

LETTER TO THE EDITOR

Cochineal extract-induced immediate allergy

Dear Editor,

Cochineal extract (carmic acid) is a natural red dye¹ that is used in cocktails, red pickles and confectionery. We encountered three patients who showed an immediate allergic response after ingesting drinks containing cochineal extract.

Patient 1 was a 35-year-old woman with a history of atopic dermatitis. She had developed facial itching and swelling after drinking Campari containing cochineal extract 3 years previously. This time, she drank Spumoni (a cocktail containing Campari and grapefruit juice). Epigastric pain and respiratory distress occurred immediately, while facial swelling, generalized erythema and diarrhea developed after 30 min. She presented to our hospital the next morning. Her symptoms subsided after i.v. infusion of a corticosteroid.

Patient 2 was a 44-year-old woman who had a history of allergic rhinitis, and had experienced itching after drinking alcohol previously. She noted discomfort 10 min after drinking a cocktail containing Campari and presented to our hospital on the next day. Her symptoms, as well as facial swelling and erythema of the upper extremities, resolved after treatment with oral anti-allergy drugs.

Patient 3 was a 52-year-old woman who had experienced urticaria before. When she drank a can of strawberry-colored juice containing cochineal extract, she developed palmar itching, pharyngeal discomfort, generalized itching and facial swelling within 30 min. The patient presented to our clinic 2 days later.

Hematology tests and biochemistry tests were conducted and the total immunoglobulin (Ig)E level was measured in all three patients. In patient 1, C-reactive protein (CRP) was slightly high (1.1 mg/dL) and total IgE was increased to 732 IU/mL (normal, ≤ 300 IU/mL). IgE radioallergosorbent test was class IV for the "konahyouhi" tick and house dust. In patients 2 and 3, hematology tests and biochemistry tests were all normal and the total IgE level was low.

Skin prick tests (SPT) were carried out on the three patients and 12 healthy volunteers, as described previously.² Cochineal extract and purified carmic acid (obtained by removal of impurities from cochineal extract) were provided by Saneigen FFI (Osaka, Japan). The color of the solutions of cochineal extract and purified carmic acid was the same as that of Campari. The cochineal extract concentrations in Spumoni and strawberry milk are lower than in Campari. In all the three patients, the SPT response to Campari was +++ or ++ and the response to cochineal extract solution was ++, similar to that for Campari. However, the SPT done with purified carmic acid showed a weak or negative reaction in all three patients. The results for Spumoni and strawberry milk were ++ or +. Boiled Campari caused a stronger reaction, suggesting that the allergen was heat-resistant and boiling increased its concentration. In 12 healthy volunteers used as controls, the SPT was always negative.

Serum levels of specific IgE were measured in patients 1 and 2, as well as the 12 healthy volunteers, by enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions. In patients 1 and 2, specific IgE for Campari and cochineal extract was positive, but IgE for purified carmic acid was negative. Specific IgE was negative in all 12 healthy volunteers.

The molecular weight of the antigenic protein was analyzed by western blotting using serum from the three patients and 12 healthy volunteers. Results of western blotting with serum from the three patients are shown in the Figure 1. It was found that patient 1 had IgE targeting a cochineal protein with a molecular weight of 39–45 kDa (and a weak reaction at 25 kDa), while patient 2 had IgE targeting a 40–45-kDa protein (and a weak reaction at 26 kDa). Patient 3 had IgE for a 39–44-kDa protein. The corresponding bands were not detected in the serum of the healthy volunteers, so they did not have specific IgE.

Correspondence: Yuko Yamakawa, M.D., Ph.D., Yamakawa Dermatology Clinic, 2F, 57-2 Oguchidoori, Kanagawa-ku, Yokohama 221-0002, Japan.
Email: yukoy@ce.netyou.jp

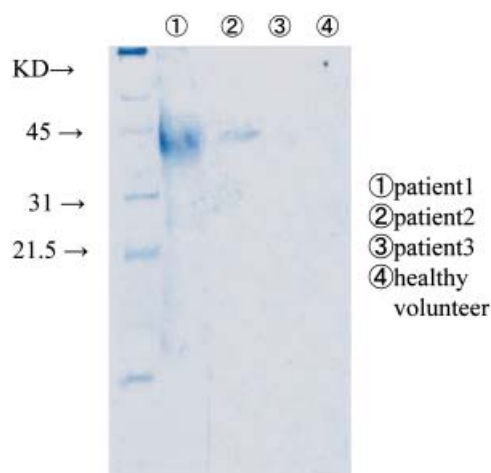


Figure 1. Western blotting using serum of the three patients and a volunteer. Patient 1 had immunoglobulin (Ig)E that responded to cochineal protein of molecular weight 39–45 kDa and slightly 25 kDa (lane 1). Patient 2 had that of 40–45 kDa and slightly 26 kDa (lane 2). Patient 3 had that of 39–44 kDa (lane 3). The corresponding band was not detected in serum of healthy volunteers (lane 4), proving that these volunteers did not have IgE.

Cochineal extract (carminic acid) is a natural red dye obtained from dried female *Dactylopius coccus Costa* (*Coccus cacti* L.), a cochineal belonging to the scale insect family, which is a parasite of *Nopalea coccinellifera*.¹ It is used in cocktail drinks such as Campari and Spumoni, other drinks such as strawberry milk and juice, red pickles, and confectionary such as red candies and red sweet bean jelly. The cochineal extract currently used by the food industry contains protein impurities originating from the insect source that remain after extraction of the pigment. Cochineal extract-induced allergic reactions that have been reported so far include occupational asthma,³ allergic alveolitis,⁴ and urticaria, dyspnea and anaphylaxis after drinking Campari,^{5,6} drinking strawberry milk or juice⁷ and eating fruit yogurt,⁸ as well as cochineal extract-containing popsicles or processed crab meat.⁹ Our hospital has managed three patients with cochineal extract-induced immediate allergy in the last 2 years. All three patients had a marked reaction to Campari and cochineal extract, but the reaction became weaker or negative when purified carmine was tested. This suggests that impurities in cochineal extract could be the cause of the immediate allergic reaction in these patients.

Measurement of serum levels of specific IgE in two patients showed that specific IgE for Campari and cochineal extract was positive, while IgE for purified carmine was at the same level as in 12 healthy volunteers. These results suggested the possibility that our patients had IgE targeting protein impurities in cochineal extract, but not purified carmine. Western blotting was conducted using patient serum and demonstrated that all three patients had IgE targeting a cochineal protein with a molecular weight of 39–45 kDa. Three cases have been reported so far, in which the allergenic proteins were 17, 28 and 50 kDa,¹⁰ 38 and 50 kDa,⁹ and 23 kDa.⁹ It has also been reported that allergy to cochineal extract is caused by protein impurities. There have been no Japanese reports before about immunoblotting in patients with cochineal extract-induced immediate allergy. The present study suggested that specific IgE responding to a protein of approximately 39–45 kDa among the impurities in cochineal extract may play a role in cochineal extract-induced anaphylaxis in Japan. If the protein impurity was eliminated and highly purified carmine was used as a food dye instead, patients with cochineal extract-induced immediate allergy would be safe from the risk of recurrence and new cases would also be prevented. Thus, the number of patients with cochineal extract-induced immediate allergy would decrease. A safer food dye would therefore be used widely.

ACKNOWLEDGMENT

We are deeply indebted to the Japan Food Chemistry Research Foundation for their assistance.

Yuko YAMAKAWA,^{1,2} Hiroyuki OOSUNA,³
Tadashi YAMAKAWA,⁴ Michiko AIHARA,³
Zenro IKEZAWA³

¹Yamakawa Dermatology Clinic, ²Department of Dermatology, Yokohama City University Medical Center, Departments of ³Environmental Immunodermatology, and ⁴Endocrinology and Diabetes, Yokohama City University Medical Center, Yokohama, Japan

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