

# References

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## Occupational allergy to papain

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**Key words:** cosmeticians; occupational allergy; papain.

● PAPAIN, a proteolytic enzyme extracted from the latex of the papaya tree and fruit (*Carica papaya*), has numerous uses and applications (meat and cephalopod tenderizer, beer clarificant, pharmaceuticals, cosmetics, etc.). It is well known that papain can induce IgE allergy reactions through different routes: respiratory, contact, or digestive (1–3). Most of them involve cases of occupational rhinitis and asthma in workers of industries where papain is handled. We report two new cases of occupational allergy to papain in two beauty workers.

### Two nonatopic cosmeticians with IgE-mediated allergy.

Patient 1 was a 22-year-old woman who had worked in a beauty salon for 5 years. Progressively, she developed contact urticaria, rhinoconjunctivitis, and asthma when she used papain tablets dissolved in water for removing adhesives; therefore, she had stopped using them several weeks before she consulted the allergist. She did not suffer these symptoms in other situations, but only slight nose blockage and sneezes when she handled detergents. She never ate papaya and she never had any problems with fruits such as pineapple or kiwi, meat, or beer. She did not have symptoms with latex and toothpaste either. She did not wear contact lenses.

Patient 2 was a 31-year-old woman who had worked in a beauty salon for 10 years. She suffered rhinitis, asthma, and contact urticaria when she used papain tablets for removing adhesives; therefore, she had stopped using them several years before she consulted the allergist. She did not have symptoms in other situations. She never ate papaya and never had any problems with meat or pineapple, but she suffered mouth itching after eating kiwi. She did not drink beer. She wore contact lenses without problems, and she tolerated contact with latex and toothpaste.

In patient 1, the prick tests with 5% papain in PBS extract obtained from the tablet and commercial extract of papain (LETI, Barcelona, Spain) were positive with wheal sizes of 15×5 mm and 4×4 mm, respectively; prick by prick with papaya was 6×6 mm. The results of the skin tests with bromelain, pineapple, kiwi, and latex (LETI) and common inhalants (ALK-Abelló, Madrid, Spain) were negative. Total IgE (CAP System, Pharmacia, Sweden) was 194 kU/l; specific IgE (CAP System) against papain was 47.3 kU/l, and it was 8.37 kU/l to papaya. Specific IgE to latex, kiwi, bromelain, and pineapple were not found. Specific IgE immunoblotting, performed according to Moneo et al. (4), showed a

strong band between 24 and 50 kDa when the extract of papain was analyzed; bands were not found for kiwi, *Ficus benjamina* latex, and fig extracts.

In patient 2, the skin prick test with commercial papain showed a wheal size of 6×5 mm, and prick by prick with papaya showed 3×2 mm (the test with papain tablet extract was not done). Skin prick tests with common inhalants, bromelain, pineapple, and latex were negative; that with kiwi resulted in a wheal of 2×2 mm. Total IgE was 48.4 kU/l.

Specific IgE to papain was 19.5 kU/l; to papaya, 4.95 kU/l; and to kiwi, 0.52 kU/l. Results for latex, bromelain, and pineapple were negative. The immunoblot demonstrated a strong band between 34 and 50 kDa and a weaker one at 24 kDa. At this value, only one band was found to kiwi extract, and none were found to *F. benjamina* latex and fig extracts.

We present two new cases of occupational type I allergic reactions to papain demonstrated by skin and sera tests. The sensitization was produced in a different workplace from those usually reported, such as the drug and food industries. We found only one reference on papain allergy in cosmeticians (5), perhaps because the patients clearly perceive the symptoms from using this substance, avoid it, and never consult an allergist for this problem. Cross-reactivity between papain and fruits, bromelain, latex, and *F. benjamina* latex has been reported (6, 7). In our patients, this was not found, but in patient 2 a similar band at 24 kDa in blotting with papain and kiwi extracts was found.

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## Long persistence of IgE antibody to cefaclor

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**Key words:** cefaclor; child; IgE.

● ADVERSE drug reactions are a common clinical problem in childhood, and antibiotics are among the major contributors to drug hypersensitivity (1). Cefaclor, a second-generation oral

cephalosporin with a  $\beta$ -lactam ring, is used for a wide range of bacterial infections, especially in children. This antibiotic may cause various kinds of reactions (erythematous or papular eruptions, urticaria, serum sickness-like reactions, hypersensitivity myocarditis, and anaphylactic reactions) (1–3).

We describe a child who presented an adverse, IgE-mediated reaction to cefaclor and a long persistence of specific IgE to cefaclor.

At the age of 8 years, the patient had taken cefaclor suspension (5 ml) (trade name Panacef, Eli Lilly, Florence, Italy, 250 mg/5 ml) for infectious bronchitis. This drug had been previously taken by the child without adverse reactions; moreover, he had not experienced adverse reactions to other drugs. Five minutes after taking cefaclor, he presented angioedema with dyspnea and generalized urticaria; 10 min later, he was treated by a medical doctor with methylprednisolone 40 mg i.m., with clinical resolution in 1 h. Afterward, no determination of the cause of this adverse reaction was done.

Only 6 years later, the child was referred to our allergy clinic to determine the cause of this type of adverse reaction. He was now 14 years old, with allergic rhinitis to house-dust mite, but without family history of allergy. Panacef suspension contains excipients such as erythrosine and strawberry which might cause adverse reactions. Erythrosine (E127) is a coloring agent able to cause the appearance of clinical manifestations in subjects with hypersensitivity to this substance (4). Therefore, we did a test (double-blind vs placebo) with this agent, which was administered *per os* (capsules of 5 and 10 mg), according to the instructions of the manufacturer (Laboratorio Lofarma,

**IgE antibody was detected up to 6 years after reaction.**

Milan, Italy). No symptoms appeared after the administrations. A skin prick test (SPT) to erythrosine (10 mg/ml) was carried out on the volar side of the forearm with a plastic lancet (1-mm tip) made by Laboratorio Lofarma (Milan, Italy). A positive control with 10 mg/ml histamine was included. SPT results were assessed as positive (wheal response  $\geq 2+$ ) according to the recommendations of the European Academy of Allergology and Clinical Immunology (5). The SPT result for erythrosine was negative (0+). This SPT was done because the presence of IgE to additives has been described (6). A skin test (prick+prick with fresh food) and a commercially available assay for specific IgE level (CAP System Pharmacia, Uppsala, Sweden) to strawberry were also performed with a negative result (0+ and  $<0.35$  kUA/l, respectively). Specific IgE level (CAP System, Pharmacia) was then performed for cefaclor with a positive result (9.89 kUA/l), and for penicilloyl G, penicilloyl V, ampicilloyl, and amoxicilloyl with a negative result ( $<0.35$  kUA/l). A SPT with a drop of Panacef (concentration 50 mg/ml) was also carried out. The SPT response to Panacef was 4+. In a control group of 20 children without family history of allergy, without appearance of adverse drug reactions, and with allergic rhinitis to house-dust mite, SPT and CAP to cefaclor were negative (0+ and  $<0.35$  kUA/l respectively).

This report shows that cefaclor causes IgE-mediated reactions, and that it is possible to demonstrate the presence of specific IgE to cefaclor 6 years after the administration of this drug.

In the literature, there are no studies reporting the persistence of IgE to cefaclor for such a long period of time, whereas the evolution of skin test sensitivity in subjects allergic to benzylpenicillin, amoxicillin, and ampicillin has been investigated (7). We can propose some hypotheses to explain the long