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## Abbreviations

SPTs: Skin Prick Tests; BAT: Basophil Activation Test

## Introduction

We report a selective anaphylaxis to yuzu (*Citrus junos*) without allergy to other citrus fruits. *Citrus junos* is a hybrid of a mandarin, *Citrus reticulata*, and a lemon fruit, *Citrus ichangensis*. The consumption of this citrus is common in the Japanese diet, with its peel being used as a condiment and its juice for flavoring. There has been a growing interest for this citrus as a new culinary fashion in recent years.

## Case Presentation

A 42-year-old woman, with no atopic history, has experienced two anaphylactic reactions after consuming yuzu. She presented urticaria 10 minutes after the consumption of bluefin tuna flavored in yuzu juice. Clinical signs disappeared within 24 hours without treatment. Two months later, 15 minutes after consuming a butter flavored with peel and juice of yuzu, she presented urticaria and hoarseness. She went to the emergency department, where she was given an antihistamine, corticosteroid IV, and inhaled adrenalin. The symptoms decreased quickly under treatment.

She consumed other citrus fruits (lemon, orange, grapefruit, and tangerine) without any reaction.

Skin prick tests (SPTs) were performed with juice, peel and pulp

## Case Report

# Anaphylaxis to the Citrus Fruit Yuzu

### Abstract

**Introduction:** We report a selective anaphylaxis to yuzu (*Citrus junos*).

**Case Presentation:** A 42-year-old woman, with no atopic history, has experienced two anaphylactic reactions after consuming yuzu. Skin prick tests (SPTs) were performed with juice, peel and pulp of commercially available lemon, orange, grapefruit, tangerine and yuzu, 2 cultivars of *Citrus junos*, 2 cultivars of *Citrus reticulata*, one *Citrus ichangensis* and food consumed during the culprit meal.

Basophil activation test and immunoblot were also performed.

**Result:** Skin prick test to juice and peel of yuzu and basophil activation test to juice of yuzu were positive. The protein recognized by IgE is a protein of 23 kDa.

**Conclusion:** Our patient presents a selective food allergy to yuzu. She consumed other citrus fruits (lemon, orange, grapefruit, and tangerine) without any reaction.

of commercially available lemon, orange, grapefruit, tangerine and yuzu, 2 cultivars of *Citrus junos* (ICVN 0110241 and SRA 846), 2 cultivars of *Citrus reticulata*, one *Citrus ichangensis* and food consumed during the culprit meal.

Basophil activation test (BAT) by flow cytometry (Flow Cast®, Bühlmann, Switzerland) was also performed with juice of *Citrus junos* ICVN 0110241. The CD63 molecules were used as activation marker.

Immunoblots were performed (Genclis SA) with the juice of *Citrus junos* cultivar ICVN 0110241. Twenty microliters of juice were separated by electrophoresis under denaturing and reducing conditions using 12 % polyacrylamide NuPage Bis-tris gels (Invitrogen). After protein transfer on PVDF membrane 0.45 µm and blocking in Tris-buffered saline with Tween (Tris 0.1 M, pH 7.5, 0.15 M NaCl and 0.1% Tween) containing 5% defatted dry milk, membranes were incubated with diluted sera (1:100 dilution). Bound IgE were detected by peroxidase-conjugated goat anti-human IgE (KPL) using ECL Western blotting kit (Amersham GE Healthcare). The approximate molecular weight (MW) of the bands was determined by comparison with the MW marker, Precision plus Protein Dual colour standard (Bio-Rad).

## Result

SPTs were positive with juice (8 mm) and peel (7 mm) of commercial yuzu, with juice of *Citrus junos* ICVN 0110241 (10 mm), juice (5 mm) and pulp (8 mm) of one *Citrus reticulata*, negative to other citrus and ingested food. Positive controls were histamine (7 mm) and codeine (5 mm). Negative control was physiological serum (no reaction).

To rule out an unspecified reaction, SPT with juice of yuzu were performed in two non-allergic persons. SPT were negative for the both.

BAT was positive, with juice of *Citrus junos* ICVN 0110241. At one-hundredth's dilution, the percentage of activated basophils was 13.4 with a positivity threshold of 5% (Figure 1).

Specific IgE (ImmunoCap®, Thermo fisher) to lemon, orange, grapefruit, tangerine, mandarin, rPru p3, cypress and tuna were negative (<0.10 kU/L).

Because ImmunoCap® to yuzu was not commercially available, specific IgE to yuzu were detected by immunoblot. Immunoblot with the serum of the patient revealed an IgE-reactive band at 23 kDa in the juice of Citrus junos ICVN 0110241 (Figure 2). In contrast, no band was observed when immune blot was performed under the same conditions with the serum of a non-allergic patient (not shown).

### Discussion

Citrus fruits belong to the Rutaceae family. Food allergy to citrus

is rare, despite the wide consumption of these fruits. Few case reports regarding allergy to citrus are available in the literature [1,2]. Oral syndrome is the most common manifestation, especially in pediatrics [2]. However, the literature shows that anaphylactic reactions of variable severity are possible [1,3].

Vovolis and et al. have suggested the possibility of a dose-dependent relationship with variable thresholds [4]. Three major allergens of orange has been identified: Cit s1 (germin-like protein, 23kDa) [5], Cit s 2 (profilin, 14 kDa) [6] and Cit s 3 (lipid-transfer protein, 9 kDa) [7]. The 23 kDa IgE-reactive protein may be homologous with Cit s 1, the major allergen of orange. A cross-reactivity between orange and pollen cypress has been reported [8]. No sensitization to cypress pollen was identified in our patient.

### Conclusion

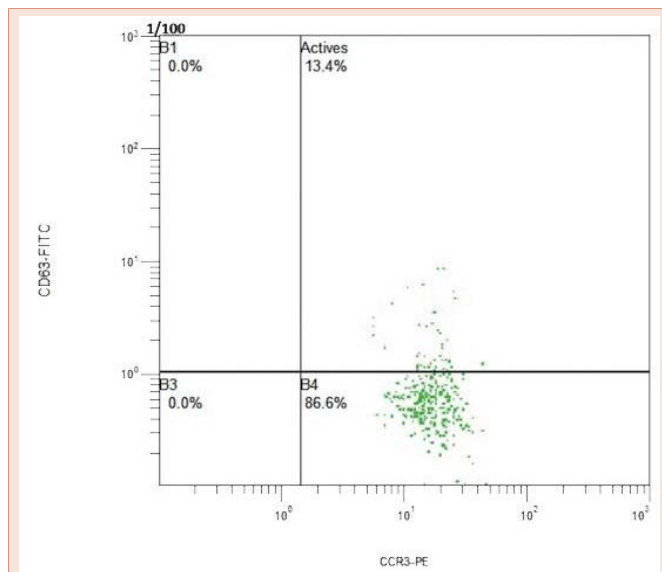
Our patient presents a selective food allergy to yuzu. It is interesting to note, as previously described with other fruits, that there is a difference of reactivity among cultivars [9]. The most reactive is Citrus junos ICVN 0110241, which is the most consumed yuzu.

### Conflict of Interest

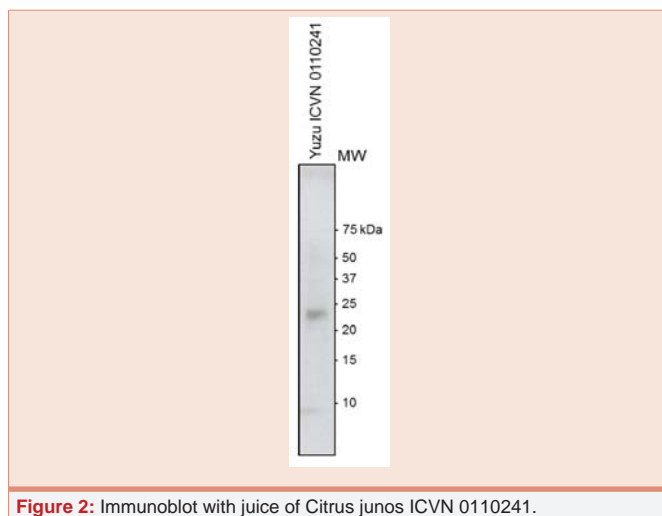
S. Jacquenet and C. Richard are employed by Genclis SA. G. Kanny has received research support from Genclis. The other authors declare that they have no relevant conflicts of interest.

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**Figure 1:** Basophil activation test at one-hundredth's dilution. The percentage of activated basophils was 13.4 with a positivity threshold of 5%.



**Figure 2:** Immunoblot with juice of Citrus junos ICVN 0110241.

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