

Potential Utility of High-Pressure Processing to Address the Risk of Food Allergen Concerns

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Abstract: High-pressure processing (HPP) technology is a novel, nonthermal processing technology for food. This special processing method can inactivate microorganisms and enzymes in food at room temperature using ultra-high pressures of above 100 MPa, while the original flavor and nutritional value of the food are maintained, with an extended refrigerated shelf-life of the food in distribution. In recent years, because of the rising prevalence of food allergies, many researchers have actively sought processing methods that reduce the allergenicity of food allergens. This study describes the effects of the current HPP technology on allergen activity. Our main goal was to provide an overview of the current research achievements of the application of HPP to eliminate the allergenicity of various foods, including legumes, grains, seafood, meat, dairy products, fruits, and vegetables. In addition, the processing parameters, principles, and mechanisms of HPP for allergen destruction are discussed, such as the induction of protein denaturation, the change in protein conformation, allergen removal using the high-pressure extraction technology, and the promotion of enzymatic hydrolysis to alter the sensitization of the allergens. In the future, the application of HPP technology as a pretreatment step for raw food materials may contribute to the development of food products with low or no allergenic ingredients, which then can effectively reduce the concern for consumers with allergies, reduce the risk of mistaken ingestion, and reduce the overall incidence of allergic reactions from food.

Introduction

Food allergy, a common disease, is an abnormal immune response of an individual triggered by the ingestion of certain foods. The phenomenon that nontoxic proteins in food with no adverse response in the majority of individuals lead to allergy symptoms in a certain sensitive population is still poorly understood, and no perfect treatment is currently available. Based on an epidemiological survey, the World Allergy Organization estimated that there are approximately 220 to 250 million people suffering from food allergies, and the incidence of food allergies is 5% to 8% for infants and children, which is higher than 1% to 2% for adults (Fiocchi and others 2011). The prevalence of food allergies is increasing every year. The statistical analyses by Sicherer and others (2010) for the United States in 1997 to 2008 showed that food allergies for children under the age of 18 increased by 18% during that time and continue to increase. Food allergies not only have a serious negative impact on the quality of life of the patients but also endanger lives. Epidemiological studies have estimated that there are approximately 125000 cases of emergency incidents and 53700 cases of systematic anaphylaxis caused by food allergies annually in the USA alone, causing 2000 patients to be hospitalized and approximately 200 severe cases that led to death (Decker and others

2008; Ross and others 2008; Sicherer and Sampson 2010; Fiocchi and others 2011). In addition, many potential allergy sufferers initiate an allergic response to specific foods after being influenced by factors such as diet and the environment; therefore, the physical conditions change with increasing age. These potential allergic patients do not realize that they are allergic to certain foods until eating those foods; therefore, food allergies seriously affect a person's life quality and food safety. The invested medical resource is a large economic burden for the entire society, indicating that food allergies are indeed a livelihood issue that cannot be ignored.

Food allergens exist widely in various food products. To reduce the incidence of food allergies, education can increase public awareness of food allergies; in addition, food manufacturers should enhance the allergen labeling in food packaging. Many developed countries such as the United States, the European Union, Australia, the United Kingdom, Japan, and People's Republic of China have expressly stipulated that all allergenic foods must be labeled to reduce the risk of mistaken ingestion by consumers. Currently, food manufacturing and processing technologies have substantially improved, and the components of many refined processed foods are difficult to identify, becoming hidden sources of allergens. The accidental allergenic response due to inadvertent ingestion of food containing allergens has been frequently reported. Therefore, research and development of processing technologies to inhibit allergen activity or to remove allergens for the preparation of hypoallergenic or nonallergenic food is a common goal for food processing industry professionals. Many studies have attempted to remove food allergens using different processing methods based on

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different principles including enzymatic hydrolysis, genetic modification, and physical methods (Shriver and Yang 2011). The hypoallergenic foods currently available on the market are primarily manufactured using enzymatic hydrolysis. Although this method has the ability to alter sensitization, considering the food quality and consumer acceptance, the proteolysis process has a negative impact on food structure and organoleptic characteristics. Therefore, it does not apply to most foods. Genetic modification produces genetically modified food without allergenic proteins using a genetic engineering technique. Based on the existing regulations and consumer perception about genetically modified food, the development of these foods remains controversial (Houska and others 2011). Accordingly, most processing technologies are still based on physical principles to destroy the food allergens. The physical methods include thermal processing using humid or dry heat treatments. Although the thermal processing technology is frequently applied in traditional food processing, the sensory quality and nutritional value of the processed food may be harmed. Therefore, the development and research of nonthermal processing technologies, such as high-pressure processing (HPP), pulsed ultraviolet light, pulsed electric field, gamma-irradiation, and ultrasound have emerged (Thakur and Nelson 1998).

HPP is a novel nonthermal processing technology which has triggered attention to its ability to inactivate pathogens in room temperature and retain the organoleptic characteristic and nutritional quality of foods. The protein structure of the food allergen is the key to its allergenicity. The HPP causes a reversible or irreversible structural modification in proteins, leading to protein denaturation, aggregation, or gelatinization (Mills and others 2009). This feature allows the HPP technology to alter allergen allergenicity. The review of the literature here introduces food allergies and HPP; the main goal is to provide an overview of the studies on the removal of food allergens through high-pressure technology including the application of high-pressure technology for promoting the inhibition of allergen activity and for assisting allergen removal.

Food Allergy

Definition and mechanism

Statistical data indicate that the extent of food allergy cases accounts for approximately 1% to 2% of the total population, and it often occurs in infants (1 to 3 y of age) whose immune systems have not yet been well developed and children (Taylor and Hefle 2001). Food allergens exist widely in various food products. More than 90% of food allergies are derived from 8 types of food including cow milk, eggs, fish, crustaceans (shrimp, crab, and lobster, and so on), peanuts, soybeans, tree nuts (almond, walnut, cashew, pistachio, and hazelnut, and so on), and wheat. These 8 food categories have been defined as the most important types causing food allergies by the Food and Agriculture Organization of the United Nations (FAO 1995). Among them, food allergy to cow milk, eggs, and peanuts often occurs in infants under 3 y of age, accounting for approximately 6% to 8%, while the occurrence of an allergy triggered by nuts and seafood showed a higher proportion in adults, with approximately 1% to 2% adults having allergies to peanuts, tree nuts, and seafood (Sampson 1996; Sicherer and others 1999; Grundy and others 2002; Untersmayr and Jensen-Jarolim 2006). The symptoms in 80% of children allergic to cow milk, eggs, soy, and wheat are relieved before reaching school age, while the allergies to peanuts, tree nuts, and seafood typically persist throughout life (Sicherer and Sampson 2006). The statistical analyses showed that the occurrence of food allergy is rising, in-

dicating that food allergy is a major issue that cannot be ignored (Sicherer and others 2010).

All abnormal physiological responses caused by diet are collectively defined as food sensitivity, which can be divided into food allergy, which is regulated by the immune system, and food intolerance, which is not regulated by the immune system (Figure 1). Food allergy is the abnormal evoked response in the immune system caused by specific components in the food, and these components are usually the proteins naturally occurring, which are nontoxic and show no adverse effects for most individuals. Based on the characteristics of the immune response, it can be divided into 2 types of reactions: the IgE-mediated immediate hypersensitivity reaction regulated by immunoglobulin IgE; and the non-IgE-mediated delayed hypersensitivity reaction. For the former, after ingestion of the allergenic food, the symptoms arise usually in a few minutes to 1 h, or even right after the moment of ingestion. The abnormal immune response is generated by the antigen-specific IgE in the humoral immune system, which is the most common food allergy and has been most widely investigated. The latter usually occurs within 6 to 24 h after ingestion, and the probability of occurrence is relatively low and with an unclear mechanism. The latter belongs to an abnormal immune response generated by sensitive T cells in the cellular immune response (Taylor and others 2000). The abnormal response of food intolerance is not caused by the immune system. For example, metabolic food disorders are genetic defects in the ability to metabolize certain food ingredients (such as lactose intolerance) or an increased sensitivity to certain food ingredients because of a genetic defect (such as favism). An anaphylactoid reaction is caused by the sensitizing factor released from mast cells and basophils. It is difficult to distinguish from the immediate food allergy regulated by IgE in clinical practice. The only difference is that an anaphylactoid reaction is not IgE-regulated. The pathogenic mechanism of idiosyncratic reaction such as sulfite-induced asthma in some individuals is poorly understood (Taylor and others 1992).

Clinical studies have confirmed that, among all abnormal immune responses caused by food, the proportion of those regulated by IgE is the highest. The allergic reactions caused by allergenic foods such as cow milk, eggs, seafood, and nuts belong to this category. Therefore, the investigations of food allergies have primarily focused on the food allergies regulated by IgE (Taylor and others 1992). The reaction mechanism of a food-induced allergy can be divided into 5 stages: recognizing the antigen; generating immunoglobulin IgE; activating the mast cells and basophils; releasing the sensitizing factors; and presenting the clinical symptoms. When a sensitive individual ingests an allergenic food, the allergen protein in this food is recognized by the immune system as an antigen, and an allergic reaction is induced. When T cells are stimulated by the antigen, they release the substances IL-4, IL-5, and IL-13 to activate and convert B cells into plasma cells that can secrete IgE. IgE with specificity to the particular allergen will bind to the receptors of the mast cells and basophils so that they are activated to be sensitive cells. When the allergen is ingested into the body again, the allergen will be recognized as the antigen and binding to the IgE on the surface of the mast cells and basophils, resulting in the degranulation of particles and the release of the vesicles containing the sensitizing factors. These sensitizing factors are then released into the blood and interact with the receptors on cells and tissues, thereby causing the symptoms of an allergic reaction. The allergic symptoms caused by food allergy and their severity depend on the individual physical conditions

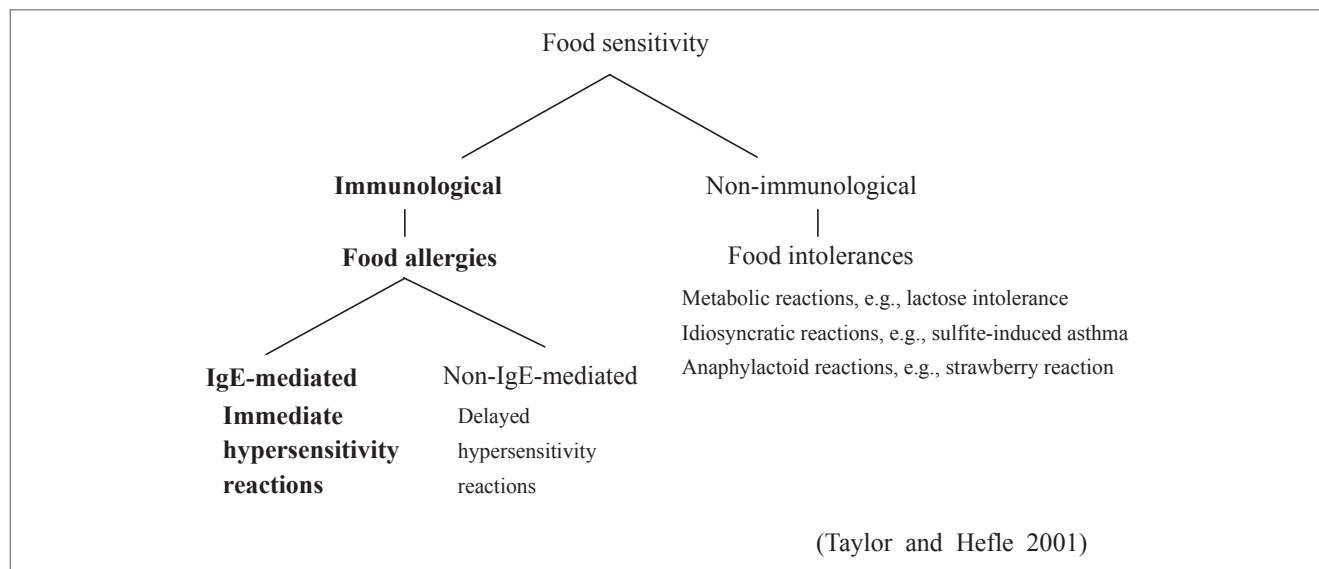


Figure 1—Relationships of the various types of food sensitivities.

and the intake amount, which may be moderate, severe, and even life-threatening symptoms in the gastrointestinal tract, the skin, or the respiratory tract (Untersmayr and Jensen-Jarolim 2006).

The pathogenesis of food allergy, including what makes one person become more allergic than others, and the factors that make some foods and food proteins more allergenic than other foods and food proteins are still unknown. No perfect treatment for food allergy is currently available (Mills and others 2009). The food allergy reaction regulated by IgE has quite a low tolerance to specific foods, and trace amounts are sufficient to cause an allergic reaction in some sensitive individuals. Therefore, sensitive individuals must avoid the ingestion of foods that cause an abnormal reaction. Food allergy sufferers must wear medical identification, fully understand their own condition, carry medications at all times, and learn emergency treatments such as self-injection of epinephrine in the early stage of allergy symptoms to avoid more serious consequences. Attention should also be paid to the incomplete cleaning of processing equipment and eating utensils as well as cross-contamination during meal preparation. In addition, patients with food allergies should carefully read the labels on packaged foods in order to avoid what must not be ingested (Taylor and others 1992; Sicherer and Sampson 2010). The 2003/13/EC of the European Union stipulates that foods containing grains (gluten), crustaceans, eggs, fish, peanuts, soybeans, cow milk, nuts, celery, mustard, sesame, and sulfites (if more than 10 mg/kg or 10 mg/L) must be labeled (EU 2003). The allergen-labeling specifications of the United Kingdom and Australia are similar to those of the European Union (Food Standards Agency 2006; Australian Food and Grocery Council 2007). In January 2006, the U.S. FDA announced the Food Allergen Labeling and Consumer Protection Act (FALCPA), which specifies the labeling of allergenic foods and products sold in the United States, including cow milk, eggs, fish, crustaceans, peanuts, tree nuts, wheat, and soybeans. The label text is required to be clear and easy to understand; for example, “milk” instead of its specific ingredient “casein.” If casein is used as a term, it must be followed by an explanation in plain text such as “casein (milk).” In Asia, according to the enforcement rules of the Food Sanitation Law by the Ministry of Health, Labor and Welfare of Japan, the labels of foods that would likely lead to an allergic reac-

tion are divided into 2 categories: mandatory and recommended labels. Eggs, cow milk, peanuts, wheat, buckwheat, shrimp, and crab require mandatory labeling by ministerial ordinance and are referred to as “specific allergenic ingredients” (Akiyama and others 2011). On the other hand, foods that require only recommended labeling include ingredients such as abalone, squid, salmon roe, kiwifruit, beef, walnut, soybean, apple, and peach, referred to as “subspecific allergenic ingredients.” In P. R. China, the Chinese Natl. Food Safety Standard stipulates labeling for 8 categories of prepackaged foods that easily lead to allergies. If any of these categories are used as ingredients or might be added during the food processing, then they must be listed among the ingredients or nearby on the label (Ministry of Health of the People’s Republic of China 2011).

Categories of food allergens

The specific components in certain foods that can trigger an abnormal immune response in the human body are known as food allergens. Only a few allergens have been isolated and identified. Most have similar characteristics such as being water-soluble glycoproteins with heat-resistance and acid-stability, and the molecular weights are located between 10 and 70 kDa (Shriver and Yang 2011). The major allergenic foods are introduced in the following sections.

Peanut

In Western and Asian countries, the numbers of cases of peanut allergy have risen in recent years. During the period of 1997 to 2002, the peanut allergy population has doubled. In the United States, approximately 3 million people suffer from allergies to peanuts and other nuts (Sicherer and others 2003). In addition to affecting a large number of people, peanut allergy is also the allergy with the highest mortality rate (Bock and others 2007). For extremely sensitive individuals, the ingestion of trace amount will cause serious symptoms (Grundy and others 2002; Leung and others 2002). Currently, 13 proteins have been identified that specifically bind with the peanut-specific IgE (Allergen Nomenclature Sub-committee 2013). Among them, Ara h 1 and Ara h 2, 64 and 17 kDa, respectively, are commonly considered the 2 most

important peanut allergens; they are recognized by the serum IgE from more than 90% of the patients with a peanut allergy (Stanley and others 1997; Shin and others 1998). Ara h 2 can induce the basophils of allergic patients to release histamine, showing stronger allergenicity than Ara h 1 (Koppelman and others 2004). Although peanut allergy occurs due to the proteins, it is difficult to ensure the complete removal of peanut allergens in the preparation of peanut oil; therefore, peanut oil still should be avoided, especially by patients with a severe allergy.

Cow milk

Cow milk is rich in nutrients and is used as a substitute for breast milk to feed infants. If cow milk causes immune system symptoms, the case is considered an allergy. Cow milk allergy is a clinical abnormality in the immune response to the proteins from cow milk, which leads to the immediate immune response regulated by IgE. The allergy differs from lactose intolerance, which is not regulated by the immune system. After a baby is born, besides breast milk, cow milk is the most common source of food. Therefore, cow milk allergy is common in infants and young children, about 90% of the children who suffer from cow milk allergy symptoms will improve before the age of 4. The main proteins in cow milk are casein and whey protein. Casein includes α -, β -, and κ -casein; whey protein includes α -lactalbumin (α -la), β -lactoglobulin (β -lg), bovine serum albumin (BSA), and immunoglobulin (Ig). Casein and β -lactoglobulin are the major allergens in cow milk (El-Agamy 2007).

Seafood

Seafood includes a wide variety of foods: fish such as cod, salmon, and tuna; crustaceans such as shrimp, crab, and lobster; and mollusks such as oysters, abalone, squid, scallops, and clams. Crustaceans and mollusks can be collectively defined as shellfish. Seafood allergies often occur in areas geographically adjacent to an ocean. The allergy symptoms caused by seafood range widely from minor urticaria to severe life-threatening symptoms. The epidemiological statistics indicate that approximately 6.6 million people, accounting for 2.3% of the population in the United States, have a seafood allergy (Sicherer and others 2004). With increasing age, the chance of seafood ingestion gradually increases; therefore, the cases of seafood allergy mostly occur in adults. Moreover, the people with a shellfish allergy are the majority in the population, with an incidence 5 times higher than those with fish allergy. The major allergen of fish is parvalbumin, with a molecular weight of 12 kDa, while that of shellfish is mainly tropomyosin, with a molecular weight of 36 to 39 kDa, which often causes an allergic reaction after ingestion (Lopata and others 2010).

Egg

Eggs are rich in nutrients and a major source of protein in the diet. An egg allergy is one of the most common food allergies in childhood. Approximately 1% to 2% of children suffer from egg allergy. Similar to cow milk allergy, egg allergy also causes the most common allergy symptom of atopic dermatitis in children (Sicherer and Sampson 2006; Savage and others 2007). With increasing age, the allergic symptoms in the majority of patients can be improved. The most important egg allergens exist in the egg white including the 43-kDa ovalbumin (OA), 78-kDa conalbumin (CA), 28-kDa ovomucoid (OM), and 14-kDa lysozyme (LY), altogether accounting for 80% of the proteins in egg whites (Hildebrandt and others 2008).

Soybean

Soybean is one of the main sources of food in Asia. Because it is not only rich in minerals, high-quality soy protein, and carbohydrates, but also has the advantage of a low fat content, the acceptance of soy in the Western countries has increased in recent years. The main allergen in soybean is GlymBd 30 k, with other allergens including the storage protein β -conglycin as well as the G1 and G2 subunits of glycinin (Peñas and others 2011).

Wheat

Wheat is the main source of cereal. A wheat food allergy regulated by IgE will cause symptoms in the skin, the gastrointestinal tract, and the respiratory tract, and it may also cause food-dependent, exercise-induced anaphylaxis (FDEIA) (Naoko 2009). Wheat allergies typically occur in childhood, the allergic symptoms of most patients will improve by the age of 3 to 5 y. Wheat allergies in adults are often FDEIA, that is, after the ingestion of wheat products, the allergic symptoms occur during or after exercise. Among such food-induced allergic reactions, the proportion of the cases caused by wheat is the highest at 57% (Teo and others 2009). Of the wheat allergens, those causing FDEIA are gluten, ω -3 gliadins, and the subunits of the high molecular weight glutenin. Other food allergies and atopic dermatitis are triggered by the water-soluble/salt-soluble and insoluble wheat proteins.

Tree nuts

Tree nuts contain abundant nutrients, and an adequate intake of tree nuts can supplement the essential elements for a body, with cardiovascular benefits. There are many types of tree nuts including hazelnuts, almonds, walnuts, chestnuts, cashews, pistachios, and so on. The allergic reactions caused by tree nuts account for 0.5% of the allergic reactions in adults (Fleischer and others 2005). Unlike the cow milk and egg allergies, once this allergy occurs, there is only a less than 10% chance for improvement. The allergic reaction in most patients will last a lifetime. Severe food allergic reactions resulting from an overdose or mistaken ingestion are common.

High-Pressure Processing Characteristic and principle

The technology of HPP of food is also called high-hydrostatic-pressure processing (HHP) technology. This technique places a sealed flexible container containing liquid food or solid food with a high water content in a pressure system mediated by water or other liquid as the pressure-transmitting medium. After treatment with pressure above 100 MPa, the pathogens in food can be killed at room temperature, and the energy consumption for the heating and subsequent cooling is avoided. The pressure-transmitting medium is recyclable after the pressure treatment, with the advantages of low energy consumption and no pollution (Toepfl and others 2006). Compared with conventional thermal processing, the original color, flavor, and nutrients can be preserved, and the addition of food additives to achieve longer shelf-life can be reduced. Currently, HPP has been approved by the U.S. Natl. Advisory Committee on Microbiological Criteria for Foods (NACMCF), the U.S. Food and Drug Administration (FDA), and the United States Dept. of Agriculture (USDA) as an alternative nonthermal pasteurization method (Yordanov and Angelova 2010). Commercial application of HPP has been actively developed in many countries including Europe, the United States, Australia, Japan, P. R. China, and South Korea, and it has been widely applied in such food products as meat, seafood, fruits, vegetables, and juice drinks (Yaldagard and others 2008). According to

statistics, the output value of the foods produced by HPP technology has reached 2 billion dollars worldwide, and the production of high-pressure food shows a steady upward trend since better food quality and health concerns are the main driving factors that consumers purchase high-pressure-processed food (Bruhn 2007; Balasubramaniam and others 2008).

The application of high-pressure technology is related to 2 basic principles: the isobaric principle and Pascal's principle. The isobaric principle indicates that, in a confined environment, when applying pressure to a liquid medium, the pressure exerted anywhere in the environment is identical, with no influence of shape or size. According to Pascal's principle, when an external force is applied to a static fluid in a sealed container, the resulting pressure change will be evenly transmitted to any part of the fluid and the container wall with no loss. Therefore, during HPP, the pressure is rapidly and evenly transmitted to the transmission medium and the food in an isobaric form, without influence by the size, shape, and appearance of the product, which is an advantage compared to traditional thermal processing. If the food contains sufficient moisture content, the microstructure of the product after the pressure treatment is not affected (Yordanov and Angelova 2010). In addition, the high-pressure treatment only affects noncovalent bonds such as the hydrogen, ionic, and hydrophobic bonds. Thus, it induces changes in the physicochemical characteristics and the functional activity of the biological macromolecules in the food such as protein denaturation and inactivation of enzymes and microbes. However, the flavor and natural nutrients (such as the small molecules of amino acids, pigments, peptides, monosaccharides, fruit acids, vitamins, and aroma compounds) as well as other low-molecular-weight colors and flavors in the food are unaffected. Accordingly, with no change in the composition and no nutrient destruction, the original nutritional value, color, and natural flavor of the food are preserved, while heat-induced aroma and browning reactions do not occur (Kadam and others 2012; Wang and others 2013.).

Equipment and packaging requirements

HPP of foods utilizes pressures above 100 MPa, requiring equipment that not only generates high pressure but also endures the pressure used. A typical HPP system consists of a high-pressure vessel and its closure, a pressure-generation system, a pressure-transmitting system, and a temperature-control system. The most important component of HPP equipment is the pressure vessel, which is usually a forged monolithic cylindrical vessel constructed from an alloy steel of high tensile strength. Several aspects should be considered for building a stable and safe high-pressure vessel. Pressure-transmitting fluids are used to transmit the pressure uniformly and instantaneously to the food inside the vessel. The most commonly used fluids are water, food-grade glycol solutions, ethanol solutions, silicone oil, and castor oil. The compression and decompression steps can result in a transient temperature change of the pressure-transmitting fluids and products during the high-pressure treatment. The temperature will be increased during the compression phase as a result of physical compression, and will return to a temperature slightly lower than its initial temperature upon decompression because of heat losses during the compression phase. Different media have unique increases in adiabatic temperature during compression in HPP (Patazca and others 2007). Water increases about 3 °C for every increase of 100 MPa at room temperature. On the other hand, fats and oils have a heat of compression increase of 8 to 9 °C per 100 MPa, and proteins and carbohydrates have intermediate heat of compression values.

Therefore, a temperature control system is necessary to regulate the operating temperature precisely during HPP treatment. High pressure can be generated either by direct or indirect compression of the pressure-transmitting fluids (Yordanov and Angelova 2010). In a direct compression system, the pressure fluids in the high-pressure vessel are directly pressurized by a piston that is driven by a low-pressure pump. This pressurized method allows for faster compression than the indirect method; however, the limitations of the high-pressure dynamic seal between the piston and the internal surface of the vessel restrict the use of this method to laboratory-scale or pilot plant-scale equipment with smaller diameters. In an indirect compression system, the pressure fluids are pumped from the reservoir into the closed high-pressure vessel by a high-pressure intensifier, until the target pressure is reached. Only static high-pressure seals are needed within the high-pressure vessel in this method, making it suitable for use in plant-scale equipment with bigger diameters (Yaldagard and others 2008).

Several considerations are needed for selecting packages for HPP products. The packaging material should be able to withstand the operating pressure, have good seal properties, and protect the contents to prevent quality deterioration during the application of HPP (Rastogi and others 2007). Because food decreases in volume during compression, and an equivalent expansion occurs upon decompression, the packaging used for HPP-treated foods must be able to accommodate up to 15% reduction in volume and return to its original volume without loss of seal integrity and barrier properties (FDA 2011). Thus, rigid materials such as metal or glass containers cannot be used. In order to ensure efficient utilization of the package as well as the space inside the pressure vessel, the headspace should be minimized while sealing the package, which also minimizes the time needed for reaching the target pressure (Rastogi and others 2007). The complete HPP procedures for food products include the following. First, food products are packaged in a flexible material. The packaged foods are then loaded into a high-pressure chamber and the vessel is sealed and filled with pressure-transmitting fluids. Once the desired pressure is reached, the pump or piston is stopped, the valves are closed, and the pressure can be maintained. After holding the product for a desired treatment time at the target pressure, the vessel is decompressed by releasing the pressure-transmitting fluid. The HPP foods are then taken out for storage and are ready for the next operating procedure (Yordanov and Angelova 2010).

Application of high pressure to reduce food allergenicity

Food allergens exist widely in various food products. With the advancements in food processing technology and refined food production processes, the component sources of a food product may consist of many ingredients from many types of foods, which can result in a potential risk of mistaken ingestion. Therefore, to reduce the incidence of food allergy reactions, complete avoidance of ingestion appears to be the only solution; however, this is extremely difficult to do. In addition to the establishment of a properly regulated labeling system, the search for an alternative solution is attracting close attention from researchers and food industry professionals. The ultimate goal is to improve the situation of food allergies through complete removal of the allergens or by reducing food allergenicity. Food allergens that commonly cause allergic reactions have several characteristics. The food allergenic proteins are quite stable under all food processing method, and it is known that some allergens are highly heat and acid resistant (Sicherer and Sampson 2010). The allergenic proteins in food are more resistant to proteolysis than other types of proteins,

and although they may be partially hydrolyzed after the digestion process in the human body, the sensitizing fragments retain their sensitization capability. Consequently, any single method will prove insufficient in removing and reducing the food allergen to achieve a satisfactory result.

Many researchers are actively seeking treatments to reduce the allergenicity of allergens. After an allergen enters the body, IgE antibodies bind to a specific allergen epitope to trigger an immune response. The specific epitope can be divided into linear or conformational types, where the former is a portion of continuous amino acids along the food allergen and the latter is formed by 3-dimensional folding of the food allergen (Shriver and Yang 2011). Therefore, an effective treatment method must be able to interfere with or mask the amino acid sequence at a specific position (cleavage or genetic modification) or to alter the protein conformation of the allergen (protein denaturation, cross-linking, or aggregation) (Sathe and others 2005, 2009). With a change in the specific epitope of the allergen, IgE will be unable to bind to it, thereby inhibiting the subsequent allergic reaction. Currently, food allergen removal methods include enzymatic hydrolysis, genetic modification (Watanabe and others 2000; Chung and others 2005; Houska and others 2011), and physical methods, based on their corresponding principles. The first 2 methods serve to destroy the amino acid sequence of the allergen. The physical methods can be divided into thermal processing (moist and dry heat treatments) (Leszczynska and others 2003; Mondoulet and others 2005; Taheri-Kafrani and others 2009; Fu and others 2010; Liu and others 2010; Blanc and others 2011) and nonthermal processing (pulsed ultraviolet light, pulsed electric field, irradiation, and ultrasound) methods (Byun and others 2002; Li and others 2006; Chung and others 2008; Kaddouri and others 2008; Johnson and others 2010; Yang and others 2010; Shriver and others 2011; Li and others 2013), all of which alter the structure of the allergen to reduce its allergenicity. Currently, there are very few practical applications of food processing that successfully eliminate allergenicity. The only feasible method of enzymatic hydrolysis is not applicable to most foods.

Although all of the above methods can reduce the allergenicity of food allergens, many limitations remain in their practical application. The most extensively discussed method is to change the activity of the food allergens through heat processing which did not demonstrate a positive effect on all allergens. For example, some allergens such as tropomyosin in crustacean can tolerate high temperatures. A study has also indicated that baking could even increase the allergenicity of certain allergens (Mondoulet and others 2005). In addition, to maintain the flavor, taste, and nutritional value of a food, high-temperature treatment is not suitable for all types of foods. Compared with conventional thermal processing, nonthermal processing methods can preserve the natural taste of a food, while retaining more nutritional value and better organoleptic properties; however, many restrictions remain in their application to improve food allergenicity. Pulsed ultraviolet light and irradiation only destroy food allergens on the food surface; the penetration of ultrasound treatment is rather poor and therefore has limited ability to have a complete and even effect on food allergen. In addition, the genetic modification method can silence the allergenic genes (gene silencing) to produce a genetically modified food without the allergen. However, this method is still under early investigation. Considering social perception, safety, environmental hazards, and other factors, the development of this type of food remains controversial. The hypoallergenic foods currently available on the market are mostly manufactured

using the enzymatic hydrolysis method, but they show a negative impact on the structure of the foods and their organoleptic properties after protein hydrolysis (Houska and others 2011; Shriver and Yang 2011). Therefore, the development of other potential processing techniques is necessary. High-pressure-processed food has excellent organoleptic quality and nutritional value which are the main reasons for its popularity in recent years.

A complete identification of how HPP may affect allergenicity requires an understanding of how HPP alters the structure and properties of food allergens. As mentioned earlier, the pressure treatment only affects noncovalent bonds such as hydrogen, ionic, and hydrophobic bonds. The impact of high pressure on the proteins is related to the rupture of the noncovalent interactions in the protein molecule. The primary, secondary, tertiary, and quaternary structures of proteins consist of different types of interactions (Rastogi and others 2007). The primary structure is composed of an amino acid sequence that is connected by covalent bonds. Covalent bonds are unaffected by high pressure, and thus the primary structure of proteins maintains integrity during HPP. The polypeptide chain forms α -helices or β -sheets/strands by intra- or intermolecular hydrogen bonds, creating the secondary structure of proteins. Secondary protein structures change at very high pressure, likely as a result of cleavage of hydrogen bonds (Yaldagard and others 2008). The tertiary structure, which is also called the protein subunit, shows how the secondary structure domains fold into a 3-dimensional configuration as a consequence of noncovalent interactions between amino acid side chains. The quaternary structure describes the spatial arrangement of the subunits, held together by noncovalent bonds. Therefore, high pressure has a substantial impact on the tertiary and quaternary structures of the protein, which are mainly maintained by noncovalent bonds. The tertiary structure of a food allergen is the key to its allergenicity; therefore, high-pressure treatment has great potential in reducing food allergenicity. In recent years, many studies have begun to explore the effects of HPP on the allergenicity of food allergens, which are explained by different mechanisms, such as protein denaturation, induction of protein conformational changes or modifications, allergen removal by extraction of allergens, and the promotion of enzymatic hydrolysis to alter the sensitization of the allergens (Table 1). HPP induces a reversible or irreversible structural modification in the proteins, leading to protein denaturation, aggregation, or gelatinization; therefore, the structure of the allergen epitope binding site for IgE might be destroyed or altered by HPP, which ultimately reduces its allergenicity. Altering the protein conformation may also change the epitopes, which will no longer be recognized by IgE antibodies or stimulate an immune response (Shriver and Yang 2011). Many researchers have also described other possible mechanisms for altering the allergenicity of food allergens. Kato and colleagues (2000) indicated that pressurization enhances the permeability of a surrounding solution into the internal structure of foods, solubilizing the allergen proteins and subsequently releasing a considerable amount into the surrounding solution, thus resulting in a decrease in allergenicity. Hu and Xie (2013) demonstrated that proteases in solution can diffuse into the internal structure of foods during HPP treatment, which lower its immunoreactivity by enhancing the enzymatic hydrolysis reaction. The application of HPP for altering food allergenicity is discussed in detail in the following section.

Peanut

In the study by Hu and others (2011), peanut allergens were treated with high pressures of 60, 90, 120, 150, and 180 MPa

Table 1—An overview of high-pressure processing on food allergens.

Mechanisms	Changes in allergenicity	Reference
Protein denaturation	Milk: β -lactoglobulin increased	Kleber and others 2007
Protein conformational changes/modification	Soybean: decreased	Li and others 2012
	Apple: Mal d 3 decreased	Johnson and others 2010
	Apple: decreased	Meyer-Pittroff and others 2007
	Peanut: Ara h 2 decreased	Hu and others 2011
	Carrot: Dau c 1 unchanged	Heroldova and others 2009
	Celery: Api g 1 unchanged	Houska and others 2009
	Carp: unchanged	Liu and Xue 2010
Extraction of allergens	Rice: decreased	Kato and others 2000
Enhance enzymatic hydrolyze reaction	Milk: β -lactoglobulin decreased	Chicón and others 2008
	Shrimp: decreased	Hu and Xie 2013
Others	Soybean: decreased	Peñas and others 2011
	Apple: Mal d 3 decreased	Husband and others 2011
	Apple: Mal d 1 decreased	Husband and others 2011
	Celery: Api g 1 decreased	Husband and others 2011
	Egg: decreased	Hildebrandt and others 2010
	Almond: unchanged	Li and others 2013

Table 2—Effect of high-pressure processing on food allergens of legumes and grains.

Food variety	Treatment conditions	Major findings	Reference
Peanut	150 to 800 MPa, 20 to 80 °C, 10 min	No changes in the secondary structure of any allergens	Johnson and others 2010
Peanut	60 to 180 MPa	High-pressure microfluidization treatment decreased the antigenicity of the peanut allergen Ara h 2, changed its secondary structure, and increased its UV absorption intensity and surface hydrophobicity. The change in conformation played a critical role in the decrease in antigenicity of Ara h 2.	Hu and others 2011
Soybean	300 MPa, 40 °C, 15 min	A significant decrease in antigenicity was observed in the sprouts obtained from HPP-treated soybean seeds. The total essential amino acid content and nutritional value, however, were reduced only by 18%. HPP could be an important technological approach for the industrial production of hypoallergenic and nutritive soybean sprouts.	Peñas and others 2011
Tofu	300 MPa, 40 °C, 15 min	HPP did not affect the protein profile of tofu protein extracts, but did lower the intensity of some protein bands, when the protein profile was visualized by PAGE. The immunoreactivity of tofu was not affected by HPP.	Peñas and others 2011
Soy protein isolate (for infant formula)	300 MPa, 15 min	The allergenicity of soy protein isolate (SPI) decreased by 48.6%. HPP induced changes in the secondary structure and molecular interactions of soy protein, which could alter the allergenicity and enhance the safety of SPI for infants who are allergic to cow milk.	Li and others 2012
Rice	100 to 400 MPa, 10 to 120 min	Pressurization promoted the release of major rice allergens into the surrounding solution. Thus, the content of these allergenic proteins decreased and almost completely disappeared in rice grains that were pressurized in the presence of proteolytic enzyme (300 MPa, 30 min/protease-N).	Kato and others 2000
Almond	600 MPa, 4 to 70 °C, 5 to 30 min	SDS-PAGE, WB, and ELISA assays showed that HPP did not affect the allergen concentration and IgE binding capacity of almond extract.	Li and others 2013

followed by enzyme-linked immunosorbent assay (ELISA) and circular dichroism to analyze the impact on its allergenicity and the structure of the peanut allergen Ara h 2 (Table 2). It was found that the binding of Ara h 2 with IgE decreased with increasing pressure, and the subsequent analysis indicated that it was closely related to the change in the structure and surface hydrophobicity of the allergen protein by the high-pressure treatment.

Soybean

A number of studies investigate the effects of HPP on food allergen of soybean are listed in Table 2. Peñas and others (2011) compared the effects of high pressure (300 MPa at 20 °C for 15 min) on the protein pattern, amino acid composition, and immunoreactivity of soybean, bean sprouts, and commercial tofu. High-pressure treatment had no effect on the distribution of protein profiles, with only a slight reduction in the content of a few proteins. The analysis of amino acid content before and after the high-pressure treatment showed that high pressure reduced the content of the essential amino acids by approximately 18%. However, it is noteworthy that the allergenicity of the soybean sprouts

germinated from the soybean after the high-pressure treatment was significantly reduced, proving that high pressure can be used in industrial production of hypoallergenic sprouts that are equally rich in nutrients. With a high nutritional value, soy protein is widely used in the food industry, and the production of infant formula is one of its important applications. Soybean is a suitable alternative food source for babies who are allergic to cow milk (El-Agamy 2007). Li and others (2012) found that high pressure could be applied to reduce the allergenicity of soy protein isolate for infant formula. With high-pressure treatment (200 to 500 MPa, 5 to 20 min), the allergenicity after the treatment of 300 MPa for 15 min was reduced 48.6%, which was achieved by a modification of the secondary structure for the allergen protein. The application of this technology can improve food safety of soybean protein isolate in the manufacture of baby food.

Rice

Kato and others (2000) found that high-pressure treatment (100 to 400 MPa) could increase the release of the major allergens in rice (Table 2). After the treatment of 300 MPa for 30 min, a

Table 3–Effect of high-pressure processing on food allergens of seafood and meat products.

Food variety	Treatment conditions	Major findings	Reference
Carp	300 MPa, 20 °C, 60 min	High-pressure treatment did not change the subunit composition, molecular weight, or the allergenicity of silver carp allergens. However, the structure of the allergens changed when treated with 300 MPa for 10 min or above.	Liu and Xue 2010
Shrimp	450 MPa, 40 °C, 55 min	Shrimp meat was immersed in 1% saline containing papain, and pressurized to obtain low-allergen or allergen-free whole brine shrimp. The proteases in the saline solution diffused into the internal structure of shrimp and hydrolyzed the allergen protein.	Hu and Xie 2013
Processed meat matrix	600 MPa, 20 °C, 10 min	The combined application of heat (70 °C) and high pressure produced synergistic effects that reduced the allergenic potential of egg white proteins in meat. The combined treatment was nearly twice as effective (resulting in an 8.9-fold decrease in allergenic potential) as the sum of individual treatments conducted separately (heat 70 °C: 1.5-fold decrease in allergenic potential; HPP: 3-fold decrease in allergenic potential).	Hildebrandt and others 2010

Table 4–Effect of high-pressure processing on dairy products.

Food variety	Treatment conditions	Major findings	Reference
Whey protein isolate	200 to 600 MPa, 30 to 68 °C, 10 to 30 min	The antigenicity of β -lactoglobulin (β -lg) increased with an increase in pressure, temperature, and holding time.	Kleber and others 2007
Skim milk	200 to 600 MPa, 30 to 68 °C, 10 to 30 min	The antigenicity of β -lg increased with an increase in pressure and holding time, and decreased with thermal treatment. However, the β -lg levels were higher in HPP-treated skim milk than in untreated milk.	Kleber and others 2007
Sweet whey	200 to 600 MPa, 30 to 68 °C, 10 to 30 min	The antigenicity of β -lg increased with an increase in pressure and holding time. Furthermore, the antigenicity of β -lg increased at 40 °C. Antigenicity decreased at higher temperatures (50, 60, and 68 °C), but was still higher than in the untreated whey.	Kleber and others 2007
Milk	>100 MPa	Treatment with chymotrypsin and trypsin under high pressure for relatively short times (20 min) accelerated the proteolysis of β -lg, leading to the rapid depletion of the intact protein. Thus, a combination of HPP and proteolysis could be used to produce hypoallergenic foods.	Chicón and others 2008

slight morphological change in the internal structure of the rice grains was observed under a scanning electron microscopy. This allowed the solution around the rice grain to enter the rice more easily, to enhance the solubility of the allergen, and to facilitate the extraction and the release of the allergen into the external solution. The study also found that the addition of proteolytic enzymes in the solution can promote the release of the allergens and enhance the effect of reducing allergenicity. Pressurization might be an applicable processing method to produce hypoallergenic rice.

Seafood

The impact of HPP on food allergens of seafood are summarized in Table 3. Liu and Xue (2010) treated the silver carp allergen with 100, 200, and 300 MPa at 20 °C for 10, 30, and 60 min. The secondary structure of the allergen had changed after the pressure treatment, while the protein composition, molecular weight, and allergenicity were not affected. Hu and Xie (2013) applied high-pressure treatment (450 MPa, 40 °C, 55 min) combined with enzymatic hydrolysis to prepare hypoallergenic shrimp. The high-pressure treatment promotes the interaction of the protease in the solution and the allergen in the shrimp tissue to destroy them with hydrolysis.

Egg

Hildebrandt and others (2010) treated a meat product containing dried egg powder with heat (70 °C) and high pressure (600 MPa, 20 °C, 10 min), and the effect on its allergenicity was investigated using the EAST inhibition assay (Table 3). The C_{50} of the control group was 145 μ g/mL. The lower the value of C_{50} (μ g/mL), the higher the inhibitory ability, indicating that the allergenicity was increased. The results showed that high-pressure treatment could

reduce the allergenicity up to 3-fold (485 μ g/mL), that is, 1.5 times higher than that of the heat treatment (214 μ g/mL). When the heat and pressure treatments were combined, a synergistic effect was observed for the inhibition of allergy response, with the inhibition rate of up to 8.9 times (1286 μ g/mL).

Cow milk

β -Lactoglobulin (β -lg) is the main allergen causing a cow milk allergy. There are various studies indicating the effects of HPP on the allergenicity of β -lg are shown in Table 4. Kleber and others (2007) investigated several solutions rich in β -lg, such as whey protein isolate solution (WPI), sweet whey, and skim milk. After treatment with 200, 400, and 600 MPa at 30 to 68 °C for 0, 30, and 60 min, the allergenicity of β -lg was analyzed. It was found that the allergenicity increased with increasing pressure (200 to 600 MPa) and time (0 to 30 min). However, in the group of skim milk, when the processing temperature was increased with the treatment of 600 MPa for 10 min (>25 °C), the allergenicity decreased with increasing temperature; however, it was still higher than that in the untreated group. Conversely, the allergenicity in the WPI group increased with an increase of the processing temperature. This result is presumably due to the unfolding of the proteins caused by the high pressure, and such unfolded states may generate new epitopes which are normally buried within the protein structure but become surface-accessible in a partially folded state (Mills and Mackie 2008). Consequently, the exposure of more binding sites to the antibody leads to an increased allergenicity. The results showed that the degree of denaturation in β -lg does not correlate to its allergenicity; in addition, the detection of allergenicity of the same allergen in different media showed different results, indicating the complexity of the food ingredients, and their difference could

Table 5—Effect of high-pressure processing on food allergens of fruits and vegetables.

Food variety	Treatment conditions	Major findings	Reference
Apple	400 to 800 MPa, 80 °C, 10 min	In the apple allergen Mal d 3, HPP treatment at 80 °C caused unfolding of the α -helix into a random coil and a decrease in the immunoreactivity at higher pressures, particularly above 400 MPa. Another apple allergen, Mal d 1b, showed small changes in secondary structure following HPP at 20 °C, and more prominent changes after HPP at 80 °C.	Johnson and others 2010
Apple	700 MPa, 115 °C, 10 min	The immunoreactivity of Mal d 3 was decreased by approximately 30% after HPP treatment at 700 MPa, 20 °C, 10 min. There was a significant loss of Mal d 3 immunoreactivity after HPP treatment at a higher temperature. The immunoreactivity and the amount of immunoreactive Mal d 1 was reduced by over 50%, after HPP treatment at 700 MPa, 115 °C for 10 min. A combination of HPP and thermal processing is an effective method for reducing the allergenicity of apple allergen.	Husband and others 2011
Apple	600 MPa, 5 min	Three patients with extreme allergy against apple, who were administered with 25 g high-pressure-treated apple every day for 3 wk, could be hyposensitized by means of specific immunotherapy.	Meyer-Pittroff and others 2007
Celeriac	700 MPa, 118 °C, 10 min	The allergenicity of the Api g 1 allergen in celeriac is reduced by a combination of HPP and thermal processing.	Husband and others 2011
Celery	500 MPa, 50 °C, 10 min	Changes in the structure of the recombinant celery allergen rApi g 1 are positively correlated with pressure. Prominent structural changes were observed in rApi g 1, after HPP treatment with 500 MPa at 50 °C for 10 min. However, there was no change in the allergenicity of rApi g 1.	Houska and others 2009
Carrot	500 MPa, 50 °C, 10 min	The secondary structure of the carrot allergen rDau c 1 was slightly altered by HPP (increased beta-sheet structure). However, the immunoreactivity of rDau c 1 remained unchanged.	Heroldova and others 2009
Carrot juice	400 to 550 MPa, 3 and 10 min 500 MPa, 30 to 50 °C, 10 min	HPP had no influence of the allergenicity of carrot juice.	Heroldova and others 2009

lead to inconsistent results after the high-pressure treatment, which increased the difficulty of the study. To reduce the allergenicity of the allergenic foods containing cow milk components, enzymatic hydrolysis is usually applied. Chicón and others (2008) found that high pressure can promote enzyme hydrolysis. The proteolytic enzymes such as chymotrypsin and trypsin were added to the buffer containing β -lg for high-pressure treatment. The results showed that the IgE-binding capacity of the enzymatic hydrolysis products with a 20-min high-pressure treatment was lower than those in the groups treated with chymotrypsin (hydrolysis for 8 h) and trypsin only (hydrolysis for 48 h). Using this method, the hypoallergenic hydrolysis products can be quite rapidly prepared for the production of hypoallergenic foods.

Fruits and vegetables

In addition, high-pressure treatment can reduce the allergen levels in fruits and vegetables (Table 5). After the treatment of 700 MPa at 20 °C for 10 min, the immunoreactivity of the apple allergen Mal d 3 was decreased. If combined with the temperature treatment at 115 °C, the inhibitory effect was more significant. Another apple allergen Mal d 1 and celery allergen Api g 1 were only decreased when the treatment condition was elevated to 700 MPa at 115 to 118 °C for 10 min. These results concluded that combination of HPP and thermal processing is an effective method to reduce the allergenicity of both apple and celery (Husband and others 2011). Johnson and others (2010) indicated that high-pressure treatment changed the secondary structure of the apple allergens Mal d 1 b and Mal d 3, and decreased the immunoreactivity of Mal d 3. The treatment of 400 MPa at 80 °C reduced the allergenicity of Mal d 3 more significantly. Meyer-Pittroff and others (2007) found that 3 patients with heavy allergy against apple who were administrated with 25 g high-pressure-treated apple slices (600 MPa, 5 min) every day for 3 wk could be hyposensitized by means of a specific immune-therapy method. However, Houska and others (2009) treated recombinant celery

allergen rApi g 1 with 400 to 500 MPa at 30 °C, 40 °C, and 50 °C for 10 and 20 min. Changes of protein structure of rApi g 1 were positively correlated with pressure (400 to 500 MPa and 10 and 20 min). The greatest structure changes were seen when treated by 500 MPa at 50 °C for 10 min but no was seen in change the allergenicity of rApi g 1. Heroldova and others (2009) detected the influence of HPP on the allergenicity of recombinant carrot allergen rDau c 1 and carrot juice by treating with 400 to 550 MPa for 3 and 10 min and 500 MPa at 30 to 50 °C for 10 min. Although the secondary structure of rDau c 1 was changed after treating by 500 MPa at 50 °C for 10 min but it did not influence the immune reactivity of rDau c 1.

Future Applications and Expectations

HPP technology changes the allergenicity of allergens through different mechanisms, such as protein denaturation, protein conformation changes, allergen extraction, and facilitating enzymatic hydrolysis (Figure 2). However, changes in the allergenicity of food allergens by processing methods are affected by many complex factors such as the food ingredients, the processing conditions, the biochemical and the immune characteristics of the allergen, the binding interaction of the allergens and allergen-specific IgE, and the sensitivity of the patients (threshold, tolerance, and persistence of allergic reactions).

Food ingredients and processing conditions

Because food ingredients are complex, the detection of the allergenicity for the same allergen in different media might produce different results. The change in protein structure under high pressure is affected by the environmental conditions. For example, under the conditions of different pH and ionic strength, the proteins might show different tolerance to the pressure. These differences have led to inconsistent results after the high-pressure treatment (Rastogi and others 2007; Yaldagard and others 2008). In addition, inhibition of the allergenicity of various allergens required

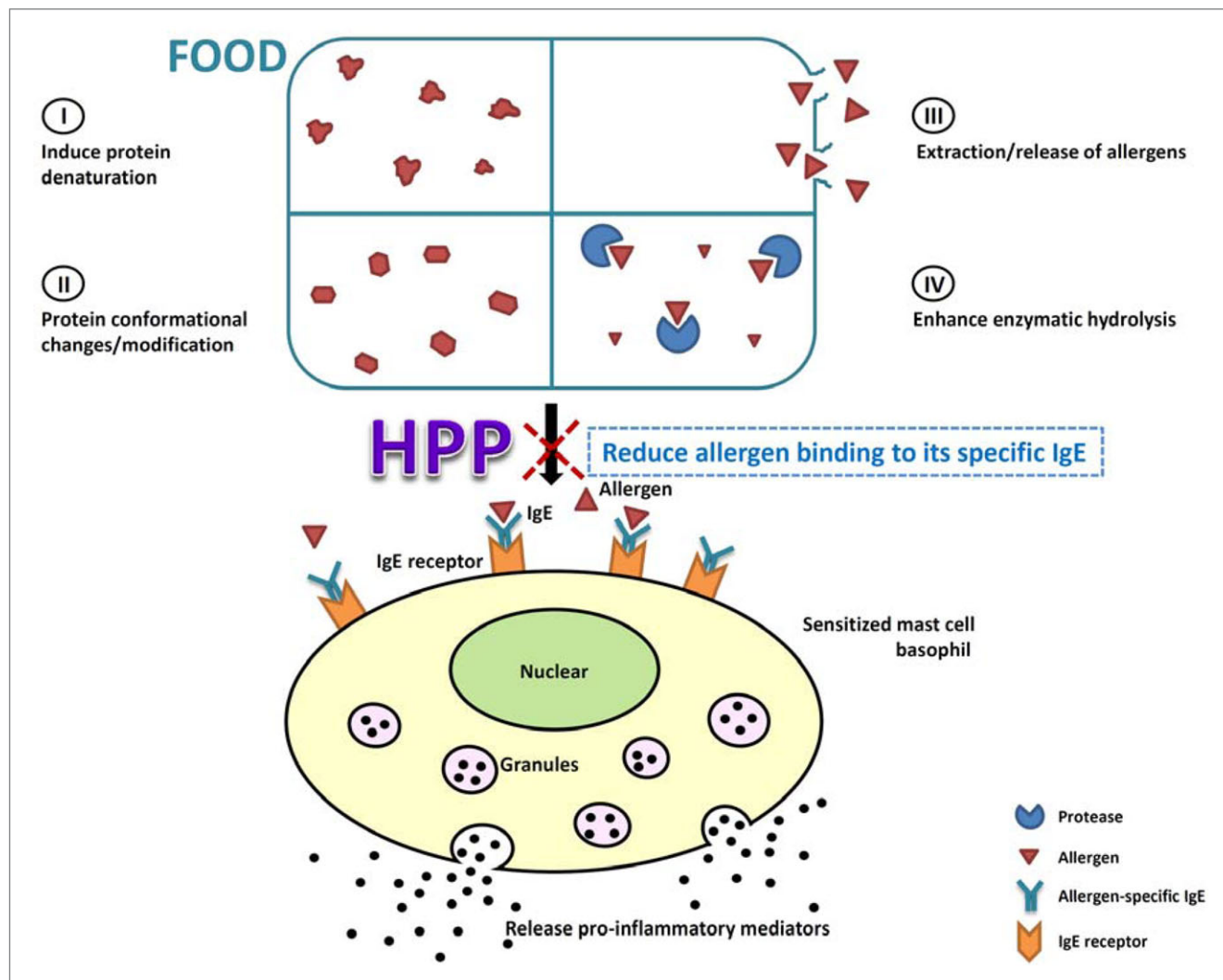


Figure 2—Mechanisms of HPP in reducing allergenicity of food allergen. HPP has the potential to reduce the binding of food allergens to its specific IgE through following mechanisms such as protein denaturation, induction of protein conformational changes or modification, allergen removal by extraction the allergens, and the promotion of enzymatic hydrolysis by increasing the diffusion of protease into food structure in HPP-treated food, and the activation of mast cells and basophils by the signal transduction of allergen and IgE cross-linking is inhibited and ultimately the allergenicity of food allergen is diminished.

different pressure-processing conditions, which increases the difficulty of study.

Hurdle concept for eliminating food allergenicity

Currently, food processing techniques are widely used in the research on the removal of food allergens. High temperature processing, enzymatic hydrolysis, and radiation are prevalent methods used in this research area. However, these methods can potentially cause varying degrees of impact on food ingredients. In contrast, the advantage of HPP of food offers the ability to preserve raw food materials and the intrinsic and natural characteristics of food. Therefore, the use of HPP to remove food allergens can easily be used in conjunction with other processing techniques. This technique can be performed without the need to change the original manufacturing process, which usually involves pretreating raw materials by destroying food allergens, and subsequently producing various kinds of food using hypoallergenic raw materials in order to effectively lower the amount of allergens present in food. An alternative method would be to use HPP as the final procedure in food processing. Applying HPP to packaged products can pro-

duce the same effect in the elimination of food allergens. From the perspective of food safety, this technique is a hurdle concept, in which high pressure acts as one of the hurdles, used simultaneously with other processing methods to attain high level of food allergen elimination. Another simultaneous effect of this technique is that it allows the removal of pathogenic microorganisms from raw materials and food. Food processing techniques in combination with HPP can reduce the intensity of other processing methods. For example, the temperature used in ultra-high temperature processing to eliminate bacteria can be reduced, the amount of additives added can be decreased, and the shelf-life of food can be increased. Meanwhile, this will allow food to maintain its natural flavor and reduce concerns about food safety. These advantages are not offered by other food processing techniques, HPP is a highly beneficial technique.

Characteristics of the allergen and the sensitivity of patients

The key factors that contribute to an allergen's allergenicity, and whether the structure of the specific epitope in the allergen can be destroyed by high-pressure treatment to lead to an inhibition of

allergic reactions, are important issues that are worth further study. Understanding the impact of HPP on the sensitization potential of food allergens and the thresholds for elicitation of allergic reactions in sensitized individuals is crucial for the management of food allergy (Mills and others 2009). Due to differences in the degree of the allergic reactions and the tolerance among different patients, it is not possible to claim that the allergic reaction has been suppressed unless it is certain that no clinical symptom will occur after ingestion. According to this reason, although high-pressure treatment can partially deactivate or eliminate the allergen, high-pressure-treated food still requires a careful *in vivo* assessment of the food allergens (Sathe and Sharma 2009).

Even though the development of high-pressure technology for the improvement of food allergies requires some advances, it still has great potential. The current application may develop with 2 strategies. The combination of high-pressure and heat-processing treatments may directly destroy the allergen structure. As an indirect method, high-pressure treatment combined with enzymes facilitates the release of the allergens in food. After allergen extraction is increased, the allergens are decomposed by the enzymes. High-pressure treatment is still unable to completely destroy the allergen activity directly. With the premise of not damaging food quality, the combination treatment with other processing methods can improve the potential of inhibiting allergen allergenicity. In addition, some studies have prepared a hypoallergenic cake using wheat flour after enzymatic hydrolysis for allergy patients and found that more than half of the patients could tolerate it and gradually accepted regular flour products. Currently, research of such immunotherapy has been conducted for foods treated with high pressure. Studies found that patients with heavy allergy against apple could be hyposensitized by administration of high-pressure-treated apple slices for several weeks (Meyer-Pittroff and others 2005, 2007). Several papers have mentioned the positive effect of high pressure for improving the allergenicity of allergens. The application of hypoallergenic ingredients after high-pressure treatment in food manufacturing can not only reduce food allergenicity, but also increase food safety while maintaining sensory quality and the natural nutritional value.

Conclusions

To date, investigations on high-pressure-treated foodstuffs have not revealed any evidence of any microbial, toxicological or allergenic risks as a consequence of high-pressure treatment. Results of presently available studies suggest that high-pressure treatment might be used for the specific reduction of the allergenicity of certain protein families. However, there are not so many successful processing methods for de-allergization of foods in real life, which is the challenge for food engineers and novel food processing technologies. High-pressure treatment has a positive effect on reducing the allergenicity of food allergens by different mechanisms, such as protein denaturation, induction of protein conformational changes or modifications, allergen removal by extraction of allergens, and the promotion of enzymatic hydrolysis to alter the sensitization of the allergens, indicating a good development potential of the high-pressure-processing technology for a decrease improvement of food allergies and still requires some advances and careful *in vivo* assessment of the food allergens. Understanding the impact of food processing and food structure on allergenic potential is central to managing allergen risks in the food chain. The practical application is surely great news for allergy sufferers which is the reason why it's worthy of further exploration.

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