APJAI
Asian Pacific Journal of
Allergy and Immunology

REVIEW ARTICLE

Buckwheat allergy

Feng Chen,[1] Yangshuhan Xu,[2] Kelong Ma,[1] Yuzhu Zhang,[3] Tengchuan Jin[4]

Abstract

Buckwheat, a gluten-free pseudocereal, is a traditional staple in parts of East Asia—particularly Japan, Korea, and northern China—as well as in Russia, but is rarely consumed in Southeast Asia where rice dominates the diet. Its growing use in gluten-free products worldwide has increased exposure, raising concerns about buckwheat allergy, which can manifest as urticaria, rhinoconjunctivitis, asthma, or life-threatening anaphylaxis. Both dietary ingestion and occupational inhalation pose risks. Despite relatively high sensitization rates in endemic regions, many individuals remain asymptomatic, complicating clinical interpretation. Conventional diagnostic methods using aqueous extracts often miss lipid-soluble allergens such as oleosins (e.g., Fag t 6), potentially leading to false-negative results. Component-resolved diagnostics targeting Fag e 2—a pepsin-resistant 2S albumin recognized by IgE in up to 90% of symptomatic patients—significantly enhances diagnostic specificity. Cross-reactivity with latex, peanut, and wheat has been reported, though its clinical relevance requires individual assessment. Strict avoidance remains the cornerstone of management, as no approved immunotherapy exists. Given buckwheat's frequent inclusion in unlabeled "gluten-free" foods, accurate diagnosis and patient education are critical. Future efforts should focus on standardized detection protocols that include non-aqueous extraction and the development of precision diagnostic tools.

Key words: buckwheat allergy, Fag e 2, oleosin, component-resolved diagnostics, cross-reactivity, food allergy diagnosis

Citation:
Chen, F., Xu, Y., Ma, K., Zhang, Y., Jin, T. (2025). Buckwheat allergy. *Asian Pac J Allergy Immunol*, 43(4), 753-761. https://doi.org/10.12932/ap-171025-2165

Affiliations:
[1] College of Integrated Chinese and Western Medicine/College of Life Science, Anhui University of Chinese Medicine, Hefei, Anhui, China
[2] Hefei University, School of Energy, Materials and Chemical Engineering, Hefei, Anhui Province, China
[3] Healthy Processed Foods Research Unit, USDA-ARS, Western Regional Research Center, Albany, California, United States
[4] Hefei National Laboratory for Physical Sciences at Microscale, the CAS Key Laboratory of Innate Immunity and Chronic Disease, School of Basic Medicine Sciences, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, China

Corresponding author:
1. Feng Chen
E-mail: cf121205@ahtcm.edu.cn
2. Tengchuan Jin
E-mail: jint@ustc.edu.cn

Introduction

In 2024, the Collegium Internationale Allergologicum (CIA) reported in its update on emerging allergens that newly recognized food allergens include legumes (such as peas and chickpeas), seeds (such as hemp seeds and chia seeds), tree nuts (such as cashew), pseudocereals (such as buckwheat and quinoa), certain fruits, and microalgae.[1] Buckwheat is a gluten-free pseudocereal rich in nutrients and beneficial for health,[2] but it is also a common allergenic food capable of triggering hypersensitivity reactions. Buckwheat allergy is more prevalent in Asian countries,[3] likely due to its widespread use as a staple grain substitute.

Buckwheat is traditionally consumed in parts of East Asia—particularly Japan, Korea, and northern China—and has gained increasing popularity in North America and Europe as a gluten-free functional food. Epidemiological data indicate that buckwheat allergy, though relatively rare, is clinically significant. In a survey of 92,680 elementary schoolchildren in Yokohama, Japan, the prevalence of buckwheat allergy was 0.22%.[4] A nationwide 2015 survey of 29,842 Korean schoolchildren reported a current prevalence of immediate-type buckwheat allergy of 0.13%[5] In contrast, data from China remain limited: a small study of 61 adults with occupational or dietary exposure to buckwheat in Shanxi Province found a sensitization rate of 1.6% (skin prick test positive), but no confirmed clinical allergy.[6]

Table 1. Reported buckwheat sensitization and allergy rates by country.

Country	Prevalence	Population	Data Type	Published
Japan	0.22%	92,680 elementary schoolchildren in Yokohama	Questionnaire-based allergy (symptoms/physician diagnosis)	1998
Korea	0.13%	29,842 schoolchildren (nationwide)	Parent-reported current allergy	2017
China	1.6%*	61 adults with buckwheat exposure in Shanxi	Asymptomatic sensitization (SPT+)	2000
Italy	3.6%	1,954 allergy clinic patients	Sensitization in allergic cohort	2013

*Sensitization rate; no clinical allergy confirmed.

In Italy, buckwheat sensitization was detected in 3.6% of 1,954 patients referred to allergy clinics—highest in the North (4.5%)—though this reflects a selected allergic population rather than the general public.[7] These findings are summarized in **Table 1**.

Nutritional and Functional Properties of Buckwheat

Buckwheat exhibits strong ecological adaptability and can thrive in diverse environments, including marginal soils and cool climates, although it is primarily cultivated in the Northern Hemisphere. Major producing countries include Russia, China, Ukraine, Kazakhstan, and several European nations such as Poland and France (FAOSTAT, 2023). China ranks second in global buckwheat production, with cultivation primarily concentrated in northern and southwestern regions, including Heilongjiang, Inner Mongolia, Shanxi, Yunnan, and Sichuan provinces. The two major cultivated species are common buckwheat (*Fagopyrum esculentum*) and tartary buckwheat (*Fagopyrum tataricum*).[8] Buckwheat is rich in high-quality protein, dietary fiber, flavonoids (notably rutin), and essential minerals, many of which exhibit bioactive properties. Its consumption is associated with multiple health benefits, including anti-aging, antidiabetic, hypotensive, immunomodulatory, gut microbiota-regulating, and cardiovascular protective effects.[9-11] Buckwheat has been processed into a variety of food products, such as bread, noodles, buckwheat tea, vinegar, and functional beverages.[12]

Clinical symptoms of buckwheat allergy

Buckwheat allergy was first documented in the early 20th century, with increasing recognition of its clinical significance in subsequent decades. It can elicit a range of allergic reactions, including dyspnea, rhinitis, urticaria, and angioedema.[13] In 2010, seven patients in China were diagnosed with buckwheat allergy, exhibiting symptoms such as sneezing, rhinorrhea, urticaria, pruritus, abdominal discomfort, and anaphylaxis.[14] The primary clinical manifestations of buckwheat allergy include cutaneous symptoms—such as urticaria, angioedema, atopic dermatitis, and erythema—and gastrointestinal symptoms, including nausea, vomiting, abdominal pain, and diarrhea. Systemic reactions involving two or more organ systems, including anaphylaxis, have also been observed.[15]

Notably, buckwheat can also induce non-IgE-mediated food allergy. Two Japanese case reports described buckwheat-induced food protein–induced enterocolitis syndrome (FPIES): a 4-year-old girl and a 2-year-old boy developed repeated vomiting, pallor, lethargy, and (in the girl) diarrhea 2–3 hours after ingesting buckwheat-containing noodles.[16,17] The absence of cutaneous or respiratory symptoms and the presence of systemic features like pallor and lethargy suggest relatively severe FPIES. These cases confirm that buckwheat may trigger both IgE- and non-IgE-mediated hypersensitivity.

Occupational buckwheat allergy has been increasingly recognized. A baker was reported to develop rhinoconjunctivitis and asthma due to inhalation of buckwheat flour.[18] In 2020, six food industry workers (three cooks, two bakers, and one grocery store employee) developed occupational asthma, rhinitis, or contact urticaria following exposure to buckwheat flour.[19] This year, a food industry worker experienced anaphylactic shock with urticaria, angioedema, and dyspnea after ingesting buckwheat, following previous episodes of rhinoconjunctival itching and sneezing due to inhalation of buckwheat flour.[2]

Clinical Note: Buckwheat allergy can present not only as typical IgE-mediated reactions such as urticaria or anaphylaxis, but also as non-IgE-mediated FPIES—characterized by vomiting and lethargy—or occupational respiratory symptoms. Buckwheat allergy should be considered in patients who develop unexplained gastrointestinal or respiratory reactions after consuming "gluten-free" products.

The mechanism of buckwheat allergy

The common mechanism of various food allergies lies in the abnormal immune response of the immune system to food proteins, leading to IgE-mediated or non-IgE-mediated diseases, such as eosinophilic esophagitis,[20] FPIES, and food protein-induced proctocolitis (FPIAP).[21] Food allergy usually starts in gastrointestinal tract, skin, and respiratory tract, which is probably related with barrier function damage or inflammation.[22,23] Like other food allergies, buckwheat allergy usually presents as an IgE-mediated immediate allergic reaction. After entering the gastrointestinal tract, food allergens can cross the epithelial barrier via specialized cells (e.g., M cells) or dendritic cell processes, are taken up by antigen-presenting cells (such as dendritic cells), processed into peptide fragments, and presented on the cell surface in complex with MHC class II molecules to activate T cells.[24,25]

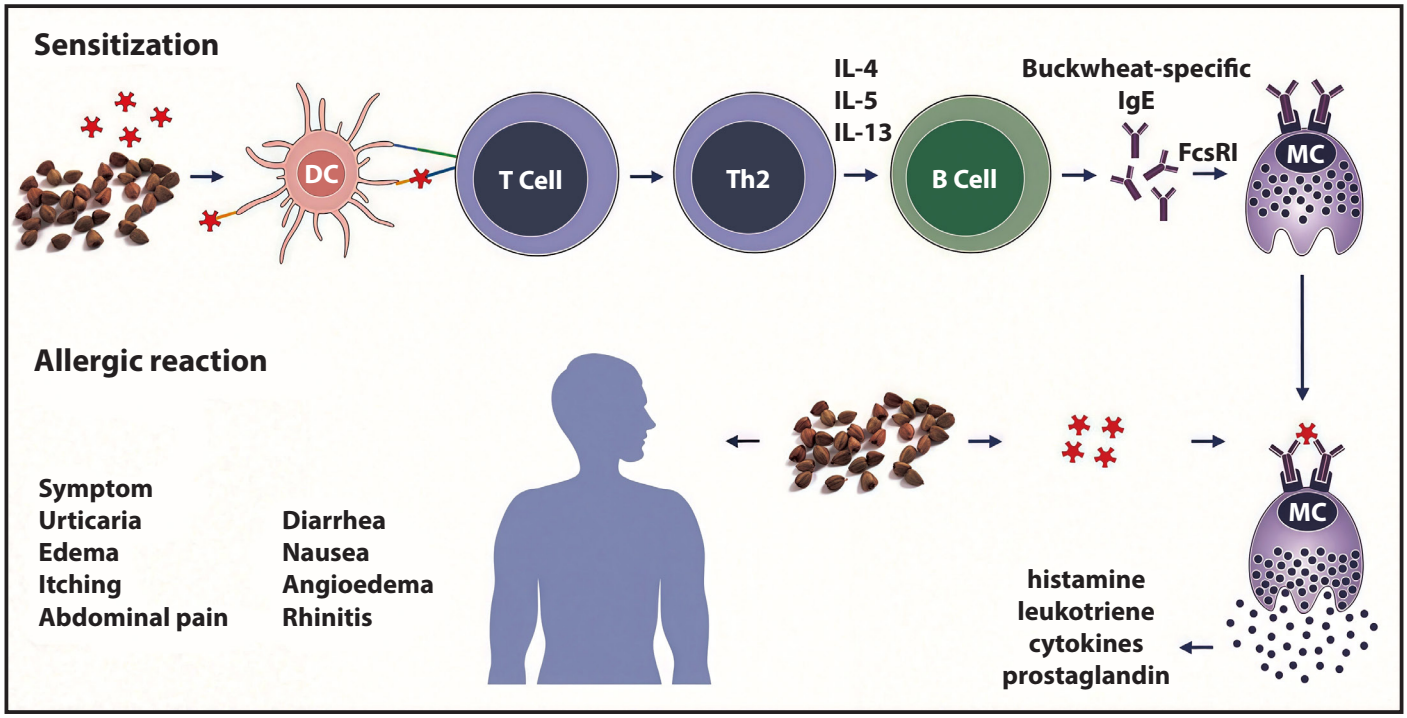

Figure 1. Allergic reaction to buckwheat.

This complex is recognized by the T cell receptor (TCR) on naive $CD4^+$ T cells, providing the first signal for T cell activation. Upon receiving co-stimulatory signals and in the presence of cytokines such as IL-4, naive T cells differentiate into type 2 helper T (Th2) cells. Th2 cells secrete cytokines, including interleukin-4 (IL-4), IL-5, and IL-13, which promote B cell class switching to produce allergen-specific IgE antibodies. These IgE antibodies bind with high affinity to FcεRI receptors on the surface of mast cells and basophils, leading to systemic sensitization. Upon re-exposure, the food allergen crosslinks allergen-specific IgE molecules bound to these cells, triggering degranulation and the release of inflammatory mediators such as histamine, leukotrienes, prostaglandins, and platelet-activating factor. These mediators cause local or systemic allergic reactions, including urticaria, asthma, and rhinitis.[24] (**Figure 1**)

Buckwheat allergen

Buckwheat contains multiple allergens. To date, five well-characterized allergens from common buckwheat (*Fagopyrum esculentum*), designated Fag e 1 to Fag e 5, and three from tartary buckwheat (*Fagopyrum tataricum*), Fag t 1, Fag t 2, and Fag t 6, have been identified. Fag e 1, a 13S globulin, was first identified in 1994 and is considered a major allergen with a molecular mass of approximately 62 kDa.[26] A cDNA encoding Fag e 1 was cloned in 1999,[27] and recombinant Fag e 1 has since been expressed and shown to be recognized by IgE in sera from buckwheat-allergic patients.[28] A Fag e 1–glucomannan conjugate prepared through glycation via the Maillard reaction reduces the IgE-binding capacity of Fag e 1, a finding also supported by studies in a BALB/c mouse model of allergy.[29] However, the clinical relevance of Fag e 1 and its utility in allergy diagnosis remain controversial.[31] Some individuals with Fag e 1–specific IgE do not experience anaphylactic reactions after consuming buckwheat, suggesting that sensitization to Fag e 1 alone may not be sufficient to predict clinical allergy.[30]

Fag e 2 is a member of the 2S albumin family, with a molecular mass of approximately 16 kDa. It is recognized by serum IgE from up to 90% of buckwheat-allergic individuals, indicating its clinical relevance.[31,32] Unlike Fag e 1, which is susceptible to digestive enzymes, Fag e 2 is resistant to pepsin digestion, contributing to its allergenic potential. Fag e 3 is a vicilin-like protein composed of a 19 kDa subunit and is considered an important allergen in buckwheat allergy.[33] Choi et al. suggested that Fag e 3 is associated with clinical buckwheat allergy, but it is less commonly involved in individuals who are sensitized without exhibiting symptoms.[34] Fag e 4, designated as antimicrobial peptides 1 and 2 (AMP1 and AMP2), is a low-abundance IgE-binding protein.[35] AMP1 and AMP2 share high sequence homology and differ by only a single amino acid residue. Fag e 5 is another member of the 7S vicilin family. In an ELISA study, serum from 6 out of 7 buckwheat-allergic patients showed IgE reactivity to Fag e 5. On SDS-PAGE, Fag e 5 separates into two bands (55 kDa and 35 kDa), suggesting the presence of disulfide bonds between its subunits.[36]

Table 2. Characterized buckwheat allergens: protein families, molecular weights, IgE reactivity, and clinical relevance.

Allergen	Protein Family	MW (kDa)	IgE Binding*	Clinical Relevance
Fag e 1	13S globulin	~62	~70%	Major but poor symptom predictor
Fag e 2	2S albumin	~16	~90%	Major allergen; digestion-resistant, high clinical relevance
Fag e 3	Vicilin-like	~19	~80%	Linked to clinical allergy
Fag e 4	Antimicrobial peptide	~ 4	~70%	Minor allergen; limited clinical role
Fag e 5	7S globulin	~55	~85%	Likely clinically relevant
Fag t 1	11S globulin	~60	~60%	Major allergen; homologous to Ara h 3/4
Fag t 2	2S albumin	~16	~40%	Minor allergen
Fag t 6	Oleosin	~18	~60%	lipid-soluble; may explain false-negative diagnoses

*IgE binding based on available patient cohort studies.

Three allergens from tartary buckwheat (*Fagopyrum tataricum*)—Fag t 1, Fag t 2, and Fag t 6—have been characterized. Fag t 1 is a major allergen that has been purified from tartary buckwheat and structurally identified.[37] Recombinant Fag t 1, expressed in *Escherichia coli*, retains the natural structure and immunological properties of the native protein.[38] It belongs to the cupin superfamily and is an 11S legumin-like protein, showing structural similarity to the peanut allergens Ara h 3 and Ara h 4.[39] Fag t 2, with a molecular mass of approximately 16 kDa, is another major allergen of tartary buckwheat and a member of the 2S albumin family. It is resistant to both pepsin digestion and heat treatment. Natural and recombinant Fag t 2 exhibit similar IgE-binding specificities.[40] Epitope mapping using ELISA and dot blot assays has identified two dominant IgE-binding epitopes: amino acid sequences at positions 108–117 and 132–141.[41]

Fag t 6, a recently identified 18-kDa allergen from tartary buckwheat reported by our group,[42] belongs to the oleosin family and is lipid-soluble. Because conventional diagnostic reagents are prepared in aqueous solutions, they may poorly extract oleosin-type allergens, potentially leading to false-negative results. The discovery of Fag t 6 improves our understanding of buckwheat and other lipid-soluble allergens and may enhance diagnostic accuracy in the future.[42] The molecular and clinical profiles of characterized buckwheat allergens are summarized in **Table 2**. Given that homologous proteins are known allergens in various foods, additional buckwheat proteins—such as oleosins in common buckwheat or antimicrobial peptides and vicilin-like proteins in tartary buckwheat—may also act as allergens.

Clinical Note: Fag e 2 is the buckwheat allergen most strongly associated with clinical reactions, and IgE positivity to Fag e 2 strongly suggests true allergy; in contrast, Fag e 1 positivity is typically linked to asymptomatic sensitization. Component-resolved diagnostics should prioritize testing for Fag e 2 to improve diagnostic specificity.

Cross-reactivity between buckwheat and other foods/agents

Cross-allergic reactions are caused by structural or sequence similarities between homologous proteins in different foods or biological sources. A patient allergic to a specific allergen in one food may also react to similar proteins in other foods due to IgE cross-reactivity. Cross-reactivity between buckwheat and various foods or materials—such as latex, rice, hazelnut (filbert), peanut, and wheat—has been reported.[43,44] In 1998, a case report described two patients with latex allergy who experienced severe allergic reactions after consuming buckwheat-containing pancakes. The first patient was a 27-year-old woman who developed contact urticaria and facial rash when wearing natural rubber gloves during her role as a football goalkeeper. Over four years, she noted worsening symptoms with new gloves. After eating a pancake made from wheat flour containing 5% buckwheat, she developed severe urticaria and expiratory dyspnea. Oral challenge with buckwheat (starting at 1 mg and increasing up to 5 g) induced nausea and vomiting. The second patient, a 23-year-old woman working in a fish processing plant, experienced pruritus, contact urticaria, rhinitis, and asthma upon exposure to natural rubber gloves. Both patients developed cyanosis and loss of consciousness after consuming the same buckwheat-containing pancake.[43] In 2014, another study reported cross-reactivity between latex and buckwheat. Immunological analyses revealed that both latex and buckwheat extracts contained allergens with a molecular mass of approximately 50 kDa. These allergens shared common IgE-binding epitopes, providing evidence for immunological cross-sensitization.[45]

While clinical co-sensitization between peanut and buckwheat has been observed, definitive evidence of IgE-mediated cross-reactivity remains limited. Although structural similarities between seed storage proteins (such as 2S albumins and 7S/11S globulins) may contribute to cross-recognition, shared IgE-binding epitopes between specific peanut and buckwheat allergens have not yet been conclusively identified.[46] Notably, many plant-derived foods contain oleosins—structural proteins associated with oil bodies. Due to their stability and lipid solubility, oleosins can act as allergens and may be missed by conventional aqueous-based diagnostic extracts. Given the structural conservation of oleosins across plant species, cross-reactivity among oleosin-containing foods (e.g., peanut, sesame, buckwheat) is biologically plausible and should be considered in patients with unexplained anaphylaxis or negative test results despite clinical reactivity.[46]

In 2014, a potential cross-reactivity between wheat and buckwheat was reported. Researchers observed that some patients with eosinophilic esophagitis (EoE) triggered by wheat also exhibited allergic reactions to buckwheat, suggesting possible immunological cross-recognition.[20] More recently, our group found that serum IgE from 5 out of 20 buckwheat-allergic patients reacted with crude wheat extracts in ELISA assays, indicating in vitro IgE cross-binding between wheat and buckwheat proteins.[41] However, the clinical relevance of this cross-reactivity requires further validation through component-resolved diagnosis and oral food challenges. In contrast, cross-reactivity between wheat and rice, as well as between buckwheat and quinoa, has been reported to be minimal and likely not clinically significant.[47] Based on these findings, rice and quinoa may serve as safer dietary alternatives for wheat-allergic individuals. However, due to the observed IgE cross-reactivity, buckwheat should not be automatically considered a safe substitute for wheat-allergic patients without individualized evaluation.[47]

In 2011, a case suggestive of cross-reactivity among buckwheat, poppy seed, and hazelnut (filbert) was reported.[44] A patient with known allergies to hazelnut and poppy seed experienced an allergic reaction after consuming a cake containing buckwheat flour. Immunological analysis indicated potential cross-reactivity between the 11S legumin-like seed storage proteins present in hazelnut and poppy seed, and the 13S globulin (Fag e 1) of buckwheat, which shares structural homology with 11S globulins.[44] However, direct evidence of IgE cross-binding between these specific proteins requires further validation through inhibition assays or component-resolved diagnostics.

Cross-reactivity between common buckwheat (*Fagopyrum esculentum*) and tartary buckwheat (*Fagopyrum tataricum*) has not been systematically studied. However, due to their close botanical relationship and high sequence homology in major seed storage proteins (such as 13S globulins and 2S albumins), immunological cross-reactivity is likely. Individuals with allergy to one species should therefore consider the potential for cross-reactive reactions when consuming the other, pending further clinical and molecular evidence.

Detection Methods and Challenges for Buckwheat Allergens

Buckwheat is often a hidden ingredient in "gluten-free" foods, posing a risk of unintended exposure for allergic individuals. Therefore, reliable detection methods are essential for food safety. Two main approaches are currently used:

Protein-based methods, such as sandwich ELISA, employ two antibodies specific to buckwheat seed storage proteins (e.g., Fag e 2) and can detect residues as low as 2 ppm in processed foods.[48] This approach directly identifies immunologically active proteins, offering high clinical relevance. However, protein degradation during thermal processing or storage may lead to false-negative results, and cross-reactivity with other pseudocereals (e.g., quinoa) remains a concern.

DNA-based methods, such as qPCR, target buckwheat-specific regions of the internal transcribed spacer (ITS) and 5.8S rRNA genes. These assays detect both cultivated (common and tartary buckwheat) and wild buckwheat species, are robust to food processing, and achieve a sensitivity of 1 ppm (w/w).[49] A key limitation is that DNA detection cannot confirm whether allergenic proteins are still intact or biologically active. Additionally, food matrix components like polysaccharides and polyphenols can inhibit PCR amplification (causing false negatives), while laboratory contamination may result in false positives.[50]

Currently, there is no internationally standardized method for quantifying buckwheat allergens, which limits the use of test results in clinical risk assessment.

Notably, commercial allergen extracts are typically prepared using aqueous solutions, which may fail to solubilize lipid-associated allergens such as oleosins. Oleosins have been identified as allergens in peanut, sesame, sunflower, and buckwheat,[42,51,52] with sesame oleosin (Ses i 6) linked to severe anaphylaxis.[53] If buckwheat oleosins (e.g., Fag e 3 or similar components in common buckwheat) are also potent allergens, current water-based detection methods may miss them, leading to false-negative diagnoses. Future testing strategies should therefore incorporate extraction and detection protocols for non-water-soluble allergens to improve diagnostic comprehensiveness and safety.

Clinical Note: Conventional aqueous-based allergen tests may overlook lipid-soluble allergens like oleosins. In patients with clear clinical reactions but negative test results, false negatives due to undetected oleosins should be considered.

Diagnosis of Buckwheat Allergy

The diagnosis of buckwheat allergy requires integration of clinical history, sensitization testing, and oral food challenge (OFC). It is crucial to emphasize that sensitization to buckwheat extract—defined as a positive skin prick test (SPT) or specific IgE (sIgE)—is relatively common in the general population, particularly in East Asian regions with high buckwheat consumption. However, the majority of these cases represent asymptomatic sensitization and do not equate to clinical allergy. This phenomenon significantly limits the specificity of SPT and sIgE, and reliance on these tests alone frequently leads to overdiagnosis

and unnecessary long-term dietary restrictions. The underlying reasons include: (1) commercial buckwheat extracts contain complex mixtures of non-allergenic proteins and cross-reactive carbohydrate determinants (CCDs), which can bind IgE non-specifically due to cross-reactivity with pollen, latex, or other plant allergens;[54] and (2) some individuals develop immunological tolerance despite being sensitized, remaining symptom-free throughout life. Therefore, a positive sensitization test must always be interpreted in the context of a compatible clinical history; otherwise, its diagnostic relevance is questionable.

In this context, SPT demonstrates superior diagnostic performance compared to sIgE for buckwheat allergy. In a study using OFC as the gold standard, sIgE showed minimal ability to predict OFC outcomes, whereas SPT wheal diameter exhibited good predictive value.[55] Although SPT also uses crude extract and has limitations, larger wheal sizes correlate with higher positive predictive values (PPV)—for example, a wheal diameter ≥ 24.1 mm corresponds to a PPV of 90%, potentially obviating the need for OFC.

To overcome these diagnostic challenges, component-resolved diagnostics (CRD) have emerged as a critical advancement. Fag e 2 (a 2S albumin) is the major clinically relevant allergen: IgE against Fag e 2 is detected in 85–90% of patients with confirmed buckwheat allergy, and this protein is heat- and digestion-resistant, strongly associated with systemic reactions.[56] In contrast, Fag e 1 positivity is often linked to asymptomatic sensitization.[30] Thus, testing for Fag e 2 effectively filters out false positives caused by crude extracts and substantially improves diagnostic specificity.

Oral food challenge (OFC) remains the diagnostic gold standard. Graded challenge protocols have been reported, starting with a very low dose (e.g., 0.1 mg buckwheat protein) and escalating to a cumulative dose of 3072 mg buckwheat protein (approximately 15 g of buckwheat flour), performed under medical supervision with a total observation period of at least 2–3 hours.[55] Open OFC is appropriate for patients with typical, objective, rapid-onset reactions; double-blind placebo-controlled food challenge (DBPCFC) is reserved only for cases with subjective or non-specific symptoms, or for research purposes.[57]

The basophil activation test (BAT), an ex vivo functional assay, has shown promising diagnostic concordance in small studies: in one cohort of 11 children, BAT results aligned with clinical history or OFC outcomes in 90.9% of tested foods.[58] Although currently limited to research settings due to lack of standardization, BAT holds potential to reduce unnecessary OFCs and may serve as an adjunctive tool for diagnosing IgE-mediated food allergy in the future.

Notably, allergic reactions often occur after consuming "gluten-free" baked goods, which frequently contain buckwheat (commonly blended with rice, corn, or quinoa). Since "gluten-free" labeling does not disclose buckwheat content, clinicians must specifically inquire about such products during history-taking. After diagnosis, patients should be educated to read full ingredient lists—not rely solely on "gluten-free" claims—and remain vigilant about cross-contamination. These steps are essential for accurate trigger identification, avoiding misdiagnosis, and ensuring effective avoidance.

In summary, we propose the following individualized diagnostic algorithm (**Figure 2**):

- For patients with typical, objective, reproducible symptoms, a positive SPT or sIgE in the appropriate clinical context is sufficient to establish a diagnosis without OFC.
- For those with atypical histories or discordant findings (e.g., asymptomatic sensitization), Fag e 2 testing should be prioritized to enhance specificity.
- OFC should be reserved only when the diagnosis remains uncertain after comprehensive evaluation, and must be conducted in a setting equipped for emergency management.

This strategy aims to minimize misdiagnosis and unwarranted dietary restrictions resulting from the poor specificity of crude buckwheat extract–based testing.

Clinical Note: Diagnosis should follow a three-step approach: (1) typical history + positive sensitization → clinical diagnosis; (2) atypical presentation → test for Fag e 2; (3) diagnostic uncertainty → proceed to open OFC. Avoid diagnosing buckwheat allergy based solely on positive SPT or sIgE to crude extract, as this risks unnecessary dietary avoidance.

Management of Buckwheat Allergy

Currently, the management of food allergies primarily revolves around strict avoidance of the allergenic food. In the event of an allergic reaction, treatment should be administered promptly based on symptom severity, using antihistamines, corticosteroids, or epinephrine—the latter being the first-line life-saving medication for anaphylaxis.[59]

However, unlike common allergens such as peanuts, there are currently no approved allergen-specific immunotherapies for buckwheat allergy. Although oral immunotherapy (OIT) has shown promise in peanut allergy (e.g., Palforzia®)[60] and is one of the most extensively researched strategies for food desensitization,[61] no mature OIT protocols for buckwheat have entered clinical trials or received approval to date. Sublingual immunotherapy (SLIT), epicutaneous immunotherapy (EPIT), and biologics (such as omalizumab and dupilumab) have demonstrated potential in other allergic conditions,[62-65] but their safety and efficacy in buckwheat allergy have not been systematically evaluated.

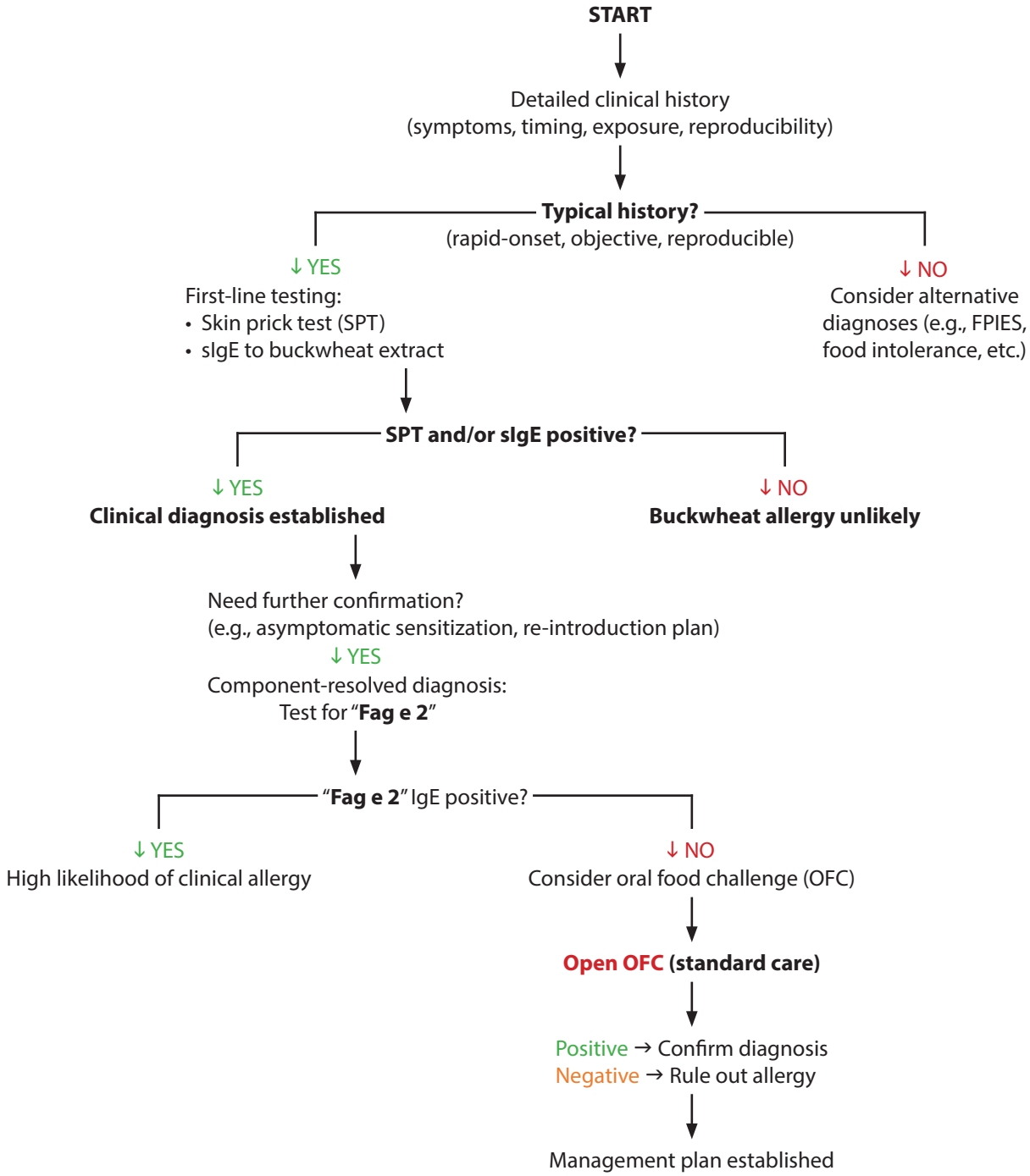

Figure 2. Stepwise diagnostic algorithm for buckwheat allergy.

In clinical practice, the management of buckwheat allergy relies heavily on strict avoidance and patient education. It is important to note that exposure routes are not limited to ingestion; inhalation of buckwheat dust (e.g., from buckwheat hull pillows) can trigger rhinitis or asthma, although skin contact rarely leads to systemic reactions.[14] A retrospective study of seven confirmed cases in China showed that all follow-up patients successfully prevented recurrence through strict buckwheat avoidance, with only one case of recurrence due to accidental ingestion.[14]

Given that buckwheat is often a hidden ingredient in "gluten-free" foods, patients need to learn to identify potential sources on food labels and carry emergency medications (such as epinephrine auto-injectors). Developing standardized diagnostic tools and specific treatments for buckwheat remains an unmet clinical need. Future research should prioritize exploring desensitization strategies based on Fag e 2 and individualized management pathways.

Clinical Note: Current management relies entirely on strict avoidance. Patients must learn to recognize hidden buckwheat in "gluten-free" foods and carry epinephrine at all times. Inhalation exposure (e.g., from buckwheat pillows) should also be avoided.

Conclusion

Buckwheat, a widely consumed pseudocereal common in Asia and increasingly popular worldwide, can trigger severe IgE-mediated allergic reactions ranging from mild urticaria to life-threatening anaphylaxis. Its frequent use as a hidden ingredient in "gluten-free" foods places allergic individuals at risk of unintentional exposure, underscoring the critical need for accurate diagnosis and effective management.

However, current sensitization tests based on crude buckwheat extracts—such as skin prick testing (SPT) and specific IgE (sIgE)—have limited specificity and often misclassify asymptomatic sensitization as clinical allergy. Component-resolved diagnostics (CRD), particularly testing for the major allergen Fag e 2, significantly improves diagnostic accuracy and helps avoid unnecessary dietary restrictions. For cases with persistent diagnostic uncertainty, open oral food challenge (OFC) remains the gold standard.

At present, management of buckwheat allergy relies entirely on strict avoidance and emergency preparedness, as no allergen-specific immunotherapies (e.g., oral immunotherapy) have been approved—a significant unmet clinical need. Future research should focus on refining the molecular characterization of buckwheat allergens, promoting the adoption of standardized diagnostic tools, and developing safe and effective desensitization strategies to improve patient outcomes and quality of life.

Author Contributions

- Conceptualization: F.C. and T.J.
- writing—original draft preparation: F.C.
- writing—review and editing: F.C., Y.X., K.M., Y.Z. and T.J.
- All authors have read and agreed to the published version of the manuscript.

Funding

Thanks to the financial support of the University Natural Sciences Research Project of Anhui Province (2023AH050730) and the Talents Support Project of Anhui University of Chinese Medicine (2022rczd006).

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Treudler R. Emerging and novel elicitors of anaphylaxis: Collegium Internationale Allergologicum update 2024. Int Arch Allergy Immunol. 2024;185(8):794–802.
2. Pilz JF, Faihs V, Kugler C, Darsow U, Biedermann T, Brockow K. Occupational buckwheat allergy in a health food store employee: from inhalative exposure to anaphylaxis. Allergol Select. 2025;9:47–49.
3. Kajita N, Yoshida K. Buckwheat allergy in Asia. Curr Allergy Asthma Rep. 2024;24(9):549–557.
4. Takahashi Y, Ichikawa S, Aihara Y, Yokota S. Buckwheat allergy in 90,000 school children in Yokohama. Arerugi. 1998;47:26–33.
5. Kim M, Lee JY, Jeon HY, Yang HK, Lee KJ, Han Y, et al. Prevalence of immediate-type food allergy in Korean schoolchildren in 2015: a nationwide, population-based study. Allergy Asthma Immunol Res. 2017;9(5):410–416.
6. Wieslander G, Norbäck D, Wang ZH, Zhang Z, Mi YH, Lin RF. Buckwheat allergy and reports on asthma and atopic disorders in Taiyuan city, Northern China. Asian Pac J Allergy Immunol. 2000;18(3):147–152.
7. Badiu I, Olivieri E, Montagni M, Guida G, Mietta S, Pizzimenti S, et al. Italian study on buckwheat allergy: prevalence and clinical features of buckwheat-sensitized patients in Italy. Int J Immunopathol Pharmacol. 2013;26(3):801–806. doi:10.1177/039463201302600328
8. Li SQ, Zhang QH. Advances in the development of functional foods from buckwheat. Crit Rev Food Sci Nutr. 2001;41(6):451–464. doi:10.1080/20014091091887
9. Zhu F. Chemical composition and health effects of Tartary buckwheat. Food Chem. 2016;203:231–245. doi:10.1016/j.foodchem.2016.02.050
10. Zhu F. Buckwheat starch: structures, properties, and applications. Trends Food Sci Technol. 2016;49:121–135. doi:10.1016/j.tifs.2015.12.002
11. Zhu F. Dietary fiber polysaccharides of amaranth, buckwheat and quinoa grains: a review of chemical structure, biological functions and food uses. Carbohydr Polym. 2020;248:116819. doi:10.1016/j.carbpol.2020.116819
12. Zhu F. Buckwheat proteins and peptides: biological functions and food applications. Trends Food Sci Technol. 2021;110:155–167. doi:10.1016/j.tifs.2021.01.081
13. Smith HL. Buckwheat-poisoning with report of a case in man (1909). Allergy Proc. 1990;11(4):193–196. doi:10.2500/108854190778880088
14. Tang R, Zhang H, Wang R. Seven Chinese patients with buckwheat allergy. Am J Med Sci. 2010;339(1):22–24. doi:10.1097/MAJ.0b013e3181bcd0a1
15. Heffler E, Nebiolo F, Asero R, Guida G, Badiu I, Pizzimenti S, et al. Clinical manifestations, co-sensitizations, and immunoblotting profiles of buckwheat-allergic patients. Allergy. 2011;66(2):264–270. doi:10.1111/j.1398-9995.2010.02469.x
16. Miyamoto M, Kato M, Yoshihara S, Terashi Y, Nakayama K, Takayanagi F, et al. Food protein-induced enterocolitis syndrome due to buckwheat: a case report. Allergol Immunopathol (Madr). 2023;51(3):25–27.
17. Satou T, Horino S, Nihei M, Miura K. Food protein-induced enterocolitis syndrome caused by buckwheat. Pediatr Int. 2019;61(10):1058–1059.
18. Erquici SP, Abraira MB, Arenas SD, Landa IU, Basterrechea IA, Moreno OB, et al. Rhinoconjunctivitis and occupational asthma due to buckwheat flour allergy. Arch Bronconeumol. 2020;56(7):466–467. doi:10.1016/j.arbres.2020.02.001
19. Jungewelter S, Airaksinen L, Pesonen M. Occupational buckwheat allergy as a cause of allergic rhinitis, asthma, contact urticaria and anaphylaxis—an emerging problem in food-handling occupations? Am J Ind Med. 2020;63(12):1047–1053. doi:10.1002/ajim.23185
20. Lopez DE, Zavala BB, Ortiz I. Cross-reactivity between buckwheat and quinoa in a patient with eosinophilic esophagitis caused by wheat. J Investig Allergol Clin Immunol. 2014;24(1):56–57.
21. Calvani M, Anania C, Cuomo B, D'Auria E, Decimo F, Indirli GC, et al. Non-IgE- or mixed IgE/non-IgE-mediated gastrointestinal food allergies in the first years of life: old and new tools for diagnosis. Nutrients. 2021;13(1):226. doi:10.3390/nu13010226
22. Brough HA, Liu AH, Sicherer S, Makinson K, Douiri A, Brown SJ, et al. Atopic dermatitis increases the effect of exposure to peanut antigen in dust on peanut sensitization and likely peanut allergy. J Allergy Clin Immunol. 2015;135(1):164–171.e249. doi:10.1016/j.jaci.2014.10.007
23. Galand C, Leyva-Castillo JM, Juhan Y, Han A, Lee MS, McKenzie ANJ, et al. IL-33 promotes food anaphylaxis in epicutaneously sensitized mice by targeting mast cells. J Allergy Clin Immunol. 2016;138(5):1356–1366. doi:10.1016/j.jaci.2016.03.056
24. Burks AW. Peanut allergy. Lancet. 2008;371(9620):1538–1546. doi:10.1016/S0140-6736(08)60659-5
25. Strobel S, Mowat AM. Oral tolerance and allergic responses to food proteins. Curr Opin Allergy Clin Immunol. 2006;6(3):207–213. doi:10.1097/01.all.0000225162.98391.81
26. Urisu A, Kondo Y, Morita Y, Wada E, Kurosawa K. Identification of a major allergen of buckwheat seeds by immunoblotting methods. Arerugi. 1994;43(12):1397–1403.
27. Nair A, Adachi T. Immunodetection and characterization of allergenic proteins in common buckwheat (Fagopyrum esculentum). Plant Biotechnol. 1999;16(5):357–362.
28. Yoshioka H, Ohmoto T, Urisu A, Mine Y, Adachi T. Expression and epitope analysis of the major allergenic protein Fag e 1 from buckwheat. J Plant Physiol. 2004;161(7):761–767. doi:10.1016/j.jplph.2004.01.010

29. Suzuki Y, Kassai M, Hirose T, Katayama S, Nakamura K, Akiyama H, et al. Modulation of immunoresponse in BALB/c mice by oral administration of Fag e 1-glucomannan conjugate. J Agric Food Chem. 2009;57(21):9787–9792. doi:10.1021/jf902490t
30. Park JW, Kang DB, Kim CW, Ko SH, Yum HY, Kim KE, et al. Identification and characterization of the major allergens of buckwheat. Allergy. 2000;55(11):1035–1041. doi:10.1034/j.1398-9995.2000.00763.x
31. Tanaka K, Matsumoto K, Akasawa A, Nakajima T, Nagasu T, Iikura Y, et al. Pepsin-resistant 16-kD buckwheat protein is associated with immediate hypersensitivity reaction in patients with buckwheat allergy. Int Arch Allergy Immunol. 2002;129(1):49–56. doi:10.1159/000065173
32. Koyano S, Takagi K, Teshima R, Sawada J. Molecular cloning of cDNA, recombinant protein expression and characterization of a buckwheat 16-kDa major allergen. Int Arch Allergy Immunol. 2006;140(1):73–81. doi:10.1159/000092038
33. Choi SY, Sohn JH, Lee YW, Lee EK, Hong CS, Park JW. Characterization of buckwheat 19-kD allergen and its application for diagnosing clinical reactivity. Int Arch Allergy Immunol. 2007;144(4): 267–274. doi:10.1159/000106315
34. Cho J, Lee JO, Choi J, Mi RP, Shon DH, Kim J, et al. Significance of 40-, 45-, and 48-kDa proteins in the moderate-to-severe clinical symptoms of buckwheat allergy. Korean J Allergy Clin Immunol. 2015; 35(6):487–494.
35. Fujimura M, Minami Y, Watanabe K, Tadera K. Purification, characterization, and sequencing of a novel type of antimicrobial peptides, Fa-AMP1 and Fa-AMP2, from seeds of buckwheat (Fagopyrum esculentum Moench.). Biosci Biotechnol Biochem. 2003;67(7):1636–1642. doi:10.1271/bbb.67.1636
36. Geiselhart S, Nagl C, Dubiela P, Pedersen AC, Bublin M, Radauer C, et al. Concomitant sensitization to legumin, Fag e 2 and Fag e 5 predicts buckwheat allergy. Clin Exp Allergy. 2018;48(2):217–224. doi:10.1111/cea.13068
37. Wang ZH, Zhang Z, Zhao ZH, Wieslander G, Norback D, Kreft I. Purification and characterization of a 24 kDa protein from tartary buckwheat seeds. Biosci Biotechnol Biochem. 2004;68(6):1409–1413. doi:10.1271/bbb.68.1409
38. Wang ZH, Wang L, Chang WJ, Li YY, Zhang Z, Wieslander G, et al. Cloning, expression, and identification of immunological activity of an allergenic protein in tartary buckwheat. Biosci Biotechnol Biochem. 2006;70(5):1195–1199. doi:10.1271/bbb.70.1195
39. Yang ZH, Li YY, Li C, Wang ZH. Synthesis of hypoallergenic derivatives of the major allergen Fag t 1 from tartary buckwheat via sequence restructuring. Food Chem Toxicol. 2012;50(8):2675–2680. doi:10.1016/j.fct.2012.03.039
40. Chen P, Guo YF, Yan Q, Li YH. Molecular cloning and characterization of Fag t 2: a 16-kDa major allergen from Tartary buckwheat seeds. Allergy. 2011;66(10):1393–1395. doi:10.1111/j.1398-9995.2011.02657.x
41. Zheng B, Zhang HN, Shen W, Wang L, Chen P. Core epitope analysis of 16 kDa allergen from tartary buckwheat. Food Chem. 2021;346:128953. doi:10.1016/j.foodchem.2020.128953
42. Chen F, Li H, Fan XJ, Li YL, Zhang CY, Zhu LX, et al. Identification of a novel major allergen in buckwheat seeds: Fag t 6. J Agric Food Chem. 2021;69(46):13315–13322. doi:10.1021/acs.jafc.1c01537
43. De Maat-Bleeker F, Stapel SO. Cross-reactivity between buckwheat and latex. Allergy. 1998;53(5):538–539.
44. Varga EM, Kollmann D, Zach M, Bohle B. Anaphylaxis to buckwheat in an atopic child: a risk factor for severe allergy to nuts and seeds? Int Arch Allergy Immunol. 2011;156(1):112–116. doi:10.1159/000321916
45. Doyen V, Lievie K, de Thier F, Ledent C, Mairesse M, Corazza F, et al. A study of allergens involved in a case of latex-buckwheat cross-allergenicity. Rev Fr Allergol. 2014;54(6):454–456. doi:10.1016/j.reval.2013.12.002
46. Kobayashi S, Katsuyama S, Wagatsuma T, Okada S, Tanabe S. Identification of a new IgE-binding epitope of peanut oleosin that cross-reacts with buckwheat. Biosci Biotechnol Biochem. 2012;76(6): 1182–1188. doi:10.1271/bbb.120063
47. Zhao JL, Li ZX, Khan MU, Gao X, Yu M, Gao HY, et al. Extraction of total wheat (Triticum aestivum) protein fractions and cross-reactivity of wheat allergens with other cereals. Food Chem. 2021;347:129064. doi:10.1016/j.foodchem.2021.129064
48. Panda R, Taylor SL, Goodman RE. Development of a sandwich enzyme-linked immunosorbent assay (ELISA) for detection of buckwheat residues in food. J Food Sci. 2010;75(5):T110–T117. doi:10.1111/j.1750-3841.2010.01683.x
49. Hirao T, Imai S, Sawada H, Shiomi N, Hachimura S, Kato H. PCR method for detecting trace amounts of buckwheat (Fagopyrum spp.) in food. Biosci Biotechnol Biochem. 2005;69(4):724–731. doi:10.1271/bbb.69.724
50. He X, Shi X. Internal amplification control and its applications in PCR detection of foodborne pathogens. Wei Sheng Wu Xue Bao. 2010;50(2):141–147.
51. Akkerdaas JH, Schocker F, Vieths S, Versteeg S, Zuidmeer L, Hefle SL, et al. Cloning of oleosin, a putative new hazelnut allergen, using a hazelnut cDNA library. Mol Nutr Food Res. 2006;50(1):18–23. doi:10.1002/mnfr.200500147
52. Pons L, Chery C, Romano A, Namour F, Artesani MC, Gueant JL. The 18 kDa peanut oleosin is a candidate allergen for IgE-mediated reactions to peanuts. Allergy. 2002;57 Suppl 72:88–93. doi:10.1034/j.1398-9995.57.s72.16.x
53. Leduc V, Moneret-Vautrin DA, Tzen JTC, Morisset M, Guerin L, Kanny G. Identification of oleosins as major allergens in sesame seed allergic patients. Allergy. 2006;61(3):349–356. doi:10.1111/j.1398-9995.2006.01013.x
54. Sindher SB, Long A, Chin AR, Hy A, Sampath V, Nadeau KC, et al. Food allergy, mechanisms, diagnosis and treatment: innovation through a multi-targeted approach. Allergy. 2022;77(10):2937–2948. doi:10.1111/all.15418
55. Yanagida N, Sato S, Takahashi K, Nagakura K, Ogura K, Asaumi T, et al. Skin prick test is more useful than specific IgE for diagnosis of buckwheat allergy: a retrospective cross-sectional study. Allergol Int. 2018;67(1): 67–71. doi:10.1016/j.alit.2017.04.005
56. Tohgi K, Kohno K, Takahashi H, Matsuo H, Nakayama S, Morita E. Usability of Fag e 2 ImmunoCAP in the diagnosis of buckwheat allergy. Arch Dermatol Res. 2011;303(9):635–642. doi:10.1007/s00403-011-1142-z
57. Vlieg-Boerstra BJ, van der Heide S, van der Valk JPM, van der Meulen GN, Otten HG, van der Ent CK, et al. Graded oral food challenges: EAACI position paper. Pediatr Allergy Immunol. 2023;34(1):e13897.
58. Lanser BJ, Giclas H, Kohlhepp A, Merkel P, Knight V. The basophil activation tests accurately predicts clinical food allergy. J Allergy Clin Immunol. 2017;139(2):AB125. doi:10.1016/j.jaci.2016.12.404
59. Oriel RC, Wang JL. Diagnosis and management of food allergy. Pediatr Clin North Am. 2019;66(5):941–956. doi:10.1016/j.pcl.2019.06.002
60. Lopes JP, Sicherer S. Food allergy: epidemiology, pathogenesis, diagnosis, prevention, and treatment. Curr Opin Immunol. 2020;66: 57–64. doi:10.1016/j.coi.2020.03.014
61. Wang JL. Advances in the management of peanut allergy (oral immunotherapy and epicutaneous immunotherapy). Allergy Asthma Proc. 2020;41(1):5–9. doi:10.2500/aap.2020.41.190011
62. Wang J, Sampson HA. Safety and efficacy of epicutaneous immunotherapy for food allergy. Pediatr Allergy Immunol. 2018;29(4): 341–349. doi:10.1111/pai.12869
63. Virkud YV, Wang JL, Shreffler WG. Enhancing the safety and efficacy of food allergy immunotherapy: a review of adjunctive therapies. Clin Rev Allergy Immunol. 2018;55(2):172–189. doi:10.1007/s12016-018-8694-z
64. Nicolaides RE, Parrish CP, Bird JA. Food allergy immunotherapy with adjuvants. Immunol Allergy Clin North Am. 2020;40(1):149–163. doi:10.1016/j.iac.2019.09.004
65. Long A, Borro M, Sampath V, Chinthrajah RS. New developments in non-allergen-specific therapy for the treatment of food allergy. Curr Allergy Asthma Rep. 2020;20(2):8. doi:10.1007/s11882-020-0897-8