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REVIEW



Soybean allergy: characteristics, mechanisms, detection and its reduction through novel food processing techniques

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ABSTRACT

Human beings have consumed soybean as an excellent food source for thousand years due to its rich protein, fatty acids, minerals, and fibers. However, soybeans were recognized as one of the big eight allergens resulting in allergic symptoms and even could lead to death. With the increasing demand for soybean products, the challenges caused by soybean allergy need to be solved urgently. This review detailedly described the pathogenesis and clinical characteristics of soybean allergy, and also the advantages and disadvantages of four different diagnostic methods were summarized. The major soybean allergens and their structures were summarized. Three types of soybean allergy including Type I, III, and IV, which could trigger allergic reactions were reported in this review. Summary in four different diagnostic methods showed that double-blind, placebo-controlled food challenge is recognized as a gold standard for diagnosing soybean allergy. Three types of processing techniques in reducing soybean allergy were discussed, and the results concluded that some novel food processing techniques such as ultrasound, cold-plasma treatment, showed potential application in the reduction of soybean allergenicity. Further, some suggestions regarding the management and treatment of food allergies were addressed in this review.

KEYWORDS

Soybean allergy;
skin prick test;
food processing techniques;
protein structure;
immunotherapy

1. Introduction

Soybean (*Glycine max*) is one of the members of the legume family, which is rich in proteins (36.5 g/100 g), total lipid (20 g/100 g), minerals (e.g., calcium, 277 mg/100 g), vitamins (e.g., vitamin B-6, 0.23 mg/100 g), fibers (6 g/100 g), and fatty acids (e.g., total polyunsaturated, 5.1 g/100 g) (Table 1). Studies reported that the protein content of soybean is 4–5 times higher than that of cereals and twice that of eggs, meat, and fish (Friedman and Brandon 2001). The Food and Drug Administration (FDA) of the United States suggests that adding soybean protein to foods can lower cholesterol levels and reduce cardiovascular disease risk (Gagnon et al. 2010). Soybean protein is a complete plant-based protein containing abundant bioactive peptides. These bioactive peptides have the functions of anti-oxidation, angiotensin-converting enzyme inhibition, and blood pressure reduction (Chatterjee, Gleddie, and Xiao 2018; Kim, Yang, and Kim 2021). In addition, soybean is the only vegetable food that contains all eight essential amino acids, and the physiological value of soybean protein can reach 100% of protein digestibility corrected for amino acid score (PDCAAS) (Rizzo and Baroni 2018).

Soybean has great potential marketing value. In 2020, the Food and Agriculture Organization (FAO) of the United

Nations reported that the total worldwide soybean production was 353,463,735 tons, and the output has increased by about 32% compared to five years ago. Furthermore, soybean has obtained significant attention from the food industry due to its unique processing properties such as emulsification and foaming characteristics. Soybean was considered as an excellent source to produce a variety of products such as soybean oil, soybean flour, soybean milk, tofu, soybean flakes, or fermented soybean products (e.g., miso and soybean sauce) for our daily consumption (Tamari, Shoyu). As a meat alternative, it shows an increasing trend and has become popular among vegetarians.

However, soybean was recognized as one of the major allergenic food items among the “big eight” (including milk, eggs, fish, shellfish, tree nuts, peanuts, wheat, and soybean), which can trigger various allergic reactions ranging from mild symptoms to life-threatening symptoms (Dick et al. 2021). Studies reported that there is approximately 0.3–0.4% of children are allergic to soybean worldwide (Savage et al. 2010). Besides, soybean may also have cross-allergic reactions with other allergens due to their sharing of similar epitopes in the proteins. Gly m 4 is a major soybean allergen which is also a homologous protein of Bet v1 present in birch pollen. Thus, those individuals with a history of birch

Table 1. Nutrients in 100 grams (g) Soybeans, mature cooked, boiled, without salt (Source: USDA Nutrient Database, 2018).

Nutrients	Ingredients	Concentration (100 g soybean)
Proximates	Energy	721kJ
	Water	62.55g
	Carbohydrate	8.36g
	Fiber	6g
	Sugar	3g
Minerals	Protein	18.21g
	Calcium	102mg
	Magnesium	86mg
	Iron	5.14 mg
	Potassium	515mg
	Phosphors	245mg
	Zinc	1.15 mg
Vitamins	Vitamin B-6	0.234 mg
	Vitamin A, IU	9IU
	Vitamin K (phylloquinone)	19.2 µg
Lipids	Fatty acids, total saturated	1.297g
	Fatty acids, total monounsaturated	1.981g
	Fatty acids, total polyunsaturated	5.064g

Table 2. Mechanisms of the four types of hypersensitivity (Marc and Olson 2009; Burks et al., 2018).

Types	Participating ingredients	Effector cells	Primary mediator	Secondary mediator	Major diseases
Type I Immediate immune	IgE	Mast cell, basophils	Vasoactive amine	leukotrienes, Cytokine, Prostaglandin D2 Platelet activating factor	Hives, redness, angioedema
Type II Cytotoxic hypersensitivities	IgG, IgM	Fragment crystallizable (Fc) receptors+ cells (phagocyte, Natural killer cells)	Complement, membrane attack complex	Lysosomal enzyme, Perforin	Hemolysis, Autoimmune hemolytic anemia
Type III Immune complex	IgG, IgM	Fc receptors+ cells, complement	Antigen-antibody complex	Lysosomal enzyme	Systemic lupus erythematosus, serum sickness, arthritis
Type IV Delayed-type	Th1, Th2, CTL	Mφ, Eosinophil	IFN-γ, IL-4, IL-5, IL-12, eotaxin	Eotaxin, Cytokine, Inflammatory factor	Contact dermatitis, Rash, Tuberculosis

pollen allergy may induce allergic reactions when exposed to soybean or related product (Mittag et al. 2004; Calamelli et al. 2019). Furthermore, one study has reported that 43% of infants with cow's milk allergy showed cross-reactivity with soybean (Ahn et al. 2003). Also, the incidence rate is increasing by year due to the increase of exposure to soybean or relevant products. Thus, solving this global challenge is urgent.

Novel techniques used in reducing the allergenicity of soybean commonly can be subdivided into thermal processing, non-thermal processing, chemical, and biological methods. The thermal and non-thermal processing includes heating, high-pressure treatment, ultrasound, cold plasma, etc. These methods generally do not involve the primary structures of protein. Chemical methods mainly include glycosylation reaction and chemical reagent treatment. This treatment method is very inefficient in reducing the allergenic potency of soybean or relevant products, and there will be chemical residues in the product. The main methods to reduce the allergenicity of soybean protein by biological methods are microbial fermentation, enzyme treatment, plant breeding, and genetic modification (Panda et al. 2015; Costa et al. 2021). Although the genetic modification method can remove endogenous genes of soybean allergens, its safety remains widely controversial.

In this review, we attempt to describe the pathogenesis and clinical characteristics of soybean allergy, and also the advantages and disadvantages of different diagnostic methods

to be covered. The main allergens present in soybeans including Gly m bd 28k, Gly m bd 30k, Gly m bd 60k were reviewed. Finally, we also discuss the advantages and disadvantages of different processing methods to reduce soybean allergenicity.

2. Pathogenesis, clinical features, diagnosis, and epidemiology of soybean allergy

2.1. Pathogenesis and clinical features

Hypersensitivity is also called allergy, which develops when the antigen was recognized by the immune system, and then sensitized lymphocytes or specific antibodies are produced under the interaction of certain conditions (Wang et al. 2019). When the patient is exposed to the antigen again, hypersensitivity reactions will occur, and four types of allergy were found (Table 2 and Figure 1). Soybean can mainly cause allergic reactions in the human body, including Type I, III, and IV.

For Type I, the soybean antigen protein enters the intestinal immune system and produces a large amount of immunoglobulin E (IgE) (Stenton, Vliagoftis, and Befus 1998). The fragment crystallizable of IgE binds to the fragment crystallizable receptor of mast cells in the tissue to make the body sensitized. When the body is exposed to the sensitizing protein again, the sensitizing protein will bind to IgE, which can cause a release of active media such as cell

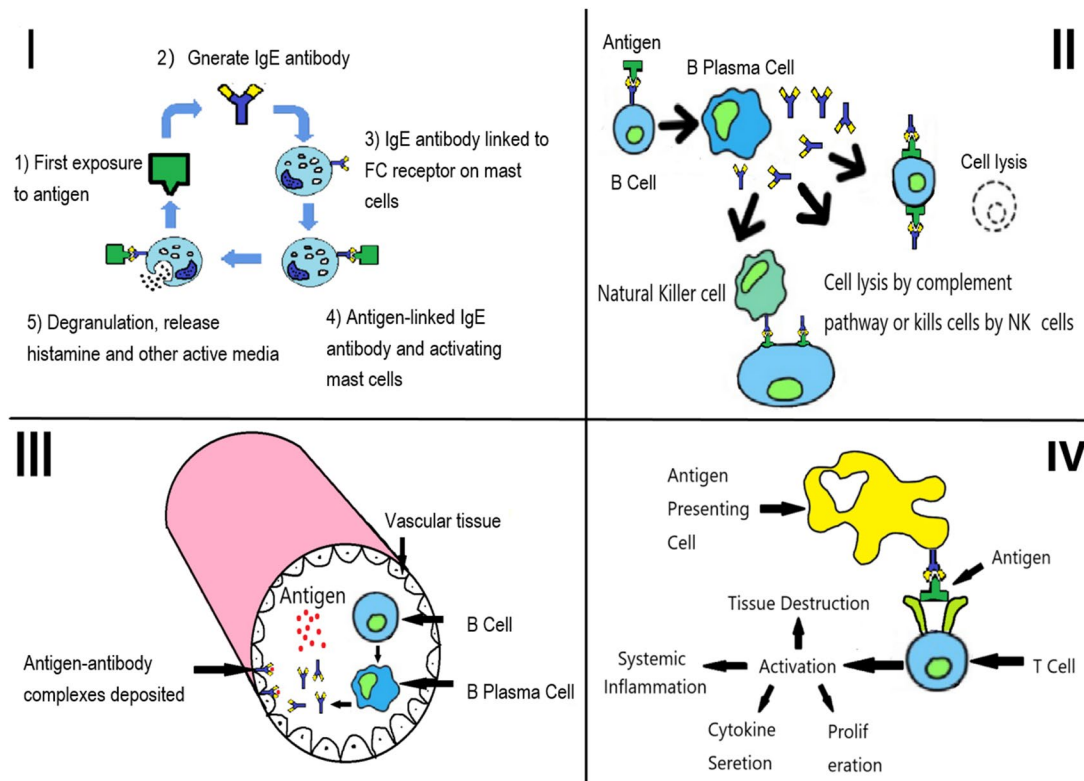


Figure 1. Four different types of food allergies and their mechanisms.

degranulation, histamine, serum toxin, prostaglandin, and enzyme. Eventually, the protein in the plasma leaks into the intestinal lumen, intestinal mucosal edema, goblet cell mucous exudation, and intestine where absorption of liquid and electrolyte occurs, leading to severe local inflammation in the intestinal mucosa and submucosa (Sun et al. 2008; Marc and Olson 2009).

In comparison with other types of allergic reactions, Type III hypersensitivities need a longer time (from several hours up to weeks) to develop. As shown in Figure 1, after soy antigen passes through the human body's intestinal wall and enters the circulation, it can stimulate lymph nodes throughout the body to produce more IgG, forming an IgG-antigen complex (Ellsworth et al. 2008). Antigen-antibody complexes are deposited in the intestinal wall tissues, which activate the complement system to release allergic toxins and vascular permeability enhancers; or adhere to platelets and promote the release of reactive amines leading to inflammation. Research has suggested that Type III reactions may contribute to systemic lupus erythematosus (SLE), serum sickness, and farmer lung (Coico and Sunshine 2009).

Type IV hypersensitivities are referred to as delayed-type hypersensitivities, mediated by specific T lymphocytes. Antigen protein activates T-lymphocytes through a specific and intricate reaction with T cells, causing a late-type allergic reaction, causing proliferation of intestinal epithelial lymphocytes in animals, and greatly accelerating the mitotic rate of crypt cells, leading to changes in the structure of intestinal villi (Gell and Benacerraf 1961).

2.2. Diagnosis and detection

2.2.1. Skin prick test (SPT)

Skin prick test is one of the most common methods which is used to identify the allergies and the relevant allergic food sources in the hospital. In an SPT, safe doses of allergens are introduced into a patient's skin. If there is a skin reaction, it means that the patient is reacting to the allergen, and the size and color of skin lesions can indicate the severity of the allergy; normally, a wheal with a mean diameter 3 mm or greater would be considered as a positive SPT (Shokouhi Shoormasti et al. 2021). According to Guidelines for the diagnosis and management of food allergy in the United States (Boyce et al. 2011), SPT effectively detects the presence of sIgE. It is valuable in identifying the food(s) responsible for IgE-mediated food allergy, but for making an initial diagnosis of food allergy, it has low positive predictive value; some patients have sIgE without clinical food allergy, so it may cause over-diagnosis.

2.2.2. Allergen-specific serum immunoglobulin E (sIgE)

sIgE test is an in vitro immunodiagnostic test that is applied to detect the concentration of sIgE in the serum and to identify foods that potentially provoke IgE-mediated food-induced allergic reactions. sIgE levels were originally measured using the radioallergosorbent test (RAST), but this test has been replaced by more sensitive fluorescence enzyme-labeled assays. The ImmunoCAP system is a new assay for sIgE (detecting sIgE down to 0.1 kU/l). It has been identified by the Food and Drug Administration (FDA).

Similarly, Enzyme-linked Immunosorbent Assay (ELISA) is another method used to determine the levels of sIgE. IgE in the patient's blood is bound to the antigen, and then enzyme-conjugated secondary antibodies are added. The complex reacts fluorescently with the developing agent. The higher the response value, the more specific IgE is present in the specimen. To evaluate the test results, the responses for the patient samples are transformed into concentrations with the use of a calibration curve. These IgE-based diagnostic methods have a high sensitivity (60% to 71%) and specificity (98% to 99%) (Wang et al. 2019).

2.2.3. Component-resolved diagnostics (CRD)

Component-resolved diagnostics (CRD) is a diagnostic test. The sIgE antibodies respond against the individual allergenic molecules when detected by using purified native or recombinant allergens. CRD can discriminate genuine sensitization from sensitization due to cross-reactivity (Calamelli et al. 2019). For example, Gly m 4 and Ara h 8 in soybean and peanut respectively, were identified as Homologous protein of Bet v1. A patient with birch pollen allergy may also be allergy to peanut or soybean because of cross-reactivity (Mittag et al. 2004; Oriel and Wang 2019). If CRD leads to a definitive diagnosis. Oral food challenge may be avoided in some patients.

2.2.4. Oral food challenge (OFC)

Oral food challenge (OFC) is the most definitive method for diagnosing of food allergies. There are three types of OFC, including Double-Blind, Placebo-Controlled Food Challenge (DBPCFC), Single-Blind Food Challenge, and Open-Food Challenge. The DBPCFC is the gold standard (Oriel and Wang 2019). The patient will receive increasing doses of the suspected food allergen and a harmless placebo. Food allergens and placebo are taken separately, at intervals of hours or days. Because allergens and placebo look similar, neither the patient nor his doctor will know which one is received, this procedure term is "double-blind." However, DBPCFC is time-consuming and expensive (Boyce et al. 2011). Detection speed of single-blind and open food challenges are faster than DBPCFC, so these two methods are more used in clinical settings, Single-blind food challenges is that the patient does not know what food is being eaten, while open food challenges is that both the patient and the doctor know what food is being eaten. But both the subjective factors of the patient and the doctor may affect the diagnosis. Overall, OFC is a good way to diagnose food allergy, but any form of OFC can expose patients to potentially severe allergic reactions.

2.2.5. Basophil activation test (BAT)

The basophil activation test (BAT) is a functional assay that measures the degree of degranulation following stimulation with allergen or controls by flow cytometry (Santos and Lack 2016). It correlates directly with histamine release and has the potential to resemble more closely the clinical phenotype of patients than allergy tests that merely detect the

presence of allergen-specific IgE. In a study, the basophil activation test (BAT) was used to examine the allergenic potential of five chemically characterized soybean protein extracts (SPE): raw SPE, SPE heated (121 °C) for 10 or 30 minutes with glucose and SPE heated (121 °C) for 10 or 30 minutes without sugar as a control (Teodorowicz et al. 2015). The results found that patients showed an increase (from 2 to 5 times; 2 patients) or decrease (from 2 to 36 times; 3 patients) allergenic potential to the processed soybean extracts. When the SPE heated for 30 minutes with glucose stimulated basophils were stronger than untreated samples for the 70% of the patients. In another study, 33 patients with documented birch pollen-associated soybean sensitization were enrolled and the BAT was used to examine their allergenic properties (Beyer, Sack, and Treudler 2012). The results found only 58% of subjects who were sensitized to soybean responded to their specific allergen, but virtually all those sensitized to wasp venom in the control group. BAT may need a higher concentrations soybean allergen (Gly m 4). The studies regarding the applications of BAT on the diagnosis of soybean allergy are very limited. Thus, further studies especially on the disadvantages and advantages about BAT are in need.

2.3. Global epidemiology of soybean allergy

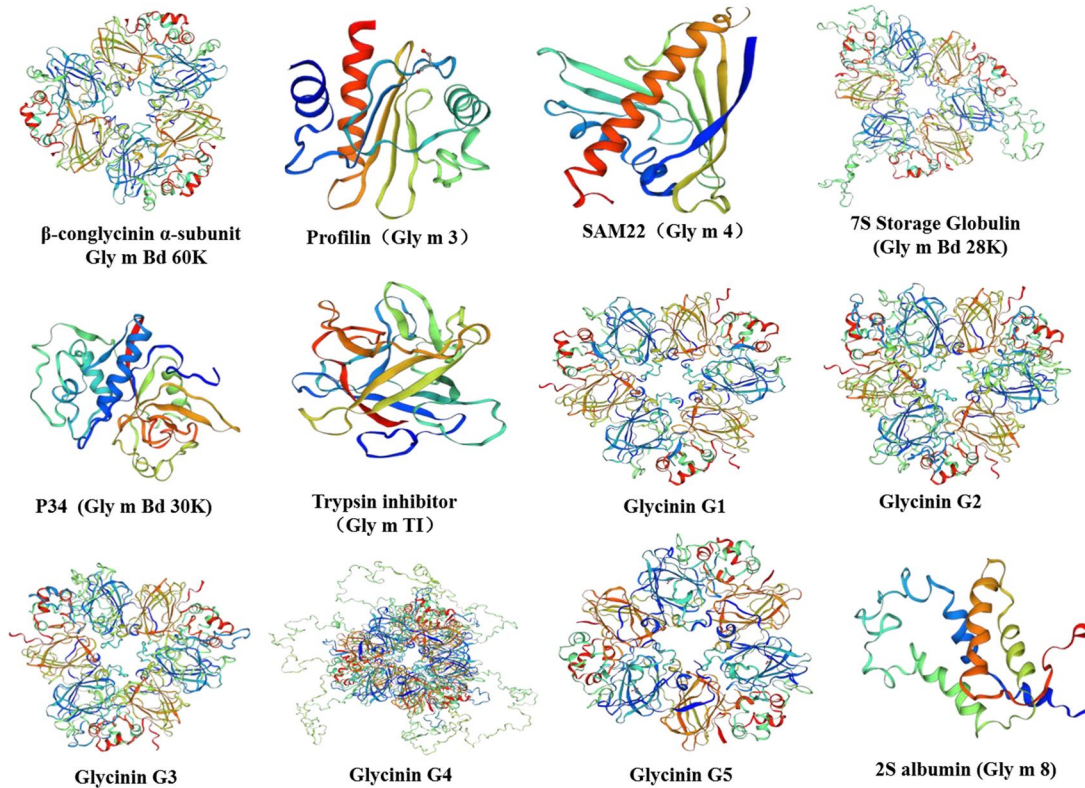
The soybean allergy has been documented since the 1980s (Ballmer-Weber and Vieths 2008). Soybeans are widely grown in Asia and the United States. According to statistics from FAO in recent years, soybean production and consumption in the world have been rising. Moreover, due to the development of food processing technology, soybean proteins and their processed products are widely used in the food industry. Allergic cases caused by it are increasing. From 1991 to 1992, Björnsson et al. (1996) surveyed 1,397 unselected adults aged 20–44. They used the RAST method to test the candidates and found that about 2% of people were allergic to soybeans. In 1999, a study performed in France among 703 patients with food allergies and found that 1.2% of patients were allergic to soybean by a food challenge (Rance et al. 1999). In 2014, a meta-analysis study reported that the overall pooled point prevalence of self-reported soybean allergy was 1.5–3.2% (95% CI 1.2–1.8, 2.7–3.6) for specific IgE positivity, and 0.3% (95% CI 0.1–0.4) for food challenge (FC) positivity (Nwaru et al., 2014). Generally, soybean allergy occurs primarily among young children with atopic dermatitis (Savage et al. 2010). But soybean allergies could also induce serious consequences. Fatal cases of anaphylaxis after ingestion of soybean have been reported (Hayashi et al. 2020). There is a high degree of concern about the allergenicity of genetically modified soybeans, but overall information about soybean allergies is scarce, epidemiologic data on soybean allergy in adults and children is still lacking.

3. Types of soybean allergens

Soybean allergens are proteins present in soybean that can trigger allergic reactions in humans. The World Health

Table 3. Main allergenic proteins of soybean and their relative characteristics.

Biochemical name	Group	MW	Types	References
Hydrophobic seed protein	Gly m 1	8 kDa	Structural protein	Lui, White, and Litster (2007) and Pi et al. (2021)
Hull Protein	Gly m 2	8 kDa	Structural protein	Lui, White, and Litster (2007), Pi et al. (2021)
Profilin	Gly m 3	14 kDa	Structural protein	Pi et al. (2021)
SAM22	Gly m 4	17 kDa	Defense protein	Pi et al. (2021)
β -conglycinin	Gly m 5	52-76 kDa	Storage protein	Li, Bu, et al. (2021), Pi et al. (2021)
7S Storage Globulin	Gly m Bd 28K	26 kDa	Storage protein	Astuti et al. (2018)
Cysteine protease (P34)	Gly m Bd 30K	32 kDa	Storage protein	Matsuo et al. (2020)
Trypsin inhibitor	Gly m TI	21.5 kDa	Defense protein	Vagadia, Vanga, and Raghavan (2017)
Glycinin	Glycinin G1, G2, G3, G4, G5	320-360 kDa	Storage protein	Luthria et al. (2018)

**Figure 2.** Protein structure of soybean allergens obtained from protein data bank (data source: www.rcsb.org).

Organization and International Union of Immunological Societies (WHO/IUIS) Allergen Nomenclature Sub-committee has identified eight key allergenic proteins present in soybean. According to the allergen database of the University of Nebraska–Lincoln, soybean allergy proteins can be subdivided into 43 types (www.allergenonline.org). As shown in Table 3, the major antigen proteins in soybean were listed, and protein structures of main soybean allergen are also presented in Figure 2.

3.1. β -Conglycinin (Gly m 5)

As shown in Table 3, β -conglycinin (Gly m 5) is one of the most allergenic proteins, which accounts for 30% of total globulin in soybean seed (Pi et al. 2021). β -Conglycinin is composed of three subunits, namely, α' (76 kDa), α (67 kDa), and β (52 kDa) (Li, Bu, et al. 2021). These three subunits

have high homology, but only α -subunit of β -conglycinin could cause allergy reactions. β -conglycinin α -subunit mRNA with a total length of 1955 nt, with poly (A) tail, encoding 605 amino acids, including a 22 amino acid signal peptide at the N-terminus, the precursor peptide after removing the signal peptide is 583 amino acids. Finally, 40 amino acids were cut from the N-terminus during processing to form a mature α -subunit of 543 amino acids. Further, studies have reported that there are about 15 linear IgE-binding epitopes in the Gly m 5 such as GEKEEDEDEQPR, EQDERQFPFPR, NDDRDSYRLQSGD, and KEEGNKGRKGP (Sun et al. 2013; He and Xi 2020).

3.2. Cysteine protease (P34, Gly m Bd 30K)

As shown in Table 3, P34 (Gly m Bd 30K) is a kind of soybean storage protein that belongs to the cysteine protease.

Table 4. Summary of recent studies regarding the effect of thermal and non-thermal processing technologies on the allergenicity of soybean.

Method	Treatment	Result	References
Moist heating	Boiled soybeans for 60 min at 100 °C	Lower IgE-binding proteins	Cabanillas et al. (2018)
Dry heating	β -conglycinin of soybean, heated at 65–125 °C	IgG binding capacity of β -conglycinin decreased by 50.30% at 125 °C compared with control	Li, Bu, et al. (2021)
Ohmic heating (OH)	Soybean protein isolate treated at 50 Hz–20 kHz, 20 V/cm at 95 °C	Immunoreactivity of soybean protein was reduced by 36% with OH at 50 Hz	Pereira et al. (2021)
Microwave heating	Microwave heated at the power of 600 W for 10 min	The allergenicity of soybean protein isolate decreased 24.7%	Li et al. (2016)
High-pressure treatment	400 Mpa, 10 min 500 Mpa, 10 min	Glycinin was denatured entirely Secondary structure α -helix and β -sheet of glycinin were destroyed and transformed into random coils	Tang and Ma (2009)
	200–400 MPa	7S globulin and 11S globulin were denatured and inactivated Gly m 1 allergenicity was reduced	Peñas, Préstamo, Polo, and Gomez (2006)
	300 MPa, 15 min	Soybean protein allergenicity decreased by 48.6%	Li et al. (2012)
Cold plasma	Microwave-driven plasma torch (2.45 GHz, 12 kW, air, 18 s/m, 10 min), Xenon PUV system 13.2 cm from the light source 235.2 J/cm ²	Immunoreactivity of soybean protein samples decreased by 89–100%	Meinlschmidt et al. (2016)
Pulsed Ultraviolet		11S Glycinin (14~34 kDa) and β -conglycinin (7S, 50 kDa) were significantly reduced	Yang et al. (2010)
Ultrasonic treatment	300 W treated soybean seeds, then germinated for 5 days 37 kHz, 10 min	Allergenicity was reduced by about 51.39% Allergenicity was reduced by about 24%	Yang et al. (2015) Choudhary et al. (2013)

Studies have reported that P34 is the most active allergenic protein in soybeans, which could be frequently recognized by IgE antibodies in the serum of patients with atopic dermatitis (Matsuo et al. 2020). The mature P34 vacuolar protein is composed of 257 amino acid residues, which is obtained by removing a portion of the 122 amino acid residues at the N-terminus from the precursor protein with a molecular weight of about 47,000 Da during maturation in the vacuole (Jeong et al. 2013). It also has 30% homology with Der p 1 (a dust mite allergen) (L'Hocine and Boye 2007). The gene structure belongs to the papain superfamily, but it is likely not to have protease activity because its active center is missing a cysteine. Studies have reported that mature P34 protein has five major linear IgE-binding epitopes (3FLVLLLFSL12, 110PQEFSSKKTQ119, 229RCKANKIQDK238, 299INHFVLLVGY308, 311GYIWIQRNTG340) (Helm et al. 2000; Pi et al. 2021). Different IgE epitopes have significant differences in serum binding capacity for different allergic patients.

3.3. 7s storage globulin (Gly m Bd 28 K)

Gly m Bd 28 K was initially isolated from soybean as a glycoprotein and was later found to be an unknown Asn glycoprotein with a mass of 26 kDa (Astuti, Palupi, and Zakaria 2018). It was identified that the Asn-N linked glycan moiety having the same sugar composition as Gly m Bd 30 K was located on the Asn20 residue of Gly m Bd 28 K. The N-terminal amino acid sequence analysis gave a result of FHDDEGGDKKSPKSLFMSDSTRVFK (Ogawa, Samoto, and Takahashi 2000). Gly m Bd 28 K is another important allergen in the 7S component and is recognized by the serum of approximately 25% of patients with soybean allergy (Pi et al. 2021). Gly m Bd 28 K cDNA is 1567 bp in length with a polyadenylated tail. It has an open reading frame of 1419 bp and a 3' untranslated region of 148 bp. One of the open reading frames encodes a protein precursor consisting of 473 amino acids (Tsuji et al. 2001).

3.4. Glycinin acidic peptides and other soybean allergenic proteins

The overall sensitizing capacity of glycinin is lower than that of the 7S component. The allergenicity is derived from the constituent subunits. Studies have shown that the acid peptides A1a, A1b, A2, A3, and A4 of 11S globulin are all allergenic proteins (Hsieh, Yu, and Tsai 2012). Also, soybean trypsin inhibitors, Gly m 1, Gly m 2, Gly m 3, and Gly m 4 (SAM22) are several soybean allergens that have been studied a lot (Vagadia, Vanga, and Raghavan 2017; Pi et al. 2021). The overall content of these allergic proteins is relatively low, accounting for only 15–20% of the total protein of soybean, and the thermal stability and antigenicity are relatively weak. Hence it can easily remove the allergenicity of these proteins (Lui, White, and Litster 2007).

4. Effect of processing techniques on the reduction of soybean allergens

Although avoiding to consume foods containing soybean allergens is the best way to prevent triggering allergic reactions suggested by the doctor, soybean as fillers, emulsifiers, and protein fillers are now widely used in the food industry (Asensio et al. 2008). Meanwhile, many food products have not been clearly labeled as containing soybean ingredients, which is a challenge to avoid the ingestion of soybean allergens completely. Therefore, it is very necessary to reduce the content of active allergens in soybeans or relevant products using different food processing techniques. In this study, we reviewed and compared three different techniques that may be used to reduce the allergenicity of soybean or related products (Table 4).

4.1. Thermal processing

Heat processing methods can be divided into three types: moist heating, dry heating, and dielectric heating (radio

frequency and microwave). Thermal processing is one of the most common food processing methods which are used to inhibit the activity of bacteria and enzymes through different temperatures and times (Verma et al. 2012). For allergic proteins present in food, heat treatment can cause damage in the spatial conformation of the protein, which in turn could result in a reduction in the allergenicity of the food. Lakemond et al. (2000) found that processing under high temperatures induced significant changes in the spatial conformation and three-dimensional structure of glycinin, which led to a decrease in the allergenicity or removed allergenicity of glycinin.

Similar studies have been reported by the previous researchers. Cabanillas et al. (2018) boiled soybean samples for 15 min, 30 min, and 60 min at 100°C (Table 4). The results showed that soybeans boiled for 15 min and 30 min rarely affected the IgE-binding capacity of soybean proteins. In comparison, the IgE-binding capacity of soybean proteins was significantly inhibited when boiled for 60 min (Cabanillas et al. 2018). In another study, one of major soybean allergens, β -conglycinin was treated with dry heat at 65–125°C (Li, Bu, et al. 2021). The results found that the IgG binding capacity of β -conglycinin decreased by 50.30% at 125°C compared with control. Whereas the IgE binding capacity of β -conglycinin increased 75.63% at 95°C when compared with the negative β -conglycinin. These differences in binding capacity of proteins with IgG and IgE may contribute to the differences in their epitope binding sites (Li, Bu, et al. 2021). Pereira et al. (2021) treated soybean protein isolate using ohmic heating (OH) with a frequency of 50 Hz–20 kHz, 20 V/cm at 95°C. The results reported that the immunoreactivity of soybean protein was reduced by 36% when treated with OH at 50 Hz. For the microwave processing, a study found that the allergenicity of soybean protein isolate decreased 24.7% when treated at the power of 600 W for 10 min (Li et al. 2016).

Although many studies have reported that thermal processing could destroy the spatial structure of proteins, resulting in a reduction in the allergenicity of soybeans. Davis, Smales, and James (2001) found that the Maillard reaction in the glycosylation product generated during the thermal processing might cause the formation of some new antigens or allergen epitopes. Similarly, Pi et al. (2021) confirmed this conclusion, and they found that high-pressure heat treatment significantly enhanced the IgE binding ability of Gly m Bd 30 K protein (a major soybean allergen). Besides, Boxtel et al. (2008) found that heat treatment did not affect the binding capacity of glycinin to IgE. The differences of effects on the allergenicity of soybean allergens resulted from various thermal processing techniques may be strongly associated with the soybean proteins from different families (Costa et al. 2021). Therefore, it is difficult to effectively reduce the allergenicity of soybean protein by heat treatment alone due to the complexity of the allergen epitope structure of soybean, and some novel food processing techniques are needed in the future.

4.2. Non-thermal processing

In contrast to heat-based processing methods, non-thermal treatments are beneficial to maintain the sensory attributes

and nutritional properties of food while changing the allergenicity. In recent years, many studies have been performed to develop non-thermal processing techniques, which could be potentially used as an alternative method to reduce the allergenicity of soybean. These food processing techniques include high-pressure treatment, cold plasma treatment, pulsed ultraviolet, and ultrasound processing.

4.2.1. High-pressure treatment

High-pressure treatment can provide pressure over 100 MPa with certain ranges of temperatures, which could be used to inhibit the activity of microorganisms and modify the enzymes, proteins, starch, and other biological macromolecules in food (Huang et al. 2014). Studies found that high-pressure treatment can effectively maintain the natural taste, flavor, and nutritional value of the food and also may produce some new textural characteristics (Huang et al. 2014). Recently, studies have reported that high-pressure processing could break down the non-covalent bonds in the protein molecule and cause significant changes in its structures (e.g., secondary structure).

As shown in Table 4, Tang and Ma (2009) treated glycinin with high-pressure treatment at 300–500 MPa for 10 min. The results found that glycinin was dissociated into subunits, and the conformation of these subunits also changed after processing at 300 MPa for 10 min (Tang and Ma 2009). At the same time, the number of sulfur-containing groups, hydrophobic regions, and amino acids showed a significant increase. After treatment at 400 MPa for 10 min, glycinin was denatured entirely. The secondary structure, including α -helix and β -sheet of glycinin, were destroyed and transformed into random coils when further increase of the pressure up to 500 MPa. Peñas et al. (2006) found that 7S globulin (β -conglycinin) and 11S globulin in soybean were denatured and inactivated under high-pressure treatment at 300–400 MPa. Further, they also found that high-pressure processing at 200–300 MPa could cause a significant reduction in the allergenicity of Gly m 1 in soybean. Similarly, Li et al. (2012) processed soybean protein isolates with high pressure at 200–300 MPa for 5–15 min, and the results found that the content of hydrophobic bonds and free sulfhydryl groups of soybean protein isolates increased significantly compared with the untreated samples during treatments. The immunoreactivity of soybean protein decreased by 48.6% when treated at 300 MPa for 15 min compared with the control group. This reduction in the allergenicity of soybean proteins was strongly associated with the protein structural changes during processing. Also, in this study, they found the interaction between the hydrophobic bond and the thiol group, which gradually decreased, and the average length of the soybean protein isolate spiral increased significantly (Li et al. 2012). The possible reason is that the soy protein allergen epitope is closely related to the α -helix and β -sheet secondary structures, and these interactions and secondary structure changes provide direct evidence for the reduction of soybean allergenicity. In summary, high-pressure treatment shows potential applications in reducing the allergenicity of soybeans through the secondary structure effect

(e.g., α -helix and β -sheet) of proteins under different pressures and further studies still needed.

4.2.2. Cold plasma

In the past decade, cold plasma technology obtains high attention from researchers due to its advantages in microbial decontamination of food products. Also, cold plasma could provide a low temperature, short processing time, high power efficiency, strong antimicrobial effect, and minimal impact on food quality (Bourke et al. 2018). Ultraviolet photons, ions, electrons, free radicals, molecules, motivated atoms, etc., are generally referred to as ionized gases in the fourth state of matter and are composed of a range of reactive substances (Dasan et al. 2017). Many studies found that cold plasma could induce the reactions between proteins resulting in their conformational structure changed and lead to a reduction in the food allergenicity (Ekezie, Cheng, and Sun 2018).

Meinlschmidt et al. (2016) used cold plasma technology to treat soybean allergen, β -conglycinin, and glycinin. The results found that after cold plasma treatment, the corresponding protein band strength decreased, and then a new protein band of 50 kDa was formed. In addition, it was found that the disappearance of protein bands in SDS-PAGE was caused by insoluble aggregates formed after treatment. Finally, in the analysis of ELISA, it was found that the immunoreactivity of soybean protein samples decreased by 89–100%. These studies illustrate that cold plasma treatment shows a potential application in reducing the allergenicity of food. The related mechanisms are still not clear, and thus further studies are needed in the future.

4.2.3. Pulsed ultraviolet (PUV)

Pulsed ultraviolet is a type of pulsed excitation technology equipped with a unique inert gas tube that is used to excite and process ultraviolet rays in a pulse form. In recent years, pulsed ultraviolet light has been applied to ionize molecules due to the formation of high energy within a short time (Meinlschmidt et al. 2016). Molecular vibrations and rotations are driven by visible and infrared light. PUV light has photothermal, photophysical, and photochemical properties, which may cause protein aggregation, loss of conformational epitopes, and thus change the allergen structure and reduce IgE-binding ability. Yang et al. (2010) treated the soybean protein extract with PUV light and found that glycinin (11S, 14–34 kDa) and β -conglycinin (7S, 50 kDa) were significantly reduced as analyzed by SDS-PAGE. Also, the results observed that protein molecules with a molecular weight of 150 to 250 kDa were crosslinked or polymerized during the processing, which may contribute to the reduction in the allergenicity of food proteins (Yang et al. 2010). However, long-time PUV light treatment could lead to increase in temperature, moisture loss, and weight loss due to the formation of photothermal effect during processing (Chung, Yang, and Krishnamurthy 2008; Krishnamurthy et al. 2008). Therefore, pulsed ultraviolet processing showed a potential application in modifying the allergic soybean proteins, while

some functional characteristics such as digestibility and nutrients content may be affected negatively during processing. Further studies are needed in the future.

4.2.4. Ultrasound processing

The frequency of mechanical waves used in ultrasonic processing varies from 20 kHz to 100 kHz (Feng, Barbosa-Cánovas, and Weiss 2011). The sound wave will spread through the medium, resulting in a series of compression and rarefaction. The interference between bubbles and the critical size of bubbles leads to fracture, which results in an increase in the temperature and pressure in the medium. When bubbles explode, the temperature and pressure in the local area may be as high as 5000 K and 1000 atm, which provides enough energy to modify the related molecules (Shriver and Yang 2011). For protein molecules, hydrogen interactions between polar and nonpolar groups can contribute to a variety of changes in the natural structure, such as conformational changes, secondary structure damage, other intra/inter molecular interactions, and the recombination of disulfide bonds (Stanic-Vucinic et al. 2012). At the same time, the high shear stress and velocity gradient will lead to the generation of micro streams, and the intense agitation of micro streams may destroy the van der Waals interaction and hydrogen bond in peptides, leading to protein denaturation. Therefore, ultrasound treatment showed potential effects on the characteristics of soybean allergens (Tian et al. 2004; Soria and Villamiel 2010).

Yang et al. (2015) treated soybean seeds with ultrasound at different power levels (0–300 W) and then germinated them for 5 days. The results found that ultrasound processing disrupted or eliminated the epitopes in the proteins, which led to a significant reduction in the allergenicity of soybeans. Specifically, the allergenicity of soybeans treated with ultrasound at 300 W was reduced by 51% when compared with the untreated samples (Yang et al. 2015). In addition, Choudhary et al. (2013) treated soybeans with a high-intensity ultrasonic processor at a frequency of 37 kHz for 10 minutes. The results reported that high-intensity ultrasound processing at 37 kHz caused significant changes in the secondary structure of soybean proteins, which resulted in a 24% reduction in the sensitization of soybean proteins (Choudhary et al. 2013).

At present, even if there is very limited literature regarding the effects of ultrasound on soybean allergens, ultrasound processing, a non-thermal processing method, might have a potential application in modifying the allergic proteins present in soybeans, and further studies are needed in the future.

4.3. Chemical method

4.3.1. Glycosylation

Glycosylation is a chemical reaction in which a carbohydrate is covalently bonded to an α or β -amino group on a protein molecule to form a glycosylated protein. Recently, studies have reported that glycosylation, as a chemical method,

Table 5. Summary of recent studies regarding the effect of chemical and biological processing methods on the allergenicity of soybean.

Type	Method	Treatment	Result	References
Chemical methods	Glycosylation	Used fructose or oligofructose (FOS) in powder and liquid systems to saccharify soy protein isolate (SPI)	Allergenicity was reduced by 90%	van de Lagemaat et al. (2007)
		Protein-galactomannan complex by Maillard reaction	Removed 34 kDa protein, Masked the recognition structure of Gly m Bd 30 K	Wilson, Blaschek, and De Mejia (2005)
Biological methods	Fermentation	Glycosylation with lactose	Antigenicity of 11S reduced 30%	Bu, Zhang, and Chen (2015)
		Fermented by <i>Aspergillus oryzae</i> GB-107 for 48 hours	Eliminated trypsin inhibitors	Hong, Lee, and Kim (2004)
	Enzymatic hydrolysis	Fermented by moromi	No longer allergenic	Kobayashi (2005)
		Autoclave (120 ° C, 0.2 kgf / cm ² for 20 minutes) inoculate 0.8 mg of dry <i>Bacillus natto</i> powder per 1 g of soybeans.	Gly mBd 30K in soybean was significantly reduced	Yamanishi, Huang, Tsuji, Bando, and Ogawa (1996)
	Breeding	Alkaline protease of Proleather FG-F (25% hydrolysis)	Hydrolyzed Gly m Bd 28K,30K,60K	Tsumura et al. (1999)
		Hydrolyzed soybean 11S globulin with pepsin and chymotrypsin	Sensitization of the 11S enzymatic fragment was reduced	Wigotzki et al. (2000)
		Gamma-rays mutation breeding	Lacking the Gly m Bd 60K	Takahashi et al. (1994)
		Natural hybridization and γ -ray irradiation	Low-sensitivity soybean varieties was induced	Sathe, Kshirsagar, and Roux (2006)
		Marker-assisted method	Selected low-P34 lines P34 reduced by 50–70%	Watanabe et al. (2017)
	Genetic modified	Gene-silencing techniques	Eliminated P34	Herman (2003)

could be used to reduce the allergenicity of soybeans. van de Lagemaat et al. (2007) used fructose or oligofructose (FOS) powder and liquid systems to saccharify soybean protein isolate (SPI) by Maillard reaction. The results of SDS-PAGE showed that the protein band of 7S and 11S fragments present in soybeans was affected during the reaction of glycosylation. Further, an ELISA test was used to confirm these changes and the results found that the antigenicity on glycated soybean protein isolate was reduced by 90% compared with non-glycated samples (van de Lagemaat et al. 2007). Similarly, Babiker et al. (1998) obtained a soybean protein-galactomannan complex by Maillard reaction. The results also found that one of the major soybean allergens, a 34-kDa protein that is easily recognized by IgE antibodies in the serum of patients with a soybean allergy history, was removed during the reaction (Babiker et al. 1998). Wilson, Blaschek, and De Mejia (2005) also reported that galactomannan prepared with guar gum masked the recognition structure of Gly m Bd 30 K antibody, thereby successfully eliminating the sensitization of Gly m Bd 30 K. And the latest research reported glycosylation with lactose could also reduce the antigenicity and IgE-binding capacity of glycinin, the antigenicity of 11S after glycosylation was reduced by approximately 30% compared with raw 11S (Bu, Zhang, and Chen 2015). These reductions in the allergenicity of soybeans during the glycosylation reactions could be attributed to the blocking of Ig-E binding epitopes of proteins by the added compounds. The second pass is the chemical solution, such as glutaraldehyde solution, copper sulfate, sodium sulfite, ethanol, which can be used to change the molecular structure of trypsin inhibitors, destroy disulfide bonds, and achieve the purpose of passivating antigens. However, Ogawa et al. (1995) performed a western blotting experiment on the hydrolyzed β -conglycinin peptide and found that the peptide that binds to IgE is not a glycopeptide. They believe that glycosylation is not a necessary

condition for binding to IgE (Ogawa et al. 1995). Another study reported that IgE can also react with deglycosylated peptides or proteins detecting by dot blot (Calabozo, Barber, and Polo 2002). Therefore, the role of sugar chains in reducing the IgE-binding capacity of allergens is different in various food allergens.

At present, there are different conclusions and opinions on glycosylation in soybean sensitization. The reasons for the disagreement are mainly due to two aspects. One is that there are many diagnostic methods for determining allergic reactions. The other one is the type of sera (animals or humans) used in the experiments are numerous. Therefore, the role of glycosyl groups and their structures in sensitization needs further studies.

4.4. Biological method: Fermentation and enzymatic hydrolysis

Fermentation is one of the traditional foods preserving methods that could be used to extend the shelf life of food products. During processing, the big food molecules like proteins could be decomposed into smaller molecule peptides and amino acids, which increased the protein content and digestibility and altered the structure of their epitopes, thereby reducing the allergenicity of food products and improving the nutritional quality of soybeans (Shekib 1994). As shown in Table 5, Hong, Lee, and Kim (2004) posted soybeans in a bed-packed solid fermenter with *Aspergillus oryzae* GB-107 for 48 hours, and then its trypsin inhibitor and nutrient content of soybeans were measured. The results showed that fermentation increased the protein content in soybeans, eliminated trypsin inhibitors, and reduced the size of peptides (Hong, Lee, and Kim 2004). In Japanese soybean sauce, after soybeans are fermented by moromi, the protein was completely degraded into peptides and amino acids by

microbial proteolytic enzymes (such as koji), and their allergenicity was in an undetectable range. At the same time, it was found that polysaccharides derived from soybean cell walls still exist in soybean sauce after fermentation treatment. These polysaccharides have effective anti-allergic activity *in vitro* and *in vivo* and are effective interventions for patients with allergic rhinitis (Kobayashi 2005). Yamanishi et al. (1996) soaked soybeans in water overnight, then autoclaved at 120° C, 0.2 kgf/cm² for 20 minutes, and inoculated 0.8 mg of dry *Bacillus natto* powder per 1 g of soybeans. The fermentation process was performed at 40° C with sufficient moisture. The results demonstrated that the sensitization of Gly mBd 30 K in soybean was significantly reduced during the fermentation of *Bacillus natto* (Yamanishi et al. 1996). During the fermentation process, the microorganisms and the internal environment of the fermentation are not very stable, the fermentation cycle is long, and unknown anti-nutritional components may appear in the fermentation process; therefore, the use of microbial fermentation cannot completely remove the antigen in soybean.

Enzymatic hydrolysis is another similar method that can be used to reduce the allergenicity of soybeans by destroying the spatial structure of proteins or breaking down the chemical bonds of soybean proteins. Tsumura et al. (1999) found an alkaline protease of *Proleather* FG-F, it can effectively hydrolyze Gly m Bd 30 K, Gly m Bd 28 K sensitized protein, and 7S globulin α subunit when the hydrolysis degree reaches 25% (Tsumura et al. 1999). In addition, Lee et al. (2007) hydrolyzed soybean 11S globulin with pepsin and chymotrypsin, and the results showed that the sensitization of the 11S enzymatic fragment was reduced up to 100% (Lee et al. 2007). However, some studies found that partial hydrolysis does not reduce or remove food allergies in a certain way because cross-contamination may occur during processing, and new allergens appear (Wigotzki et al. 2000). Cabanillas et al. (2010) hydrolyzed lentils with protein and found that proteolysis destroyed an important Ig E binding epitope in *in-vitro* experiments, but protein allergens were still detected in the patient's serum indicating that enzymatic hydrolysis can destroy some protein allergen but not completely removed. In general, in the enzymatic hydrolysis process, due to the different types of enzymes and the enzymatic hydrolysis process, the enzymatic hydrolysis conditions are not easy to control, and there are also differences in the components and antigenicity in the final product obtained.

4.5. Breeding and genetically modified methods

Breeding is a traditional method for removing allergenic protein from soybeans. In 1994, scientists cultivated soybean lacking the β -subunit of β -conglycinin through mutation breeding (Ohtake et al. 1994). In 2005, researchers at Kyoto University in Japan used natural hybridization and γ -ray irradiation to induce low-sensitivity soybean varieties by inducing plant mutations and the preferred method, and clinical experiments showed that the taste of this low-sensitivity soybean did not change (Sathe, Kshirsagar,

and Roux 2006). In 2007, scientists cultured a new variety of soybean which excluded allergenic proteins such as P34, Gly m 2, Gly m 1.0101, Gly m 1.0102, and r Gly m 3 through breeding pathways (L'Hocine and Boye 2007). In 2013, scientists developed molecular markers and polyclonal antibodies to select soybean lines that express P34 at low levels efficiently. The selected soybean lines can continue to be crossed with other non-allergenic soybean varieties to breed low-allergenic soybean varieties (Jeong et al. 2013). In 2017, researchers used a marker-assisted method, selected low-P34 lines from a cross-population. Concentrations of the P34 protein, as identified with a polyclonal antibody, were reduced by 50–70% (Watanabe et al. 2017). Although plant breeding pathways are used to cultivate low-sensitized soybean varieties, the antigenic protein can be fundamentally removed. However, most antigen proteins are used for defense. Decreasing the content of antigen proteins may cause adverse effects on soybeans, such as yield and disease resistance (Clarke and Wiseman 2000a, 2000b). Finally, whether the breeding method will bring some negative effects on nutrition and function or whether it will express new antigenic components also needs further investigation.

Genetically modification could eliminate the allergenicity of soybean allergens by eliminating endogenous genes. In a study, scientists successfully removed major allergens Gly m Bd 30 K in soybeans by applying the genetic modification method (Herman 2003). However, the removal of allergens by genetic engineering is controversial, which may bring new potential allergens, and there are no clear standards to evaluate the safety of genetically modified foods. A widely publicized report on allergenicity has fueled speculation on the safety of genetically modified foods that genetically modified foods may be responsible for the rise in global allergies (Maghari and Ardekani 2011). In 1966, methionine-rich albumin from Brazilian triangular walnut was introduced into soybeans to make up for the lack of this essential amino acid in soybeans. But Nordlee research found that allergen proteins were also introduced into the blood of human volunteers and recognized by the serum, triggering an allergic reaction (Nordlee et al. 1996). Thus, further studies regarding the genetically modified technology used to reduce the allergenicity of soybean are still needed.

5. Management and treatment of food allergy

5.1. Dietary management

Currently, there are no effective medical methods that could be used to cure soybean allergy. One of the most effective treatments for people with a soybean allergy history is to avoid ingestion of corresponding foods or related products. Further, learn about how to deal with allergic reactions that may occur after the accidental ingestion of soybean or related products is also very necessary. Soybean is a versatile ingredient in food processing due to its rich protein content and inexpensive properties. Thus, avoiding the ingestion of soybean is difficult. Meanwhile, there are multiple allergenic

proteins in soybean. The list of potential cross-reactive foods is significant. For those patients with soybean allergies, it is difficult for them to know their dietary restrictions and a complete list of allergens related to the cross-reactivity of soybean allergies. Even in developed countries, food ingredients in the food are unclear, and/or incorrect labeling is very common. Consumers who are allergic to soybean should carefully read the detailed ingredient information of each product before purchasing them.

5.2. Emergency treatment

Food allergy could trigger a rapid multi-organ allergic reaction and even result in some serious or fatal health conditions (Bird, Lack, and Perry 2015). Thus, timely identification of signs and symptoms of an allergic reaction is essential for proper management. The U.S. Food and Drug Administration (FDA) in 1987, approved epinephrine as available as a self-injectable medicine that is highly active and secure for the management of anaphylaxis. For patients with a severe allergy, intramuscular epinephrine is the first-line treatment in all instances of anaphylaxis in both inpatient and outpatient situations. But many studies have shown that patients do not get enough adrenaline when they have a severe allergic reaction (Wang et al., 2017). Part of the reason may be related to the fear of needles or adverse drug reactions. On the other hand, it may be that the patient lacks relevant knowledge, does not realize the importance of self-administration, and does not know how to use the adrenaline device (Shemesh et al. 2017). In a 384-case study on severe allergic reactions, the results found that those who used adrenaline before the hospital needed fewer hospitalizations than those who used it after arriving at the hospital (Fleming et al. 2015). Thus, the emergency treatment is very helpful for the individuals with the history of certain food allergy.

6. Future immunotherapy

Currently, no immunotherapy can cure food allergies. The primary purpose of allergen immunotherapy is desensitization, a temporary increase in the response threshold that provides a degree of safety, the latter depending on continuous therapeutic exposure. Ideal treatment should allow patients to eat whatever they want without being affected by stimulants such as disease or exercise, that is, to achieve true, complete tolerance. At present, the hottest areas of immunotherapy are research on oral immunotherapy (OIT), epicutaneous immunotherapy (EPIT), BASALIT trial, and sublingual immunotherapy (SLIT) routes.

The formation mechanism of oral tolerance is very complicated, and it is not clear so far. It is generally considered to be related to the regulation of immune response, which may be related to the loss or disability of immune cells and the activation of immune regulatory cells (Burks et al. 2018). But most clinical trials currently focus on the three most common allergens: peanuts, eggs, and milk, and get some positive results (Burks et al. 2018). Although oral

immunotherapy research on other food allergens is ongoing, this method is time consuming and at risk of allergies. SLIT is another therapy for allergic reactions, which requires allergen extracts to be given sublingually every day during the treatment (sublingual 2–3 minutes after swallowing). SLIT therapy can desensitize to a certain extent, is well tolerated, and has mild adverse reactions, usually only oropharyngeal itching and tingling. However, it rarely achieves sustained unresponsiveness (Burks et al. 2018). EPIT therapy is a new therapy that is still in the research stage and needs further research. EPIT therapy involves applying a small patch of allergen patch to the back or upper arm and changing the patch every 24 hours for several years. The efficacy of this therapy is weaker than OIT and SLIT, but it is the safest and well-tolerated. Most patients will only have mild local skin irritation symptoms at the patch site (Burks et al. 2018). To sum up, these therapies pose a risk of allergies to patients. Therefore, there is still much work to do, and more novel effective immunotherapy treatments need to be developed in the future.

Conclusion

Soybean is one of the eight major allergens, which could cause some cross-reactivity, with other related allergens, such as birch pollen, leading to an increasing trend all over the world. Soybean can cause a series of allergic symptoms, even could lead to death. With the increasing demand for soybean products, the problem of allergenicity of soybean protein needs to be solved urgently. In this review, we reported major soybean allergens in soybean such as Gly m Bd 28 K, P34 (Gly m Bd 30 K), and β -conglycinin α -subunit (Gly m Bd 60 K). In the food industry, some physical or chemical treatments are often used to reduce the allergenicity of soybean by changing the protein structure or IgE binding site of allergens. However, different processing methods have shown various effects on the modification of proteins and their functional characteristics, and currently, the effective processing methods are still very limited. Thus, more novel food processing techniques are still needed. Further, the processed soybean products should be evaluated using medical methods like skin prick test and blood test to detect their allergenicity. Finally, education on proper management of soybean allergy patients and the development of desensitization strategies can improve the physical condition and quality of life of patients with food allergy history.

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