

飲酒前後のカキ‘西条’果実摂取がヒト血中のエタノール濃度に及ぼす影響

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Effect of Ingestion of the Japanese Persimmon ‘Saijo’ Fruit on Ethanol Levels in the Blood of Humans and Rats

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The Japanese astringent-type persimmon ‘Saijo’ fruit is considered to contain bioactive compounds that help to alleviate the deconditioning seen after excessive intoxication with alcohol in humans. To evaluate the contribution of ingestion of persimmons in lowering blood ethanol levels in intoxicated humans, we investigated the blood ethanol concentration with the ingestion of persimmons (fresh or semi-dried persimmon fruit and persimmon extract) before or after alcohol consumption (including a comparison with that of apples before alcohol consumption). For rats, we investigated their blood ethanol concentration with the ingestion of persimmon extract before alcohol administration, and also detected the antioxidant activity (measured as ferric reducing antioxidant potential (FRAP)) and flavonoid content in their blood after administration of persimmon extract. Ingestion of persimmons before alcohol consumption significantly reduced human blood ethanol levels compared with control values 1 h after alcohol consumption, and this was even more effective than that observed with apple ingestion. Rat data also suggested the same tendency of persimmon extract, but the difference was not significant. There was no significant difference in the human blood level of ethanol between ingestion of persimmons after alcohol consumption and that of control. In addition, neither an increase in the level of flavonoids nor an increase in antioxidant activity were detected in rat plasma; there was even a slight decrease in FRAP after administration of persimmon extract. Taken together, these data showed that the functional compound kaki-tannin alone or together with other components in persimmon fruit ingested by humans before alcohol consumption was effective in lowering blood ethanol levels. These components are not entirely absorbed to blood capillaries, so they might adsorb the ethanol in the human digestive system to depress the absorption coefficient of ethanol on the surface of the gastrointestinal epithelium.

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Key words : ‘Saijo’ persimmon, drunken sickness, blood ethanol levels, kaki-tannin, gastrointestinal epithelium
西条柿, 悪酔い, 血中エタノール濃度, カキタンニン, 胃腸上皮組織

Persimmon (*Diospyros kaki* Thunb.) has been cultivated in Japan for several centuries, and is thought to have originated in Southern China¹⁾. It contains many bioactive compounds, including carotenoids, tannins, sugars, hydrocarbons, lipids, aromatics, flavonoids, terpenoids, steroids, naphthoquinones, amino acids²⁾ and minerals³⁾. It is also a good source of nutritional antioxidant polyphenols^{4),5)}, β -carotene⁶⁾ and dietary fiber³⁾. The fruit and leaves of the persimmon are used to treat coughs²⁾ and hypertension^{7),8)}. The fruit and leaves of the persimmon as well as extract from the peel also have several health-promoting effects. These include: free radical-scavenging activity⁹⁾; prevention of a rise in the level of lipids in plasma¹⁰⁾; anti-oxidative effects (from the whole fruit³⁾); an improvement in lipid levels in plasma and the liver (from compounds in the leaves¹¹⁾); anti-oxidative and anti-genotoxic effects (from compounds in the peel extracts¹²⁾); and an anti-mutagenic effect against ultraviolet irradiation (found in kaki-shibu (crude kaki-tannin extract) and its tannin-degraded products¹³⁾). Using gas chromatography (GC), OGATA¹⁴⁾ showed that Japanese persimmon 'Fuyu' (sweet-type) fruit juice (including the peel) significantly decreased the ethanol level in blood and alleviated excessive drunkenness in rabbits after alcohol administration. OGATA suggested that the pectin and/or kaki-tannin contained in persimmon fruit juice may "coat" the gastrointestinal epithelium and exert an uptake-inhibitor effect. KOIKEDA *et al.*¹⁵⁾ reported that taking 'Saijo' persimmon extract before drinking alcohol could significantly help in lowering the ethanol concentration in blood for people who have a low tolerance for alcohol.

In the present study, we examined the activity of 'Saijo' persimmon in lowering the concentration of ethanol in blood after administration of the whole fruit or fruit extract to humans or rats. We also established a time-course for absorption of the persimmon extract from the gastrointestinal epithelium to the blood vessels of rats. Using a ferric-reducing antioxidant power (FRAP) assay, we also examined changes in antioxidant activity in the plasma of rats after administration of persimmon extract.

Materials and Methods

1. Ethical approval of the study protocol

The animal studies were approved by the Ethics

Committee for Animal Experimentation at Shimane University (Matsue, Japan). The animals were handled according to institutional guidelines. All subjects provided written informed consent to participate in all experiments in compliance with the certification of the Shimane University Health Administration Center.

2. Reagents and solutions

Ethanol (99.5%) was obtained from Wako Pure Chemical Industries (Osaka, Japan). Distilled water was used to prepare the solutions. The standard curve for calculation of ethanol concentration was prepared in the range of 0.0~400 ppm (326 μ g/ml) using samples of whole blood obtained from each human subject before administration of fruit or alcohol. All standards were prepared at 0 °C. Artificial stomach liquid was prepared with 0.2% NaCl (Wako), 0.32% pepsin (Sigma-Aldrich, St Louis, MO, USA) and adjusted to pH 2 by HCl (0.1% final concentration)^{16),17)}. Purified kaki-tannin was obtained from Maruzen Pharmaceuticals Company Limited (Onomichi, Japan).

3. Plant materials

(1) **Fresh persimmon fruit** We used the mature persimmon (*Diospyros kaki* Thunb. 'Saijo') fruit after removal of astringency. The fruits used were of uniform weight (~200 g/fruit, containing ~1.5% kaki-tannin), without visual defects, and were harvested in Shimane prefecture (Japan). For the measurement of polyphenol content, 'Saijo' persimmon harvested from farm fields in the Shimane prefecture were used. Astringency was removed from fruit by dry ice (1.5% of total fruit weight).

(2) **Semi-dried persimmon fruit** The fresh persimmon 'Saijo' fruit is available only from October to December. It is not available for experimentation during other seasons. JUNG *et al.*⁶⁾ found that the contents of dietary fibers and trace elements in fresh and equivalent quantities of dried persimmon fruit were comparable, and proposed that the latter could substitute for the fresh fruit. We therefore used the semi-dried persimmon fruit (containing 32% of the water content of the fresh fruit) made from the fresh, mature persimmon. This semi-dried fruit was used in the experiments carried out in winter in place of the fresh persimmon 'Saijo' fruit.

(3) **Persimmon extract** The fruit extract was used in the experiments carried out in winter as a substitute for the persimmon fruit. Fruit without

calyces were washed and crushed in a food processor or blender. The crushed fruit was extracted in hot water for 30 min and filtered through a clean cloth. The filtered extract was subsequently centrifuged at 3,000 rpm for 10 min at room temperature, and the supernatant (designated 'persimmon extract') stored at -20°C until use. A 35-ml persimmon extract was equivalent to ~ 200 g of fresh fruit based on the amount of tannin content.

4. Animals

Male WKY / Izm rats (SLC, Incorporated, Hamamatsu, Japan) were used for the alcohol administration experiment. Male Wistar rats (Charles River Laboratories, Tokyo, Japan) were used for the FRAP assay and extraction of flavonoids from plasma. All animals were housed at the Institute of Animal Experiment of Shimane University with a controlled lighting period (lights on from 07 : 00 to 19 : 00). Rats were fed a commercial diet (CLEA Japan, Incorporated, Tokyo, Japan) with tap water *ad libitum* for 1 week.

5. Experimental procedures

(1) Experiment 1 : ingestion of the persimmon fruit before alcohol administration

1) **Human subjects** : The age range of the recruited subjects was 20 ~ 50 years. A study population of 10 individuals (7 males and 3 females) who showed homo- or heterologous expression of the acetaldehyde - dehydrogenase 2 (ALDH2) gene were selected from 20 healthy adults by the results of the alcohol patch test¹⁸⁾ and the score of Tokyo University ALDH2 Phenotype Screening Test (TAST)¹⁹⁾.

This experiment was undertaken using fresh mature (in October), semi-dried persimmon and fresh apple fruit (in February). Each subject was fasted for 10 h before the experiment. At the end of fasting, the first baseline blood sample (5 ml / subject) was taken from each subject (0 h).

In control subjects, each volunteer drank a 90-ml serving of the Japanese alcoholic beverage sake (containing 15~16% or 11.0 g ethanol) over a 15-min period. There was an interval of 5 ~ 7 days between conduction of the control experiment and treatment experiment because the same subject could not repeat alcohol consumption in a short period. In the treatment group, each subject ingested either a single ripe fresh persimmon fruit or two semi-dried persimmon fruits or one fresh

apple fruit 30 min before consuming sake, the same way as in the control subjects.

The second, third, and fourth samples of blood in the control and treatment subject were taken at 1, 2, and 3 h after alcohol administration, respectively.

2) **Rats** : Male rats (age, 24 weeks; 380~440 g) were randomly divided into two groups of five after overnight fasting. The control group received vehicle (distilled water) only, whereas each rat in the test group received a dose of 10 ml / kg of 10% persimmon extract. Persimmon extract was administered orally using a gastric tube (Magensonde) before 30 min of alcohol loading. Both groups were given alcohol (2.0 g / kg). Baseline blood samples were collected before alcohol administration (0 h) and test samples were collected at 1, 2, 4 and 6 h after alcohol loading.

(2) Experiment 2 : ingestion of persimmon fruit after alcohol administration

1) **Human subjects** : A study population of 16 individuals (11 males and 5 females) was chosen from 33 healthy adults using the subject test selection methods described above. The ratio of the sex of subjects (male : female = 2 : 1) was designed to be consistent with that in experiment 1 (i.e., ingestion of the persimmon fruit was before alcohol administration). This experiment was undertaken using persimmon extract of the same persimmon cultivar from the fruit used in the earlier experiments. Each subject fasted for 10 h before the experiment. At the end of fasting, baseline blood samples (5 ml / subject) were taken from each subject (0 h). After drawing the blood sample, each subject immediately drank a 70-ml serving of alcohol ('shochu', containing 25% or 14.3 g ethanol) over a 15-min period. Persimmon extract was not given after alcohol consumption for the control experiments.

After a 2-day interval, each subject repeated the experiment except that, 20 min after alcohol consumption, they drank a 35-ml persimmon extract containing approximately the same concentration of soluble polyphenols found in the whole fruit. The second, third, and fourth blood samples were taken at 1, 2, and 3 h after alcohol administration, respectively.

(3) **Ethanol concentration in blood** Whole blood (0.5 ml) was added to a 5.0-ml screw-cap vial (SY-2 ; Nichiden-Rika Glass, Kobe, Japan). The vial was immediately sealed with a silicone-septum cap,

placed in an incubator at 27°C for 25 min, and heated at 40°C for 30 min in a water-bath. The 25-G needle of a glass syringe (volume, 1ml) was then inserted into the septum. A 0.5-ml volume of the headspace vapor was drawn into the syringe and rapidly injected into the GC port at 210°C.

(4) GC condition The GC analysis was carried out on a GC 14 A series gas chromatograph with flame ionization detector (FID) (Shimadzu, Kyoto, Japan). The GC conditions were as follows: column temperature, 90°C (the retention time of ethanol was ~10.2 min) or 90°C to 150°C (the retention time of ethanol was ~9.4 min: 7 min hold at 90°C, 30°C/min from 90°C to 150°C, and 8 min hold at 150°C); injection temperature, 210°C; detection temperature, 210°C; and helium flow rate, 60 ml/min. A Chromosorb 101 (80/100 mesh) pre-conditioned glass column (1.6 m × 3.2 mm I.D.; Shimadzu) was used. For GC quantification, the peak area of each compound was used. Ethanol was quantified with a calibration curve fit using 0.0~400 ppm (326 µg/ml) ethanol solutions prepared in whole-blood samples from each subject.

(5) Experiment 3: flavonoids levels in the plasma of rats administered persimmon extract

1) Sampling method of the blood for detection of the absorption of kaki-tannin from the gastrointestinal epithelium to the blood vessels:

Each rat (age, 5 weeks; 120~140 g) was fasted for 16 h before the experiments were started. At the end of fasting, a baseline blood sample (3ml/rat) was taken from each rat (0 h), and each rat was immediately given persimmon extract (1ml/rat) using a gastric tube (Magensonde). The second and third blood samples were taken at 2 h and 4 h after administration, respectively.

2) FRAP assay: We carried out the FRAP assay according to the methods of LOTITO and FREI²⁰⁾. In this assay, the antioxidant capacity of plasma was measured as ferric-reducing antioxidant potential using sampled blood.

3) Extraction and determination of flavonoids from plasma: We extracted the flavonoids from the plasma of rats administered persimmon extract according to the methods of SESINK *et al.*²¹⁾. The extract product (20 µl) was analyzed by high-performance liquid chromatography (HPLC). The HPLC system (LaChrom, Hitachi, Tokyo, Japan) was fitted with an ODS-80 Ts column (4.6 × 250mm). The system conditions were as follows: solvent was

varied from 0 min to 10 min with acetonitrile/0.1% formic acid (10:90) followed by 10~20 min with a linear gradient of acetonitrile/0.1% formic acid (10:90) to acetonitrile/0.1% formic acid (30:70) and 20~50 min with acetonitrile/0.1% formic acid (30:70); flow rate, 1ml/min; and electron capture detector (ECD) detection was set at 800 mV.

(6) Experiment 4: changes in soluble polyphenol content in persimmon fruit after incubation in artificial stomach liquid

Persimmon flesh was cut into fine pieces, and ground into paste in a mortar and pestle. Four grams of the fruit paste with 20ml of artificial stomach liquid or distilled water was added to a 50-ml centrifuge tube, and the tube was shaken. The centrifuge tube was incubated in an ultrasonic automatic washer at 37°C for 5 min. After further incubation (without an ultrasonic automatic washer) at 37°C for 0.5, 1, 2, and 3 h, the solution was centrifuged at 10,000 rpm for 30 min at 4°C.

The content of total polyphenols in the supernatant was measured by the Folin-Denis method as described by SWAIN and ELLIS²²⁾. Briefly, 1ml of sample (200 µl of supernatant diluted with 800 µl of distilled water) was made up to 7ml with distilled water, and mixed with 0.5ml of Folin-Denis reagent. After 3 min, 1ml of saturated Na₂CO₃ solution was added. The mixture was made up to 10 ml with distilled water and left at room temperature for 60 min. The absorbance was measured with a spectrophotometer (Hitachi U-1100) at 725 nm. The determination was carried out thrice. The amount of phenolics (expressed as mg catechin/100 g fresh weight) was calculated from a standard curve (0.01~0.1mg catechin/ml) prepared at the same time.

(7) Experiment 5: determination of the adsorption effect of kaki-tannin on ethanol gas/liquid

First, purified kaki-tannin (powder; 100 mg) was sealed in a 6-ml glass vial with an open-top screwcap and Teflon/silicon disk (Nippon Electric Glass, Shiga, Japan). In the control experiment, kaki-tannin was not added. Half a milliliter of saturated ethanol gas or 2 ml of ethanol (99.5%) liquid was added to the sample or control 6-ml vial. The vial was shaken well to ensure mixing. Saturated ethanol gas was prepared as follows. Four milliliters of ethanol (99.5%) solution was sealed in a 19-ml vial and incubated at 35°C for 20 min: the headspace gas was assumed to be saturated ethanol gas.

The ethanol gas concentration and amount of ethanol in ethanol solution in the vials were determined 2 h after incubation. Headspace gas (0.2 mL) or 1 μ l of the solution was injected into the gas chromatograph. The GC condition was identical to that described in Experiment 2 except that the column, injection and detector temperatures were 160°C, 200°C, and 200°C, respectively.

6. Statistical analyses

The mean \pm SE value from experiments was determined. Time - dependent changes in the concentration of ethanol in human blood between control and fresh persimmon or persimmon extract groups was evaluated by two-factor analysis of variance (ANOVA) with only one observation in each cell ($P < 0.05$). Among the controls, semi-dried persimmon and apple, pairwise comparisons were made using the Ryan-Einot-Gabriel-Welsch Q test ($P < 0.05$). Time-dependent changes in the ethanol concentration in rat blood between control and persimmon extract groups were evaluated by one-factor ANOVA ($P < 0.05$). A multiple comparison method for mean values of changes in the FRAP assay in rat plasma among different time points was undertaken using the Tukey-Kramer test ($P < 0.05$).

Results

1. Ingestion of the persimmon fruit before alcohol consumption

(1) **Human subjects** Among the data of 10 subjects, we excluded outlier values from 3 subjects. The mean values of the remaining 7 subjects who had a similar tendency with respect to changes in blood ethanol level were calculated and statistical analyses undertaken.

In the control group, the ethanol concentration in whole blood ($n = 7$) peaked 1 h after alcohol administration and returned to baseline level at 3 h. Blood ethanol levels in the fresh and semi-dried persimmon and fresh apple almost returned to the baseline level by 2 h (Fig.1).

1) **Baseline results before alcohol consumption :** The subjects in each group had whole-blood ethanol concentrations of ~ 0 mg/ ℓ .

2) **One hour after alcohol consumption :** Fig.1-A shows that blood ethanol levels were lower in subjects treated with fresh persimmon (101.85 ± 29.89 mg/ ℓ) than those in the control (184.16 ± 29.27 mg/ ℓ), and that this difference was significant at

the 1% level. Fig.1-B shows that the blood ethanol levels were lowest in the semi-dried persimmon (96.37 ± 15.74 mg/ ℓ), and also that levels in the fresh apple (133.11 ± 14.33 mg/ ℓ) were lower than those in the control group (174.75 ± 13.95 mg/ ℓ). There were significant differences among each treatment and control at the 5% level.

3) **Two hours after alcohol consumption :** In the fresh persimmon group, the ethanol concentrations were lower (8.57 ± 8.57 mg/ ℓ) than in the control group (61.11 ± 28.99 mg/ ℓ), but there was no significant difference at the 5% level (Fig.1 A). In the semi-dried persimmon (16.38 ± 12.38 mg/ ℓ) and fresh apple (17.58 ± 14.69 mg/ ℓ), the ethanol concentrations were almost identical with those in the control group (29.44 ± 19.15 mg/ ℓ) (Fig.1 B).

4) **Three hours after alcohol consumption :** The mean whole - blood ethanol concentration of

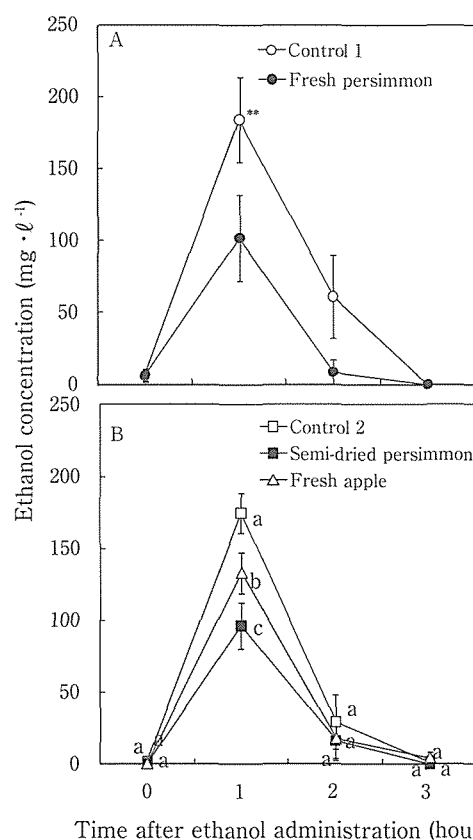


Fig. 1 Time-course of the whole-blood ethanol level in 7 human subjects who ingested fresh persimmon (A), or semi-dried persimmon fruit and fresh apple (B) before alcohol consumption

Each value is expressed as the mean of 7 replications \pm SE. A: ** significant at $P < 0.01$ (two-factor ANOVA); B: pairwise comparisons were made using the Ryan-Einot-Gabriel-Welsch Q test, different letters annotating values within each hour indicate significance at $P < 0.05$ among treatments and control.

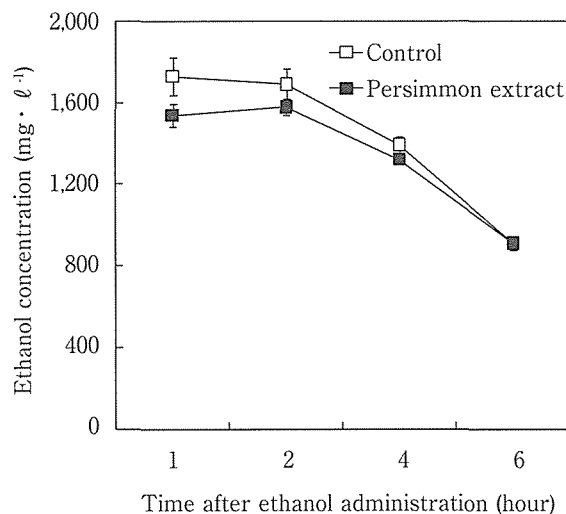


Fig. 2 Time-course of the whole-blood ethanol level in male rats who ingested persimmon extract before alcohol consumption

Each value is expressed as the mean of five replications \pm SE. Significant differences between treatment and control were tested by one-factor ANOVA at the $P < 0.05$ level. Each value was not significant.

subjects in each group returned to baseline levels (Fig.1).

(2) **Rats** Blood ethanol concentrations measured at appropriate intervals after administered alcohol are shown in Fig.2. The peak blood level was reached between 1 h and 2 h after alcohol administration. The persimmon extract group showed lower blood ethanol concentrations 1, 2 and 4 h compared with the control group, though the difference was not statistically significant.

2. Ingestion of persimmon extract after alcohol consumption in human subjects

There was no statistical significance at the 5% level in changes in whole - blood ethanol concentrations ($n = 16$) between persimmon (persimmon extract)-treated groups and control groups 1~3 h after alcohol consumption. However, the results suggested that blood ethanol levels in the treatment group were even higher than those in the control groups 1 h and 2 h after alcohol consumption (Fig.3).

3. Flavonoid levels in the plasma of rats after administration of persimmon extract

In the plasma of rats given persimmon extract, kaki-tannin consisting of four types of catechins was not detectable by HPLC (data not shown), and an increase in FRAP was not seen. However, there

was a slight decrease in antioxidant activity over 4 h (Fig.4).

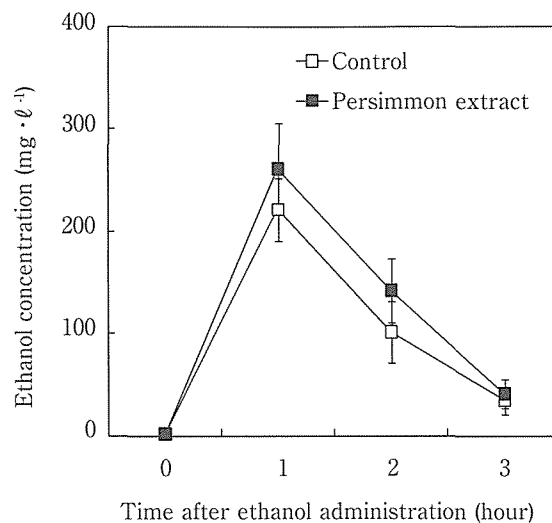


Fig. 3 Time-course of whole-blood ethanol levels in human subjects who ingested persimmon extract after alcohol consumption

Each value is expressed as the mean of 16 replications \pm SE. Significant differences between treatment and control were tested by two-factor ANOVA at the $P < 0.05$ level. Each value was not significant.

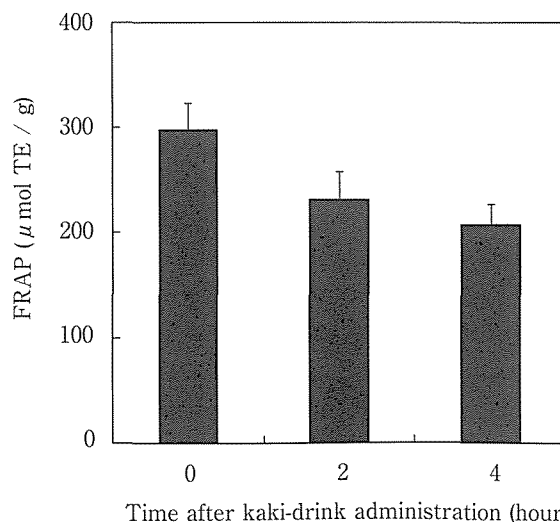


Fig. 4 Time-course of plasma antioxidant capacity in male rats after consumption of persimmon extract

Each value is expressed as the mean of 2~5 replications \pm SE. Statistical analyses were undertaken by one-factor ANOVA at the $P < 0.05$ level. Significant differences among respective time periods were tested by the Tukey-Kramer *post-hoc* analysis. Each value was not significant.

4. Changes in soluble polyphenol content in persimmon fruit after incubation in artificial stomach liquid

There was a larger content of soluble polyphenols in 'Saijo' persimmon extract when it was incubated with artificial stomach liquid than when it was incubated in distilled water. The polyphenol content being incubated with artificial stomach liquid was significantly larger than that when it was incubated with water at 3 h (Fig.5).

5. Adsorption effect of kaki-tannin on ethanol gas /liquid

The level of ethanol gas (0.03mg/ml) after 2-h incubation with kaki-tannin was significantly lower than that in the control (1.5mg/ml) (Fig.6 A). Ethanol liquid after 2-h incubation with kaki-tannin showed no significant difference in ethanol amount compared with that in the control (Fig.6 B).

Discussion

In the present study, we studied the effects of 'Saijo' persimmon in lowering blood ethanol levels after alcohol consumption in humans. The time of ingestion of persimmon fruit, either before or after alcohol consumption, is an important factor in decreasing the ethanol concentration in blood. The effects of different times of fruit ingestion were also distinguished in this work.

Subjects who ingested fresh persimmon fruit before the consumption of alcohol showed a decrease in blood ethanol levels when compared with their corresponding control levels in which they did not receive fruit before drinking sake alcohol. One hour after alcohol consumption, the decrease in blood ethanol levels was significant (Fig. 1 A). The results for the semi-dried persimmon were nearly identical to those for the fresh persimmon (Fig.1 B). We also observed a similar (but not significant trend) in adult rats (Fig.2). Although there was a tendency of lowering blood ethanol levels by administration of persimmon extract in rats, this effect was not significant at the 5% level. This might have been due to the excessively high administration of alcohol, which was almost tenfold that used in humans.

These results that ingestion of persimmon before alcohol consumption can reduce blood ethanol levels are in accordance with those obtained from adult rabbits in the study of OGATA in which the fruit juice and peel of the 'Fuyu' (sweet type) fruit was

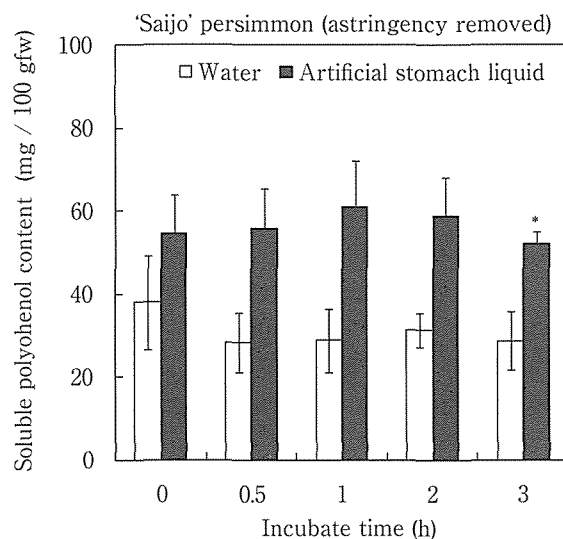


Fig. 5 Time-course of soluble polyphenol content in Saijo persimmon fruit after incubation in distilled water and artificial stomach liquid (pH 2) at 37°C

Each value is expressed as the mean of three replications \pm SE. *significant at $P < 0.05$ (one-factor ANOVA).

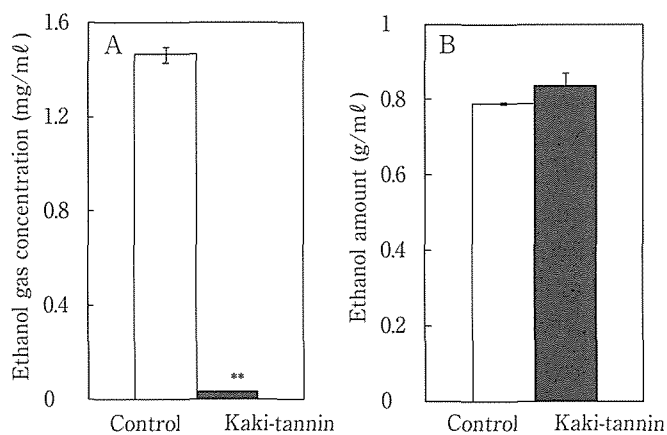


Fig. 6 Ethanol gas concentration (A) or ethanol amount in liquid (B) 2 h after incubation with kaki-tannin at room temperature compared with that in the control

Each value is expressed as the mean of three replications \pm SE.

**significant at $P < 0.01$ (one-factor ANOVA) between kaki-tannin treatment and control.

used; blood ethanol levels were reduced markedly only if fruit juice or peel had been administered 30 min before alcohol administration¹⁴⁾. Conversely, subjects who ingested persimmon extract after consuming alcohol had blood ethanol levels nearly identical to the controls at each time point after alcohol consumption (Fig.3). These results show that the whole-blood ethanol concentrations of subjects were affected only by the ingestion of persimmon fruit before alcohol consumption.

These results suggest that the ingestion of

persimmon fruit before alcohol consumption may alleviate the deconditioning seen after excessive intoxication in humans. KOIKEDA, *et al*¹⁵⁾, also reported that taking 'Saijo' persimmon extract before drinking alcohol could lower the ethanol concentration in human blood. This is an important finding, particularly for subjects who have low tolerance for alcohol, because the reduction in ethanol concentration was significant compared with control values.

However, it remains unclear which components of the persimmon fruit are involved in decreasing blood ethanol levels. According to our *in vitro* study, we showed that kaki-tannin (water-soluble) was extremely efficient in adsorbing ethanol gas (Fig.6 A), but it could not adsorb ethanol liquid (Fig.6 B). It is therefore likely that the highly functional compound kaki-tannin is related to the reduction of ethanol gas but not ethanol liquid in the human stomach. Usually, astringent-type persimmon fruit contains kaki-tannin in an exclusively soluble form (1.5 g/100 gfw [fresh weight]). After the removal of astringents in order to be edible, nearly all of the soluble tannin (high-molecular-weight) condenses to a higher-molecular-weight, insoluble tannin. Insoluble kaki-tannin is then ingested in the stomach, and part of it (15mg/100 gfw) is de-polymerized to soluble

tannin under acid conditions, which was proved by our artificial stomach liquid experiment (Fig.5). Kaki-tannin was not absorbed from the surface of the gastrointestinal epithelium to the blood capillaries in our rat experiments (Fig.4), so we do not think that it plays a part in the ethanol concentration-decreasing effect in the blood and other organs (e.g., liver). Thus, we hypothesize that inside the stomach these de-polymerized soluble kaki-tannins (15mg/100 gfw) with the initial low-molecular-weight polyphenols (30mg/100 gfw; total, 45mg/100 gfw), as well as some dietary fibers (or probably in addition with the insoluble-type tannin) form a type of "film" to adsorb the ethanol gas which is released from the ingested ethanol liquid. This results in the disturbance of total ethanol absorption by the human digestive system (Fig.7). OGATA¹⁴⁾ also proposed that the intoxication-alleviating effect of the persimmon fruit was dependent upon depression of the absorption coefficient of ethanol on the surface of the gastrointestinal epithelium in the presence of persimmon fruit juice. OGATA's hypothesis supports our hypothesis to a certain extent.

Based on the above hypothesis, we might explain the different effects of persimmon and apple in decreasing blood ethanol levels (Fig.1 B). These might be due to the complete deficiency of soluble

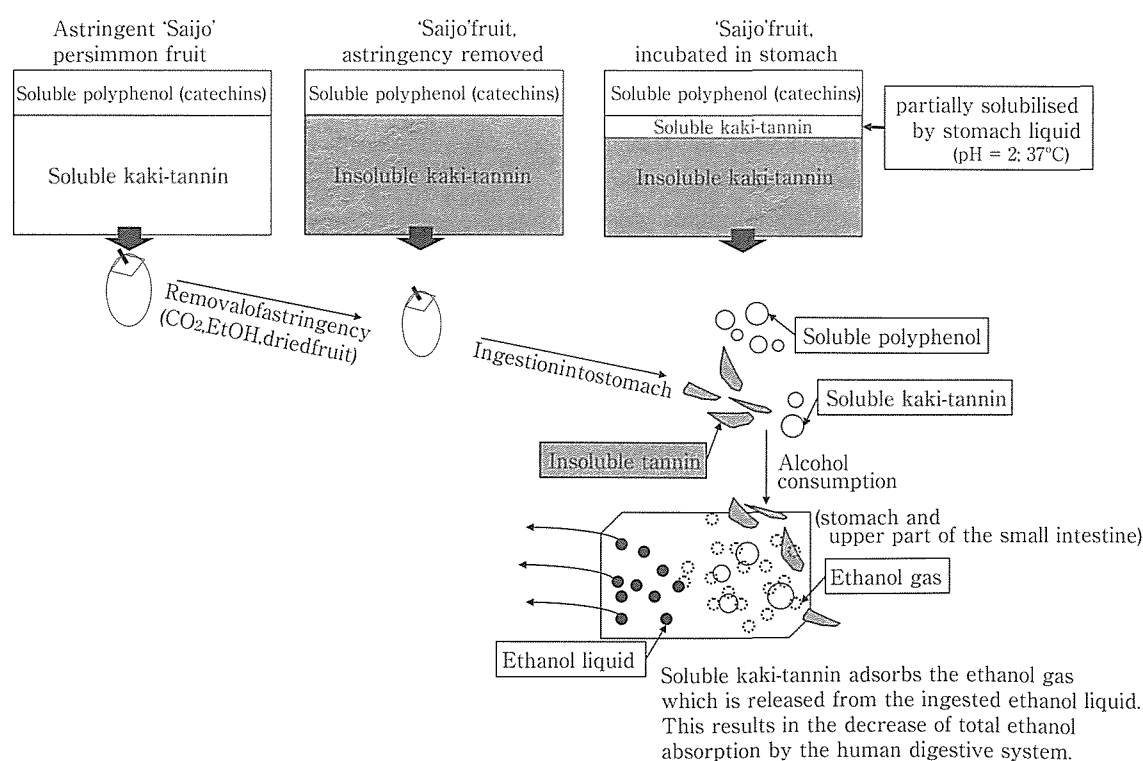


Fig. 7 Interactions of soluble kaki-tannin and ethanol in the human digestive system with respect to reduction in blood ethanol levels after alcohol consumption (schematic)

Table 1 Dietary fibers and tannin (polyphenol) contents in persimmons and apples (g/100 gw)

		Dietary fibers ^z		Tannin ^y		Total polyphenols ^x
		Soluble	Insoluble	Soluble	Insoluble	
Japanese Persimmons	Astringent, raw	0.5	2.3	1.5~2.0	Tr ^w	1.51 ^v
	Astringency removed, raw	0.5	2.3	Tr	1.5	1.51
	Dried	1.3	12.7	Tr	2.2~4.2	7.48
Apples	Raw	0.3	1.2	0	0	1.2~2.4 ^u

^z Data for persimmons and apples are cited from Tables of Food Composition 2009 (Fifth Revised and Enlarged Edition) 2009²³⁾.

^y Data for persimmons are cited from study of TAIRA *et al.*, 1992²⁴⁾, 1998²⁵⁾, and 2008²⁶⁾.

^x In persimmon, total polyphenols contain kaki-tannin and other catechins;

In apple, total polyphenol usually includes variety of soluble flavonoids and other phytochemicals.

^w Tr means the content is trace level.

^v Data for persimmons are cited from study of JUNG *et al.*, 2005⁶⁾.

^u Data for apples are cited from study of BOYER and LIU, 2004²⁷⁾.

kaki-tannin, or both soluble and insoluble tannin in apple. Also, the contents of dietary fibers in apple fruit are lower than that of persimmons (Table 1). Both of these aspects might contribute to the higher efficiency in ethanol alleviation in persimmon.

Future experiments (including those with animals) will be essential for resolving the mechanisms by which the persimmon fruit decreases blood ethanol levels after alcohol consumption in humans.

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飲酒前後のカキ‘西条’果実摂取がヒト血中のエタノール濃度に及ぼす影響

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渋ガキ‘西条’果実は、酩酊したヒトの体調の悪化を緩和できることが知られている。本研究では、カキを摂取することで飲酒後血中エタノール濃度の低下に寄与できるかどうかを評価するために、ヒトを対象に飲酒前後にカキ（カキ果実、あんぼガキまたはカキ抽出液）を摂取したときの血中エタノール濃度を調査するとともに、飲酒前のリンゴ摂取との比較も行った。また、ラットに対して、アルコール摂取前にカキ抽出液を投与して血中濃度を測定した。さらに、カキ抽出液を投与したラットの血漿中の抗酸化力（鉄還元能FRAP値）の変化とフラボノイドの有無を調べた。その結果、ヒトへの飲酒前のカキ摂取において、血中エタノール濃度はアルコール摂取後1時間で対照およびリンゴ摂取よりも有意に低くなった。さらに、アルコール摂取前にカキ抽出液を投与したラットについても、有意差はないものの同様の傾向が

認められた。一方、飲酒後にカキを摂取した被験者の血中エタノール濃度は、対照と比べて有意差が認められなかった。カキ抽出液を投与したラットの血漿中にはフラボノイドは検出されず、FRAP値の増加も認められず、むしろFRAP値は減少する傾向さえみられた。これらのことから、本研究は、飲酒前のヒトに、カキ果実に含まれる機能性成分であるカキタンニンを、単独もしくは他の成分とともに摂取させることによって、血中エタノール濃度を低下させる効果があることを示した。カキの機能性成分は血中に移行しないため、これらはヒトの胃の中でエタノールを吸収し、胃腸の上皮表面からのエタノールの吸収を抑制するものと考えられる。

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