**Introduction**

Yuzu (Citrus junos Sieb. ex Tanaka) is a typical Japanese citrus fruit with a desirable smell. Yuzu was brought via Korea from China to Japan more than 1,000 years ago. Yuzu peel and juice are used in making vinegar and seasonings in Japan. It is reported that the components of yuzu peel have anti-allergic, relaxation, and antioxidant effects. However, no studies have been performed on the effects of yuzu seeds because yuzu seed oil is a new material. In this study we show that yuzu seed oil may be suitable as a new curative method for atopic dermatitis.

### The study design

This type of mouse develops human atopic-like skin lesions with elevated serum IgE level when kept in conventional conditions.

**Induction of atopic dermatitis**

- **Antigen**: Mite antigen ointment (Biostir AD®)
- **Application of yuzu seed oil**
  - We applied yuzu seed oil to NC/Nga mice every day.
  - We used olive oil as a negative control.
  - We used betamethasone sodium phosphate (topical steroid) as a positive control.

**Clinical features**

This photograph was taken 4 weeks after sensitization. Atopic dermatitis induced by topical application of the antigen resulted in immediate clinical signs and symptoms of itching, erythema, and hemorrhage on the ear and back. This was followed by edema, superficial erosion, deep excoriation, scarring, and dryness of the skin. These clinical signs were markedly alleviated in both the yuzu seed oil groups.

### The effect of yuzu seed oil on serum IgE level

As shown in this figure, IgE level in the serum of the negative control group increased with the periodical topical application of the antigen. The IgE level in the serum had no significant correlation with the progression of dermatitis. Application of yuzu seed oil did not inhibit the increase of IgE in the serum.

### The inhibitory effect of yuzu seed oil on histamine levels in serum and skin lesions

This figure shows changes in the histamine levels in the serum and skin lesions of NC/Nga mice. Samples were taken 4 weeks after sensitization and histamine levels were measured using the ELISA system. The histamine levels in the serum and skin lesions of the negative control group, which were sensitized with the antigen under SPF conditions, increased from the beginning of the sensitization. Application of yuzu seed oil significantly inhibited the increase of the histamine levels in the serum and skin lesions in comparison with the negative control group. Particularly, the effect on the cutis was remarkable.

### A hypothesis of the effect of yuzu seed oil on atopic dermatitis

Yuzu seed oil inhibited atopic dermatitis symptoms and signs in the antigen-treated NC/Nga mice.

1. We showed that yuzu seed oil reduced the pathosis of the atopic dermatitis but did not prevent pathogenesis in NC/Nga mice.
2. In conclusion, yuzu seed oil is a good candidate to be used as an alternative medicine against atopic dermatitis.

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**Clinical Score**

A three-point evaluated: 0 (none), 1 (mild), 2 (moderate)

- **Purified**
  - 0
  - 1
  - 2
- **Non-Purified**
  - 0
  - 1
  - 2

**Clinical features**

- **Eosinophils**
  - **Histamine**
  - **Itching**

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**Concentration**

- **Histamine**
  - **Eosinophils**

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**Water**

- **Histamine**
  - **Itching**

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**Histamine**

- **Activation**
  - **Histamine**
  - **Eosinophils**