

Flavorings and colorings

Taylor SL, Dormedy ES. Flavorings and colorings.
Allergy 1998; 53 (Suppl 46): 80–82. © Munksgaard 1998.

S. L. Taylor, E. S. Dormedy

Food Allergy Research and Resource Program,
University of Nebraska, Lincoln, NE, USA

Dr Steve L. Taylor
University of Nebraska
Food Allergy Research and Resource Program
Lincoln, NE 68583-0919
USA

Flavorings are concentrated preparations that are used to impart flavor to food products. Flavoring preparations often contain dozens of chemicals, sometimes including flavoring adjuvants and carriers. Colorants are concentrated preparations of chemicals added to foods to impart color. Both flavoring and coloring substances are intended for use as food additives. Given the concentrated nature of these preparations, flavoring and coloring preparations are typically used at low levels in finished food products. In the USA, where food ingredients must be listed on labels in decreasing order of prevalence in the food product, colors and flavors are often the final ingredient to be listed.

Allergists sometimes suspect flavoring and coloring substances to be the cause of otherwise unexplained allergic reactions to specific food products. In these cases, the major ingredients listed on the incriminated product's labeling have been clinically tested and eliminated as possible causative agents. The physician is then left to wonder whether minor ingredients such as flavoring and coloring substances could be the causative factors. However, very little proof exists of the allergenicity of these substances. The possible role of flavoring substances in food allergies and intolerances was recently reviewed extensively (1).

Nature and composition of flavors

Those components of flavoring preparations that actually impart flavor are typically small-molecular-weight, volatile chemicals. Examples include various esters, ketones, lactones, aldehydes, terpenes, pyrazines, amines, phenols, and sulfur compounds. These flavoring substances can be manufactured by chemical synthesis or may be entirely natural in origin. Naturally occurring flavors may be inherent in foods or generated from precursors during cooking or processing of

foods. Commercially, flavors may be isolated from natural sources by various extraction, distillation, and concentration processes. Flavors can also be generated by thermal reactions between naturally occurring compounds in foods, such as the creation of meat flavor by the thermal reaction of certain amino acids and sugars. Flavors may also be generated by enzymatic reactions or enzymatic modification, as in cheese flavor, or by microbial fermentation, as in butter flavor. These process flavors generated by thermal or enzymatic action are becoming increasingly popular in the generation of the flavoring preparations needed in today's complex processed foods. Extraction, distillation, and concentration may also be used in the manufacture of process flavors to generate more concentrated flavor preparations. Synthetic flavors are manufactured from a variety of chemical reactions that often yield chemicals that are identical to naturally occurring compounds found in foods. However, chemical synthesis may be a way to produce flavors more economically than their isolation from natural sources.

Nonproteinaceous substances, such as esters, ketones, etc., make up the majority of flavors. Some flavors, especially certain process flavors, can include proteins from eggs, peanuts, milk, seafood, soybean, tree nuts, and wheat, which are considered to be common allergenic foods. The protein content of process flavors is highly variable depending upon the source materials used in the formulation, the protein content of these substances, processing conditions, and extraction conditions.

Carriers may also be present in flavoring formulations, often at concentrations exceeding that of the flavors themselves. Occasionally, allergenic materials such as whey may be used as carriers for flavor preparations.

Flavoring substances are typically used at low

levels in finished food products, and thousands of flavoring substances are allowed for use in foods. Complete labeling of flavoring substances is not required in any country, to our knowledge.

Assessment of the allergenic potential of food flavoring substances

Food allergens are typically proteins of natural origin. As noted above, flavors and flavor preparations rarely contain proteins. Thus, flavoring substances have been rarely implicated in allergic reactions. Flavoring substances would be unlikely to elicit allergic reactions because of the nonproteinaceous nature of most flavors, the extraordinary diversity of flavoring substances used in foods, the removal of any proteins in the flavor manufacturing process, and the very low levels of use of most of these substances (1).

IgE-mediated allergic reactions from flavoring substances in food products are rarely reported. In most such cases, the flavoring contained proteins from well-known allergenic foods such as milk or peanuts. Gern et al. (2) described four milk-allergic patients who had reactions after eating meats that were labeled as "nondiary" or "pareve" (containing no milk products). The natural flavoring of hot dogs and bologna was found to contain hydrolyzed sodium caseinate. St Vincent & Watson (3) documented the cases of two milk-allergic patients who developed allergic reactions after consumption of dill pickle-flavored potato chips. The package label listed "dill pickle seasoning"; milk was identified as an ingredient of this seasoning. McKenna & Klontz (4) described the case of a woman who suffered a severe, life-threatening, systemic allergic reaction from ingestion of a soup mix. The product was found to contain peanut flour as a component of the natural flavoring. Although the only examples in the literature involve milk and peanuts, the possibility exists that similar reactions could occur to soybeans, eggs, seafood, and other known allergenic materials used in the formulation of certain flavorings. However, the level of allergen in foods resulting from flavors would be extremely low even in the few formulations where allergenic materials were used.

Spices may also be considered as flavoring substances. Allergic reactions to spices have been widely reported (1). Spice allergies probably involve IgE-mediated reactions in most cases. However, the diagnosis of spice allergy is complicated by possible irritant reactions occurring in skin tests (1). While allergic reactions to spices have been reported more frequently than allergic reactions to other flavoring substances, such reactions are still considered rather rare.

Allergic reactions to flavors have also been reported to flavoring substances found in toothpaste, dental materials, tobacco products, hard candy, and chewing gum (1). These reactions are probably contact sensitivity reactions resulting from the flavor acting as a hapten, binding to mucosal proteins in the mouth, and eliciting a localized, cell-mediated immune response. Such contact sensitivity reactions require repeated exposure to comparatively higher concentrations of the offending substance and prolonged contact with the affected tissue (1). Certain flavoring substances are noteworthy for their ability to induce such contact sensitivity reactions. These flavoring substances include balsam of Peru, cinnamon and cinnamic compounds, eugenol, menthol, peppermint oil, spearmint oil, vanillin, and anethole (1). While contact sensitivity reactions are encountered with flavoring substances, the number of substances involved in such reactions is few, the reactions tend to occur with a few products that have long residence times in the mouth such as hard candy and chewing gum, sensitization often occurs through dermal exposure from the use of such substances in cosmetics, and the reactions are typically localized and comparatively mild (1).

Adverse reactions have also been reported to flavor enhancers such as monosodium glutamate (MSG). Some evidence exists to suggest that certain people may develop short-term, subjective reactions (flushing, etc.) when they consume large doses (3 g or more) of MSG (1). However, these reactions are not IgE-mediated. Some individuals with severe asthma may respond to large doses (3 g or more) of MSG (5). However, the mechanism of MSG-induced asthma is unknown, and the role of MSG in asthma has not been confirmed (6, 7). The association of MSG and hydrolyzed proteins with adverse reactions in some individuals remains to be clearly documented.

Nature and composition of colorings

Food colorings can be either synthetic or natural. Synthetic colorings fall into two general structural categories: the azo dyes and the nonazo dyes. Examples of azo dyes include tartrazine or FD&C Yellow No. 5, sunset yellow or FD&C Yellow No. 6, and FD&C Red No. 40. Examples of nonazo dyes include FD&C Blue No. 1 and FD&C Red No. 3. Natural colorings used in foods include carmine, annatto, turmeric, paprika, and several of the carotenoids. Foods sometimes contain more than one of these coloring substances.

Assessment of the allergenic potential of food-coloring substances

Adverse reactions have been most frequently reported with tartrazine. While many studies have purported to show a causative role for tartrazine in asthma, chronic urticaria, and, occasionally, other food sensitivities, a cause-and-effect role for tartrazine in these illnesses has not been established (8, 9). Considerable debate exists relative to the proper method to conduct challenge trials with tartrazine, especially with respect to the withdrawal of medications before challenge (8, 9). Only one of 24 patients with chronic urticaria developed urticaria on challenge with tartrazine if antihistamines were not withheld (8). In a study of 43 aspirin-tolerant and 194 aspirin-sensitive asthmatics, none reacted on challenge with up to 50 mg of tartrazine when beta agonists, cromolyn, and antihistamines were withheld but theophylline, bronchodilators, and inhaled and systemic corticosteroids were continued during challenge (9).

A few reactions have been reported to other synthetic food colors. However, these studies are plagued by many of the same methodological problems that occur in tartrazine studies. Thus, there is no compelling evidence for the involvement of other synthetic food colors in asthma, urticaria, or angioedema.

Food sensitivities have been reported to several of the natural food colorings. Annatto and carmine have been implicated in IgE-mediated allergic reactions. Both of these natural colorings do contain natural protein residues, so allergic sensitization is possible. Several studies have implicated annatto in chronic urticaria and/or angioedema (10, 11). However, antihistamines were withheld from the patients in these challenge studies; thus, the results are somewhat questionable. A single convincing case report of an IgE-mediated allergic reaction to annatto exists (12). This patient had a positive skin test, and an IgE-binding protein was identified in the annatto extract. The evidence for IgE-mediated reactions to carmine is fairly compelling, although only a small number of cases have

been reported (13–16). Carmine does contain protein and is probably a rare cause of IgE-mediated allergic reactions to food.

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