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Original Research

Saponin contents and anticarcinogenic effects of ginseng depending on types and ages in mice

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KEY WORDS ginseng; plant roots; plant extracts; saponins; benzo(a)pyrene; lung neoplasms; anticarcinogenic agents; phytogenic antineoplastic agents; pharmacognosy

AIM: To compare the anticarcinogenic effects of fresh, white, and red ginseng (*Panax ginseng* C A Meyer) roots and their saponins. **METHODS:** Lung adenoma in newborn N : GP (S) mice was induced by a subcutaneous injection of benzo(a)pyrene 0.5 mg. After weaning, ginseng powders or extracts were given in the drinking water for 6 wk. In the 9th wk the incidence and multiplicity of lung adenoma were counted. **RESULTS:** Anticarcinogenic effects were found in 5-year-dried fresh ginseng, 5- and 6-year white ginseng, and 4-, 5-, and 6-year-red ginseng powders. Anticarcinogenic effects were also found in 6-year-dried fresh ginseng, 5- and 6-year-white ginseng, and 4-, 5-, and 6-year-red ginseng extracts. The content of major ginsenosides R_{b1}, R_{b2}, R_c, R_d, R_e, R_f, R_{g1} showed a little higher tendency in fresh or white ginsengs than red ginseng. This tendency was increased as the cultivation ages were increased. But there was no relationship was found between ginsenoside contents and preparation types or cultivation ages. **CONCLUSION:** Long-cultivated ginseng and red ginseng contain a higher amount of anticarcinogenic components.

Prolonged administration of ginseng (*Panax ginseng* C A Meyer) to experimental animals protected against the carcinogenesis induced by urethane, aflatoxin B_1[1,2], benzo(a)pyrene[3,4], diethylnitrosamine[5], and *N*-methyl-*N*-nitrosourea[6]. Continuous consumption of ginseng might reduce the risk of human cancer[7,8]. Red ginseng extract made from 6-year fresh ginseng showed positive results in the majority of these studies. White or fresh ginseng had a weak or no anticarcinogenic effect. The present study was to compare the anticarcinogenic efficacies of fresh, white, and red ginsengs and their major saponin contents.

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MATERIALS AND METHODS

Mice Non-inbred N:GP(S) mice were obtained from National Cancer Institute (NIH), USA and bred at random *inter se*.

Ginseng Roots of fresh ginseng (*Panax ginseng* C A Meyer) at 1.5, 3, 4, 5, and 6 years were used. Fresh ginseng was dried at room temperature, finely powdered, and extracted in a water bath for 8 h, 3 times for fresh ginseng (yield of extract: 45 %). White ginseng was processed in the same way as fresh ginseng after removal of its cortex and fine root (yield of extract: 47 %). For red ginseng, fresh ginseng was steamed, dried, and processed in the same way as fresh ginseng (yield of extract: 51 %).

Bioassay of anticarcinogenicity We used the 9-wk medium-term bioassay model[3,4]. Newborn mice, < 24 h old, were injected sc in the scapular region with 0.02 mL of a suspension of 0.5 mg of benzo(a)pyrene (BP, Sigma, USA) in 1 % aqueous gelatin. After weaning, ginseng powders 5 g $\cdot L^{-1}$ or extracts 2.5 g $\cdot L^{-1}$ were given in drinking water for 6 wk. Mice were killed in the 9th wk by asphyxiation. The lungs were fixed in Tellyesniczky's solution (70 % ethanol 100 mL + formalin 5 mL + glacial acetic acid 5 mL). The incidence and multiplicity of lung adenoma were counted with the naked eye.

Saponin contents Crude saponin was extracted from dried fresh, white, and red ginseng powders or extracts as previously[9], and subjected HPLC (Waters 244) to quantitative major ginsenosides (R_{b1}, R_{b2}, R_c, R_d, R_e, R_f, and R_{g1}. Lochrosorb column, differential refractometer RI 401 detector and acetonitrile/water/*n*-butanol (80:20:0.25, v/v) mobile phase was used.

Statistics We used Chi-square test for tumor incidence and *t*-test for multiplicity.

RESULTS

The mice well tolerated carcinogen and ginseng. There was no death attributable to the treatment, and overall weight gains over the 9 wk period were almost the same between control and treated mice. The mean relative lung weights did not show significant differences between groups.

In dried fresh ginseng treated groups, the incidence of lung adenoma induced by BP was 41.3 % which was reduced to 31.2 %, 30.0 %, 31.3 %, 30.3 %, and 27.8 % after co-treatment with 1.5-, 3-, 4-, 5-, and 6-year-dried fresh ginseng powders, respectively. In extract treated groups, the incidence of lung adenoma in BP group was 63.9 % which was also reduced to 48.3 %, 52.5 %, 51.8 %, 47.5 %, and 44.1 % after co-treatment with 1.5-, 3-, 4-, 5-, and 6-year-dried fresh ginseng extracts, respectively. A significant effect was seen in the groups treated with powders or extracts of 6-year-dried fresh ginseng ($P<0.05$) (Tab 1).

In the white ginseng treated groups, the incidence of lung adenoma by BP was 45.0 % which was decreased to 41.3 %, 38.0 %, 31,6 %, and 25.3 % after co-treatment with 3-, 4-, 5-, and 6-year-white ginseng powders, respectively. Lung adenoma incidence by BP was 41.3 % which became 32.0 %, 46.0 %, 44.0 %, and 26.5 % after co-treatment with 3-, 4-, 5-, and 6-year-white ginseng extracts, respectively. Five- and 6-year-ginseng powders ($P < 0.05$ and $P < 0.01$, respectively) and 6-year-ginseng extract ($P<0.05$) showed inhibitions of lung adenoma (Tab 1). In BP with 6-year white ginseng powder treated group, lung tumor multiplicity decreased *vs* that in BP alone group.

In the red ginseng treated group, the incidence of lung adenoma by BP was 48.6 % which diminished to 37.9 %, 41.7 %, 31.7 %, 28.3 %, and 25.4 % after co-treatment with 1.5-, 3-, 4-, 5-, and 6-year-red ginseng powders, respectively. In the extract treated groups, the incidence by BP was 47.5 % which diminished to 40.7 %, 35.0 %, 30.1 %, 30.0 %, and 26.3 % after co-treatment with 1.5-, 3-, 4-, 5-, and 6-year-red ginseng extracts, respectively. In 4-, 5-, and 6-year-ginseng powder ($P<0.05$, $P<0.05$, and $P<0.01$, respectively) or extract ($P < 0.05$) treated groups (Tab 1).

We determined level of ginsenosides in various ginseng powders or extracts. The multiplicity reduced in the 6-year red ginseng treated group. Crude saponin and the contents of all the ginsenosides increased accordingly as cultivation age increased. However, there is no relationship between anticarcinogenicity and amount of each ginsenoside (Tab 2).

DISCUSSION

The present study showed that the anti-carcinogenicities of ginseng powders or extracts were different according to their preparation types or cultivation ages.

A significant anticarcinogenic effect was observed in 6-year-dried fresh ginseng, 5- and 6-year-white ginsengs, and 4-, 5-, and 6-year-red ginseng powders. The extract showed patterns of anticarcinogenicity similar to those of ginseng powders. The dosage of ginseng extracts would be equivalent to ginseng powders because ginseng extracts were given at a dose of 1/2 of that of the powders.

From above results, the active components of ginseng which exert anticarcinogenic activity might be richer in older and red ginseng. Typical ginsenoside responsible for the anticarcinogenicity of ginseng was not found and there was no relationship between ginsenoside contents and anticarcinogenic effect of ginseng. Because we did not examine all of the ginsenosides that are contained in ginseng, it is difficult to exclude ginsenosides as active components of ginseng that exerts anticarcinogenic activity. There are other possibilities of components other than ginsenosides and a combination effect of these components which might be responsible for the anticarcinogenicity of ginseng.

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REFERENCES

1 Yun TK, Yun YS, Han IW. An experimental study on tumor

Tab 1. Effects of ginseng on incidence of lung adenoma in mice induced by benzo(a)pyrene (BP).
$^aP>0.05$, $^bP<0.05$, $^cP<0.01$ *vs* BP alone.

Treatment (age of ginseng)	Ginseng powder: Mice Sex	n	Incidence/ %	Multiplicity $\bar{x} \pm s$	Ginseng extract: Mice Sex	n	Incidence/ %	Multiplicity $\bar{x} \pm s$
Fresh ginseng								
Untreated control	M	36	0	0	M	30	0	0
	F	36	2.8	0.03 ± 0.14	F	30	0	0
	M + F	72	1.4	0.01 ± 0.03	M + F	60	0	0
BP	M	40	40.0	0.68 ± 1.08	M	26	57.7	1.75 ± 2.06
	F	40	42.5	0.73 ± 0.37	F	30	70.0	1.30 ± 1.26
	M + F	80	41.3	0.70 ± 0.89	M + F	56	63.9	1.78 ± 2.12
1.5-year	M	38	2.6	0.03 ± 0.13	M	30	0	0
	F	38	0	0	F	29	0	0
	M + F	76	1.3	0.01 ± 0.08	M + F	59	0	0
BP + 1.5-year	M	38	28.9	0.34 ± 0.56	M	30	46.7	1.77 ± 3.01
	F	39	33.3	0.56 ± 1.05	F	29	50.0	1.47 ± 2.71
	M + F	77	31.2^a	0.46 ± 0.65^b	M + F	59	48.3^a	1.61 ± 2.84^a
3-year	M	38	2.6	0.03 ± 0.12	M	30	0	0
	F	38	0	0	F	30	4.0	0.04 ± 0.28
	M + F	76	1.3	0.01 ± 0.03	M + F	60	2.0	0.02 ± 0.14
BP + 3-year	M	40	22.5	0.35 ± 0.58	M	30	53.3	1.27 ± 1.63
	F	40	37.5	0.78 ± 1.39	F	29	51.7	1.72 ± 3.66
	M + F	80	30.0^a	0.56 ± 0.97^a	M + F	59	52.5^a	1.59 ± 2.86^a
4-year	M	38	0	0	M	30	0	0
	F	38	2.6	0.03 ± 0.13	F	30	0	0
	M + F	76	1.3	0.01 ± 0.08	M + F	60	0	0
BP + 4-year	M	40	32.5	0.85 ± 1.21	M	30	50.0	1.13 ± 1.89
	F	40	30.0	0.45 ± 0.75	F	29	53.6	1.14 ± 1.38
	M + F	80	31.3^a	0.65 ± 1.07^a	M + F	59	51.8^a	1.13 ± 1.65^a
5-year	M	38	0	0	M	30	0	0
	F	37	2.7	0.03 ± 0.13	F	30	4.0	0.04 ± 0.28
	M + F	75	1.3	0.01 ± 0.07	M + F	60	2.0	0.02 ± 0.14
BP + 5-year	M	37	29.7	0.43 ± 0.87	M	30	46.7	1.70 ± 0.28
	F	39	30.8	0.62 ± 1.12	F	29	48.3	2.00 ± 2.66
	M + F	76	30.3^a	0.53 ± 0.98^a	M + F	59	47.5^a	1.79 ± 3.48^a
6-year	M	38	0	0	M	30	0	0
	F	37	0	0	F	30	0	0
	M + F	75	0	0	M + F	60	0	0
BP + 6-year	M	39	38.5	0.72 ± 0.78	M	27	48.3	1.02 ± 1.58
	F	40	17.5	0.38 ± 0.60	F	30	40.0	1.30 ± 2.07
	M + F	79	27.8^b	0.54 ± 0.68^a	M + F	57	44.1^b	1.16 ± 1.72^a
White ginseng								
Untreated control	M	25	0	0	M	25	0	0
	F	25	0	0	F	25	0	0
	M + F	50	0	0	M + F	50	0	0
BP	M	40	32.5	0.68 ± 1.08	M	40	35.0	0.43 ± 0.68
	F	40	57.5	1.08 ± 1.70	F	40	47.5	0.70 ± 1.32
	M + F	80	45.0	0.85 ± 1.56	M + F	80	41.3	0.55 ± 0.83

Treatment (age of ginseng)	Ginseng powder Mice Sex	n	Incidence/ %	Multiplicity $\bar{x} \pm s$	Ginseng extract Mice Sex	n	Incidence/ %	Multiplicity $\bar{x} \pm s$
3-year	M	30	0	0	M	24	0	0
	F	30	0	0	F	25	4.0	0.04 ± 0.28
	M + F	60	0	0	M + F	49	2.0	0.02 ± 0.14
BP + 3-year	M	40	27.5	0.35 ± 0.60	M	25	28.0	0.32 ± 0.56
	F	40	55.0	1.05 ± 1.80	F	25	36.0	0.72 ± 1.37
	M + F	80	41.3[a]	0.70 ± 1.32[a]	M + F	50	32.0[a]	0.52 ± 1.05[a]
4-year	M	25	0	0	M	25	4.0	0.04 ± 0.28
	F	25	4.0	0.04 ± 0.28	F	25	0	0
	M + F	50	2.0	0.02 ± 0.14	M + F	50	2.0	0.02 ± 0.14
BP + 4-year	M	40	25.0	0.30 ± 0.57	M	25	36.0	0.64 ± 1.08
	F	39	51.3	1.08 ± 1.57	F	25	56.0	1.16 ± 1.70
	M + F	79	38.0[a]	0.68 ± 0.99[a]	M + F	50	46.0[a]	0.90 ± 1.43[a]
5-year	M	25	0	0	M	25	8.0	0.08 ± 0.20
	F	25	4.0	0.04 ± 0.28	F	25	4.0	0.04 ± 0.28
	M + F	50	2.0	0.02 ± 0.14	M + F	50	6.0	0.06 ± 0.24
BP + 5-year	M	30	27.5	0.53 ± 0.82	M	25	36.0	0.44 ± 0.65
	F	30	35.9	0.74 ± 0.96	F	25	52.0	1.00 ± 1.35
	M + F	60	31.6[b]	0.63 ± 0.89[a]	M + F	50	44.0[a]	0.68 ± 1.08[a]
6-year	M	25	0	0	M	25	4.0	0.04 ± 0.28
	F	25	0	0	F	25	4.0	0.04 ± 0.28
	M + F	50	0	0	M + F	50	4.0	0.04 ± 0.28
BP + 6-year	M	40	31.3	0.25 ± 0.57	M	24	20.8	0.28 ± 0.61
	F	39	18.5	0.62 ± 0.79	F	25	32.0	0.40 ± 0.65
	M + F	79	25.4[c]	0.43 ± 0.70[c]	M + F	49	26.5[c]	0.41 ± 0.81[a]
Red ginseng								
Untreated control	M	26	0	0	M	25	0	0
	F	30	0	0	F	25	0	0
	M + F	56	0	0	M + F	50	0	0
BP	M	36	44.4	0.44 ± 0.72	M	40	40.0	0.45 ± 0.60
	F	38	52.6	0.63 ± 1.08	F	40	55.0	1.15 ± 1.70
	M + F	74	48.6	0.54 ± 0.96	M + F	80	47.5	0.80 ± 1.32
1.5-year	M	25	0	0	M	24	0	0
	F	25	0	0	F	25	0	0
	M + F	50	0	0	M + F	49	0	0
BP + 1.5-year	M	28	46.4	0.89 ± 1.12	M	29	34.5	0.48 ± 0.87
	F	30	30.0	0.40 ± 0.68	F	30	46.7	0.50 ± 0.57
	M + F	58	37.9[a]	0.64 ± 1.08[a]	M + F	59	40.7[a]	0.49 ± 0.73[a]
3-year	M	29	0	0	M	25	0	0
	F	30	0	0	F	25	4.0	0.04 ± 0.28
	M + F	59	0	0	M + F	50	2.0	0.02 ± 0.14
BP + 3-year	M	30	33.3	0.67 ± 1.12	M	30	23.3	0.30 ± 0.60
	F	30	50.0	0.90 ± 0.99	F	30	46.7	0.80 ± 1.21
	M + F	60	41.7[a]	0.80 ± 1.06[a]	M + F	60	35.0[a]	0.51 ± 0.97[a]
4-year	M	25	0	0	M	25	0	0
	F	25	3.3	0.03 ± 0.21	F	25	0	0
	M + F	50	1.7	0.02 ± 0.12	M + F	50	0	0

Treatment (age of ginseng)	Ginseng powder Mice Sex	n	Incidence/ %	Multiplicity $\bar{x} \pm s$	Ginseng extract Mice Sex	n	Incidence/ %	Multiplicity $\bar{x} \pm s$
BP + 4-year	M	30	33.3	0.83 ± 1.24	M	29	24.1	0.31 ± 0.60
	F	30	30.0	0.50 ± 0.68	F	30	36.7	0.83 ± 1.39
	M + F	60	31.7[b]	0.67 ± 0.89[a]	M + F	59	30.1[c]	0.58 ± 1.10[a]
5-year	M	28	0	0	M	25	4.0	0.04 ± 0.28
	F	30	0	0	F	25	4.0	0.04 ± 0.28
	M + F	58	0	0	M + F	50	4.0	0.04 ± 0.28
BP + 5-year	M	30	33.3	0.60 ± 0.76	M	30	20.0	0.30 ± 0.65
	F	30	23.3	0.46 ± 0.58	F	30	40.0	0.57 ± 0.82
	M + F	60	28.3[b]	0.53 ± 0.68[a]	M + F	30	30.0[c]	0.43 ± 0.75[a]
6-year	M	28	0	0	M	25	4.0	0.04 ± 0.28
	F	30	3.3	0.03 ± 0.21	F	25	4.0	0.04 ± 0.28
	M + F	58	1.7	0.02 ± 0.12	M + F	50	4.0	0.04 ± 0.28
BP + 6-year	M	32	31.3	0.50 ± 0.66	M	27	22.2	0.37 ± 0.62
	F	27	18.5	0.44 ± 0.54	F	30	30.0	0.37 ± 0.79
	M + F	59	25.4[c]	0.48 ± 0.62[a]	M + F	57	26.3[c]	0.37 ± 0.70[c]

Tab 2. Dry weights (%) of crude saponin and major ginsenosides in fresh, white, and red ginseng roots of various cultivation ages.

		Ginseng powder 1.5-year	3-year	4-year	5-year	6-year	Ginseng extract 1.5-year	3-year	4-year	5-year	6-year
Crude saponin	Fresh	10.20	10.73	10.50	11.54	11.46	4.38	4.80	4.86	5.64	5.70
	White	9.10	9.14	9.36	9.30	9.28	3.86	3.95	4.03	4.18	4.25
	Red	7.90	8.20	8.15	9.21	9.54	4.35	4.72	4.82	5.69	5.73
Ginsenoside-R_{b1}	Fresh	1.32	1.40	1.43	1.62	1.68	0.54	0.60	0.66	0.78	0.81
	White	1.25	1.30	1.37	1.28	1.24	0.48	0.52	0.56	0.54	0.53
	Red	1.20	1.34	1.40	1.48	1.50	0.60	0.68	0.72	0.84	0.89
Ginsenoside-R_{b2}	Fresh	0.63	0.64	0.72	0.78	0.75	0.21	0.28	0.30	0.36	0.34
	White	0.51	0.53	0.63	0.56	0.54	0.18	0.24	0.26	0.27	0.24
	Red	0.54	0.56	0.58	0.64	0.68	0.23	0.31	0.36	0.40	0.38
Ginsenoside-R_e	Fresh	0.62	0.67	0.73	0.80	0.84	0.23	0.30	0.31	0.37	0.40
	White	0.64	0.68	0.71	0.66	0.62	0.26	0.28	0.30	0.28	0.27
	Red	0.56	0.59	0.65	0.67	0.72	0.31	0.34	0.36	0.40	0.43
Ginsenoside-R_d	Fresh	0.35	0.37	0.38	0.40	0.39	0.13	0.15	0.18	0.21	0.19
	White	0.30	0.31	0.33	0.34	0.30	0.13	0.14	0.15	0.18	0.16
	Red	0.25	0.28	0.31	0.34	0.36	0.14	0.16	0.17	0.18	0.19
Ginsenoside-R_c	Fresh	0.86	0.87	0.86	0.91	0.94	0.36	0.39	0.40	0.48	0.47
	White	0.70	0.76	0.80	0.81	0.79	0.31	0.32	0.35	0.36	0.38
	Red	0.64	0.66	0.65	0.72	0.76	0.33	0.37	0.38	0.46	0.47
Ginsenoside-R_f	Fresh	0.18	0.20	0.18	0.20	0.19	0.07	0.09	0.08	0.10	0.09
	White	0.14	0.16	0.15	0.18	0.17	0.06	0.07	0.07	0.08	0.07
	Red	0.14	0.16	0.16	0.17	0.15	0.07	0.09	0.08	0.10	0.09
Ginsenoside-R_{g1}	Fresh	1.05	1.15	1.14	1.21	1.23	0.44	0.51	0.52	0.59	0.58
	White	0.93	1.00	0.97	0.96	0.98	0.39	0.43	0.46	0.40	0.44
	Red	0.78	0.85	0.86	0.92	0.94	0.43	0.49	0.50	0.56	0.54

inhibitory effects of red ginseng in mice and rats exposed various chemical carcinogens. Proc 3rd Intl Ginseng Symp. Seoul: Korea Ginseng Research Institute Press, 1980; 87 - 113.

2 Yun TK, Yun YS, Han IW. Anticarcinogenic effect of long-term oral administration of red ginseng on newborn mice exposed to various chemical carcinogens. Cancer Detect Prev 1983; 6: 515 - 25.

3 Yun TK, Kim SH. Inhibition of development of benzo(a)pyrene-induced mouse pulmonary adenoma by natural products in medium-term bioassay system. J Korean Cancer Assoc 1988; 30: 133 - 42.

4 Yun TK, Kim SH, Lee YS. Trial of a new medium-term model using benzo(a)pyrene induced lung tumor in newborn mice. Anticancer Res 1995; 15: 839 - 46.

5 Wu XG, Zhu DH. Influence of ginseng upon the development of liver cancer induced by diethylnitrosamine in rats. J Tongji Med Univ 1990; 10: 141 - 5.

6 Bespalov VG, Aleksandrov VA, Davydov VV, Limarenko AY, Molokovshii DS, Petrov AS, *et al*. Mammary carcinogenesis suppression by ginseng tissue culture biomass tincture. Experimentalnoi Biologii i Meditsiny 1993; 115: 59 - 61.

7 Yun TK, Choi SY. A case-control study of ginseng intake and cancer. Int J Epidemiol 1990; 19: 971 - 6.

8 Yun TK, Choi SY. Preventive effect of ginseng intake against various human cancers: A case-control study on 1987 pairs. Cancer Epidemiol Biomarkers Prevent 1995; 4: 401 - 8.

9 Ko SR, Choi KJ, Kim MW. Contents of crude saponin and ginsenosides in white ginsengs. Korean J Pharmacog 1989; 20: 170 - 4.

2P3 - 2P8

各种不同年龄人参的皂苷含量及其抗小鼠肿瘤的作用

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关键词 人参；植物根；植物提取物；皂苷类；苯并(a)吡；肺肿瘤；抗肿瘤药；植物源的抗肿瘤药；生药学

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