



Irradiation technology: An effective and promising strategy for eliminating food allergens

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ABSTRACT

Food allergies are one of the major health concerns worldwide and have been increasing at an alarming rate in recent times. The elimination of food allergenicity has been an important issue in current research on food. Irradiation is a typical nonthermal treatment technology that can effectively reduce the allergenicity of food, showing great application prospects in improving the quality and safety of foods. In this review, the mechanism and remarkable features of irradiation in the elimination of food allergens are mainly introduced, and the research progress on reducing the allergenicity of animal foods (milk, egg, fish and shrimp) and plant foods (soybean, peanut, wheat and nuts) using irradiation is summarized. Furthermore, the influencing factors for irradiation in the elimination of food allergens are analyzed and further research directions of irradiation desensitization technology are also discussed. This article aims to provide a reference for promoting the application of irradiation technology in improving the safety of foods.

1. Introduction

Food allergy refers to the abnormal immune response of a certain tissue, organ, or even the whole body to certain food items or food additives, which can cause various tissue damage or organ dysfunction. (Chinthrajah, Hernandez, Boyd, Galli, & Nadeau, 2016; Lin & Alcocer, 2017; Sharma, Bansil, & Uygungil, 2015). At present, 10% of the world's population suffers from food allergies (Carrard, Rizzuti, & Sokollik, 2015; Korte & Brockmeyer, 2016). With the development of food processing technology and the increasing variety of foods raw materials (such as new resource food), the variety of food that can cause allergies is increasing (Arakali, Green, & Dinakar, 2017; Lepski & Brockmeyer, 2013; L'Hocine, Achouri, & Mélanie, 2019). Food allergies have become a prominent global health and food safety issue. Only a small number of proteins in allergenic food have the biological activity to induce allergies, which were named "food allergens" (Cabanillas & Novak, 2019; Penumarti & Kulis, 2020). Altering the allergenic epitopes in food allergens through food processing for elimination or reduction of food allergenicity has attracted extensive attention from the researchers and is also crucial for food industry development (Crevel & Cochrane, 2014).

Recently, non-thermal food processing methods such as irradiation, cold plasma, high-voltage pulse and ultrasound have been increasingly

studied. (Dong, Wang, & Raghavan, 2020; Gavahian & Khaneghah, 2020; Yuan et al., 2021). These kinds of food processing methods can not only effectively preserve the nutrients, freshness, and flavor of the food item but can also change the structure of food allergens in a larger operating space to achieve a better allergen elimination effect (Alves et al., 2019; Zhang et al., 2019). As a typical non-thermal food processing technology, food irradiation is a process in which food or raw materials are irradiated by high-energy and high-penetrating rays, resulting in physical or chemical reactions of food components or organisms (Shahbaz, Akram, Ahn, & Kwon, 2016; Pillai & Shayanfar, 2017). This process can effectively inhibit or destroy metabolism and even lead to the death of cells and tissues, making it a very important application in food sterilization and prolonging food storage time (Pillai & Shayanfar, 2017; Kim, Shahbaz, Kyung, & Kwon, 2018). The irradiation energy that is commonly used can be divided into two categories: γ -rays and X-rays (<5 MeV) from ^{60}Co or ^{137}Cs radioactive sources and electron beams (<10 MeV) from electron accelerators (Zehi, Afshari, Noori, Jannat, & Hashemi, 2020). Food irradiation has been demonstrated to have a beneficial effect on improving food quality and extending shelf life (Odueke, Farag, Baines, & Chadd, 2016; Zehi et al., 2020). The process of irradiation treatment can be performed in large quantities and without any chemical reagents, having the advantages of

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easy operation, less pollution, and energy efficiency (Pereira et al., 2017; Vanga, Singh, & Raghavan, 2017). In view of these characteristics, food irradiation has become an important processing method to improve food quality and safety.

As reported, food irradiation can effectively destroy the structure and epitopes of food allergenic proteins and thus reduce or even eliminate their immunogenicity. This process can bypass the disadvantages of the uncertain effects of ultrahigh pressure and ultrasonic wave treatment, as well as the high cost and complications of changing the food flavor and quality by enzymatic hydrolysis and fermentation (Rahaman, Vasiljevic, & Ramchandran, 2016; Zhu, Wang, Shen, Xu, & Zhou, 2018). However, due to the wide variety of foods and the different allergenic proteins contained, it is difficult to evaluate the correlation between irradiation dose and desensitization effect of specific allergens, resulting in the lack of sufficient theoretical support and reference in practical application. In addition, although irradiation technology has long been allowed to be used in the processing of various foods in many countries, the safety of the dose residues in food caused by strong irradiation is also one of the problems that people are generally concerned about (Shahbaz et al., 2016; Vaz et al., 2013). Therefore, it is necessary to review the mechanism and features of food irradiation, especially to summarize the current studies about food irradiation eliminating the allergenicity of allergens, which is conducive to promoting the in-depth research and application of food irradiation technology in improving the safety of food.

This paper provides a detailed introduction to the mechanism and features of irradiation technology in eliminating or reducing the allergenicity of food and reviews studies on irradiation-based elimination of animal- and plant-derived allergens in recent years. The influencing factors of food irradiation on the elimination of allergens were further analyzed to clarify the rules and advantages of irradiation desensitization technology. Future directions for research and development in irradiation desensitization technology were also pointed out to offer the references for its further research and applications.

2. Eliminating food allergens by irradiation

2.1. Mechanism of irradiation desensitization

The allergenic ingredients in food are mostly proteins, which are composed of different amino acids and have a complex spatial structure. Linear epitopes based on the amino acid sequence and conformational epitopes based on the protein spatial structure are the basis for the immune response to food allergens (Boye, Danquah, Thang, & Zhao, 2012; Husslik et al., 2016; Breiteneder, 2018). During irradiation, the energy from γ -rays, X-rays, or electron beams is directly absorbed, leading to changes in the spatial structure and conformation of the allergenic proteins, thereby reducing their allergenicity. Fig. 1 shows the widely accepted mechanism of irradiation for eliminating food allergens. Upon irradiation treatment, the allergenic proteins of chicken ovalbumin

(OVA) and prawn stable protein have not only had substantial structural polymerization but also obvious differences in surface hydrophobicity. High doses of irradiation could destroy the epitopes of β -lactoglobulin, making it unable to accurately identify the binding sites of IgE; when the irradiation dose was higher than 7 kGy, its IgE binding capacity decreased to less than 50% (Chen & Gao, 2012; Matsuo, Yokooji, & Taogoshi, 2015; Fu, Cherayil, Shi, Wang, & Zhu, 2019; Wang et al., 2020).

Another mechanism for irradiation eliminating food allergies is thought to be the action of rays irradiated on water molecules, producing large amounts of free radicals such as $\cdot\text{OH}$, $\text{H}\cdot$, and e_{aq}^- (Brasoveanu et al., 2013; Mladenova, Aleksieva, & Nacheva, 2019). These free radicals can oxidize, deoxidize or decarboxylate sulfhydryl-containing amino acids of allergic proteins, or oxidize the free radicals from phenol and polycyclic amino acids, causing the cleavage and cross-linking of peptide bonds and the destruction of allergen secondary or tertiary structures (Fig. 2). The leakage of R groups of hydrophobic amino acids decreases the solubility of allergenic proteins, thus reducing the content of allergens in food (Vaz et al., 2013a; Liu et al., 2017a). This reduction was verified in irradiation-based elimination experiments with the allergen tropomyosin (Guan et al., 2018). Low irradiation doses damaged the secondary structures of these allergenic proteins, causing the hydrophobic groups of amino acids to leak out. After increasing the irradiation dose (7–10 kGy), the peptide chains of proteins were repolymerized and cross-linked to form new polymers and degraded peptides, leading to a reduction in food allergenicity. The secondary structures of peanut allergens Ara h 2 and Ara h 6 were verified to have obvious changes after irradiation treatment (Luo et al., 2013). Irradiation treatment with a dose of 10 kGy eliminated the antigenicity of the two allergens (brought down to 5%). These results further demonstrate the powerful function of irradiation in eliminating food allergens.

2.2. Features of irradiation for eliminating food allergens

Compared with other physical, chemical, or biological methods for eliminating food allergens, irradiation technology is considered of a green, safe, and efficient strategy (Ehlermann, 2016; Ekezie, Cheng, & Sun, 2018). Treatment by irradiation has marked advantages, which are shown mainly in the following aspects: (1) Maintaining the original ingredients and flavor of the food to the maximum extent (Kuan, Bhat, Patras, & Karim, 2013). Radiation treatment for eliminating food allergens is generally performed under normal temperature and pressure, thus preventing the loss of inherent food ingredients under harsh environments and preserving the flavor and quality of food, which is very important in modern food processing. Muanghorn et al. found that γ -irradiation had little effect on essential mineral content in freshwater prawns, and under the tested dose (5 kGy), there was almost no loss of nutrients (Muanghorn et al., 2018); (2) High efficiency. The γ -rays, X-rays, or electron beams used for irradiation generally have very high energy, which can quickly and effectively eliminate the allergenicity of

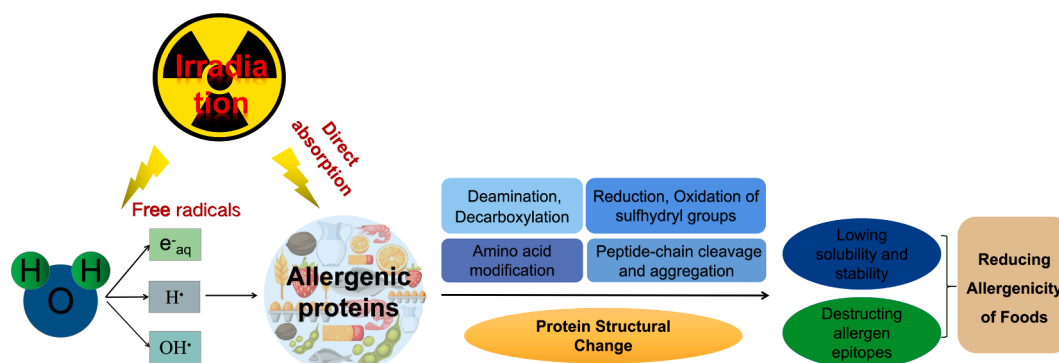


Fig. 1. Schematic mechanism of irradiation technology in reducing the allergenicity of food.

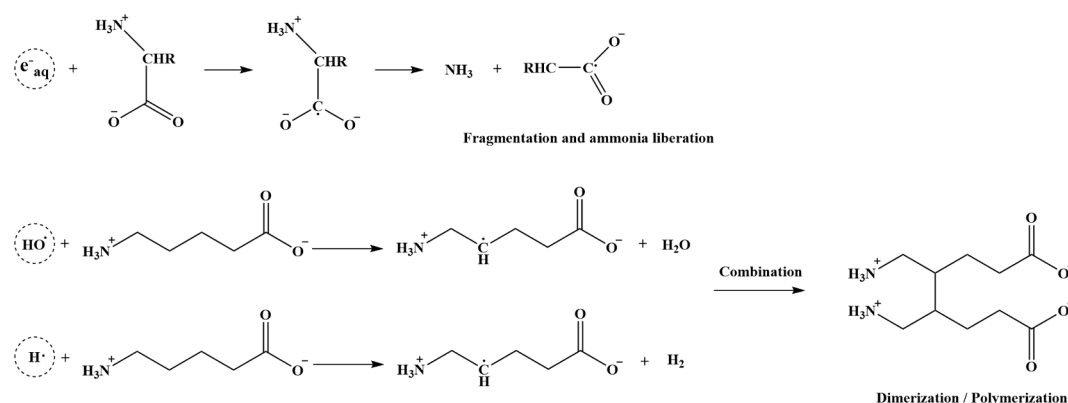


Fig. 2. Possible depolymerization and cross-linking reactions of protein chains with free radicals generated from irradiated water.

food allergens. Additionally, irradiation treatment has been shown to be effective for most types of food allergens (Jiménez-Saiz, Benedé, Molina, & López-Expósito, 2015; Luo & Hu, 2019). This concept is well in line with the rapid and high-throughput processing requirements for food products suitable for rapid consumption; (3) Less pollution and environmental safety (Solanki, Prasad, Sonawane, & Gupta, 2012). Irradiation treatment does not require the addition of chemical reagents or auxiliaries and produce chemical residues, thus reducing the possibility of contamination of food and the environment (Ravindran & Jaiswal, 2019); (4) Simple operation, stable effects, and strong industrial applicability. Compared with the other processes for allergen elimination, the irradiation strategy does not require complicated equipment or facilities, and the process is relatively simple, with strong controllability and stable treatment effect (Mittendorfer, 2016). These characteristics make it suitable for the industrial processing of large quantities of food.

2.3. Irradiation-based elimination of typical food allergens

2.3.1. Animal-derived food allergens

Animal-derived food, including meat, eggs, milk, and aquatic products, provides large amounts of high-quality proteins that play a very important role in improving physical quality (Groetch, Metcalfe, Sampson, Simon, & Lack, 2014; Tellez et al., 2015; Pan et al., 2019). However, the presence of various food allergens in these foods can also cause serious threats to human health. To date, researchers have carried out relatively complete and systematic studies on various allergens and their elimination methods in milk, eggs, fish, shrimp and other foods (Chen, Wu, & Deng, 2015; Han, Chen, & Ge, 2016). Irradiation technology can destroy the ordered structure of animal-derived food allergens and has been verified to be an effective strategy for allergen elimination. Table 1 illustrates the research investigating the use of irradiation to reduce the animal-derived food allergens in food products.

2.3.1.1. Milk allergens. Bovine milk is rich in nutrients, with a protein content of approximately 3.3–3.5%, and is the best substitute for breast milk (Perdijk, van Splunter, Savelkoul, Brugman, & van Neerven, 2018; Shafqat, Naheed, Ayesha, & Amir, 2018). However, the protein composition of bovine milk is markedly different from the protein composition of human milk. Bovine milk contains α -casein and β -lactoglobulin, which are not present in human milk, and a relatively low content of α -lactalbumin and immunoglobulin (Jiang, Du, & Lonnerdal, 2014). Milk allergy, with an incidence of 2–7.5%, is a common allergic disease in infants and young children that seriously affects their growth and may even be life-threatening (Biscola et al., 2018; Schoemaker et al., 2015). The main allergens in milk are α -casein, β -lactoglobulin, and α -lactalbumin, all of which have linear epitopes and conformational epitopes that can be recognized by IgE (Villa, Costa, Oliveira, & Mafra, 2020). Casein is the most abundant protein in milk,

up to approximately 80%, and has flexibility and thermal stability. β -lactoglobulin accounts for approximately 10% of the total milk protein, is resistant to digestion by gastric acid and pepsin and can pass through the intestine into the bloodstream. Approximately 82% of the cases of milk allergies are due to this protein. Approximately 74% of the amino acids of α -lactalbumin in bovine and human milk are homologous. However, because its immunogenicity depends mainly on the conformational epitope, α -lactalbumin is still a major milk allergen (Villa, Costa, Oliveira, & Mafra, 2018; Yan, 2018).

Some studies have demonstrated that irradiation at a certain dose can change the structure of milk-allergy proteins and mask their epitopes, thus reducing the allergenicity of milk proteins (Bu, Luo, Chen, Liu, & Zhu, 2013; Robichaud, Bagheri, Aguilar-Uscanga, Millette, & Lacroix, 2020). Meng et al. (2016) used ^{60}Co γ -rays at different doses (1–10 kGy) to irradiate the α -lactalbumin allergen in milk and further investigated the change in its immunogenicity (Meng et al., 2016). Interestingly, after irradiation at a low dose (3 kGy), α -lactalbumin protein was found to begin to polymerize, and all molecules of this allergen formed a polymer at a 10 kGy dose, which proved that irradiation treatment caused irreversible changes in the ordered spatial structure of this allergenic protein. The immunological activity of irradiated α -lactalbumin was found to be reduced by more than 80% in experiments evaluating its binding capacity to IgG and IgE. Additionally, irradiated α -lactalbumin showed considerable improvement in the inhibition of Ca^{2+} levels in KU812 cells and a decrease in the degranulation ability of basophils mediated by IgE. These results confirmed that irradiation could reduce the ability of α -lactalbumin to trigger an immune response. This group further validated the effect of irradiation on the allergenicity of α -lactalbumin using an in vivo experimental mouse model. Feeding α -lactalbumin irradiated at a 10 kGy dose triggered Th2 allergic reactions in mice. The levels of the Th2 cytokines, IL-17E and IL-21, which play a synergistic role with Th2 cytokines, were substantially decreased in mice, indicating that irradiation treatment can reduce the allergenicity of α -lactalbumin and allergic reactions in mice. Yang et al. (2020) investigated the effect of ultrasound-assisted irradiation in reducing the allergenicity of β -lactoglobulin (Yang et al., 2020). The results indicated that surface hydrophobicity was reduced and the aggregation of β -lactoglobulin was increased after treatment with irradiation, both with and without sonication. IgE binding capacity and release of inflammatory mediators were substantially reduced, and the reduction induced by irradiation after sonication was the greatest, suggesting that irradiation after sonication can be a safe and effective method to reduce the allergenicity of β -lactoglobulin in dairy processing. These studies demonstrated that irradiation has a positive effect on the elimination of allergenicity of milk allergens.

2.3.1.2. Egg allergens. Eggs, with high nutritional value, are a common food in daily life and are also one of the most allergenic foods reported

Table 1

Research investigating the use of irradiation reducing the allergens in milk, egg, fish and shrimp products.

Products	Target allergen	Irradiation dose	Observation	Reference
Milk	α -lactalbumin	1–10 kGy	α -lactalbumin began to polymerize at a low dose (3 kGy). All molecules of this allergen had formed the polymer and the immunological activity was reduced by more than 80% at 10 kGy dose.	Meng et al., 2016
Milk	β -lactoglobulin	5 kGy	The surface hydrophobicity was reduced and the aggregation of β -lactoglobulin was increased after treatment by irradiation, IgE binding capacity and release of inflammatory mediators were substantially reduced.	Yang et al., 2020
Milk	Casein, β -lactoglobulin	0.75, 10 kGy	Irradiation affects the antigenicity of allergenic food residues at low levels depending on the food matrices and the processing methods.	Gomaa & Boye, 2015
Pork	Porcine serum albumin (PSA)	1, 2, 4, 6, 8 kGy	The secondary and tertiary structures of gamma irradiated PSA were altered, the allergenicity of PSA was lowered by boosting the amount of irradiation. A high correlation between depletion in the α -helix and immunoglobulin E-binding capability of PSA.	Zhu et al., 2018
Pork muscle	Myofibrillar and sarcoplasmic protein	0, 3, 5, 7 kGy	Irradiation at 3 kGy could promote the actomyosin formation in myofibrillar protein, but ≥ 5 kGy irradiation favored its depolymerization.	Li et al., 2018
Egg	OVA	3, 5, 7, 10 kGy	The OVA epitopes undergo conformational changes, the binding abilities of the irradiated OVA against the monoclonal IgG and the egg allergic patients' IgE decreased, but	Kim et al., 2014

Table 1 (continued)

Products	Target allergen	Irradiation dose	Observation	Reference
Egg	OVA	0, 1, 3, 5 kGy	differences from using the two different radiation types were not observed. The γ -ray irradiation can improve the dispersion, significantly reduced the droplet size, increased the fluidity, and decreased elasticity and viscosity of egg white protein emulsion.	Liu, He, Zhang, Zhao, Yang, Liang, and Jing (2020)
OVA	OVA	1 kGy	Mice treated with γ -irradiated OVA had less OVA-specific IgE, but no difference in levels of OVA-specific IgG + A + M, IgG1, and IgG2a.	Yang et al., 2016
Turbot	Parvalbumin	1, 3, 5, 7, 10, 13 kGy	Binding ability of irradiated parvalbumin to IgE decreased markedly upon increasing the irradiation dose; the carbonyl content in parvalbumin was positively correlated with the irradiation effect.	Li et al., 2014
Tegillarca granosa	Myofibrillar protein	0–9 kGy	Total sulfhydryl content and Ca^{2+} -ATPase activity declined with increasing irradiation dose; the actin, paramyosin and myosin heavy chain contents of myofibrillar protein partially degraded.	Lv, Mei, Zhang, Xu, and Yang (2018)
Grass carp	Myofibrillar protein	Up to 10 kGy	Irradiation decreases emulsifying properties of fish protein. Irradiation up to 6 kGy distinctly decreases the content of myosin heavy chains.	Shi et al., 2015
Shrimp	Pen a 1	7, 10 kGy	Fragmentation, cross-linking and aggregation of the Pen a 1 occurred by treated with irradiation, the immunoreactivity decrease after irradiation with 7 kGy and 10 kGy	Mou et al., 2014
Shrimp	Tropomyosin	3, 5, 7, 10 kGy	Irradiation significantly	Liu et al., 2017

(continued on next page)

Table 1 (continued)

Products	Target allergen	Irradiation dose	Observation	Reference
Shrimp	Tropomyosin	0, 1, 3, 5, 7, 9 kGy	changes the IgE binding capacity of frozen shrimp at 10 kGy doses by 20% IgG binding capacity of tropomyosin has a significant decrease, and the most significant effect observed at 7 kGy. The structural changes were consistent with changes in IgG binding capacity of tropomyosin	Guan et al., 2018

by the Food and Agriculture Organization (FAO) of the United Nations (Urisu, Kondo, & Tsuge, 2015). Egg allergens are the second largest food allergen accounting for 35% of food allergies in children and 12% in adults. The allergenicity of egg allergens poses a great threat to the dietary safety of allergic patients. The adverse immune reactions caused by egg allergenic proteins include IgE-mediated allergic reactions, non-IgE-mediated allergic reactions, and immune disorders jointly mediated by IgE and cells, which clinically manifest as allergic colitis and gastrointestinal disorders (Rupa, Nakamura, Katayama, & Mine, 2014; Dona & Suphioglu, 2020). The allergens in egg yolk are mainly yolk glycoprotein and vitellogenin, whereas ovomucoid (OVM), ovomucoid (OVT), ovalbumin (OVA), and lysozyme (LYS) are believed to be present in egg whites (Amo et al., 2010; Park, Yoon, Kim, Han, & Choi, 2017; Stănciuc, Banu, Turturică, & Aprodu, 2016).

For eggs and their products, irradiation technology was first used in the sterilization process, and in recent years, it has gradually been used in egg allergen elimination. Some studies have demonstrated that irradiation dose, irradiation source, synergistic effect with other conditions and food matrix affect the elimination of egg allergens upon irradiation to some extent. Liu et al. has investigated the effects of different doses (0, 1, 3, 5 kGy) of ^{60}Co γ -ray irradiation on the structural and emulsifying properties of egg white protein. γ -ray irradiation improved the dispersion, significantly reduced the droplet size, increased the fluidity, and decreased the elasticity and viscosity of the egg white protein emulsion. All these results suggested that irradiation treatment can improve the emulsification characteristics and stability of egg white protein (Liu, He, Zhang, Zhao, & Jiang, 2020). In the study of Kim (Kim et al., 2014), the egg allergenic protein OVA, upon being irradiated by two forms of radiation (electron and X-ray), showed no differences in the structural properties of OVA by spectrometric and electrophoretic analyses. However, in the competitive indirect enzyme-linked immunosorbent assay (ELISA), OVA samples irradiated by electron beam or X-ray irradiation showed different immunological responses in reactions with monoclonal and polyclonal antibodies (immunoglobulin G) produced against nonirradiated OVA, which indicates that electron beam irradiation and X-ray irradiation produced different patterns of structural changes to the OVA molecule. In fact, allergens do not exist alone in food, and complexity of the food matrix is also an important factor affecting the elimination of allergens by irradiation. The research group of Gomaa and Boye has evaluated the impact of irradiation and thermal processing on the immunochemical detection of milk and egg allergens in foods. Different food matrices (bread, boiled pasta and extruded cereal) were selected for γ -irradiation and thermal processes. By comparison, γ -irradiation at 0.75 and 10 kGy did not affect the antigenicity of food allergens and the allergen recoveries in γ -irradiated samples

depended on the irradiation dose, the tested matrix, and the processing method (Gomaa & Boye, 2015). At the same time, irradiation with γ -rays and electron beams has obvious differences in the reduction of OVA antigenicity, demonstrating that the selection of radiation sources should also be considered in practical applications.

Irradiation, in conjunction with heat, ionic strength (pH), gas, and other factors, can accelerate the curing of egg allergens, which is a more efficient treatment method for removing allergens. The synergistic effect of irradiation and thermal processing was found to enhance the sensitivity of egg allergens. O_2 has a protective effect on the activity of OVM, slows the rate of irradiation-induced inactivation, and promotes the reduction of OVA activity, which might be due to the differences in the spatial structure of OVM caused by different ionic strengths. Therefore, irradiation or its combination with other processing technologies is considered an effective technical means of removing the allergenicity of egg allergens. Because the irradiation effect could be affected by the food matrix, pH value, gas environment, and other factors, it is necessary to have standardized and comprehensive parameters during the irradiation procedure for its further application.

2.3.2. Aquatic products allergens

Aquatic products, including fish and crustaceans, account for two of the eight categories of food that can easily cause allergies as reported by the FAO (Pedrosa, Boyano-Martinez, Garcia-Ara, & Quirce, 2015; Leung et al., 2014; Wong, 2015). Allergenic proteins in aquatic products have also attracted considerable attention (Sharp & Lopata, 2014; Prester, 2016; Ma, Pavase, Li, & Lin, 2017). Irradiation with high energy is also applied to eliminate the allergenicity of allergic proteins in aquatic products, which might improve the digestibility and adsorption level of aquatic products.

2.3.2.1. Fish allergens. Fish are rich in high-quality proteins and phosphorus and are easily digested and absorbed by the human body, becoming a popular food. However, fish and their products contain proteins that may cause severe allergic reactions in sensitive people through direct consumption or indirect contact. The prevalence of fish allergies is usually less than 8%, depending on the population's dietary habits, diagnostic criteria, exposure style, and age (Kobayashi et al., 2016; Kourani, Corazza, Michel, & Doyen, 2019). To date, only 0.5% of fish, including tuna, cod, carp, and salmon, have been studied at the molecular level for allergens (Stephen et al., 2017). Parvalbumin is a Ca^{2+} -binding protein widely found in fish muscle and bone cells and can regulate multiple cellular processes by controlling intracellular Ca^{2+} ion exchange (Guo, Kubota, & Shiomi, 2012; Lapteva, Uversky, & Permyakov, 2013). Parvalbumin is the most important allergen in fish and can cause allergic reactions in 90% of people who are allergic to fish. Most allergic reactions are caused by the presence of β -parvalbumin (Fernandes, Costa, Carrapatoso, Oliveira, & Mafra, 2017; Moonesinghe et al., 2016; Zhang et al., 2020). Li et al. evaluated the effect of irradiation on the immunogenicity and carbonyl content of parvalbumin in turbot (Li et al., 2014). The binding ability of irradiated parvalbumin to IgE decreased markedly upon increasing the irradiation dose, and the carbonyl content in parvalbumin was positively correlated with the irradiation effect, suggesting the possibility that the carbonylation of parvalbumin under irradiation is one reason for its allergic elimination, which provides a very important reference for studying irradiation-based reduction of allergenic stimulation by fish.

The high energy of γ -rays or electron beams used for irradiation can cause changes in the physicochemical properties and structure of fish proteins, such as hardness, gumminess, chewiness or resilience, further improving food quality. Lv et al. investigated the effect of electron beam irradiation at doses of 0–9 kGy on the biochemical properties and structure of myofibrillar protein from *Tegillarca granosa* (Lv et al., 2018). Although irradiation had no effect on the surface hydrophobicity of the myofibrillar protein, the total sulfhydryl content and Ca^{2+} -ATPase

activity both declined to varying extents with increasing doses of irradiation. With increasing dose of irradiation, the actin, paramyosin and myosin heavy chain contents of the myofibrillar protein were partially degraded. In the study of Shi et al. (2015), γ -irradiated myofibrillar protein from grass carp exhibited decreased emulsifying properties and increased surface hydrophobicity. This study demonstrated that γ -irradiation decreased the myofibrillar protein ordered structure and generated the crosslinking and provided a possible reference for the identification of irradiated fish products.

2.3.2.2. Shrimp allergens. Irradiation, which breaks chemical bonds in food molecules and destroys protein structures in organisms, reduces the activity of food-sensitizing proteins and is considered a new method to reduce the allergenicity of shrimp products (Han et al., 2016). Mou et al. examined the function of each epitope of Pen a1 (a major allergen in shrimp) in the sensitization process by analyzing the variations of their immunoreactivity following irradiation, heat treatment, or a combination of both (Mou et al., 2014). The variation in the IC_{50} values of epitope 3 was consistent with the IC_{50} values measured from the whole Pen a1 protein, which suggests that epitope 3 is the determinative epitope in the allergenicity and epitope 5 was stable following irradiation and heat treatments.

The main allergens in shrimp products are tropomyosin and arginine kinase. Tropomyosin (36 kDa, pI 4.5) has a double helical structure formed by two identical intertwined α -helix subunits and has excellent thermal stability and digestive resistance (Peixoto et al., 2018; Ruethers et al., 2020). Due to the large number of antigenic epitopes and high cross-reactivity among different shrimp species, tropomyosin has become the main subject of research on shrimp allergens (Long, Yang, Wang, Hu, & Chen, 2015; Lv, Lin, Li, Ahmed, & Chen, 2017; Zhang, Xiao, & Zhou, 2019). Arginine kinase (40 kDa, pI 6.4) is an acid- and alkali-resistant protein with poor heat resistance and is the second most important allergen in shrimp products after tropomyosin (Margaret, Jinap, & Faizal, 2015). These allergens pose a threat to health. The elimination of these allergens during food processing is very challenging (Lasekan & Nayak, 2016).

Electron beam irradiation can also substantially reduce the immune activity of allergenic proteins in shrimp products (Liu et al., 2017b). Specific IgE binding results showed that the capacity of shrimp extracts and TM initially increased by 10% after irradiation at 3 kGy doses and then decreased by 20% with irradiation doses increased to 10 kGy. This result suggests that electron beam irradiation significantly changes the IgE binding capacity of frozen shrimp at 10 kGy doses by 20% and has the potential to reduce shrimp allergy risk. Guan et al. found that the binding capacity of tropomyosin in shrimp meat was reduced by 59% with 7 kGy irradiation treatment using an electron beam (Guan et al., 2018). According to the results of circular dichroism and Fourier transform infrared spectroscopy, the structure of tropomyosin was destroyed. The allergenicity of whole shrimp and shrimp meat extracts decreased with an increase in irradiation dose. Due to the differences in the state of shrimp food, irradiation technology is generally believed to have a better reduction effect on liquid shrimp products, whereas allergens in solid products (shrimp meat and whole shrimp) usually require a higher dose of irradiation.

2.3.3. Plant-derived food allergens

2.3.3.1. Soybean allergens. Soybean is rich in proteins (35–38%) and unsaturated fatty acids, and its amino acid composition is balanced. Soybean is widely used in food, feed, and other fields as an important raw material (Fiorda et al., 2016; Preece, Hooshyar, & Zuidam, 2017; Wang et al., 2018). Soybean and its products have the functions of enhancing the immunity of the body, preventing vascular sclerosis, and promoting bone development but also have food allergens that lead to allergic diseases (Matsuo et al., 2020; Natarajan et al., 2016; Villa,

Mónica, Moura, Costa, & Mafra, 2020). Nearly 20 kinds of allergy proteins have been identified in soybean, among which Gly-m Bd 30 K and Gly-m Bd 28 K in 7S globulin and Gly-m Bd 60 K in β -soybean globulin are three major allergens (Murakami, Ogawa, Takafuta, Yano, & Moriyama, 2018; Tsuji et al., 2014).

Allergic reactions induced by soy proteins are mainly type I hypersensitivity reactions that are mediated by a specific IgE (He & Xi, 2020; Sun, Shan, Yan, Zhang, & Guan, 2013). Therefore, reducing the immunoreactivity of soybean allergenic proteins is a very effective means of reducing allergenicity. Vaz et al. (2013b) investigated the relationship between allergenicity and molecular structure of a food allergen after gamma irradiation, which confirmed that high-dose radiation may render protein food allergens innocuous by irreversibly compromising their molecular structure. Although the allergenicity of soy protein can be reduced by irradiation, irradiation can easily affect the quality of food because of the limitation of using high-energy irradiation. Therefore, they are not used frequently in production processes. Some studies have shown that radiation combined with heat treatment can change the secondary and tertiary structure of proteins, substantially affect the surface hydrophobicity and free sulfhydryl content of soybean isolates, and improve their solubility, foaming, and emulsifying ability (Cabanillas, Jappe, & Novak, 2018; Zu, Hua, Gong, Yang, & Chen, 2014). Soybean trypsin inhibitor (STI) is a known antinutrient and food allergen present in soybean. Mallikarjunan and coworkers systematically studied the influence of different moisture levels during γ -irradiation on the structure and function of STIs (Mallikarjunan, Marathe, Deshpande, Jamdar, & Sharma, 2012). According to the results obtained, both the structure and function of STI were almost destroyed at the 10 kGy dose in aqueous solution. With 50% moisture and in the dry state, the loss in functional and structural attributes was discernible only at 30 and 100 kGy. Up to irradiation doses of 100 and 50 kGy, the STI activity was found to be unaffected in dry and soaked soybean seeds.

In studies on the elimination of allergens in eggs, milk, peanuts, kidney beans, and black beans, the effects of irradiation on plant allergens were found to be much higher than those animal allergens (Table 2). Irradiation, used in combination with heat treatment, greatly reduced soluble proteins and insoluble proteins in leguminous plants, with a particularly marked reduction in allergic reactions, which was much higher than the reduction in allergic reactions obtained by irradiation or heating alone (Kasera et al., 2012; Moriyama et al., 2013). Meinschmidt et al. have investigated the effects of pulsed ultraviolet light (PUV), cold atmospheric pressure plasma (CAPP), and γ -irradiation on the immunoreactivity of soy protein isolates (Meinschmidt et al., 2016). With increasing doses and times of PUV light, direct CAPP, and γ -irradiation, a loss of soy immunoreactivity was confirmed using sandwich ELISA using specific anti-Gly m5 monoclonal antibodies (mAbs), verifying that these innovative technologies have great potential for industrial application due to their effectiveness in reducing soy immunoreactivity. Wang et al. combined irradiation with the glycosylation modification method. Irradiation was proven to be able to the Maillard reaction between the soybean protein isolate and maltose and significantly improve the functional properties of the modified protein, providing theoretical and technical support for expanding the application of the soy protein isolate in the food industry (Wang et al., 2020).

2.3.3.2. Peanut allergens. Peanut is not only a nutritious and delicious food but can also be widely used as a raw material or ingredient in various other food items. As a food allergen recognized by the FAO/WHO, peanut contains 18 allergenic proteins with immunogenicity, 11 of which, viz., Ara h 1–11, can be recognized by specific IgEs (Anagnostou & Clark, 2015; Sicherer, Sampson, & Burks, 2015; Chen et al., 2016). Among these proteins, Ara h 1, Ara h 2, Ara h 3, and Ara h 6 are considered the major allergenic proteins in peanuts (Koppelman et al., 2015; Koppelman et al., 2016; Palladino & Breiteneder, 2018).

Most of the proteins in peanuts were stable upon irradiation

Table 2

Research investigating the use of irradiation reducing the plant-derived allergens.

Products	Target allergen	Irradiation dose	Observation	Reference
Soybean	β -conglycinin, Gly m Bd 30 K, STI, Gly m 4	0, 2.5, 5, 7.5, 10, 20, 30 kGy	No significant changes in the allergen contents, except for a decrease in the STI. The IgE binding allergenic protein patterns were not changed by irradiation up to 30 kGy.	Moriyama et al., 2013
Bean	Cramoll	1, 10, 25 kGy	High-dose radiation may render protein food allergens innocuous by irreversibly compromising their molecular structure.	Vaz et al., 2013a
Soybean	STI	10, 30 100 kGy	Different moisture levels during γ -irradiation has a different loss on functional and structural attributes of STI.	Mallikarjunan et al., 2012
Soy protein isolate	β -conglycinin, Gly m5, glycinin Gly m6	3–100 kGy	A loss of soy immunoreactivity was confirmed with increasing dose and time of PUV light, direct CAPP, and γ -irradiation.	Meinlschmidt et al., 2016
Soybean protein	Glycosylated soybean proteins	7.5 kGy	Irradiation could promote the Maillard reaction between the soybean protein isolate and maltose, and significantly improve the functional properties of the modified protein.	Wang et al., 2020
Peanut protein extracts solution and defatted powder	Ara h 1, Ara h 2, Ara h 3	2, 4, 6, 8, 10, 15, 20 kGy	The allergen in solution was found to be more sensitive to irradiation than that in solid state. The concentration and turbidity of the allergen solution increased with the increasing of irradiation dose.	Xu, et al. 2012
Peanut	Ara h 6	1–5 kGy	The content of secondary structure α -helix of the Ara h 6 was markedly reduced, and the binding ability of Ara h 6 allergens with IgG decreased.	Luo et al., 2013
Wheat	Wheat germ lectin	1, 10, 25 kGy	Loss of intrinsic activity and the formation of insoluble amorphous aggregates with a lack of native conformational structures after irradiation. The allergenic epitopes of wheat germ lectin became less active and antigenic after high-dose radiation.	Vaz et al., 2012
Pistachio	–	1, 10, 100 kGy	The antibody binding rate of pistachio allergens showed a negative dose response relationship with irradiation dose	Vahid et al., 2019
White sesame seeds	2S albumin (Ses i 1)	2.5, 5.0, 10.0 kGy	Sesame allergenicity was not significantly affected by irradiation up to 10.0 kGy	Zoumpoulakis et al., 2012
Moringa oleifera seed	Moringa oleifera seed lectin	10 mGy, 10 Gy	There was no loss of protein molecules but conformational change was detected at 10 Gy.	Santos et al., 2020

(Verhoeckx, Vissers, Baumert, Faludi, & Kimber, 2015; Zhang et al., 2019). Irradiation at a low dose (<1.0 kGy) had little effect on peanut allergens in protein powder or solution. High-dose irradiation of 2–20 kGy led to conformational changes and polymerization of proteins with small molecular weights, thus reducing the allergenicity of allergenic proteins. These results indicate that the elimination of peanut allergenic activity depended on the irradiation dose, which had an important effect on the secondary structure but little effect on the tertiary structure of peanut protein. Luo et al. (2013) irradiated Ara h 6 allergens with γ -rays and found that the content of secondary structure α -helix of the peanut allergy protein was markedly reduced, and the binding ability of Ara h 6 allergens with IgG decreased. The results further demonstrated that the secondary structure of the α -helix was closely related to the allergenicity of Ara h 6. As the irradiation dose increased from 1 kGy to 5 kGy, peanut allergy proteins gradually accumulated and eventually formed insoluble aggregates, indicating that high-dose irradiation leads to considerable changes in the conformational epitopes of peanut allergens, thus reducing their allergenicity, possibly because some peanut ingredients can prevent a decrease in the allergenicity of peanut allergens at low-dose irradiation, but this similar protective function no longer exists at high doses. Xu et al. investigated the effect of electron beam irradiation on the allergenicity and biochemical properties of peanut protein (Xu, et al. 2012). Peanut protein extract solution and defatted powder were irradiated at different doses (2, 4, 6, 8, 10, 15 and 20 kGy). The allergen in solution was found to be more sensitive to irradiation than the allergen in the solid state. When the irradiation dose was higher than 10 kGy, the immunoreactivity decreased. The concentration and turbidity of the allergen solution increased with increasing irradiation dose. These results demonstrated that the biochemical properties of peanut allergens were altered and immunoreactivity was reduced by irradiation, and the effect of electron beam irradiation on peanut allergens in the solid state was more significant. Heavy-ion beam irradiation has high linear energy transfer capable of breaking the double-stranded DNA molecules, which is applied to produce hypoallergenic peanut lacking major allergens, Ara h 2 and 3, indicating that heavy-ion beam irradiation is a powerful means of producing knockout hypoallergenic peanuts (Cabanos et al., 2012).

2.3.3.3. Wheat allergens. Wheat is one of the main food crops, with an annual output of 600 million tons. With the increase in wheat consumption, allergic diseases caused by wheat have also attracted great attention (Lu, Zhang, Ouyang, Liu, & Li, 2015; Quirce, Boyano-Martinez, & Diaz-Perales, 2016; Ji, Meng, & Gao, 2018). Wheat allergies include mainly celiac disease, baker's asthma, specific dermatitis, and allergies caused by food-related activities (Graham, Caubet, Ramadan, Spoerl, & Eigenmann, 2020; Okolie, Aryee, & Udenigwe, 2018). According to previous studies, wheat proteins can be divided into water-soluble albumin, salt-soluble globulin, wheat gliadin, and gluten. Among these wheat proteins, gliadin and glutenin account for approximately 80% of the total protein content of wheat (Pritchard & Brock, 2010; Sievers, Rawel, Ringel, Niggemann, & Beyer, 2016). Most patients with wheat allergies are allergic to the pentapeptide structure of Glu-Glu-Glu-Pro subunits of gluten. Albumin and globulin in wheat are the main allergens in baker's asthma and wheat-specific dermatitis allergies, whereas gliadin, an isolectin, is considered to be the allergen that causes celiac disease and food-dependent exercise-induced allergies (Battais et al., 2003; Morita, Yamamura, Mihara, Kameyoshi, & Yamamoto, 2015).

For patients with wheat allergies, it is important to avoid allergens or eat wheat products with a low level of allergens. Irradiation technology can promote the oxidation, dissociation, and aggregation of proteins, thus reducing their allergenicity. Vaz et al. irradiated wheat germ lectin (WGA) at different doses of 1, 10, and 25 kGy, and found that the activity of the allergenic epitopes of WGA worsened after high-dose irradiation (Vaz et al., 2012). This is because when the irradiation dose exceeds 10 kGy, the polypeptide chain of the WGA molecule breaks, resulting in the destruction of the molecular folding structure and the formation of amorphous polymers. In subsequent mouse experiments, the levels of two types of eosinophils, IL-4 and IL-5, were markedly reduced in WGA-fed mice. The amount of lymphocyte osmosis in the intestinal tissue sections of the mice was reduced, which in turn reduced the inflammatory response of the mice. These results show that high doses of irradiation reduced WGA sensitization. Since wheat gliadin is also an agglutinin, it indirectly confirmed the role of irradiation in reducing wheat allergenicity, providing a theoretical basis for wheat allergy-elimination processing.

2.3.3.4. Nut allergens. Allergenic proteins are found in nuts such as almonds, cashews, and walnuts, which may also cause allergic reactions in some people (Geiselhart, Hoffmann-Sommergruber, & Bublin, 2018; Vanga & Raghavan, 2016). Since the surfaces of these nuts are usually covered with a hard shell, the allergenic proteins in the nuts are more stable to irradiation. In the study of Zoumpoulakis et al. (2012), the lipid content in white sesame seeds decreased after irradiation at a 2.5 kGy dose, but the allergenicity of seed proteins was not significantly affected by irradiation up to 10.0 kGy. In some studies, irradiation alone has been shown not to affect allergenic proteins in nuts. However, irradiation combined with heat treatment, high-pressure steam, frying, and other processing methods can effectively reduce the allergenicity of nut allergens (Venkatachalam et al., 2008). Vahid et al. found a negative dose-response relationship between the antibody binding rate of pistachio allergens and γ -irradiation dose, indicating a promising finding that irradiation appears to be an effective method for reducing the allergenicity of pistachio nuts (Vahid et al., 2019). At the same time, γ -irradiation, especially at a high dose, caused adverse changes in the sensory properties of pistachios, which also proved that the dose must be controlled in the process of eliminating allergens by irradiation.

3. Future research outlook

Irradiation has been widely considered in food processing because of its advantages such as effectiveness against most allergens in foods, low-cost and easy of industrialization. As far as the current study is concerned, many follow-up studies are still needed. First, the mechanism for irradiation elimination of food allergens needs to be studied further. Existing conclusions on the degradation or cross-linking of allergenic proteins are mostly speculative, so more effective strategies are needed to analyze and verify the structural changes of proteins before and after irradiation. This analysis and verification are also meaningful for the evaluation of the safety of irradiated foods. Second, irradiation treatment may change the structure of other components in the food matrix, which may affect the nutritional value, flavor or quality of the food. Because the elimination effect is affected by irradiation dose, allergen characteristics and food matrices, it is of great significance to study precise radiation desensitization according to different food matrices and allergen characteristics. Third, the combination of irradiation treatment and other food processing methods may be more effective in reducing the allergenicity of food, which is very meaningful to promote the practical application of irradiation desensitization technology.

4. Conclusions

In summary, the elimination or reduction of the allergenicity of animal and plant food through irradiation treatment is feasible because irradiation can change the structure of allergic proteins through free radical reactions or direct absorption. In practice, irradiation has been proven to be effective for most food allergens in foods, achieving different elimination effects. Although the elimination of some allergenic proteins needs to be improved, further improvements have been made by combining with other food processing methods such as high pressure, high-voltage pulse, ultrasound. All these results have confirmed that irradiation is an appropriate and potential strategy to eliminate or reduce most food allergens in foods.

CRediT authorship contribution statement

Mingfei Pan: Funding acquisition, Investigation, Writing – original draft. **Jingying Yang:** Writing – review & editing, Visualization, Data curation. **Kaixin Liu:** Data curation, Writing – review & editing. **Xiao-qian Xie:** Formal analysis. **Liping Hong:** Software. **Shan Wang:** Data curation. **Shuo Wang:** Supervision.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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