Preventive Effect of Ginseng Intake against Various Human Cancers: A Case-Control Study on 1987 Pairs

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Abstract
This study presents the risk of various cancers in relation to ginseng intake based on the data from a case-control study conducted in the Korea Cancer Center Hospital. Ginseng intakers had a decreased risk (odds ratio = 0.50, 95% confidence interval (CI) = 0.44–0.58) for cancer compared with nonintakers. On the type of ginseng, the odds ratios for cancer were 0.37 (95% CI = 0.29–0.46) for fresh ginseng extract intakers, 0.57 (95% CI = 0.48–0.68) for white ginseng extract intakers, 0.30 (95% CI = 0.22–0.41) for white ginseng powder intakers, and 0.20 (95% CI = 0.08–0.50) for red ginseng intakers. Intakers of fresh ginseng slice, fresh ginseng juice, and white ginseng tea, however, showed no decreasing risk. There was a decrease in risk with the rising frequency and duration of ginseng intake, showing a dose-response relationship. On the site of cancer, the odds ratios were 0.47 for cancer of the 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; and 0.15 for ovarian cancer. In cancers of the female breast, uterine cervix, urinary bladder, and thyroid gland, however, there was no association with ginseng intake. In cancers of the lung, lip, oral cavity and pharynx, and liver, smokers with ginseng intake showed decreased odds ratios compared with smokers without ginseng intake. These findings support the view that ginseng intakers had a decreased risk for most cancers compared with nonintakers. In conclusion, further studies will be necessary to elucidate what type of compounds caused this effect. To elucidate the mechanisms involved, extensive chemical, biochemical, molecular biological, immunological, and intervention studies must be conducted.

Introduction
The ginseng root has been used empirically for thousands of years in Asian countries. Since 1965, several pharmacological activities have been reported for ginseng extracts or ginseng dammarane saponins, including effects on the central nervous system; antipsychotic action; tranquilizing effects; protection from stress ulcers; increase of gastrointestinal motility; anti-fatigue action; endocrinological effects; enhancement of sexual behavior; acceleration of metabolism; or synthesis of carbohydrates, lipids, RNA, and proteins (1–5).

The species of ginseng are Panax ginseng C. A. Meyer (Korean ginseng), which is cultivated in Korea, Japan, China and Russia; Panax quinquefolius L. (American ginseng), which is raised in the eastern United States and Canada; Panax japonicus C. A. Meyer (Japanese ginseng), which is also called Bamboo ginseng; and Panax notoginseng (Burk) F.H. Chen (Sanchi-ginseng), a native of southwest China (Yunnan and Kwangsi Provinces). In Korea, Panax ginseng C. A. Meyer is collected after 2 to 6 years of cultivation, and it is classified into three types depending on how it is processed: (a) fresh ginseng (less than 4 years old and can be consumed in the fresh state); (b) white ginseng (4–6 years old and then dried after peeling); and (c) red ginseng, which is harvested when 6 years old and then steamed and dried (Fig. 1). Each type of ginseng was categorized further into several forms of ginseng products: fresh sliced; juice; extract (tincture or boiled extract); powder; tea; tablet; capsule; and other forms.

We hypothesized that the life-prolonging effect of ginseng described by Shennong (6) during the Liang Dynasty in China may be due to the preventive activity of ginseng against the development of cancers. We therefore carried out extensive animal experiments in 1978 to investigate whether ginseng inhibited carcinogenesis. We demonstrated that the red ginseng extract has anticarcinogenic effects against pulmonary tumors induced by various chemical carcinogens including 9,10-dimethyl-1,2-benzanthracene, urethane, aflatoxin B1, and N2-fluorenylacetamide in a long-term carcinogenesis model using mice (7, 8). This anticarcinogenic mechanism was partly involved in the elevation of the natural killer cell activity (9). The medium term (9 weeks) model system also revealed the anticarcinogenicity of ginseng on pulmonary adenomas induced by benzo(a)pyrene in newborn mice (10–12). We further investigated whether fresh ginseng or white ginseng has similar anticarcinogenic effects, and also if their anticarcinogenic effects are related to types and ages of ginseng using benzo(a)pyrene. A significant anticarcinogenic effect was observed in 6-year-old dried powder or extracted fresh ginseng; 5- and 6-year-old white ginseng powder or extract; and 4-, 5-, and 6-year-old red ginseng powder or extract (13, 14).

It has recently been shown that the biomass of ginseng tincture protected Ehrlich ascitic tumor cells against the mutagenic action of urea nitrosomethyl in vitro and in vivo (15). Sanchi ginseng inhibited the early antigen activation of Epstein-Barr virus in Raji cells induced by TPA and n-butylic acid, pulmonary tumorigenesis induced in mice by 4-nitroquinoline-N-oxide and diethylene-N-oxide in rats (18). It has also been reported more recently that tissue culture biomass tincture...
obtained from culture cells of Panax ginseng C. A. Meyer had a marked inhibitory effect on mammary tumors, mostly adenocarcinoma, induced by N-methyl-N-nitrosourea administration in rats (19).

We have previously reported the results on the effect of ginseng intake in a case-control study conducted on patients admitted to Korea Cancer Center Hospital (20). There was a decrease in cancer risks for ginseng intakers.

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 which can be prevented by ginseng, and (e) the effect of ginseng on cancers associated with smoking, we extended the number of subjects for a case-control study on 1987 pairs.

Patients and Methods

The sites studied which are classified according to the 9th Revision of the International Classification of Diseases for Oncology, WHO (21), were as follows: cancers of the lip, oral cavity and pharynx, esophagus, stomach, colorectum, liver, pancreas, larynx, lung, female breast, uterine cervix, ovary, urinary bladder, thyroid gland, and others. All the cases were confirmed by cytological and/or histopathological examination as primary cases admitted between February 1987 and December 1990 at the Korea Cancer Center Hospital, which specializes in cancer control and functions as a general hospital for the neighborhood.

The controls were selected from a pool of patients diagnosed as having noncancerous diseases at the hospital. Each case was matched with 1 control based on the year of birth (within 2 years), sex, and the admission date (within 3 months). When there were too many candidates for controls, the patient who was admitted on the nearest date was selected. The disease sites in male control patients were the stomach (495), thyroid (120), colon (81), kidney (93), oral cavity (85), lung (51), and others (95); for females, they were the uterus (351), breast (177), thyroid (170), ovary (75), stomach (46), liver (25), colon (16), and others (55). The types of diseases of controls were mainly acute diseases, that is, acute or unspecified gastritis in the stomach, goiter in the thyroid gland, acute appendicitis and obstruction in the colon, acute pyelonephritis and stone in the kidneys, tonsilitis and laryngopharyngitis in the oral cavity, or pneumonia and pleurisy in the lungs.

Cases and controls were selected among patients who were admitted to the hospital as new patients at the beginning of the study and were interviewed personally in the hospital by three trained interviewers. Almost every respondent was willing to answer the questionnaire. Those who had difficulty in answering because of serious illness were excluded from the study. Of the eligible cases and controls, 2.2% refused to answer from the outset or in the course of answering. To obviate biases caused by the interviewers, the category of the study subjects, i.e., case or control, was not known to the interviewers (22). Each study subject was interviewed according to a standard questionnaire.

All questionnaires were checked for consistency and verified for accuracy of coding. When information in questionnaires was incomplete or inconsistent, they were sent back for correction. The questionnaire included information on sociodemographic characteristics, life-long occupational history, and smoking and drinking habits. To obtain detailed information about ginseng intake, we asked subjects to specify their age at initial intake, their frequency and duration of intake, and the kind of ginseng. In the case of fresh ginseng, the categories include fresh slice (thinnly sliced pieces taken with or without honey), fresh extract (ginseng soup boiled for more than 3 h), or boiled young fresh ginseng root with chicken. For white ginseng, the categories include powder (white ginseng in powder form), extract (boiled white ginseng soup), and tea. Red ginseng was classified into extract (boiled red ginseng soup) and powder. In addition, multiple combinations among fresh, white, and red ginseng were included. Interviews on ginseng intake were carried out by asking the following questions in order to exactly characterize life-long ginseng intake: (a) have you ever consumed ginseng; (b) at what age did you take ginseng for the first time; (c) what type of ginseng products have you taken; and (d) how long (duration) have you used it? The frequency of ginseng intake was divided into four categories: (a) no intake; (b) 1–3 times/...
The abbreviations used are: OR, odds ratio; CI, confidence interval.

The distribution of total studied cancers and their controls was used for significance. The ORs3 and 95% CIs were computed for ginseng intake. These estimates were obtained by multiple logistic regression to control confounding factors such as age, sex, education, marital status, smoking, and alcohol consumption (24-25).

Results
The distribution of total studied cancers and their controls according to demographic and social characteristics is shown in Table 1. Among 1987 cases, 1072 (54.0%) were males and 915 (46.0%) were females. The average ages at diagnosis for the case groups of males and females were 53.5 and 49.8 years, respectively. There were no significant differences in age, marital status, educational level, religion, and occupation by sex between cases and controls. Female cases had fewer years of schooling and were more often widowed than male cases.

The ORs for cancers according to ginseng intake are shown in Table 2. Control groups (69.6%) had more ginseng intake compared with that of cancer patients (53.6%). The OR for ginseng intakers was 0.50 (95% CI = 0.44-0.58) compared with nonintakers. According to the type of ginseng product, the ORs for fresh ginseng intake was 0.50 (95% CI = 0.44-0.58) compared with nonintakers. The ORs for ginseng intakers were 0.37 (95% CI = 0.29-0.46) for fresh ginseng extract intakers, 0.57 (95% CI = 0.48-0.68) for white ginseng powder intakers, and 0.20 (95% CI = 0.08-0.50) for red ginseng intakers. However, intakers of fresh ginseng showed no decreasing risks. Intakers of fresh ginseng slice, fresh ginseng juice, and white ginseng tea showed no decreasing risks.

Table 3 shows the ORs for frequency and lifetime consumption of ginseng. There was a decrease in risk with rising frequency of ginseng intake. The OR ranged from 0.60 for 1-3 times/year to 0.36 for intakers of more than 12 times/year on more).

To evaluate the accuracy of the answers to the questionnaire, 10% of both cases and controls were selected and reinterviewed 1 year after the first interview. κ is a measure of agreement with desirable properties. Landis and Koch (23) have characterized different ranges of values for κ with respect to the degree of agreement: κ values less than 0.40, poor agreement beyond chance; 0.40-0.70, fair to good agreement beyond chance; 0.70-0.80, excellent agreement beyond chance; and greater than 0.75, excellent agreement beyond chance. The κ value for this study was 0.78 (P < 0.01), which indicated excellent agreement of answers.

Contingency tables were constructed for cases and controls by demographic and social characteristics, and the χ² test was used for significance. The ORs and 95% CIs were computed for ginseng intake. These estimates were obtained by multiple logistic regression to control confounding factors such as age, sex, education, marital status, smoking, and alcohol consumption (24-25).

\* The abbreviations used are: OR, odds ratio; CI, confidence interval.
for stomach cancer; 0.42 for colon and rectal cancer; 0.48 for liver cancer; 0.22 for pancreatic cancer; 0.18 for laryngeal cancer; 0.55 for lung cancer; and 0.15 for ovarian cancer. In cancers of the female breast, uterine cervix, urinary bladder, and thyroid gland, however, there was no association with ginseng intake.

Table 6 shows the effect of ginseng on the risk of cancer associated with smoking. Smokers without ginseng intake for cancers of the lung, lip, oral cavity, pharynx, and liver showed significantly increasing risks. However, the ORs for smokers who had consumed ginseng decreased, showing 1.99 for lung cancer; 2.36 for cancer of the lip, oral cavity, and pharynx; and 2.09 for liver cancer compared with nonsmokers who had consumed ginseng. There was no association with ginseng intake in cancers of the esophagus, stomach, and colorectum.

**Discussion**

In our previous case-control study conducted on 905 pairs of inpatients at Korea Cancer Center Hospital, we had observed that cancer risk decreased in ginseng intakers (20). In the present study we extended the number of subjects to 1987 pairs, including the above-mentioned pairs, and studied: (a) the types of the most prominent cancer-preventive ginseng products; (b) the reproducibility of the dose-response relationship; (c) the significant preventive duration of ginseng consumption; (d) types of cancer which can be prevented by ginseng; and (e) the effect of ginseng on cancers associated with smoking. The proportion of ginseng intakers to controls of this study, 69.6%, was similar to the 71.6% average of other sources from four major ginseng cultivation areas (Kangwa-eup, 70.7%; Keumsan-eup, 85.4%; Muju-eup, 89.4%; Punggi-eup, 81.8%) and in a comparison area (Keumchon-eup, 61.4%) for performing a prospective study in August 1988. The OR for cancer in relation to ginseng intake, 0.50, was similar to the previous data (0.56).

Ginseng is believed to have been used for about 2000 years in Oriental countries. Even some highly educated or high income people who preferred Western medicine to Korean traditional medicine took mainly white ginseng extract or powder that could be preserved as a tonic. In the past it was rather expensive, and only a few high level people could afford it. As the socioeconomic status of Korea began to improve about 15 years ago, and Koreans began to prefer Korean traditional teas, and the effect of ginseng became widely known, a lot of

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**Table 3** Odds ratios for cancers according to frequency and lifetime consumption of ginseng

<table>
<thead>
<tr>
<th>Frequency of ginseng intake</th>
<th>Cases</th>
<th>Controls</th>
<th>OR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>921</td>
<td>605</td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td>1-3 times/year</td>
<td>417</td>
<td>440</td>
<td>0.60</td>
<td>0.51-0.71</td>
</tr>
<tr>
<td>4-11 times/year</td>
<td>324</td>
<td>394</td>
<td>0.51</td>
<td>0.43-0.61</td>
</tr>
<tr>
<td>1 time/month or more</td>
<td>325</td>
<td>548</td>
<td>0.36</td>
<td>0.30-0.43</td>
</tr>
</tbody>
</table>

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**Table 4** Odds ratios for cancers according to duration of ginseng intake

<table>
<thead>
<tr>
<th>Duration of ginseng intake (yr)</th>
<th>Cases</th>
<th>Controls</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>921</td>
<td>605</td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td>1</td>
<td>361</td>
<td>362</td>
<td>0.64</td>
<td>0.54-0.77</td>
</tr>
<tr>
<td>2</td>
<td>162</td>
<td>197</td>
<td>0.53</td>
<td>0.42-0.66</td>
</tr>
<tr>
<td>3</td>
<td>116</td>
<td>201</td>
<td>0.36</td>
<td>0.26-0.47</td>
</tr>
<tr>
<td>4</td>
<td>82</td>
<td>114</td>
<td>0.45</td>
<td>0.33-0.61</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>116</td>
<td>0.31</td>
<td>0.22-0.44</td>
</tr>
</tbody>
</table>

---

**Table 5** Odds ratios for various cancers according to ginseng intakers

<table>
<thead>
<tr>
<th>Site of cancer</th>
<th>Cases Never taken/ever taken</th>
<th>Controls Never taken/ever taken</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip, oral cavity, and pharynx</td>
<td>67/92</td>
<td>40/119</td>
<td>0.47</td>
<td>0.29-0.76</td>
</tr>
<tr>
<td>Esophagus</td>
<td>40/47</td>
<td>14/73</td>
<td>0.20</td>
<td>0.09-0.38</td>
</tr>
<tr>
<td>Stomach</td>
<td>142/158</td>
<td>76/224</td>
<td>0.36</td>
<td>0.25-0.52</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>55/63</td>
<td>32/86</td>
<td>0.42</td>
<td>0.24-0.74</td>
</tr>
<tr>
<td>Liver</td>
<td>108/156</td>
<td>67/197</td>
<td>0.48</td>
<td>0.30-0.70</td>
</tr>
<tr>
<td>Pancreas</td>
<td>12/11</td>
<td>5/18</td>
<td>0.22</td>
<td>0.05-0.95</td>
</tr>
<tr>
<td>Larynx</td>
<td>21/19</td>
<td>8/32</td>
<td>0.18</td>
<td>0.06-0.54</td>
</tr>
<tr>
<td>Lung</td>
<td>120/156</td>
<td>81/195</td>
<td>0.55</td>
<td>0.30-0.79</td>
</tr>
<tr>
<td>Female breast</td>
<td>82/92</td>
<td>70/109</td>
<td>0.63</td>
<td>0.40-1.05</td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>156/146</td>
<td>132/170</td>
<td>0.72</td>
<td>0.52-1.01</td>
</tr>
<tr>
<td>Ovary</td>
<td>17/5</td>
<td>8/14</td>
<td>0.15</td>
<td>0.04-0.60</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>23/40</td>
<td>16/47</td>
<td>0.64</td>
<td>0.26-1.47</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>16/24</td>
<td>14/26</td>
<td>0.96</td>
<td>0.38-2.44</td>
</tr>
<tr>
<td>Others</td>
<td>53/61</td>
<td>35/79</td>
<td>0.48</td>
<td>0.27-0.85</td>
</tr>
</tbody>
</table>

* Adjusted for age, sex, marital status, education, smoking, and alcohol consumption.
* Adjusted for age, marital status, education, smoking, and alcohol consumption.
Table 6  Odds ratios for cancers according to ginseng intake and smoking*  

<table>
<thead>
<tr>
<th>Cancers</th>
<th>Ginseng intake</th>
<th>Nonsmokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Lung</td>
<td>Ever taken</td>
<td>1.00 (27)*</td>
<td>1.99 (81)</td>
</tr>
<tr>
<td></td>
<td>Never taken</td>
<td>2.11 (40)</td>
<td>4.13 (126)</td>
</tr>
<tr>
<td>Lip, oral cavity, and pharynx</td>
<td>Ever taken</td>
<td>1.00 (23)</td>
<td>2.36 (43)</td>
</tr>
<tr>
<td></td>
<td>Never taken</td>
<td>2.13 (24)</td>
<td>4.41 (69)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Ever taken</td>
<td>0.51 (5)</td>
<td>0.38 (42)</td>
</tr>
<tr>
<td></td>
<td>Never taken</td>
<td>2.73 (80)</td>
<td>1.90 (101)</td>
</tr>
<tr>
<td>Stomach</td>
<td>Ever taken</td>
<td>1.00 (31)</td>
<td>2.90 (62)</td>
</tr>
<tr>
<td></td>
<td>Never taken</td>
<td>2.11 (35)</td>
<td>1.90 (101)</td>
</tr>
<tr>
<td>Colorectum</td>
<td>Ever taken</td>
<td>1.00 (31)</td>
<td>3.25 (20)</td>
</tr>
<tr>
<td></td>
<td>Never taken</td>
<td>1.68 (27)</td>
<td>2.50 (125)</td>
</tr>
</tbody>
</table>

* Adjusted for age, sex, education, and alcohol consumption.

Numbers in parentheses, number of cancer patients.

Fig. 2  Fresh state of Panax ginseng C. A. Meyer at 1.5, 3, 4, 5, and 6 years.

people began to drink ginseng tea. Ginseng tea is served as much as coffee. At home some take white ginseng powder with honey by the spoon. Since electric appliances have become widely available, others purchase the 4-year-old fresh ginseng roots from the ginseng market, boil them with dates and ginger for about 3 h as white ginseng, store its brownish soup in the refrigerator, and drink it every day. Some people often buy red ginseng extract powder or ginseng tincture from department stores or ginseng distribution centers and drink it in hot water with sugar like instant coffee. Some take sliced fresh ginseng or ginseng juice at home or at Insam Chajip (ginseng drink corners in Korean).

The preventive effect of ginseng against cancers was observed in almost all types of ginseng product, which include fresh ginseng extract, white ginseng extract, white ginseng powder, and red ginseng products but exclude fresh ginseng slice, fresh ginseng juice, and white ginseng tea. The absence of a preventive effect with fresh ginseng slice and fresh ginseng juice intake is consistent with our previous data (20); this again was supported by the results of animal studies on a medium term benzo(a)pyrene anticarcinogenicity bioassay system with the use of 4-year-old fresh ginseng root (10) and 1.5- to 5-year-old dried fresh ginseng (13, 14; Fig. 2). The number of subjects who consumed expensive red ginseng was too small to evaluate any beneficial effect in the earlier study, but in this study the OR of red ginseng products intakers was the lowest at 0.20.

To examine the reproducibility of dose-response relationships between ginseng consumption and cancer, all types and forms of ginseng products were combined, and the frequency of ginseng intake was categorized into four levels as in the earlier study. The ORs for decreasing levels of ginseng intake were similar to those in the earlier study in males and females, and a trend test showed a significant decrease in the proportion of cancer cases, with an increasing frequency of intake for both males and females, respectively. To confirm the cumulative effect of ginseng intake, total lifetime frequencies of ginseng intake were calculated, and the ORs were reduced gradually as the total frequency of ginseng intake increased as in the earlier study. The OR began to decrease after 1 year of ginseng intake and progressively declined until after 5 years of intake. The
ORs in those who consumed ginseng for 6–10 and 11–12 years gradually decreased further. We also analyzed the effect of age of first ginseng intake on risk for cancers. There was no significant difference in the OR between those who began to use ginseng between the ages of 30–39 and after age 60. In both groups the preventive effect appeared 1 year after the first ginseng intake and increased with the duration of consumption (data not shown).

According to the site of cancer, ginseng intake decreased the OR for cancers of the lip, oral cavity, pharynx, esophagus, stomach, colorectum, liver, pancreas, larynx, lung, and ovary. However, there were inconsistent and weak associations between ginseng intake and cancers of the female breast, uterine cervix, urinary bladder and thyroid gland. The ORs for cancers of the breast and uterine cervix showed 0.63 (95% CI = 0.40–1.05) and 0.72 (95% CI = 0.52–1.01), respectively. Considering that biomass tincture obtained from culture cells of Panax ginseng C. A. Meyer showed a marked inhibitory effect on mammary adenocarcinoma in rats induced by N-methyl-N-nitrosourea (19), and also that the upper limits of the 95% confidence interval of cancers of the breast and uterine cervix were close to 1.00, we expect an inhibitory effect in these cancers. The total number of other cancers shown in Table 5, 114 cases, included cancers of the kidney (22), bile duct (21), nasal cavity (20), and malignant lymphoma (20). The rest were cancers of the corpus uteri, prostate gland, vagina, bone, testis, penis, abdomen, duodenum, pleura, and placenta. The OR for all other cancers was 0.48 (95% CI = 0.27–0.85). Therefore, it suggests that most cancers could be prevented by intake of ginseng.

It is well recognized that β-carotene, retinol, 13-cis-retinoic acid, vitamin C, vitamin E, and isorretinoin act as inhibitors of lung and skin cancers; 4-OH phenyl-retinamide (phenoretinide) and tamoxifen of breast cancer; folate acid and trans-retinoic acid of cervix cancer; and β-carotene, fiber, calcium vitamin C, vitamin E, and piroxicam of colon cancer (26–29). However, ginseng prevented almost all types of cancer irrespective of the pathologival types in our study. It is very hard to understand how the intake of ginseng could prevent the development of nearly all cancers. Ginseng might be effective in the primary prevention of cancers and have an effect in the early initiation stage of carcinogenesis. Considering the reports on the higher incidence of lung cancer among men who received β-carotene (30); on the lack of anticancer effects of antioxidant vitamins including vitamin C, vitamin E, and β-carotene (31); and on high grade endometrial carcinoma in patients and hepatocarcinogenic activity in rats treated with tamoxifen (which was expected to prevent breast cancer; Refs. 32 and 33), interest should be taken in the cancer-preventive effects of ginseng.

It is well known that the incidence of lung cancer is high in smokers (34, 35), and it has also been reported that smoking enhanced the risk of cancers of the oral cavity (35, 36), pharynx (35, 37), esophagus (35, 38), stomach (39), and liver (40, 41). In the present study, the risk of cancers of the lung, lip, oral cavity, pharynx, and liver associated with smoking was reduced with ginseng intake. Smokers with ginseng intake for these cancers showed significantly increasing risks, but the ORs decreased compared with smokers without ginseng intake. The result that risk was reduced in smokers is congruent with our report that the inhibition of mouse pulmonary tumors was induced by benzo(a)pyrene, an environmental carcinogen contained in tobacco smoke (10–14), and supports the view that the ethanol extract of Panax ginseng exhibited a selective induction of epoxide hydrazide and cytosolic glutathione transferase activity without the concurrent induction of arylhydrocarbon hydroxylase activity (42).

The above mentioned results of this study support the results of our previous animal experiments and a case-control study. They were also supported by the fact that the average age-adjusted annual cancer incidence per 100,000 population was 134.8 in both sexes (183.0 in males and 99.5 in females between 1983 and 1987 surveyed in Kangwha county, which is one of the most well known ginseng cultivation areas near Seoul) to identify the population-based rate in Korea (43). These data were lower than those from seven population-based cancer registries in Japan (44) and also lower than those of the United States in 1987 (45).

Since there have been no epidemiological studies on the preventive effect of ginseng against cancers conducted by others, we have been performing a prospective study in 4 major ginseng cultivation areas (Kangwha, Keumsan, Miju, and Punggi) and in 1 comparison area (Keumchon) with 14,651 participants over age 40 since August 1988. The ginseng takers among the participants in ginseng cultivation areas were 70.7% in Kangwha-eup, 85.4% in Keumsan-eup, 89.4% in Miju-eup, and 81.8% in Punggi-eup, and 61.4% in Keumchon-eup. The prospective study of Kangwha-eup, which was conducted for 7 years, is now under analysis.

The possible biases that may affect this study of ginseng intake are as follows; information, selection, and interview biases, and uncontrolled confounding variables. It is unlikely that information biases will have any effect since at the time of data collection, this hypothesis was unknown to the interviewers and the patients. The possibility of selection bias cannot be ruled out easily. Differential rates of hospitalization for exposed and unexposed cases and controls can distort the OR determined in the hospital from that in the population. Cancer generally requires hospitalization for treatment. Particularly, most persons with cancer will be admitted to this hospital, which specializes in cancer. An effect due to selection bias appears unlikely in this study since 97.8% of the subjects approached for interview participated in this hospital. Cases and controls are selected by a scheme that is equivalent to sampling from the admission logs (incident cases) and not on the basis of a hospital register of current patients (prevalent cases). The distribution of ginseng intake among controls was similar to that of the participants in four major ginseng cultivation areas and one comparison area for cohort study, although we have no data on ginseng intake rates in the whole population. Biases resulting from selective admission to hospital are unlikely because all subjects had to be admitted regardless of whether they consumed ginseng. Perhaps the greatest drawback in our methodology was the inability to adjust for potential confounding variables, particularly those related to diet for cancers of the digestive organs and sexual behavior for cancers of the reproductive systems.

It is still unknown what components of ginseng work in reducing cancer risks. On the basis of our observation of the fact that the administration of ginseng extract decreased the incidence of lung adenomas induced by urethan and reversed the decrease of natural killer cell activity induced by urethan in the early stage of our study, we thought that the anticarci- nogenic activity of ginseng extract against urethan-induced carcinogenesis might be related partly to the augmentation of natural killer cells. In consideration that ginseng has been taken as a herb medicine for a long time in Korea, however, we are attaching more importance in our study to confirming whether ginseng has as great an anticarcinogenic effect in human beings as it has in mice rather than studying its active components.
Since Shibata et al. (1) isolated a number of tetracyclic dammarane saponins (ginsenosides) from ginseng in 1965, which was the first example of dammarane saponins in nature, 28 saponins of this type have been isolated from the roots and leaves of ginseng (46). In 1969, Breckman proposed the presence of “adaptogen” in ginseng (47). Adaptogen is a term for a prophylactic against aging and diseases that recovers homeostasis. In other words, an adaptogen is a compound that increases nonspecific resistance against toxic environmental agents, as well as physical stress. The concept of adaptogen suggests the possibility of using ginseng as a prophylactic or delaying agent against carcinogenesis rather than as a therapeutic agent (17). According to Oliver and Nouri (48), a case-control study in which regular ginseng consumption increased resistance to cancer reported by us (20) supports the view that the immune reaction which regular ginseng consumption increased resistance to cancer in mice (52, 53). The polysaccharide revealed anticomplement activity (49), neticuloendothelial system-potentiating activity (54), and for reverse transformation in cultured Morris adenocarcinoma cells (SW620), human uterus carcinoma cells (HeLa cells), and mouse fibroblast-derived tumor cells (L929 cells), human colon adenocarcinoma cells (SW620), human uterus carcinoma cells (HeLa cells) and human erythroleukemic cells (K562 cells) (49) for growth inhibition of human ovarian cancer cells in nude mice (50), for reverse transformation in cultured Morris hepatoma cells (51), and for immunomodulating activity in mice (52, 53). The polysaccharide revealed anticomplementary activity (54), reticuloendothelial system-potentiating activity and alkaline phosphatase-inducing activity (55), and cytoprotective activity (56). Lately, various polyacylates are reported to have been extracted from ginseng (57, 58), and they are known to have cytotoxic activity (59). Judging from the fact that each constituent has its own characteristics, one or more than one in cooperation seem to reduce cancer risks. It is, of course, possible that some unknown constituents are related to the reduction of cancer risks. In order to elucidate what type of compounds played a part in this process and their mechanisms, extensive chemical, biochemical, molecular biological, immunological, and epidemiological studies must be conducted.

In conclusion, all ginseng products such as fresh ginseng extract, white ginseng extract, white ginseng powder, and red ginseng products except fresh ginseng slice, juice, and white ginseng tea showed preventive effects with a dose-response relationship. The OR began to decrease with intake of ginseng for 1 year and progressively declined until 20 years of intake. Ginseng had a preventive effect against most types of cancers (lip, oral cavity and pharynx, esophagus, stomach, colorectum, liver, larynx, lung, pancreas, and ovary) except cancers of the female breast, uterine cervix, urinary bladder, and thyroid gland. Ginseng also reduced the risk of cancers associated with smoking. However, further studies will be necessary to confirm the cancer preventive effect of ginseng and to identify its active components and their mechanism of action.

References


Preventive effect of ginseng intake against various human cancers: a case-control study on 1987 pairs.

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