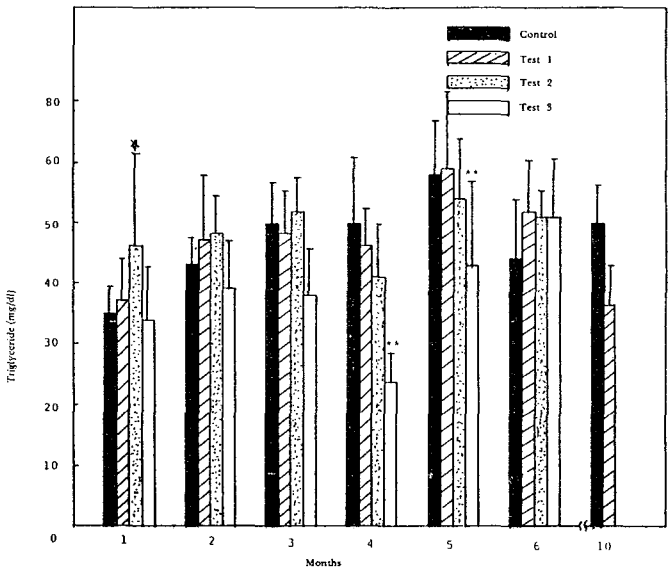

Fig. 3. Serum triglyceride of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

3) Free Fatty Acid

Serum free fatty acid was lower in test groups compared to the control groups (Figure 4). Among the 3 month fed animals, subgroup 2 showed 16% lower, and subgroup 3 showed 21% lower than the controls. Subgroup 3 also showed 16% lower level after 5 months of treatment.

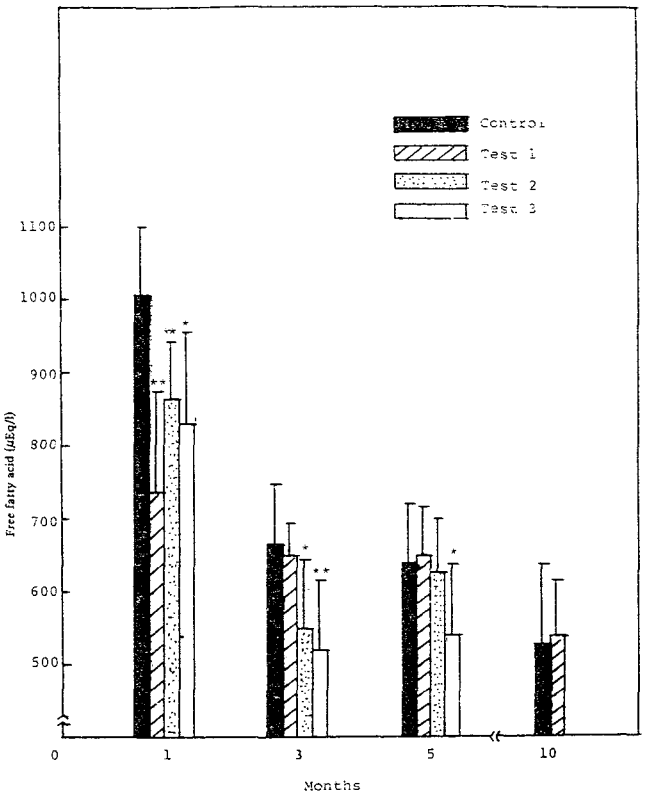

Fig. 4. Serum free fatty acid of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

4) Total Lipid

The total serum lipid content in test animals was lower than the control's in the 2 and 3 month-fed groups (Figure 5). Among the 2 month-fed groups, subgroup 2 showed 37.9%, and subgroup 3, 17% lower level than the controls, while the 3 months treated subgroup 1 was 40% lower, and subgroup 2 was also lower than the controls.

5) Phospholipid

Figure 6 shows the serum phospholipid content with the test animals showing approximately 10-30% increase over the control animals.

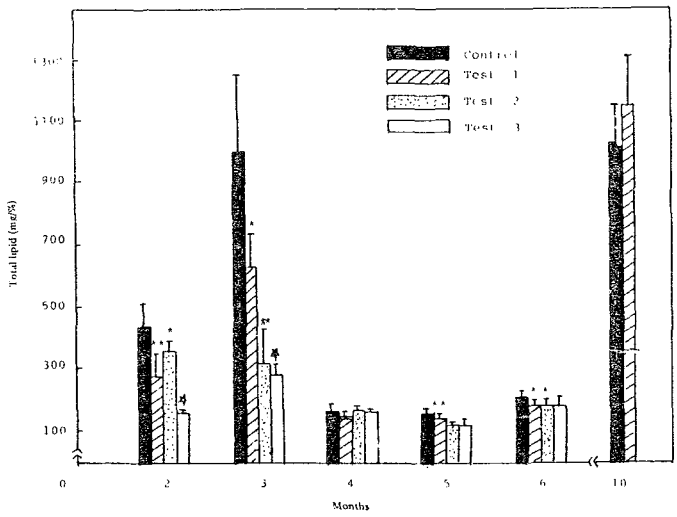

Fig. 5. Total serum lipid of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

Particularly noteworthy is the 30.6% increase in the 4 month fed subgroup 2 and a 12% increase in the 1 month fed subgroup 2. That red-ginseng fed groups had a higher level of phospholipid was evident at every experimental period.

Joo et al.[3,4] have suggested that ginseng saponin stimulates biosynthesis of phospholipid and our results support this claim.

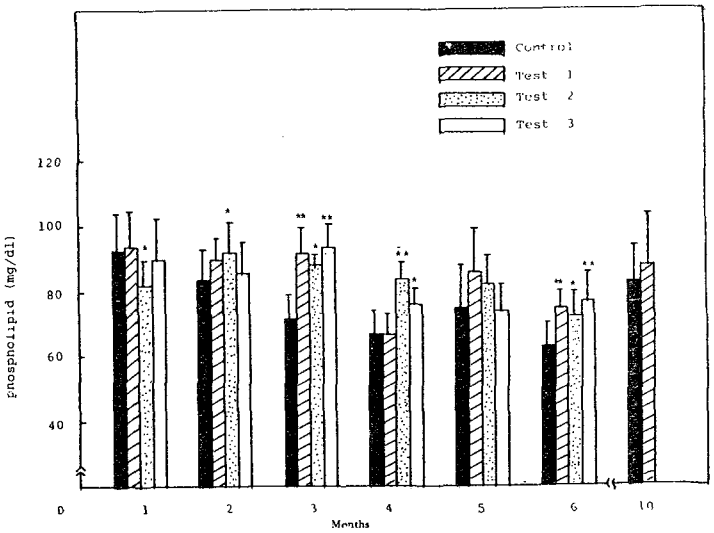

Fig. 6. Serum phospholipid of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

6) Total Serum Protein

The total serum protein increased among the test animals, as shown in Figure 7, with the 4-month fed subgroup 3 showing 13% increase, and the 5-month fed subgroup 1 and 2 showing a 10% and 14% increase respectively. The 6-month fed animals had levels similar to the controls. Overall, the test animals showed a slight increase in the amount of protein present and this agrees with the reports that ginseng stimulates protein synthesis.[5,6]

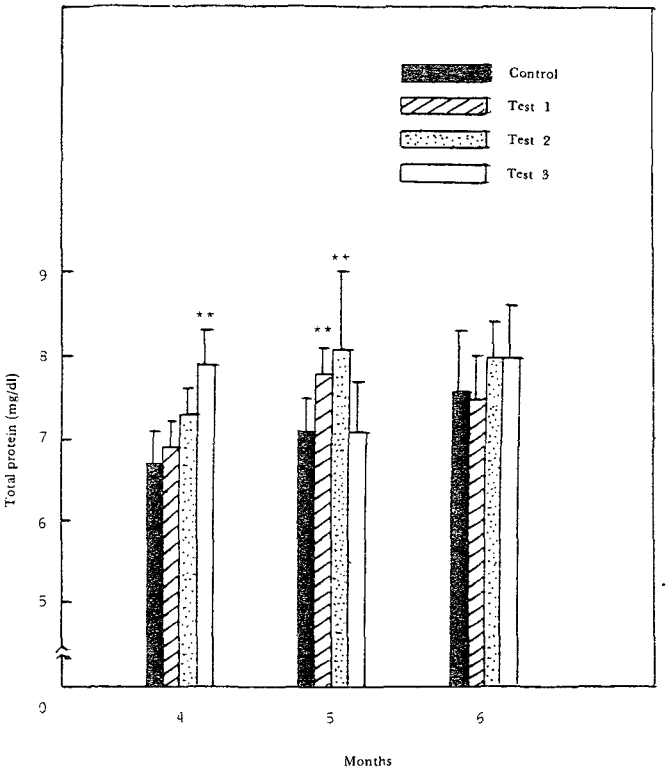

Fig. 7. Total serum protein of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

7) Total Serum Cholesterol

As shown in Figure 8, total serum cholesterol increased 20% in the 1 month-fed subgroup 1 and 12% in subgroup 2. Among those fed for 2 months, subgroups 1 and 2 showed an increase while subgroup 3 showed a decrease with respect to the control animals. The 3-month fed groups, on the other hand, showed a 10% increase in

subgroup 1, a 15% decrease in subgroup 2, and no change from the controls in subgroup 3. The 4-month fedgroup had a 29% increase in subgroup 2 and a 20% increase in subgroup 3. The 5 and 6-months fed groups had total cholesterol values similar to those of the controls.

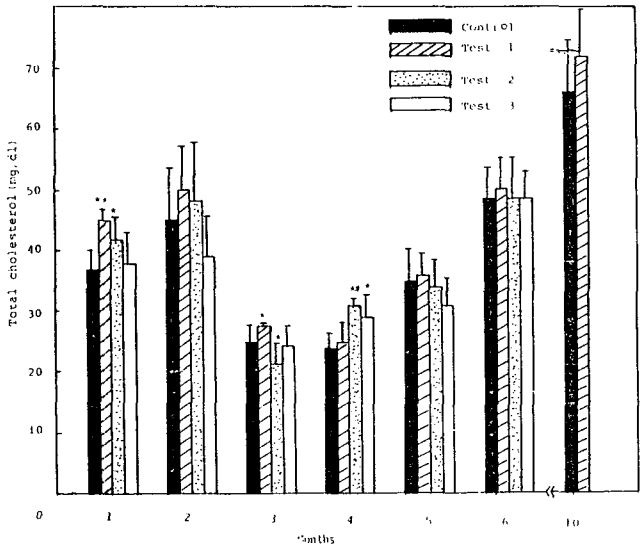

Fig. 8. Total serum cholesterol of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

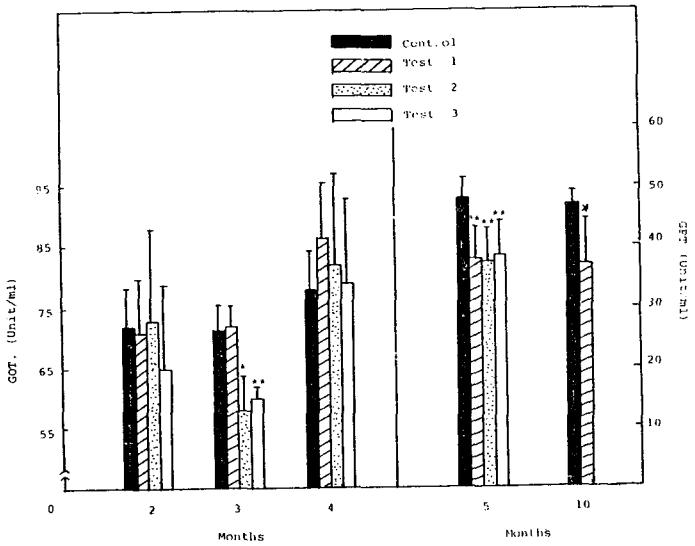

Fig. 9. Sera GOT and GPT of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

8) S-GOT and S-GPT

S-GOT and S-GPT levels are shownin Figure 9. Subgroups 1 and 2 in the 2-month fed group showed a similar S-GOT levels as the controls while subgroup 3 had a lower value. The 3-month fed subgroups 2 and 3 had 17% and 15% lower values respectively. Subgroups 1 and 2 in the 4-month fed group showed a slight increase but this was not statistically significant. Subgroup 3 had a value similar to the control's.

S-GPT, on the other hand, decreased 18-23% in all 3 subgroups in the 5-months fed rats.

9) Serum Free Cholesterol

As shown in Figure 10, the 2 and 6-month ginseng fed animals showed a decrease in serum free cholesterol regardless of the amount of ginseng in the feed. However, it was not significant. The 5-month fed groups showed no difference from the control.

10) HDL-Cholesterol

Serum HDL-cholesterol levels, as shown

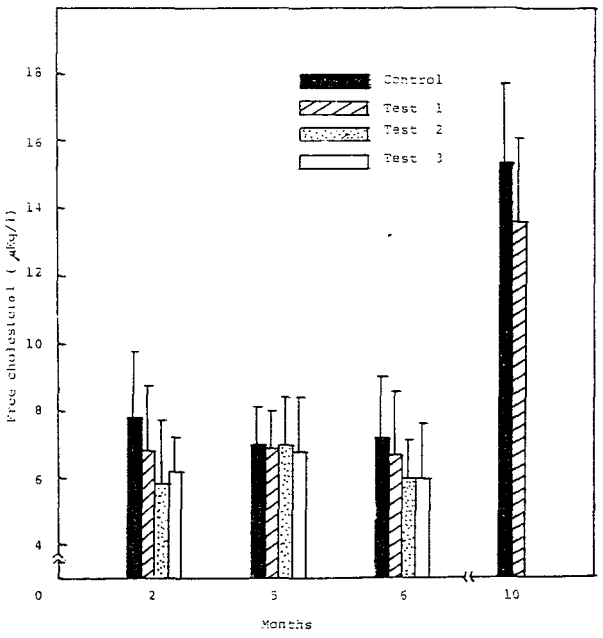

Fig. 10. Serum free cholesterol of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

in Figure 11, showed a 20% increase among the subgroups 1 and 2, and a 40% increase in subgroup 3 among those fed red ginseng for 2 months. Those fed for 3 months showed no difference from the controls in subgroups 1 and 3 while subgroup 2 showed a modest increase of 9.2%. 24% increase occurred with subgroup 2 in the 4-month fed animals but the other subgroups showed no change.

The 5-month fed group exhibited a 18.7% and 13.9% increase in subgroups 1 and 2 but this was not statistically significant. Subgroup 3 was no different than the control.

Subgroup 1 in the 6 month fed group had a 12.6% significant increase but the other subgroups showed no great change.

In general, the subgroups 1 and 2 showed an increase in HDL-cholesterol level in the serum.

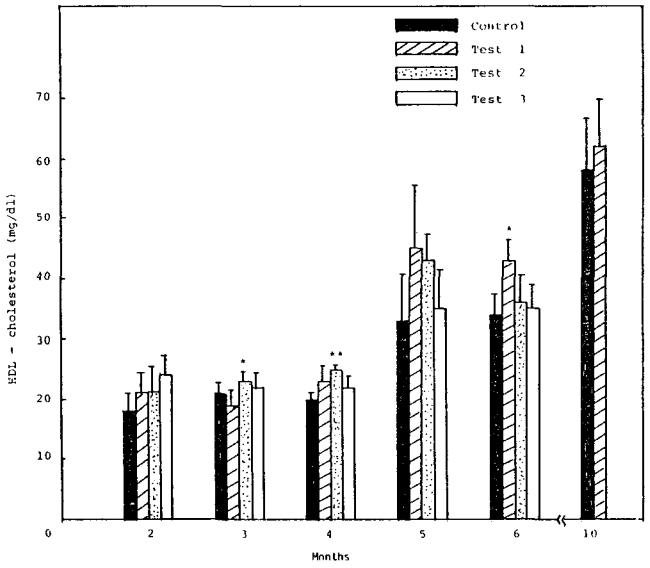

Fig. 11. Serum HDL-cholesterol of ginseng powder-fed rats.

* : $P < 0.05$
** : $P < 0.01$
☆ : discard $F < 0.05$

11) Red Blood Cell (RBC) Count

As shown in Table 9, the test and control groups had RBC count of approximately 6.0-9.0 x 10^{12}/L and the comparable groups showed similar values. The 3-month fed groups, both test and control, had the highest RBC count at 8.0-9.0 x 10^{12}/L. The 5-month fed subgroup 3 showed a 20% increase in RBC count, 7.29 x 10^{12}/L compared to the 6.07 x 10^{12}/L of the control, and this was statistically significant.

12) White Blood Cell (WBC) Count

The WBC count of both the control and test animals, fed from 2 to 6 months, were similar with values ranging from 5.0-9.0 x 10^9/L (Table 10). The exception was the 4-month fed subgroup 1 which had a 15.5% lower WBC count of 6.09 x 10^9/L compared to the 7.21 x 10^9/L of the control.

13) Hemoglobin

Hemoglobin content was similar between the control and the test groups. As shown in Table 11, the animals had values of 12.0-13.0 g/dl hemoglobin after 1 month of feeding (2 months of age) and this value increased as the animals grew to 14.0-15.0 g/dl found in the 6-month fed rats.

14) Hematocrit

The hematocrit was similar in both the ginseng-fed and control animals throughout the period of the experiment and ranged from 42-48% (Table 12).

The above data on blood composition and blood count indicate that ginseng administration tended to decrease the serum free fatty acid as well as the total lipid. This suggests that ginseng may stimulate lipid metabolism *in vivo*. Phospholipids, in particular, are an important constituent of cellular membrane and plays an important role in the body along with neutral lipids and non-polar lipids like cholesterol. The reports that ginseng increases phospholipid biosynthesis[3,4] may be due to the ginseng mediated increase in the absorption and metabolism of water-insoluble lipids.

The ginseng-fed animals tended to show an increase in HDL-cholesterol levels and this may be the result of an increase in the absorption and

Table 9. Red blood cell counts in rats fed diets containing various amount of ginseng powder for 1 - 10 months.

(10^{12}/L)

Group / Month	Control	Test 1	Test 2	Test 3
1	6.86 ± 0.44	6.65 ± 0.38	6.50 ± 0.65	6.79 ± 0.40
2	6.98 ± 0.60	6.83 ± 0.36	7.16 ± 0.41	6.10 ± 0.30
3	8.89 ± 0.50	8.33 ± 0.79	8.80 ± 0.38	9.00 ± 0.23
4	6.90 ± 0.70	6.41 ± 0.34	6.13 ± 0.29	6.16 ± 0.21
5	6.07 ± 0.30	6.28 ± 0.35	6.41 ± 0.37	7.29 ± 0.55
6	7.12 ± 0.46	7.33 ± 0.82	6.95 ± 0.96	6.46 ± 0.29
10	8.67 ± 0.50	8.74 ± 0.98	–	–

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 10. White blood cell counts in rats fed diets containing various amount of ginseng powder for 2 - 10 months.

(10^{9}/L)

Group / Month	Control	Test 1	Test 2	Test 3
2	5.03 ± 0.39	5.42 ± 0.62	5.30 ± 0.57	–
3	6.71 ± 1.69	6.75 ± 0.57	6.90 ± 0.95	6.54 ± 1.75
4	7.21 ± 0.67	6.09 ± 0.46	6.72 ± 1.02	6.91 ± 1.02
5	6.97 ± 0.93	8.26 ± 1.52	7.21 ± 1.59	–
6	6.07 ± 1.84	5.82 ± 0.72	7.05 ± 1.30	6.31 ± 0.74
10	6.60 ± 1.10	5.50 ± 0.91	–	–

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

metabolism of lipids as discussed above.

This effect of ginseng on blood lipid content could be the result of the detergent-like activity of saponin, one of ginseng's active components, on increasing the dispersion of water-insoluble cholesterol and neutral lipids.

RBC, WBC and hematocrit showed no difference between the test and control animals. This agrees with a previous report by Kim et al.[7-9]

The above results indicate that the use of ginseng as a food substance helps maintain health through stimulating metabolism and absorption, especially with respect to lipids. Ginseng is a safe and useful food substance that may help prevent atherosclerosis and other diseases of old age.

Table 11. Hemoglobin in rats fed diets containing various amount of ginseng powder for 1 - 10 months.

(g/dl)

Group / Month	Control	Test 1	Test 2	Test 3
1	12.3 ± 1.1	12.4 ± 0.6	12.2 ± 0.9	12.7 ± 0.4
2	15.0 ± 0.5	14.7 ± 0.5	15.0 ± 0.6	14.8 ± 0.3
3	15.7 ± 0.4	15.8 ± 0.8	15.6 ± 0.6	15.8 ± 0.6
4	15.0 ± 0.7	14.8 ± 0.6	14.7 ± 0.6	14.6 ± 0.4
5	15.1 ± 0.7	15.2 ± 0.5	15.5 ± 0.3	15.6 ± 0.7
6	14.9 ± 0.8	14.7 ± 0.8	14.9 ± 0.9	15.4 ± 0.9
10	16.0 ± 0.7	16.2 ± 0.7	–	–

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

Table 12. Hematocrit value in rats fed diets containing various amount of ginseng powder for 1 - 10 months.

(%)

Group / Month	Control	Test 1	Test 2	Test 3
1	48.3 ± 6.2	48.5 ± 1.7	43.8 ± 5.0	44.0 ± 4.3
2	42.1 ± 4.3	42.2 ± 5.2	45.7 ± 3.1	45.6 ± 1.0
3	44.1 ± 4.3	42.2 ± 9.6	43.4 ± 3.3	47.4 ± 3.1
4	46.3 ± 2.9	46.3 ± 2.1	46.5 ± 2.4	42.8 ± 1.5
5	48.3 ± 1.4	45.3 ± 3.0	47.9 ± 1.5	49.3 ± 2.7
6	45.4 ± 2.4	45.9 ± 2.6	43.5 ± 4.7	41.9 ± 4.5
10	45.2 ± 2.5	47.2 ± 0.8	–	–

* Test 1 : 0.625 g/kg diet
Test 2 : 1.25 g/kg diet
Test 3 : 2.5 g/kg diet

4. F_1, F_2 Generations

Table 13 and 14 shows the organ weight, blood cell count, hematocrit and the hemoglobin content of the F_1 and F_2 progeny from the ginseng fed animals. No difference was detected in litter size between the control and the F_0 and F_1 of both the subgroup 1 (0.625 g/kg diet) and the sub group 3 (2.5 g/kg diet). In addition, neither abnormal development nor histopathological irregularities were observed. Organ weight and hematological data, as shown in Tables 13, 14 was similar to that of the control, leading us to conclude that ginseng has no undesirable side-effects.

Hess et al.[10] fed ginseng extract to Sprague-Dawley rats through the F_2 generation and studied the reproductive pattern in these animals. They detected no visible abnormalities and the serological and histopathological examinations proved normal.

Hayashi et al.[11] also orally administered ginseng extract (*P. ginseng* C.A. Meyer) to ICR-SLC and Wistar Imamich rats in a teratological experiment, and observed no more abnormal external appearance than in the controls.

Table 13. Organ weights of F_1 and F_2 rats fed diets containing various amount of ginseng powder for 1 month.

(g)

Group	Organ	Heart	Liver	Kidney	Lung	Spleen	Brain	Body weight
Control	male	0.3 ± 0.1	2.4 ± 0.3	0.7 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	1.6 ± 0.1	69 ± 4.7
	female	0.3 ± 0.1	2.6 ± 0.3	0.7 ± 0.1	0.5 ± 0.0	0.3 ± 0.1	1.5 ± 0.1	62 ± 4.9
F_1	male Test 1	0.3 ± 0.1	2.5 ± 0.4	0.7 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	1.5 ± 0.0	70 ± 5.2
	female Test 1	0.3 ± 0.0	2.4 ± 0.3	0.7 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	1.6 ± 0.1	68 ± 4.6
F_2	male Test 1	0.4 ± 0.1	2.3 ± 0.2	0.7 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	1.6 ± 0.1	70 ± 5.3
	male Test 3	0.4 ± 0.1	2.3 ± 0.2	0.9 ± 0.1	0.7 ± 0.1	0.4 ± 0.1	1.6 ± 0.1	82 ± 6.9
	female Test 1	0.3 ± 0.0	2.3 ± 0.3	0.7 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	1.5 ± 0.1	65 ± 3.8
	female Test 1	0.4 ± 0.1	2.7 ± 0.4	0.8 ± 0.1	0.6 ± 0.1	0.3 ± 0.1	1.5 ± 0.1	70 ± 6.2

* Test 1 : 0.625 g/kg diet
Test 3 : 2.5 g/kg diet

Table 14. Red blood cell, white blood cell, hematocrit and hemoglobin values of F_1 and F_2 fed diets containing various amount of ginseng powder.

		RBC (10^{12}/L)	WBC (10^9/L)	HCT (%)	Hgb (g/d)
Male	Control	5.11 ± 0.26	3.20 ± 0.80	34.0 ± 2.0	13.3 ± 1.1
	Test 1 F_1	4.88 ± 0.26	3.12 ± 0.56	32.3 ± 2.6	13.4 ± 0.6
	Test 1 F_2	4.83 ± 0.31	2.90 ± 0.40	31.2 ± 2.7	13.1 ± 0.5
	Test 3 F_2	5.21 ± 0.28	3.48 ± 0.49	34.9 ± 2.0	13.4 ± 0.5
Female	Control	5.14 ± 0.21	2.72 ± 0.26	32.7 ± 1.9	13.0 ± 0.3
	Test 1 F_1	5.00 ± 0.36	2.84 ± 0.64	30.9 ± 1.5	13.2 ± 0.8
	Test 1 F_2	5.12 ± 0.35	2.65 ± 0.51	31.8 ± 2.2	13.1 ± 0.9
	Test 3 F_2	5.26 ± 0.25	2.78 ± 0.36	33.4 ± 2.1	13.3 ± 0.3

* Test 1 : 0.625 g/kg diet
Test 3 : 2.5 g/kg diet

5. Histopathological Study

Histopathological studies were performed on organs of rats administered ginseng. In test groups given ginseng (0.625g/kg diet, 125g/kg diet and 2.5g/kg diet) allocated to administered durations (1, 2, 3, 4, 5 and 6 months), the liver, kidney, lung, heart and small intestine were manifested normal appearance histologically. The liver showed normal hepatic cells and cell cords. The kidney showed also normal tubular epithelium and renal corpuscles. The lung showed normal appearance of alveoli with the primary and secondary bronchi. The heart showed normal cardiac muscle fibers and endocardium, and the small intestine showed normal intestinal glands and villi.

In particular, the megakaryocytes in the spleen were encountered frequently in the control group rats (Photo 1). On the other hand little or no megakaryocytes in the spleen were found in the test group rats without correspondence to administered durations (Photos 2, 3, 4). It is suggestive that the administration of ginseng might be correlated to hematopoietic functions. Therefore, the disappearance or decrement of megakaryocytes in the rat spleen administered ginseng might be indicative that extramedullary hematopoiesis in the spleen were not needed since the normal hematopoiesis of bone marrow were enhanced.

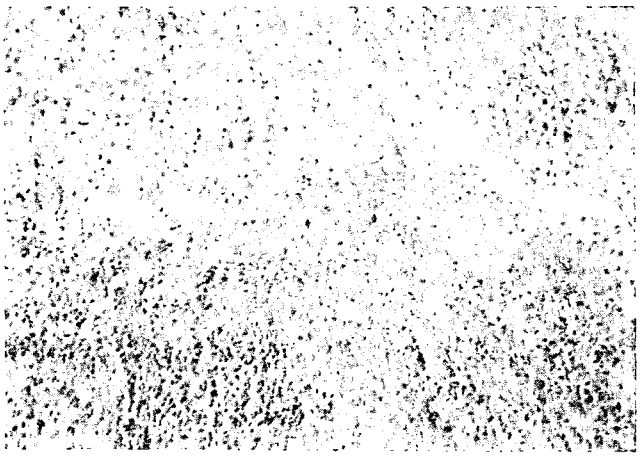

Photo 1. Rat spleen of control group with common diet (X400)

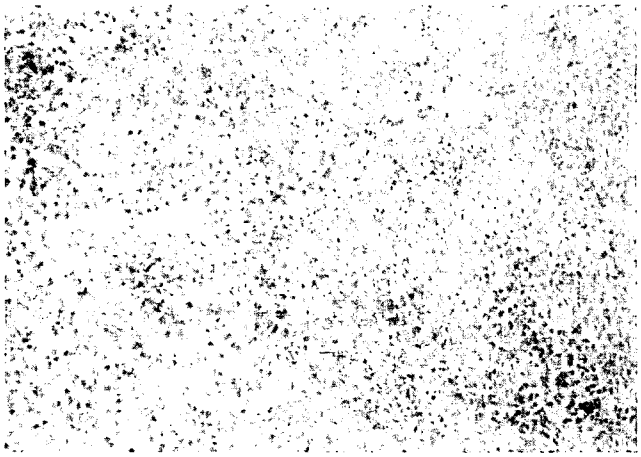

Photo 2. Rat spleen of test 3 with ginseng powder containing fed diet for 1 month (X400)

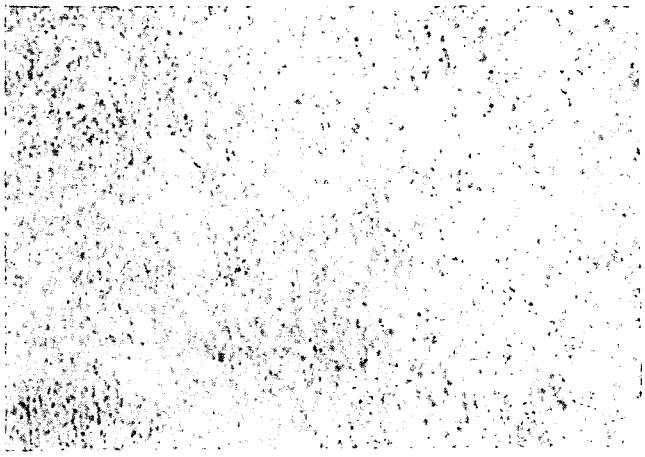

Photo 3. Rat spleen of test 3 with ginseng powder containing fed diet for 3 months (X400)

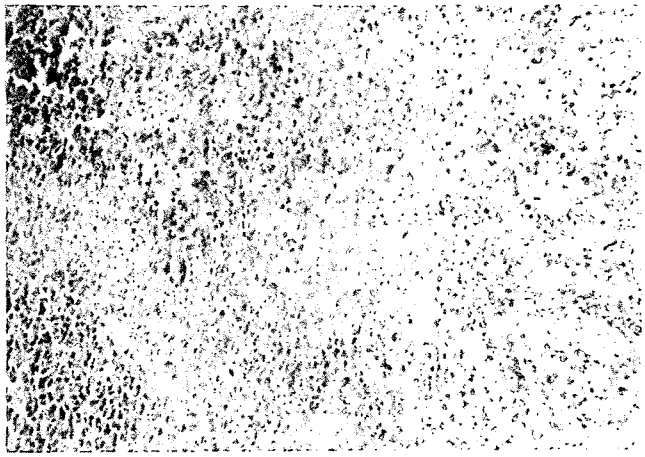

Photo 4. Rat spleen of test 3 with ginseng powder containing fed diet for 6 months (X400)

CONCLUSION

1. The growth rates were similar between the test and control groups.
2. Liver, spleen, kidney, brain, lung and heart weights were similar between the test and the control groups.
3. RBC, WBC, hematocrit, and hemoglobin values were similar between the test and control animals. The blood composition determination showed a similar level of alkaline phosphatase, triglyceride, total cholesterol, S-GOT and free cholesterol between the test and controls. However, free fatty acid, total lipid and S-GPT levels decreased while phospholipid, total protein, and HDL-cholesterol levels tended to increase.
4. F_1, F_2 generations showed no abnormal values in blood count, organ weight nor in external appearance.
5. No histopathological differences were observed between the test and control animals even after a long-term administration of ginseng. However, there was evidence that ginseng promotes hematopoiesis in test animals.
6. These results suggest that ginseng is not only safe as a food substance but may indeed strengthen the body and help prevent diseases of old age.

F.J. Lee: I'm just wondering whether all the animals survived till the end of the experimental period.

Hong: We didn't find any dead animals.

Chong: You fed ginseng powder between 1 to 6 months on all twelve rats. I think it was quite a long period. How long were they given Korean Ginseng? What was the mean period of the feeding?

F.J. Lee: All the test animals were fed ginseng for 6 months.

Chong: Did you look at the platelet counts in the blood? Was there any difference between the controls and ginseng fed rats.

Hong: Yes, I looked at the platelet counts but there was no difference.

고려인삼의 식품안전성 연구

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홍삼 분말을 혼합하여 제조한 사료로 60~80g 의 Sprague Dawley Rat(♂) 12마리를 1군으로 하여1~6개월간 사육하였다. 사육기간동안, 체중증가, 혈청의 생화학적 분석, 장기(심장, 폐, 신장, 간, 비장, 뇌)의 무게와 이들 장기의 병리조직검사를 하였다.

인삼 사육군과 대조군의 성장율, 장기 무게와 혈구수는 통계적 유의성은 없었으나 혈청중의 triglyceride, total cholesterol, free cholesterol 함량은 대조군과 유사하였고 total lipid, free fatty acid는 대조군에 비해 약간씩 감소하였다. 그러나 실험군의 total protein, phospholipid, HDL-cholesterol은 대조군에 비해 증가하였다. 실험군의 병리조직검사에서도 대조군과 차이가 없었으나, 특히 대조군의 비장에서는 조혈기능을 지닌 거핵구세포가 다수 출현하였으며 인삼 투여기간과 용량에는 비례하지 않았다.

F_1, F_2세대의 적혈구, 백혈구, 장기 무게와 병리조직검사는 대조군과 유사하였으며 외형적 기형도발견되지 않았다.

이상의 결과들로 고려인삼은 건강식품으로도 매우 안전하며 조혈기능도 촉진시킴을 시사해 준다.

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