Food Allergy and Risk Management

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Abstract

Food allergy is an adverse immune response to a normally tolerated food protein.⁴⁴ Generally, food allergic reactions are mediated by immunoglobulin E (IgE) and occur in individuals who are genetically predisposed to the allergy and who have been previously exposed to the allergen. Food allergies have become an important health concern worldwide. The symptoms of food allergy include respiratory, gastrointestinal and cardiovascular symptoms and a rare life threatening symptom includes anaphylactic shock. The substance that causes an allergic reaction is called an allergen. More than 160 foods are identified as allergenic. Approximately 90 percent of all the allergenic reactions to food are caused by eight major foods namely milk, eggs, fish, crustacean, shellfish, tree nuts, peanuts, wheat, and soybeans.¹⁰ Currently there is no cure for food allergy. Therefore, proper management is very much important to reduce the risk of food allergy. Several research efforts are ongoing to develop anti-allergenic as well as hypoallergenic foods by using various processing technologies to eliminate the causative factor. Hence, understanding the recent status of food allergy and advanced processing technologies are required for reducing allergenicity of foods.

Keywords: Food allergy; Allergen; Anaphylactic shock; Anti allergenic food; Hypoallergenic food.

Introduction

Food is necessary for survival, but sometimes a morsel can kill. Food allergies have become a burning health concern worldwide. It is an adverse reaction to specific food by the immune system. Food allergy is a major health problem affecting up to 5% of adults and 8% of children worldwide. ¹⁹ It has been defined as an IgE-mediated abnormal response to very low quantities of certain food

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proteins.³⁸ Symptoms are diverse ranging from relatively mild to severe or sometimes even fatal consequences.⁴³ Clinical manifestations of food allergies in sensitized individuals can range from minor digestive disorders and skin irritations to more severe symptoms that can even lead to life threatening situations. To provide all consumers with better information and to protect the health of certain consumers, several countries have introduced into their legislation the obligation to indicate the presence of certain allergenic ingredients on food labels.

Food allergies are an abnormal response of the body to otherwise harmless foods involving the immune system. Normally, our immune system defends against possibly harmful substances, such as bacteria, viruses, and toxins. However, the immune system of allergic individuals incorrectly identifies certain food constituents as harmful. The severity of an allergic reaction may vary between individuals. While one person may have to rush

to the nearest emergency room within minutes of eating a food allergen because of life-threatening symptoms, another person may only develop itching in the mouth. The reaction may develop within a few minutes or a few hours.

Currently there is no cure for food allergy and food allergic individuals must completely avoid the sensitive foods.36 Absolute avoidance of the foods is difficult in the modern days because of the use of major allergens as ingredients in other food products and contamination caused by processing in same facility that handles allergenic foods.⁴⁹ Risk assessment and management of food allergy is very difficult because of several reasons: (1) Non-allergic people can consume different food allergens without any risk unlike other chemical and microbiological hazards like toxins and harmful bacteria. (2) Almost all of the major allergenic foods provide nutrition and are part of daily food consumption for survival. (3) The sensitivity to food allergens varies vastly from one patient to other who is allergic to the same food. Hence no two allergenic foods can have similar risk management strategies.⁷

Prevalence of food allergy

Food allergies are an important health issue that are considered by the World Health Organization among the five most important public health concerns, 24,16 particularly industrialized in countries, where the affected population represents approximately 2% of adults and up to 4-8% of young children.^{20,12} Globally 200-500 million people suffer from food allergy and it affects the quality of life mainly children (5-8%). In adults, the prevalence is considerably low (1-2%) and no country has reported decline in food allergy in the last decade.³⁹ India reflects 1–2% prevalence of food allergy which is found more among children when to compared to adults.30

Allergens

A substance that causes an allergic reaction is called an allergen. Food allergens are the components of food that can cause adverse immunological reactions when consumed. More than 160 foods are identified as allergenic. Approximately 90 percent of all the allergenic reactions to food are caused by eight major foods namely milk, eggs, fish, crustacean, shellfish, tree nuts, peanuts, wheat, and soybeans. The other 10 percent of the allergenic food reactions are caused by remaining foods that are identified as allergens and are less prominent.⁴⁰

Table 1: Food allergens from animal sources

Food	Major allergenic proteins	References
Cow's Milk	b-lactoglobulin Casein a-lactalbumin	[34] [52]
Egg	Hen's Egg White Ovomucoid Ovalbumin Ovotransferrin Lysozyme Egg yolk a-livetin	[5] [21] [50] [41]
Fish	Parvalbumin	[41]
Shrimp	Pen a 1 (Tropomyosin)	[3]

Table 2: Food allergens from plant sources

Food	Major allergenic proteins	References
Tree nuts	Pru du 6 from almond	[14]
	Ber e 1 from Brazil nut	[42]
	Ana o 1 and Ana o 2 from cashew	
	Cor a 1 from hazelnut	
Peanut	Ara h 1	[31]
	Ara h 2	[32]
	Ara h 3	[25]
Soybean	Gly m Bd 30 K	[37]
•	Gly m Bd 60 K	[54]
	Glv m Bd 28 K	

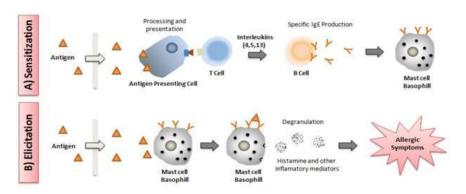


Fig. 1:

Mechanism of food allergy

The development of an allergy occurs in two stages (Figure 1):

Sensitisation: When a person is first exposed to a food (may be before birth), the food may trigger immune system cells to produce large amounts of IgE that specifically recognizes that food.

Reaction: Once sensitised, even a tiny quantity of that allergen can lead to an allergic reaction. When the person eats the same food again, the allergen triggers the newly armed immune system, which leads to allergy symptoms.

Signs and symptoms: Clinical symptoms that are associated with the ingestion of foods by sensitive persons include urticaria, itching, edema, bronchoconstriction, rhinitis, vomiting, diarrhea, cramps, and, in severe cases, cardiovascular symptoms that may lead to anaphylactic shock, which may have fatal consequences.⁵

Risk management of food allergy

Currently there is no cure for food allergy and food allergic individuals must completely avoid the sensitive foods.⁴⁷ Absolute avoidance of the foods is difficult in the modern days because of the use of major allergens as ingredients in other food products and contamination caused by processing in same facility that handles allergenic foods.⁴⁹ Therefore, a proper risk management strategy is very much essential to eliminate the seriousness of food allergy. The development of food allergy could be prevented by blocking any steps in the allergic reaction sequence, from allergen absorption to inflammatory reaction. Food allergy can be prevented by

- (i) Blocking allergen invasion/recognition
- (ii) Blocking T-cell activation
- (iii) Blocking the binding of allergens with IgE antibodies
- (iv) Blocking the release of chemotransmitters.

Risk management of allergenicity by foodoriented approach

1. Exclusive breastfeeding: Breast milk contains a host of immunologically active compounds, such as transforming growth factor – beta, lactoferrin, lysozymes, long-chain fatty

- acids, antioxidants and secretory IgA (sIgA), all of which have an effect on immune development, including oral tolerance and help to reinforce the gut-epithelial barrier. 8,22 There is evidence that exclusive breastfeeding for the first 6 months from birth protects against wheezing in early life. 18 On the other hand infant formulas should be given in the first 4 to 6 months only if exclusive breastfeeding is not possible for some reason.
- 2. Avoid the allergenic food: The elimination of the allergenic food from the diet of an individual with allergy is the simplest way to reduce allergy. But food avoidance should always be parallel with inclusion of food substitutes to balance the nutritional intake. On the other hand, eating meals away from home can be risky for individuals with food allergies. Whether at a fancy restaurant or a fast-food establishment, inadvertent exposure to an allergen can occur, even among the most knowledgeable individuals.
- 3. Label reading: Labeling is an important part of a food package and it helps the consumers to identify the potential allergen present in it. Since January 1, 2006, the Food Allergen Labeling and Consumer Protection Act (FALCPA) requires the top 8 allergens to be listed clearly on the food labels. This includes ingredients in any amount and also mandates specific ingredients to be listed such as the type of nut or seafood.

Risk management of allergenicity by food processing

Food Processing may alter the structures and availability of epitopes for binding to IgE. Processing may be thermal or non-thermal.

Thermal Processing

The effect of thermal treatment on food allergens has been widely researched due to its wide application in food processing. Heat treatment can denature some proteins and thus change the native structure. The conformational epitopes are altered during denaturation due to the modification of secondary and tertiary structure which may reduce the IgE binding. Depending on the type of protein, temperature and extent of heating, heat treatment may induce unfolding which can be reversible or irreversible. Each protein exhibits different resistance to heat treatment. Moreover the response

of a food allergen to heat depends on whether the heat is dry or moist.⁶ Fruit allergens such as Mal d 1 and Pru av 1 are more heat labile, whereas Gly m 4 of soy are more heat stable.⁴⁴ Examples of food allergens that are highly resistant to heat treatment include casein,¹ tropmyosin⁴⁵ and ovomucoid.⁴

Thermal treatment may also lead to formation of neoantigens that are not present originally. The generation of neoantigens may enhance the allergenic problem in sensitized patients. One of the factors responsible for the formation of neoantigens maybe maillard reaction, e.g., the interaction of the protein component with sugar residues upon heating, generating sugar conjugated protein derivatives, that in turn increases the allergenicity of protein.⁵¹

The effect of heating on allergenicity of different foods-

- 1. Legumes: Boiled lentils extract keeps its allergenicity. Soybean allergen globulin, when heated, lost partly its allergenicity. Decrease allergenicity of chickpea on boiling, but may have no change on antigenic behaviour as in the case of boiling pea allergens.
- 2. Fish and seafood: Cooking of fish caused denaturation and coagulation of proteins but some bands presented IgE binding. Canning of fish caused the reduction in IgE binding.
- 3. *Meat and meat products:* Allergenicity of pork sausages decreases after autoclave treatment.
- 4. Peanuts and other nuts: Roasting, autoclaving, blanching, microwave heating of almonds indicated antigenic stability of almond proteins when compared with that of the unprocessed nuts. Hazelnut protein presented high heat stability and can be detected even after treatment at 185 °C. Peanut roasting, increases the allergenicity of the final product.
- 5. *Fruits and vegetables:* In case of peach, sterilization is not able to decrease the allergenicity of the Pru p 1 protein.
- 6. Milk and milk products: In cow milk, α -casein is the most stable, bovine serum albumin is the most heat labile and β -lactoglobulin is relatively heat stable. Bu *et al.* (2013) studied the effect of thermal processing on milk proteins and reported that α -latalbumin and β -lactoglobulin had increased allergenicity from 50 to 90 °C whereas the allergenicity decreased when heated above 90 °C.

Non - thermal Processing

Although thermal treatment may reduce allergic reactions of some thermal labile proteins, non-thermal processing offers several advantages over non-thermal processing because of retention of nutrition and natural attributes such as aroma, color, and flavor. Nonthermal treatments are proved to be effective in killing harmful bacteria in different food products with minimum effect on the quality.⁴

Recent research on the effect of nonthermal treatments in altering allergenicity of food proteins showed that these treatments can reduce the allergencity of different food allergens.35 Pulse ultraviolet light, high intensity ultrasound, nonthermal atmospheric plasma, gamma irradiation, genetic modification, physical, chemical and enzymatic processing are some of the nonthermal treatments shown to have the ability to alter the allergenicity of different food allergens.³⁵ Some of these processes have been described below:

- a. *Enzyme Treatment*: Enzymatic treatment hydrolyzes the protein with enzymes and reduces the allergenicity. This treatment destroys the structure of proteins and alters its properties. Development of off flavor and bitterness due to the release of peptides and amino acids makes the enzymatic hydrolyzed product often unacceptable for consumption.¹⁵ Expensive equipment and ingredients were the major disadvantages of this treatment.
- b. *Bacterial Culture*: Mesophillic and thermophillic strains of bacterial cultures were shown to have reduced the allergenicity of cow milk proteins when tested with in vitro system. Lactic acid bacteria fermentation can reduce the immunoreactivity of sterilized cow milk by 90% while preserving the organoleptic properties of the product.²³
- c. Genetic Modification: Genetic modification process can be applied to prevent translation of selected allergens using post-transcriptional gene silencing or co-suppresion. Stability of these foods has not been determined and this process might lead to the change in functional and physical properties of foods.⁴⁶
- d. *Gamma Irradiation:* Gamma irradiation was regarded as an effective method to reduce the allergenicity of shrimp and milk allergens.²⁸ However consumer resistance and need for large investments makes it difficult for application in food industry.²⁹

e. *Ultraviolet Light:* Researchers used ultraviolet (UV) light as a bactericidal agent since the year 1928.⁵² The effect of UV radiation on food allergenicity varies depending on the amino acid composition and molecular structure of the protein.¹⁷ A 7 fold reduction in IgE binding of peanut allergens in Ci-ELISA analysis was obtained by treating peanut extract and liquid peanut butter with pulsed UV light treatment.¹¹

Development of product based on proceesing techniques

Development of hypoallergenic food

Currently, food allergy is mainly treated symptomatically through medication and removal of the causal food. However, the elimination of allergen-containing food from the diet of growing infants is undesirable, as it may lead to nutritional deficiency or developmental disturbance. The development of hypoallergenic food through the degradation or denaturation of allergens is essential to prevent nutritional disorders or growth disturbance and to maintain a rich and varied diet. Therefore, it is required that hypoallergenic food is nutritionally identical to normal food and shows minimum allergenic activity.

To date, several methods for reducing allergens in crops or food products have been developed and applied to commercial products. One such example is "Fine Rice," which has been developed through joint research between Shiseido, the Faculty of Agriculture of The University of Tokyo and the School of Medicine of Yokohama City University, and was commercialized in 1991. Fine Rice has been produced through the protease treatment of rice, which has led to the decomposition of globulin, an allergenic protein. The product was approved by the Ministry of Health and Welfare as the first "food for specified health uses" in June 1993 and as "food for medical purpose" in June 1997. Another example of hypoallergenic rice is that developed by Mitsui Toatsu Chemicals, Inc. (currently Mitsui Chemicals, Inc.) and the National Institute for Agro - Environmental Sciences, in which the expression of allergenic proteins has been suppressed by genetic engineering. The National Agricultural Research Center for Tohoku Region has developed a hypoallergenic soybean variety named "Yumeminori" lacking two of the three major allergens found in soybeans.

Development of anti-allergic food

Anti-allergic food prevents or controls food allergy by inducing oral tolerance or utilizing gut immunity and anti-allergic food components.

- (1) Anti-allergic food based on oral tolerance induction: Oral tolerance is a phenomenon in which proteins in orally ingested food do not induce excessive immune responses, despite the fact that food has a vast amount of antigenic substances containing foreign proteins. Food allergy is induced when a specific allergen is orally ingested and absorbed by the body via the digestive tract. It has been reported that oral tolerance to acertain antigen is induced by the protein itself or by a peptide of the protein. In other words, it may be possible to suppress an allergic reaction by inducing oral tolerance using a peptide that reacts with the T-cell but does not bind to the IgE antibody involved in the allergic reaction.
- (2) Anti-allergic food based on mucosal immunity in the gut: Microbes such as lactic bacteria in cheese, yogurt and other fermented dairy products improve the storage quality and taste of milk and its nutritional value through proteolysis, lactose degradation and vitamin synthesis. They also improve the gut microflora and have other health effects such as intestinal regulation, normotension and immune stimulation. Recently, probiotics have attracted attention for their effect of enhancing the immune regulatory function of the digestive tract and suppressing or ameliorating allergic symptoms. There is a difference in gut microflora between people with and without allergy, and smaller numbers of lactobacillus, a kind of lactic bacteria, have been found in the former compared to the latter group. This report has triggered a series of research projects on probiotics including lactic bacteria and the development of probioticbased products with anti-allergic effects.
- (3) Use of anti-allergic components: One way to prevent the development of food allergy is to suppress the production or action of chemotransmitters such as histamine and leukotriene that trigger the inflammatory response in the allergic reaction sequence. The production or action of chemotransmitters is called anti-allergic action. While hypoallergenic food involves antigen-specific suppression, anti-allergic action works in a non-specific manner, suppressing allergic reactions independent of the allergen type. Many food components are known to have anti-allergic

actions. For example, highly unsaturated fatty acids such as eicosa pentaenoic acid and docosa hexaenoic acid, which are abundant in fish, suppress leukotriene production, and tea polyphenol suppresses histamine and leukotriene release. Anti-allergic actions have also been reported in tea catechin and caffeine. Additional anti-allergic components have been identified in various foods, including flavonoids, sesamin and perilla leaf extract, development of probiotic-based products with anti-allergic effects.

Conclusion

Lucretius of Greece once said, "One man's food might be another man's poison." Food allergy is a significant health problem, with increasing prevalence and potentially life-threatening sequelae. Over-diagnosis of food allergy may also lead to unnecessary avoidance of food, resulting in an impaired quality of life. Recent advances in various processing techniques offer great promise to the food processors to develop hypoallergenic foods and to ensure delivery of safe food to consumers. Future progress in research and development requires not only setting individual research tasks but also discussing the evaluation of the efficacy and safety of anti-allergic foods and their application to allergic diseases. Therefore, cooperation with the medical profession is essential for the research and development of food products. Thus, further careful evaluation has to be conducted for determining the influence of specific process on the allergens. However, much more research is needed into the causes of food allergy. Such research will help to develop strategies for prevention and management that could improve the health, and quality of life of many people.

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