Anti-allergic Effects of *Acanthopanax senticosus* Root Extract and *Perilla frutescens* Seed Extract

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SUN CHLORELLA Corp.

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[Abstract]

*Acanthopanax senticosus* Root Extract (EUE) and *Perilla frutescens* Seed Extract (OSE) have been examined for their anti-allergic effects when used individually or in combination. The results are summarized as follows: (1) EUE and OSE significantly inhibited histamine release induced by Compound 48/80 (*p*<0.01, vs. the vehicle control). Histamine release was more potently inhibited by a mixture of EUE and OSE (5:1) than by either EUE or OSE alone. (2) In a PCA test in rats sensitized with mouse antiserum against ovalbumin, 14-day repeated oral administration of EUE resulted in dose-dependent inhibition of pigment leakage elicited as the PCA reaction in the animals. Comparison with the control group indicated significant inhibitions of PCA reaction in groups treated with EUE alone as well as in those with EUE and OSE in combination (*p*<0.01). In the PCA test, no significant synergic or additive inhibitory effect was noted in the group concomitantly treated with EUE and OSE. The effect in the group treated with EUE and OSE, however, was apparently higher than that in the group treated with DSCG (Intal® inhalant solution). (3) EUE tended to inhibited not only histamine- but also serotonin-induced leakage of pigment in a dose-dependent manner although no significant differences from the vehicle control group were detected at any doses examined.

[Key words]

*Acanthopanax senticosus*, *Perilla frutescens*, allergy, histamine release inhibition, passive cutaneous anaphylaxis (PCA)

INTRODUCTION

Allergic diseases such as allergic rhinitis, bronchial asthma, and pollinosis are characterized as Type I allergies mediated by IgE antibodies. Because of the prevalence of Type I allergies in recent years, anticipation for establishment of effective prevention and treatment methods has been growing. The pathogenesis of allergy, however, has not been fully understood yet. Furthermore, currently available treatments with an antihistamine agents or steroids are only symptomatic and require special care for preventing the development of serious adverse effects of these therapeutic agents. Under these circumstances,
in addition to symptomatic relief by treatment with a therapeutic agent, a long-term improvement of physical conditions by food materials is considered effective in treating allergic diseases.

The Araliaceae plant, Ezo Ukogi in Japanese name (scientific name: *Acanthopanax senticosus* Harms), naturally grows in cold regions such as Sakhalin, Korea, Amurskaya, and the northern china, but only in Hokkaido in Japan.\(^1\) *Acanthopanax senticosus* is used as a pharmaceutical in China and Russia although *Acanthopanax senticosus* is used only as a raw material for production of pharmaceuticals and health foods in Japan. Pharmacological effects of *Acanthopanax senticosus* have been extensively studied in China and the former Soviet Union, and many studies have been reported mostly on its antifatigue effects,\(^2,3\) but hardly on its anti-allergic effects. Seeds of the Lamiaceae plant, Egoma in Japanese name (scientific name: *Perilla frutescens* var. japonica Hara), have been consumed in Japan as daily food for a long time. Yamamoto et al\(^4\) have reported on anti-allergic effects of *Perilla* seed.

In general, medicinal plants of the same scientific name differ in composition of effective components and their contents, depending upon its growing place and conditions. In addition, the extraction method is another major factor to determine the composition of effective components and their contents in the resulting extract from the plant. Therefore, extracts even from a certain medicinal plant hardly show the same pharmacological effect.

In keeping these facts in mind, we have examined *Acanthopanax senticosus* root extract (abbreviated as EUE, which stands for *Ezo Ukogi* Extract) manufactured by Guangyuan Pharmaceutical (Heilongchiang, China) and *Perilla* seed extract (abbreviated as OSE, which stands for *Ocymoidas* seed extract) manufactured by Oryza Oil & Chemical Co., Ltd. (Aichi, Japan) for its effects on histamine release, passive cutaneous anaphylaxis (PCA), and histamine- and serotonin-induced pigment leakage. The results are described in the present report.

**MATERIALS AND METHODS**

1. Animals

The following animals were purchased from Japan Slc (Shizuoka): 9 weeks old male Slc:SD rats for collecting intraperitoneal mast cells to be used in the histamine release test, 6 weeks old male C57BL/6CrSlc mice for preparing antiserum to be used in the PCA test, 10 weeks old male Slc:SD rats for determining titers of the antiserum prepared, and 6 weeks old male Slc:SD rats for the PCA test and pigment leakage test. Animals were quarantined and acclimated for 1 week, and those showing no abnormalities in general conditions were used in the experiments. Animals were allowed free access to solid feed (Labo-MR Stock, Nihon Nosan Kogyo, Kanagawa) and tap water. Animals were treated in accordance with the NIH guideline.\(^5\)

2. Test Substance

EUE was a dry powder product of Guangyuan Pharmaceutical Co., Ltd. (Heilongchiang, China) manufactured from *Acanthopanax senticosus* roots via the following process: pulverization, extraction with 6 volumes of water for 2–3 hr at 90–100°C, removal of sediments following the addition of ethanol, concentration under reduced pressure, and drying by a spray dryer.
The product contained isofraxidine, eleuteroside B and E, and chlorogenic acids as components. OSE was a dry powder product of Oryza Oil & Chemical (Aichi, Japan) prepared from concentrated extract of 15–20 g of Perilla seeds with aqueous ethanol. The product contained polyphenols at 3% or higher in total concentration. Since EUE and OSE were orally ingested in common practice, these extracts were suspended in distilled water for injection and orally administered (by using a gastric tube) in in vivo experiments. Disodium cromoglicate (DSCG, Sigma) and Intal Inhalant (Fujisawa Pharmaceutical) were used as the positive control.

3. Histamine Release Inhibition Test

3.1 Collection of mast cells

Twenty-five rats (11 weeks old) were exsanguinated by decapitation under anesthesia with ether, and the abdominal cavity was washed with 20 mL of Tyrode solution containing 0.1% bovine serum albumin (BSA) for 2 min with gentle rubbing the abdomen. The abdominal cavity was cut open to collect the Tyrode solution. The collected solution was centrifuged at 450×g for 10 min at 4°C. The resulting supernatant was removed, and the sediment was washed three times with Tyrode solution containing 0.1% BSA. The resulting cell suspension was placed on a blood cell counting plate to determine the number of mast cells in 0.1 μL of the suspension. The cell suspension was diluted with Tyrode solution containing 0.1% BSA to give a cell concentration of 10^5 cells/1.7 mL.

3.2 Histamine Release Test

A cell suspension prepared as described above was preincubated at 37°C for 5 min. After the additions of 100 μL of a test substance solution and 200 mL of 2.0 μg/mL Compound 48/80 (to give a final concentration of 0.4 μg/mL), the suspension was incubated at 37°C for 10 min. All additions were made by using solutions in Tyrode solution containing 0.1% BSA. After the incubation, the incubation mixture was placed in an ice-water bath to terminate the reaction and centrifuged at 450×g for 10 min at 4°C. Each of the resulting supernatant and sediment (mast cells) mixed with HClO₄ to give a final concentration of 3%(w/v) and a final volume of 3 mL. The resulting mixture was alternatively frozen and thawed three times and then centrifuged to obtain the supernatant as a sample for histamine measurement.

In Experiment I, the assay was performed in duplicate in each of the vehicle control group, the EUE groups (100 and 1000 μg/mL), and the positive control DSCG group (25 μg/mL). In Experiment II, six determinations were performed in each of the vehicle control group, the EUE groups (50, 150, 500, and 1000 μg/mL), the OSE group (100 μg/mL), and the concomitant treatment group (EUE 500 μg/mL + OSE 100 μg/mL).

3.3 Measurement of Histamine

The samples obtained in the histamine release test as described above were subjected to measurement of histamine concentrations by the method of Komatsu et al. A 2.0 mL of each sample (histamine extract) was mixed with 200 μL of 6 mol/L NaOH and about 1 g of NaCl and extracted with 3.3 mL of an organic solvent mixture (n-butanol/chloroform=3:2) by shaking for 5 min. The mixture was then centrifuged at 900×g for 5 min at room temperature. A 3.0-mL portion of the separated organic layer (the resulting supernatant) was transferred into another test
tube and mixed with 3.0 mL of hexane and 1.2 mL of 0.1 mol/L HCl. The mixture was shaken for 5 min and centrifuged at 600×g, for 5 min at 4°C. The separated organic layer (the resulting supernatant) was removed, and 1.0 mL of the remaining aqueous layer was transferred into another test tube and mixed with 150 μL of 1 mol/L NaOH and 100 μL of 0.2%(w/v) o-phthalaldehyde. The mixture was incubated for 40 min in an ice-water bath. The mixture was further incubated for 20 min at room temperature after the addition of 140 μL of 0.25 mol/L H₂SO₄.

A 1.39-mL portion of the resulting reaction mixture (solution for concentration measurement) was subjected to fluorescence intensity measurement by using a fluorometer (Hitachi Model F-2000, Hitachi) with the excitation wavelength set at 360 nm and the emission wavelength set at 440 nm.

Histamine concentrations in the samples were calculated from the fluorescence intensity-concentration calibration curve. From the histamine concentrations, histamine contents were calculated from the original volume of the samples (3 mL), the volume of their histamine extracts (2 mL), and the volume of the fluorometry samples (1.39 mL) by using Equation (1). In addition, histamine release rates and percent inhibitions of histamine release were calculated by using Equations (2) and (3), respectively.

\[
\text{Histamine content (ng)} = \text{Histamine concentration (ng/mL)} \times 1.39 \times 3/2
\]  
Equation (1)

\[
\text{Histamine release rate (％)} = \left( \frac{\text{Histamine content in the supernatant} \times 100}{\text{Histamine content in the supernatant} + \text{Histamine content in the sediment}} \right)
\]  
Equation (2)

\[
\text{Percent inhibition of histamine release (％)} = \frac{(A-B) \times 100}{A}
\]  
Equation (3)

A: Histamine release rate in the absence of any test substance (the rate in the presence of Compound 48/80−the rate in the absence of Compound 48/80)

B: Histamine release rate in the presence of a test substance (the rate in the presence of Compound 48/80−the rate in the absence of Compound 48/80)

4. Rat PCA Test Induced by Mouse Antiserum

4.1 Preparation of mouse antiserum and measurement of the titer

Seven weeks old mice were sensitized by intraperitoneal administration of a mixture of ovalbumin (OVA, 2 mg/kg) and 50 μL of Alum (Al(OH)₃, 1 mg) in a relative dosing volume of 10 mL/kg. The sensitization was performed three times at 1-week intervals. Blood was collected from the sensitized animals 12 days after the final sensitization. The serum samples separated from the collected blood samples were determined for their titers in rat PCA reaction. For provocation of PCA reaction in rats, anti-OVA serum was subjected to serial dilutions. Each diluted serum was taken in a relative dosing volume of 0.1 mL and intradermally administered to a shaved site on the back. A solution of the antigen together with Evans Blue was intravenously administered 24 hr after the intradermal administration of the diluted serum.

In addition, when the anti-serum preparation was heated at 56°C for 30 min, no
provocation of PCA reaction was observed, indicating IgE-mediated nature of the PCA reaction induced by the anti-serum preparation used in this study.

4.2 Effects of EUE and OSE on Mouse Antiserum-induced PCA Reaction

For examining effects of EUE and OSE on mouse antiserum-induced PCA reaction, SD rats (7 weeks old) were used. In Experiment I, seven animals each were allocated in the vehicle control group, the EUE groups (60, 200, and 600 mg/kg), the OSE group (120 mg/kg), and the co-administration group (EUE 600 mg/kg + OSE 120 mg/kg). In Experiment II, six animals each were allocated in the vehicle control group, the co-administration groups (EUE 85 mg/kg + OSE 15 mg/kg, EUE 250 mg/kg + OSE 50 mg/kg), and the positive control DSCG group (Intal® Inhalant, 10 mg/kg). Distilled water for injection was used as the vehicle control and orally administered in the same relative dosing volume.

To the animals in the groups other than the positive control group, EUE alone or in combination with OSE was administered by oral administration in a dosing volume of 10 mL/kg once a day for 14 consecutive days from the day after the grouping. To the animals in the positive control group, the positive control substance was administered once on Day 14. In Experiment II, animals were not allowed any access to food from the early evening on Day 13. On Day 14, antiserum (with 8-fold dilution in Experiment I or 16-fold dilution) and physiological saline (0.1 mL each) were intradermally administered to a shaved site on the back of each rat 1 hr after the final administration of the test substances or immediately after the administration of the positive control.

Immediately after the intradermal administration, animals were challenged by intravenous administration of a solution of the antigen (2.5 mg/mL) together with 0.5% Evans Blue in a relative dosing volume of 2 mL/kg. The animals were decapitated under anesthesia with ether 30 min after the challenge. The skin in the area where antiserum was intradermally administered was removed and immersed and kept in 1 mol/L KOH at 37°C for 24 hr. The pigment was then extracted with a mixture of 0.2 mol/L H₃PO₄/acetone (1:13), and quantitated by reading the absorbance at 600 nm in a spectrophotometer (Shimadzu Model 160A UV spectrometer, Shimadzu).

5. Histamine- and Serotonin-induced Pigment Leakage Tests

In the histamine- and serotonin-induced pigment leakage tests, SD rats (7 weeks old) were allocated in the vehicle control group and the EUE groups (100 and 200 mg/kg). In a manner similar to that described above for the PCA test, EUE was administered by oral administration once a day for 14 consecutive days from the day after the grouping. After the final administration, animals were challenged with histamine (0.001%) or serotonin (0.001%). Pigment leakage was quantitated in the same manner as that described above for the PCA test.

6. Statistical analysis

For each parameter, the mean and standard deviation in each experimental group were calculated from the measured values. The differences between experimental groups were tested for statistical significance as follows. In the initial step, the variances in the groups were examined for homogeneity by Bartlett method (at a significance level of 5%). When
the variances were demonstrated to be homogenous, one-way analysis of variance was further applied. When a significant difference was detected, the means were compared by Turkey method. When the variances were not homogenous, Kruskal-Wallis $H$-test was further applied. When a significant difference was detected, mean ranks were compared by Turkey method. All analyses were performed at significance levels of 5 and 1%.

### Table 1  Histamine Release Inhibition Test

<table>
<thead>
<tr>
<th>Concentration of test substance (µg/mL)</th>
<th>n</th>
<th>Histamine release (%) in the presence of Compound 48/80 (mean±S.E.)</th>
<th>Inhibition of histamine release (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2</td>
<td>48.9</td>
<td>—</td>
</tr>
<tr>
<td>EUE 100</td>
<td>2</td>
<td>34.1</td>
<td>35.7</td>
</tr>
<tr>
<td>EUE 1000</td>
<td>2</td>
<td>25.9                                                          * 55.8</td>
<td></td>
</tr>
<tr>
<td>DSCG</td>
<td>2</td>
<td>1.40                                                          * 98.1</td>
<td></td>
</tr>
<tr>
<td>Experiment II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>6</td>
<td>49.3 ± 0.5                                                     —</td>
<td></td>
</tr>
<tr>
<td>EUE 50</td>
<td>6</td>
<td>48.4 ± 0.4                                                     1.5</td>
<td></td>
</tr>
<tr>
<td>EUE 150</td>
<td>6</td>
<td>33.5 ± 0.4                                                     * 36.7</td>
<td></td>
</tr>
<tr>
<td>EUE 500</td>
<td>6</td>
<td>30.4 ± 0.3                                                     * 44.0</td>
<td></td>
</tr>
<tr>
<td>EUE 1000</td>
<td>6</td>
<td>25.7 ± 0.2                                                     * 54.6</td>
<td></td>
</tr>
<tr>
<td>OSE</td>
<td>6</td>
<td>25.2 ± 0.1                                                     * 55.6</td>
<td></td>
</tr>
<tr>
<td>EUE 500 + OSE</td>
<td>100 6</td>
<td>17.0 ± 0.1                                                   * 74.9</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.01

### Table 2  PCA Test Using Mouse Antiserum

<table>
<thead>
<tr>
<th>Test substance and dose (mg/kg/day)</th>
<th>n</th>
<th>Pigment leaked (µg/mL) (mean ± S.E.)</th>
<th>Inhibition of pigment leakage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>7</td>
<td>30.06 ± 0.74                       —</td>
<td></td>
</tr>
<tr>
<td>EUE 60</td>
<td>7</td>
<td>15.89 ± 2.08                       47.1</td>
<td></td>
</tr>
<tr>
<td>EUE 200</td>
<td>7</td>
<td>13.47 ± 0.67                       * 55.2</td>
<td></td>
</tr>
<tr>
<td>EUE 600</td>
<td>7</td>
<td>10.97 ± 0.89                       ** 63.5</td>
<td></td>
</tr>
<tr>
<td>OSE 120</td>
<td>7</td>
<td>13.33 ± 0.10                       * 55.7</td>
<td></td>
</tr>
<tr>
<td>EUE 600 + OSE</td>
<td>120 7</td>
<td>10.81 ± 1.07                      ** 64.0</td>
<td></td>
</tr>
<tr>
<td>Experiment II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>6</td>
<td>17.87 ± 1.40                       —</td>
<td></td>
</tr>
<tr>
<td>EUE 85 + OSE</td>
<td>15 6</td>
<td>6.81 ± 0.26                       61.9</td>
<td></td>
</tr>
<tr>
<td>EUE 250 + OSE</td>
<td>50 6</td>
<td>5.29 ± 0.19                       ** 70.4</td>
<td></td>
</tr>
<tr>
<td>DSCG 1)</td>
<td>10mg/kg 6</td>
<td>5.69 ± 0.33                      ** 68.2</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01

1)Intal Inhalant Solution

### Table 3  Histamine- and Serotonin-induced Pigment Leakage Test
<table>
<thead>
<tr>
<th>Dose (mg/kg/day)</th>
<th>n</th>
<th>Pigment leaked (µg/mL) (mean ± S.E.)</th>
<th>Inhibition of pigment leakage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.001% Histamine</td>
<td>0.001% Serotonin</td>
</tr>
<tr>
<td>Vehicle control</td>
<td>6</td>
<td>4.38 ± 0.67 [8.56]</td>
<td>8.56 ± 1.64 [42.1]</td>
</tr>
<tr>
<td>EVE</td>
<td>100</td>
<td>3.55 ± 0.86 [18.9]</td>
<td>4.96 ± 0.83 [42.1]</td>
</tr>
<tr>
<td>EUE</td>
<td>200</td>
<td>2.53 ± 0.79 [42.2]</td>
<td>4.26 ± 0.62 [50.2]</td>
</tr>
</tbody>
</table>
RESULTS

1. Histamine Release Inhibition Test

Table 1 shows histamine release rates and inhibition rates of histamine release. Comparison with the vehicle control group revealed statistically significant inhibitions of histamine release in the EUE 1000 μg/mL group in Experiment I as well as in the EUE 150, 500, and 1000 μg/mL groups and the OSE 100 μg/mL group, in Experiment II. In addition, the inhibition in the EUE 500 μg/mL + OSE 100 μg/mL co-administration group was apparently higher than that in the group treat with EUE or OSE alone at the same dose.

2. Rat PCA Test Using Mouse Antiserum

Table 2 shows amount of pigment leaked and inhibitory rates of pigment leakage. When compared with the vehicle control group, statistically significant inhibitions of pigment leakage were detected in the EUE 200 and 600 mg/kg groups, the OSE 120 mg/kg group, and the EUE 600 mg/kg + OSE 120 mg/kg co-administration group in Experiment I as well as in the EUE 250 mg/kg + OSE 50 mg/kg co-administration group in Experiment II. EUE inhibited pigment leakage in a dose-dependent manner when administered alone or together with OSE.

3. Histamine- and Serotonin-induced Pigment Leakage

Table 3 shows amount of pigment leaked and inhibitory rates of pigment leakage. EUE 100 and 200 mg/kg groups revealed insignificant, but dose-dependent inhibitions of pigment leakage.

DISCUSSION

The present study was performed to examine anti-allergic effects of EUE and OSE, in terms of their individual effects and their combined effects, in the standard tests for evaluating anti-allergic activities.

Compared with the vehicle control, EUE, OSE, and a mixture of EUE and OSE showed significant inhibitory effects on histamine release from rat intraperitoneal mast cells. A mixture of EUE and OSE (5:1) showed a more potent inhibitory effect than either one of the components.

The fact that EUE and OSE inhibited degranulation of mast cells prompted us further to examine anti-allergic effects of these extracts in a PCA test using mouse antiserum against OVA.

From comparison with the vehicle control group, significant inhibitions of OVA-induced PCA reaction were noted in the groups treated with either EUE or OSE alone and in the group concomitantly treated with EUE and OSE (EUE/OSE dose ratio=5:1) in Experiment I. In Experiment II, EUE and OSE were co-administered at a lower dose level, keeping the dose ratio at 5:1. As a result, 70.4% inhibition was observed in the EUE 250 mg/kg + OSE 50 mg/kg group. The inhibition was statistically significant when compared with the vehicle control group (p<0.01). Furthermore, the inhibition was more potent when compared with 68.2% inhibition attained by DSCG (Intal® Inhalant Solution). In the group concomitantly treated with EUE and OSE at the lowest dose level examined in this study (EUE 85 mg/kg + OSE 15mg/kg group), 61.9% inhibition was observed although the inhibition was insignificant, compared with the vehicle control group. From these results, the anti-allergic effect of EUE alone or its
combination with OSE is considered comparable with that of DSCG.

In the histamine- and serotonin-induced pigment leakage tests, EUE showed statistically insignificant but dose-dependent inhibitions of pigment leakage. These results suggest that EUE has histamine- and serotonin-antagonistic effects at high doses.

A number of studies have reported various antifatigue effects of EUE. Those include effects to increase activities of oxidation enzymes and superoxide dismutase (SOD) in skeletal muscles in an exercise loading test in mice,\(^7\) to prolong the times requiring for increase in maximal oxygen consumption and in total workload and the time to develop distress in humans,\(^8\) to prolong exercise endurance time and to decrease liver glycogen content in an exercise loading test in mice (these were shown as effects of a stem bark extract),\(^2\) and to increase \(\beta\)-endorphin concentration in the blood.\(^9\) In addition, antifatigue effects under acute stress and antistress effects under chronic stress have also been reported as effects of *Acanthopanax senticosus* root extracts.\(^10,\,11\) Moreover, EUE has been reported to have antioxidation effects, such as inhibitory effects on lipid peroxidation by rat liver microsomes\(^12\) and protective effects against radiation by increasing SOD activity in the liver.\(^13\) In a clinical study, Enack Tablets, a revitalizing drug containing *Acanthopanax senticosus* as the major component, has been shown to have improving effects in patients with indefinite complaints.\(^14\) Eleuterosides E, B1, and B, isofraxidine, and chlorogenic acids have been identified as the major EUE components with pharmacological activities.\(^15\) No components, however, have been shown to be responsible for the anti-allergic effects of EUE. Accordingly, multiple components, including unknown components, may be involved in the anti-allergic effects of EUE. EUE inhibited degranulation of inflammatory cells to an extent comparable with that observed with the positive control DSCG. EUE, however, showed antagonistic effects toward histamine and serotonin or anti-inflammatory effects. These results suggest that EUE exerts its effect via a mechanism different from that for DSCG. In this connection, it is noteworthy that EUE increased SOD activity since active oxygen species are involved in pathogenesis of a wide variety of diseases including allergic diseases by directly injuring cells.\(^16\) Accordingly, the SOD-activity increasing activity may be involved in the anti-allergic effects of EUE.

As for OSE, the following pharmacologic effects have been reported: antibacterial effects on oral pathogenic bacteria,\(^17\) and anti-inflammatory effect on changes in mouse auricles induced by TPA, a tumor promoter.\(^18\) In rats given *Perilla* seed oil, the development of breast cancer was retarded, or breast cancer was limited in its volume.\(^19\) In relation to anti-allergic effects, it has been reported that some components of OSE fractions, such as luteolin, chrysoeilol, rosmalnic acid, and methyl rosmalinate, have inhibitory effects on arachidonate lipoxygenase\(^4\) and that OSE reduced oxazolone-induced auricular edema in mice.\(^18\)

EUE, when used in combination with OSE, is expected to have anti-allergic effects associated with inhibitory effects on release of chemical mediators from inflammatory cells such as basophils and mast cells, inhibitory effects on leukotrienes production by inhibiting arachidonate lipoxygenase, SOD activity, histamine- and serotonin-antagonistic activity, or anti-inflammatory effects. Thus, EUE is expected to have a potential as a long-term improving drug for allergic rhinitis, atopic
Anti-allergic effects of *Acanthopanax senticosus* roots and *Perilla frutescens* seeds

Since a long-term oral application is possible with EUE and OSE, co-administration of these extracts appears to be more beneficial than DSCG, an anti-allergic agent widely used in clinical settings. In addition, neither EUE nor OSE has any serious adverse effects characteristic to steroids. However, further studies are needed to examine if any adverse effects are observed in association with co-administration of EUE and OSE and to determine their optimal doses for co-administration.

We have a plane to study effects of co-administration of EUE and OSE in animal models for asthma and allergic dermatitis, and possibly in clinical studies.

**CONCLUSIONS**

Both EUE and OSE showed inhibitory effects on histamine release from mast cells. In addition, EUE seemed to have histamine- and serotonin-antagonistic activities at high doses. Further studies are needed to identify the components responsible for the pharmacological effects and to clarify the mechanism of the actions.

**ACKNOWLEDGMENT**

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