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Anticarcinogenic Effect of Ginseng Powders Depending on the Types and Ages using Yun's Anticarcinogenicity Test (I)

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Abstract□The authors have already shown that 6 year old red ginseng extract or its powder has remarkable anticarcinogenic effects. In this study, we further investigated whether fresh ginseng or white ginseng has similar anticarcinogenic effects and also if their anticarcinogenic effects are related to the types and ages of ginseng using Yun's anticarcinogenicity test (9 week medium term bioassay model). Dried fresh ginseng and red ginseng at 1.5, 3, 4, 5 and 6 years, and white ginseng at 3, 4, 5 and 6 years were used. The following results were obtained: 1) In the dried fresh ginseng treated groups, the incidence of lung adenoma induced by benzo(a)pyrene was 41.3% and its incidence was reduced to 31.2%, 30.0%, 31.3%, 30.7% and 27.8% after co-treatment with 1.5, 3, 4, 5 and 6 year-dried fresh ginseng, respectively. A significant effect was observed only in 6 year-dried fresh ginseng. 2) In the white ginseng treated groups, the incidence of lung adenoma induced by benzo(a)pyrene was 45.0% and its incidence decreased to 41.3%, 38.0%, 31.6%, and 25.3% after co-treatment with 3, 4, 5 and 6 year-white ginseng, respectively. Five and 6 year-ginsengs showed significant inhibition of lung adenoma. 3) In the red ginseng treated groups, the incidence of lung adenoma induced by benzo(a) pyrene was 48.6% and its incidence diminished to 37.9%, 41.7%, 31.7%, 28.3% and 25.5% after co-treatment with 1.5, 3, 4, 5 and 6 year-red ginseng, respectively. In 4, 5 and 6 year-ginsengs, the anticarcinogenic effect was prominent. From the above results, we concluded that 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 ginsengs.

Key words□Ginseng powder, types and ages, Yun's anticarcinogenicity test, anticarcinogenic effect

Introduction

Ginseng has been used as one of the most valuable natural tonics in the orient for over 2,000 years. Although numerous studies have reported that ginseng has various pharmacological activities, its efficacy is still unclear. Several investigators have demonstrated the anticancer effect of ginseng in various transplantable tumor models using rodents.[1-3]

The authors hypothesized that the life prolongation effect of ginseng described by Shennong of China in the sixth century,[4] may be due to the preventive activity of ginseng against the development of cancers. We have already shown that 6 year old red ginseng extract had remarkable anticarcinogenic effects on lung tumors induced by dimethylbenz(a)anthracene, urethan, and aflatoxin B_1 in long term carcinogenesis models,[5] and that the increment of NK cells may be one of its anticarcinogenic mechanisms.[6] The anticarcinogenicity of red ginseng extract was also shown in Yun's anticarcinogenicity test (9 week medium-term bioassay model induced by benzo(a)pyrene).[7] Therefore, in this study, we further investigated whether fresh ginseng or white ginseng has similar anticarcinogenic effects, and if also their anticarcinogenic effects are related to the types and ages of ginseng using Yun's anticarcinogenicity test.

Materials and Methods

1. Experimental animals

Non-inbred N:GP(S) mice were obtained from the NCI (National Cancer Institute, U.S.A. [NIH]) and bred at random *inter se*. All mice were housed in a controlled room, fed solid pellets prescribed by NIH-7-open formular and given water *ad libitum*.

2. Preparation of ginseng

Fresh ginseng at 1.5, 3, 4, 5 and 6 years was processed in three ways.

① Fresh ginseng was dried at room temperature and finely powdered for dried fresh ginseng.

② White ginseng was processed in the same way as fresh ginseng after removal of the ginseng cortex and fine roots.

③ For red ginseng, fresh ginseng was steamed overnight three times and dried at 50℃.

3. Bioassay of anticarcinogenicity

The present experiment adopted the 9 week medium-term bioassay model established in the author's laboratory, and called 'Yun's anticarcinogenicity test' in our laboratory to distinguish this test from other medium-term bioassay models.

4. Administration of carcinogen

Newborn mice, less than 24 hours old, were injected subcutaneously in the scapular region with 0.02 m*l* of the suspension, containing 0.5 mg of benzo(a) pyrene (BP, Sigma Chemical Co., U.S.A.) in 1% aqueous gelatin.

Table 1. Changes in body and lung weights of mice treated with benzo(a)pyrene, ginseng powders or combination of the two

Experimental groups	Sex	Ginseng powders					
		Fresh ginseng		White ginseng		Red ginseng	
		Boty wt*	Lung wt**	Body wt	Lung wt	Body wt	Lung wt
Untreated control	M	33.9± 2.6	8.1± 1.4	27.7± 3.3	7.9± 2.0	32.5± 2.8	8.5± 1.1
	F	26.9± 2.9	8.3± 1.2	25.0± 6.9	8.6± 2.5	28.4± 2.8	8.5± 1.1
BP	M	32.7± 2.5	8.6± 1.6	35.9± 2.4	7.5± 0.9	32.8± 5.3	8.1± 1.0
	F	26.3± 2.5	9.3± 1.5	29.5± 3.4	8.5± 2.7	27.4± 2.1	9.7± 1.4
1.5 year***	M	34.2± 3.2	7.9± 1.1	–	–	35.3± 3.6	8.6± 1.7
	F	27.3± 2.3	9.5± 1.3	–	–	28.2± 1.8	8.6± 1.4
BP+1.5 year	M	35.0± 2.4	9.0± 1.7	–	–	33.1± 3.1	8.5± 1.3
	F	28.6± 2.7	8.9± 1.5	–	–	26.9± 2.2	8.5± 1.1
3 year	M	34.0± 2.9	9.1± 1.5	31.9± 9.5	6.9± 1.9	35.4± 2.4	8.4± 0.9
	F	26.5± 2.7	10.0± 1.6	28.7± 9.0	7.0± 1.9	29.2± 3.1	8.2± 1.6
BP+3 year	M	33.4± 2.8	8.6± 1.4	33.8± 2.7	8.0± 1.0	34.3± 3.1	8.4± 0.9
	F	28.1± 2.0	9.6± 1.7	29.2± 3.4	8.0± 1.2	27.2± 2.0	8.6± 1.6
4 year	M	33.3± 2.6	9.1± 1.4	32.0± 9.6	7.4± 2.1	34.7± 2.6	8.4± 0.9
	F	27.2± 2.6	10.5± 2.0	27.3± 7.7	8.6± 2.0	27.8± 2.4	8.8± 1.9
BP+4 year	M	32.5± 4.5	8.8± 1.4	33.5± 2.7	7.1± 1.4	32.4± 2.5	8.6± 0.9
	F	27.1± 2.9	9.2± 1.7	28.7± 2.8	7.9± 1.8	27.1± 2.6	9.8± 1.6
5 year	M	32.7± 2.6	8.9± 2.2	34.8± 3.3	7.7± 0.9	35.4± 2.4	8.0± 1.4
	F	27.1± 2.9	10.1± 2.2	26.4± 2.5	9.5± 1.2	28.1± 2.0	9.2± 1.9
BP+5 year	M	32.9± 2.1	8.5± 1.1	33.1± 2.9	7.3± 1.0	33.7± 2.8	7.8± 1.2
	F	24.9± 2.2	9.3± 1.6	35.8± 2.7	7.6± 1.1	26.1± 2.0	9.4± 2.1
6 year	M	32.5± 2.3	9.3± 1.8	34.3± 3.4	7.4± 1.1	34.9± 2.2	7.3± 1.3
	F	25.7± 2.0	9.0± 1.8	25.5± 2.1	9.8± 1.8	28.6± 2.6	9.4± 1.9
BP+6 year	M	31.9± 3.3	8.1± 1.7	35.8± 2.7	7.7± 1.0	32.7± 2.4	8.5± 1.0
	F	26.8± 2.6	8.8± 1.9	28.6± 3.2	8.4± 1.4	26.6± 1.9	8.9± 1.3

Data represent Mean± S.D.
BP : Benzo(a)pyrene.
*Gram, **mg/g body weight, ***Age of ginsengs.
– : 1.5 year-white ginseng treated group was not present.

5. Administration of ginseng powders

After weaning, dried fresh ginseng, white ginseng or red ginseng powders of various ages at a concentration of 5 mg/ml were orally administered in the drinking water for 6 weeks.

6. Scoring of lung tumors

All mice were sacrificed at the 9th week. To determine the number of tumors per lung, the animals were killed by asphyxiation. The lungs were excised, fixed in Tellyesniczky's solution,[8] and the incidence and multiplicity of lung adenoma were counted with the naked eyes.

7. Statistical analysis

Chi-square test was used for tumor incidence and

Table 2. Effect of fresh ginseng powders on the incidence of lung adenoma in mice treated with benzo(a)pyrene

Groups and treatment	Mice		Incidence (%)	Multiplicity (Mean± S.D.)
	Sex	Number		
Untreated control	M	36	0	0
	F	36	1(2.8)	0.03± 0.14
	M+F	72	1(1.4)	0.01± 0.03
Benzo(a)pyrene	M	40	16(40.0)	0.68± 1.08
(BP, 0.5 mg)[1]	F	40	17(42.5)	0.73± 0.37
	M+F	80	33(41.3)	0.70± 0.89
1.5 years[2]	M	38	1(2.6)	0.03± 0.13
(5 mg/ml)[3]	F	38	0	0
	M+F	76	1(1.3)	0.01± 0.08
BP+1.5 years	M	38	11(28.9)	0.34± 0.56
	F	39	13(33.3)	0.56± 1.05
	M+F	77	24(31.2)	0.46± 0.65
3 years	M	38	1(2.6)	0.03± 0.12
	F	38	0	0
	M+F	76	1(1.3)	0.01± 0.03
BP+3 years	M	40	9(22.5)	0.35± 0.58
	F	40	15(37.5)	0.78± 1.39
	M+F	80	24(30.0)	0.56± 0.97
4 years	M	38	0	0
	F	38	1(2.6)	0.03± 0.13
	M+F	76	1(1.3)	0.01± 0.08
BP+4 years	M	40	13(32.5)	0.85± 1.21
	F	40	12(30.0)	0.45± 0.75
	M+F	80	25(31.3)	0.65± 1.07
5 years	M	38	0	0
	F	37	1(2.7)	0.03± 0.13
	M+F	75	1(1.3)	0.01± 0.07
BP+5 years	M	37	11(29.7)	0.43± 0.87
	F	39	12(30.8)	0.62± 1.12
	M+F	76	23(30.3)	0.53± 0.98
6 years	M	38	0	0
	F	37	0	0
	M+F	75	0	0
BP+6 years	M	39	15(38.5)	0.72± 0.78
	F	40	7(17.5)	0.38± 0.60
	M+F	79	22(27.8)*	0.54± 0.68

BP : Benzo(a)pyrene.

[1]Per mouse, subcutaneous injection, [2]Age of fresh ginsengs, [3]ml in drinking water.

Significantly different from BP alone group at *$p<0.05$.

Student's t-test was used for multiplicity, organ and body weight.

Results

Table 1 shows that the animals were tolerated carcinogen or carcinogen combined with various types of ginseng powders. There was no mortality attributable to the treatment, and overall weight gain over the 9 week period was almost the same between control and treated animals. Mean relative lung weight of each group did not show any differences among groups. In dried fresh ginseng powder treated groups, the incidence of lung adenoma induced by BP was 41.3% (33/80) and its incidence was reduced to 31.2% (24/77), 30.0% (24/80), 31.3% (25/80), 30.3% (23/76) and 27.8% (22/79) after co-treatment with 1.5, 3, 4, 5 and 6 year-dried fresh ginseng powders, respectively. A significant effect was observed only in 6 year-dried fresh ginseng powder ($p<0.05$) (Table 2). In the white ginseng powder treated groups, the incidence of lung adenoma induced by BP was 45.0% (36/80) and its incidence decreased to 41.3% (33/80), 38.0% (30/79),

Table 3. Effect of white ginseng powders on the incidence of lung adenoma in mice treated with benzo(a)pyrene

Groups and treatment	Mice		Incidence (%)	Multiplicity (Mean± S.D.)
	Sex	Number		
Untreated control	M	25	0	0
	F	25	0	0
	M+F	50	0	0
Benzo(a)pyrene	M	40	13(32.5)	0.63± 1.21
(BP, 0.5 mg)[1]	F	40	23(57.5)	1.08± 1.70
	M+F	80	36(45.0)	0.85± 1.56
3 years**	M	25	0	0
(5 mg/m*l*)***	F	25	0	0
	M+F	50	0	0
BP+3 years	M	40	11(27.5)	0.35± 0.60
	F	40	22(55.0)	1.05± 1.80
	M+F	80	33(41.3)	0.70± 1.32
4 years	M	25	0	0
	F	25	1(4.0)	0.04± 0.28
	M+F	50	2(2.0)	0.02± 0.14
BP+4 years	M	40	10(25.0)	0.30± 0.57
	F	39	20(51.3)	1.08± 1.57
	M+F	79	30(38.0)	0.68± 0.99
5 years	M	25	0	0
	F	25	1(4.0)	0.04± 0.28
	M+F	50	1(2.0)	0.02± 0.14
BP+5 years	M	40	11(27.5)	0.53± 0.82
	F	39	14(35.9)	0.74± 0.96
	M+F	79	25(31.6)**	0.63± 0.89
6 years	M	25	0	0
	F	25	0	0
	M+F	50	0	0
BP+6 years	M	40	6(15.0)	0.25± 0.57
	F	39	14(35.9)	0.62± 0.79
	M+F	79	20(25.3)*	0.43± 0.70

BP : Benzo(a)pyrene.
[1]Per mouse, subcutaneous injection, [2]Age of fresh ginsengs, [3]m*l* in drinking water.
Significantly different from BP alone group at *$p<0.01$ and **$p<0.05$.

31.6% (25/79), and 25.3% (20/79) after co-treatment with 3, 4, 5 and 6 year-white ginseng powders, respectively. Five and 6 year-ginseng powders showed significant inhibition of lung adenoma ($p<0.05$ and $p<0.01$, respectively) (Table 3). In the red ginseng powder treated groups, the incidence of lung adenoma induced by BP was 48.6% (36/74) and its incidence diminished to 37.9% (22/58), 41.7% (25/60), 31.7% (19/60), 28.3% (17/60) and 25.4% (15/59) after co-treatment with 1.5, 3, 4, 5 and 6 year-red ginseng powders, respectively. In 4, 5 and 6 year-ginsengs, the anticarcinogenic effect was prominent ($p<0.05$, $p<0.02$ and $p<0.01$, respectively) (Table 4).

Table 4. Effect of red ginseng powders on the incidence of lung adenoma in mice treated with benzo(a)pyrene

Groups and treatment	Mice		Incidence (%)	Multiplicity (Mean± S.D.)
	Sex	Number		
Untreated control	M	26	0	0
	F	30	0	0
	M+F	56	0	0
Benzo(a)pyrene	M	36	16(44.4)	0.44± 0.72
(BP, 0.5 mg)[1]	F	38	20(52.6)	0.63± 1.08
	M+F	74	36(48.6)	0.54± 0.96
1.5 years[2]	M	30	0	0
(5 mg/ml)[3]	F	30	0	0
	M+F	60	0	0
BP+1.5 years	M	28	13(46.4)	0.89± 1.21
	F	30	9(30.0)	0.40± 0.68
	M+F	58	22(37.9)	0.64± 1.08
3 years	M	29	0	0
	F	30	0	0
	M+F	59	0	0
BP+3 years	M	30	10(33.3)	0.67± 1.12
	F	30	15(50.0)	0.90± 0.99
	M+F	60	25(41.7)	0.80± 1.06
4 years	M	30	0	0
	F	30	1(3.3)	0.03± 0.21
	M+F	60	1(1.7)	0.02± 0.12
BP+4 years	M	30	10(33.3)	0.83± 1.24
	F	30	9(30.0)	0.50± 0.68
	M+F	60	19(31.7)***	0.67± 0.89
5 years	M	28	0	0
	F	30	0	0
	M+F	58	0	0
BP+5 years	M	30	10(33.3)	0.60± 0.76
	F	30	7(23.3)	0.46± 0.58
	M+F	60	17(28.3)**	0.53± 0.68
6 years	M	28	0	0
	F	30	1(3.3)	0.03± 0.21
	M+F	58	1(1.7)	0.02± 0.12
BP+6 years	M	32	10(31.3)	0.50± 0.66
	F	27	5(18.5)	0.44± 0.54
	M+F	59	15(25.4)*	0.48± 0.62

BP : Benzo(a)pyrene.
[1]Per mouse, subcutaneous injection, [2]Age of fresh ginsengs, [3]ml in drinking water.
Significantly different from BP alone group at *$p<0.01$, **$p<0.02$ and ***$p<0.05$.

Discussion

The present study has shown that anticarcinogenicity of ginseng powders varies according to their types and ages.

The root of *Panax ginseng* C.A. Meyer has been used for several thousand years as a tonic in traditional oriental medicine. Recently, there are some data including the author's about its anticarcinogenic or cancer preventive effect-e.g., chronic administration of *Panax ginseng* extracts to experimental animals was reported to exert a protective effect against chemical carcinogenesis induced by urethan, aflatoxin B1, 3-methylcholanthrene, benzo(a)pyrene, and diethylnitrosamine.[5, 7, 9, 10] Furthermore, we also suggested that the high consumption of ginseng reduced the risk of developing cancer in an epidemiological study.[11] However, red ginseng extract was used in the majority of these studies, and white ginseng or fresh ginseng showed weak or non-anticarcinogenic effect. Therefore, we tried this study to elucidate whether this anticarcinogenic activity of ginseng was exerted only by 6 year old red ginseng extract. First, we tested the powders of various types and ages of ginseng on the effect of development of lung tumor induced by BP over 9 weeks, a model which was established in our laboratory through assessment over the past 10 years [7, 12] and called Yun's anticarcinogenicity test in our laboratory. In the dried fresh ginseng powder treated groups, the incidence of lung adenoma induced by BP was reduced by 24.5%, 27.4%, 24.2%, 25.7% and 32.6% after co-treatment with 1.5, 3, 4, 5 and 6 year-dried fresh ginseng powders, respectively. A significant effect was observed only in 6 year-dried fresh ginseng. In the white ginseng powder treated groups, the incidence of lung adenoma induced by BP decreased by 8.2%, 15.6%, 29.8% and 43.8% after co-treatment with 3, 4, 5 and 6 year-white ginseng powders, respectively. Five and 6 year-ginsengs showed significant inhibition of lung adenoma. In the red ginseng powder treated groups, the incidence of lung adenoma induced by BP was diminished by 22.0%, 14.2%, 34.8%, 41.8% and 47.5% after co-treatment with 1.5, 3, 4, 5 and 6 year-red ginseng powders, respectively. In 4, 5 and 6 year-ginsengs, the anticarcinogenic effect was prominent.

From the above results, we concluded that 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 ginsengs. Therefore, the active components of ginseng which exert anticarcinogenic activity might be present at a higher percentage in older ginseng and in red ginseng. Further study using three types of ginseng extracts is in progress and we hope that more interesting results will be obtained.

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