



Comprehensive Review on Banana Fruit Allergy: Pathogenesis, Diagnosis, Management, and Potential Modification of Allergens through Food Processing

Priyanga Suriyamoorthy¹ · Alluru Madhuri² · Srikanth Tangirala^{1,3} · Karunai Raj Michael¹ · Vignesh Sivanandham² · Ashish Rawson^{1,3} · Arunkumar Anandharaj¹

Accepted: 19 May 2022 / Published online: 3 June 2022

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

Abstract

The pulp of the banana fruit is rich in bioactive compounds like dietary fibers, low glycemic carbohydrates, natural sugars, vitamins, minerals and antioxidants. These beneficial compounds are responsible for the proper functioning of immune system and enhance prevention against various deadly diseases like cancer, diabetes and heart diseases. Despite having, positive effects, the fruit are recognized as an important source for causing allergy to 0.6% of people in general population and up to 67 and 46% for people with asthma or atopic dermatitis. Fruit allergy is one of the most common food allergies witnessed worldwide. Banana fruit allergy results from the abnormal immune response to the banana proteins soon after its consumption. Symptoms range from oral allergy syndrome (OAS) to the life-threatening anaphylaxis. IgE reactivity of banana is associated with different proteins of which six proteins have been identified as major allergens, viz., Mus a1 (Profilin-actin binding protein), Mus a 2 (Class 1 chitinase), Mus a 3 (Nonspecific lipid transfer protein), Mus a 4 (Thaumatococcus protein), Mus a 5 (Beta 1,3 glucanase) and Mus a 6 (Ascorbate peroxidase). This review focuses on pathogenesis, clinical features, diagnosis, and different food processing methods to mitigate the allergenicity of banana fruit.

Keywords Banana allergy · Latex allergy · Skin prick test · Oral allergy syndrome (OAS) · Urticaria · Food processing

Introduction

Banana fruit is the most important staple food in the world across different ethnicities and has been an extensively studied fruit for edible purpose. One of the earliest reports to link

allergies originating due to fruit and vegetable consumption and pollen allergy was published in 1942. Since then, several fruits like kiwi, avocado, melon, citrus fruits and tomatoes including banana etc., have been reported as a source of allergy due to their own properties as well as their cross-reactivity pattern [1]. Although, worldwide the prevalence of allergy to the consumption of banana among the general population is uncommon, there are few individuals showing hypersensitive reaction who are estimated to be at 0.04 to 1.2%. However, an increasing trend is being noticed on the number of cases that exhibit hypersensitive reactions to banana in infants as well as in adults are being reported till date [2]. Banana allergy can be associated in two forms: first allergic to tree pollen, like birch and second allergic to banana latex. Individuals allergic to birch pollen are often susceptible to banana and develop symptoms after taking either fresh banana or banana containing food immediately or an hour later. Symptoms are local reactions like itching and inflammations in mouth and throat and termed as OAS [2]. Alternatively, the allergy develops in reaction with the banana allergen and natural rubber latex (e.g., gloves,

✉ Ashish Rawson
ashishrawson@gmail.com; ashish.rawson@iifpt.edu.in

✉ Arunkumar Anandharaj
arunkumar@iifpt.edu.in

¹ Department of Food Safety and Quality Testing,
National Institute of Food Technology, Entrepreneurship
and Management (NIFTEM), Thanjavur,
Tamil Nadu 613005, India

² Academics and Human Resources Department, National
Institute of Food Technology, Entrepreneurship
and Management (NIFTEM), Thanjavur,
Tamil Nadu 613005, India

³ Centre of Excellence in Non-Thermal Processing,
National Institute of Food Technology, Entrepreneurship
and Management (NIFTEM), Thanjavur,
Tamil Nadu 613005, India

balloons etc.) known as latex fruit syndrome. Symptoms exhibited by susceptible individuals are such as urticaria, abdominal pain, vomiting and sometimes life-threatening reactions called anaphylaxis. The impact of banana as a source of food allergic reaction was investigated, it has been observed that nearly 20–50% of individuals allergic to natural rubber latex (NRL) have reported to show hypersensitivity after eating banana. Despite the evidence for cross-reacting allergens in NRL and banana, most incidents of banana allergy are connected with profilin susceptibility while banana-latex association is less common [3].

The occurrence of food related allergy has increased in current decades and it is now considered as a significant public health issue in developing countries. Allergies of food originate from the cross linking of proteins (allergens) present in the food and human immunoglobulin E (IgE) [4]. Currently, there is no curative measure for food allergic reactions. Predominantly IgE mediated allergies are involved in different health related problems including the skin, gastrointestinal and respiratory tracts, and cardiovascular system and even cause life threatening reactions like anaphylaxis. However, the identification of specific genes (food allergen) involved in the allergic reactions are of main interest among the researchers to understand the pathogenesis, structural characteristics in allergenicity and its adoption in molecular level protocols for diagnosis, treatment and prevention. Food allergy (FA) is the general mechanism of clinical and immunological involvement against ingested foods. This break-down result in IgE mediated diseases (Table 1) as well as non-IgE-mediated reactions, like eosinophilic oesophagitis, allergic proctocolitis and

enterocolitis. Recently, allergies to fruits are increasing at an unknown rate and the rising prevalence of food allergies in both young and elderly populations has a significant impact on the quality of life. Food-related anaphylaxis was the second most common cause of death between 2004 and 2015 [12]. Nearly 40% of latex allergy individuals have latex–fruit syndrome, which is caused by cross-reactivity with food allergens (primarily banana, avocado, chestnut, and kiwifruit), for which Hev b 2, Hev b 6.02, Hev b 7, Hev b 8, and Hev b 12 allergens have been implicated. Profilins are panallergens because of their widespread presence, eliciting IgE responses in 10–20% of pollen allergic patients. Indeed, depending on the geographical location of the analysed populations, the prevalence of banana sensitised patients varies, ranging from approximately 5% in Swedish birch pollen–allergic patients to 20–30% in Austria, France, Portugal, and Italy, and 60% in Spain [13]. According to clinical studies, 11–26 million people in Europe suffer from food allergies, whereas the global figure is between 220 and 520 million people [3]. Banana sensitivity was found in 67 [14] and 40.6% [15] of asthmatic patients, respectively, while banana allergy was found in 5.6% of atopic dermatitis patients worldwide [16]. However, till date there is no detailed review on banana allergy and its clinical responses, the main objective of this work is to address the current issue on its pathogenesis and clinical characteristics and also diagnostic methods based on proteins involved in *in vivo* reactions. Further here we describe for the first time few food processing techniques through which the allergenicity of banana can be mitigated to ensure the safety of consumption.

Table 1 Food hypersensitivity (allergic) disorders by predominant organ affected

Banana allergen	PR proteins	Organ affected	Clinical manifestations	Reference
Mus a 1	PR-10 (Profilin)	Gut	Abdominal cramps, flatulence, blood in the stools, nausea, abdominal distension, colic, pain, vomiting, meteorism, diarrhea, constipation, malabsorption	[5, 6]
Mus a 2	PR-3 (Chitinase types I, II, III, IV, V, VI, and VII)	Skin	Atopic dermatitis, contact dermatitis, eczema, skin rashes, itching or flushing, tingling, swelling of the lips, palate, tongue or throat erythema, urticaria, angioedema	[7–9]
Mus a 5	PR-2 (β -1,3-Glucanases)	Respiratory	Recurrent wheezing, nasal congestion, itchiness or sneezing, asthma, laryngeal edema, cough, rhinoconjunctivitis cold, shortness of breath, dyspnea	[5, 9]
Mus a 4	PR-5(Thaumatococcus-like proteins)	Mouth, neck, ears	Stomatitis, otitis, pharyngitis, oral allergy syndrome	[7, 10]
Mus a 3	PR-14 (Lipid transfer protein)	Nervous system	Irritability, restlessness, fatigue, migraine	[11]

IgE-Mediated Food Reactions

FA present in the food is absorbed through the epithelium of intestinal cells along with other nutrients by accessing the mucosa and finally enters the blood stream; where the effector cells come into action with the allergen. Then the ingested food allergens react with IgE high-affinity Fc receptor (FcεRI; also known as high-affinity immunoglobulin ε receptor (FCER1) on mast cells present in mucosal lining and with basophils present in circulation, leads to the activation of immuno cells (Fig. 1). FcεRI crosslink with the tyrosine kinase result in exocytosis mediated hypersensitivity reactions includes secretions of histamine, tryptase and chymase. This crosslink also activates the *de novo* synthesis of lipid metabolites like leukotrienes, prostaglandins and platelet-activating factor

(PAF). Activation of these mediators involves a range of various physiological responses like vasodilation, increased vascular permeability, activation of nociceptive nerves which induces itch and smooth muscle constriction. When dispersed systemically, the allergen and IgE-sensitized circulating basophils and tissue-resident mast cells can react, resulting in anaphylaxis (a rapid systemic allergic reaction that can cause death).

Pathogenesis Related (PR) Proteins

PR proteins are diverse polypeptides synthesized by the plants in response to various biotic and abiotic stress. Chitinases, categorized under PR-3 family are the most abundant proteins in the pulp of unripe bananas. The main function of these proteins is the defensive

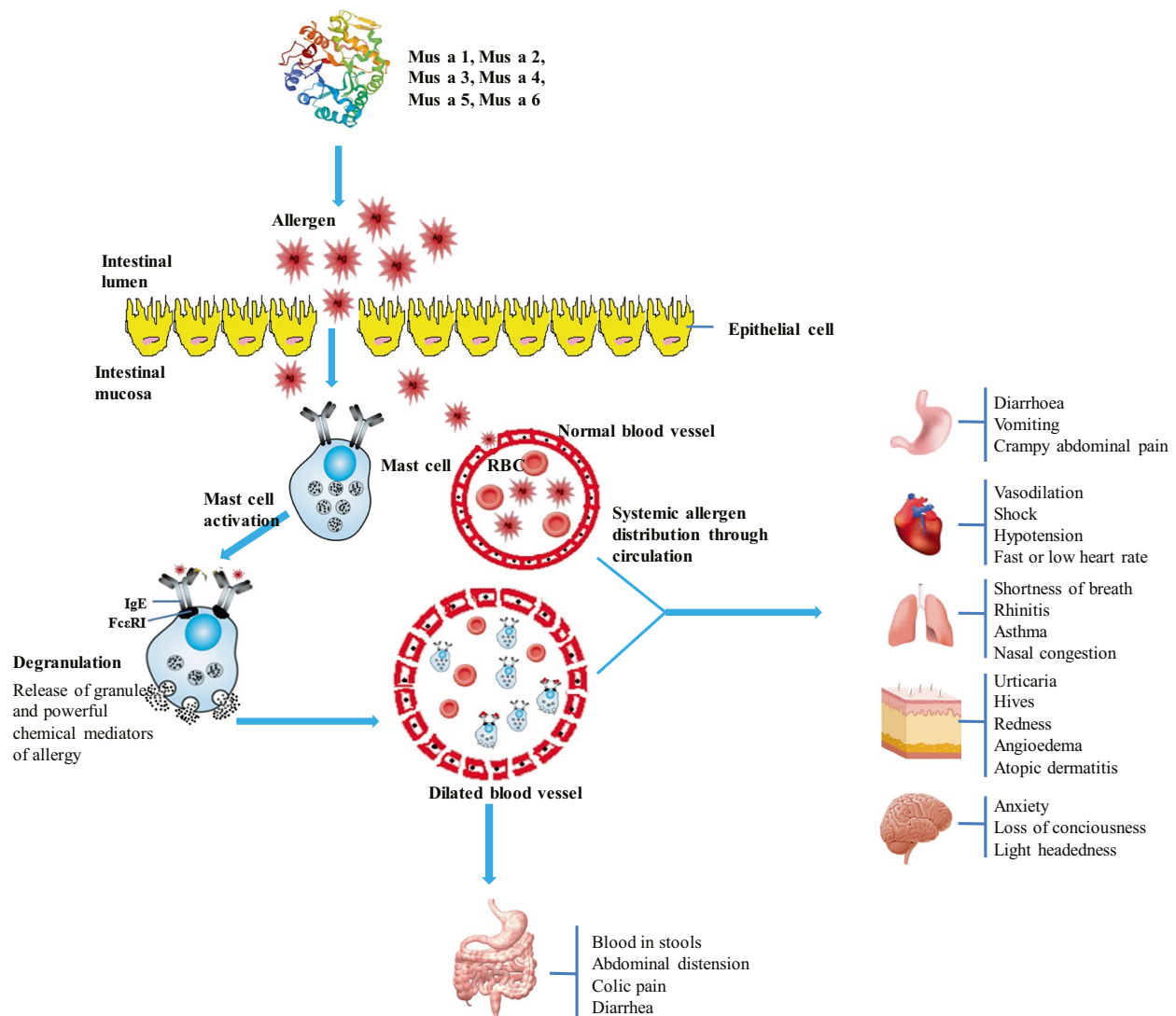


Fig. 1 Ingested food allergens pass through the intestinal epithelium by a variety of mechanisms

mechanism against the pathogens that invade the plant. These proteins hydrolyze a glycosidic bond in chitin – a major component present in the cell wall of the pathogen and diffuse the pathogen invasion process. PR proteins expressed in different plant parts due to its exposure to biotic and abiotic stresses are accumulated in the edible parts such as fruits, seeds and pollen grains (Supplementary Fig. 1). These proteins on ingestion or inhalation leads to interaction with IgE which triggers the immune response through antigen-antibody interaction, leading to specific allergenic responses and development of symptoms like OAS, allergy, asthma, anaphylaxis, conjunctivitis, rhinitis, nausea, and hypertension, etc.

Characterization of Banana Allergens

Banana (Mus a 2) are Class I chitinases with hevein-like domains that have IgE binding capabilities. Mus a2 protein and Pers a1 have a 74.0% similarity in the amino acid sequence and includes the hevein-like domain in both the proteins. The presence of cysteine residues in these proteins ensures the stability. Individuals who have been exposed to latex prohevein or hevein are prospective candidates for cross-reaction with some fruits and vegetables to cause allergy, since these proteins have a conserved hevein-related structure [17]. The expression of Beta 1,3-glucanase (Mus a5), increases significantly during fruit ripening which has five IgE binding epitopes that are comparable to Hev b 2. The crystal structure of allergic TLP from banana (Mus a 4) was characterized by its three unique domains: a core domain made up of two β -sheets sandwiched together, an extended α -helix domain, and a hairpin segment made up of two short strands joined by an extended loop, eight disulphide bridges to stabilise the structure, which are conserved in other thaumatin-like compounds [18].

Pathogenesis and Manifestations of Banana Allergy

Banana allergy is an abnormal immune response experienced by susceptible individuals after ingestion of the fruit. Allergy develops when the proteins present in the banana are recognized by the immune system as allergen and an inappropriate type of immune response is generated. This allergenic response leads to the release of allergen-specific antibodies termed as sensitization [19]. These newly formed IgE antibodies connected with the specific effector immune cells called mast cells. Upon subsequent exposure to banana fruit or related banana products leads to the activation of high affinity IgE receptors on the surface of mast cells against the allergen [20]. The activation of mast cells resulted in the secretion of histamine and other inflammatory

mediators leads to primary symptoms of banana allergy. People who are sensitive to tree pollen may have developed pollen-specific IgE molecule. This IgE molecule also may recognize similar proteins with complimentary structure in banana leads to the activation of IgE bound mast cell. This in turn cause significant reactions to banana fruit directly or through cross sensitization with other allergens of similar nature. The intensity of symptoms is determined in part by the route of sensitization with the highest risk of severe anaphylactic reactions [21].

Cross Reactions

Reindl et al. [22] reported that 44% of banana allergenic individuals developed sensitivity to recombinant banana profilin protein which was confirmed by immunoblot analysis and Enzyme Allergo sorbent Test (EAST). There is a consensus of about 131 amino acids between the birch pollen and profilin protein, thus high cross reactivity of birch pollen protein Bet v2 and latex profiling Hev b8 was demonstrated by immunoblot and EAST inhibition experiments. It was found that Mus a 1 gene in banana is the important mediator for the IgE cross reactions between the pollen and exotic fruits.

Immunoglobulin- E (IgE) associated food allergies appear to develop in early childhood period and the process of immune responses is termed allergic sensitization. Banana allergy was first reported by Lotfi et al. [23] in latex allergic individuals. According to the studies reported so far, nearly 88% of latex fruit syndromes were associated with particular IgE-mediated reactions to various plant-derived foods. The susceptibility to food antigens may be mediated by many ways, such as through the skin, by inhalation, through the gastrointestinal tract, through direct exposure or directly through breast milk. Further it is also stated that exposure to fresh bananas may have increased the severity of symptoms, given that the major allergens of bananas may have heat sensitivities [24] (Supplementary Fig. 2a). Ricci et al. [25] reported a case of anaphylaxis after banana ingestion and the individuals' skin test was negative. Individual with anaphylaxis after banana ingestion shows atopic dermatitis, Urticaria, angioedema, vomiting, respiratory symptoms started 2 h after banana intake, and there was no history of reactions to latex and other foods that could cross-react with bananas. In previously reported cases, specific IgE values of two cases with symptoms after banana intake were found to be 5.21 and 5.24 kU/L.

Dayıoğlu et al. [7] reported that the specific IgE value of tested case was 8.7 and 0.194 kU/L respectively, while the values for normal persons without allergy may show IgE levels between 0.35 to 0.69 kU/L. Pollen-food allergy syndrome (PFAS) is an immunoglobulin E (IgE)-mediated immediate allergic reaction that occurs after ingesting fruits, vegetables,

or nuts that have cross-reactivity with pollens in individuals with pollinosis [26]. PFAS caused by cross-reactivity between pollen in autumn and various foods is called celery-mugwort-spices syndrome and ragweed-melon-banana syndrome [27] (Supplementary Fig. 2b).

Banana Oleosins and Hirudin

Neutral lipids in plant seeds are stored in lipid droplets and are utilized as a source of energy and carbon during seed growth. Lipid droplets have a core surrounded by a monolayer of phospholipids and proteins. The major protein present in the monolayer of these lipid droplets is oleosin. Oleosins have been identified as allergenic molecules in peanut (Ara h 10, Ara h 11, Ara h 14 and Ara h 15), sesame (Ses i 4 and Ses i 5), and hazelnut (Cor a 12, Cor a 13, and Cor a 15). The molecular mass of oleosins ranges between 14 and 17.5 kDa and have a central hydrophobic hairpin adjacent to the N- and C-terminal domains that can penetrate the phospholipid monolayer and contact the hydrophobic core of the oil droplet [28]. The use of transgenic plants to produce biopharmaceutical products, vaccines, antibodies, hormones, enzymes and drugs is gaining importance over the years. A number of plant species containing a naturally occurring polysaccharide matrix have been explored for the introduction of transgenes which provides stability to the humanized proteins upon production [29]. One of the preferred species for these applications are *Musa acuminata* and *Musa balbisiana*. In such cases the recombinant protein expressed in the transgenic plant has the possibility to be trapped in the oil bodies by expressing as oleosin-fusion proteins. It is thought that the oleosin-fusion proteins can be by products and also can cut-back on the production cost of biopharmaceuticals [30]. If this occurs, the allergenicity caused by these fusion proteins in human system is unknown. A classical example of this fusion protein system is the production of oleosin-hirudin fusion protein in *Brassica napus* seeds and purified by flotation centrifugation for commercial production in Canada [31]. However, this approach has not been tried in banana fruit.

Oral Allergy Syndrome (OAS)

OAS also known as pollen-food syndrome and an IgE mediated allergic response that primarily manifest in the oral cavity, including pruritus and edema on the lips, tongue or palate, immediately after food intake. This is caused by allergens found in fruits; vegetables and pollen that react in a sensitized subject. Although symptoms are usually limited to the mouth, some individuals may

also have extra-oral complaints, including pharyngeal edema, changes in skin color, or respiratory symptoms. OAS Allergy with banana has been identified (0.04% to 1.2%) in different studies, yet rarely anaphylaxis has been reported with banana, otherwise oral-cutaneous allergy is mostly observed. Symptoms of systemic reactions such as skin involvement, hypotension, angioedema, respiratory arrest have been reported only in individuals with anaphylaxis. Betv 2-specific IgE antibodies have been shown to recognize profilins in apple, banana, carrot, celery, cherry, hazelnut, pear, pineapple, potato and tomato [32] (Supplementary Fig. 2c).

Common Diagnosis and Detection Methods of Banana Allergy

Clinical diagnostic tools for the detection of banana allergy include double blind placebo-controlled food challenge (DBPCFC), skin prick test (SPT), enzyme linked immunosorbent assay (ELISA), and immunoCAP [21]. DBPCFC is widely considered as a gold standard diagnostic tool. In this method a sample of food given to sensitive individual, both the subject and treating physician are unaware that the food contains allergens or a placebo. After consumption of banana, if the individual develops any clear signs and symptoms of allergic response then the test is considered as positive. This kind of diagnostic challenge may need several days to complete because individuals vary in their immune responses. Allergic reactions can only be triggered after taking sufficient doses of allergen or placebo [33]. Due to the tedious process involved in DBPCFC, SPT is considered as a more accessible diagnostic tool. This test involves placing small amounts protein extract from banana pulp on the subjects' skin (arm) which is scratched or pricked by needle. This leads to the contact of the protein extract with the individual's blood through skin and is exposed to the mast cells. Individuals allergic to banana produce specific IgE on cutaneous mast cells result in the secretion of histamine a localized allergic reaction. The skin is examined after 10 to 15 min for redness (flare) or any inflammation (wheal). A wheal size of 3 mm or bigger than the negative control (0.9% saline), then the test is considered as positive. SPT is quick and easy to perform and simultaneously, multiple allergens can be tested at the same time. On the contrary, SPT method has significant false positive rate ranging upto 50 to 60%, which limits the utility of this diagnostic method [34].

ELISA and immune CAP are the two similar blood test methods mainly based on recognition of specific IgE present in the blood of susceptible individuals. These methods can be used to diagnose sensitized individuals to banana fruit or other banana based commercial food extracts. The allergens which are specific to banana allergy are measured by colorimetric reaction after the binding of specific enzyme labeled

antibodies and later quantified by standard curves. This kind of IgE based method has high sensitivity rate ranging from 6 to 70% and specificity from 98 to 99% and are estimated rapidly as compared to other diagnostic methods [35].

DNA (Deoxyribo nucleic acid) based detecting methods like PCR (Polymerase chain reaction) and RT-PCR (Reverse transcriptase polymerase chain reaction) are used to detect specific allergen in food products. Compared to clinical diagnostic methods these methods are used to test the concentration of allergen in banana [36]. DNA is more stable than the proteins, due to the fact that proteins get modified under different processing conditions. The practical applications of these DNA methods are limited in food industries due to its complexity in protocols and expensive equipments. Therefore, there is the need for the development of novel detecting and diagnostic methods with improved specificity, sensitivity, easy protocols, and relatively low cost.

Grob et al. [8] reported that two latex sensitized individuals were also hypersensitive and allergic to banana. Also, immunoblot of the blood analyses revealed that there was a new protein of 70kDa that caused banana allergy to one of the tested two individuals. The study also found the new banana allergen showed 70% homogeneity with the allergen profilin that may have cross reacted with IgE to elicit an allergic response. Aleksik and co-workers reported the molecular characterization of Mus a 5 with the fresh banana extracts, and evaluated the allergenic properties. IgE reactions of Mus a 5 were confirmed in 74% of individuals with banana sensitivity (Table 2). The upregulation of basophil activation markers like CD63 and CD203c was achieved with Mus a 5 allergen in a concentration-dependent manner and found Mus a 5 as a functional allergen and a novel candidate for the diagnosis of banana allergy. IgE reactivity of three major banana allergens Mus a 2, Mus a 4 and Mus a 5 were confirmed with the molecular techniques and clinically from sera of banana allergic individuals. Nikolic et al. confirmed major 3 allergens with the a three-step purification protocol (a combination of anion exchange, cation exchange and reversed phase chromatography) using banana extract and obtained sufficient yield with high purity [37, 38].

Rapid Method for Allergen Detection

The first allergen-related rapid immunoassay was developed for peanut in the year 1997 and the first commercialized Lateral flow kits were made available in the market by 2004. Lateral flow devices provide a quick and rapid method for allergen detection, nevertheless little is known about their general usage, sensitivity, and specificity [45]. For the detection of allergenic chemicals, devices such as biosensors using nanoparticles have been developed. Due to their simplicity of manufacture, gold nanoparticles are the most commonly utilized nanomaterial. Furthermore, research focuses

on the creation of novel nanoparticles for use in assessing allergenic chemicals in food and the association of nanoparticles to improve detection. Alternative protein sources, allergic food processing, and the use of diverse transducer systems and nanomaterials in combination with innovative absorbents (immobilization methods) to enhance biosensor detection limits are one of the recent trends observed [38].

Effect of Food Processing on Banana Allergens

Processing of food is a common method to improve the palatability of food, to extend the shelf life of food, improve its quality etc. However, processing of food leads to various physiochemical changes in food depending on the processing techniques used. These changes in food may in turn also affect the structural integrity of various allergy causing components. This information could be useful to food processors in selection of the processing technique to not only make the food palatable and microbiologically safe but also lead to an allergen safe food product.

Effect of Food Processing on Major Allergens Classes

The availability of literature on the effect of food processing on banana allergens is scarce, the effect of food processing on some of the major allergens classes are discussed in this section.

Profilin Various processing techniques (*i.e.*, microwave heating, cooking, γ irradiation, ultra-high pressure treatment and high voltage impulse treatment) effects on the immunochemical stability of celery root allergens were studied [46]. Microwave processing effect on profilin allergen was evaluated and was reported that celery processing with microwave treatment at 100 °C for 30 min showed the reduced binding capacity of profiling with IgE. However, microwave treatment exceeding 20 min are not recommended due to overheating and charring of food product.

Thaumatococcus Conformational changes of thaumatococcus-like (Mal d 2) apple allergen, induced by food processing was studied and reported that industrial practice involving varying temperature treatments (20 min at 60, 85, and 100 °C), pH (3.5 and natural pH), modification of redox potential, addition of sugar (15%) in manufacturing of apple products or digestive enzymes (pepsin, trypsin, and chymotrypsin) cannot lead to a destruction of the molecular stability of Mal d 2. Gastrointestinal digestion and synergistic combination of thermal treatment (70 °C) with pH (acidic and neutral pH) on Mal d 2 were evaluated. It was reported that even after 4 h of digestion treatment the protein secondary structure was intact. Thermal treatment at acidic pH unfolded the protein structure, refolding on cooling down was observed and this

Table 2 Banana allergens and identification techniques

S.No	Food source	Techniques used	Subjects	Allergen identified-banana	Clinical condition	References
1	Banana	Immunoblotting DBPCFC	4 subjects with a history of banana allergy	Bet v 2 Profilin Class 1 chitinases	Birch pollinosis	[8]
2	Banana	IgE ELISA, SDS PAGE 2D PAGE, Basophil activation test (BAT), MALDI-TOF	23 subjects	Mus a 5	OAS	[39]
3	Banana	SDS-PAGE, 2D-PAGE Mass fingerprint, N-terminal sequencing, Immunodetection	5 subjects	Mus a 2, Mus a 4 and Mus a 5	Clinical history of banana allergy	[37]
4	Banana	Skin prick test Oral banana challenge IgE ELISA	80 children with allergic diseases	Banana specific IgE in serum	2 groups of allergic children with and without history of banana allergy	[40]
5	Banana	Skin prick test, RAST inhibition, immunospot inhibition assay, crossed-line immunoelectropho- resis and crossed-line radioim- munoelctrophoresis	47 subjects	Banana specific IgE	History of latex allergy	[41]
6	Banana	CAP RAST assay and SDS PAGE immunoblotting	19 subjects (17 female, 2 male)	33 kD allergen was detectable in 15 of 19 sera (88%) and 37 kD allergen in 13 of 19 sera (76%).	History of latex allergy	[42]
7	Banana	Affinity chromatography, cation- exchange chromatography, N-terminal sequencing, enzy- matic activity assays, immuno- blotting	15 subjects	Two major IgE-binding proteins of 34 and 32 kDa	Banana allergy	[43]
8	Banana	Immunodetection assays, Skin prick tests, IgE determination and ELISA-inhibition assays	51 subjects	Mus a 3, Mus a 4, Mus a 5	Banana allergy	[44]

did not affect the IgE binding capacity. The refolding was not present in thermal treatment with neutral pH [47]. Similar thermal treatment (95 °C) in combination with pH (acidic and neutral pH) effect was evaluated in Kiwi fruit for thaumatin-like (Act d 2) protein. The Act d 2 results were similar to that of Mal d 2 as no reduction in IgE binding capacity.

Nonspecific Lipid Transfer Protein (nsLTP) These proteins has heat resistant property (up to 90 °C). In apples, nsLTP (Mal d 3) has characteristic stability due to 3–4 intramolecular disulphide bonds in its structure. Variation in IgE binding capacity of Mal d 3 as result of thermal treatment and in presence or absence of glucose was studied. It was reported that thermal treatment for short duration (90 °C for 20 min) and with or without the presence of glucose has no effect on IgE binding capacity. However, upon exposure to severe conditions viz. 100 °C for 2 h the secondary structural deviation and reduction of IgE binding capacity was observed. Moreover, presence of glucose has mild synergistic effect in IgE binding capacity in the latter treatment [35]. In case of Peaches, nsLTP is majorly located in the fruit peel, chemical peeling followed in industrial processing significantly reduced the allergenicity caused by nsLTP.

In recent years has also evidenced the use of newer technologies for processing of food whereas conventional technologies are well established and commonly used in food industries which includes thermal methods such as boiling, roasting, grilling, frying, etc., and not limited to emerging processing technologies such as ultra-sonic treatment, high-pressure processing, pulsed electric field treatment, etc. Some of these methods are used as a major technical approach to reduce risk of food allergens by deactivating their allergenic epitope sequence after their identification [48]. Apart from this, there are some studies which shown that food processing may increase or have no effect on allergenicity. Though there is no literature available especially on the impact of food processing on banana allergens. However, for profilin (Mus a1) an allergen, which also has been reported in Hazel nut is found to be heat stable which avoids its structure unfolding even at temperatures upto 400 K, which shows its non-destructive nature during its processing. Further at temperatures 450 to 500 K, profilin generated cross reactivity with other food allergens [49]. Along with this, Profilin from lichi fruit also did not change its allergenicity during processing. Another allergen of banana, chitinase (Mus a 2) which is also present in maize survives during processing in which its stability can be explained by its 3D structure [48]. It is observed that profilin subjected to temperatures of 450 and 500 K could generate cross-reactivity with other food allergens. Further work is warranted to see the implications of novel technologies on banana allergen as a standalone technology or in combination with conventional technology as it can impact the ability of proteins to cause the achievement of allergic sensitization.

Protein's physicochemical modifications, viz., structural unfolding, aggregation, proteolysis, glycosylation, glycation, solubility, pH effects, and networking to gel formation, may alter its allergenic potential. The nature of the allergen, food matrix composition, processing conditions, etc., has an impact on allergenic potential/activity. Hence it is difficult to generalize processing effects on food allergen as the allergenic potential/activity may increase, decrease or remain unchanged [50].

Effect of Thermal and some Non-thermal Processing on Food Allergens

Thermal Processing and Types of Thermal Treatment

During thermal processing of foods, significant structural changes in protein depend on various parameters like treatment temperature, an intrinsic characteristic of protein, and physicochemical conditions of the protein. Structural changes in protein during thermal treatment influences protein's stability and activity. Characteristically, protein tertiary structure loss is followed by secondary structure loss (55–70 °C), disulphide bonds cleavage (70–80 °C), formation of new intra- /inter-molecular interactions, disulphide bonds rearrangements (80–90 °C) and formation of aggregates (90–100 °C) [51]. Other chemical modifications may take place at high temperatures (100–125 °C and higher), with the rest of the food constituents in the matrix, leading to various adducts [51].

Thermal treatment leads to conformation changes, viz., conformational epitopes are generally destroyed by cleavage of the protein, linear epitopes may be maintained, and exposure of hidden epitopes in the native conformation. The treatment may lead to generation of new immunologically reactive structures (neoallergens), among which are the advanced glycation end-products (AGEs) produced as a result of the Maillard reaction [52].

Thermal treatment can be applied as dry heating and as wet heating. Dry heating unit operation, like roasting hazelnut at 140 °C for 40 min reduced the allergenicity approximately by 100-fold, contrarily roasting peanuts increased Ig-E binding capacity of allergen by 90-fold. Application of wet heat (boiling at a lower temperature, < 100 °C and frying at high temperature, 120 °C) and dry heating (dry heating at high temperature) on peanut had increased and decreased the allergen's potential [53]. However, thermal treatment significance on allergenicity are usually impulsive. Certain allergenic foods are designated as heat stable (e.g., fish, egg, milk, peanuts, etc), while others are considered partially stable (e.g., cereals, soybean, tree nuts, etc.) or heat-labile (fruits of the Rosaceae family and carrots).

Non-thermal Processing Methods

High-Pressure Processing (HPP) HPP, a non-thermal technique referred to also as high hydrostatic pressure or ultra high pressure processing. It affects only non-covalent bonds of protein resulting in denaturation and conformational changes [50]. By and large, conformational changes in proteins are ascertained when the pressure reaches to a range of 200–300 MPa [54]. Conformation changes lead to the destruction of conformational epitopes while linear epitopes are exposed for enzymatic action. HPP treatment resulted in allergenicity reduction in soy sprouts by making protein more available for enzymatic action. In case of rice HPP treatment released allergenic protein into an aqueous solution. Immunoreactivity of soy protein decreased by 55.5% when treated at 300 MPa for 15 min, in walnuts by 46.64% reduction when treated at 550 & 650 MPa, and in ginkgo seed protein complete reduction in ginkgo seed protein at 600 & 700 MPa [55]. Antigenicity reduction up to 92.7% was observed with HPP treatment at 200–500 MPa for 5–20 min in 1% β -conglycinin [56].

Structural changes brought by denaturation can increase allergenicity by exposing hidden epitopes. It was found that antigenicity of β -lactoglobulin in whey protein isolates increased with an increase in treatment parameters pressure (200–600 MPa), temperature (30–68 °C), and duration of the treatment (10–30 min). The immunoreactivity of β -lactoglobulin increase with pressure enhancement of in HPP treatment, it reached maximum at 400 MPa. The increase in immunoreactivity is attributed to the revelation of IgG linear epitopes after HPP, which stemmed in the tertiary structural changes [57]. HPP reported as a better method for preserving freshness and essential compounds of food [58], albeit it may increase the immunoreactivity of food allergens in many cases. Hence HPP is not a recommended approach and further more investigation is required regarding its application in food allergenicity reduction.

2) Pulsed Light/Pulsed UV-Light Pulsed light is a part of electromagnetic spectrum consisting of ultraviolet light, visible light and infrared light parts. It constitutes of short and high energy pulses of white light [59]. Pulsed ultraviolet light has 200 to 1000 nm wavelength range and its intensity is thousand-time greater than convention ultraviolet light [59]. The inactivation mechanism of PUV light occurs by chemical and structural modifications, varying heating rates and discharge of high energy discontinuous pulses [60]. Apropos to the application of PUV light to food system for reducing the allergenicity, the processing technique bring changes to the food allergens in structural conformation and induce protein aggregation. Due to the above said protein aggregations hyper reactive conformational neo-epitopes can be augmented aggravating allergenicity [61]. Application

of PUV light with varying operating parameters like time of treatment, intensity, distance between light and sample depicted the reduction in immunoreactivity of allergens in soy [62], peanut [63], and in milk [64]. Immunoreactivity of allergens in eggs were unaltered with this treatment [65]. Admitting the influence of PUV light processing in immunoreactivity reduction, it can be suggested as an alternative processing technology. Nevertheless there is a dire need for clinical and *in vivo* studies for its application in food industry.

Pulsed Electric Field (PEF) In food industry pulsed electric field (PEF) application is blooming. High electric field strength generally from 0.1 to 80 kV/cm is applied to food across two electrodes for a very brief period ranging from nanoseconds to milliseconds [66]. Enzyme and microbial inactivation, modification of food protein structures for functional properties alterations are some applications of PEF. Specific protein molecules are polarized led by explosion of the hydrophobic amino acids to the solvent. Subsequently with the high intensity electric field, unfolding proteins form into aggregates [67]. PEF processing has the potential to decrease the immunoreactivity of ovalbumin by altering conformational structure as reported by Yang et al. [68]. It was reported that there was no conformational changes in either in purified food allergens such as Ara h 2,6 (peanut), Mal d 1 and Mal d 3 (apple) [69], and in whole celery [70]. Juxtaposition of PEF with other non-thermal and thermal treatments, the effects PEF on allergen reduction is minimum. Therefore, this processing needs further studies.

Cold Plasma Plasma is the fourth state of matter, which is a partially ionized gas consisting of reactive species, such as ions, UV photons, electrons, free radicals, molecules, and excited atoms. These ionized species can interact with proteins and alter their conformations. In this processing technology IgE-mediated reactions are reduced due to exposure of conformational epitopes to free radicals of plasma [71]. Cold plasma application resulted in antigenicity reduction in dry, defatted peanut and whole peanut flours [72], wheat [71], untoasted soy protein extract [62]. It was found that no significant difference in milk [64]. Cold plasma processing affects food quality by accelerating lipid oxidation, reduction in vitamin and sensory attributes descent during its application. Hence, it can be stated as this processing technology is not an ideal one and explore other technologies.

Ultrasound Ultrasound is specified as sound waves bearing a frequency of up to 20 kHz. As an efficient and emerging food processing technology, its applications are involved in extraction, microbial and enzymatic inactivation, cutting, homogenization, drying, surface cleaning, etc. [73]. Mechanical waves generate the sonication bubble, which

undergoes compression, intermittent refraction, and collapses at critical radius. The explosions of bubbles generate localized high temperatures (upto 5000 K) and pressures (upto 1013.25 bar). Such dynamic conditions have the chance to induce structural changes in allergens. Reduction in immunoreactivity of allergens was observed in peanut [74], shrimp and soy [75], but there was no effect in milk [64]. Ultrasound processing realized momentous consideration due to its advantages such as handling of higher mass, energy conservativeness, environmental friendliness and lesser reduction of sensory attributes of food products during processing [21]. Effectiveness of ultrasound processing enhances when applied in combination of heat rather than its solo application. Thus ultrasound can be as an alternative method of processing for food immunoreactivity reduction.

Fermentation Food fermentation involves protein's partial hydrolysis by the enzymes produced by the added culture. Fermentation reported the inactivation of allergen-causing epitopes and reducing IgE binding capacity by protein gelation and other aggregates. Immunoreactivity was reduced in α -lactalbumin and β -lactoglobulin of skim milk [76], soy-containing products, *viz.*, tempeh, miso, yogurt [77]. Albeit, allergenicity is retained in a fermented soy sauce containing both soy and wheat [78].

Hydrolysis Enzymatic and chemical hydrolysis are common methods to reduce allergenicity. Enzymatic hydrolysis is the most common process used industrially to reduce the protein allergenicity. The nature and the degree of hydrolysis depend on the structure and on post-translational modifications. The site of hydrolysis depends on enzyme specificity and the degree of hydrolysis depends on working conditions. Most proteolytic treatments generate partial hydrolysis so that not all epitopes are destroyed. Proteolysis can destroy some epitopes and unmask linear epitopes making them available for IgE binding [50]. Chemical hydrolysis is less commonly used industrially and it is used in combination with thermal or hyper-hydro-baric treatment. The result of chemical hydrolysis depicted less allergenicity in wheat [79] and reduced IgE binding capacity in Sletten et al. [80]. Deamidation is a chemical hydrolysis method for altering the protein structure to increase solubility. Application of deamidation technique to foods has increased the allergic reaction in case of wheat.

In conclusion juxtaposing non-thermal technologies for reducing food allergenicity, HPP, cold plasma are not recommended as in some case where there was increase in allergenicity. Considering the processing technologies like ultrasound, PUV, PEF treatments they are recommended for processing but still the effects of these processing

technologies are still scarce. Fermentation especially long-term fermentation has the potentiality for allergenicity reduction. As per the case of hydrolysis enzymatic hydrolysis can be preferred over other types but the specificity of the enzymes and enzyme costs plays a crucial role in selecting this type of processing technology.

Future Scope

Currently, there has been no treatment and cure for the banana allergy. The identification and characterization of fruit allergen is necessary to diagnose and combat the disease. The management of banana allergy is to completely avoid this fruit and also manage accidental exposure to banana and its related products. Several studies have reported that some processing methods like steam cooking, boiling, sterilization and microwave heating may help to reduce FA [81]. Most of the allergic proteins are stable, resists thermal treatment and proteolysis. While intake of fruit, there is a chance of getting interactions between the allergenic proteins and phenolic compounds in the food matrix forms a stable structure and more intact, hence leads to increase in temperature for denaturation [82]. Thermal treatments are one of the useful strategies for eliminating immunoreactive proteins or allergens among the different approaches used to make protein hypoallergenic. Thermal treatment procedures are mostly used to improve flavour, texture, digestibility, eliminate toxins, and protect against germs, in addition to lowering allergenicity [83]. Sensitization to profilin has been clinically increased when patients with OAS [99]. Thus, high-temperature food processing followed by γ -irradiation may be beneficial in lowering the likelihood of food hypersensitivity responses in sensitive people. It is presumed that these processing techniques may alter the immune-reactive epitomes of the allergic proteins. However, processing techniques have shown to destroy existing epitopes on an allergic protein, simultaneously there are also higher chances to generate new ones (formation of neoallergens) as a result of conformational changes that cannot be avoided [84]. Further, the diversity in individuals' sensitivity levels, also play a significant role that causes an allergic reaction. Genetic background of banana allergy and its molecular targets are though well established the prevention and treatments are lagging behind for IgE mediated food allergenicity. The immunotherapeutic treatment of this banana fruit allergy is a major challenge for susceptible individuals in coming years. The scientific community has a tremendous task upfront in improving the quality of life of people suffering from this illness.

Conclusion

Overall the diagnosis of allergy based on the molecules responsible for this allergy is critical for the evaluation of sensitized individuals to banana fruit. Even though many processing procedures, such as steam boiling, microwave heating, enzyme treatment, and ethylene treatment, helps to reduce banana allergenicity, but also their efficacy needs to be enhanced and well-studied. In addition to that, new processing techniques must be created to complete desensitization of allergy causing allergens in banana. Recognition of banana allergy, its knowledge on proper care, and the development of desensitization methods would also help individuals with this FA, improve their results and quality of life. Further visions into the pathophysiology and the mechanisms of IgE mediated food allergy will lead to the progress of methods for the prevention, diagnosis, and management.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11130-022-00976-1>.

Acknowledgements We would like to thank National Institute of Food Technology Management and Entrepreneurship, Thanjavur, India.

Author Contributions AR and AA conceptualized, PS and AM wrote the manuscript, KRM, VS, AR and AA reviewed the manuscript.

Declarations

Conflict of Interest The authors declare no competing interests.

References

- Louis Tuft GIB (1942) Studies in food allergy: II. Sensitization to fresh fruits: clinical and experimental observations. *J Allergy* 13:574–582
- Thongkhom R, Oncham S, Sompornrattanaphan M, Laisuan W (2020) Banana anaphylaxis in Thailand: case series. *Asia Pac Allergy* 10:1–7. <https://doi.org/10.5415/apallergy.2020.10.e4>
- Mrkic I, Abughren M, Nikolic J et al (2014) Molecular characterization of recombinant Mus a 5 allergen from banana fruit. *Mol Biotechnol* 56:498–506. <https://doi.org/10.1007/s12033-013-9719-8>
- Ansotegui IJ, Melioli G, Canonica GW et al (2020) IgE allergy diagnostics and other relevant tests in allergy, a world allergy organization position paper. *World Allergy Organ J* 13. <https://doi.org/10.1016/j.waojou.2019.100080>
- Kocacik Uygün DF, Filiz S, Bingöl A (2018) An evaluation of banana allergy in children living in the Mediterranean region. *Turkish J Med Sci* 48:469–475. <https://doi.org/10.3906/sag-1705-140>
- Beyer K, Grishina G, Bardina L, Grishin A, Sampson HA (2002) Identification of an 11S globulin as a major hazelnut food allergen in hazelnut-induced systemic reactions. *J Allergy Clin Immunol* 110(3):517–523. <https://doi.org/10.1067/mai.2002.127434>
- Dayoğlu A, Akgiray S, Nacaroglu HT, Bahçeci Erdem S (2020) The clinical Spectrum of reactions due to banana allergy. *Bagcilar Med Bull* 5:60–63. <https://doi.org/10.4274/bmb.galenos.2020.04.013>
- Grob M, Reindl J, Vieths S et al (2002) Heterogeneity of banana allergy: characterization of allergens in banana-allergic patients. *Ann Allergy Asthma Immunol* 89:513–516. [https://doi.org/10.1016/S1081-1206\(10\)62090-X](https://doi.org/10.1016/S1081-1206(10)62090-X)
- Novembre E, Martina D (1988) Foods and respiratory allergy. *Med Hyg (Geneve)* 81:1059–1065
- Sinha M, Singh RP, Kushwaha GS, et al (2014) Current overview of allergens of plant pathogenesis related protein families. *Sci World J* 2014. <https://doi.org/10.1155/2014/543195>
- Guariso G, Bertoli S, Cernetti R et al (1993) Migraine and food intolerance: a controlled study in pediatric patients. *La Pediatr e Chir Med Surg Pediatr* 15:57–61
- Al-Rabia M (2016) Food-induced immunoglobulin E-mediated allergic rhinitis. *J Microsc Ultrastruct* 4:69. <https://doi.org/10.1016/j.jmau.2015.11.004>
- Alessandri C, Alessandri C, Ferrara R et al (2020) Molecular approach to a patient's tailored diagnosis of the oral allergy syndrome. *Clin Transl Allergy* 10:1–18. <https://doi.org/10.1186/s13601-020-00329-8>
- Aba-Aikhail BA, El-Gamal FM (2000) Prevalence of food allergy in asthmatic patients. 81–87
- Mandal J, Das M, Roy I et al (2009) Immediate hypersensitivity to common food allergens: an investigation on food sensitization in respiratory allergic patients of Calcutta, India. *World Allergy Organ J* 2:9–12. <https://doi.org/10.1097/wox.0b013e318194c0de>
- Rokaite R, Labanauskas L, Vaideliene L (2004) Role of the skin patch test in diagnosing food allergy in children with atopic dermatitis. *Medicina (Kaunas)* 40:1081–1087
- Gabrielli S, Clarke AE, Morris J et al (2021) Fruit-induced anaphylaxis: clinical presentation and management. *J Allergy Clin Immunol Pract* 9:2825–2830.e2. <https://doi.org/10.1016/j.jaip.2021.02.055>
- Leone P, Menu-Bouaouiche L, Peumans WJ et al (2006) Resolution of the structure of the allergenic and antifungal banana fruit thaumatin-like protein at 1.7-Å. *Biochimie* 88:45–52. <https://doi.org/10.1016/j.biochi.2005.07.001>
- Valenta R, Hochwallner H, Linhart B, Pahr S (2015) Food allergies: the basics. *Gastroenterology* 148:1120–1131.e4. <https://doi.org/10.1053/j.gastro.2015.02.006>
- Yu W, Freeland DMH, Nadeau KC (2016) Food allergy: immune mechanisms, diagnosis and immunotherapy. *Nat Rev Immunol* 16:751–765. <https://doi.org/10.1038/nri.2016.111>
- Wang J, Vanga SK, McCusker C, Raghavan V (2019) A comprehensive review on kiwifruit allergy: pathogenesis, diagnosis, management, and potential modification of allergens through processing. *Compr Rev Food Sci Food Saf* 18:500–513. <https://doi.org/10.1111/1541-4337.12426>
- Reindl J, Rihs HP, Scheurer S et al (2002) IgE reactivity to profilin in pollen-sensitized subjects with adverse reactions to banana and pineapple. *Int Arch Allergy Immunol* 128:105–114. <https://doi.org/10.1159/000059400>
- Lotfi M'Raihi CD, Pons Alain BP, Daniel V (1991) Cross-reactivity between latex and banana. *J Allergy Clin Immunol* 87:129–130. [https://doi.org/10.1016/0091-6749\(91\)90224-c](https://doi.org/10.1016/0091-6749(91)90224-c)
- O'Keefe AW, Ben-Shoshan M (2014) A 4-month-old baby boy presenting with anaphylaxis to a banana: a case report. *J Med Case Rep* 8:6–8. <https://doi.org/10.1186/1752-1947-8-62>
- Ricci A, Avanzini MA, Scaramuzza C et al (2005) Toll-like receptor 2-positive and toll-like receptor 4-positive cells in adenoids of children exposed to passive smoking [1]. *J Allergy Clin Immunol* 115:631–632. <https://doi.org/10.1016/j.jaci.2004.11.044>
- Jeon YH (2020) Pollen-food allergy syndrome in children. *Korean J Pediatr* 63:463–468. <https://doi.org/10.3345/cep.2019.00780>

27. Oberhuber C, Bulley SM, Ballmer-Weber BK et al (2008) Characterization of bet v 1-related allergens from kiwifruit relevant for patients with combined kiwifruit and birch pollen allergy. *Mol Nutr Food Res* 52:230–240. <https://doi.org/10.1002/mnfr.20080146>
28. Huang AHC (2018) Plant lipid droplets and their associated proteins: potential for rapid advances. *Plant Physiol* 176:1894–1918. <https://doi.org/10.1104/pp.17.01677>
29. Khan F, Szmigielski R, Gul A, Volkan Altay MO (2020) Advancements in plant transgenomics approach for the biopharmaceutics and vaccines production. In: Ozturk M, Dilduza Egamberdieva MP (eds) *Biodiversity and biomedicine*. Academic Press, pp 317–333
30. Sarkar A (2009) *Molecular Farming*. Discovery Publishing House
31. Boothe J, Nykiforuk C, Shen Y et al (2010) Seed-based expression systems for plant molecular farming. *Plant Biotechnol J* 8:588–606. <https://doi.org/10.1111/j.1467-7652.2010.00511.x>
32. Kivity S (2012) Adult-onset food allergy. *Isr Med Assoc J* 14:70–72
33. Lieberman JA, Sicherer SH (2011) Diagnosis of food allergy: epicutaneous skin tests, *in vitro* tests, and oral food challenge. *Curr Allergy Asthma Rep* 11:58–64. <https://doi.org/10.1007/s11882-010-0149-4>
34. Asha'ari ZA, Suhaimi Y, Yusof RA et al (2011) Comparison of serum specific ige with skin prick test in the diagnosis of allergy in Malaysia. *Med J Malaysia* 66:202–206
35. Sancho AI, Rigby NM, Zuidmeer L et al (2005) The effect of thermal processing on the IgE reactivity of the non-specific lipid transfer protein from apple, mal d 3. *Allergy Eur J Allergy Clin Immunol* 60:1262–1268. <https://doi.org/10.1111/j.1398-9995.2005.00876.x>
36. Hindson BJ, Ness KD, Masquelier DA et al (2011) High-throughput droplet digital PCR system for absolute quantitation of DNA copy number. *Anal Chem* 83:8604–8610. <https://doi.org/10.1021/ac202028g>
37. Nikolic J, Mrkic I, Grozdanovic M et al (2014) Protocol for simultaneous isolation of three important banana allergens. *J Chromatogr B Anal Technol Biomed Life Sci* 962:30–36. <https://doi.org/10.1016/j.jchromb.2014.05.020>
38. Aquino A, Conte-Junior CA (2020) A systematic review of food allergy: nanobiosensor and food allergen detection. *Biosensors* 10:1–19. <https://doi.org/10.3390/bios10120194>
39. Aleksic I, Popovic M, Dimitrijevic R et al (2012) Molecular and immunological characterization of Mus a 5 allergen from banana fruit. *Mol Nutr Food Res* 56:446–453. <https://doi.org/10.1002/mnfr.201100541>
40. El-Sayed ZA, El-Ghoneimy DH, El-Shennawy D, Nasser MW (2013) Evaluation of banana hypersensitivity among a group of atopic egyptian children: Relation to parental/self reports. *Allergy, Asthma Immunol Res* 5:150–154. <https://doi.org/10.4168/aaair.2013.5.3.150>
41. Mäkinen-Kiljunen S (1994) Banana allergy in patients with immediate-type hypersensitivity to natural rubber latex: Characterization of cross-reacting antibodies and allergens. *J Allergy Clin Immunol* 93:990–996. [https://doi.org/10.1016/S0091-6749\(94\)70046-X](https://doi.org/10.1016/S0091-6749(94)70046-X)
42. Delbourg MF, Guilloux L, Moneret-Vautrin DA, Ville G (1996) Hypersensitivity to banana in latex-allergic patients. Identification of two major banana allergens of 33 and 37 kD. *Ann Allergy, Asthma Immunol* 76:321–326. [https://doi.org/10.1016/S1081-1206\(10\)60032-4](https://doi.org/10.1016/S1081-1206(10)60032-4)
43. Sanchez-Monge R, Blanco C, Díaz-Perales A et al (1999) Isolation and characterization of major banana allergens: Identification as fruit class I chitinases. *Clin Exp Allergy* 29:673–680. <https://doi.org/10.1046/j.1365-2222.1999.00526.x>
44. Palacin A, Quirce S, Sanchez-Monge R et al (2011) Sensitization profiles to purified plant food allergens among pediatric patients with allergy to banana. *Pediatr Allergy Immunol* 22:186–195. <https://doi.org/10.1111/j.1399-3038.2010.01125.x>
45. Courtney Rachel C (2016) Evaluation of qualitative food allergen detection methods and cleaning validation approaches. University of Nebraska, Lincoln
46. Jankiewicz A, Aulepp H, Baltes W et al (1996) Allergic sensitization to native and heated celery root in pollen-sensitive patients investigated by skin test and IgE binding. *Int Arch Allergy Immunol* 111:268–278
47. Smole U, Bublin M, Radauer C et al (2008) Mal d 2, the thaumatin-like allergen from apple, is highly resistant to gastrointestinal digestion and thermal processing. *Int Arch Allergy Immunol* 147:289–298. <https://doi.org/10.1159/000144036>
48. Leoni C, Volpicella M, Dileo MCG et al (2019) Chitinases as food allergens. *Molecules* 24:1–10. <https://doi.org/10.3390/molecules24112087>
49. O'Keefe AW, Ben-Shoshan M, Ansotegui IJ et al (2020) Food processing and allergenicity. *World Allergy Organ J* 25:463–468. <https://doi.org/10.1021/acsomega.8b02288>
50. EFSA-Panel (2014) Scientific opinion on the evaluation of allergenic foods and food ingredients for labelling purposes. *EFSA J* 12:3894. <https://doi.org/10.2903/j.efsa.2014.3894>
51. Davis PJ, Williams SC (1998) Protein modification by thermal processing. *Allergy Eur J Allergy Clin Immunol* 53:102–105. <https://doi.org/10.1111/j.1398-9995.1998.tb04975.x>
52. Clare Mills EN, Sancho AI, Rigby NM et al (2009) Impact of food processing on the structural and allergenic properties of food allergens. *Mol Nutr Food Res* 53:963–969. <https://doi.org/10.1002/mnfr.200800236>
53. Mondoulet L, Paty E, Drumare MF et al (2005) Influence of thermal processing on the allergenicity of peanut proteins. *J Agric Food Chem* 53:4547–4553. <https://doi.org/10.1021/jf050091p>
54. Kurpiewska K, Biela A, Loch JI et al (2019) Towards understanding the effect of high pressure on food protein allergenicity: β -lactoglobulin structural studies. *Food Chem* 270:315–321. <https://doi.org/10.1016/j.foodchem.2018.07.104>
55. Zhou H, Wang C, Ye J et al (2016) Effects of high hydrostatic pressure treatment on structural, allergenicity, and functional properties of proteins from ginkgo seeds. *Innov Food Sci Emerg Technol* 34:187–195. <https://doi.org/10.1016/j.ifset.2016.02.001>
56. Xi J, He M (2018) High hydrostatic pressure (HHP) effects on antigenicity and structural properties of soybean β -conglycinin. *J Food Sci Technol* 55:630–637. <https://doi.org/10.1007/s13197-017-2972-2>
57. Meng X, Bai Y, Gao J et al (2017) Effects of high hydrostatic pressure on the structure and potential allergenicity of the major allergen bovine β -lactoglobulin. *Food Chem* 219:290–296. <https://doi.org/10.1016/j.foodchem.2016.09.153>
58. Muntean M-V, Marian O, Barbieru V et al (2016) High pressure processing in food industry – characteristics and applications. *Agric Agric Sci Procedia* 10:377–383. <https://doi.org/10.1016/j.aaspro.2016.09.077>
59. Shriver SK, Yang WW (2011) Thermal and nonthermal methods for food allergen control. *Food Eng Rev* 3:26–43. <https://doi.org/10.1007/s12393-011-9033-9>
60. Krishnamurthy K, Irudayaraj J, Ali Demirci A, Yang W (2008) UV pasteurization of food materials. In: *Processing Food* (ed) Jun S, Irudayaraj JM. *Operations Modeling, Design and Analysis*, Second Edition, pp 281–302
61. Thomas K, Herouet-Guicheney C, Ladics G et al (2007) Evaluating the effect of food processing on the potential human allergenicity of novel proteins: international workshop report. *Food Chem Toxicol* 45:1116–1122. <https://doi.org/10.1016/j.fct.2006.12.016>

62. Meinlschmidt P, Ueberham E, Lehmann J et al (2016) The effects of pulsed ultraviolet light, cold atmospheric pressure plasma, and gamma-irradiation on the immunoreactivity of soy protein isolate. *Innov Food Sci Emerg Technol* 38:374–383. <https://doi.org/10.1016/j.ifset.2016.06.007>
63. Yang WW, Mwakatage NR, Goodrich-Schneider R et al (2012) Mitigation of major peanut allergens by pulsed ultraviolet light. *Food Bioprocess Technol* 5:2728–2738. <https://doi.org/10.1007/s11947-011-0615-6>
64. Tammineedi CVRK, Choudhary R, Perez-Alvarado GC, Watson DG (2013) Determining the effect of UV-C, high intensity ultrasound and nonthermal atmospheric plasma treatments on reducing the allergenicity of α -casein and whey proteins. *LWT - Food Sci Technol* 54:35–41. <https://doi.org/10.1016/j.lwt.2013.05.020>
65. Manzocco L, Panozzo A, Nicoli MC (2012) Effect of ultraviolet processing on selected properties of egg white. *Food Chem* 135:522–527. <https://doi.org/10.1016/j.foodchem.2012.05.028>
66. Bhat ZF, Morton JD, Mason SL, Bekhit AEDA (2019) Current and future prospects for the use of pulsed electric field in the meat industry. *Crit Rev Food Sci Nutr* 59:1660–1674. <https://doi.org/10.1080/10408398.2018.1425825>
67. Zhao W, Yang R (2009) Effect of high-intensity pulsed electric fields on the activity, conformation and self-aggregation of pepsin. *Food Chem* 114:777–781. <https://doi.org/10.1016/j.foodchem.2008.10.016>
68. Yang W, Tu Z, Wang H et al (2018) Immunogenic and structural properties of ovalbumin treated by pulsed electric fields. *Int J Food Prop* 20:S3164–S3176. <https://doi.org/10.1080/10942912.2017.1396479>
69. Johnson PE, Van Der Plancken I, Balasa A et al (2010) High pressure, thermal and pulsed electric-field-induced structural changes in selected food allergens. *Mol Nutr Food Res* 54:1701–1710. <https://doi.org/10.1002/mnfr.201000006>
70. Paschke A (2009) Aspects of food processing and its effect on allergen structure. *Mol Nutr Food Res* 53:959–962. <https://doi.org/10.1002/mnfr.200800187>
71. Nooji JK (2011) Reduction of wheat allergen potency by pulsed ultraviolet light, high hydrostatic pressure, and non-thermal plasma
72. Venkataratnam H, Sarangapani C, Cahill O, Ryan CB (2019) Effect of cold plasma treatment on the antigenicity of peanut allergen Ara h 1. *Innov Food Sci Emerg Technol* 52:368–375. <https://doi.org/10.1016/j.ifset.2019.02.001>
73. Feng H, Barbosa-Cánovas GV, Weiss J (2011) *Ultrasound Technologies for Food and Bioprocessing*. Springer, New York
74. Li H, Yu J, Ahmedna M, Goktepe I (2013) Reduction of major peanut allergens Ara h 1 and Ara h 2, in roasted peanuts by ultrasound assisted enzymatic treatment. *Food Chem* 141:762–768. <https://doi.org/10.1016/j.foodchem.2013.03.049>
75. Dong X, Wang J, Raghavan V (2020) Critical reviews and recent advances of novel non-thermal processing techniques on the modification of food allergens. *Crit Rev Food Sci Nutr* 0:1–15. <https://doi.org/10.1080/10408398.2020.1722942>
76. Bu G, Luo Y, Zhang Y, Chen F (2010) Effects of fermentation by lactic acid bacteria on the antigenicity of bovine whey proteins. *J Sci Food Agric* 90:2015–2020. <https://doi.org/10.1002/jsfa.4046>
77. Song YS, Frias J, Martinez-Villaluenga C et al (2008) Immunoreactivity reduction of soybean meal by fermentation, effect on amino acid composition and antigenicity of commercial soy products. *Food Chem* 108:571–581. <https://doi.org/10.1016/j.foodchem.2007.11.013>
78. Hefle SL, Lambrecht DM, Nordlee JA (2005) Soy sauce retains allergenicity through the fermentation/production process. *J Allergy Clin Immunol* 115:2005
79. Akiyama H, Sakata K, Yoshioka Y et al (2006) Profile analysis and immunoglobulin E reactivity of wheat protein hydrolysates. *Int Arch Allergy Immunol* 140:36–42. <https://doi.org/10.1159/000092000>
80. Sletten G, Van Do T, Lindvik H et al (2010) Effects of industrial processing on the immunogenicity of commonly ingested fish species. *Int Arch Allergy Immunol* 151:223–236. <https://doi.org/10.1159/000242360>
81. Kasera R, Singh AB, Kumar R et al (2012) Effect of thermal processing and γ -irradiation on allergenicity of legume proteins. *Food Chem Toxicol* 50:3456–3461. <https://doi.org/10.1016/j.fct.2012.07.031>
82. Verhoeckx KCM, Vissers YM, Baumert JL et al (2015) Food processing and allergenicity. *Food Chem Toxicol* 80:223–240. <https://doi.org/10.1016/j.fct.2015.03.005>
83. Verma AK, Kumar S, Das M, Dwivedi PD (2012) Impact of thermal processing on legume allergens. *Plant Foods Hum Nutr* 67:430–441. <https://doi.org/10.1007/s11130-012-0328-7>
84. Fernández-Rivas M, Benito C, González-Mancebo E, Dolores Alonso Díaz De Durana M (2008) Allergies to fruits and vegetables. *Pediatr Allergy Immunol* 19:675–681. <https://doi.org/10.1111/j.1399-3038.2008.00821.x>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.