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Food allergens: identification, cross-reactivity, and advances in detection strategies

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Abstract

A food allergen is a protein in food that causes an immune system overreaction, resulting in an allergic reaction. Food allergens, including common triggers like milk, eggs, peanuts, and tree nuts, provoke immune responses mediated by IgE antibodies. With food allergies on the rise, particularly among young children in Western nations, the need for accurate identification and management has never been more critical. The article focuses on newly identified allergens from the Cupin and Prolamin superfamilies-groups of proteins that play key roles in seed storage and cereal grains-highlighting their potential to cause severe allergic reactions. A particularly fascinating aspect discussed is cross-reactivity among different food allergens. This happens when IgE antibodies, initially produced in response to one allergen, mistakenly recognize similar proteins in another food, creating a cascade of allergic reactions. For instance, those allergic to peanuts may also react to tree nuts, or individuals with fish allergies may experience symptoms when exposed to other seafood. Such cross-reactions underscore the complexity and unpredictability of food allergies. Different data management strategies for diagnosing and managing food allergies are described, emphasizing a detailed clinical history, which remains the most essential diagnostic tool. Effective management requires a multidisciplinary approach, with clinicians, dietitians, gastroenterologists, and psychologists working together to ensure a holistic care plan for individuals affected by food allergies. Allergen detection technologies, including DNA-based methods, SDS-PAGE, ELISA, and Lateral Flow Immunoassay (LFIA), each offering unique advantages and challenges, are also discussed.

1. Introduction

Anything that reacts with IgE antibodies causes allergic sensitization or triggers allergic reactions is classified as a food allergen. While some allergens bind IgE but do not cause mast cell degranulation, others merely cause allergic sensitization and no symptoms. An antigen's potential to be a potent food allergy cannot be predicted by any common structure (Bush and Hefle, 1996). Food and nonfood sources, more than 700 allergens have been discovered (Bannon, 2004).

Studies indicate that up to 10% of individuals in Western countries may have undiagnosed food allergies, with younger children being particularly affected. In children under five, challenge-proven food allergies are estimated at 4% in the UK, 3.6% in Denmark, and 6.8% in Norway. In Australia, the prevalence is reported to be over

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10% at 12 months and more than 4% at 04 years of age. According to the Melbourne-based HealthNuts study, the occurrence of peanut allergies at 12 months was 3.0%, egg allergies 8.9%, and sesame allergies 0.80%. The prevalence of peanut, egg, and sesame allergies at the four-year follow-up was 1.9%, 1.2%, and 0.4%, respectively. An estimated 10.8% of individuals in the US were found to have a confirmed food allergy, while 19.0% claimed to have one. The most reported allergies included shellfish (2.9%), milk (1.9%), peanuts (1.8%), tree nuts (1.2%), and finfish (0.9%) (Loh and Tang, 2018).

IgE antibodies can recognize, bind to, and initiate an immune response to similar allergenic molecules, a process known as cross-reactivity. This often occurs when allergy-causing particles from genetically similar species or structurally similar molecules with the same function are found in different species within the corresponding protein family. Examples of cross-reactivity include groups of cross-reactive allergens, family-specific homologous molecules, pan allergens, and cross-reactive carbohydrate determinants (CCDs). In the field of allergies, proteomics has been used more and more to (i) assess the genetic and phenotypic diversity of allergens, (ii) acquire well-defined allergens, and (iii) identify and measure allergens in complex foods, such as bread and cookies, in either their original or processed forms (Popescu, 2015).

Food allergies, which have been called the second phase of hypersensitivity after asthma, are becoming more widely acknowledged as a rising public health concern. More than half (n = 51) of the 83 countries that were members of the World Allergy Organization and six non-member countries surveyed lack data on the prevalence of food allergies, while a quarter (n = 23) relied on patient or parent reports for data, only 10% (n = 9) had data derived from oral food challenges (OFCs) (Loh & Tang, 2018). Although there isn't much research that uses IgE testing and a compelling medical record to establish the frequency of food allergies, those that do exist reveal food allergy rates that fall within the same range as the studies based on oral food challenges (OFCs). The frequency of food allergies in preschool-aged children, as determined by the past and food-specific IgE, was 3.20% in northern Europe (Sweden) and 3.4% in Asia (Taiwan). Through symptom assessment and IgE testing, the frequency in older children, however, ranged from just 0.30% in Korea to 5.30% in Sweden & 7.60% in Taiwan (Prescott *et al.,* 2013).

Since children often overcome their allergies, about 10% of children and about 3% of adults suffer from allergies. Compared to their contemporaries who are not allergic, people with allergies in North America & Europe report a lower quality of life, higher healthcare costs (46%), and higher food expenditures (19%). The incidence of food allergies appears to be increasing, especially in adolescent people (Kopko *et al.,* 2022).

2. Sources of food allergens

Milk, eggs, fish, shellfish, tree nuts, peanuts, wheat, and soybeans are considered the eight primary allergenic foods. The USA Food Allergen Labeling Act (FALCPA) requires that certain foods, which make up almost 90% of all food allergies in the US, be disclosed on any processed food (Monaci *et al.,* 2006). Proteins or glycoproteins make up almost all allergies, also known as antigens. While most allergens are oligomers with molecular weights exceeding 200 kDa, polypeptide masses typically fall between 5 and 70 kDa. To assess whether a substance or food product is allergenic, human IgE binding from the serum of individuals with hypersensitivity related to a specific clinical condition is commonly used. Food allergies differ globally due to various factors, including age, region, genetic diversity, and dietary choices. For instance, buckwheat (in Japan) & the edible nest of the swiftlet, commonly referred to as bird's nest (in Singapore), are widespread allergies, while sesame is a prevalent food allergy in Israel (Monaci *et al.,* 2006).

3. Major classes of food allergens

3.1. Cupin superfamily

The term 'cupin' was coined to refer to the functionally varied superfamily of proteins known as cupins, which contain two short, conserved sequence motifs and a β-barrel core structural domain. Bicupins have 2 of these conserved cupin domains, whereas single domain Geigercupins have just one (Breiteneder and Ebner, 2004).

The three types of seed storage proteins that make up cupin allergens are legumins (11S globulins), vicilins (7S globulins), and germins (< 7S protein). The canonical protomeric structure of these allergens is composed of two α-helical arms connected to either one cupin motif (germin) or two cupin motifs (vicilin, legumin). When consumed accidentally by previously sensitized consumers, cupin allergens serve as significant allergens that can cause serious anaphylactic reactions (Barre *et al.,* 2018). There are 26 isoallergens and 24 food allergens in the Cupin superfamily. The members of this family are primarily seed

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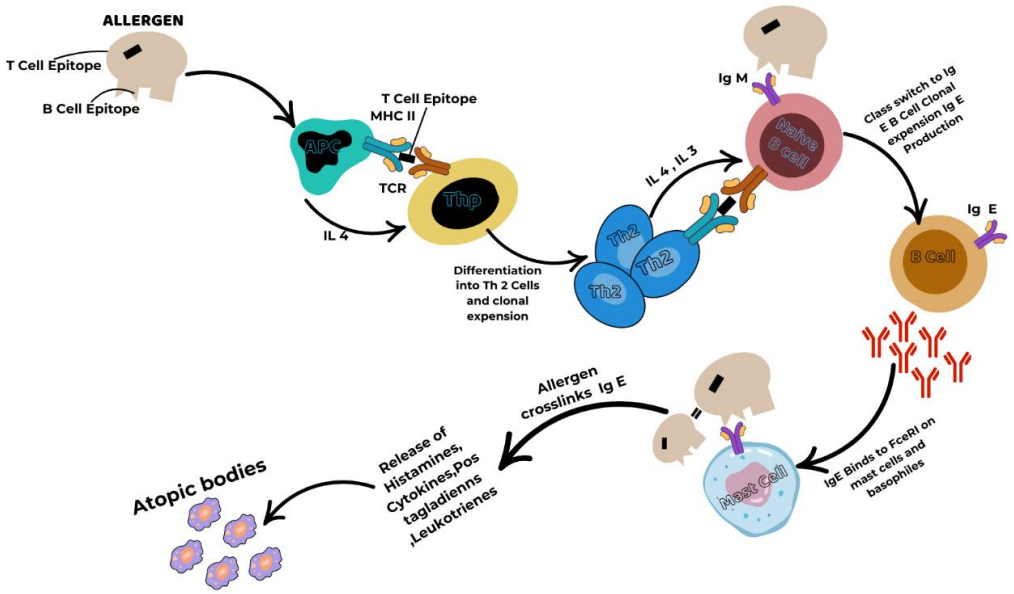


Figure 1. Cross-reactivity due to allergens binding Ig E.

storage globulins, which can be categorized into two subfamilies: 7/8S vicilins and mature 11S legumins (Wang *et al.,* 2014). The 7S globulinsBreiteneder found in soybean (β-conglycinin), peanut (conarachin; Ara h 1), walnut (Jug r 2), and lentil, along with the 11S globulins in peanut (arachin; Ara h 3), soybean (glycinin) and maybe coconut and walnut, have been discovered as important cupin food allergens (Mills *et al.,* 2002). The major peanut allergen, Ara h, which is responsible for the most fatal anaphylactic reactions triggered by plant-based foods, is the best-analyzed allergenic vicilin. Despite being comparatively rare, cashew nut allergies can be fatal (Breiteneder and Ebner, 2004).

3.2. Prolamin superfamily

The predominant storage proteins found in cereals and other grass family members are a class of storage proteins in seeds, called prolamins. Another important class of lipid-binding proteins found in cereal seeds are indolines, which are Lipid-binding proteins (nonspecific) that belong to the prolamin superfamily. The α-globulin group of storage proteins was initially identified in corn and rice (Breiteneder and Radauer, 2004). The existence of this superfamily was suggested due to the proteins' sequences including eight conserved cysteine residues. Except for oats and rice, cereal Prolamins serve as the primary storage proteins and are named for their high proline and glutamine levels (Breiteneder and Radauer, 2004).

Because of their high glutamine and proline concentrations and solubility in alcohol and water combinations, prolamins are core storage protein fractions found in grain crops. Up to 80% of the total protein content in wheat, barley, and rye is made up of these proteins (Daly *et al.,* 2020). Some common examples of prolamins Superfamily Include 2S albumins, Cereal prolamins (i.e.glutenins and gliadins) & Nonspecific lipid transfer proteins (nsLTPs) (Breiteneder and Radauer, 2004). The 2S albumins Sin a (from yellow mustard seeds) and Braj (from oriental mustard seeds) were found to be the proteins that cause allergic responses to mustard. The conglutin protein family, associated with 2S albumin family, includes Ara h 2, 6, and 7. It was discovered that Ara h 2 functions as a mild trypsin inactivator, shielding Ara h 1 from trypsin destruction. In Mediterranean populations, nsLTPs are the main allergens for peaches (Pru p 3), apples (Mal d 3), and apricots (Pru ar 3) (Breiteneder and Radauer, 2004).

3.3. Pathogen-related allergens

Pathogen-related (PR) proteins are proteins that are induced in response to abiotic stimuli, pathogen attacks, and various stress conditions (Jurkaninová, 2002). Some food allergens are related to pathogen proteins). There are 14 families into which PRs have been divided. Examples of

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Table 1. Sources, nature, cross-reactivity, and mechanism of cross-reactivity of different allergen families.

Allergen Family	Source	Specific Allergenic Protein(s)	Cross-Reactivity	Mechanism of Cross-Reactivity	References
Cupin Superfamily	Cashew Nut *(Anacardium occidentale)*	7S Globulin (vicilin-like), 11S Globulin (legumin-like)	Pistachio Nut *(Pistacia vera)*, Walnut, Peanut	Similar 3D structure and shared epitopes that trigger IgE binding	(Sicherer and Sampson, 2014)
	Pistachio Nut (*Pistacia vera*)	11S Globulin (legumin-like)	Cashew Nut, Hazelnut, Brazil Nut	Homologous proteins across nuts increase allergenic response	(Wang et al., 2014)
Prolamin Superfamily	Fish	Parvalbumin	Cod, Salmon, Tuna	IgE binding due to conserved parvalbumin structure	(Gazzaz and Rasco, 1993)
	Egg (*Gallus domesticus*)	Ovomucoid, Ovalbumin	Minor cross-reactivity with avian proteins	Cross-reactivity within avian proteins due to structural similarities	(Baumgartner and Schubert-Ullrich, 2010)
	Wheat (*Triticum aestivum*)	Gliadins, α-amylase/trypsin inhibitors	Rye, Barley, Oats	Cross-reactive IgE epitopes across cereal grains	(Battais et al., 2008)
	Peanut	2S Albumin, nsLTP	Walnut, Almond	Cross-reactive IgE-binding sites among legumes	(Bremer, 2009)
Pathogen-Related Allergens on Food	Mold-contaminated Food Products	Fungal Amylase, Beta-glucan	Cereals, Nuts, Fruits	Pathogen-produced enzymes tsichat can elicit allergenic responses	(Jurkaninová et al., 2024)
	Bacterial Contamination (LPS)	Lipopolysaccharides (LPS), Enterotoxins	Meat, Dairy, Fresh Produce	LPS proteins act as potent allergens and immunomodulators	(Daly, 2020)

allergens related to pathogenesis-related (PR) proteins include chitinases (PR-3) from avocado, banana, and chestnut; antifungal thaumatin-like proteins (PR-5) found in cherries and apples; proteins similar to the primary birch pollen allergen Bet v 1 (PR-10) from various fruits or vegetables; and lipid transfer proteins (PR-14) present in fruits and cereals (Breiteneder and Ebner, 2004). Fruits including avocado (Pers a 1), bananas and chestnuts (Cas s 5) contain class I chitinases, which are strong allergens that cross-react with latex allergens (Hev b 6.02).

PR-5 family includes thaumatin-like proteins (TLPs). In people with apple allergies, IgE-mediated symptoms are linked to Mal d 2, apple fruit-derived allergenic thaumatin-like proteins (TLPs). Using recombinant tobacco, Mal d 2 was produced in Nicotiana benthamiana plants. mosaic virus vector. Other allergens including Heme-containing enzymes called peroxidases employ H2O2 to carry out several oxidative processes. PR-9 are lignin-forming peroxidases that are triggered by pathogens and contribute to plant defense against them. After consuming specific plant foods, people with pollen allergies often experience allergic reactions. Most of these reactions are brought on by allergens of Apiaceae vegetables (like carrot and celery) and fruits (like apple and pear) that react with allergens found in birch tree-derived pollen, especially main birch pollen Bet v 1, and other tree pollens (Breiteneder and Ebner, 2004).

4. Cross-reactivity between food allergens

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Cross-reactivity refers to the ability of an IgE antibody to identify, bind, and initiate an immune response to similar allergenic molecules (homologs) (Popescu, 2015). Some examples of cross activity of various food allergens are given as:

The bird-egg syndrome is a condition where individuals with allergic respiratory issues, caused by inhaling bird feathers or dander, also experience allergic reactions upon consuming eggs, is a possible variant of cross-reactivity with eggs (Kazatsky and Wood, 2016). Pathologic, IgE-driven immune reaction to fish proteins is known as a fish allergy. Fish aeroallergens can trigger sensitization through the respiratory system, skin contact, or ingestion, with the gastrointestinal tract being the primary route for sensitization (Kuehn *et al.,* 2014).

Allergens found in wheat are gliadin and glutenin protein subunits. The primary structural protein of wheat, gluten, is made up of two main fractions based on how soluble they are in aqueous alcohols: the insoluble glutenins, which are divided into high-molecular-weight (HMW) and low-molecular-weight (LMW) subunits, and the monomeric soluble gliadins, which are categorized into α, β, γ, and Ω types based on their primary structures. Gluten-derived peptides cause an autoimmune reaction mediated by T cells in celiac disease (CD). Immunoglobulin E (IgE) antibodies play a key role in triggering the inflammatory response to various allergenic proteins in wheat allergy, including gliadins, HMW glutenins, non-specific lipid transfer protein (nsLTP), and alpha-amylase/trypsin inhibitors (Elli *et al.,* 2015).

The main allergen in fish is parvalbumin (Sharp *et al.,* 2015). In the baltic cod, beta-parvalbumin was initially

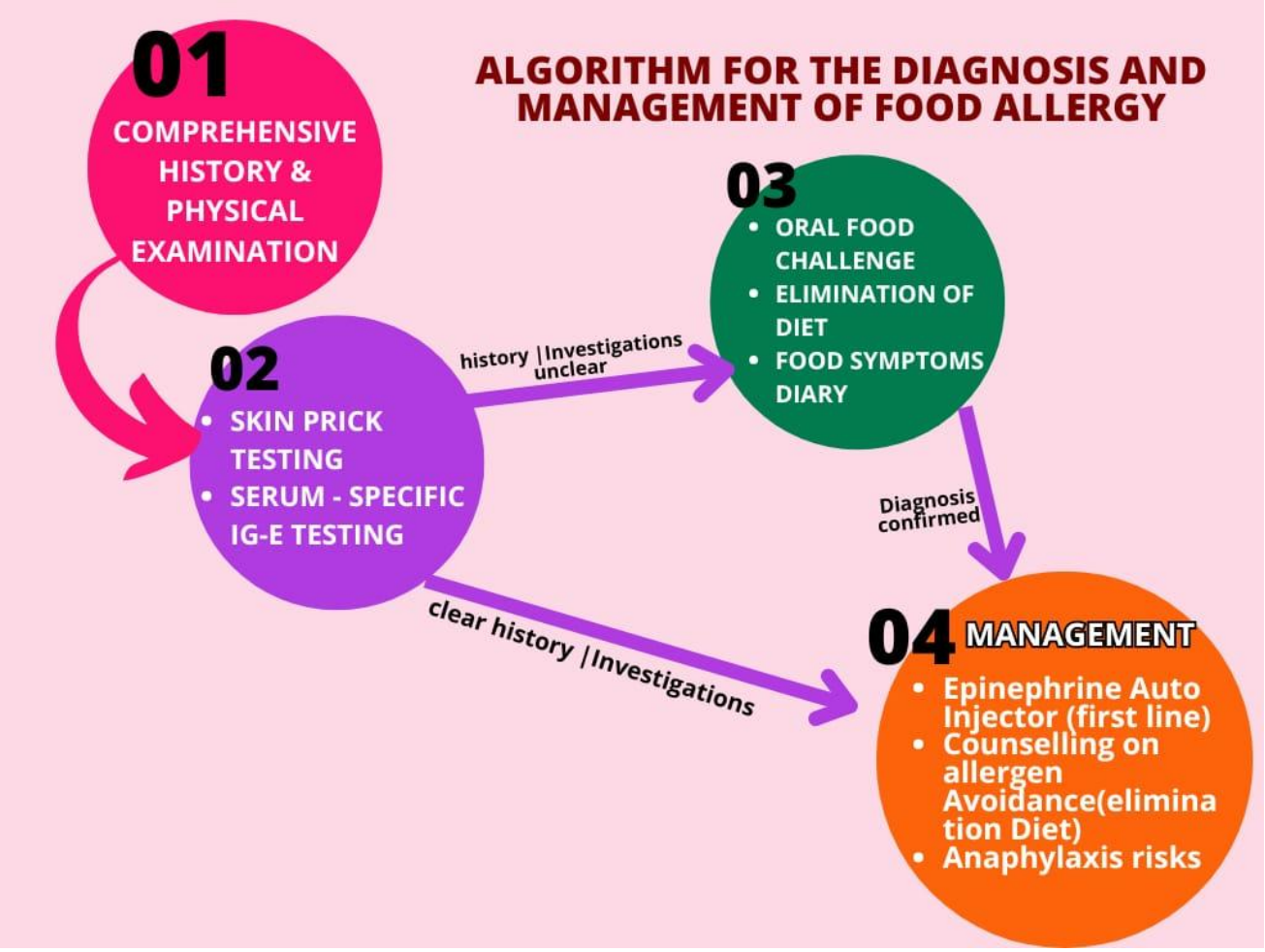


Figure 2. Algorithm for diagnosis and management of food allergy

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discovered to be a hypersensitivity due to fish. Pathologic, IgE-associated immune response for fish proteins is known as a fish allergy. Individuals encounter allergens via the respiratory system through fish-based aeroallergens, by skin contact, or through the digestive system after consuming them, with ingestion being the primary pathway for sensitization (Kuehn *et al.,* 2014).The primary allergens in cashews are Ana o1, Ana o2, and Ana o3. Like other food hypersensitivities, most of the cashew nut sensitivity reactions start with skin lesions and progress to respiratory and gastrointestinal symptoms (Mendes *et al.,* 2019).

IgE-mediated allergy responses have been documented in the tree nut known as pistachio (Pistacia vera) (Noorbakhsh *et al.,* 2010). Pistachio nuts are officially classified as containing five different allergenic proteins (Pis v1, Pis v2, Pis v3, Pis v4, and Pis v5) (Costa *et al.,* 2019). Alpha-livitin appears to be the most reported allergy to egg yolks. The most common egg allergen in egg white is ovalbumin (Walsh *et al.,* 1987). Hen's egg allergy (HEA) is a primary trigger for IgE-driven food hypersensitivity (Popescu *et al.,* 2020).

5. Advances in allergen detection

5.1. DNA detection

A sensitive and precise technology based on molecular biology methods is DNA detection in food. It uses polynucleotide probes to measure DNA amplified by the polymerase chain reaction (PCR). However, food product preparation, such as heat treatments or DNA fragmentation, can impact the precision of DNA-based techniques. Detecting DNA in food does not necessarily indicate the presence of allergenic proteins. Although DNA sequence markers cannot identify the types or quantities of allergens, they can identify contamination from allergic sources. This approach is not appropriate for evaluating how well food processing techniques reduce allergenicity (Tuppo *et al.,* 2022). Research teams creating such techniques take into consideration two primary strategies regarding DNA targets: (i) by utilizing the coding sequences of allergenic proteins, or (ii) by focusing on specific DNA markers from the allergenic substances in question. Among the possible DNA targets, single-copy or multiple-copy sequences like mitochondria, chloroplasts, or other highly repetitive sequences are frequently employed. Single copy nuclear DNA is thought to be highly practical if a dependable quantitative approach is needed because of its increased consistent number of copies in various cells & tissues, however, the latter targets offer the benefit of increased sensitivity, as they have a greater number of copies in each sample (Tuppo *et al.,* 2022).

Unlike proteins, DNA may be extracted from food matrices with efficiency and is less sensitive to extraction conditions. Then, the number of DNA techniques for detecting food allergies has been increasing in recent years.Hazelnut, peanut, soybean, sesame, (celery), mustard, lupine, pistachio, almond, and other nuts have all been detected using end-point PCR or real-time PCR techniques (Tuppo *et al.,* 2022).

5.2. SDS -PAGE

Food allergies are separated using SDS-PAGE and immunoblotting, which are one-dimensional PAGE and immunoblotting techniques. Using radio-labeled or enzyme-labeled antibodies, these procedures segregate allergenic proteins according to their molecular mass. These approaches, however, are time-consuming and tedious, which makes them inappropriate for consumer goods industries that move quickly, including the food sector (Iqbal *et al.,* 2018). These methods denature proteins, give them a negative charge, and then separate them based on molecular mass. Human IgE blotting enables the detection and characterization of specific allergens. These methods are used extensively for identifying new allergens and qualitatively determining potentially allergenic food contaminants (Monaci *et al.,* 2006)

For Example, A study examined allergenic proteins in shrimp through anion exchange column chromatography and sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). Shrimp proteins were extracted using Phosphate Buffered Saline (PBS) at pH 7.2, followed by centrifugation at 10,000 rpm for 10 minutes at 4°C. The highest protein yield was identified via SDS-PAGE. The protein profile and molecular weight of the shrimp extract were determined by SDS-PAGE, with cooked shrimp displaying a protein band at a molecular weight of 37.77 kDa (Monaci *et al.,* 2006).

5.3. Dot immunoblotting

One low-cost, semi-quantitative technique for identifying allergens in food samples is dot immunoblotting. This semi-quantitative assay uses radio-labeled and enzyme-labeled antibodies for complex analysis to identify allergenic proteins on nitrocellulose membranes. This technique replicates protein bands on thin membranes, allowing antigens to be easily accessible to specific

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antibodies. The ideal system would be a replica of the electrophoresis gel, with all protein bands represented in their native conformation. Antigens are detected in two layers: antibody-specific and detection system-conjugated molecules, which may include an amplification system for increased sensitivity. The antigen content in blotted membrane bands can be quantified using a radiolabeled probe and a transmission densitometer on an autoradiograph or fluorograph. Colored bands on a membrane can be quantified using reflectance or transmission densitometry after soaking in an organic solvent to make it transparent (Iqbal *et al.,* 2018).

This technique was utilized to assess the interaction of 10 candidate antigen epitopes with a specific protein. The peptides were applied to Nitrocellulose membranes, blocked using skim milk, and incubated with both patient sera and sera from non-allergic individuals. The membranes were subsequently treated with mouse anti-human IgE conjugated with horseradish peroxidase and visualized using ECL Plus Western blotting detection reagents (Zhang *et al.,* 2019). The overall immunogenicity of the sample was evaluated since proteins were not separated based on molecular weight. If the sample includes a purified protein, individual proteins can also be analyzed; however, the resolution of the blotting membrane limits detection for proteins with very high or low molecular weights (Zhang *et al.,* 2019).

5.4. Mass spectrometry

A non-immunological protein-based technique for identifying allergens, mass spectrometry (MS) necessitates costly equipment, intricate procedures, and laborious data analysis (Zhang *et al.,* 2019). Proteins in food samples and allergenic proteins in intricate mixtures, like those found in refined foods, can be identified using mass spectrometry-based techniques. A widely used approach known as 'bottom-up proteomics' involves the use of a specific protease to digest proteins, followed by mass spectrometry to analyze the resulting fragments. This method allows for the identification of multiple proteins or allergens in a single test. Denatured and fragmented proteins can also be detected by mass spectrometry, and extracts can be sorted using SDS-PAGE before proteolytic processing. However, there are two limitations: the ability to detect proteins that have been altered during processing and the availability of protein sequences in databases. Despite these challenges, mass spectrometry-based methods can help elucidate food allergy profiles and provide insights into unidentified allergens (Tuppo *et al.,* 2022).

Seven sesame allergens could be sensitively and specifically quantified in a single run according to recent SRM study by Ma & coworkers who used LC-MS/MS analysis based on trypsin digestion. In a diverse collection of food matrices, the study found preserved and thermally stable peptides appropriate for precise allergen identification and measurement. Additionally, pointing out the differences in allergens among sesame types, the study recommends that each allergy protein be quantified separately. Recently a study established an LC–MS/MS approach to identify gluten-containing cereals (i.e., Triticum species, including wheat and spelt, barley, and oats) and Fagopyrum esculentum Moench (buckwheat) in processed meals. This technique enables the sensitive, specific, and concurrent detection of the grains specified in food allergen labeling regulations, without requiring expensive kits or lengthy experimental procedures from sampling to results. It is also applicable for testing a broad variety of processed food products (Zhang *et al.,* 2019).

5.5. ELISA

Because of its great sensitivity and simplicity of use, ELISA is the most employed method. to identify food allergies. This technique identifies dietary proteins as indicators of allergic foods using monoclonal or polyclonal antibodies. ELISA frequently targets foods that cause allergies, including fish, shrimp, peanuts, eggs, and milk. Based on factors such as food composition, sensitivity, and the attributes of the antibody and target molecule, the ELISA format may be either sandwich (s-ELISA) or competitive (c-ELISA). In the c-ELISA experiment, an immobilized allergen and the target allergen compete on a plate. It may be augmented, indirect, or direct. Indirect ELISA employs an unlabeled immunoglobulin-specific antibody, whereas direct ELISA uses a detector antibody that has been enzyme-labeled. A chemical such as biotin is used in enhanced ELISA to increase sensitivity. The biophysical and chemical characteristics of the target allergens determine the sensitivity and specificity of ELISA formats. Protein extractability and antibody recognition may be impacted by changes in allergen structure brought on by food preparation. Allergen recovery may be impacted by heat and nonthermal processing that lowers ELISA kit performance. In complicated food matrices, denaturing and reducing agents can improve extraction efficiency. The

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sensitivity and specificity of immunochemical techniques are increased by choosing the right target analytes, detection antibodies, and extraction techniques (Zhang *et al.,* 2019).

The food industry and government use ELISA to identify allergenic proteins, particularly peanut allergies. Commercial kits like Veratox, BioKits, ELISA-TEK, and Ridascreen are available. However, heat treatment and food processing techniques can affect protein quality and cross-reactivity (Zhang *et al.,* 2019). A recent study evaluated three commercial ELISA kits, the AgraQuant Fish ELISA kit from Romer Labs and the Common Bone Fish Antigen EIA ELISA kits, versions 2 and 3 from XEMA—for detecting 57 fish species. All three test kits found only 21 percent of the species, which included rainbow trout (Oncorhynchus mykiss), European carp (Cyprinus carpio), & Atlantic cod (Gadus morhua). Only a few commercially significant fish species from the Asia-Pacific area were detected. These were the red snapper (Lutjanus erythropterus), frypan bream (Argyrops spinifer), and king threadfin (Polydactylus macrochir).

5.6. LFIA

A tool known as Lateral Flow Immunoassay (LFIA) is used to find molecules in food samples. If the target molecule is present, it binds to the antibody on a strip containing IgG antibodies unique to it. The development of an antigen-antibody complex is indicated by a signal displayed by a reporter molecule. Food samples have been successfully tested for allergens using LFIA, which is faster than ELISA (Tuppo *et al.,* 2022). The LFA platform is useful for routine food safety analysis since it offers a quick, accurate, and sensitive way to find toxins in food and water. Multiplexed LFA (xLFA) is primarily achieved through the following approaches: (i) placing multiple strips in a single cassette, with each strip targeting a different analyte; (ii) spatially organizing the detection sites on a single strip; and (iii) utilizing distinct signal reporters that emit unique signals. A step toward enabling 2-D multiplexing in LFAs (for example, by using multiple probes that produce distinguishable signals within one detection site along with several separate detection sites) involves the use of probes with different colors, which are easily integrated with standard LFIA materials and (bio)reagents. This enhances the detection capacity of the method considerably (Tuppo *et al.,* 2022).

5.7. Biosensors

In food analysis, surface plasmon resonance (SPR)--based biosensors are being utilized more and more to identify high molecular weight substances such as allergens. These biosensors identify allergens in real-time by using certain antibodies that have been immobilized on the chip surface. Modern biosensors provide label-free detection, automation, quick assay times, and high-throughput, multi-analyte measurements. Nevertheless, they are costly and necessitate skilled laboratory workers. It is anticipated that allergy test kits will be made commercially available, and certain biosensor immunoassays for allergen detection have been created.

Surface plasmon resonance (SPR) biosensing has recently been developed for detecting protein levels due to its high sensitivity to various species, including food allergens, harmful proteins, biomarker proteins, antibodies, and therapeutic proteins (Wang et al, 2016). The detection of various compounds found in food samples & biosensors may be derived from nanoparticles (NPs) is another area in which nanotechnology shows promise. Combining biological elements with physical-chemical sensors offers significant advantages for detecting and analyzing food allergens. As a result, advancements in nanoparticle technology have enhanced the use of biosensors alongside nanoparticles for ensuring food safety. Nanoparticle-based biosensors provide several important advantages over conventional techniques, such as lower costs and quicker analysis times (Kuehn *et al.,* 2014).

6. Management strategies

A food allergy can be diagnosed using clinical history, which is considered the most essential test (Sicherer and Sampson, 2018). A multidisciplinary team is the best way to manage food allergies. This group should consist of healthcare professionals such as clinicians to diagnose and determine underlying causes and risks, dietitians to identify uncommon allergens and prevent nutritional deficiencies, gastroenterologists to exclude other conditions, and psychologists to assist individuals dealing with significant anxiety or challenges to their quality of life (Muraro *et al.,* 2022)

To diagnose food allergies, in vivo, skin prick testing is frequently used. Skin prick testing (SPT) uses a variety of food extracts, some of which may differ from batch to batch and contain allergens. It is therefore common practice to do prick-to-prick testing with the food source, particularly when evaluating plant food allergy sources (fresh fruits,

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vegetables, and nuts) (Sicherer and Sampson, 2018). In vitro testing for certain IgE antibodies based on extracts has been around for a while and is still used for regular diagnosis (Sicherer and Sampson, 2018).

To confirm the existence of allergen-induced IgE in patients' blood plasma & its capacity to activate basophils, cellular assays are available. Either donor autologous cells or pre-existing cell lines are used in these assays. Cell activation can be assessed by measuring the production of histamine or sulfidoleukotrienes following passive sensitization with serum and the addition of allergen extracts or allergens (Hoffmann-Sommergruber *et al.,* 2015)

7. Conclusion

Recent advancements in allergen detection methods have enhanced the identification and management of food allergies. Techniques like SDS-PAGE, dot immunoblotting, mass spectrometry, ELISA, LFIA, and biosensors each have distinct advantages and limitations. SDS-PAGE and dot immunoblotting are effective for protein identification but less suitable for rapid, high-throughput needs. Mass spectrometry offers precise allergen detection in complex food matrices but is costly and resource-intensive. ELISA remains the most popular method due to its sensitivity and versatility, while LFIA and biosensors provide rapid detection options with varying levels of complexity and cost.

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7. Conflict of Interest

The authors declare no conflict of interest.

8. Authors' Contribution

Noor ul Ain: Conceptualization, Literature review, and Manuscript writing. Saira Ali Anjum: Data analysis, Literature review, and Manuscript editing.

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