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Food intolerance due to wine gums: Identification of copper chlorophyll (E141) as a possible pseudoallergen

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To the Editor:

Food intolerance is a commonly perceived problem in the general population and may lead to a variety of symptoms. We present a report of a young woman with relapsing angioedema, rhinoconjunctivitis, and asthma-like symptoms caused by exposure to copper chlorophyll (E141).

A 28-year-old woman had a history of sudden facial swelling associated with asthma-like symptoms and rhinorrhea. She remembered having eaten in a Chinese restaurant and having consumed various alcoholic beverages including a cocktail and an herb-flavored liqueur on the day of her symptoms. She had a history of allergic rhinoconjunctivitis and atopic eczema in her childhood. She also recalled symptoms of an oropharyngeal allergy syndrome after eating carrots, nuts, and kiwifruit. Her physical examination findings were unremarkable. Routine blood test results were normal including concentration and activity of serum C1-esterase inhibitor. Skin prick test results were positive against anise, caraway, mugwort, celery, coriander, paprika, carrot, nuts, and kiwifruit. Her total serum IgE level was elevated to 676 kU/L. Allergen-specific IgE antibodies against various spices and herbs were found in her serum. Allergic angioedema and rhinitis were diagnosed. She was

advised to avoid the suspected foods and beverages and instructed to keep a food diary.

One month later she again had multiple episodes of acute eyelid swelling, dyspnea, and rhinoconjunctivitis. Her food diary revealed that she had consumed milk, rice, orange juice, cheese, bread, 2 alcoholic cocktails, and English wine gums (a jelly bean–like chewy, sweet confection of different colors and fruit flavors without a hard sugar coat) as possible triggers. An open challenge was performed in which these foods and beverages were individually given in 1-hour intervals. Facial angioedema and rhinorrhea were provoked within 10 minutes after the patient had eaten a mixture of wine gums. Challenges with these gums (7 gums of each color in 45-minute intervals) showed green wine gums to elicit an anaphylactoid response within 10 minutes, whereas other colors were tolerated. Because the green wine gums differed from the others by the presence of E141 and gooseberry flavor, single-blind challenges were performed. Placebo-controlled challenges were performed with the substances hidden in wheat starch capsules and given at increasing amounts (45-minute intervals between each dosage) on 2 separate days. Angioedema and rhinoconjunctivitis were elicited only by E141 and developed after the patient had eaten 1 mg of E141 (equivalent to 5 green wine gums). Skin prick tests with green wine gums, E141, and copper sulfate yielded negative results. A cellular allergen stimulation test¹ with E141 was also nonreactive. After strict avoidance of E141, the patient has been free of any symptoms for more than 3 years.

It is known that food colors can act as allergens and pseudoallergens. Artificial dyes and synthetic and natural colors can provoke urticaria and anaphylaxis.^{2,3} E141 is a natural food color made from edible plants, grass, lucerne (alfalfa), and stinging nettles. It is used in foods, beverages, and pharmaceuticals (Table I).

Table I. Possible sources of copper chlorophyll and copper chlorophyllin (E141)* in foodstuffs[†]

Source	Examples
Sweets	Jelly beans, fruit gums, wine gums, candy floss or foamy sweets (eg, marshmallows), candies, chocolate products with colored coatings (eg, chocolate lentils), chewing gum
Fruit products	Jam, toppings (eg, on cake), jelly
Vegetable products	Some preserves with vegetables (eg, cucumbers or chilis)
Flavored dairy products	Fruit yogurt, milkshakes, ice cream and other dairy products, Sage Derby-Cheese (English specialty)
Beverages	Soft drinks, iced tea, flavored syrup, isotonic beverages
Alcoholic drinks	Cocktails, liqueurs, flavored wine- containing drinks
Other	Pharmaceutical products

*Coding of E141 includes the lipophilic copper chlorophyll and the hydrophilic copper chlorophyllin. In the latter dye the phytol ester is removed.

†Permitted as a foodstuff in most European countries according to European Parliament and Council Directive 94/36/EC of June 1994 on colors intended for use in foodstuffs (Official Journal L237, 10.09.1994; L 259, 07.10.1994; L252, 04.10.1996).

During the commercial production of E141, the plant extract is treated with dilute acids to replace magnesium with copper.⁴ Impurity of the dye can lead to an increased amount of ionizable copper, which by legislation, must not exceed 200 mg per kilogram dye.⁵ However, our patient did not have copper sensitization. Theoretically, mastication, exposure to digestive enzymes, and pH changes in the gastrointestinal tract may hydrolyze the ester bonds and cleave the isocyclic ring of E141, generating an antigen. Because the minimum amount of the coloring agent (copper pheophytine) is only 10% of the total dye,⁵ other residual pigments and remnants of the extracted original plant material may act also as an allergen or pseudoallergen. Thus our failure to provoke a positive reaction of green wine gums and E141 on skin prick test and cellular allergen stimulation test does not exclude an IgE-mediated reaction. On the basis of its potential to provoke anaphylactoid reactions, the presence of E141 in foods, beverages, and pharmaceuticals should be watched for in the future.

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