INTRODUCTION

The ginseng root has been used empirically for thousands of years in Asian countries. Since 1965, several pharmacological activities of ginseng extracts or ginseng dammarane saponin have been reported, including effects on the central nervous system, antipsychotic action, tranquilizing effects, protection from stress ulcers, increase of gastrointestinal motility, antifatigue action, endocrinological effects, enhancement of sexual behavior, acceleration of metabolism, syntheses of carbohydrates, lipids, RNA, and proteins (1-4).

The ginseng plant is deciduous perennial belonging to the Araliaceae family. Of the 13 species (5, 6), the most prominent are Panax ginseng C.A. Meyer, which is cultivated in Korea, Japan, China, Russia, the United States of America, and Germany, P. quinquefolius L. (American ginseng) found...
in southern Canada and the U.S.A., and *P. japonicus* C.A. Meyer (Japanese ginseng) grown in Japan.

We have proposed that the life-prolonging effect of ginseng described by Shennong (7) during the Liang Dynasty in China may be due to the preventive activity of ginseng against the development of cancers. Employing a long term anticarcinogenesis model using newborn mice (8, 9), we carried out extensive experiments in 1978 to investigate whether ginseng inhibited carcinogenesis, and demonstrated that the red ginseng extracts of *Panax ginseng* C.A. Meyer cultivated in Korea had anticarcinogenic activity against lung tumors and liver cancer induced by urethane or aflatoxin B1.

The extract was found to partly elevate natural killer cell activity (10), the results providing the hope for natural products preventing human cancers. The medium-term (9 weeks) model system also revealed anticarcinogenicity of ginseng on pulmonary adenoma induced by benzo(a)pyrene (BP) in newborn mice (11-14).

Employing BP as carcinogen, we further investigated whether fresh ginseng or white ginseng also had the similar anticarcinogenic effects, and whether the anticancer effects depended on types and ages of ginseng. We found a significant anticarcinogenic effect of 6-yr-old dried powder or fresh ginseng extract, 5- and 6-yr-old white ginseng powder or extract, and 4-, 5-, and 6-yr-old red ginseng powder or extract (15-17). The results demonstrated that the anticarcinogenicity was more prominent in aged or heat treated extract of fresh ginseng and red ginseng prepared by steaming.

In light of the above described evidences, in 1987 we began a case-control study with 905 pairs (18) to confirm whether red ginseng extracts had anticarcinogenic effect on human cancers as much as on mice, and we later extended the number of subjects to 1,987 pairs (19) from 905 pairs.

Also, a prospective study (20) was started to find whether ginseng intake was related to the type of cancers, and to evaluate the preventive effect of ginseng among the population residing in ginseng cultivation area 6 months after the first case-control study (in August 1987) and compared the results with three independent analyses in 10 yr of follow up period.

**MATERIALS AND METHODS**

**Case-control study with 905 pairs**

The cases and controls were selected from the patients admitted to the Korea Cancer Center Hospital (KCCH), Seoul. As a major cancer centre in Korea, the KCCH diagnosed average 5,000 new cancer patients annually between 1 July 1982 and 30 June 1987. These represent an average of 14% of all cancer patients diagnosed annually in 66 hospitals in Korea (21). Selection criteria for cases were: newly diagnosed cancer during the period of 1 February 1987 through 31 January 1988, diagnosis of cancer by pathological examination, and 20 yr of age or older at diagnosis. Patients admitted to the intensive care unit or the otolaryngology department were excluded from the study, because of the difficulty in answering questions. A total of 905 cases met these criteria and all cases agreed to participate in the study.

One control was selected for each case from a pool of patients diagnosed with non-cancerous diseases at the same hospital by matching gender, age at diagnosis (± 2 yr), and date of admission (± 3 months). When more than one control fell within the selection range, the control which had the admission date closest to that of the cancer patient was selected as the matched control. Patients whose final diagnoses were not cancer but whose diseases were associated with smoking or alcohol consumption were also excluded from the control group. Among the controls were those suffering from cardiovascular disease, chronic obstructive pulmonary disease, peptic ulcer, and liver cirrhosis.

Two trained interviewers visited the 905 case-control pairs in the hospital. To prevent possible bias between the interviewers, a standardized questionnaire was administered to each case-control pair by the same interviewer. During the interview, some information on demographic characteristics (i.e., age, marital status, education, occupation and income), life-style (i.e., cigarette smoking, alcohol consumption and others), and ginseng consumption were obtained (18).

In order to collect information on ginseng intake, a dietary-recall method commonly employed in epidemiological studies on diet and disease was used (22). In the questionnaire, ginseng types were classified into fresh ginseng, white ginseng and red ginseng. Fresh ginseng is less than four yr old and can be consumed in the fresh state. White ginseng is grown for four to six year, peeled and dried to reduce the water content to 12% or less. Red ginseng is harvested after six year, steamed, and dried. In the questionnaire, each type of ginseng was further grouped into several forms of ginseng product; i.e., fresh sliced, juice, extract, powder, tea, tablet, capsule and other forms. The lifetime consumption of ginseng was assessed by asking types and products used, frequency of intake per day, week, and month for each decade of life. In addition, multiple combinations among fresh, white and red ginsengs were included.

Interviews on ginseng intake were carried out by asking the following series of questions: 1) Have you ever consumed ginseng? 2) At what age did you first take ginseng? 3) What type of ginseng products have you taken? and 4) How often (frequency) and how long (duration) have you used it? The frequency of ginseng intake was divided into four categories: no intake, 1-3 times per year, 4-11 times per year, and more than once a month (12 times or more per year). The trained interviewers obtained information by using a precoded ques-
To measure the reliability of recall of ginseng use, a second interview was carried out with 180 randomly selected subjects by the same interviewer one year after the first interview, using the same questionnaire. The strength of agreement on ginseng intake information obtained from the two interviews was measured by Kappa statistic (23).

Case-control study with 1,987 pairs

In order to explore further (a) the types of ginseng products that have the most prominent cancer preventive effect, (b) the reproducibility of the dose-response relationship, (c) the duration of ginseng consumption that has a significant preventive effect, (d) the types of cancer that can be prevented by ginseng, and (e) the effect of ginseng on cancers associated with smoking, we increased the number of subjects to 1987 pairs for a case-control study (20).

All the cases were admitted to the Korea Cancer Center Hospital between February 1987 and December 1990, and were confirmed by cytological and/or histopathological examination.

The cases and controls were selected as described in the previous study (18). The disease sites of male control patients were stomach (495), thyroid (120), colon (81), kidney (93), oral cavity (85), lung (51), and others (95). For female control patients, they were uterus (351), breast (177), thyroid (170), ovary (75), stomach (46), liver (25), colon (16), and others (55). The types of diseases of the controls were mainly acute diseases; acute or unspecified gastritis, goiter, acute appendicitis, colon obstruction, acute pyelonephritis, kidney stone, tonsillitis, laryngopharyngitis, pneumonia and pleurisy. All questionnaires were checked as described in the earlier case-control study (18) of 905 pairs. To evaluate the accuracy of the answers to the questionnaire, 10% of each cases and controls were evaluated by k value (24).

Prospective study with population

The study population was selected from persons who were listed in the 1987 resident’s list which was registered at the provincial government offices of the ginseng production areas. These lists contain the name, sex, date of birth, and permanent and present addresses. Subjects born before 1947 (over 40 yr) were selected. A cohort of 4,634 persons over 40 yr of age residing in Kangwha-eup was interviewed and examined between August 1987 and December 1989. Each study subject was interviewed by means of a standard questionnaire about demographic characteristics, life-long occupation, smoking and drinking habits, and past history of diseases, etc. In an attempt to obtain detailed information on ginseng intake, we used the same questionnaire as used in the previous two case-control studies (18, 19). The interviewers had been instructed and trained beforehand to ensure uniformity in the method of inquiry. We carried out follow-up studies on all cohort members to document development of cancer and other illnesses and to update exposure information. Length of follow-up was calculated for each individual in the study as the number of days elapsed since completion of the questionnaire until death from cancer or other diseases. Deaths among the cohort from August 1987 to December 1997 were traced by population registration cards with no follow-up loss. A cohort member was classified as a cancer case if they had any disease code of cancer in hospital records, death certificates of the provincial government, privileged data of Korea Medical Insurance Corporation, etc.

RESULTS

905 pairs case-control study

Distribution of selected cases by cancer site for each gender is shown in Table 1. Of the 905 cases, 562 (62%) had a history of ginseng intake compared to 674 (75%) of the controls (p<0.01). The odds ratio (OR) for cancer in relation to ginseng intake is shown in Table 2. The odds ratio (OR) for cancer in relation to ginseng intake is shown in Table 2.

Table 1. Distribution of cancer sites in 905 case subjects

| Site of cancer | Male | Female |
|---------------|------|--------|
| Liver         | 101  | 13     |
| Lung          | 82   | 29     |
| Stomach       | 80   | 42     |
| Larynx        | 14   | 3      |
| Cervix        | 0    | 178    |
| Breast        | 0    | 84     |
| Thyroid       | 0    | 27     |
| Others        | 136  | 92     |
| Total         | 436  | 469    |

Table 2. Odds ratios and 95% confidence intervals (CI) for cancers by ginseng intake in 905 pairs

| Type of ginseng | Cases | Controls | Odds ratio | 95% CI* |
|----------------|-------|----------|------------|--------|
| No intake of ginseng | 343   | 231      | 1.00       | Reference |
| Intake of ginseng | 562 (62%) | 674 (75%) | 0.56      | 0.46-0.69 |
| Fresh ginseng |       |          |            |        |
| Slice | 103   | 94       | 0.74       | 0.53-1.04 |
| Juice  | 39    | 34       | 0.77       | 0.46-1.30 |
| Extract | 13    | 64       | 0.14      | 0.07-0.26 |
| White ginseng |       |          |            |        |
| Powder | 28    | 43       | 0.44       | 0.26-0.75 |
| Extract | 247   | 261      | 0.64      | 0.50-0.82 |
| Tea | 37   | 27       | 0.93      | 0.53-1.61 |
| Red ginseng |       |          |            |        |
| Extract | 2     | 3        | 0.45      | 0.06-3.32 |
| Combination | 10    | 25       | 0.27     | 0.13-0.53 |

Adjusted for age, sex, marital status, educations, smoking, and alcohol consumption. *CI: confidence interval
to ginseng intake was 0.56 [95% confidence interval (CI), 0.45-0.69]. Ginseng extract and powder were shown to be more effective than fresh sliced ginseng, the juice, or tea in reducing the OR (Table 2). With the increased frequency of ginseng intake, ORs decreased in both male and female (Table 3). A trend test showed a significant decrease in the number of cancer cases among those who reported an increased frequency of ginseng intake for males \( (p<10^{-5}) \) as well as for females \( (p<0.05) \). The reliability of recall for ginseng use was assessed by twice interviewing one-tenth of the randomly selected subjects using the same questionnaire. The overall agreement in reported ginseng use between the two interviews was 0.85, and the k value was 0.71 \( (p<0.01) \) (Table 4). These results strongly support the hypothesis that ginseng has cancer preventive effects, as suggested by the previous animal experiments (8-17).

### Table 3. Odds ratios of cancer in ginseng intake frequency and 95% confidence intervals in 905 pairs case-control study

| Frequency of ginseng intake | Male Cases | Male Controls | Odds ratio (95% CI) | Female Cases | Female Controls | Odds ratio (95% CI) |
|-----------------------------|------------|---------------|---------------------|--------------|-----------------|---------------------|
| No intake                   | 117        | 56            | 1.00                | 226          | 175             | 1.00                |
| 1-3 times/yr                | 132        | 108           | 0.58 (0.38-0.90)    | 111          | 106             | 0.81 (0.57-1.15)    |
| 4-11 times/yr               | 104        | 115           | 0.43 (0.28-0.67)    | 75           | 103             | 0.56 (0.39-0.82)    |
| Once/month or more          | 83         | 157           | 0.25 (0.16 - 0.39)  | 57           | 85              | 0.52 (0.35-0.78)    |
| Total                       | 436        | 436           |                     | 469          | 469             |                     |

Linear trend test (1 d.f.) \( 45.59 \ (p<0.001) \), \( x^2 \) homogeneity test (3 d.f.) \( 47.28 \ (p<0.001) \).  

### Table 4. Subjects response to ginseng intake questions at two different interviews

| Second interview | First interview | None | Fresh ginseng | White ginseng | Total |
|------------------|----------------|------|---------------|---------------|-------|
| None             | 0.57 (104)     | 0.05 (9)     | 0.01 (2)     | 0.63 (115)   |       |
| Fresh ginseng    | 0.02 (4)       | 0.21 (39)    | 0.01 (1)     | 0.27 (48)    |       |
| White ginseng    | 0.02 (4)       | 0.01 (1)     | 0.07 (12)    | 0.10 (17)    |       |
| Total            | 0.64 (116)     | 0.27 (49)    | 0.07 (15)    | 1.00 (180)   |       |

Overall proportion of observed agreement \( P_o=0.57+0.21+0.07=0.85 \)  
Overall proportion of chance-expected agreement \( p_e=0.64 \times 0.63+0.27 \times 0.27+0.09 \times 0.11=0.49 \)  
Kappa value \( \kappa = 0.85-0.49 = 0.71 \ (p<0.01) \)  

### Table 5. Odds ratios and 95% confidence intervals for cancers by ginseng intake in 1,987 pairs

| Type of ginseng | Cancer patients | Controls | Odds ratio | 95% CI |
|-----------------|-----------------|----------|------------|--------|
| No intake of ginseng | 921 | 605 | 1.00 | Reference |
| Intake of ginseng   | 1,066 (62%) | 1,382 (75%) | 0.50 | 0.44-0.58 |
| Fresh ginseng Slice | 210 | 172 | 0.79 | 0.63-1.01 |
| Juice              | 69   | 63  | 0.71 | 0.49-1.03 |
| Extract            | 146  | 255 | 0.37 | 0.29-0.46 |
| White ginseng Powder | 60  | 129 | 0.30 | 0.22-0.41 |
| Extract            | 373  | 442 | 0.57 | 0.48-0.68 |
| Tea                | 43   | 41  | 0.69 | 0.45-1.07 |
| Red ginseng Extract | 6   | 17  | 0.20 | 0.08-0.50 |
| Combination        | 22   | 58  | 0.16 | 0.10-0.25 |

Adjusted for age, sex, marital status, education, smoking, and alcohol consumption.

In this study, as with the previous study, ginseng users had a lower risk \( (OR; 0.50) \) for cancer compared with non-users. With respect to the type of ginseng, the ORs for cancer were 0.37 for fresh ginseng extract users, 0.57 for white ginseng extract users, 0.30 for white ginseng extract users, 0.30 for white ginseng powder users, and 0.20 for red ginseng users (Table 5). Those who took fresh ginseng slices, fresh ginseng juice, and white ginseng tea, however, showed no decrease in the risk. Overall, the risk decreased as the frequency and duration of ginseng intake increased, showing a dose-response relationship (Table 6). With respect to the site of cancer, the odds ratios were 0.47 for cancer of lip, oral cavity, and pharynx; 0.20 for esophageal cancer; 0.36 for stomach cancer; 0.42 for colorectal cancer; 0.48 for liver cancer; 0.22 for pancreatic cancer; 0.18 for laryngeal cancer; 0.55 for lung cancer; 0.15 for ovarian cancer; and 0.48 for other cancers (Table 7). With cancers of the female breast, uterine cervix, urinary bladder, and thyroid gland, however, there was no benefit with ginseng intake. In cancers of lung, lip, oral cavity, pharynx, and liver, smokers who took ginseng showed decreased OR compared with smokers with no ginseng intake. These findings supported the view that the use of ginseng decreased the risk for most cancer compared to the non-user. Smokers without ginseng intake showed significantly increased risks for cancers of lung, lip, oral cavity, pharynx, and liver. However, the ORs for smokers who had consumed ginseng decreased, showing 1.99 for lung, 2.36 for lip, oral cavity, and pharynx cancers, and 2.09 for liver cancer compared with nonsmokers who had consumed ginseng. In cancers of esophagus, stomach, and colorectum, there...
was no association with ginseng intake (Table 8).

**Cohort study on population**

The total number of subjects interviewed was 4,675. Out of them, 41 prevalent cancer cases were excluded, and the remaining 4,634 eligible subjects (2,362 men and 2,272 women) were selected for analysis. From 4,634 people eligible for analysis, 47 unknown diseases were excluded, and 54.7% of 137 cancer cases had history of ginseng intake in comparison with 71.2% of 4,450 non-cases, showing similar proportion to those of the control groups in the previous case-control studies [74.5% (Table 2) and 69.6% (Table 5) (18, 19)]. The present study showed a significant reduction of relative risk (RR) (0.40) by the intake of ginseng (Table 9), as shown in the previous case-control studies. On the type of ginseng, the RRs for cancer in fresh ginseng extract consumers and consumers with multiple combinations were significantly reduced (Table 9). The RRs for other types of ginseng including white ginseng tea showed a decreasing trend, but was not statistically significant. Among 24 red ginseng consumers, there were no deaths from cancer. The results showed no relationship between fresh ginseng consumers and cancer, which was consistent with the experimental study (12-17) and case-control studies (18, 19).

There was a decreased risk with increased frequency of ginseng consumed, showing a significant dose-response relationship (Table 10). During the study period, 137 cases including 42 stomach, 24 lung, 14 liver and 57 at other sites were diagnosed as cancers. The RRs in ginseng consumers were 0.33 (95% CI: 0.12-0.88) for gastric cancer, 0.30 (95% CI: 0.14-0.65) for lung cancer, showing a statistical significance (Table 11). Among ginseng preparations, only fresh ginseng extract consumers, a decreased risk for gastric cancer (RR=0.33, 95% CI: 0.12-0.88 was observed), while other types of ginseng

| Table 6. Distribution of ginseng intake frequency in cases and controls by sex: Odds ratios for cancer and 95 percent confidence interval in case-control study with 1,987 pairs |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Ginseng intake  | Males           | Females         | Males           | Females         |
| Frequency of ginseng intake | Case | Controls | Odds ratio | 95% CI | Case | Controls | Odds ratio | 95% CI |
| None            | 409 | 234 | 1.00 | Reference | 512 | 371 | 1.00 | Reference |
| 1-3 times/yr    | 246 | 231 | 0.62 | 0.49-0.79 | 171 | 209 | 0.60 | 0.47-0.76 |
| 4-11 times/yr   | 197 | 223 | 0.48 | 0.37-0.62 | 127 | 171 | 0.54 | 0.42-0.71 |
| 1 time/month or more | 220 | 384 | 0.31 | 0.25-0.39 | 105 | 164 | 0.47 | 0.39-0.62 |
| Total lifetime consumption of ginseng | None | 409 | 452 | 1.00 | Reference | 512 | 371 | 1.00 | Reference |
| 1-50            | 452 | 501 | 0.51 | 0.42-0.63 | 322 | 402 | 0.58 | 0.48-0.71 |
| 51-100          | 75 | 100 | 0.41 | 0.29-0.58 | 28 | 39 | 0.56 | 0.34-0.93 |
| 101-300         | 80 | 131 | 0.32 | 0.23-0.44 | 29 | 54 | 0.39 | 0.25-0.61 |
| 301-500         | 20 | 29 | 0.33 | 0.18-0.62 | 8 | 21 | 0.29 | 0.14-0.63 |
| 500+            | 36 | 77 | 0.25 | 0.16-0.38 | 16 | 28 | 0.42 | 0.23-0.79 |

| Table 7. Odds ratios for various cancers according to ginseng intake in case-control study with 1,987 pairs |
|-----------------|-----------------|-----------------|
| Site of cancer  | Cases           | Controls         | Odds ratios | 95% CI |
| Lip, oral cavity, and pharynx | 67/92 | 40/119 | 0.47 | 0.29±0.76 |
| Esophagus       | 40/47 | 14/73 | 0.20 | 0.09±0.38 |
| Stomach         | 142/159 | 76224 | 0.36 | 0.09±0.52 |
| Colon and rectum| 55/63 | 32/86 | 0.42 | 0.24±0.74 |
| Liver           | 108/156 | 67/197 | 0.48 | 0.33±0.70 |
| Pancreas        | 12/11 | 5/18 | 0.22 | 0.05±0.95 |
| Larynx          | 21/19 | 8/32 | 0.18 | 0.06±0.54 |
| Lung            | 120/156 | 81/195 | 0.55 | 0.38±0.79 |
| Female breast   | 82/92 | 70/109 | 0.63 | 0.40±1.05 |
| Cervix uteri    | 156/146 | 312/170 | 0.72 | 0.52±1.01 |
| Ovary           | 175 | 8/14 | 0.15 | 0.04±0.60 |
| Urinary bladder | 23/40 | 16/47 | 0.64 | 0.28±1.47 |
| Thyroid gland   | 16/24 | 14/26 | 0.96 | 0.36±2.44 |
| Other           | 52/61 | 35/79 | 0.48 | 0.27±0.85 |

Adjusted for age, sex, marital status, education, smoking, and alcohol consumption.
showed a decreasing trend.

**DISCUSSION**

In China, red ginseng was found to inhibit development of diethylnitrosamine-induced liver cancer in rats (25) and skin cancer in mice (26). In Russia, tissue-culture biomass tincture obtained from cultured *Panax ginseng* cells was shown to have a strong inhibitory effect on rat mammary adenocarcinoma induced by methyl-N-nitrosourea (27) as well as development of experimental uterine cervix and vaginal tumors (28). The result that 12-0-tetradecanoylphorbol-13-acetate (TPA)-induced production of tumor necrosis factor in mouse skin was inhibited by methanol extract of heat-processed neoginseng pretreatment was obtained in Korea (29). Recently, Japanese workers observed that, dietary administration of red ginseng powder during the initiation stage of carcinogenesis suppressed preneoplastic lesions in the colon of rats induced by 1,2-dimethylhydrazine (30). In MCF-7 breast cancer cells, the ability of American ginseng to induce the oestrogen-regulated gene $pS2$ and to regulate the cell-cycle were assessed in the U.S.A. Both American ginseng and oestradiol equally induced $pS2$ RNA expression, but only the ginseng caused a dose-dependent decrease in cell proliferation (31).

In case-control studies with 905 pairs and 1,987 pairs, there was noticeable decrease in risk by intake of ginseng extract compared to intake of fresh ginseng and there was a dose-response relationship depending on frequency of ginseng intake. The ORs of ginseng consumers decreased in all kinds of cancers. These results strongly support the hypothesis that ginseng has cancer preventive effects, as suggested by the earlier animal experiments. Lancet stated in an editorial that our study was one example of needed research into non-organ specific strategies for cancer control (32). Furthermore, the results of the cohort study also suggest that *Panax ginseng* C.A. Meyer has non-organ specific preventive effect against cancer, providing support for the previous case-control studies.

By comparing experimental results of types and ages of ginseng including two case-control and one cohort studies, the result with less than 5 yr-fresh ginseng was negative in both experimental and epidemiological studies but positive.
in fresh ginseng extract (Table 12). On the other hand, there was no cancer death among 24 red ginseng consumers, and red ginseng products showed prominent preventive effect in the 9 week antitumorogenicity test model (Yun’s model) and both case-control and cohort studies.

In order to compare the dose-response relationship between ginseng consumption and trend test of the above described results showed a significant decrease in proportion of cancer cases with increasing frequency of intake for both males and females (Table 13).

Experimental studies on ginseng has been widely carried out in many countries including Korea, China, Japan and Russia. The results indicated ginseng as an agent for anti-

Table 11. Adjusted relative risks for selected cancers by ginseng intake in cohort study

| Ginseng intake | Stomach (42) | Lung (24) | Liver (14) |
|---------------|--------------|-----------|------------|
|               | No. of subjects | No. RR | 95% CI | No. of subjects | No. RR | 95% CI | No. of subjects | No. RR | 95% CI |
| No intake     | 1,283         | 23       | 1.00   | -            | 14      | 1.00   | -            | 4        | 1.00   | -        |
| Ginseng intake| 3,167         | 19       | 0.33*  | 0.18-0.57   | 10      | 0.30*  | 0.14-0.65  | 10       | 0.86   | 0.25-2.94 |
| Slices & juice| 236           | 2        | 0.57   | 0.17-1.94   | 1        | 0.67   | 0.15-3.43  | 2        | 1.97   | 0.34-2.95 |
| Extract       | 296           | 1        | 0.33*  | 0.12-0.88   | 1        | 0.26   | 0.04-2.17  | -        | -      | -         |
| White ginseng Powder | 147     | 1        | 0.24   | 0.03-1.84   | -        | -      | -            | -        | -      | -         |
| Extract       | 68            | 2        | 1.34   | 0.30-5.97   | -        | -      | -            | -        | -      | -         |
| Tea           | 442           | 6        | 0.64   | 0.26-1.61   | 4        | 0.80   | 0.26-2.44  | 2        | 1.72   | 0.15-4.87 |
| Red ginseng   |               |          |        |             |          |        |              |          |        |           |
| Extract       | 381           | 5        | 0.43   | 0.12-1.43   | 1        | 0.35   | 0.08-1.95  | 1        | 0.85   | 0.15-4.87 |

RR: Relative risks, adjusted for age, sex, education, smoking and alcohol consumption; *: p<0.05; CI: Confidence interval; Value in parentheses indicate number of cancer cases.

Table 12. Comparison of relative risks for cancer by type of ginseng intake by medium-term experiment, case-control studies and cohort study

| Kind of ginseng | Antitumorogenicity confirmed by Yun’s test model | Case-control studies | Cohort study based on population |
|---------------|-----------------------------------------------|----------------------|---------------------------------|
|               | Relative risks by medium-term experiments       | Relative risks       | Odds ratios                      |
|               | 905 pairs | 1,987 pairs | 4,634 persons/5 yr |                        |
| Ginseng intake|                                               |                      |                                |
| Fresh ginseng |                                               |                      |                                |
| Fresh slices  |                                              |                      |                                |
| 1.5, 3, 4 and 5 yr-old | 0.74 | 0.79 | 0.67 |
| 6 yr-old only * |                      |                      |                                |
| Extract      |                                              |                      |                                |
| 1.5, 3, 4 and 5 yr-old | 0.14* | 0.37* | 0.31* |
| 6 yr-old only * |                      |                      |                                |
| White ginseng|                                               |                      |                                |
| Powder       |                                              |                      |                                |
| 1.5, 3 and 4 yr-old | 0.44* | 0.30* | 0.49 |
| 5 and 6 yr-old* |                     |                      |                                |
| Extract      |                                              |                      |                                |
| 1.5, 3 and 4 yr-old | 0.64* | 0.57* | 0.50 |
| 5 and 6 yr-old* |                     |                      |                                |
| Red ginseng  |                                               |                      |                                |
| Extract      |                                              |                      |                                |
| 1.5 and 3 yr-old | 0.45 | 0.20* | No cancer death = |
| 4.5 and 6 yr-old* |                     |                      |                                |
| Powder       |                                              |                      |                                |
| 1.5 and 3 yr-old | 0.27* | 0.16* | 0.34* |
| 4.5 and 6 yr-old* |                     |                      |                                |
| Combination  |                                              |                      |                                |

Adjusted for age, sex, education, smoking, alcohol consumption; *: Statistically significant.

in ginseng extract (Table 12). On the other hand, there was no cancer death among 24 red ginseng consumers, and red ginseng products showed prominent preventive effect in the 9 week antitumorogenicity test model (Yun’s model) and both case-control and cohort studies.

In order to compare the dose-response relationship between ginseng consumption and trend test of the above described results showed a significant decrease in proportion of cancer cases with increasing frequency of intake for both males and females (Table 13).

Experimental studies on ginseng has been widely carried out in many countries including Korea, China, Japan and Russia. The results indicated ginseng as an agent for antitumorogenicity as well as antipromoter. However, epidemiological studies were published only by our groups, including two case-control and one cohort studies.

In these three epidemiological studies, we demonstrated that Panax ginseng C.A. Meyer decreased the risks for most types of human cancers with dose response relationship, that is, non-organ specific cancer preventive effects (32-35). The need for clinical studies of ginseng has been strongly recommended (36-40). Clinical trials of Panax ginseng extracts and its active compounds are now warranted to be tested for a question of whether “Can this herb prevent all kinds of cancer?”
Table 13. Comparison of dose response relationship with frequency of ginseng intake in two case-control studies and three cohort analysis

| Frequency of ginseng intake | Case-control studies | Cohort analysis (4,634 Participants) |
|----------------------------|----------------------|-------------------------------------|
|                            | Male | Female | Both sex | 5 yr | 7 yr | 10 yr | Both sex | Both sex | Both sex | Both sex |
| No intake                  | 1.00 | 1.00   | 1.00     |      |      |       |         |         |         |         |
| 1-3 times/yr               | 0.58 | 0.81   | 0.60     | 0.46 | 0.29 | 0.52  |         |         |         |         |
| 4-11 times/yr              | 0.43 | 0.56   | 0.51     | 0.35 | 0.51 | 0.44  |         |         |         |         |
| 1 time/month <             | 0.25 | 0.52   | 0.36     | 0.54 | 0.34 | 0.47  |         |         |         |         |

RR adjusted for age, sex, education, smoking, alcohol consumption.

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