Short Communication

On the Antitumor Activity of Fresh Green Tea Leaf[†]

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According to the vital statistics provided by the Ministry of Health and Welfare in Japan,^{1,2)} the death rate from cancer (especially stomach cancer) in both sexes in Shizuoka Pref. is much lower than the average for Japanese people. We further investigated this phenomenon epidemiologically and obtained the following results.^{3~5)} (1) The death rate for cancer of all sites and stomach cancer in the midwest areas of Shizuoka Pref. where green tea is the staple product was much lower compared with the national average in both sexes. (2) Significant differences in green tea habits between "3K Town" with a low death rate and "O Town" with a high death rate due to stomach cancer were noted in both sexes. These findings motivated us to further investigate whether fresh green tea leaf has an antitumor activity. The results are described in this paper.

Fresh green tea leaves (*Camellia sinensis* L., *Yabukita*) were lyophilized and pulverized. Fifty grams of the pulverized green tea leaves were extracted with 500 ml of boiling water for 5 minutes. The aqueous extracts were extracted with chloroform to eliminate caffeine and dyes, and were then lyophilized. The dried

powder weighed 9.6 g. This material was dissolved in potassium phosphate buffered saline (pH 7.4) at a certain concentration as a test sample before use. A suspension (0.1 ml; 1×10^7 cells/mouse) of sarcoma 180 ascites was transplanted subcutaneously into the right flank of ICR mice. The mice used were 5 weeks old. For the examination of antitumor activity, the test sample was orally administered once a day for 4 days, starting 24 hrs after tumor implantation of sarcoma 180 cells into the ICR mice. Tumor weight was compared with that of the control (10 mice/group) on the 21st day after the inoculation. Experimental results are shown in Table I. The extracts of the leaves inhibited the growth of mouse sarcoma 180 at a dose of 400 mg/kg by oral administration ($p < 0.05$), the inhibition ratio being about 60% at a level of 800 mg/kg ($p < 0.01$).^{3,4)} Hara *et al.*⁶⁾ reported the suppression of the growth of implanted sarcoma 180 tumors in mice by (–)-epigallo-catechin gallate (EGCg), one of the main components of Japanese green tea. In addition, Kada *et al.*⁷⁾ found that EGCg has an antimutagenic effect on spontaneous reverse mutations in bacterial systems, while Okuda *et al.*⁸⁾ found that EGCg inhibited the

TABLE I. EFFECTS OF FRESH GREEN TEA LEAVES EXTRACT ON THE GROWTH OF MOUSE SARCOMA 180 TUMOR

The extracts of fresh green tea leaves were daily administered to ICR mice orally for 4 days after subcutaneous transplantation of sarcoma 180 cells (1×10^7 cells/mouse). Tumor weight was compared with that of the control (10 mice/group) on the 21st day after inoculation.

Dose (mg/kg/day)	Average tumor ^a weight (g)	Inhibition ratio (%)
0	2.04 ± 0.82	—
200	1.85 ± 1.34	9.3
400	1.02 ± 0.20	50.0 ^b
800	0.82 ± 0.55	59.8 ^c

^a The means $\pm$ S.D. ^b $p < 0.05$. ^c $p < 0.01$.

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mutagenicity of Trp-p-1 from a tryptophan pyrolysate.

Carcinogenic mechanisms are composed of at least two steps, initiation and promotion.⁹⁾ Tomita and Nakamura *et al.*^{10,11)} found that the extracts of Japanese green tea and EGCg inhibited *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine(MNNG)-induced mutagenicity in *Escherichia coli* and decreased the 12-*O*-tetra-decanoyl-phorbol-13-acetate (TPA)-mediated promotion of neoplastic transformation in mouse epidermal JB6 cells *in vitro*. Fujiki and Sugimura *et al.*¹²⁾ demonstrated that EGCg also inhibited the tumor promoting activity induced by teleocidin, a potent promoter, in two-stage skin carcinogenesis experiments with mice. These results suggest that the extracts of green tea leaves and EGCg may have inhibitory effects on both stages of initiation and promotion in carcinogenesis. Furthermore, our epidemiological data indicated that the death rate from cancer of all sites and stomach cancer in the midwest areas of Shizuoka Pref. where green tea is the staple product was much lower than the average of Japanese people in both sexes.^{3~5)} Significant differences in habitual green tea drinking between "3K Town" with a low death rate and "O Town" with a high death rate due to stomach cancer in Shizuoka Pref. were noted in both sexes on the questionnaires such as "times of green tea drinking a day" and "the frequency of making green tea leaves afresh in the tea-pot." That is, this indicated that the inhabitants in "3K Town" seemed to have been much more habitual in drinking green tea compared with those of "O Town."^{3~5)}

Our present data and these results support the possibility that the green tea may play a role in the prevention of cancer formation.

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