

Clinical effect and safety of oolong tea “ogonkei” for seasonal allergic rhino-conjunctivitis caused by pollen

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A national survey in Japan (1998) reported that the prevalence of seasonal allergic rhino-conjunctivitis was 13–16%. Recently, alternative therapy for allergic rhinitis using natural products has drawn increasing attention. A randomized trial was conducted to confirm the safety and efficacy of oolong tea “ogonkei” for seasonal allergic rhino-conjunctivitis. Adult patients with various symptoms of seasonal allergic rhino-conjunctivitis caused by pollen were tested continuously for six weeks to evaluate the effect of drinking the oolong tea beverage “ogonkei.” In this clinical study, the safety of this beverage was confirmed. Even during the period when pollen counts are high, this oolong tea was confirmed effective for relief of allergy symptoms, such as sneezing ($P<0.05$), nasal discharge ($P<0.001$), nasal obstruction ($P<0.01$), or tears ($P<0.001$). The amount of anti-allergic agent used could also be decreased. Based on the foregoing, it is suggested that drinking oolong tea “ogonkei” daily may be effective, a) allows less use of an anti-allergic agent and b) has an additive effect to attenuate allergy symptoms with anti-allergic agent during the period when so much cedar pollen is airborne.

Key words Oolong tea, Ogonkei, Epigallocatechin gallate, Pollinosis, Allergic rhino-conjunctivitis, Randomized trial.

Introduction

The prevalence of seasonal allergic rhino-conjunctivitis caused by pollen (herewith cedar pollinosis) is 13–16% in Japan (1998).¹⁾ If the prevalence of the cedar pollinosis patient is assumed to be 10%, the annual medical expense is projected to be about 286 billion yen according to a “general study for overcoming pollinosis (1997–1999).”²⁾

Many studies have been conducted on the health benefits of tea, and its effects on cancer, diabetes, hypertension, and other so-called lifestyle-related diseases, have been reported.^{3–5)} Many results have also been reported regarding the relief of allergy symptoms by tea: tea polyphenols and caffeine inhibit I and IV type allergies in rats;^{6–8)} caffeine suppresses the production of tumor necrosis factor- α (TNF- α), and a strong anti-inflammatory effect is shown when mice are stimulated with lipopolysaccharide;⁹⁾ gallated catechins such as (-)-epigallocatechin gallate (EGCG) and (-)-epicatechin gallate (ECG) inhibit histamine release from rat’s mast cell;¹⁰⁾ and saponin inhibits the bronchitis syndrome of guinea pigs.¹¹⁾ Moreover, recent studies have demonstrated that (-)-epigallocatechin-3-*O*-(3-*O*-methyl) gallate (EGCG3”Me) exhibits more anti-allergic effects than EGCG alone.^{12–15)}

Alternative therapy for allergic rhinitis using natural products is drawing increasing attention since allergic symptoms annoyingly interfere with every aspect of daily

life. Many foods such as benifuki extract,¹⁶⁾ *Perilla frutescens* extract,^{17,18)} and lactic acid bacteria^{19–21)} have been reported to affect allergic rhinitis.

We selected a tea variety to evaluate attenuating allergic symptoms by examining an inhibitory effect of a passive cutaneous anaphylaxis (PCA) reaction in rats. A trial against seasonal allergic rhino-conjunctivitis caused by pollen was begun in February before cedar pollen was airborne and March when it peaked in Japan. We report here the effect and safety of this tea beverage in relieving various symptoms of cedar pollinosis.

Materials and Methods

Materials. Ogonkei, tetsukannon (spring flush oolong tea at Fujian, China), houosuisen (spring flush green tea at Guangxi, China), and tocho oolong (spring flush, Taiwan) were obtained from O’will Co. (Tokyo, Japan). Yabukita and benifuki (second flush green tea at Shizuoka, Japan) were obtained from Ito En Ltd. (Tokyo, Japan). Aluminium sulfate octadecahydrate was purchased from Wako Pure Chemical Industries Ltd. (Osaka, Japan), ovalbumin (OVA) and cyproheptadine hydrochloride from Sigma-Aldrich Co. (St. Louis, MO) and Evans blue from Kanto Chemical Co., Inc. (Tokyo, Japan). Experimental rats were purchased from Clea Japan Inc. (Tokyo, Japan). All chemicals were of analytical or guaranteed reagent grade.

Preparation of tea extract for PCA reaction. Twenty

grams of each tea leaf was extracted in 800 ml of distilled water at 90°C for 5 min with moderate agitation. Leaves were removed and quickly cooled to 30°C. The resulting extract was centrifuged at 3,000 g for 10 min and filtered through a 1.0- μ m cellulose acetate filter (Advantec MFS Inc., Tokyo, Japan). The supernatant was freeze-dried and used for PCA reaction.

Preparation of antiserum. Aluminum hydroxide gel (alum) was prepared using the method described by Ouchi.²²⁾ Briefly, aluminium sulfate octadecahydrate (22.2 mg/mL) was gradually added to 100 mL of 2N sodium hydroxide with vigorous agitation. The generated gel was ground with a waring blender, and then centrifuged at 10,000 g for 10 min. The precipitation was washed with distilled water five times, and drying by heating. An antigen sensitization solution (0.1 mL) was adjusted to 0.5 mg/ml of OVA in alum (20 mg/ml in normal saline), and then was injected intraperitoneally into a brown norway rat (7 weeks old, male). Anti-OVA-IgE serum was collected after 14 days.

Determination of anti-allergic activity. Type I allergic activity was evaluated using PCA reaction. Wistar rats (6-7 weeks old, male) were sensitized by intradermal injection of anti OVA-IgE serum (0.1 ml/site, antibody titer 625) on either side of the dorsum, and were challenged by intravenous injection of 0.2 ml OVA (5 mg/ml) and 0.1 ml Evans blue (5 mg/ml) into tail vein after twenty-four h. Tea extracts were administered orally three hours before the challenge. Thirty min after challenge, rats were sacrificed under diethyl ether anesthesia and the back skin was stripped. The diameter in the blue dye leakage area was measured, and the inhibitory ratio of anti-allergic activity was evaluated in comparison with control in the test of each tea variety.^{6,8)}

Test beverage. Ogonkei leaves were extracted in 25 volumes of ion-exchanged water at 95°C for 15 min followed by filtering to remove the leaves. The filtrate was added ascorbic acid (final concentration 400 mg/L) and adjusted to pH 6.2 with sodium hydrogen carbonate solution and 0.35% of soluble solids with ion-exchanged water. The percent soluble solids were measured by DD-7 differential refractometer (Atago Co., Ltd., Tokyo, Japan). This preparation was

heat-sterilized at 130°C for 30 sec with ultra high temperature sterilization and packed in 250 mL plain white tetrapack® (Nihon Tetrapack Co., Ltd., Tokyo, Japan) in the sterile condition. The test beverage contents are listed in Table 1. A preparation diluted to 1/10 the test beverage was used as the control. Three packs a day were imbibed.

Subjects. Persons were targeted who had not received treatment at a medical institution, who frequently admitted suffering from nasal obstruction, tears, throat pain, and sneezing (2002-2004), and showed a positive seasonal reaction to specific IgE of cedar pollen. A total of 24 persons (17 healthy adult men, 7 women, (20 to 51 years old, average 26.8 ± 9.6) were enrolled.

Two groups were randomly selected for the oolong tea or control group. No deviation was observed in height, weight, and specific IgE antibody level of cedar pollen between the groups. A code for each of the two beverages was assigned to each subject, and was not disclosed to either the contracted test organization or the test conducting organization until testing was completed.

Since 6 subjects dropped out after week 4, 18 subjects (11 men and 7 women of 20 to 51 years old, average 28.8 ± 10.3) were tested. Personal reasons were cited by the dropouts; neither the oolong tea beverage nor any symptom exacerbation was the cause. There were no changes in the background factors of the dropouts, such as age and specific IgE antibody level of cedar pollen.

Trial schedule. The trial schedule is shown in Fig. 1. The protocol was reviewed and approved by an institutional review board (Hyakusai Clinic, Tokyo, Japan), and experiments were performed in accordance with the Helsinki Declaration. The trial duration was 6 weeks. Blood test, urine test, medical examination, blood pressure measurement, weight measurement, body fat measurement, and an electrocardiogram were performed in the evening prior to the test (week 0), then at week 2, week 4, and week 6. Subjects were instructed not to take other supplements, including tea (green tea, black tea, oolong tea, jasmine tea, tien tea (*Rubus suavissimus*), mixed tea, pu-er tea), nutrition drink agent, amino acid beverages, lactobacillus beverages, coffee, cocoa, cola, drinks containing caffeine as well as anti-allergic agents. However, continuation of vitamin tablets was admitted on the condition that the dose was maintained.

Distribution of masks and emergency alternative medicine. To prevent sudden exposure to cedar pollen, subjects also wore a mask (Iwatsuki Co., Ltd., Tokyo, Japan) as

Table 1 Catechin and caffeine composition of test beverage

constituents	mg/pack (250 ml)
(-)-epigallocatechin gallate (EGCG)	32.0
(-)-epigallocatechin (EGC)	16.9
(-)-epicatechin gallate (ECG)	6.1
(-)-epicatechin (EC)	5.4
(-)-gallocatechin gallate (GCG)	29.7
(-)-gallocatechin (GC)	29.4
(-)-catechin gallate (CG)	4.7
(+)-catechin (+C)	5.7
(-)-epigallocatechin-3-O-(3-O-methyl) gallate (EGCG3"Me)	3.5
(-)-gallocatechin-3-O-(3-O-methyl) gallate (GCG3"Me)	4.5
caffeine	52.2

Tea catechins and caffeine were analyzed with HPLC.²⁴⁾

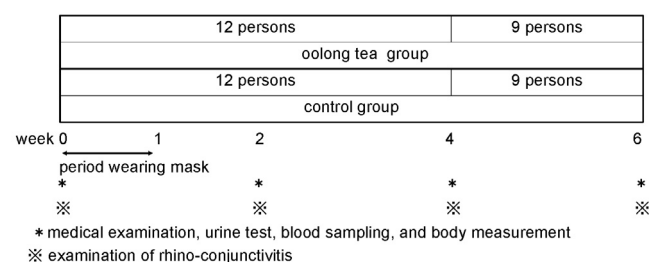


Fig. 1 Trial schedule for seasonal allergic rhino-conjunctivitis caused by pollen.

provided by the test conducting organization for seven days when going outside. Thereafter, it was prohibited to wear the mask. In consideration of quality of life (QOL), emergency alternative medicine was distributed to subjects beforehand as recommended at the nasal allergy medical examination and treatment guideline.¹⁾

When symptoms of cedar pollinosis became intolerable, subjects were permitted to use emergency alternative medicine, anti-histamine, upon examination by the doctor responsible.

Two tablets of Clemastine fumarate (Tavegil) (Novartis Pharma K. K. Tokyo, Japan) per day were permitted for rhino-conjunctivitis, and up to 4 cromolyn sodium eyedrops (Intal) (Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan) a day for eye symptoms. These medications were available only by doctor's prescription, and had to be entered in the patient's record.

Subjective symptoms. Subjects were each given a diary to record their daily routine during the intake period, and they were asked to record meals (frequency and amount), exercise amount, bowel movement, and sleeping time. They were also to enter subjective symptoms such as sneezing, nasal discharge, nasal obstruction, itchy eyes, tears, and disturbance of any daily living activities to allow a full understanding of their symptoms. For a description of symptoms, refer to Table 2-1, and to Table 2-2 for the evaluation criteria for sneezing and nasal discharge.

Table 2-1 Description of symptoms for diary

Symptom	Evaluation
Sneezing	Number of sneezing fits (counting 3 continuous sneezes as one fit)
Nasal discharge	Enter frequency with blowing your nose.
Nasal obstruction	3: Virtually impossible to breathe with nasal obstruction. 2: Hard to breathe with nasal obstruction. 1: Nose is little stuffed up. 0: No nasal blockage.
Itchy eyes	3: Often rub my eyes. 2: Sometimes rub them. 1: Not itchy enough to rub. 0: No itchy symptoms.
Tears	3: Often wipe tears away. 2: Sometimes wipe tears away. 1: Not enough to wipe. 0: No watery symptoms.
Disturbance of daily living activities *	3: Feel bad. Can't concentrate on my work. 2: Feel bad. 1: Feel somewhat bad. 0: Don't feel bad.

All symptoms were evaluated three times a day, in the morning, daytime and night.

* Disturbance of daily living activities involves work, study, housework, sleeping, and going out.

Table 2-2 Evaluation criteria for sneezing and nasal discharge

Symptom \ Level	3	2	1	0
Sneezing	over 11 fits	10-6 fits	5-1 fits	0 fits
Nasal discharge	over 11 times	10-6 times	5-1 times	0 times

Nasal discharge indicates frequency of blowing nose per day.

Method for adding points regarding medications.

Subjects recorded the number of tablets and frequency of eyedrops in their symptom diary. When clemastine fumarate was taken, 30 points were added to scoring of the frequency of sneezing, and 20 points to the frequency of nasal discharge per day. The highest score for a nasal obstruction was 9 points a day. When cromolyn sodium was applied, the highest score on a day of itchy eyes and tears was 9 points. Whichever medicine was used, the maximum score was 9 points for the disturbance of daily living activities.

Immune and safety examination. Blood sampling was performed in the evening (5-6 pm), when subjects had refrained from eating and drinking for 2 hours. Biochemical tests, immune response tests, and urine tests (protein, occult blood, urobilinogen, and sugar) were performed. Blood analysis was performed in Kotobiken-Medical Laboratories Inc. (Tokyo, Japan).

Safety. The presence or absence and level of health hazards, observation of body condition, and transition in clinical examination or vital signs, all of which factors originated in the oolong tea beverage, were taken as a whole, and the safety was evaluated in four stages according to Table 3.

Statistical analysis. The anti-allergic effects of model rats were analyzed by Bonferroni's multiple comparison test. In the clinical study, comparisons between groups were made using Student's t-test for sleeping times, weight, body mass index (BMI), body fat and blood pressure, and using Mann-Whitney's U test for bowel movement and nose or eye symptoms. Comparisons to week 0 were made using paired t-tests for sleeping time, bowel movement, weight, BMI, body fat and blood pressure. Multiple comparison of each blood inspection was performed by Dunnett test after executing a one-way ANOVA. The significance level was 5% or less with a two-sided test. Data were analyzed using SPSS Ver.13.0J (SPSS Japan Inc., Tokyo, Japan).

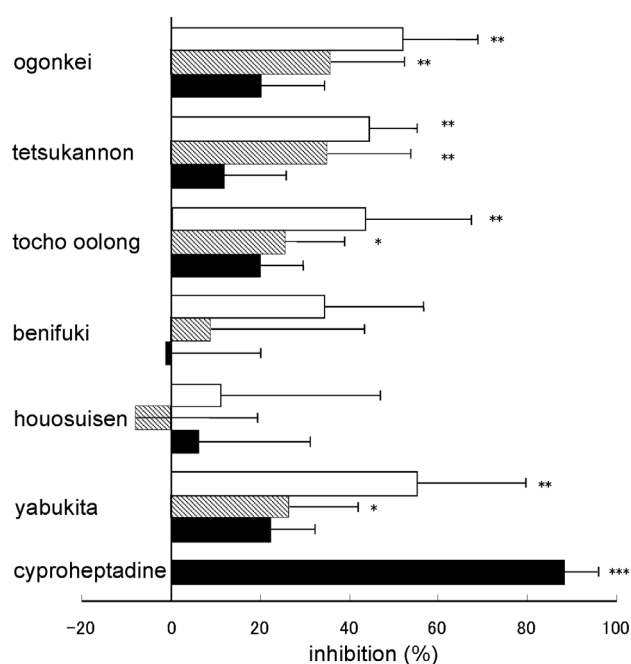
Table 3 Level of safety

Stage	Diagnosis	Details
1	Safe	No side effect at all.
2	Almost safe	Trial could be continued without some treatment by doctor despite slight side effects.
3	Some problems	Trial continued although doctor treated some side effects.
4	Unsafe	Trial discontinued or should have been because of some side effects.

Results

PCA reaction. PCA reaction on some kind of tea varieties, showed that ogonkei, tetsukannon, tocho oolong and yabukita had a higher inhibitory effect, dose-dependently. However, the contents of EGCG, and EGCG3"Me were the highest in houosuisen, which had a lower inhibitory effect. There was no correlation between the effect and the contents of each known active ingredient (Fig. 2).

Clinical trial. The oolong tea "ogonkei", which has a



	EGCG	total catechins	EGCG3'Me	caffeine
ogonkei	12.62	24.79	1.29	14.18
tetsukannon	10.97	25.04	0.78	14.95
tocho oolong	15.28	30.34	0.61	13.82
benifuki	18.69	36.35	1.65	11.26
houosuisen	25.37	36.25	2.12	14.81
yabukita	16.02	29.39	0.05	10.39

Fig. 2 Anti-allergic effect of various tea varieties from PCA reaction in rats.

Data are presented as means $\pm$ standard deviation (n=8). Cyproheptadine was examined as the positive control (n=3). There were significant differences from 0 mg/kg (control). *P<0.05, **P<0.01, ***P<0.001, Bonferroni's multiple comparison test.

□ 100 mg/kg; ▨ 30 mg/kg; ■ 10 mg/kg

The table indicates the content in freeze-dried tea extract being used for the PCA reaction. Data are presented as means of duplicate experiences. Total catechins indicate the sum of EGCG, EGC, ECG, EC, GCG, GC, CG, and +C.

better smell like orange osmanthus, and inhibitory effect on PCA reaction was used for the clinical trial on allergic rhino-conjunctivitis.

The distribution of airborne cedar pollen is shown in Fig. 3. The pollen count was lower from week 1 to week 4, and suddenly higher counts were measured at week 5 to 6 when the temperature rose dramatically. No concomitant health

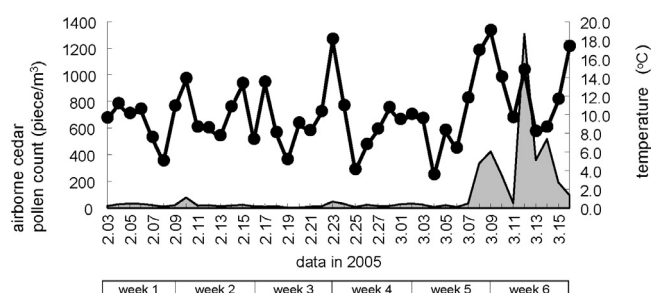


Fig. 3 Amount of airborne cedar pollen in Tama area

The Tama area (Hachioji City and Tama City, Metropolitan Tokyo) where most subjects resided was monitored using the pollen conditions system of the Ministry of the Environment. Airborne cedar pollen (solid); Temperature (●)

hazards or accompanying difficulties such as stomachache due to caffeine were mentioned in the subjects' diary. Changes in sleeping hours and bowel movement are shown in Table 4. Bowel movement was graded as normal, 1; few, 0.5; and none, 0. There was a significant difference between sleeping time in the oolong tea group at week 5 (P<0.01) and the control group at week 2 (P<0.05) by comparing with week 1. Moreover, significant differences were recognized between the oolong tea and the control group at week 5 to week 6 (week 5: P<0.01; week 6: P<0.05) in sleeping time. A significant difference was also found between groups at week 6 (P<0.05) in bowel movement. Although significant differences were recognized for both sleeping time and bowel movement, no clinical problems were found.

The subjective symptoms and disturbance level in daily life in terms of the frequency of nose and eye problems were totaled once a day, including morning, daytime and evening, and the weekly averages are shown in Fig. 4. Improvements in some symptoms were recognized in the oolong tea group. Relief of perennial allergy symptoms was also confirmed from a decrease in the scores for sneezing, nasal obstruction, itchy eyes, tears and disturbance from week 2, a time of little airborne cedar pollen, to week 3 as compared to week 1. Subjects' radioallergosorbent test (RAST) values against non-specific IgE, house dust, and cedar pollen were evaluated, and the following were measured as blood immune functions; CD4, CD8, CD4/CD8, CD16, CD56, Th1, Th2, Th0 (IFN γ + and -), Th1/Th2 and eosinophil cationic protein (ECP). There was no significant difference between and within groups.

Table 4 Sleeping time and bowel movement

	Group	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Sleeping time (hr)	Oolong	6.8 $\pm$ 1.6	6.7 $\pm$ 1.4	6.6 $\pm$ 1.5	6.4 $\pm$ 2.0	6.1 $\pm$ 1.3**††	6.4 $\pm$ 1.9†
	Control	7.0 $\pm$ 1.2	6.6 $\pm$ 1.2*	6.7 $\pm$ 1.4	6.8 $\pm$ 1.3	6.8 $\pm$ 1.5	6.9 $\pm$ 1.5
Bowel movement	Oolong	0.8 $\pm$ 0.3	0.8 $\pm$ 0.3	0.8 $\pm$ 0.3	0.8 $\pm$ 0.3	0.7 $\pm$ 0.4	0.7 $\pm$ 0.7+
	Control	0.9 $\pm$ 0.3	0.9 $\pm$ 0.3	0.9 $\pm$ 0.3	0.8 $\pm$ 0.3	0.8 $\pm$ 0.3	0.8 $\pm$ 0.3

Data are presented as means $\pm$ standard deviation (week 1-4: n=12, week 5-6: n = 9)

Significant difference from week 1 (*P<0.05, **P<0.01: paired t-test)

Significant difference compared between groups in sleeping time (†P<0.05, ††P<0.01: Student's t-test)

Significant difference between groups in bowel movement (+P<0.05: Mann-Whitney's U test)

Bowel movement was calculated as normal, 1; few, 0.5; and none, 0.

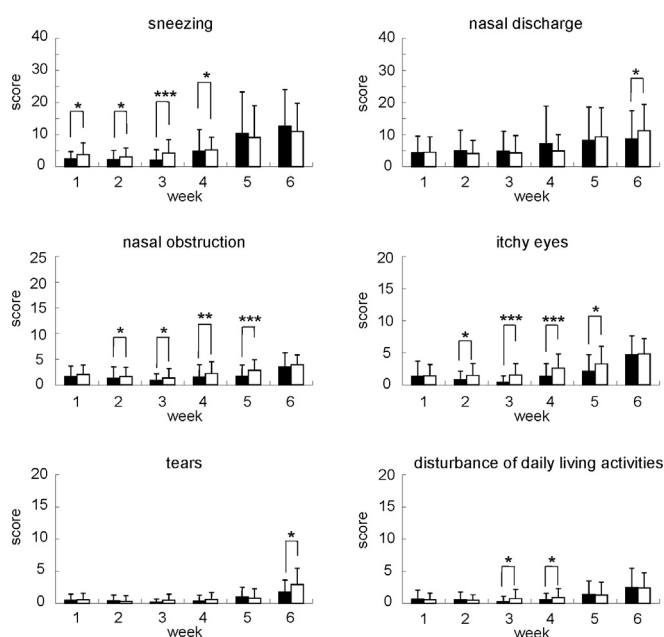


Fig. 4 Effect on subjective symptoms before considering emergency alternative medicine.

Score was the weekly average of subjective symptoms. All symptoms were evaluated according to Table 2-2 three times a day, in the morning, daytime and night. The daily score was the sum of three times.

Data are presented as means $\pm$ standard error (week 0, 2, 4: n=12, week 6: n=9)

Significant differences between groups (*P<0.05, **P<0.01, ***P<0.001: Mann-Whitney's U test).

■ oolong tea group; □ control group

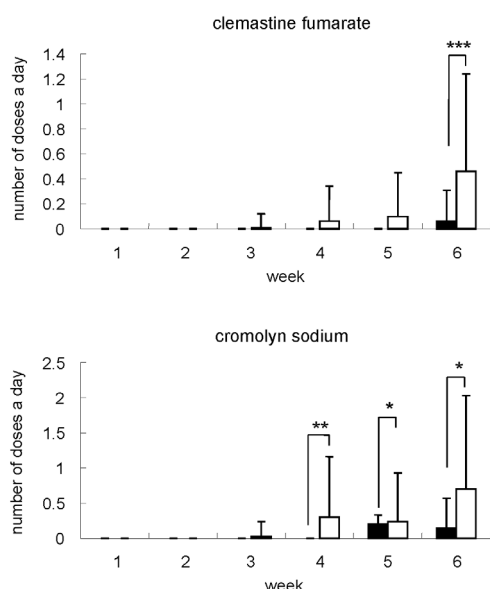


Fig. 6 Frequency of using the rescue medicine.

The number is weekly average of daily dose per person.

Data are presented as means $\pm$ standard error (week 0, 2, 4: n=12, week 6: n=9)

Significant differences between groups (*P<0.05, **P<0.01, ***P<0.001: Mann-Whitney's U test)

■ oolong tea group; □ control group

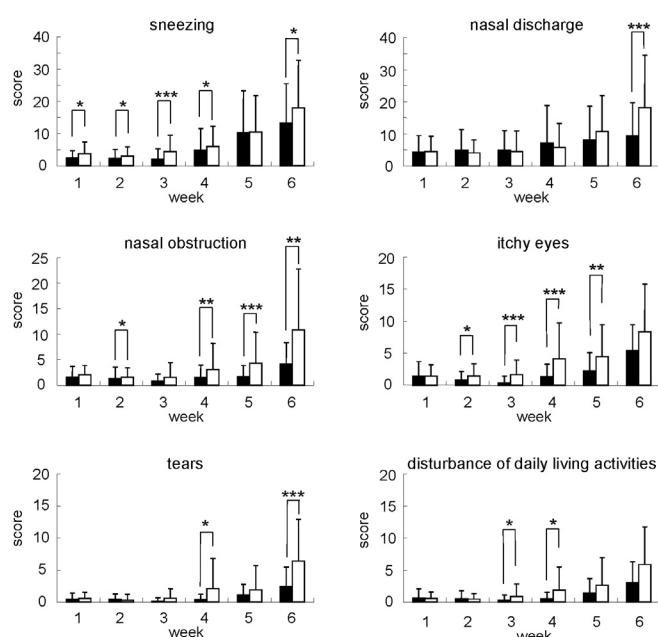


Fig. 5 Effect on subjective symptoms after considering the rescue medicine.

When clemastine fumarate was taken, 30 points were added to scoring of the frequency of sneezing, and 20 points to the frequency of nasal discharge per day. The highest score for a nasal obstruction was 9 points a day. When cromolyn sodium was applied, the highest score on a day of itchiness and tears was 9 points. Whichever medicine was used, the maximum score was 9 points for the disturbance of daily living activities.

Data are presented as means $\pm$ standard error (week 0, 2, 4: n=12, week 6: n=9)

Significant differences between groups (*P<0.05, **P<0.01, ***P<0.001: Mann-Whitney's U test)

■ oolong tea group; □ control group

The number of clemastine fumarate and cromolyn sodium applications are shown in Fig. 6. In the oolong tea group, no subject used either medication until week 4. One subject used cromolyn sodium at week 5 and two subjects used both cromolyn sodium and clemastine fumarate at week 6. In the control group, one subject used both medications at week 3, when airborne distribution of cedar pollen had begun. One subject used both medications and another used only cromolyn sodium at week 4. One subject used both medications and two subjects used only cromolyn sodium at week 5, and three persons used both medications at week 6. The dosage of both medicines increased as the pollen count increased. Subjective symptoms and the disturbance level of daily living activities, which were considered emergency alternative medicine, are shown in Fig. 5. Improvements in symptoms were recognized in the oolong tea group. Even at week 6 when pollen counts are high, the oolong tea group was confirmed effective for relief of allergy symptoms on sneezing (P<0.05), nasal discharge (P<0.001), nasal obstruction (P<0.01), and tears (P<0.001).

Medical examination revealed no contribution of the test beverage to health hazards. No significant difference was found in weight, BMI, body fat, and blood pressure. Electrocardiographic findings indicated no problem.

Biochemical tests and urine tests were performed. The

Table 5 Profile of blood component with significant difference

	Standard	Unit	Group	Week 0	Week 2	Week 4	Week 6
Blood function							
Eosinophils	1—5	%	Oolong	2 ± 2	2 ± 1	3 ± 1	4 ± 3 *
			Control	3 ± 2	3 ± 2	3 ± 2	5 ± 3
MCH	28.2—34.7	pg	Oolong	30.9 ± 1.7	29.5 ± 1.8	29.9 ± 1.5	30.0 ± 1.7
			Control	30.4 ± 0.8	29.3 ± 0.6**	29.6 ± 0.8 *	29.2 ± 0.7**
MCHC	31.8—36.4	%	Oolong	34.2 ± 1.0	33.0 ± 1.3*	33.5 ± 1.0	32.9 ± 1.1*
			Control	33.6 ± 0.9	33.1 ± 0.9	33.2 ± 0.9	32.7 ± 1.0
Serum chemistry							
Total protein	6.5—8.2	g/dl	Oolong	7.6 ± 0.3	7.4 ± 0.3	7.3 ± 0.3 ††	7.3 ± 0.3*
			Control	7.7 ± 0.5	7.7 ± 0.5	7.7 ± 0.4	7.7 ± 0.5
A/G ratio	1.00—2.00		Oolong	1.71 ± 0.20	1.77 ± 0.26	1.91 ± 0.33	1.92 ± 0.29
			Control	1.65 ± 0.19	1.71 ± 0.18	1.84 ± 0.21*	1.68 ± 0.17
Potassium	3.5—5.0	mEq/l	Oolong	4.1 ± 0.3	3.9 ± 0.3	3.9 ± 0.3	3.7 ± 0.3*
			Control	4.0 ± 0.3	3.9 ± 0.2	4.0 ± 0.2	3.8 ± 0.2
Chloride	98—108	mEq/l	Oolong	103 ± 2	103 ± 2	104 ± 2 †	102 ± 2
			Control	102 ± 1	102 ± 1	102 ± 2	101 ± 1

Data are presented as means ± standard deviation (week 0, 2, 4: n=12, week 6: n=9)

Significant difference from week 0 (*P<0.05, **P<0.01: Dunnett test)

Significant difference between groups (†P<0.05, ††P<0.01: Student's *t*-test)

following were measured: leukocytes, neutrophils, eosinophils, eotaxin, monocytes, lymphocytes, erythrocytes, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean cell hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet as blood function, and total bilirubin, direct reacting bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), γ -glutamyl transpeptidase (γ -GTP), glucose, creatine phosphokinase (CPK), total protein, albumin, A/G ratio, urea nitrogen, creatinine, sodium, potassium, chloride, total cholesterol, and neutral fat as serum chemistry. The items with a significant difference are shown in Table 5. No significant change outside the standard value range was observed, so no health hazards resulted from this oolong tea beverage, no abnormalities of clinical laboratory test were noted, and there were no safety problems.

Discussion

EGCG, EGCG3"Me, and caffeine have been shown to inhibit PCA reaction of rodents in earlier studies.^{6-8,12-14)} Six tea varieties were examined in the present study, suggesting that ogonkei could provide a higher inhibitory effect on type I allergic reaction such as perennial and seasonal allergic rhino-conjunctivitis. Also, there were no correlations between the effects and content of each of the known active ingredients. These findings indicate that tea varieties having a lower inhibitory effect may include some competitive substances against active ingredients.

We selected the oolong tea "ogonkei" to evaluate the effect on attenuating allergic symptoms due to having better smell like orange osmanthus and anti-allergic activity on

PCA reaction. First of all, in an earlier open study against perennial allergic rhino-conjunctivitis, volunteers took three times the standard dose of the oolong tea "ogonkei" for two weeks, and no side effects were observed. Moreover, the rate of improvement of nose symptoms (sneezing, nasal discharge, and nasal obstruction) was 30%, with an overall improvement factor of 35%. The findings of the study suggested that the oolong tea "ogonkei" beverage provided effective alternatives to relief of allergic rhino-conjunctivitis symptoms within a short intake period of 14 days.²³⁾

This time, eighteen healthy adults excluding the drop-outs continuously took the prescribed amount for one day (3 packs/day) for six weeks, and each subjective symptom, medical examination, body measurement, blood test, urine test, and electrocardiogram was examined to confirm the efficacy and safe relief of cedar pollinosis by intake of the oolong tea "ogonkei" containing epigallocatechin gallate. Regarding safety, no excessive symptoms caused by compounds in the test beverage had any serious adverse effects on health. Nor were there any health hazards that caused difficulties judging from the symptom diary. The hematological test revealed no significant change, and since all changes were within the standard range, it was considered that there was no problem especially in terms of safety. The biochemical test pointed out a significant change in the total proteins within and between groups, or in total cholesterol between groups. However, since these were changes within the normal range, no safety problems were posed. Although some subjects' CPK exceeded the standard values, the diary record would suggest the increase in the amount of subject exercise, not to the test beverage. When an allergen invades the body, a type I allergic reaction takes place because of physiologically active substances such as cytokines that are

produced and discharged by activation of immunocompetent cells. From the immune response test, no significant change was found in the IgE of non-specific, house dust, and cedar pollen. Therefore, it was thought that there was no safety problem even with intake of this beverage.

A significant difference in clinical efficacy was found in all symptoms, i.e. sneezing, nasal discharge, nasal obstruction, itchy eyes, tears, and disturbance of daily living activities. Although relief of such conditions was seen after week 2 and week 3 with little dispersion of airborne cedar pollen in the oolong tea group, this was thought sufficient to relieve perennial rhino-conjunctivitis. As to the frequency of medications, three subjects in the control group took clemastine fumarate, and two persons took clemastine fumarate every day at week 6 while one did so continuously for the last four days. One subject in the oolong tea group took it continuously over the last three days. The reason for no significant difference in symptoms between groups at week 6 was presumably because the subjects' symptoms had been relieved in the control group by the medications. Consequently, when the medications were totaled, there were significant differences in symptoms, except for the disturbance level. Also, despite the extremely high pollen count at week 5 and 6, the symptoms were alleviated among those taking the test beverage and they experienced little hindrance in their daily lives, explaining why they took medications less frequently. Thus, it was thought that medical treatment expenses could be reduced.

A key factor was thought to be that they had taken the beverage 3 weeks before the heavy cedar pollen period began, and thus their symptoms were readily alleviated. It is, therefore, suggested from the result of the intake period (42 days) that the oolong tea "ogonkei" is a beverage which can attenuate these cedar pollinosis symptoms together with anti-allergic agents.

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