

# AN EXPERIMENTAL STUDY ON TUMOR INHIBITORY EFFECT OF RED GINSENG IN MICE AND RATS EXPOSED TO VARIOUS CHEMICAL CARCINOGENS

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## Abstract

This experiment was carried out to evaluate the effects of Korean ginseng extract on carcinogenesis induced by various chemical carcinogens. Red ginseng extract was used for this study and was administered orally to the experimental animals. Carcinogens that were injected in subscapsular region of ICR newborn mice within 24 hours after birth were 9,10-dimethyl-1,2-benzanthracene (DMBA), urethane, N-2-fluorenylaceta-mide(AAF), aflatoxin B<sub>1</sub> and tobacco smoke condensate. N-methyl-N-nitroso-N'-nitroguani-dine(MNNG) was injected subcutaneously at the back of wistar rats. Experimental animals were autopsied in immediately after being sacrificed. All major organs were examined grossly and weighted. After fixation histopathological prepara-tions were made for microscopical study.

Following results were obtained.

In DMBA group sacrificed at the 26th week after the treatment with DMBA, the incidence of lung adenoma was 77% and the average number of the tumor was 17. However, in DMBA com-bined with red ginseng group, the incidence was 78% and the average number of lung adenoma was 14.1. This indicates that ginseng extract had no effect on the incidence of lung adenoma but

decreased the average number of lung adenoma by 17%.

In DMBA group sacrificed at the 48th week after the injection of DMBA, the lung adenoma incidence was 88%. The average diameter of the largest lung adenoma was 3.5 cm, the incidence of diffuse pulmonary infiltration was 18% and the average lung weight of male experimental mice was  $528.2 \pm 469.1$  gm.

On the other hand, in DMBA combined with red ginseng group sacrificed at the 48th week, the incidence of lung adenoma was 96%. The average diameter of the largest adenoma was 2.7 cm, the incidence of diffuse pulmonary infiltra-tion was 7% and the average lung weight of male mice was  $418.0 \pm 520$  gm.

These observations show that ginseng extract did not have any inhibitory effect on the incidence of lung adenoma but decreased the average diame-ter of the largest lung adenoma by 23%, the incidence of duffuse pulmonary infiltration by 63% and the average lung weight of male experi-mental mice by 21%.

From these results we have found that the prolonged administration with ginseng extract showed no inhibitory effect on the incidence of adenoma but it had the inhibitory effect on the proliferation of lung adenomas induced by DMBA.

In urethane group sacrificed at the 28th week

after the injection of urethane, the incidence of lung adenoma was 94% and the average number of lung adenoma was 8.6. In urethane combined with red ginseng group, the incidence of lung adenoma was 73% and the average number of adenoma was 6.0. These results indicate that there were 22% decrease of the lung adenoma incidence and 31% decrease of the average number of adenoma in urethane combined with red ginseng group.

And in urethane group sacrificed at the 50th week, the incidence of lung adenoma was 98% and the incidence of diffuse pulmonary infiltration was 14%. In urethane combined with ginseng group the incidence of lung adenoma was 85% and the incidence of diffuse pulmonary infiltration was 12%. Therefore the ginseng administration resulted in 15% decrease of the lung adenoma incidence and 14% decrease of the diffuse pulmonary infiltration incidence.

From these results we knew that the prolonged administration with ginseng extract inhibited the incidence and also the proliferation of the lung adenoma induced by urethane.

Lung adenoma and hepatoma were induced in the experimental mice sacrificed at the 68th week but not in the experimental mice sacrificed at the 28th week after the injection of AAF. In AAF group sacrificed at the 68th week after the injection of AAF the incidence of lung adenoma was 18% and the incidence of hepatoma was 27%. And in AAF combined with ginseng group the lung adenoma incidence was 12% and the hepatoma incidence was 37%. So the ginseng seemed to decrease the lung adenoma incidence by AAF, but we were unable to conclude the significant inhibitory effect of the ginseng extract on the incidence of lung adenoma by AAF because the above incidence of lung adenoma were similar to that of control group which was 11%. And these experimental data revealed that ginseng extract didn't have any inhibitory effect on the incidence of hepatoma induced by AAF.

In aflatoxin B<sub>1</sub> group sacrificed at the 56th week, the incidence of lung adenoma was 24% and hepatoma was 11%. However in aflatoxin

B<sub>1</sub> combined with ginseng group the incidence of lung adenoma was 17% and hepatoma was 3%. These results indicate that there were 29% decrease of the lung adenoma incidence and 75% decrease of the hepatoma incidence in aflatoxin B<sub>1</sub> combined with ginseng group.

In tobacco smoke condensate experimental group sacrificed at 67th week, no tumors were induced except just a few lung adenoma. The lung adenoma incidence both in tobacco smoke condensate group and in tobacco smoke condensate combined with ginseng group was 8%. And this incidence rate was similar to that of control group. These results indicate that the injection of 320  $\mu$ g tobacco smoke condensate per ICR newborn mouse was unable to induce lung adenoma in our experiments.

In MNNG group sacrificed at the 27th week the tumor incidence was 38.5% and in MNNG combined with ginseng extract group was 37%. In MNNG group for investigation of the life span of tumor bearing rats the tumor incidence was 93% and the average life span of tumor bearing rats was 318 days. And in MNNG combined with ginseng extract group the tumor incidence was 96% and the average life span was 337 days. Tumor induced by MNNG was almost sarcoma. This indicates that there was no inhibitory effect of ginseng extract on the tumor incidence, but the extract prolonged the average life span of tumor bearing rats by approximately 19 days.

## Introduction

As the life pattern of mankind becomes more civilized and sophisticated, cancer hazard of the myriad chemicals to which our environment exposes all of us, remains one of our most pressing health problems. Furthermore conventional treatment programs for most forms of cancer, such as surgical therapy, radiation therapy and chemotherapy using 43 kinds of potent chemical therapeutics, are faced with some limitations in effects.

Therefore, as a trial to develop new anti-cancer and cancer prophylactic agents among natural products, there have been many reports

on screening natural products, including plant extracts, and examining their potency of anticancer effect and their degree of side effect in cancer treatments. Especially among these natural products, ginseng extract occupies a particular place because of its well-known capacity to increase nonspecific resistance of the organism to various untoward influence.

Lazarev (1962) reported that ginseng extract inhibits the growth of Ehrlich ascites tumor transplanted in mice by 15% to 45% and has no effect in case of Walker carcinoma and CCK tumor transplanted in rats. Yaremenko (1966) found that the effect of ginseng extract on transplantation rate of tumor and average tumor size for each treatment group were not consistent in mice and rats injected intravenously Ehrlich ascites and Walker carcinoma cells. But Lee and Huemer (1971) reported that ether extract of ginseng inhibits the growth of Sarcoma 180 and Adenocarcinoma 755 transplanted in mice in proportion to weight loss of the host. According to them, ethanol extract of ginseng also shows significant anticancer effect on Sarcoma 180 tumor cells regardless of amount of administration, but L1210 leukemia are not inhibited by administration of three different extracts of ginseng; ether, ethanol, and water extract.

On the other hand, according to Murata and Hirono (1973), after surgical removal of cancers such as stomach cancer, pancreas cancer, colon cancer, breast cancer, thyroid cancer and sarcoma etc., long-term administration of protisol, effective fraction of ginseng extract, makes 70% of cancer patients improve various symptoms and reduce the recurrence rate of cancer. They suggested that this phenomenon results from rather increasing nonspecific resistance of the organism than direct anticancer effect.

Summing up these reports on the effect of ginseng extract, characteristics of the anticancer effect of ginseng extract would be summerized as follows: first, it is only observed in slow growing tumor such as Ehrlich ascites tumor and Sarcoma 180. Secondly, it is lack of dose-response relationship and has no repeatability. Finally in case of

rapidly growing tumor such as L1210 leukemia and p388 of mice and Walker carcinoma of rat which is very useful for assessment of clinical trial of new developed anticancer agent, it is not observed.

Therefore, the inconsistent anticancer effects of ginseng extract seems to support the suggestion of Brekman and Dardymov (1969) which the effect of ginseng extract is its capacity to increase nonspecific resistance of the organism. If it is the case, as Brekman and Dardymov suggested, it is more desirable to pursuit the possibility of ginseng extract rather as preventing or delaying agent for growth of cancer induced by myriad chemical carcinogens than as therapeutic agents. This experiment was carried out to evaluate the effect of Korean ginseng extract on chemical carcinogenesis induced by various carcinogen.

## Materials and methods

### Experimental animal

Mouse—Non inbred ICR mice were bred at random inter se. Within 24 hours after birth various carcinogens (total volume 0.02ml) were injected subcutaneously in subscapular region of ICR newborn mice. The mice were kept in polycarbonate boxes. 5 animals in each (27cm × 27 cm × 14cm) and in temperature (20°C ± 2°C)-controlled room and given solid pellet prescribed by NIH-7-open-fomular (1977) and tap water mixed with ginseng extract (1mg/1ml) ad libitum. Rat-7 weeks-old Wistar rats weighing from 90g to 140g which were bred at random inter se were kept in polycarbonate boxes, 3 animals in each and in same other conditions as the above.

### Chemical carcinogens

All chemical carcinogens were used within 1 hour after emulsification in the experiment. The injection volume of all chemical compounds except aflatoxin B<sub>1</sub> and MNNG was 0.02ml. The injection volume of aflatoxin B<sub>1</sub> was 0.01ml and MNNG was 0.6ml.

A single subcutaneous injection of 30μg

of DMBA (9, 10-dimethyl-1,2-benzanthracene, calbiochem. Co., Lot. I00769) in 1% aqueous gelatin was given to newborn mice in subscapular region (Pietra et al. 1959). 1 mg of Urethane (ethyl urethane, Fischer Scientific Co., Lot., 715518) in 1% aqueous gelatin was given to newborn mice the same way as the above (Pietra et al. 1961).

A subcutaneous injection of 100  $\mu$ g of AAF (N-2-fluorenyl acetamide, Eastman Kodak Co., Lot., C<sub>2</sub>A) in 1% aqueous gelatin was administered to newborn mice once a day for 5 days (Walters et al., 1967). 8  $\mu$ g of Aflatoxin B<sub>1</sub> (Calbiochem. Co) in suspension of DMSO (Dimethyl sulfoxide, Merck) and 320  $\mu$ g of tobacco smoke condensate were also given to newborn mice in the same way. Tobacco smoke condensate was made as the following procedure; first, after cigarette "Han-san-do" (Korean Monopoly product) was smoked by automatic smoking machine, the smoke was collected at -70°C. And then, it was dissolved in ethyl ether and finally removed ethyl ether completely in vacuo and suspended in 1% aqueous gelatin (Antonia, 1966).

A single subcutaneous injection of 3mg of MNNG (N-methyl-N'-nitroso-N-nitroguanidine, K & K Co., Lot. 16066) in saline solution was given into the backs of Wistar rat once a week for 10 weeks (Sugimura et al. 1966).

### Autopsy and Histological Examination

After slaughtering animals, each tumor developed in various organ was clearly observed with the naked eye. Various organs and tumors were excised to weigh out by chemical balance (Mettler) and fixed in 10% formalin and stained by hematoxylin-eosin staining method.

In case of vertebra, it was treated in 5% nitric acid solution to remove calcium from bone and neutralized in 85% alcohol. The same treatment of staining was performed as the above.

## Results and Discussion

If the mysterious effect of ginseng extract on the organism, as Brekman suggested, are its capa-

city to increase nonspecific resistance of the organism or to induce macromolecular synthesis, it is more desirable to examine the possibility of ginseng extract as a prophylactic or delaying agent for the growth of cancer than to try to use ginseng extract as a therapeutic agent of cancer induced by myriad chemical carcinogens. This experiment was performed to observe the effect of ginseng extract on carcinogenesis induced by various chemical carcinogens such as DMBA, Urethane, AAF, Aflatoxin B<sub>1</sub>, tobacco smoke condensate, and MNNG. The following results were obtained.

### I. Weaning rate of ICR new born mice injected with various chemical carcinogens.

The weaning rate of ICR new born mice injected with various chemical carcinogens are summarized in table 1. The weaning rates were over 90% in DMBA, Urethane, AAF, and tobacco smoke condensate groups, while in aflatoxin group only it was 52%.

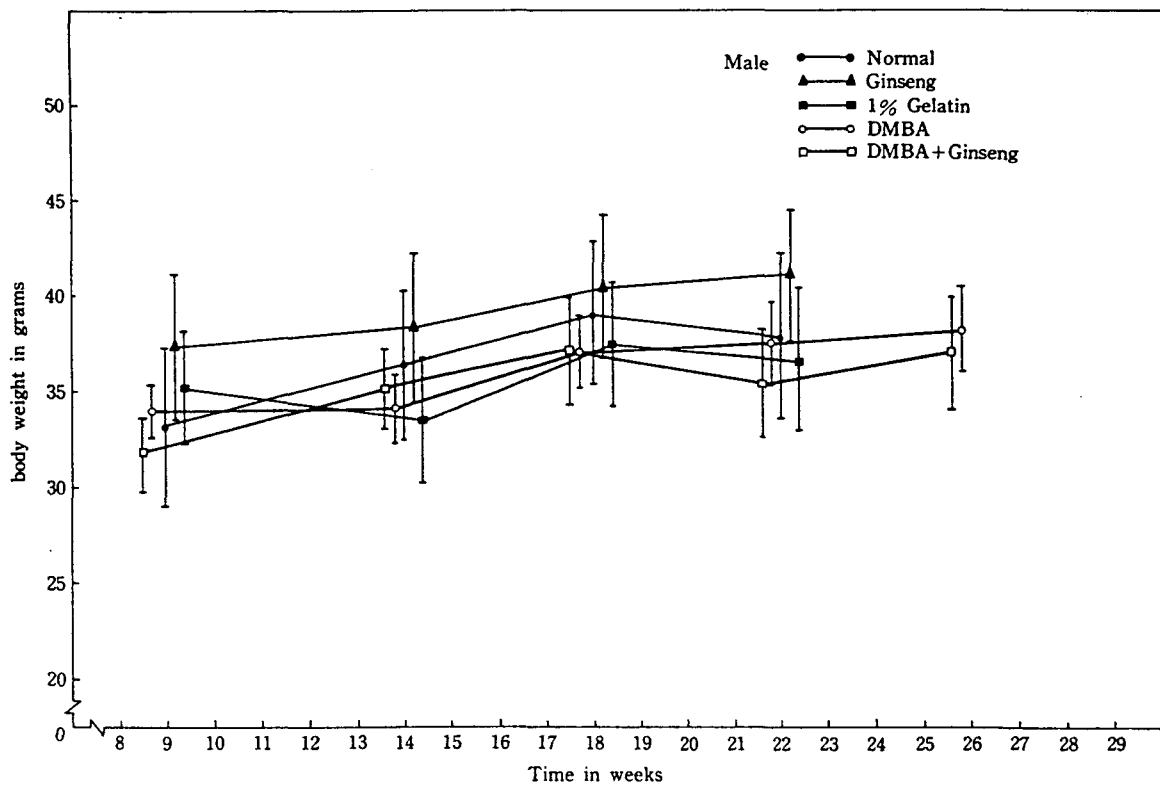
**Table 1.** Weaning rate in ICR new-born mice injected with various chemical carcinogens.

| Substance injected       | dose & route       | Vehicle          | No. mice | No. survivors at weaning | % survivor at weaning |
|--------------------------|--------------------|------------------|----------|--------------------------|-----------------------|
| 1% Gelatin               | 0.02ml×1, S.C      | H <sub>2</sub> O | 199      | 194                      | 97.5                  |
|                          | 0.02ml×5, S.C      | H <sub>2</sub> O | 201      | 196                      | 97.5                  |
| DMSO                     | 0.01ml×1, S.C      |                  | 200      | 192                      | 96.0                  |
| DMBA                     | 30 $\mu$ g×1, S.C  | 1% gelatin       | 210      | 204                      | 97.1                  |
| Urethane                 | 1mg×1, S.C         | 1% gelatin       | 200      | 186                      | 93.0                  |
| AAF                      | 100 $\mu$ g×5, S.C | 1% gelatin       | 201      | 178                      | 88.6                  |
| Aflatoxin B <sub>1</sub> | 8 $\mu$ g×1, S.C   | DMSO             | 200      | 104                      | 52.0                  |
| Tobacco Smoke Condensate | 320 $\mu$ g×1, S.C | 1% gelatin       | 200      | 188                      | 94.0                  |

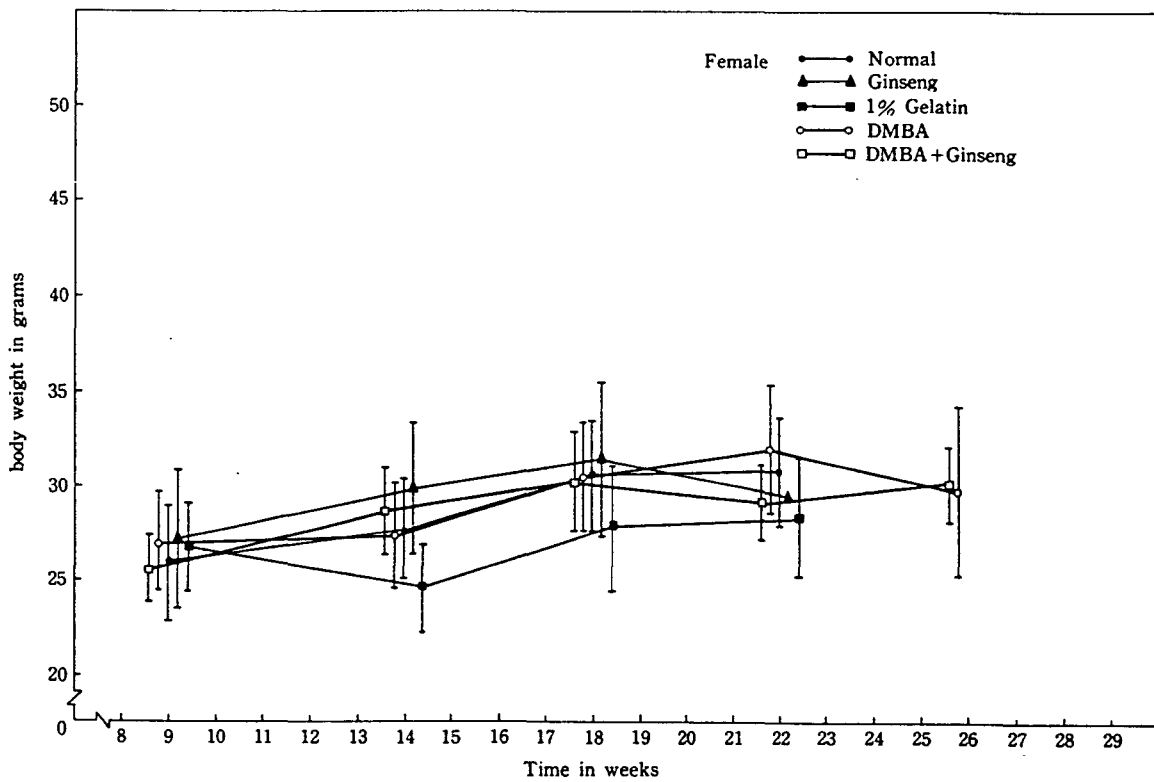
### II. DMBA group

#### 1) Changes of body weights

Fig. 1, Fig. 2, Fig. 3, and Fig. 4 show weekly increases of body weights of mice of each group sacrificed at 26th week or 48th week after the treatment with DMBA. As shown in these figures, there are normal increases of body weights, but the body weights of mice given red ginseng (Red ginseng



**Fig. 1.** Body weights of mice treated with DMBA and DMBA + Ginseng extracts.



**Fig. 2.** Body weights of mice treated with DMBA and DMBA + Ginseng extracts.

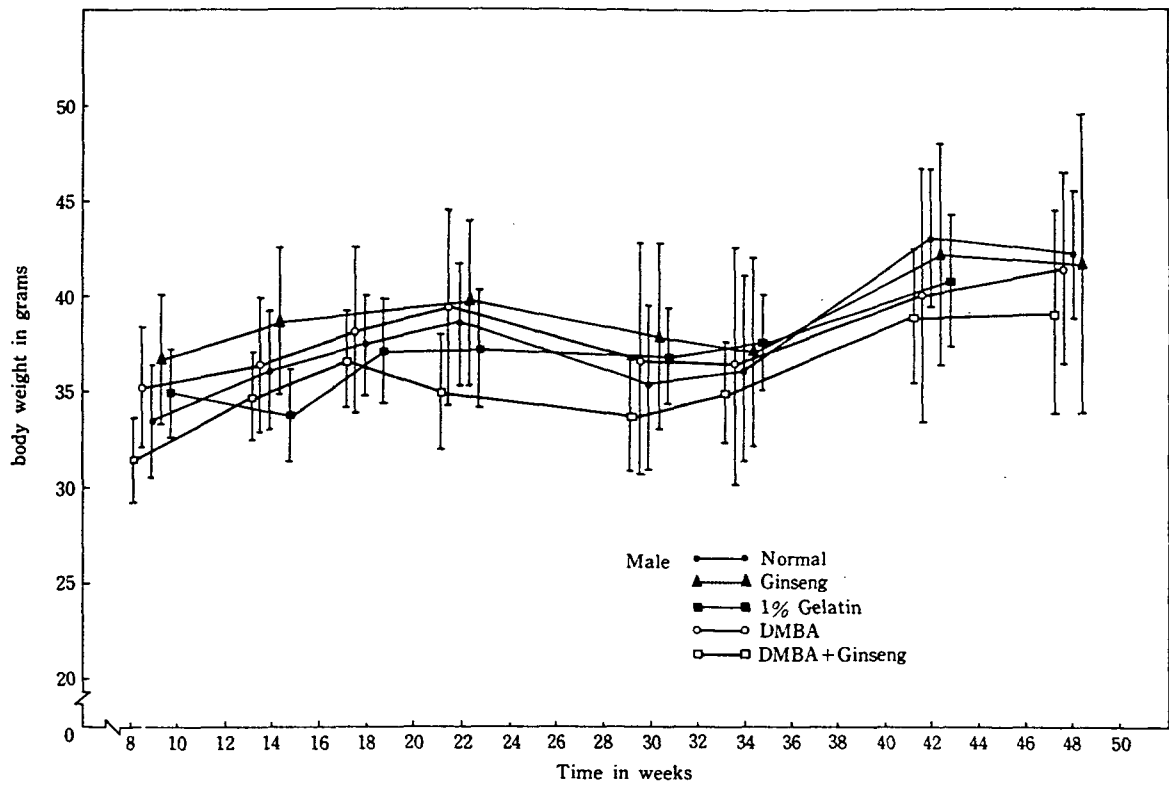


Fig. 3. Body weights of mice treated with DMBA and DMBA + Ginseng extracts.

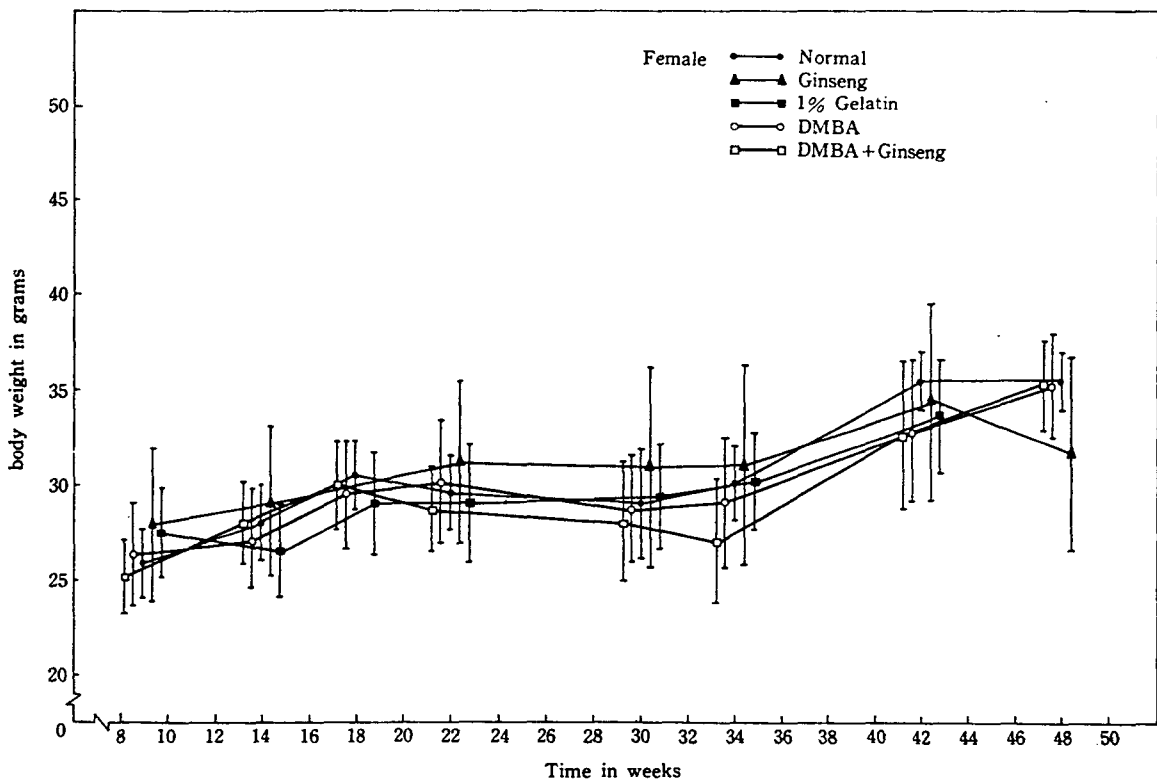


Fig. 4. Body weights of mice treated with DMBA and DMBA + Ginseng extracts.

control group) were increased to higher level than in other groups.

2) Changes of organ weights

The weight changes of various organs of mice of each group sacrificed at 26th week or 48th week after the treatment of DMBA are summerized in table 2 and table 3. Mouse organs examined here are lung, heart, salivary gland, liver, thymus, pancreas, spleen, kidney, brain, pituitary gland, testes and ovary.

In each group sacrificed at the 26th week after treatment with DMBA (Table 2,) there are little differences of weights of the organ between normal control group and other experimental groups. But in the case of the group sacrificed at the 48th week after treatment with DMBA (Table 3), compares with three control groups, weights of lung in DMBA group and DMBA combined with red ginseng group increased significantly. It results from increased pulmonary infiltration and growth

of lung adenoma for 48 weeks. Furthermore, compared DMBA group with DMBA combined with red ginseng group, the average weight of lung in DMBA group ( $528 \pm 469.1$  g) is more than those in DMBA combined with Red ginseng group ( $418 \pm 250$  g).

This means that ginseng extract inhibits the growth and pulmonary infiltration of lung adenoma induced by DMBA in mice by 21%.

3) The effect of ginseng extract on the incidence and the average number of lung adenoma induced by DMBA.

Table 4 and Fig. 5 show the incidence of lung adenoma in each group sacrificed at the 26th week after the treatment with DMBA. In DMBA group sacrificed at the 26th week after the treatment with DMBA, the incidence of lung adenoma was 77% (male, 79%; female, 75%) and the average number of the tumor was 17.0 (male, 16% ; female, 18.2%). However, in DMBA combined with red

**Table 2.** Organ weights of mice treated with DMBA and DMBA + Ginseng extracts at 26 weeks after the injection.

| Substance treated | Sex | No. mic | Lung          | Heart        | Salivary gland | Liver          | Thymus       | Pancreas | Kidney |   | Testes (ovary) |   | Brain | Pituitary |
|-------------------|-----|---------|---------------|--------------|----------------|----------------|--------------|----------|--------|---|----------------|---|-------|-----------|
|                   |     |         |               |              |                |                |              |          | R      | L | R              | L |       |           |
| ① Normal          | m   | 30      | 228.7 ± 42.4  | 199.9 ± 30.0 | 261.7 ± 38.7   | 2253.2 ± 312.9 |              |          |        |   |                |   |       |           |
|                   | f   | 29      | 210.2 ± 44.3  | 174.8 ± 36.5 | 226.9 ± 51.3   | 1951.5 ± 470.0 |              |          |        |   |                |   |       |           |
| ② Ginseng         | m   | 35      | 231.6 ± 34.5  | 229.0 ± 39.7 | 274.2 ± 35.8   | 2149.5 ± 335.9 |              |          |        |   |                |   |       |           |
|                   | f   | 39      | 223.9 ± 52.3  | 142.1 ± 27.9 | 203.9 ± 69.5   | 1831.8 ± 512.0 |              |          |        |   |                |   |       |           |
| ③ 1% gelatin      | m   | 39      | 223.6 ± 39.8  | 190.2 ± 30.2 | 267.4 ± 58.1   | 1912.1 ± 384.5 |              |          |        |   |                |   |       |           |
|                   | f   | 30      | 190.5 ± 40.0  | 132.8 ± 16.5 | 184.9 ± 42.9   | 1524.5 ± 308.8 |              |          |        |   |                |   |       |           |
| ④ DMBA            | m   | 19      | 228.0 ± 104.0 | 185.3 ± 19.8 | 288.2 ± 35.0   | 2128.9 ± 340.3 | 29.1 ± 15.2  |          |        |   |                |   |       |           |
|                   | f   | 16      | 235.7 ± 87.4  | 141.8 ± 19.8 | 193.5 ± 35.4   | 1583.1 ± 219.3 | 85.2 ± 141.5 |          |        |   |                |   |       |           |
| ⑤ DMBA + ginseng  | m   | 18      | 233.6 ± 59.7  | 191.7 ± 28.3 | 301.3 ± 55.0   | 2008.7 ± 335.6 | 29.4 ± 15.7  |          |        |   |                |   |       |           |
|                   | f   | 19      | 250.4 ± 76.3  | 147.1 ± 18.0 | 202.9 ± 27.5   | 1675.6 ± 224.0 | 49.1 ± 34.6  |          |        |   |                |   |       |           |

\* Unit: mg

**Table 3.** Organ weights of mice treated with DMBA and DMBA + Ginseng extracts at 48 weeks after the injection.

| Substance treated | Sex | No. mice | Lung          | Heart        | Salivary gland | Liver          | Thymus      | Pancreas      |
|-------------------|-----|----------|---------------|--------------|----------------|----------------|-------------|---------------|
| ① Normal          | m   | 11       | 224.5 ± 40.5  | 211.7 ± 28.0 | 276.1 ± 37.2   | 2339.5 ± 329.5 | 35.3 ± 12.5 | 281.5 ± 67.6  |
|                   | f   | 16       | 213.3 ± 25.7  | 154.8 ± 15.2 | 168.2 ± 30.5   | 1829.3 ± 281.5 | 52.4 ± 17.3 | 282.9 ± 52.4  |
| ② Ginseng         | m   | 46       | 287.1 ± 149.6 | 220.2 ± 51.1 | 256.3 ± 53.7   | 2499.1 ± 488.9 | 36.5 ± 32.8 | 332.3 ± 89.1  |
|                   | f   | 43       | 232.4 ± 75.2  | 159.0 ± 27.7 | 161.3 ± 44.2   | 1857.7 ± 460.0 | 63.3 ± 48.4 | 256.1 ± 65.9  |
| ③ 1% gelatin      | m   | 60       | 235.9 ± 88.9  | 193.3 ± 74.9 | 239.8 ± 47.2   | 2093.5 ± 483.5 | 18.0 ± 11.9 | 313.9 ± 100.0 |
|                   | f   | 48       | 233.3 ± 95.3  | 155.7 ± 32.9 | 172.4 ± 45.6   | 1850.3 ± 388.3 | 52.3 ± 23.3 | 325.1 ± 93.0  |
| ④ DMBA            | m   | 19       | 528.2 ± 469.1 | 198.2 ± 25.3 | 269.2 ± 65.6   | 2112.4 ± 383.2 | 43.6 ± 22.3 | 306.3 ± 69.3  |
|                   | f   | 14       | 317.3 ± 152.0 | 147.7 ± 18.2 | 185.7 ± 43.9   | 1691.7 ± 200.6 | 38.6 ± 13.6 | 325.4 ± 62.5  |
| ⑤ DMBA + ginseng  | m   | 9        | 418.0 ± 520.0 | 206.3 ± 25.5 | 272.6 ± 46.2   | 2182.0 ± 286.8 | 24.5 ± 11.7 | 337.0 ± 53.4  |
|                   | f   | 18       | 321.5 ± 155.4 | 153.5 ± 22.1 | 208.8 ± 75.1   | 1728.6 ± 370.8 | 53.1 ± 23.3 | 292.5 ± 68.5  |

|   | Spleen        | Kidney       |              | Testes (ovary) |              | Brain        | Pituitary |
|---|---------------|--------------|--------------|----------------|--------------|--------------|-----------|
|   |               | R            | L            | R              | L            |              |           |
| ① | 113.8 ± 49.7  | 387.9 ± 64.6 | 369.4 ± 58.4 | 138.5 ± 18.5   | 131.4 ± 18.8 | 462.4 ± 22.0 | 2.8 ± 0.8 |
|   | 208.7 ± 263.1 | 224.5 ± 28.2 | 221.5 ± 27.4 | 21.9 ± 29.6    | 13.7 ± 4.9   | 477.9 ± 41.8 | 2.2 ± 1.5 |
| ② | 238.6 ± 314.6 | 406.4 ± 69.1 | 383.9 ± 65.3 | 142.2 ± 20.2   | 136.4 ± 19.2 | 497.1 ± 29.5 | 2.5 ± 1.4 |
|   | 174.5 ± 94.4  | 236.6 ± 45.2 | 230.5 ± 46.5 | 19.6 ± 44.7    | 13.3 ± 8.1   | 501.7 ± 36.9 | 2.5 ± 1.2 |
| ③ | 171.7 ± 99.2  | 351.3 ± 64.3 | 235.2 ± 63.6 | 114.8 ± 19.2   | 108.7 ± 21.5 | 462.2 ± 31.5 | 2.5 ± 1.8 |
|   | 198.2 ± 100.7 | 306.1 ± 82.4 | 293.6 ± 79.4 | 14.5 ± 7.3     | 15.1 ± 8.4   | 467.4 ± 60.4 | 2.1 ± 1.4 |
| ④ | 173.9 ± 131.5 | 326.3 ± 63.3 | 317.5 ± 48.9 | 132.0 ± 24.0   | 124.4 ± 21   | 488.5 ± 23.5 | 1.8 ± 0.4 |
|   | 137.7 ± 43.5  | 224.4 ± 20.4 | 210.8 ± 21.6 | 11.5 ± 16.0    | 12.1 ± 10.8  | 493.0 ± 32.7 | 1.7 ± 0.8 |
| ⑤ | 168.7 ± 159.6 | 347.0 ± 53.1 | 333.0 ± 52.5 | 128.2 ± 14.7   | 121.4 ± 18.8 | 501.2 ± 37.9 | 1.8 ± 0.5 |
|   | 172.9 ± 94.3  | 222.5 ± 42.8 | 216.8 ± 46.7 | 111.3 ± 293.4  | 14.8 ± 15.4  | 487.6 ± 36.6 | 1.5 ± 0.5 |

\* Unit: mg

**Table 4.** Lung adenoma in ICR mice treated with DMBA and DMBA + Ginseng extracts.

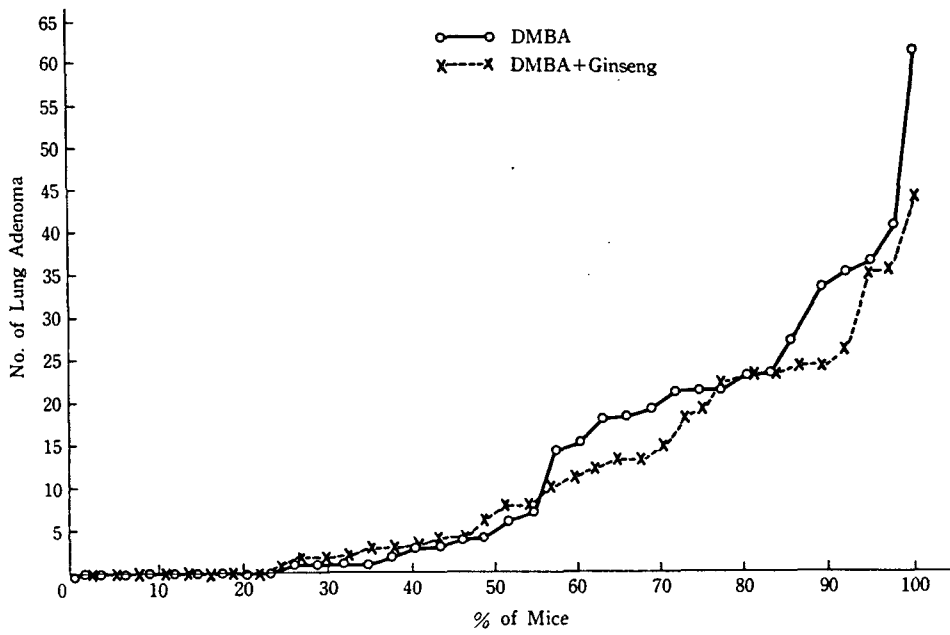
| Substance treated | No. of mice | No. (%) surv. at 26 weeks | No. (%) surv. with lung adenomas | Mean No. of lung adenomas per surv. |
|-------------------|-------------|---------------------------|----------------------------------|-------------------------------------|
| Normal            | m           | 30                        | 30 (100%)                        | 0 (0%)                              |
|                   | f           | 30                        | 29 (97%)                         | 0 (0%)                              |
|                   | m + f       | 60                        | 59 (98%)                         | 0 (0%)                              |
| Ginseng           | m           | 40                        | 35 (88%)                         | 1 (3%)                              |
|                   | f           | 40                        | 39 (98%)                         | 1 (3%)                              |
|                   | m + f       | 80                        | 74 (93%)                         | 2 (3%)                              |
| 1% gelatin        | m           | 40                        | 39 (98%)                         | 0 (0%)                              |
|                   | f           | 30                        | 30 (100%)                        | 0 (0%)                              |
|                   | m + f       | 70                        | 69 (99%)                         | 0 (0%)                              |
| DMBA              | m           | 20                        | 19 (95%)                         | 15 (79%) *(100%)                    |
|                   | f           | 18                        | 16 (89%)                         | 12 (75%) *(100%)                    |
|                   | m + f       | 38                        | 35 (92%)                         | 27 (77%) *(100%)                    |
| DMBA + Ginseng    | m           | 20                        | 18 (90%)                         | 16 (89%) *(113%)                    |
|                   | f           | 20                        | 19 (95%)                         | 13 (68%) *(91%)                     |
|                   | m + f       | 40                        | 37 (93%)                         | 29 (78%) *(101%)                    |

\*; % of DMBA Control

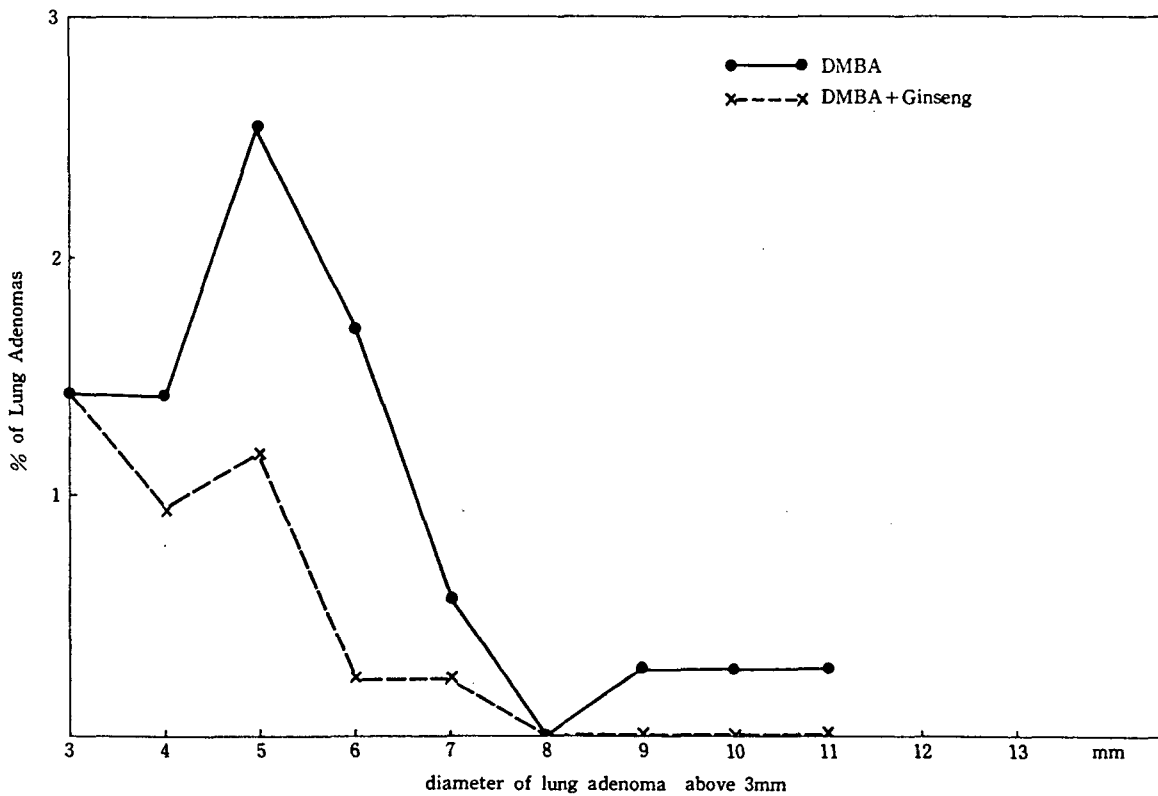
ginseng group, the incidence was 78% (male, 89%; female, 68%) and the average number of lung adenoma was 14.1 (male, 12%; female, 16.8%).

There was no pulmonary infiltration of lung adenoma in both group sacrificed at the 26th week after the treatment of DMBA. These results indi-





**Fig. 5.** The effects of Ginseng extracts on the incidence and No. of lung adenomas at 26 weeks after the injection.



**Fig. 6.** The effects of Ginseng extracts on the size (growth) of lung adenomas at 48 weeks after the injection.

cate that ginseng extract has no effect on the incidence of lung adenoma but decreases the average number of lung adenoma by 17%.

The incidence of lung adenoma in each group

sacrificed at the 48th week after the treatment of DMBA was summarized in table 5 and shown in Fig. 6. In DMBA group sacrificed at the 48th week after the injection of DMBA, the incidence of the

**Table 5.** Lung adenoma in ICR mice treated with DMBA and DMBA + Ginseng extracts.

| Substance treated | No. mice | No.(%) Survivors at 48 weeks | No.(%) Survivors with Lung adenomas | Mean size of largest Lung adenoma per tumor bearing survivors (mm) | No. (%) of mice with diffuse infiltrated Lung lobes. | Mean No.(%) of diffuse infiltrated Lung lobes per diffuse infiltrated Lung lobe bearing mice |              |
|-------------------|----------|------------------------------|-------------------------------------|--|--|--|--------------|
| Normal            | m        | 20                           | 11 (55%)                            | 2 (18%)  | 1.0  | 0 ( 0%)  | 0            |
|                   | f        | 20                           | 16 (80%)                            | 1 ( 6%)  | 1.0  | 0 ( 0%)  | 0            |
|                   | m+f      | 40                           | 27 (68%)                            | 3 (11%)  | 1.0  | 0 ( 0%)  | 0            |
| Ginseng           | m        | 60                           | 46 (77%)                            | 9 (20%)  | 1.0  | 0 ( 0%)  | 0            |
|                   | f        | 60                           | 43 (72%)                            | 1 ( 2%)  | 2.0  | 0 ( 0%)  | 0            |
|                   | m+f      | 120                          | 89 (74%)                            | 10 (11%)   | 1.1  | 0 ( 0%)  | 0            |
| 1% gelatin        | m        | 69                           | 60 (87%)                            | 2 ( 3%)  | 1.5  | 4 ( 7%)  | 0.24         |
|                   | f        | 55                           | 48 (87%)                            | 2 ( 4%)  | 1.0  | 2 ( 4%)  | 0.12         |
|                   | m+f      | 124                          | 108 (87%)                           | 4 ( 4%)  | 1.3  | 6 ( 6%)  | 0.19         |
| DMBA              | m        | 33                           | 19 (58%)                            | 16 ( 84%) *(100%)  | 3.7 *(100%)  | 6 (32%)  | 2.17         |
|                   | f        | 30                           | 14 (47%)                            | 13 ( 93%) *(100%)  | 3.2 *(100%)  | 0 ( 0%)  | 0            |
|                   | m+f      | 63                           | 33 (52%)                            | 29 ( 88%) *(100%)  | 3.5 *(100%)  | 6 (18%) *(100%)  | 2.17 *(100%) |
| DMBA + ginseng    | m        | 33                           | 9 (27%)                             | 9 (100%) *(119%)   | 2.8 *(76%)   | 0 ( 0%)  | 0            |
|                   | f        | 30                           | 18 (60%)                            | 17 ( 94%) *(101%)  | 2.7 *(84%)   | 2 (11%)  | 2            |
|                   | m+f      | 63                           | 27 (43%)                            | 26 ( 96%) *(109%)  | 2.7 *(77%)   | 2 ( 7%) *(39%)   | 2 *(92%)     |

\*; % of DMBA control

lung adenoma was 88% (male, 84%; female, 93%). The average diameter of the largest lung adenoma was 3.5cm, and the incidence of diffused pulmonary infiltration was 18%.

On the other hand, in DMBA combined with red ginseng group sacrificed at the 48th week, the incidence of the lung adenoma was 96% (male, 100% ; female, 94%). The average diameter of the largest adenoma was 2.7cm and the incidence of diffuse pulmonary infiltration was 7%.

There is rather increase of incidence of lung adenoma in DMBA combined with ginseng extract group by 8%, compared with DMBA group. Considering that the incidence rate of lung adenoma was 11% in normal control group and 11% in ginseng control group and 4% in gelatin control group, it might be experimental error due to individual variation. These observations show that ginseng extract did not have any inhibitory effect on the incidence of lung adenoma but decreased average diameter of the largest lung adenoma by 23%, the incidence of diffuse pulmonary infiltration by 61% and the average lung weight of male experimental mice by 21%.

From these results we have found that the

prolonged administration with ginseng extract showed no inhibitory effect on the incidence of adenoma but it showed the inhibitory effect on the proliferation of lung adenoma induced by DMBA.

On the other hand Lazarev(1965) reported that tumorigenesis of mouse induced by DMBA was inhibited or delayed by administration of eleuterococcus extract but there has been no reports until now that tumorigenesis induced by DMBA was inhibited by administration of ginseng extract.

DMBA has been used frequently in the experiment of carcinogenesis in addition to 3-methyl cholanthrene which is most potent carcinogen among polycyclic, hydrocarbons. There is also many similarity in carcinogenesis between DMBA and benz(a)pyrene which is a most typical carcinogen among polycyclic aromatic hydrocarbon and has been in exhaust gas of internal combustion engines, soot, carbon black, coal tar, pitch and cigarette smoke et al. Therefore, it is desirable to perform this experiment more systematically and extensively.

### III. Urethane group

#### 1) Changes of body weights

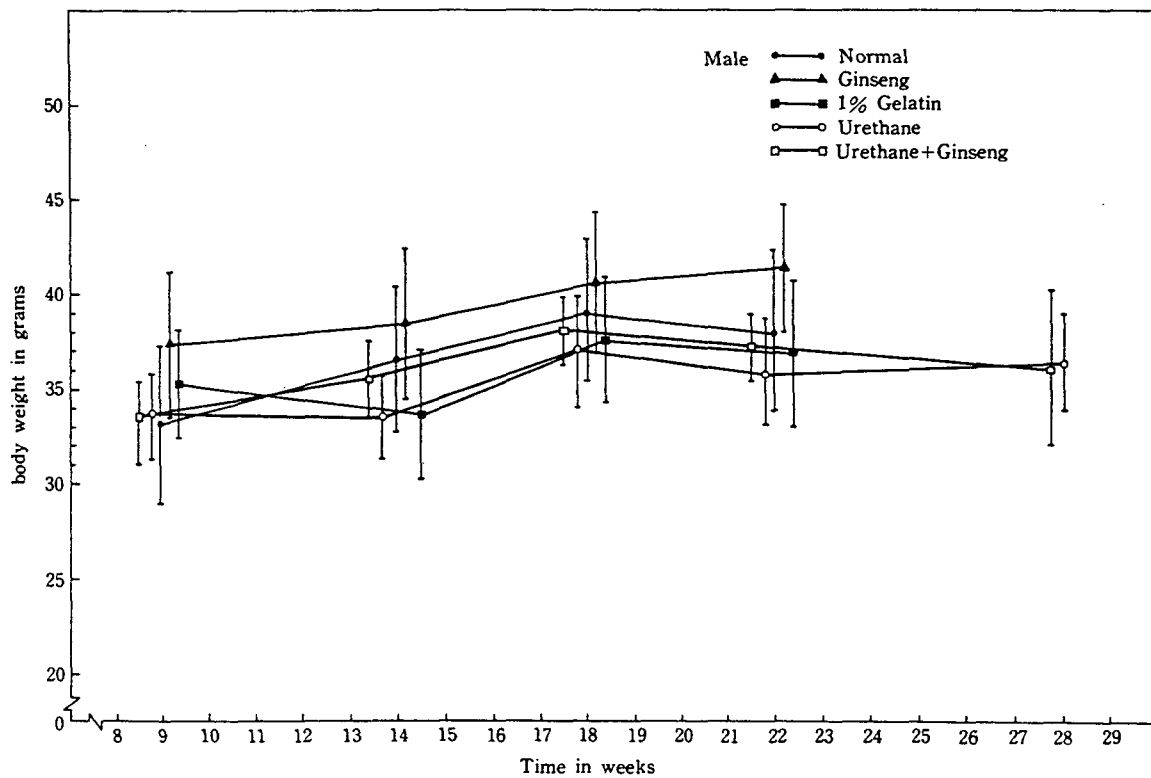


Fig. 7. Body weights of mice treated with urethane and urethane + Ginseng extracts.

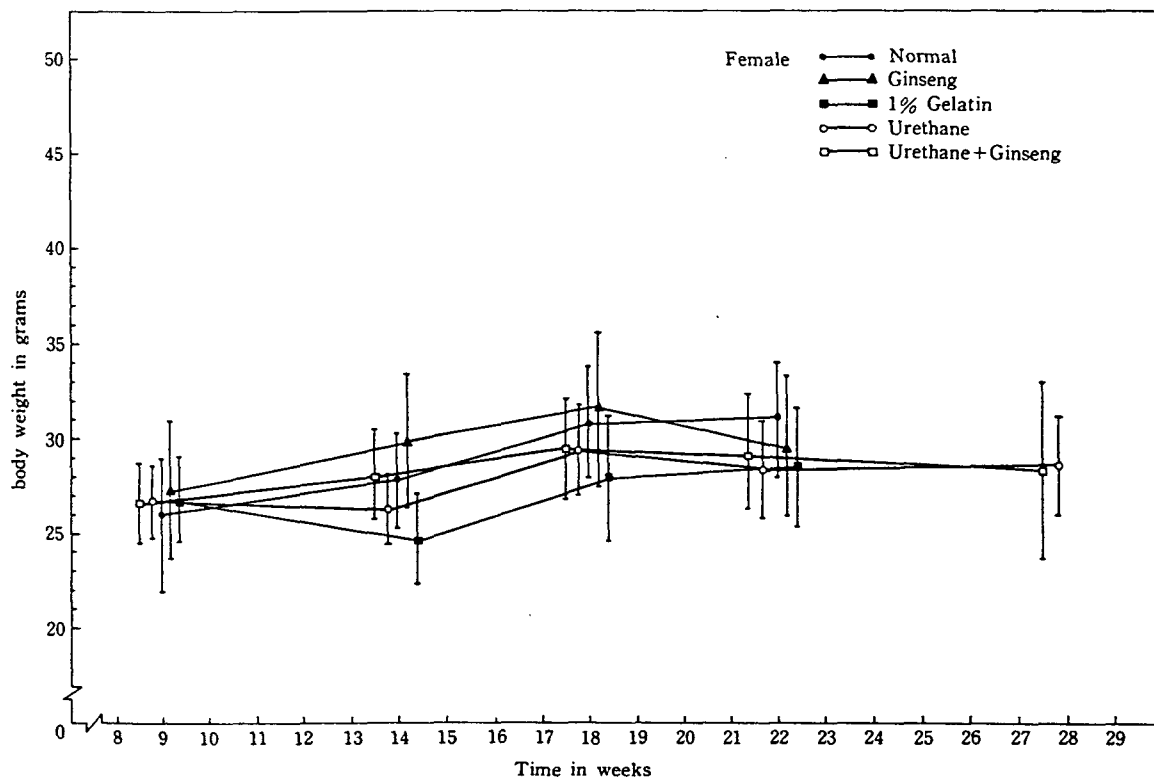


Fig. 8. Body weights of mice treated with urethane and urethane + Ginseng extracts.

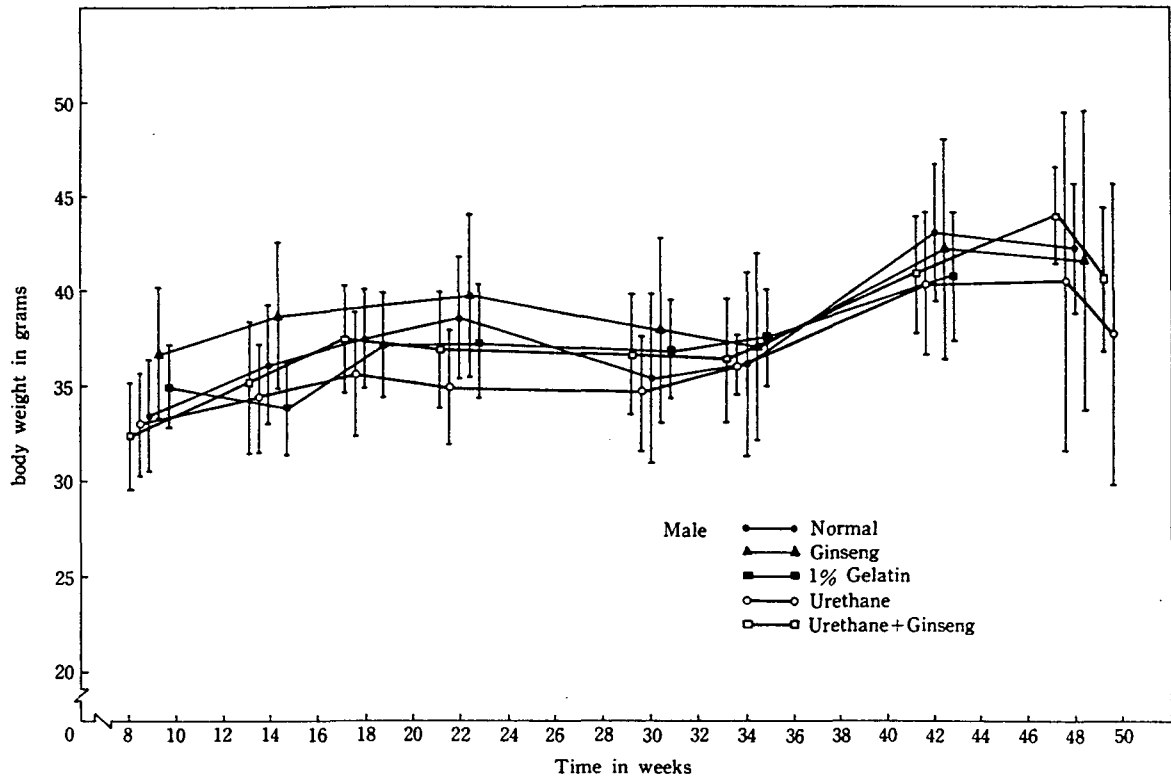


Fig. 9. Body weights of mice treated with urethane and urethane + Ginseng extracts.

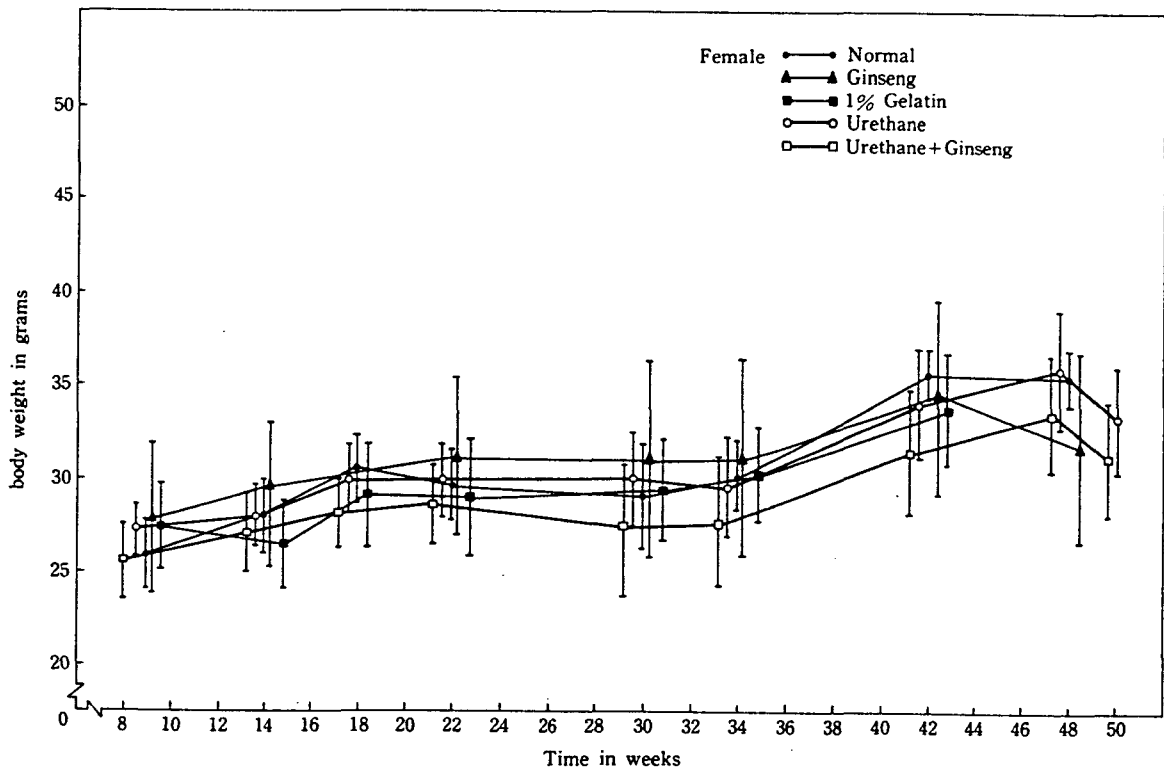


Fig. 10. Body weights of mice treated with urethane and urethane + Ginseng extracts.

**Table 6.** Organ weights of mice treated with Urethane and Urethane + Ginseng extracts at 28 weeks after the injection.

| Substance treated    | No. mice | Lung |              | Heart        |              | Salivary gland |             | Liver        |   | Thymus |   | Pancreas |   |
|----------------------|----------|------|--------------|--------------|--------------|----------------|-------------|--------------|---|--------|---|----------|---|
|                      |          | m    | f            | m            | f            | m              | f           | m            | f | m      | f | m        | f |
| ① Normal             | m        | 30   | 228.7 ± 42.4 | 199.9 ± 30.0 | 262.7 ± 38.7 | 2253.2 ± 312.9 | —           | 256.6 ± 52.7 |   |        |   |          |   |
|                      | f        | 29   | 210.2 ± 44.3 | 174.8 ± 36.5 | 226.9 ± 51.3 | 1951.5 ± 470.0 | —           | 246.8 ± 50.7 |   |        |   |          |   |
| ② Ginseng            | m        | 35   | 231.6 ± 34.5 | 229.0 ± 39.7 | 274.2 ± 35.8 | 2149.5 ± 335.9 | —           | 279.1 ± 87.1 |   |        |   |          |   |
|                      | f        | 39   | 223.9 ± 52.3 | 142.1 ± 27.9 | 203.9 ± 69.5 | 1831.8 ± 512.0 | —           | 225.5 ± 40.1 |   |        |   |          |   |
| ③ 1% gelatin         | m        | 39   | 223.6 ± 39.8 | 190.2 ± 30.2 | 267.4 ± 58.1 | 1912.1 ± 384.5 | —           | 260.0 ± 57.5 |   |        |   |          |   |
|                      | f        | 30   | 190.5 ± 40.0 | 132.8 ± 16.5 | 184.9 ± 42.9 | 1524.5 ± 308.8 | —           | 247.7 ± 30.2 |   |        |   |          |   |
| ④ Urethane           | m        | 14   | 238.0 ± 37.0 | 196.1 ± 27.9 | 274.8 ± 24.6 | 1940.8 ± 208.7 | 34.0 ± 8.2  | 264.4 ± 37.6 |   |        |   |          |   |
|                      | f        | 20   | 208.4 ± 28.5 | 132.5 ± 15.5 | 192.8 ± 32.1 | 1382.5 ± 210.4 | 55.0 ± 16.2 | 232.7 ± 39.3 |   |        |   |          |   |
| ⑤ Urethane + Ginseng | m        | 14   | 265.4 ± 96.2 | 204.9 ± 38.2 | 311.0 ± 36.6 | 2190.2 ± 264.4 | 46.8 ± 13.4 | 269.1 ± 33.8 |   |        |   |          |   |
|                      | f        | 16   | 220.3 ± 56.3 | 133.9 ± 19.0 | 203.0 ± 32.0 | 1526.8 ± 480.8 | 52.8 ± 31.8 | 230.1 ± 55.3 |   |        |   |          |   |

|   | Spleen        |               | Kidney       |              | Testes (ovary) |              | Brain        |            | Pituitary    |            |              |              |           |           |
|---|---------------|---------------|--------------|--------------|----------------|--------------|--------------|------------|--------------|------------|--------------|--------------|-----------|-----------|
|   | m             | f             | R            | L            | R              | L            | m            | f          | m            | f          |              |              |           |           |
| ① | 134.1 ± 65.8  | 123.9 ± 64.2  | 368.5 ± 68.6 | 206.4 ± 31.3 | 357.9 ± 62.1   | 199.5 ± 34.9 | 145.4 ± 28.9 | 15.9 ± 4.3 | 177.5 ± 96.0 | 13.6 ± 3.8 | 479.3 ± 27.0 | 500.5 ± 59.9 | 2.8 ± 1.2 | 2.9 ± 0.9 |
|   | 191.9 ± 252.1 | 226.7 ± 330.3 | 382.3 ± 58.1 | 208.4 ± 34.1 | 364.6 ± 51.6   | 200.6 ± 33.7 | 154.1 ± 20.2 | 16.1 ± 5.7 | 145.8 ± 18.6 | 15.4 ± 5.7 | 505.3 ± 19.4 | 507.9 ± 38.6 | 2.3 ± 0.9 | 3.0 ± 0.7 |
| ③ | 110.2 ± 45.6  | 119.6 ± 81.0  | 343.2 ± 39.4 | 182.3 ± 28.8 | 326.4 ± 37.4   | 177.4 ± 28.7 | 118.4 ± 23.9 | 14.2 ± 6.7 | 121.9 ± 22.5 | 13.5 ± 6.4 | 481.5 ± 32.5 | 504.2 ± 20.5 | 1.9 ± 1.0 | 2.5 ± 1.0 |
|   | 116.0 ± 42.2  | 112.5 ± 27.5  | 212.7 ± 27.4 | 183.8 ± 24.8 | 307.2 ± 41.9   | 179.5 ± 24.9 | 146.1 ± 17.2 | 9.4 ± 3.6  | 141.3 ± 14.5 | 10.5 ± 5.3 | 478.2 ± 14.2 | 500.6 ± 19.3 | 2.6 ± 0.9 | 1.5 ± 0.4 |
| ⑤ | 131.3 ± 55.2  | 181.3 ± 166.1 | 349.7 ± 46.9 | 185.2 ± 27.2 | 353.5 ± 50.2   | 174.6 ± 31.7 | 144.4 ± 9.2  | 10.2 ± 5.1 | 143.1 ± 13.0 | 10.6 ± 4.0 | 496.5 ± 29.0 | 499.5 ± 35.5 | 2.4 ± 1.0 | 2.4 ± 0.7 |

\* Unit: mg

Fig. 7, Fig. 8, Fig. 9 and Fig. 10 show weekly increases of body weights of mice of each group sacrificed at the 28th or 50th week after the treatment of urethane. As shown in these figures, body weights increased normally in all group, but body weights of mice given red ginseng (Red ginseng control group) were increased to higher level than in any other groups.

### 2) Changes of organ weights

The weight changes of various organs of mice of each group sacrificed at 28th or 50th week after treatment of urethane are summarized in table 6 and table 7. Mouse organs examined here are the same as DMBA group. In each group sacrificed 28th week after treatment of urethane (table 6), there are a little differences of weights of the organ between normal control group and other experimental groups.

But in case of the group sacrificed the 50th week after treatment of DMBA (table 7), compared

with three control groups, weights of lung in urethane group and urethane combined with red ginseng group increased significantly. It results from increased pulmonary infiltration and growth of lung adenoma for 50 weeks. This fact was confirmed with the naked eye.

Furthermore, compared urethane group with urethane combined with red ginseng group, the average weight of lung of female mice in urethane group ( $409.4 \pm 272.7$  g) is more than those in urethane combined with red ginseng group ( $350.7 \pm 395.5$  g).

This means that ginseng extract inhibits the growth and pulmonary infiltration of lung adenoma induced by urethane.

### 3) The effect of ginseng extract on the incidence and the average number of lung adenoma induced by the treatment of urethane

The incidence of lung adenoma in each group sacrificed at the 28th week after the treatment of

**Table 7.** Organ weights of mice treated with Urethane and Urethane + Ginseng extracts at 50 weeks after the injection.

| Substance treated    | No. mice | Lung |               | Heart        |              | Salivary gland |             | Liver         |   | Thymus |   | Pancreas |   |
|----------------------|----------|------|---------------|--------------|--------------|----------------|-------------|---------------|---|--------|---|----------|---|
|                      |          | m    | f             | m            | f            | m              | f           | m             | f | m      | f | m        | f |
| ① Normal             | m        | 11   | 224.5 ± 40.5  | 211.7 ± 28.0 | 276.1 ± 37.2 | 2339.5 ± 329.5 | 35.3 ± 12.5 | 281.5 ± 67.6  |   |        |   |          |   |
|                      | f        | 16   | 213.3 ± 25.7  | 154.8 ± 15.2 | 168.2 ± 30.5 | 1829.3 ± 281.5 | 52.4 ± 17.3 | 282.9 ± 52.4  |   |        |   |          |   |
| ② Ginseng            | m        | 46   | 287.1 ± 149.6 | 220.2 ± 51.1 | 256.3 ± 53.7 | 2499.1 ± 488.9 | 36.5 ± 32.8 | 332.3 ± 89.1  |   |        |   |          |   |
|                      | f        | 42   | 232.4 ± 75.2  | 159.0 ± 27.7 | 161.3 ± 44.2 | 1857.7 ± 460.0 | 63.3 ± 48.4 | 256.1 ± 65.9  |   |        |   |          |   |
| ③ 1% Gelatin         | m        | 60   | 235.9 ± 88.9  | 193.3 ± 74.9 | 239.8 ± 47.2 | 2093.5 ± 483.5 | 18.0 ± 11.9 | 313.9 ± 100.0 |   |        |   |          |   |
|                      | f        | 48   | 233.3 ± 95.3  | 155.7 ± 32.9 | 172.4 ± 45.6 | 1850.3 ± 388.3 | 52.3 ± 23.3 | 325.1 ± 93.0  |   |        |   |          |   |
| ④ Urethane           | m        | 19   | 390.5 ± 265.4 | 211.5 ± 47.3 | 258.5 ± 36.7 | 2013.9 ± 307.2 | 31.3 ± 19.0 | 324.4 ± 68.1  |   |        |   |          |   |
|                      | f        | 24   | 409.4 ± 272.7 | 145.6 ± 21.1 | 200.7 ± 79.9 | 1675.5 ± 290.7 | 54.0 ± 23.7 | 325.4 ± 71.5  |   |        |   |          |   |
| ⑤ Urethane + Ginseng | m        | 22   | 393.8 ± 276.6 | 196.2 ± 27.1 | 262.6 ± 42.1 | 2632.5 ± 830.7 | 29.5 ± 25.1 | 347.4 ± 61.0  |   |        |   |          |   |
|                      | f        | 19   | 350.7 ± 395.5 | 112.3 ± 32.1 | 170.3 ± 35.7 | 1560.1 ± 269.4 | 47.3 ± 31.1 | 311.4 ± 60.1  |   |        |   |          |   |

|   | Spleen | Kidney        |              | Testes (ovary) |              | Brain        | Pituitary    |           |
|---|--------|---------------|--------------|----------------|--------------|--------------|--------------|-----------|
|   |        | R             | L            | R              | L            |              |              |           |
| ① | m      | 113.8 ± 49.7  | 387.9 ± 64.6 | 369.4 ± 58.4   | 138.5 ± 18.5 | 131.4 ± 18.8 | 462.4 ± 22.0 | 2.8 ± 0.8 |
|   | f      | 208.7 ± 263.1 | 224.5 ± 28.2 | 221.5 ± 27.4   | 21.9 ± 29.6  | 13.7 ± 4.9   | 477.9 ± 41.8 | 2.2 ± 1.5 |
| ② | m      | 238.6 ± 314.6 | 406.4 ± 69.1 | 383.9 ± 65.3   | 142.2 ± 20.2 | 136.4 ± 19.2 | 497.1 ± 29.5 | 2.5 ± 1.4 |
|   | f      | 174.5 ± 94.4  | 236.6 ± 45.2 | 230.5 ± 46.5   | 19.6 ± 44.7  | 13.3 ± 8.1   | 501.7 ± 36.9 | 2.5 ± 1.2 |
| ③ | m      | 171.7 ± 99.2  | 351.3 ± 64.3 | 325.2 ± 63.6   | 114.8 ± 19.2 | 108.7 ± 21.5 | 462.2 ± 31.5 | 2.5 ± 1.8 |
|   | f      | 198.2 ± 100.7 | 306.1 ± 82.4 | 293.6 ± 79.4   | 14.5 ± 7.3   | 15.1 ± 8.4   | 467.4 ± 60.4 | 2.1 ± 1.4 |
| ④ | m      | 128.6 ± 60.8  | 263.6 ± 72.6 | 255.0 ± 68.0   | 132.0 ± 19.6 | 124.9 ± 18.8 | 474.9 ± 25.5 | 2.8 ± 0.7 |
|   | f      | 184.9 ± 180.0 | 207.0 ± 28.3 | 201.5 ± 22.7   | 10.0 ± 5.6   | 38.4 ± 113.8 | 503.8 ± 28.8 | 2.1 ± 1.0 |
| ⑤ | m      | 180.9 ± 126.2 | 342.9 ± 81.4 | 331.7 ± 61.1   | 125.5 ± 19.2 | 123.3 ± 15.9 | 472.9 ± 24.4 | 2.3 ± 1.1 |
|   | f      | 169.5 ± 158.8 | 197.0 ± 25.0 | 191.3 ± 33.2   | 11.6 ± 4.8   | 12.0 ± 4.7   | 472.4 ± 41.3 | 2.0 ± 0.7 |

\*Unit: mg

**Table 8.** Lung adenoma in ICR mice treated with Urethane and Urethane + Ginseng extracts.

| Substance treated  | No. mice | No. (%) survivors at 28 weeks | No. (%) survivors with lung adenomas | Mean No. of lung adenomas per survivors |
|--------------------|----------|-------------------------------|--------------------------------------|---|
| Normal             | m        | 30                            | 30 (100%)                            | 0 (0%)                                  |
|                    | f        | 30                            | 29 (97%)                             | 0 (%)                                   |
|                    | m+f      | 60                            | 59 (98%)                             | 0 (0%)                                  |
| Ginseng            | m        | 40                            | 35 (88%)                             | 1 (3%)                                  |
|                    | f        | 40                            | 39 (98%)                             | 1 (3%)                                  |
|                    | m+f      | 80                            | 74 (93%)                             | 2 (3%)                                  |
| 1% Gelatin         | m        | 40                            | 39 (98%)                             | 0 (0%)                                  |
|                    | f        | 30                            | 30 (100%)                            | 0 (0%)                                  |
|                    | m+f      | 70                            | 69 (99%)                             | 0 (0%)                                  |
| Urethane           | m        | 16                            | 14 (88%)                             | 13 (93%) *(100%)                        |
|                    | f        | 20                            | 20 (100%)                            | 19 (95%) *(100%)                        |
|                    | m+f      | 36                            | 34 (94%)                             | 32 (94%) *(100%)                        |
| Urethane + Ginseng | m        | 16                            | 14 (88%)                             | 10 (71%) *(76%)                         |
|                    | f        | 18                            | 16 (89%)                             | 12 (75%) *(79%)                         |
|                    | m+f      | 34                            | 30 (88%)                             | 22 (73%) *(78%)                         |

\*; % Urethane Control

urethane was summarized in table 8 and shown in Fig. 11. In urethane group sacrificed at the 28th weeks after the injection of urethane, the incidence

of lung adenoma was 94% (male, 93% ; female, 95%) and the average number of lung adenoma was 8.6 (male, 9.7 ; female, 7.9). In urethane com-

**Table 9.** Lung adenomas in ICR mice treated with Urethane and Urethane + Ginseng extracts.

| Substance treated  | No. mice | No. (%) Survivors at 50 weeks | No. (%) Survivors with lung adenomas | Mean size of largest lung adenoma per tumor bearing survivors (mm) |             |
|--------------------|----------|-------------------------------|--------------------------------------|--|-------------|
| Normal             | m        | 20                            | 11 (55%)                             | 2 (18%)  | 1.0         |
|                    | f        | 20                            | 16 (80%)                             | 1 (6%)   | 1.0         |
|                    | m+f      | 40                            | 27 (68%)                             | 3 (11%)  | 1.0         |
| Ginseng            | m        | 60                            | 46 (77%)                             | 9 (20%)  | 1.0         |
|                    | f        | 60                            | 43 (72%)                             | 1 (2%)   | 2.0         |
|                    | m+f      | 120                           | 89 (74%)                             | 10 (11%)   | 1.1         |
| 1% gelatin         | m        | 69                            | 60 (87%)                             | 2 (3%)   | 1.5         |
|                    | f        | 55                            | 48 (87%)                             | 2 (4%)   | 1.0         |
|                    | m+f      | 124                           | 108 (87%)                            | 4 (4%)   | 1.3         |
| Urethane           | m        | 28                            | 20 (71%)                             | 20 (100%) *(100%)  | 3.4 *(100%) |
|                    | f        | 30                            | 24 (80%)                             | 23 (96%) *(100%)   | 4.0 *(100%) |
|                    | m+f      | 58                            | 44 (76%)                             | 43 (98%) *(100%)   | 3.7 *(100%) |
| Urethane + Ginseng | m        | 28                            | 22 (79%)                             | 20 (91%) *(91%)  | 3.8 *(112%) |
|                    | f        | 30                            | 19 (63%)                             | 14 (74%) *(77%)  | 3.2 *(80%)  |
|                    | m+f      | 58                            | 41 (71%)                             | 34 (83%) *(85%)  | 3.6 *(97%)  |

| Substance treated  | No. mice | No. (%) Survivors with diffuse infil. lung lobes | Mean No. of diff. infil. lung lobe per diff. infil. lung lobe bearing mice | Mean weight of survivor's lung |                       |
|--------------------|----------|--|--|--------------------------------|-----------------------|
| Normal             | m        | 20   | 0 (0%)   | 0                              | 224.5 ± 40.5          |
|                    | f        | 20   | 0 (0%)   | 0                              | 213.3 ± 25.7          |
|                    | m+f      | 40   | 0 (0%)   | 0                              | 217.8 ± 32.3          |
| Ginseng            | m        | 60   | 0 (0%)   | 0                              | 287.1 ± 149.6         |
|                    | f        | 60   | 0 (0%)   | 0                              | 232.4 ± 75.2          |
|                    | m+f      | 120  | 0 (0%)   | 0                              | 261.6 ± 121.3         |
| 1% gelatin         | m        | 69   | 4 (7%)   | 0.24                           | 235.9 ± 88.9          |
|                    | f        | 55   | 2 (4%)   | 0.12                           | 233.3 ± 95.3          |
|                    | m+f      | 124  | 6 (6%)   | 0.19                           | 234.8 ± 90.9          |
| Urethane           | m        | 28   | 2 (10%) *(100%)  | 3 *(100%)                      | 390.5 ± 265.4 *(100%) |
|                    | f        | 30   | 4 (17%) *(100%)  | 3 *(100%)                      | 409.4 ± 272.7 *(100%) |
|                    | m+f      | 58   | 6 (14%) *(100%)  | 3 *(100%)                      | 400.8 ± 266.4 *(100%) |
| Urethane + Ginseng | m        | 28   | 3 (14%) *(140%)  | 3.7 *(123%)                    | 393.8 ± 276.6 *(101%) |
|                    | f        | 30   | 2 (11%) *(65%)   | 4 *(133%)                      | 350.7 ± 395.5 *(86%)  |
|                    | m+f      | 58   | 5 (12%) *(86%)   | 3.8 *(127%)                    | 373.9 ± 333.2 *(93%)  |

\*; % of Urethane Control

combined with red ginseng group, the incidence of lung adenoma was 73% (male, 71%; female, 75%) and the average number of adenoma was 6.0 (male, 7.0 ; female, 5.1).

These results indicate that there were decrease of the incidence of lung adenoma by 22% and of the average number by 31% in urethane combined with red ginseng group.

There was no pulmonary infiltration of lung adenoma in the both groups sacrificed at the 28th

week after the treatment of urethane.

Table 9 and Fig. 12 show the incidence of lung adenoma in each group sacrificed at the 50th week after treatment of urethane. And in urethane group sacrificed at the 50th week, the incidence of lung adenoma was 98% (male, 100% ; female, 96%) and the incidence of diffuse pulmonary infiltration was 14%. In urethane combined with red ginseng group the incidence of lung adenoma was 85% (male, 91% ; female, 77%) and the incidence

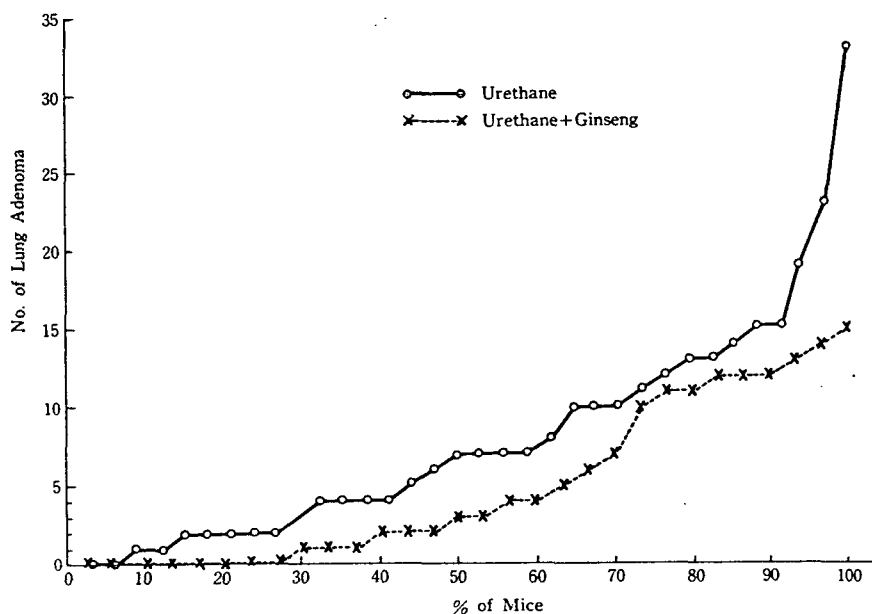


Fig. 11. The effects of Ginseng extracts on the incidence and No. of lung adenomas at 28 weeks after the injection.

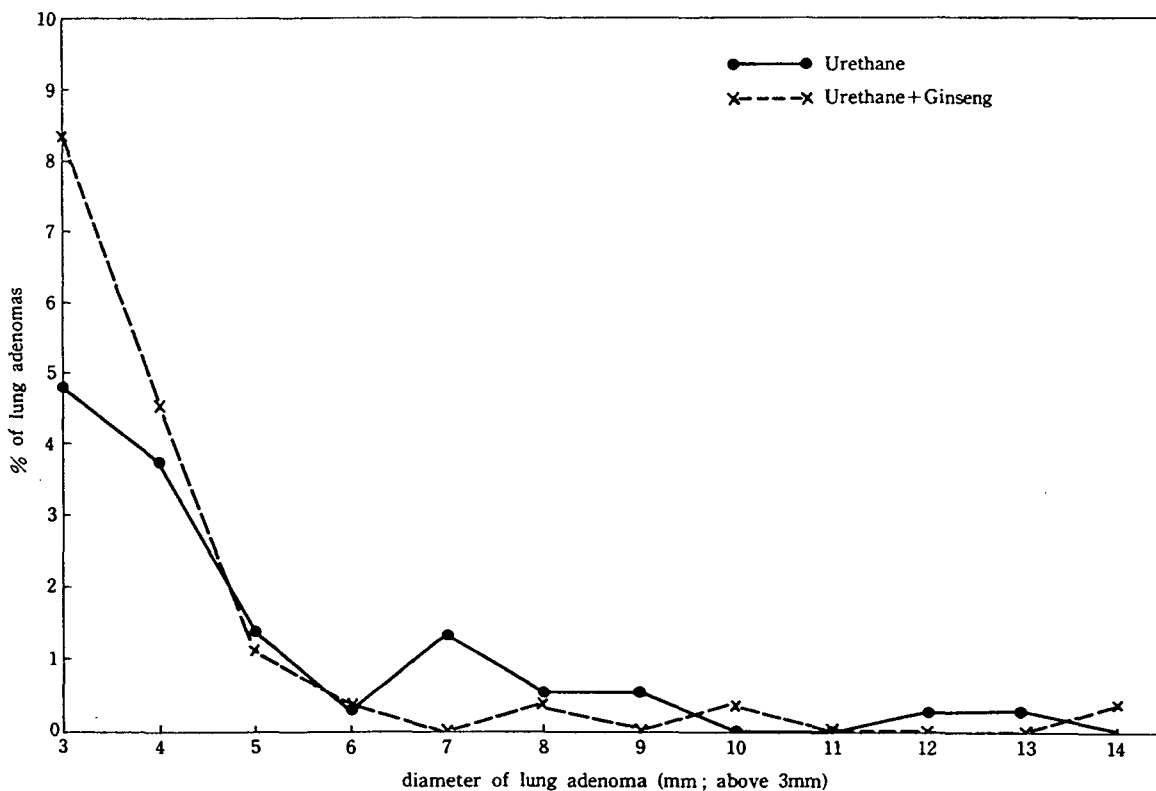


Fig. 12. The effects of Ginseng extracts on the size (growth) of lung adenomas.

of diffuse pulmonary infiltration was 12%. Therefore the ginseng administration resulted in the decrease of lung adenoma incidence by 15% and of diffuse pulmonary infiltration incidence by 14%.

From these results we knew that the prolonged administration with ginseng extract inhibited the incidence and also the proliferation of the lung adenoma induced by urethane.



Dzioev (1965) reported that the incidence of lung adenoma induced by urethane was inhibited to 20–30% by the long-term administration of eleuterococcus extract and ginseng extract. From our result, we confirmed that long term administration of ginseng extract has its inhibitory effect on tumor induced by urethane, as Dzioev reported.

#### IV. AAF group

In all AAF groups sacrificed at the 28th week after the treatment of AAF, there was no incidence of tumor. Therefore, only the results for the AAF group sacrificed at the 68th week after the treatment of AAF were mentioned as following.

##### 1) Changes of body weight

As shown in Fig. 13 and Fig. 14, the weights of mice in all group after the treatment of AAF seemed to be increased in normal way.

##### 2) Changes of organ weight

As shown in table 10, there was no noticeable

changes of organ weight between control group and other experimental groups. Organs examined here are the same as the above.

##### 3) The effect of ginseng extract on the incidence of lung adenoma and hepatoma induced by treatment of AAF.

As shown in table II, lung adenoma and hepatoma were induced in the experimental mice sacrificed at the 68th week but not in the experimental mice sacrificed at the 28th week after the injection of AAF. In AAF group sacrificed at the 68th week after the injection of AAF the incidence of lung adenoma was 18% and the hepatoma incidence was 27%. And in AAF combined with ginseng group the incidence of lung adenoma was 12% and the hepatoma incidence was 37%.

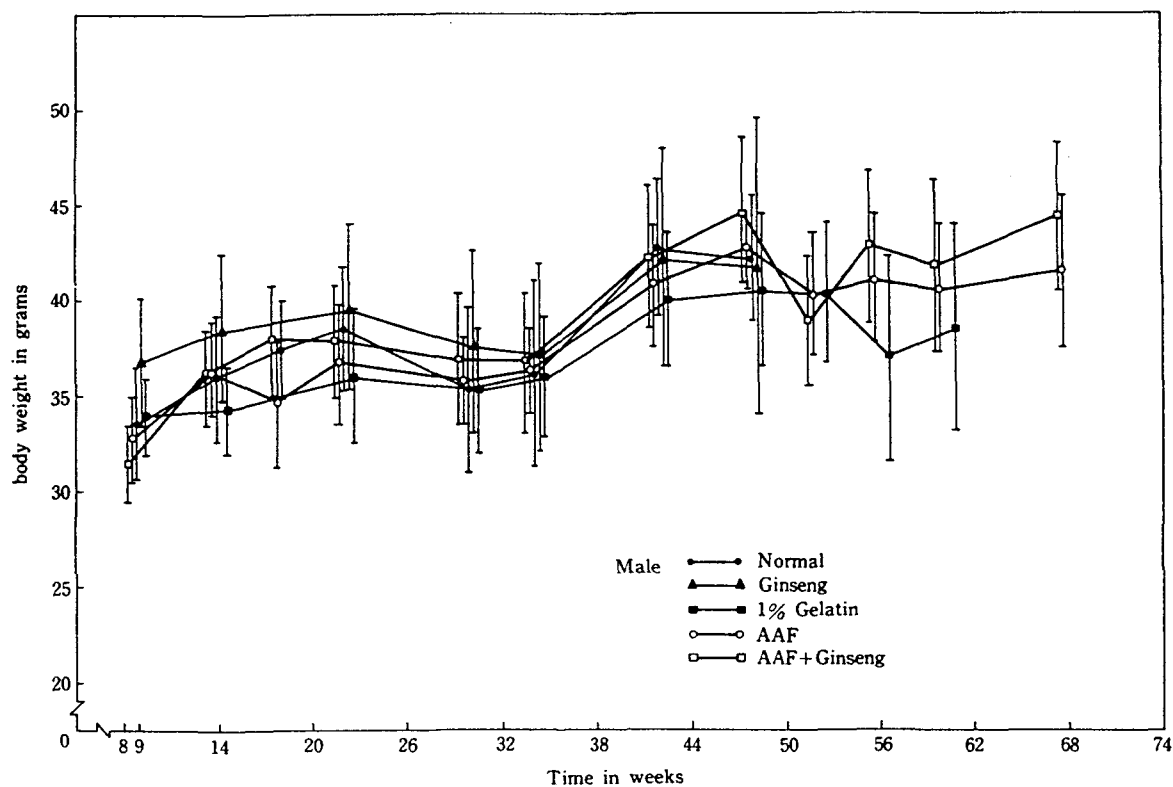
So the ginseng seemed to decrease the incidence of lung adenoma induced by AAF, but we were unable to conclude the significant inhibitory effect of the ginseng extract on the incidence of

**Table 10.** Organ weights of mice treated with AAF and AAF + Ginseng extracts at 68 weeks after the injection.

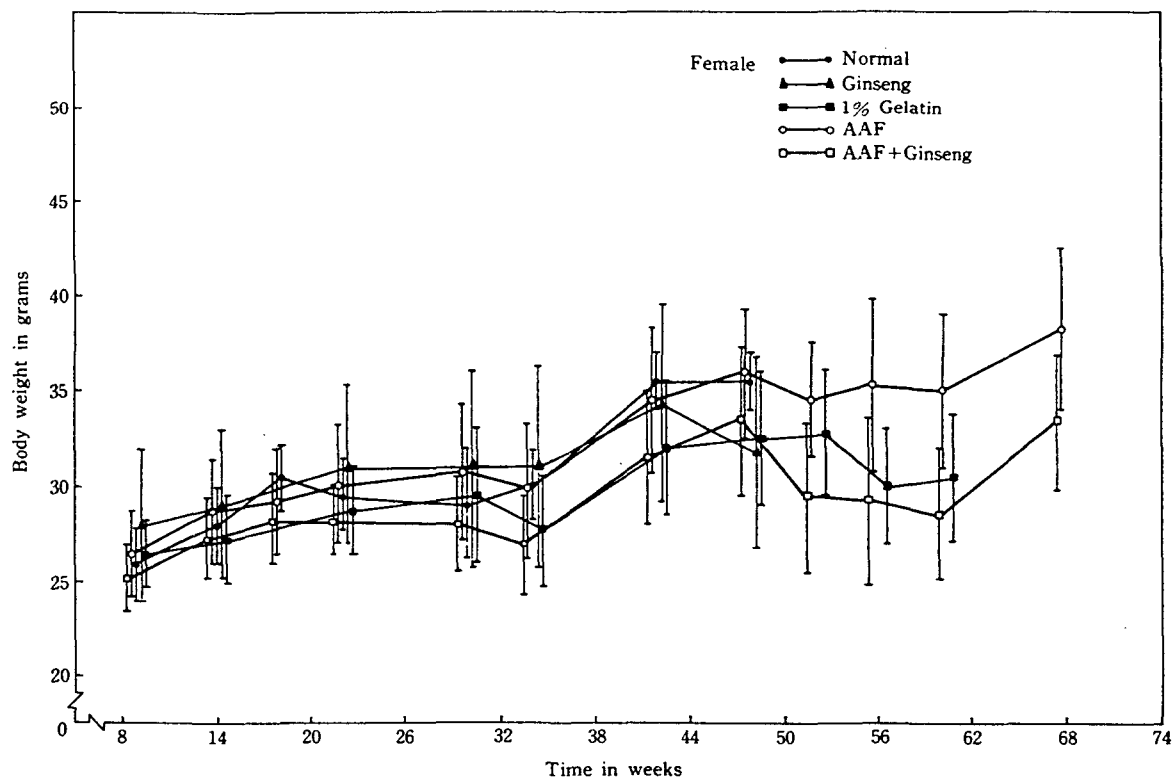
| Substance treated | No. mice | Lung          | Heart        | Salivary gland | Liver           | Thymus      | Pancreas     |
|-------------------|----------|---------------|--------------|----------------|-----------------|-------------|--------------|
| ① Normal          | m 20     | 224.5 ± 40.5  | 211.7 ± 28.0 | 276.1 ± 37.2   | 2339.5 ± 329.5  | 35.3 ± 12.5 | 281.5 ± 67.6 |
|                   | f 20     | 213.3 ± 25.7  | 154.8 ± 15.2 | 168.2 ± 30.5   | 1829.3 ± 281.5  | 52.4 ± 17.3 | 282.9 ± 52.4 |
| ② Ginseng         | m 46     | 287.1 ± 149.6 | 220.2 ± 51.1 | 256.3 ± 53.7   | 2499.1 ± 488.9  | 36.5 ± 32.8 | 332.3 ± 89.1 |
|                   | f 43     | 232.4 ± 75.2  | 159.0 ± 27.7 | 161.3 ± 44.2   | 1857.6 ± 460.0  | 63.3 ± 48.4 | 256.1 ± 65.9 |
| ③ 1% gelatin      | m 31     | 318.2 ± 118.5 | 195.6 ± 49.1 | 252.4 ± 55.1   | 1830.9 ± 327.2  | 37.5 ± 18.9 | 288.0 ± 79.7 |
|                   | f 32     | 295.0 ± 127.7 | 140.9 ± 22.3 | 187.2 ± 64.4   | 1738.3 ± 280.0  | 72.7 ± 45.8 | 225.3 ± 45.8 |
| ④ AAF             | m 14     | 434.9 ± 216.6 | 233.0 ± 35.1 | 279.2 ± 39.4   | 2672.0 ± 1231.8 | 29.8 ± 16.9 | 284.9 ± 59.2 |
|                   | f 19     | 321.7 ± 129.4 | 149.4 ± 38.5 | 188.6 ± 46.0   | 1879.9 ± 401.6  | 77.3 ± 41.2 | 243.1 ± 50.4 |
| ⑤ AAF + Ginseng   | m 12     | 327.3 ± 79.6  | 222.6 ± 51.4 | 286.8 ± 30.6   | 2664.7 ± 612.5  | 34.1 ± 15.8 | 301.7 ± 59.5 |
|                   | f 21     | 261.8 ± 45.0  | 138.7 ± 27.6 | 178.4 ± 51.0   | 1603.5 ± 317.5  | 81.7 ± 45.6 | 271.4 ± 78.1 |

|   | Spleen        | Kidney       |              | Testes (ovary) |              | Brain        | Pituitary gland |
|---|---------------|--------------|--------------|----------------|--------------|--------------|-----------------|
|   |               | R            | L            | R              | L            |              |                 |
| ① | 113.8 ± 49.7  | 387.9 ± 64.6 | 369.4 ± 58.4 | 138.5 ± 18.5   | 131.4 ± 18.8 | 462.4 ± 22.0 | 2.8 ± 0.8       |
|   | 208.7 ± 263.1 | 224.5 ± 28.2 | 221.5 ± 27.4 | 21.9 ± 29.6    | 13.7 ± 4.9   | 477.9 ± 41.8 | 2.2 ± 1.5       |
| ② | 238.6 ± 314.6 | 406.4 ± 69.1 | 383.9 ± 65.3 | 142.2 ± 20.2   | 136.4 ± 19.2 | 497.1 ± 29.5 | 2.5 ± 1.4       |
|   | 174.5 ± 94.4  | 236.6 ± 45.2 | 230.5 ± 46.5 | 19.6 ± 44.7    | 13.3 ± 8.1   | 501.7 ± 36.9 | 2.5 ± 1.2       |
| ③ | 154.9 ± 118.1 | 341.6 ± 60.3 | 325.4 ± 61.2 | 127.1 ± 22.9   | 120.3 ± 22.2 | 441.5 ± 36.3 | 0.9 ± 0.4       |
|   | 284.2 ± 227.7 | 215.5 ± 27.4 | 210.2 ± 32.5 | 13.3 ± 8.5     | 11.2 ± 5.3   | 444.6 ± 42.4 | 2.2 ± 0.9       |
| ④ | 254.2 ± 266.5 | 374.7 ± 50.6 | 355.0 ± 50.1 | 142.2 ± 32.6   | 139.7 ± 11.9 | 448.7 ± 31.6 | 1.9 ± 0.7       |
|   | 265.2 ± 197.4 | 217.6 ± 30.2 | 215.1 ± 35.3 | 20.0 ± 20.4    | 18.5 ± 13.6  | 472.1 ± 32.1 | 2.0 ± 0.7       |
| ⑤ | 348.2 ± 336.1 | 399.8 ± 47.9 | 388.2 ± 56.5 | 137.7 ± 35.3   | 116.0 ± 24.5 | 445.7 ± 37.9 | 3.2 ± 1.3       |
|   | 216.1 ± 122.7 | 201.3 ± 27.7 | 194.2 ± 39.0 | 14.7 ± 13.5    | 13.2 ± 10.4  | 454.1 ± 31.6 | 1.3 ± 0.9       |

\* Unit: mg



**Fig. 13.** Body weight of mice treated with AAF and AAF + Ginseng extracts.



**Fig. 14.** Body weight of mice treated with AAF and AAF + Ginseng extracts.

**Table 11.** Lung adenomas and hepatomas in ICR mice treated with AAF and AAF + Ginseng extracts.

| Substance treated | No. mice | No. (%) survivors at 68 weeks | No. (%) survivors with lung adenomas | No. (%) survivors with hepatomas | Mean No. of hepatomas per survivors | Mean size of largest hepatomas per tumor bearing mice (mm) |
|-------------------|----------|-------------------------------|--------------------------------------|----------------------------------|-------------------------------------|--|
| Normal*           | m        | 20                            | 11 (55)                              | 2 (18)                           | 0                                   | —  |
|                   | f        | 20                            | 16 (80)                              | 1 (6)                            | 0                                   | —  |
|                   | m+f      | 40                            | 27 (68)                              | 3 (11)                           | 0                                   | —  |
| Ginseng*          | m        | 60                            | 46 (77)                              | 9 (20)                           | 0                                   | —  |
|                   | f        | 60                            | 43 (72)                              | 1 (2)                            | 0                                   | —  |
|                   | m+f      | 120                           | 89 (74)                              | 10 (11)                          | 0                                   | —  |
| 1% gelatin        | m        | 60                            | 31 (52)                              | 0 (0)                            | 0                                   | —  |
|                   | f        | 61                            | 32 (52)                              | 2 (6)                            | 0                                   | —  |
|                   | m+f      | 121                           | 63 (52)                              | 2 (3)                            | 0                                   | —  |
| AAF               | m        | 24                            | 14 (58)                              | 4 (29)**(100)                    | 9 (64)**(100)                       | 2.9**(100)   |
|                   | f        | 24                            | 19 (79)                              | 2 (11)**(100)                    | 0 (0)                               | 0  |
|                   | m+f      | 48                            | 33 (69)                              | 6 (18)**(100)                    | 9(23)**(100)                        | 1.2**(100)   |
| AAF +Ginseng      | m        | 30                            | 12 (40)                              | 2 (17)**(59)                     | 10 (83)**(130)                      | 2.7**(93)  |
|                   | f        | 30                            | 21 (70)                              | 2 (10)**(91)                     | 3 (14)                              | 0.1  |
|                   | m+f      | 60                            | 33 (55)                              | 4 (12)**(67)                     | 13 (39)**(144)                      | 1.1 **(92)   |

\* ; data at 48 weeks

\*\* ; % of AAF control

lung adenoma by AAF because the above incidence of lung adenoma were similar to that of control group which was 11%. And these experimental data also revealed that ginseng extract didn't have any inhibitory effect on the incidence of hepatoma induced by AAF.

## V. Aflatoxin B<sub>1</sub> group

### 1) Changes of body weight

The changes of body weight of mice sacrificed at the 56th week after the treatment of Aflatoxin B<sub>1</sub> are shown in Fig. 15 and Fig. 16. As shown in Fig. 15 and Fig. 16, there were normal increases of body weight in all groups. The increase rate of weight of mice in ginseng extract control group was higher than those in any other groups.

### 2) Changes of organ weight

As shown in table 12, there were noticeable differences in changes of organ weight between normal control group and other experimental groups.

### 3) The effect of ginseng extract on the incidence of lung adenoma and hepatoma induced by the treatment of aflatoxin B<sub>1</sub>.

The incidence of lung adenoma and hepatoma in each group sacrificed at the 56th week was

summerized in table 13. In aflatoxin B<sub>1</sub> group sacrificed at the 56th week, the lung adenoma incidence was 24% and the hepatoma incidence was 11%. However in aflatoxin B<sub>1</sub> combined with ginseng group the incidence of lung adenoma was 17% and the incidence of hepatoma was 3%. These results indicate that there were 29% decrease of the lung adenoma incidence and 75% decrease of the hepatoma incidence in aflatoxin B<sub>1</sub> combined with ginseng group.

It is very difficult to conclude that there are much decrease of incidence of hepatoma in aflatoxin B<sub>1</sub> combined with ginseng group because the incidence of hepatoma in aflatoxin B<sub>1</sub> group was very low.

## VI. Tobacco smoke condensate(TSC) group

The incidences of lung adenoma, changes of body weights and organ weights in each group sacrificed at the 67th week after the treatment of tobacco smoke condensate are shown in Fig. 17, Fig. 18, Table 14 and Table 15. In each group, changes of body weights are relatively normal and there are no noticeable differences in weight changes of various organs ; lung, heart, salivary gland, liver, thymus, pancreas, spleen, kidney,

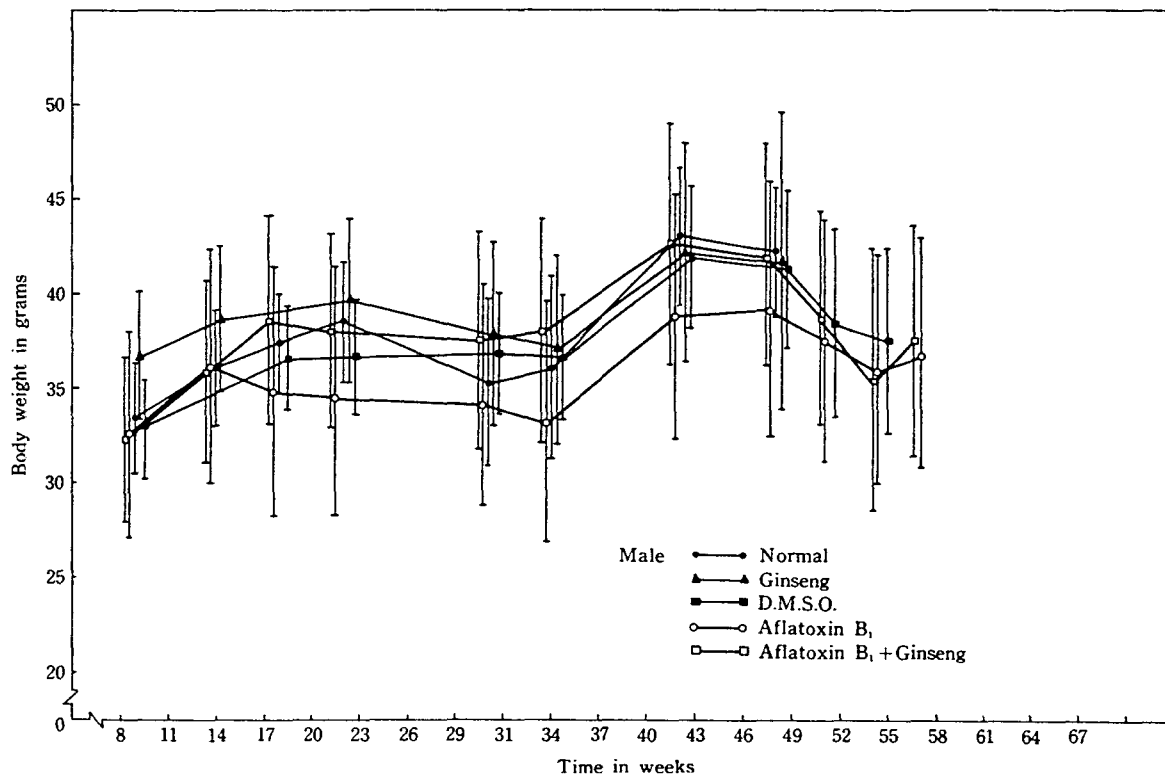


Fig. 15. Body weights of mice treated with aflatoxin-B<sub>1</sub> and aflatoxin-B<sub>1</sub> + Ginseng extracts.

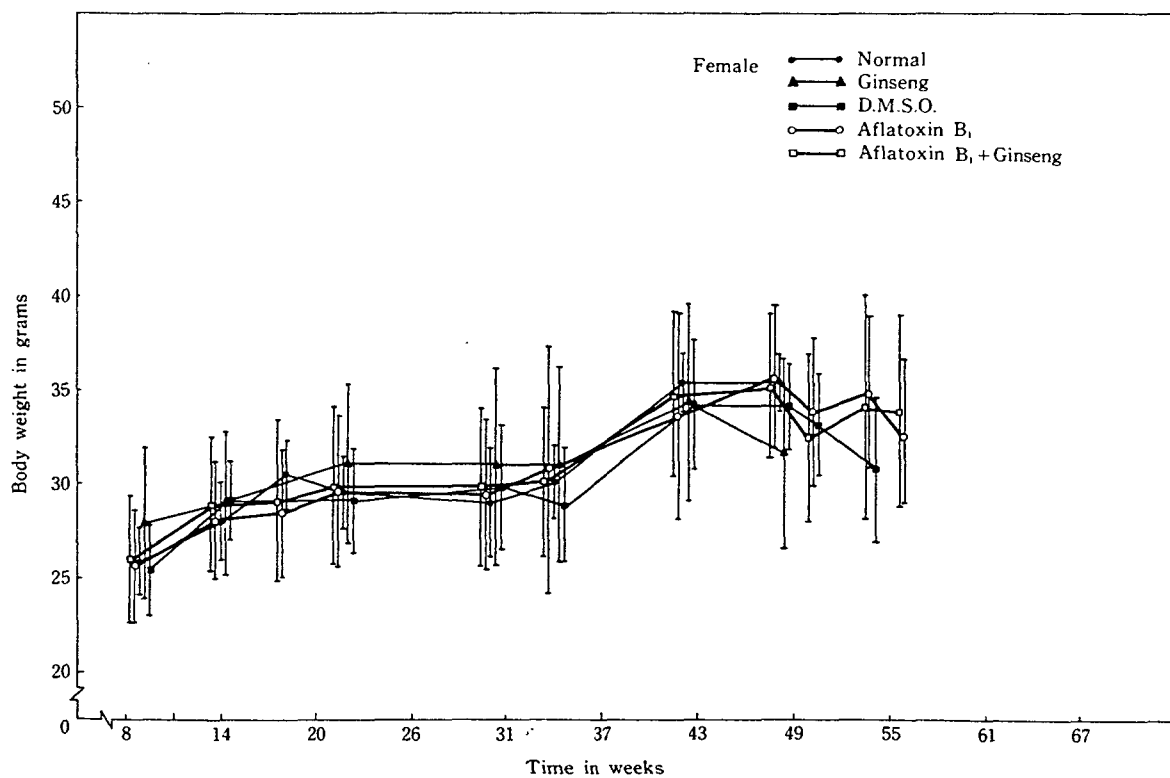


Fig. 16. Body weights of mice treated with aflatoxin-B<sub>1</sub> and aflatoxin-B<sub>1</sub> + Ginseng extracts.

**Table 12.** Organ weights of mice treated with Aflatoxin B<sub>1</sub>, and Aflatoxin B<sub>1</sub> + Ginseng extracts at 56 weeks after the injection.

| Substance treated                    | No. mice | Lung          | Heart        | Salivary gland | Liver          | Thymus      | Pancreas      |
|--------------------------------------|----------|---------------|--------------|----------------|----------------|-------------|---------------|
| ① Normal                             | m 11     | 224.5 ± 40.5  | 211.7 ± 28.0 | 276.1 ± 37.2   | 2339.5 ± 329.5 | 35.3 ± 12.5 | 281.5 ± 67.6  |
|                                      | f 16     | 213.3 ± 25.7  | 154.8 ± 15.2 | 168.2 ± 30.5   | 1829.3 ± 281.5 | 52.4 ± 17.3 | 282.9 ± 52.4  |
| ② Ginseng                            | m 46     | 287.1 ± 149.6 | 220.2 ± 51.1 | 256.3 ± 53.7   | 2499.1 ± 488.9 | 36.5 ± 32.8 | 332.3 ± 89.1  |
|                                      | f 43     | 232.4 ± 75.2  | 159.0 ± 27.7 | 161.3 ± 44.2   | 1857.7 ± 460.0 | 63.3 ± 48.4 | 256.1 ± 65.9  |
| ③ DMSO                               | m 66     | 341.3 ± 162.4 | 205.3 ± 49.8 | 248.8 ± 47.2   | 2254.8 ± 510.3 | 24.3 ± 15.5 | 312.8 ± 105.6 |
|                                      | f 52     | 277.2 ± 146.6 | 144.3 ± 17.6 | 163.0 ± 44.4   | 1936.1 ± 464.9 | 54.0 ± 48.6 | 296.4 ± 67.8  |
| ④ Aflatoxin B <sub>1</sub>           | m 23     | 258.3 ± 98.6  | 188.2 ± 62.5 | 200.7 ± 47.1   | 1869.5 ± 542.1 | 40.4 ± 24.7 | 287.2 ± 50.0  |
|                                      | f 15     | 245.0 ± 73.7  | 150.9 ± 31.3 | 162.9 ± 17.8   | 1806.0 ± 671.6 | 75.0 ± 36.7 | 283.8 ± 68.8  |
| ⑤ Aflatoxin B <sub>1</sub> + Ginseng | m 12     | 437.8 ± 317.9 | 202.0 ± 46.0 | 246.2 ± 49.1   | 2018.2 ± 578.9 | 55.7 ± 56.9 | 292.1 ± 66.2  |
|                                      | f 17     | 243.2 ± 77.1  | 150.7 ± 26.6 | 204.8 ± 34.7   | 1868.0 ± 414.6 | 73.5 ± 26.2 | 322.8 ± 47.6  |

|   | Spleen        | Kidney        |               | Testes (ovary) |              | Brain        | Pituitary |
|---|---------------|---------------|---------------|----------------|--------------|--------------|-----------|
|   |               | R             | L             | R              | L            |              |           |
| ① | 113.8 ± 49.7  | 387.9 ± 64.6  | 369.4 ± 58.4  | 138.5 ± 18.5   | 131.4 ± 18.8 | 462.4 ± 22.0 | 2.8 ± 0.8 |
|   | 208.7 ± 263.1 | 224.5 ± 28.2  | 221.5 ± 27.4  | 21.9 ± 29.6    | 13.7 ± 4.9   | 477.9 ± 41.8 | 2.2 ± 1.5 |
| ② | 238.6 ± 314.6 | 406.4 ± 69.1  | 383.9 ± 65.3  | 142.2 ± 20.2   | 136.4 ± 19.2 | 497.1 ± 29.5 | 2.5 ± 1.4 |
|   | 174.5 ± 94.4  | 236.6 ± 45.2  | 230.5 ± 46.5  | 19.6 ± 44.7    | 13.3 ± 8.1   | 501.7 ± 36.9 | 2.5 ± 1.2 |
| ③ | 215.8 ± 180.7 | 364.2 ± 60.9  | 346.0 ± 56.5  | 132.4 ± 16.5   | 122.7 ± 20.2 | 464.0 ± 31.0 | 2.2 ± 1.4 |
|   | 335.6 ± 426.6 | 250.2 ± 82.8  | 229.0 ± 35.6  | 14.0 ± 7.4     | 15.2 ± 9.3   | 481.7 ± 33.3 | 2.3 ± 1.2 |
| ④ | 190.0 ± 174.6 | 311.8 ± 102.2 | 308.5 ± 69.1  | 123.8 ± 18.2   | 119.8 ± 20.4 | 447.4 ± 42.1 | 1.7 ± 0.9 |
|   | 230.3 ± 259.8 | 231.7 ± 63.7  | 222.1 ± 49.5  | 18.5 ± 16.3    | 19.0 ± 10.5  | 477.4 ± 45.4 | 2.9 ± 1.4 |
| ⑤ | 222.6 ± 178.6 | 374.3 ± 91.6  | 353.4 ± 105.5 | 131.6 ± 23.5   | 126.5 ± 20.1 | 448.1 ± 28.9 | 2.3 ± 1.0 |
|   | 210.5 ± 181.1 | 228.0 ± 42.3  | 222.1 ± 41.6  | 17.2 ± 9.4     | 16.7 ± 10.3  | 480.0 ± 26.9 | 2.7 ± 1.7 |

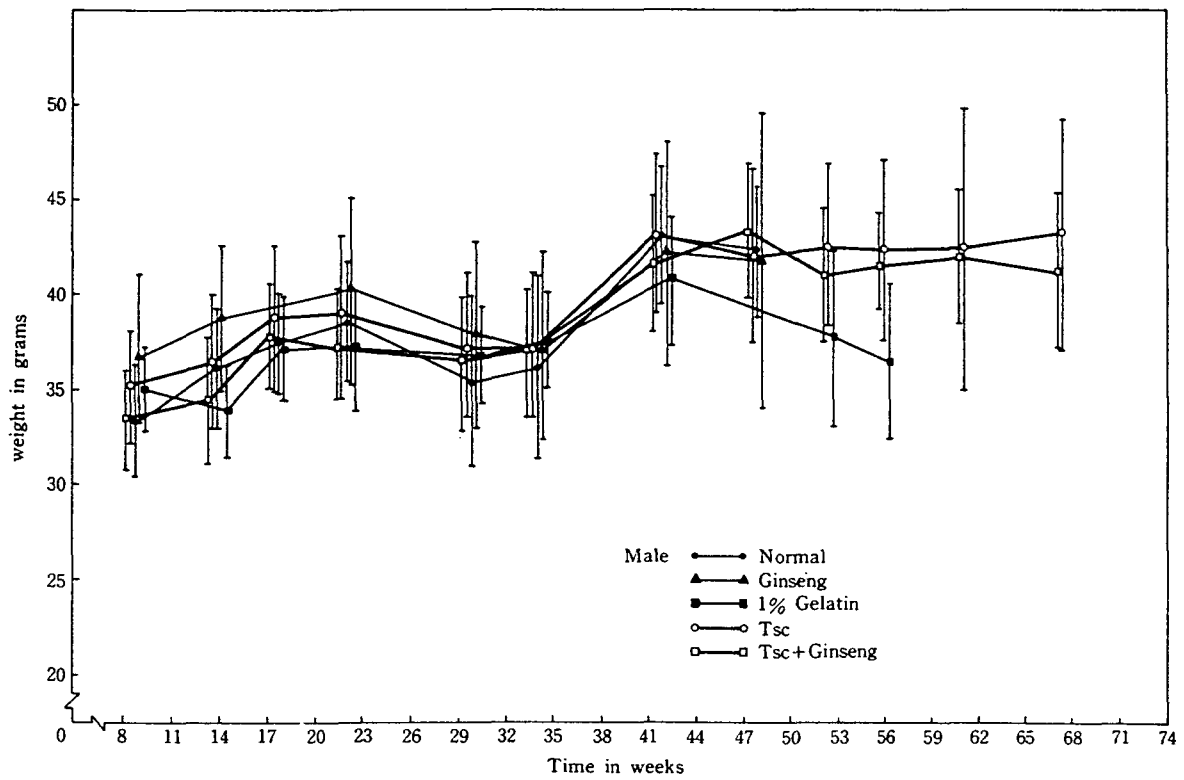
\*Unit: mg

**Table 13.** Lung adenomas and hepatomas in ICR mice treated with aflatoxin-B<sub>1</sub> and aflatoxin-B<sub>1</sub> + Ginseng extracts.

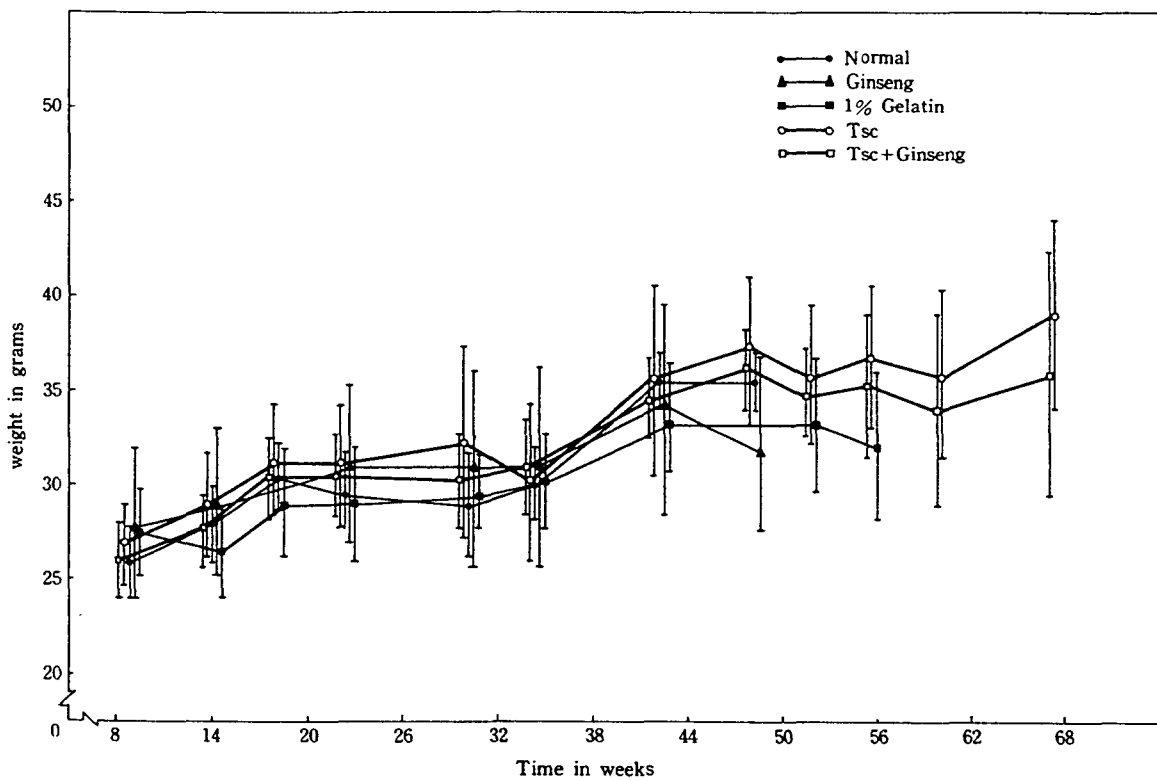
| Substance treated                  | No. mice | No.(%) survivors at 56 weeks | No.(%) survivors with lung adenomas | No.(%) survivors with hepatomas |
|------------------------------------|----------|------------------------------|-------------------------------------|---------------------------------|
| Normal*                            | m 20     | 11 (55%)                     | 2 (18%)                             | 0                               |
|                                    | f 20     | 16 (80%)                     | 1 ( 6%)                             | 0                               |
|                                    | m+f 40   | 27 (68%)                     | 3 (11%)                             | 0                               |
| Ginseng*                           | m 60     | 46 (77%)                     | 9 (20%)                             | 0                               |
|                                    | f 60     | 43 (72%)                     | 1 ( 2%)                             | 0                               |
|                                    | m+f 120  | 89 (74%)                     | 10 (11%)                            | 0                               |
| DMSO                               | m 105    | 66 (63%)                     | 2 ( 3%)                             | 1 (1.5%)                        |
|                                    | f 87     | 52 (60%)                     | 2 ( 4%)                             | 1 (1.9%)                        |
|                                    | m+f 192  | 118 (61%)                    | 4 ( 4%)                             | 2 (1.7%)                        |
| Aflatoxin B <sub>1</sub>           | m 28     | 23 (82%)                     | 6 (25%) ** (100%)                   | 4 (17%)                         |
|                                    | f 22     | 15 (68%)                     | 3 (20%) ** (100%)                   | 0 ( 0%)                         |
|                                    | m+f 50   | 38 (76%)                     | 9 (24%) ** (100%)                   | 4 (11%) ** (100%)               |
| Aflatoxin-B <sub>1</sub> + Ginseng | m 19     | 12 (63%)                     | 2 (17%) ** ( 65%)                   | 0 ( 0%)                         |
|                                    | f 28     | 17 (61%)                     | 3 (18%) ** ( 90%)                   | 1 ( 6%)                         |
|                                    | m+f 47   | 29 (62%)                     | 5 (17%) ** ( 71%)                   | 1 ( 3%) ** ( 25%)               |

\*; Data at 48 weeks

\*\*; % of Aflatoxin B<sub>1</sub> control



**Fig. 17.** Body weight of mice treated with tobacco's smoke condensate and tobacco's smoke condensate + Ginseng extracts.



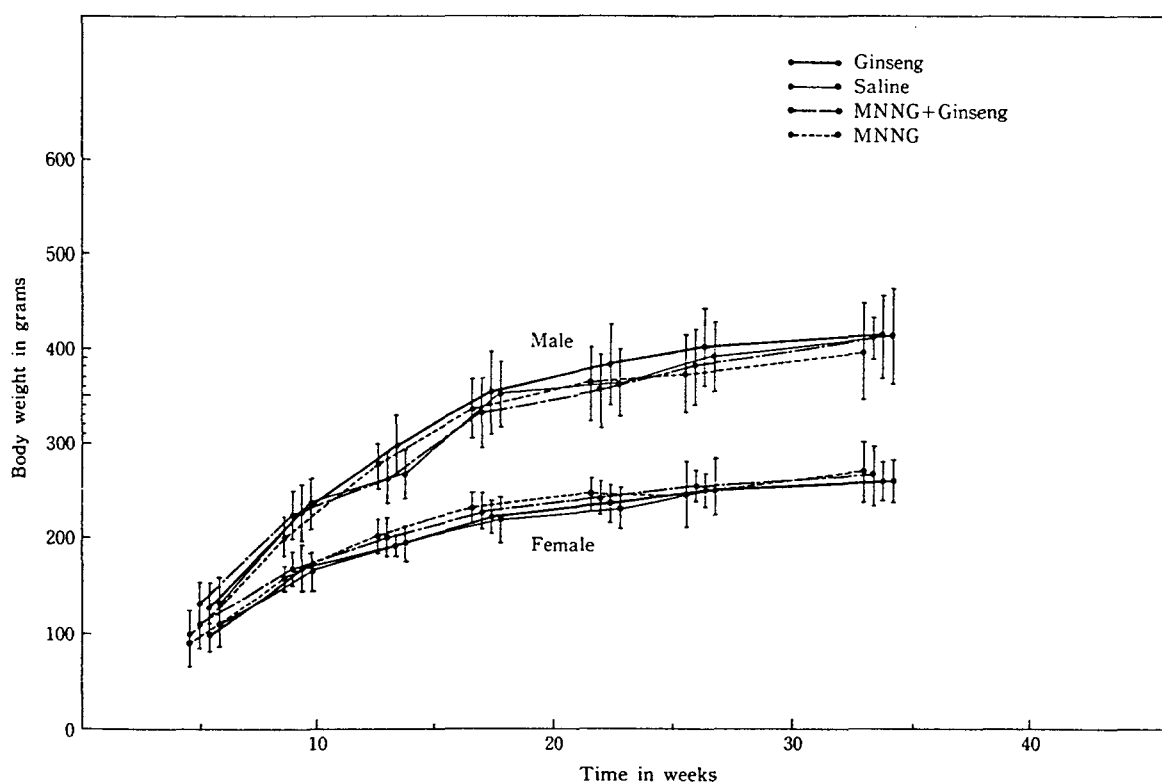
**Fig. 18.** Body weight of mice treated with tobacco's smoke condensate and tobacco's smoke condensate + Ginseng extracts.



**Table 15.** Lung adenomas in ICR mice treated with tobacco smoke condensate and tobacco smoke condensate + ginseng extracts.

| Substance treated                  | No. mice | No. survivors at 67 weeks | No. (%) survivors with lung adenomas | Mean No. of lung adenomas per survivors | Mean size of largest lung adenomas per tumor bearing survivors (mm) |
|------------------------------------|----------|---------------------------|--------------------------------------|---|---|
| Normal*                            | m        | 20                        | 11 (55%)                             | 2 (18%)                                 | 0.8   |
|                                    | f        | 20                        | 16 (80%)                             | 1 (6%)                                  | 0.06  |
|                                    | m+f      | 40                        | 27 (68%)                             | 3 (11%)                                 | 0.11  |
| Ginseng*                           | m        | 60                        | 46 (77%)                             | 9 (20%)                                 | 0.19  |
|                                    | f        | 60                        | 43 (72%)                             | 1 (2%)                                  | 0.05  |
|                                    | m+f      | 120                       | 89 (74%)                             | 10 (11%)                                | 0.12  |
| 1% gelatin*                        | m        | 69                        | 60 (87%)                             | 2 (3%)                                  | 0   |
|                                    | f        | 55                        | 48 (87%)                             | 2 (4%)                                  | 0.1   |
|                                    | m+f      | 124                       | 108 (87%)                            | 4 (4%)                                  | 0.03  |
| Tobacco smoke condensate           | m        | 40                        | 29 (73%)                             | 2 (7%)                                  | 1   |
|                                    | f        | 37                        | 24 (65%)                             | 2 (8%)                                  | 2   |
|                                    | m+f      | 77                        | 53 (69%)                             | 4 (8%)                                  | 1.5   |
| Tobacco smoke condensate + ginseng | m        | 47                        | 35 (74%)                             | 3 (9%)                                  | 1   |
|                                    | f        | 38                        | 26 (68%)                             | 2 (8%)                                  | 1   |
|                                    | m+f      | 85                        | 61 (72%)                             | 5 (8%)                                  | 1   |

\*; data at 48 weeks



**Fig. 19.** Body weight of rats treated with MNNG and MNNG + Ginseng extracts.

life span of tumor bearing rats by about 19 days (In MNNG group ; 318 days ; In MNNG combined with ginseng extract, 337 days).

This experiment was performed to evaluate the effect of ginseng extract on the incidence of tumor induced by various carcinogens in mice



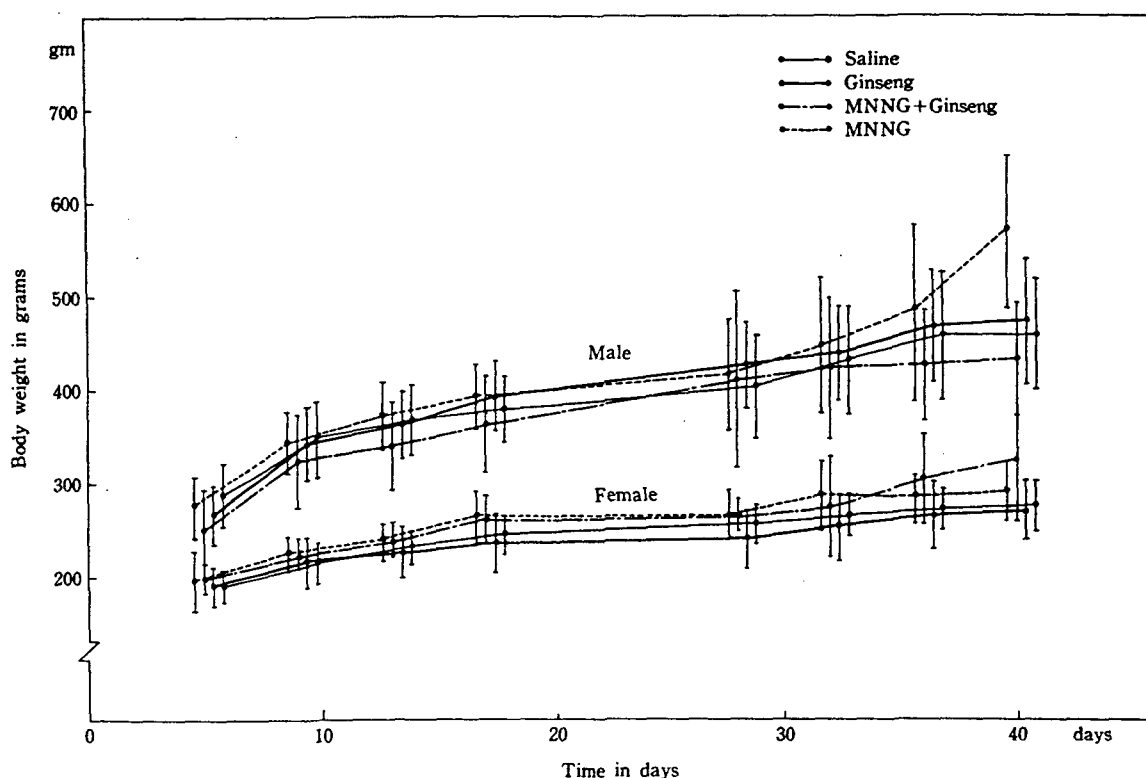


Fig. 20. Body weight of rats treated with MNNG and MNNG + Ginseng extracts.

Table 16. Organ weights of wistar rats treated with MNNG and MNNG + ginseng extracts.

| substance treated | No. mice | lung        | heart       | salivary gland | liver        | thymus      | pancreas    |
|-------------------|----------|-------------|-------------|----------------|--------------|-------------|-------------|
| ① Saline          | m 15     | 3.66 ± 0.56 | 2.98 ± 0.23 | 1.52 ± 0.12    | 30.79 ± 3.09 | 0.52 ± 0.19 | 2.21 ± 0.44 |
|                   | f 15     | 4.57 ± 0.67 | 3.24 ± 0.33 | 1.70 ± 0.23    | 34.44 ± 3.89 | 0.66 ± 0.22 | 2.93 ± 0.40 |
| ② Ginseng         | m 15     | 3.84 ± 0.74 | 3.12 ± 0.45 | 1.54 ± 0.19    | 32.59 ± 4.12 | 0.47 ± 0.17 | 2.31 ± 0.31 |
|                   | f 15     | 4.40 ± 0.56 | 2.98 ± 0.35 | 1.59 ± 0.27    | 29.72 ± 2.79 | 0.64 ± 0.16 | 2.94 ± 0.43 |
| ③ MNNG            | m 14     | 3.70 ± 0.89 | 2.95 ± 0.40 | 1.61 ± 0.38    | 29.45 ± 3.13 | 0.42 ± 0.16 | 2.22 ± 0.47 |
|                   | f 12     | 4.39 ± 0.83 | 3.35 ± 0.42 | 1.83 ± 0.68    | 33.65 ± 3.59 | 0.75 ± 0.26 | 3.16 ± 0.72 |
| MNNG              | m 14     | 3.58 ± 0.51 | 2.96 ± 0.31 | 2.41 ± 1.07    | 35.61 ± 4.43 | 0.44 ± 0.19 | 2.63 ± 0.35 |
| ④ + ginseng       | f 12     | 5.61 ± 3.96 | 3.21 ± 0.34 | 1.60 ± 0.35    | 31.93 ± 5.34 | 0.61 ± 0.20 | 3.03 ± 0.72 |

|   | spleen      | kidney      |             | testes (ovary) |             | brain       | pituitary   |
|---|-------------|-------------|-------------|----------------|-------------|-------------|-------------|
|   |             | R           | L           | R              | L           |             |             |
| ① | 1.49 ± 0.11 | 3.10 ± 0.17 | 3.06 ± 0.22 | 4.33 ± 0.45    | 4.08 ± 0.79 | 4.90 ± 0.44 | 24.5 ± 5.0  |
|   | 1.94 ± 0.27 | 3.54 ± 0.28 | 3.25 ± 0.59 | 0.23 ± 0.03    | 0.21 ± 0.05 | 6.51 ± 0.68 | 45.0 ± 12.2 |
| ② | 1.70 ± 0.13 | 3.16 ± 0.23 | 3.14 ± 0.22 | 4.18 ± 0.80    | 4.22 ± 0.84 | 4.64 ± 0.40 | 21.4 ± 4.9  |
|   | 1.94 ± 0.19 | 3.45 ± 0.28 | 3.34 ± 0.27 | 0.25 ± 0.22    | 0.22 ± 0.05 | 6.92 ± 0.75 | 50.6 ± 12.0 |
| ③ | 2.16 ± 1.22 | 2.95 ± 0.47 | 2.94 ± 0.45 | 4.01 ± 0.26    | 3.86 ± 0.66 | 4.92 ± 0.53 | 22.3 ± 7.3  |
|   | 3.01 ± 2.27 | 3.35 ± 0.32 | 3.30 ± 0.30 | 0.23 ± 0.06    | 0.24 ± 0.09 | 6.75 ± 0.22 | 51.5 ± 8.9  |
| ④ | 2.09 ± 1.06 | 3.12 ± 0.44 | 3.07 ± 0.36 | 3.74 ± 0.86    | 3.88 ± 0.94 | 4.79 ± 0.54 | 26.4 ± 7.2  |
|   | 2.50 ± 0.19 | 3.31 ± 0.37 | 3.25 ± 0.47 | 0.21 ± 0.06    | 0.21 ± 0.07 | 6.72 ± 0.62 | 55.8 ± 14.2 |

\*Unit: g/kg, body weight

or rats, such as typical polycyclic hydrocarbon (DMBA), urethane having various carcinogenicity, typical aromatic amin (AAF), carcinogenic natural product (Aflatoxin B<sub>1</sub>, and tobacco smoke condensate) and nitroso compound (MNNG).

Summing up the result of the effect of ginseng extract on the incidence and growth of tumor, it would be summarized as follows. First, ginseng extract inhibits the growth of lung adenoma induced by DMBA, also the incidence and the growth of lung adenoma by urethane. Secondly, ginseng extract seems to have the tendency to in-

**Table 17.** Sarcoma in Wistar rats treated with MNNG and MNNG + ginseng extracts at 27 weeks after the injection.

| Substance treated | No. rats at autopsy | No.(%) survivors with sarcoma | Mean weight of sarcoma |
|-------------------|---------------------|-------------------------------|------------------------|
| Saline            | m                   | 15 0 (0)                      | 0 (0)                  |
|                   | f                   | 15 0 (0)                      | 0 (0)                  |
|                   | m + f               | 30 0 (0)                      | 0 (0)                  |
| Ginseng           | m                   | 15 0 (0)                      | 0 (0)                  |
|                   | f                   | 15 0 (0)                      | 0 (0)                  |
|                   | m + f               | 30 0 (0)                      | 0 (0)                  |
| MNNG              | m                   | 14 7 (50)                     | 39.9                   |
|                   | f                   | 12 3 (28)                     | 19.1                   |
|                   | m + f               | 26 10 (38.5) *(100)           | 29.6 *(100)            |
| MNNG + ginseng    | m                   | 14 6 (42.9)                   | 24.8                   |
|                   | f                   | 13 4 (30.8)                   | 40.4                   |
|                   | m + f               | 27 10 (37) *(96.1)            | 31.0 *(104.7)          |

\*; % of MNNG Control

**Table 18.** Survival days of tumor bearing wistar rats treated with MNNG and MNNG + ginseng extracts.

| Substance treated | No. rats at autopsy | No.(%) rats with sarcoma | survival days of tumor bearing rats |
|-------------------|---------------------|--------------------------|-------------------------------------|
| Saline            | m                   | 15 0                     |                                     |
|                   | f                   | 15 0                     |                                     |
|                   | m + f               | 30 0                     |                                     |
| Ginseng           | m                   | 15 0                     |                                     |
|                   | f                   | 15 0                     |                                     |
|                   | m + f               | 30 0                     |                                     |
| MNNG              | m                   | 15 14 (93)               | 302                                 |
|                   | f                   | 14 13 (93)               | 335                                 |
|                   | m + f               | 29 27 (93) *(100)        | 318 *(100)                          |
| MNNG + ginseng    | m                   | 13 13 (100)              | 323                                 |
|                   | f                   | 11 10 (91)               | 355                                 |
|                   | m + f               | 24 23 (96) *(100)        | 337 *(106)                          |

hibit the incidence of lung adenoma induced by AAF and the incidence of hepatoma induced by aflatoxin B<sub>1</sub>.

Finally, ginseng extract has no effect on the incidence of sarcoma induced by MNNG. It might be concluded from these results that systematic and active research on this field will be carried out, ginseng extract will be able to use as an anti-cancer prophylactic agent or delaying agent for growth of cancer induced by some environmental carcinogens

### Acknowledgement

This investigation was supported by the research grant of the Korea Ginseng Research Institute, and of the Asian Foundation, Seoul, Korea.

**Chairman:** Now the time is open to discussion.

**Yamamoto:** How do you think about the mechanism of anticarcinogenic effect of ginseng, immunomodulation or stimulation of metabolism of carcinogenesis that?

**Yoon:** I am not sure about the mechanism of inhibition of chemical carcinogenesis but I suppose that non-specific response of the ginseng might be worked in this experiment.

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