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Inhibition by Dietary Tea Polyphenols of Chemical Mediator Release from Rat Peritoneal Exudate Cells

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Male Wistar rats were given purified diets containing safflower (SAF), perilla (PER), or palm (PAL) oils with or without 1% tea polyphenols (TP) for 3 weeks, and chemical mediator releasing activity from rat peritoneal exudate cells (PEC) was measured. Histamine releasing activity was not influenced by TP, while histamine release and intracellular histamine content were significantly increased in the PAL-fed group. On the contrary, leukotriene B_4 (LTB_4) release was significantly lower in rats fed PER than in those fed SAF and PAL, and TP significantly decreased the release in all fat groups. TP also significantly inhibited the release of LTB_5, which was generated only in rats fed PER. TP significantly decreased the proportion of arachidonic acid (AA) in PEC in the SAF-fed group and that of eicosapentaenoic acid (EPA), the precursor of LTB_5 in the PER-fed group, but did not influence that of AA in the PAL- and PER-fed group. These results suggest that ingestion of TP improves type I allergic symptom through the inhibition of LT release though the inhibition by TP could not be totally explained by the reduction of substrate fatty acid.

Key words: dietary fats; tea polyphenols; histamine; leukotriene; peritoneal exudate cells

Recently, there has been an increasing incidence of allergic disorders from food or air-borne allergens.[1-3] According to Coombs and Gell,[4] allergic reactions are divided into four types, and the immediate hypersensitive reaction is generally classified as a type I allergy. The allergic reaction includes a series of events; production of allergen-specific IgE, its binding to the FcεRI receptor on the surface of mast cells or basophils, cross-linking of IgE by newly absorbed allergens, and a release of chemical mediators from these cells.[5,6] The pathogenesis is induced by histamine release after degranulation of mast cells and by newly generated mediators such as prostaglandins and leukotrienes (LT) as well. Inhibition of any steps of these sequential reactions may attenuate allergic symptoms. In fact, several agents such as corticosteroids, epinephrine, histamine antagonists, and LT synthesis inhibitors exert an antiallergic potential through the specific inhibition of these reactions.[7]

Foods contain many physiological factors that may prevent the incidence of several diseases and may promote our health, in addition to their functions as nutrients. For example, dietary fats can modulate atherogenesis,[8] carcinogenesis,[9] and inflammatory reactions.[10] Tea polyphenols (TP) have many physiological and pharmacological functions such as antioxidative,[11,12] antibacterial,[13] antifungal,[14] antiviral,[15] antiatherogenic,[16] and anticancer[17-20] activities.

In addition to these preferable functions of TP, we also reported that TP inhibit the release of histamine, a typical preformed mediator, and LTB_4, a newly generated mediator, from rat peritoneal exudate cells (PEC) and rat basophilic leukemia (RBL-2H3) cells *in vitro*.[21,22] In this study, the effects of dietary TP on chemical mediator release from rat PEC were examined using different types of dietary fats.

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Abbreviations: TP, tea polyphenols; LT. Leukotriene; PC, Phosphatidylcholine; PE, Phosphatidyletanolamine

Material and Methods

Chemicals. Tea polyphenols (TP) were kindly donated by Taiyo Kagaku Co. (Yokkaichi, Japan) and composed by weight percentage of catechin (2.2), epicatechin (3.8), gallocatechin (9.5), epigallocatechin (8.3), epicatechin gallate (4.7), gallocatechin gallate (7.9), and epigallocatechin gallate (21.4). Calcium ionophore, A23187, prostaglandin B_2, and LTB_4 and LTB_5 were purchased from Sigma Chemical Co. (St. Louis, MO). Histamine dihydrochloride and *o*-phthalaldehyde (OPT) were the products of Wako Pure Chemical Industries (Osaka, Japan). Bovine serum albumin (BSA) was purchased from Boehringer Mannheim Biochemicals (Mannheim, Germany). Tyrode buffer, pH 7.2, consisted of 137 mM NaCl, 2.7 mM KCl, 1.8 mM $CaCl_2$, 1.1 mM $MgCl_2$, 11.9 mM $NaHCO_3$, 0.4 mM NaH_2PO_4, and 5.6 mM glucose.

Animals and diets. Male four-week-old Wistar rats were purchased from Seiwa Experimental Animals (Fukuoka, Japan), and given commercial pellets (type NMF, Oriental Yeast, Tokyo, Japan). After acclimation for 1 week, the animals were fed *ad libitum* one of the AIN-93 type purified diets containing different dietary fats and/or TP throughout. The composition of the experimental diet was by weight percentage, casein, 20; fat, 10; vitamin mixture, 1.0; mineral mixture, 3.5; chorine bitartrate, 0.25; L-cystine, 0.3; cellulose, 5; corn starch 36.8; dextrinized corn starch, 13.2; and sucrose to 100. The vitamin and mineral mixture were the products of Nihon Nosan Kogyo, Tokyo, Japan. The dietary fats used were edible grade safflower oil (SAF, Rinoru Oil Mill, Nagoya, Japan), perilla oil (PER, Ajinomoto Co., Tokyo, Japan), and palm oil (PAL, Fuji Oil Co., Osaka, Japan). The fatty acid composition of dietary fats is shown in Table 1 Three different dietary fats (SAF, PER, and PAL) with or without 1% TP were given. TP were added at the expense of corn starch in these experiments. After three weeks of feeding the experimental diets in both experiments, peritoneal exudate cells (PEC) were collected under light diethylether anesthesia as described below. The heart, liver, lung, spleen, kidney, and epididymal adipose tissue were excised and weighed. This experiment was done under the control of the guideline for Animal Experiment in Faculty of Agriculture and the Graduate Course, Kyushu University and the Law (No. 105) and Notification (No. 6) of the Government.

Preparation of PEC. PEC were isolated by the method as described by Matsuo *et al.*[21] Tyrode buffer containing 0.1% BSA was injected into the peritoneal cavity of rats. After the abdomen was gently massaged, the cavity was opened, and then the fluid containing the PEC was collected with a Pasteur pipette. Cells were gently washed with Tyrode buffer and then centrifuged at $200 \times g$ for 10 min at 4°C. To remove contaminating erythrocytes by hypotonic lysis, the cell pellets were resuspended in a modified-ammonium chloride buffer (150 mM NH_4Cl, 10 mM $KHCO_3$ and 10 mM EDTA-2Na, pH 7.4) and incubated for 5 min at 4°C. The remaining cells were resuspended in Tyrode buffer. Cell viability was measured by trypan blue staining and mast cells were identified by toluidine blue staining. Cell viability was above 95% and the proportion of mast cells was 7–10% of the total cells. These values were not significantly different in any dietary groups.

Table 1. Fatty Acid Composition of Dietary Fats

Fatty aci[d]	SAF	PER	PAL
		(Weight%)	
16:0	11.1	7.4	38.2
18:0	2.4	2.1	4.2
18:1n-9	17.9	21.9	44.0
18:2n-6	66.6	12.7	11.5
18:3n-3	0.1	53.7	0.2

SAF; safflower oil, PER; perilla oil, PAL; palm oil

Measurement of chemical mediator releasing activity of PEC. PEC (1×10^6 cells) were incubated with 5 μM calcium ionophore A23187 for 20 min at 37°C to measure histamine and LT release. The cells were sonicated to measure the intracellular histamine content. The amount of histamine, and LTB_4 and LTB_5 in the supernatants were measured by the fluorometric assay and HPLC assay, respectively, as described previously.[21] The percentage of histamine release (histamine release activity) was calculated as follow: histamine releasing activity (%) = (A23187-induced histamine release in the supernatant/intracellular histamine content) × 100.

Fatty acid analysis of liver and PEC phospholipids. Lipids were extracted from liver and PEC by the method of Folch *et al.*[23] and liver phospholipids were separated into phosphatidylcholine and phosphatidylethanolamine by thin-layer chromatography.[24] The fatty acid compositions of these phospholipids were analyzed by gas-liquid chromatography.[25]

Statistical analysis. Data were analyzed by two-way ANOVA to inspect the interaction of dietary variables in each group. To establish the exact nature of the difference between the groups, one-way analysis of variance was followed by Duncan's new multiple range test.[26]

Results

Effects of dietary TP and fats on food intake, growth, and tissue weights

We examined the combinational effects of dietary TP and fats on chemical mediator release from PEC. During 3 weeks of feeding, food intake was similar in the six groups of rats. However, body weight gain was significantly lower in the three TP groups, causing a significant reduction of food efficiency (0.27 ± 0.01 and 0.22 ± 0.01 g gain/g intake in TP-free and TP-fed groups, respectively, $p < 0.05$). Dietary fats did not influence weight gain. Weights of heart and lung were similar in the six dietary groups. Liver, kidney, and spleen weights were slightly lower in the TP-fed groups than in the TP-free groups, but the difference was not statistically significant. The reduction of epididymal adipose tissue weight of TP-fed groups was especially large, ranging from 35 to 55% of the TP-free groups.

Effects of dietary TP and fats on chemical mediator release from PEC

PEC were stimulated by A23187 for 20 min, and then the histamine and LT contents of the supernatant were measured. As shown in Table 2, both A23187-induced histamine release and intracellular histamine content were not different between the SAF- and PER-fed groups and significantly increased in the PAL-fed groups, however, histamine releasing activity was not different in all fat groups. TP also did not affect the histamine releasing activity of the cells in all groups.

On the other hand, LTB_4 releasing activity was significantly lower in rats fed PER compared with those fed SAF and PAL (Fig. 1). There was no difference in the activity in latter two groups of rats. TP significantly decreased LTB_4 releasing activity in all dietary fat groups. The extent of the decrease in the activity by TP was approximately 60% in the SAF group, 35% in the PER group, and 25% in the PAL group. LTB_5 release was observed only in rats fed PER. LTB_5 releasing activity decreased slightly but significantly when TP was fed with PER, as seen in

Table 2. Effect of Dietary TP and Fats on Histamine Release from PEC

	A23187-induced histamine release (ng/10^6 cells)	Intracellular histamine content (ng/10^6 cells)	Histamine releasing activity (%)
TP (−)			
SAF	630 ± 12^a	696 ± 11^a	90.4 ± 0.6
PER	609 ± 18^a	677 ± 7^a	90.0 ± 1.8
PAL	769 ± 15^b	806 ± 40^b	93.4 ± 2.5
TP (+)			
SAF	637 ± 21^a	664 ± 10^a	95.3 ± 1.6
PER	595 ± 41^a	651 ± 19^a	95.7 ± 3.4
PAL	821 ± 23^b	859 ± 15^b	95.2 ± 1.5

Cells, isolated from rats fed various diets, were stimulated with A23187 for 20 min at 37°C. The histamine content in the supernatant and cell homogenate were measured by the fluorometric assay. Results are the mean ± SE ($n = 5$) and ^{ab}values not sharing a common letter are significantly different at $p < 0.05$. SAF; safflower oil, PER; perilla oil, PAL; palm oil, TP; tea polyphenols, PEC; peritoneal exudate cells.

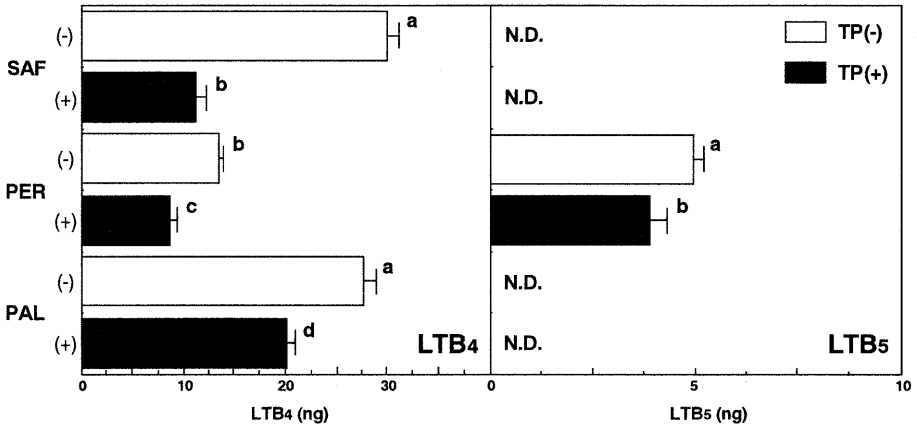

Fig. 1. Effects of Dietary TP and Fats on LT Release from PEC.

PEC isolated from rats fed various fats with or without TP were stimulated with A23187 for 20 min at 37°C. The histamine and LT contents in the supernatant were measured by the fluorometric and HPLC assays, respectively. Results are the mean ± SE ($n = 5$). $^{a\text{-}d}$Values not sharing a common letter are significantly different at $p < 0.05$. A; histamine, B; LTB_4, C; LTB_5, SAF; safflower oil, PER; perilla oil, PAL; palm oil, TP; tea polyphenols, PEC; peritoneal exudate cells.

LTB_4 release. The inhibition rate in LTB_5 releasing activity by TP was about 20%.

Effects of dietary TP and fats on fatty acid composition of liver and PEC phospholipids

LTB_4 is produced by the lipoxygenase oxidation of arachidonic acid (AA, 20:4n-6) released from membrane phospholipids. On the other hand, LTB_5 is generated from eicosapentaenoic acid (EPA, 20:5 n-3) in a similar manner. Since the eicosanoid production depends on the substrate availability of membrane phospholipids, the fatty acid composition of liver and PEC phospholipids was measured.

As shown in Table 3, the proportion of AA in liver phosphatidylcholine of the PER group was significantly lower than in the SAF and PAL groups, while that of EPA was significantly higher in this group. However, TP did not seemingly influence the proportion of AA and EPA, the substrate of eicosanoids, in all groups of rats. The proportion of docosahexaenoic acid (DHA, 22:6 n-3) was significantly low in rats fed SAF than in those fed PAL and PER, irrespective of the presence or absence of TP. A similar tendency was observed in the proportion of AA and EPA in liver phosphatidylethanolamine (data not shown).

The fatty acid composition of PEC phospholipids is shown in Table 4. The proportion of AA in the PER group was significantly lower than in the SAF and PAL groups, while that of EPA was significantly higher in this group, as seen in liver phospholipids. In contrast to the case of liver, TP significantly decreased the proportion of AA in rats fed SAF, but not in those fed PER and PAL. The proportion of EPA also was significantly reduced by TP in rats fed PER. Again, DHA was significantly lower in the SAF group than in the other groups.

Discussion

Type I allergy is an immediate hypersensitive reaction such as allergies against food or environmental allergens.[1-3] In this type of allergy, mast cells play a crucial role in the pathogenesis of allergic symptoms

Table 3. Dietary Effects of TP and Fats on Fatty Acid Composition of Liver Phosphatidlycholine (%)

	16:0	16:1	18:0	18:1 (n-9)	18:2 (n-6)	18:3 (n-3)	20:3 (n-6)	20:4 (n-6)	20:5 (n-3)	22:6 (n-3)
TP (−)										
SAF	21.7 ± 0.8^{ac}	0.9 ± 0.1^{a}	18.2 ± 0.5^{a}	6.7 ± 0.3^{a}	17.0 ± 0.8^{a}	ND^{a}	0.4 ± 0.0^{a}	29.8 ± 0.8^{ae}	0.1 ± 0.1^{a}	2.5 ± 0.2^{ac}
PER	22.3 ± 1.3^{a}	1.8 ± 0.2^{b}	17.0 ± 0.2^{a}	9.6 ± 0.3^{b}	20.2 ± 1.2^{b}	1.8 ± 0.1^{b}	1.4 ± 0.2^{b}	10.3 ± 0.4^{b}	9.5 ± 0.4^{b}	4.3 ± 0.3^{b}
PAL	19.7 ± 0.9^{ab}	1.4 ± 0.1^{b}	21.8 ± 0.9^{b}	11.9 ± 0.4^{c}	10.5 ± 0.7^{c}	ND^{a}	1.5 ± 0.1^{b}	26.3 ± 0.9^{c}	0.0 ± 0.0^{a}	4.3 ± 0.2^{b}
TP (+)										
SAF	19.0 ± 0.8^{bc}	0.6 ± 0.1^{a}	21.9 ± 0.5^{b}	5.3 ± 0.3^{d}	15.9 ± 0.7^{a}	ND^{a}	0.4 ± 0.0^{a}	31.3 ± 0.6^{a}	ND^{a}	2.2 ± 0.2^{a}
PER	19.4 ± 1.5^{ab}	0.7 ± 0.2^{a}	23.1 ± 0.6^{bc}	6.8 ± 0.4^{a}	18.0 ± 0.9^{ab}	1.3 ± 0.1^{c}	1.5 ± 0.1^{b}	12.4 ± 0.5^{d}	11.2 ± 1.3^{c}	3.7 ± 0.7^{b}
PAL	18.1 ± 0.5^{b}	1.0 ± 0.1^{a}	24.1 ± 0.9^{c}	10.0 ± 0.4^{b}	11.8 ± 0.5^{c}	ND^{a}	1.3 ± 0.3^{b}	27.8 ± 0.6^{ce}	0.5 ± 0.2^{a}	3.9 ± 0.4^{b}
ANOVA f value										
Oil	NS	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$
TP	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	NS	$p<0.01$	NS	$p<0.01$	NS	NS
Interaction	NS	$p<0.05$	$p<0.05$	NS	NS	$p<0.01$	NS	NS	NS	NS

Data are presented as mean ± SE for 5 rats. Data were analyzed by two-way ANOVA. $^{a\text{-}d}$Values without a common superscript letter are significantly different at $p<0.05$. SAF; safflower oil, PER; perilla oil, PAL; palm oil, TP; tea polyphenols. ND; not detected. NS; not significant.

Table 4. Dietary Effects of TP and Fats on Fatty Acid Composition of PEC Phospholipids (%)

	16:0	16:1	18:0	18:1 (n-9)	18:2 (n-6)	18:3 (n-3)	20:3 (n-6)	20:4 (n-6)	20:5 (n-3)	22:6 (n-3)
TP (−)										
SAF	22.4 ± 1.0	1.4 ± 0.5^{ab}	20.7 ± 2.0	12.5 ± 2.1^{a}	11.9 ± 0.6^{ab}	0.3 ± 0.1^{a}	1.5 ± 0.4	20.9 ± 1.3^{a}	0.2 ± 0.1^{a}	3.0 ± 0.2^{ac}
PER	22.6 ± 0.3	1.3 ± 0.3^{ab}	22.3 ± 1.0	16.0 ± 0.4^{ab}	9.3 ± 0.4^{a}	2.1 ± 0.2^{ac}	1.6 ± 0.6	8.7 ± 1.0^{b}	4.0 ± 0.3^{b}	5.7 ± 0.6^{b}
PAL	21.7 ± 1.0	1.8 ± 0.9^{a}	16.5 ± 0.8	17.4 ± 1.3^{b}	13.0 ± 0.6^{b}	1.1 ± 0.5^{ac}	1.1 ± 0.4	14.1 ± 2.4^{c}	0.4 ± 0.4^{a}	4.6 ± 0.9^{ab}
TP (+)										
SAF	21.3 ± 0.9	3.1 ± 0.7^{a}	20.4 ± 2.2	15.1 ± 0.5^{ab}	13.1 ± 1.1^{b}	0.1 ± 0.1^{a}	1.0 ± 0.2	14.2 ± 0.8^{c}	0.6 ± 0.3^{a}	1.7 ± 0.2^{c}
PER	21.2 ± 1.1	2.3 ± 0.8^{ab}	20.3 ± 0.9	16.3 ± 0.9^{ab}	12.8 ± 0.8^{bc}	4.6 ± 0.7^{b}	3.2 ± 1.8	7.2 ± 0.7^{b}	2.7 ± 0.1^{c}	4.2 ± 0.8^{ab}
PAL	18.1 ± 2.9	0.9 ± 0.5^{b}	18.1 ± 2.8	14.6 ± 1.1^{ab}	9.6 ± 1.9^{ac}	2.3 ± 1.4^{c}	3.5 ± 1.4	14.2 ± 2.0^{c}	0.3 ± 0.2^{a}	4.4 ± 0.6^{ab}
ANOVA f value										
Oil	NS	NS	$p<0.05$	NS	$p<0.05$	$p<0.01$	NS	$p<0.01$	$p<0.01$	$p<0.05$
TP	NS	NS	NS	NS	$p<0.05$	NS	NS	$p<0.05$	$p<0.05$	NS
Interaction	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

Data are presented as mean ± SE for 5 rats. Data were analyzed by two-way ANOVA. $^{a\text{-}d}$Values without a common superscript letter are significantly different at $p<0.05$. SAF; safflower oil, PER; perilla oil, PAL; palm oil, TP; tea polyphenols, PEC; peritoneal exudate cells. ND; not detected. NS; not significant.

through the production and release of chemical mediators such as histamine and eicosanoids. These chemical mediators cause various pathophysiologic events in the acute allergic reaction, including increased vascular permeability, induction of bronchial smooth-muscle contraction or mucus production, and neutrophil chemotaxis.[27-29] Thus, it is important to reduce the mediator release for the prevention and/or alleviation of allergic symptoms. We previously reported that TP and polyunsaturated fatty acids (PUFA) inhibited the release of chemical mediators from rat RBL-2H3 cells and rat PEC *in vitro*.[21,22,30] In this study, the effect of TP feeding on chemical mediator releasing activity of rat PEC was examined in combination with different types of dietary fats aiming at an improvement of the antiallergic effects of TP *in vivo*.

During the feeding periods, food intake was similar in the six groups of rats. However, body weight gain and food efficiency in rats fed TP were significantly lower than those fed no TP. This tendency was especially observed in adipose tissue weight. Because TP administration has been reported to increase fecal excretion of total lipids and cholesterol and reduce the absorption of triglyceride and cholesterol,[31,32] these results suggested that the decrease in body weight by dietary TP was caused at least in part by the inhibition of lipid absorption. Furthermore, lower levels of dietary TP, which did not influence these parameters, also inhibited the release of LT (Matsuo *et al.* unpublished results), and hence, the effects of TP seemed to be exerted through their direct interaction with PEC.

This study indicated that A23187-induced histamine release and intracellular histamine content were not different in the SAF- and PAL-fed group, while significantly increased in the PAL-fed group (Table 2). As shown in Table 1, SAF and PER mainly contained linoleic (18:2n-6) and a-linolenic (18:3n-3) acids, respectively, while there was no difference the total amount of PUFA (66%, w/w) between them. On the contrary, PAL contained mainly palmitic (16:0), oleic (18:1n-9) and a small amount of linoleic acid (11%, w/w). Hashimoto *et al.* reported that histamine release from mast cells was not different in rat fed the diets enriched a-linolenate and linoleate.[33] These results suggest that the type of PUFA does not affect the histamine release activity. However, the reduction of PUFA or the increase of saturated and/or monosaturated fatty acids may increase A23187-induced histamine release and the intracellular histamine content, while their histamine release activity did not affect among dietary fat group.

In the case of LT, PER decreased LTB_4 release from PEC compared with SAF and PAL. LTB_5 release was observed only in rats fed PER. LTB_4 is produced by the lipoxygenase oxidation of AA derived from membrane phospholipids and LTB_5, from EPA. PER reduced the proportion of AA in PEC phospholipids and increased that of EPA, compared with SAF and PAL. It has been reported that the fatty acid composition of membrane phospholipids is readily modified by dietary fatty acids, and in turn, eicosanoid production.[34] LT of 5-series exerts an antiallergic effect by competing with the 4-series counterpart, although the activity is generally low.[35] It is therefore likely that n-3 PUFA may suppress the allergic reactions by the reduction of the generation and release of 4-series LT through the modification of fatty acid composition of mast cell phospholipids. On the other hand, TP significantly decreased LTB_4 releasing activity of rat PEC in all dietary fat groups, while TP did not affect histamine releasing activity. Interestingly, TP inhibited the release of LTB_4 from PEC in rats fed PER to the lowest level observed, and also decreased the release of LTB_5, which was generated only in rats fed PER. In order to discover their inhibitory mechanism, we examined the relationship between the inhibition rate and the proportion of AA in membrane phospholipids. The magnitude of the inhibitory activity of TP on LTB_4 release differed depending on the source of dietary fats, and the inhibition rate was higher in rats fed SAF (62%) than in those fed PER (37%) and PAL (27%). In this context, the proportion of AA in PEC phospholipids was decreased by TP only in rats in the SAF-fed group (32%) (Table 4), in spite of the significant decrease in the LTB_4-releasing activity in all groups. These results suggested that the difference in the magnitude of inhibitory activity may not be explained by the difference in the proportion of LTB_4 precursor alone.

We have observed that TP did not influence the increase in intracellular Ca^{2+} concentration as a consequence of cross-linking of IgE with antigen in RBL-2H3 cells.[22] Thus, the inhibitory activity may be exerted through an interaction with metabolic events following an increased intracellular Ca^{2+} concentration. Several lipoxygenase inhibitors inhibit the LT release from mast cells.[36,37] In this regard, TP has been reported to inhibit lipoxygenase activity.[38] Thus, the inhibitory effect of TP seemed to be expressed through their direct interaction with the LT producing system in mast cells, such as inhibition of lipoxygenase activity, rather than the reduction of the availability of substrate fatty acids. Furthermore, dietary TP decreased LTB_4-releasing activity alone, though TP inhibited the release of both histamine and LTB_4 *in vitro*.[21,22] Histamine is a typical preformed mediator that is produced by decarboxylation of histidine and stored in the granules. Maeda *et al.*[39] reported that tea extracts inhibited the hyaluronidase activity, suggesting a modification of membrane permeability. The ID_{50} of tea extract to the hyaluronidase activity is reported to be 0.5–1.2 mg/ml, while that to the lipoxygenase activity of

epigallocatechin gallate was around 5–10 μg/ml.[38] These suggest that the inhibition of these two mediators by TP is under regulation by different mechanisms. Therefore, it is plausible that TP bifunctionally inhibits histamine release by affecting membrane fluidity, and LTB_4 release by affecting lipoxygenase activity.

The number of allergy patients is currently increasing at a considerable rate, and it is believed that the changes in eating style and living circumstances strongly influenced the prevalence of allergy.[1–3] On the contrary, food contains physiologically active components which can maintain our health.[40] In humans, TP are absorbed and finally excreted in urine and feces.[41] Further, TP administration has been reported to reduce cardiovascular disease[16] and the risk of some types of cancer.[18,19] The results obtained in this study suggest that the ingestion of TP is useful for the prevention and/or improvement of allergic symptoms and an appropriate combination of TP with n-3 fat may help in the application of this physiologically functional factor.

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