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Research on the prevention and management of soy protein-related allergies in children

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ABSTRACT
Soy products are commonly used as food flavoring agents and in the weaning process of Asian children with lactose intolerance or cow's milk protein allergy; however, soy protein itself can also induce allergies in children. This article reviews the sensitization mechanisms, risk factors, detection methods, and management approaches of soy protein-induced allergies in children, aiming to prevent soy protein allergies in Chinese children and increase soy intake.

KEYWORDS
Soy protein; Allergy; Review

1 Introduction

Soy protein, as a vital plant-based protein source, exhibits dual characteristics in the field of pediatric nutrition and allergy management: it is both a potential allergen [1] and a key alternative nutritional source for children with cow ' s milk protein allergy [2]. With the global prevalence of childhood food allergies steadily rising [3], in-depth exploration of the complex relationship between soy protein and pediatric allergies has become an interdisciplinary research focus [4]. A Singaporean cohort study of healthy children under 10 years old [5] revealed that 70% of children had consumed soy products, with 95% having their first exposure before 18 months of age; soy products are commonly used as flavoring agents and milk substitutes for children with lactose intolerance [6]. However, current diagnostic approaches for soy allergy face significant limitations: among suspected allergic populations, only 14% of studies employ oral food challenge (OFC) as the diagnostic standard [7], while most rely on caregiver-reported atypical clinical histories [8] lacking objective evidence such as sIgE testing [9]. Consequently, it is essential to elucidate sensitization mechanisms and risk factors, systematically review scientific prevention strategies and efficient management approaches for soy protein-related childhood allergies, and conduct a comprehensive synthesis. This article reviews the sensitization mechanisms, risk factors, diagnostic methods, and management protocols for soy protein-induced allergies in children, aiming to prevent soy protein allergies among Chinese children while promoting increased soy consumption where appropriate.

2 Sensitization mechanisms of soybean protein

Current domestic research on soybean allergenic proteins has conducted multiple studies, with soybean remaining one of many food allergens. Its major allergenic proteins include Gly m Bd 60K (α-subunit), Gly m Bd 30K, and Gly m Bd 28K. Guan Rongxia et al [10]. utilized 175 Chinese soybean varieties as materials, employing SDS-PAGE electrophoresis and Western blotting to analyze the contents of 11S and 7S protein subunits, as well as the absence of two allergenic proteins, Gly m Bd 28K and Gly m Bd 30K. The results demonstrated that the 11S and 7S contents of tested varieties exhibited a highly significant negative correlation ($r = -0.95$), with 11S/7S ratios ranging from 0.77 to 4.67. One variant naturally lacking the β-subunit was identified. Among the 175 varieties, no materials deficient in the 30K allergenic protein were detected; however, 77 varieties lacking the 28K allergenic protein were discovered, accounting for 44.0% of tested materials. Correlation analysis indicated that the absence of the 28K allergenic protein positively correlated with protein content ($r = 0.14$) and 11S content ($r = 0.17$), while negatively correlating with 7S content ($r = -0.18$). Song Bo [11] employed the developed α-subunit-deficient near-isogenic line "cgy-2-NIL" (genetic background: soybean cultivar "Dongnong 47") as experimental material. Through backcross breeding, SSR whole-genome scanning, RNA-Seq transcriptome sequencing, and qPCR technologies, its nutritional quality (crude protein, amino acids, etc.), processing characteristics (allergenicity), and gene expression were analyzed. Results showed this genetic line exhibited significant improvements in nutritional quality (e.g., increases in crude protein, total amino acids, essential amino acids, and sulfur-containing amino acids; free arginine content reached twice that of controls) alongside reduced allergenicity. Both studies indicate that higher soybean protein content correlates with increased absence of the 28K allergenic protein and reduced soybean allergenicity. Zhou Mingming et al [12]. utilized 29 soybean germplasms from Shanxi Province (including low-allergen target germplasms) as materials. Through polyclonal antibody preparation, Western blotting, gene sequence analysis, and quantitative fluorescence PCR, they analyzed Gly m Bd 30K protein content, related gene variations, and expression mechanisms in these germplasms. The study screened two low-Gly m Bd 30K germplasms (No. 134 and Daqingdou) from

the 29 accessions, revealing that their low allergenicity relates to TA-repeat polymorphisms in the Gly m Bd 30K promoter regulating gene transcription. Among these, No. 134 represents ideal breeding material. The developed detection methods and variation markers provide technical and material support for low-allergen soybean breeding. This research constitutes the first identification of low-allergen soybeans within Shanxi germplasms, laying the foundation for cultivating new varieties. Current Chinese research on soybean protein allergenicity primarily focuses on Gly m Bd 28K. Food allergic reactions involve complex immunological mechanisms, and most allergens are heat-stable and digestion-resistant. As no effective treatment exists for food allergies—with allergen avoidance remaining the sole approach—this inevitably increases food processing costs. Future research should prioritize breeding soybean varieties lacking allergenic proteins. Thus, it is imperative to screen China's abundant soybean resources to discover materials naturally deficient in allergenic proteins, particularly those lacking the 30K allergenic protein, thereby providing elite genetic resources for soybean breeding.

3 Risk factors of soybean protein

Allergic asthma represents a relatively typical clinical condition with high prevalence, and children constitute the primary affected population. In recent years, the incidence rate of this disease has demonstrated a year-on-year increasing trend. Major inducing factors of allergic asthma exhibit close associations with food intolerance. Feng Zhigang et al [13]. conducted serum food-specific IgG antibody testing on 196 children with allergic asthma admitted between January 2017 and December 2018. Results revealed 77.0% of patients tested positive, with soybean as the primary allergen accounting for 25.8% of cases; notably, boys showed significantly lower positive rates for these allergens than girls, and the variety of food intolerances decreased with age. This indicates that the sensitization potential of soybean protein constitutes a significant trigger for childhood allergic asthma. Serum IgG antibody detection may assist etiological diagnosis, necessitating prioritized screening for girls and younger patients, while targeted dietary modifications may alleviate symptoms. Xia Yiru et al [14]. performed serum food-specific IgG antibody testing on 60 pediatric allergic asthma patients admitted between April 2017 and April 2019, analyzing plant-based (soybean) food antibody positivity rates along with gender and age differences. Results demonstrated significantly higher soybean intolerance positivity rates in girls than boys. Children aged 1-7 years exhibited greater susceptibility to ⩾2 food intolerances, while those aged 8-12 years showed higher proportions of single-food intolerance. This confirms significant correlations between childhood allergic asthma and food intolerance, with girls bearing higher soybean intolerance risks. Younger patients (1-7 years) require vigilance for multiple food intolerances. Testing enables precise identification of intolerable foods, facilitating age-specific dietary strategies where targeted nutritional adjustments may improve asthma symptoms. The above studies collectively indicate significant associations between childhood allergic asthma and soybean protein intolerance, necessitating prioritized soybean screening for girls, while children aged 1-7 years require vigilance against multiple intolerances.

4 Testing methods for soy protein allergenicity

4.1 PCR method

Xie Wenjia et al [15]. employed probe-primer fluorescent PCR quantification (steps: DNA extraction, concentration measurement, fluorescent quantitative PCR) to address P34 gene variants in soybeans from polluted areas induced by environmental contaminants—a challenge undetectable by conventional methods. They analyzed technical sensitivity, practical applicability, and environmental correlations. Results demonstrated successful detection of P34 gene variants in contaminated soybeans (missed by traditional methods), with applicability across the entire supply chain from raw materials to processed foods. This indicates environmental pollution directly induces P34 gene mutations that generate novel allergenic proteins. The technique establishes the world's first fluorescent PCR detection standard for P34 genes, providing technical support for "pollution tracing + allergy risk early warning." Functioning like a "gene radar," it exposes hidden allergens induced by pollutants, eliminating food safety risks at the source.

4.2 Immunological methods

4.2.1 Enzyme-linked immunosorbent assay (ELISA)

Guo Wenwei et al [16]. performed sIgE antibody testing via ELISA on 73,711 allergic children (aged 0–14) from January 2020 to August 2022, analyzing overall positivity rates, age distribution, allergen types, demographic differences, and key allergen trends. Results showed: 41.96% overall positivity; preschool children (4–6 years) had highest positivity; boys exhibited higher overall positivity than girls except for dust mites/egg yolk allergens; food allergen (including soybean) positivity decreased with age (highest risk in infancy), while inhalant allergen positivity increased (peak risk in school age). This reveals "age-gender" dual-dimensional patterns in pediatric allergies. Age is a critical factor: 4–6 years marks peak food allergy susceptibility; >6 years shifts to inhalant dominance. Soy sensitization decreases with age, necessitating strict

soybean avoidance in infancy and broader screening for boys, while monitoring dust mite/egg yolk allergies in girls with age-stratified interventions.

4.2.2 Combined sIgG (ELISA) and sIgE (Immunoblot) Testing

Zhang Yi et al [17]. evaluated combined sIgG (ELISA) and sIgE (immunoblot) testing for early diagnosis in 90 allergic children, analyzing food allergen positivity, primary sensitizing foods, inhalant allergen distribution, and combined diagnostic value. Results showed: sIgG positivity 93.33% (top foods: milk, egg, soybean; severe sensitivity: milk/egg); sIgE positivity 44.44% (top foods: beef/lamb/milk; severe sensitivity: egg/shellfish); inhalant sIgE positivity 34.44% (primary allergen: dust mites). Significant inconsistency and strong complementarity between methods were observed, with soybean ranking top 3 in sIgG—indicating non-IgE-mediated delayed allergy risks. Sole reliance on sIgE misses 56% of allergies; sIgG better detects food allergies (especially soybean). Combined testing provides comprehensive coverage for immediate/delayed allergies, forming a "gold standard combination" for early diagnosis and essential for managing soybean-related delayed allergies to guide personalized interventions.

4.3 Mass spectrometry, chromatography, and chromatography-mass spectrometry

4.3.1 Liquid chromatography-tandem high-resolution mass spectrometry (LC-HRMS)

Liu Huanlong [18] utilized LC-HRMS to study four major allergenic foods (milk, peanut, egg, soybean), analyzing allergenic protein identification, signature peptide screening, methodological validation, and practical applications. The method identified signature allergens and quantitative peptides (soybean: Gly m 6, peptide VIVPONFVAAR), demonstrating high sensitivity (detection limits: 1 mg/kg for milk/egg in biscuits, 2.5 mg/kg for peanut/soybean) with excellent accuracy/precision. This achieves simultaneous quantification of four major allergens for the first time, providing a gold standard for food regulation. Targeting soybean ' s signature peptide enables precise risk monitoring and exposes food labeling loopholes. Functioning as a "food safety guardian," it accurately detects hidden soybean allergens.

4.3.2 Chromatography and chromatography-mass spectrometry

Chromatography initially separated substances, but technological advances enabled methods like HPLC to separate and identify food components. Since certain proteins cannot be definitively identified by chromatography or mass spectrometry alone, liquid chromatography-mass spectrometry (LC-MS) is also applied in allergen detection [19].

4.4 Radioallergosorbent inhibition test (EAST/RAST Inhibition)

Zhu Liyan et al [20]. developed dual-path immunoassays (sandwich ELISA + competitive ELISA) for soybean complex allergens (Gly m 5/6/7), establishing high-precision detection to address hidden allergens in processed foods. Analyses covered method performance, real-sample applicability, and comparative evaluations. Results showed: sandwich ELISA linear range 0.0078–30 ng/mL (ultra-sensitive), competitive ELISA linear range 10–100,000 ng/mL (sensitivity 10 ng/mL). Sandwich ELISA achieved higher recovery in simple matrices, while competitive ELISA excelled in complex/fermented foods. This indicates sandwich ELISA (detecting intact proteins at ppt-level sensitivity) is optimal for lightly processed foods, whereas competitive ELISA (tolerating denatured proteins with anti-matrix interference) suits deeply processed foods. The complementary dual-ELISA strategy achieves "zero missed detection" for soybean allergens across all processed food categories, establishing dual safeguards for food safety.

5 Management approaches for soy protein allergenicity

5.1 Probiotic treatment

Zhu Jierui [21] utilized eight industrial lactic acid bacteria strains and a soy protein-sensitized mouse model, employing multidimensional immunological analysis (including in vitro co-culture, in vivo mouse models, flow cytometry, 16S rRNA sequencing) to investigate mechanisms of lactic acid bacteria in alleviating soy allergy and identify probiotic alternatives to drug therapy. Analyses covered strain screening, allergic phenotypes, immunomodulation, and gut microbiota-immune axis interactions. Results identified Lactobacillus melissus CICC6081, Lactobacillus plantarum subsp. plantarum CICC20988, and Lactobacillus melissus (formerly L. gallinarum) CICC6103 as top three anti-allergenic strains. These significantly elevated IFN- γ/IL-4 ratios to reverse Th2-type allergic responses, clinically manifesting as reduced allergy scores, repaired intestinal barriers, decreased gut inflammation, lowered serum allergic antibodies (IgE/IgG1 reduction > 50%), modulated T-cell differentiation (↓ Th2/Th17 cells, ↑ Treg cells), and regulated gut microbiota (↑ Firmicutes/Bacteroidetes, ↓ harmful Bacillales). Mechanistic analyses revealed these probiotics exert anti-allergic effects through dual pathways: an immunomodulatory route ("inhibiting Th2/Th17 differentiation + promoting Treg differentiation") and a microbiota regulation route ("microbiome remodeling + enhanced gut barrier + reduced allergen permeation"). These strains demonstrate clinical value by combining "immune braking (Treg) + microbial shielding" to suppress soy allergy at its inception.

5.2 Extrusion processing

Chang Yongfeng [22] (affiliated with food engineering institution) investigated dual mechanisms of allergenicity reduction and functional enhancement in soy protein isolate (SPI) using extrusion modification systems (precisely controlled temperature, rotation speed, moisture content) coupled with multidimensional analysis (immunoassays: ELISA/Western blot; structural characterization: SDS-PAGE/UV-fluorescence/FTIR/electron microscopy; functional evaluation: emulsification/antioxidant properties). Results demonstrated under optimal parameters (140°C, 110 rpm, 42% moisture): allergenicity decreased precipitously with 81.90% antigen inhibition and key epitope inactivation; structural reorganization occurred where 75/115 allergen proteins degraded in primary structure, α-helices decreased/random coils increased in secondary structure, fluorescence red-shifted/surface hydrophobicity decreased in tertiary structure, and aggregates transformed from spherical to coarse clusters with dominant molecular forces shifting from hydrophobic to hydrogen bonding; simultaneous safety-functionality synergy emerged through improved digestive safety (reduced potential allergenicity + increased digestibility) and enhanced functionality (improved emulsification/antioxidant properties despite reduced foaming). This extrusion protocol establishes 140°C/110rpm/42% moisture as gold-standard parameters, transforming SPI into a "high-emulsification + heat-tolerant + hypoallergenic" super-protein while cautioning against functional degradation from over-processing. Extrusion ultimately converts allergenic soy protein into a safe, versatile industrial ingredient.

5.3 Enzymatic hydrolysis technology

Hui Tianran et al. [23] (Changshu Institute of Technology & Troy University) systematically reviewed four major allergen-reduction technologies (thermal processing, ultra-high pressure, enzymatic treatment, genetic engineering) targeting key soy allergens (β-conglycinin/glycinin/Gly m Bd 28K/P34). Analyses covered allergen specificity, reduction principles, comparative efficacy, and application bottlenecks. Key findings: thermal processing achieved 30%-60% allergenicity reduction (pros: simple/low-cost; cons: nutrient loss/flavor deterioration); ultra-high pressure achieved 50%-80% reduction (pros: nutrient retention/chemical-free; cons: expensive equipment/high energy consumption); enzymatic hydrolysis achieved 70%-95% reduction (pros: high specificity/mild conditions; cons: enzyme cost/bitter peptides); genetic engineering achieved >90% reduction (pros: permanent/source-level solution; cons: regulatory restrictions/public acceptance issues). Critical conclusions identified enzymatic hydrolysis as the most effective current technology, ultra-high pressure as the most industrializable, and CRISPR gene editing as the future paradigm. Enzyme-ultrapressure synergy enables >95% allergen reduction with zero nutrient loss, while gene-edited varieties may yield natural hypoallergenic "golden soybeans". Thermal processing risks generating neo-allergenic epitopes requiring monitoring. Enzymatic hydrolysis represents the current "surgical scalpel" for soy desensitization, with genetic editing as the future "beacon of hope".

5.4 Epitope-targeted treatment

Rui Xin et al. [24] (College of Food Science, Nanjing Agricultural University) employed multi-scale systems analysis (epitope mapping/peptide scanning/molecular docking, processing impact assessment, digestive fate tracking, immune interaction profiling) to investigate soy allergenic epitopes (antigenic determinants). Analyses examined epitope structural basis, processing interventions, digestive outcomes, and immune regulation blind spots to establish structure-function models guiding precision desensitization technologies. Key revelations: 7S globulins feature linear epitopes vulnerable to enzymatic cleavage; 11S globulins contain heat-resistant conformational epitopes; Gly m Bd 30K harbors immunodominant epitopes surviving gut passage to activate dendritic cells. Processing efficacy: enzymatic treatment achieved 70%-95% epitope destruction via peptide bond cleavage; extrusion achieved 60%-85% via mechanical shearing + thermal denaturation; ultra-high pressure achieved 40%-70% via hydrogen bond disruption; thermal processing achieved 30%-50% with partial epitope thermostability. Digestive-immune findings: intact β-conglycinin epitopes resist proteases and activate Th2 polarization while evading immune tolerance via Treg suppression. Future strategies involve epitope shielding/deletion/transformation, with cautions against neo-epitope generation during over-processing requiring dynamic monitoring systems. The ultimate conclusion asserts that conquering soy allergy hinges on "neutralizing epitopes first", where future foods will be dominated by "epitope-free formulations".

6 Summary

In Asian children's diets, soy protein serves both as a crucial nutritional alternative for those with lactose intolerance or cow's milk protein allergy and as a potential allergen. Current limitations in soybean allergy diagnosis necessitate systematic elucidation of related mechanisms and prevention strategies. Studies have identified Gly m Bd 28K, 30K, and P34 as major allergenic proteins, with Chinese scholars achieving breakthroughs in hypoallergenic soybean breeding; clinical investigations revealed a notably higher proportion of soybean intolerance among children with allergic asthma, demonstrating distinct gender and age disparities; testing methodologies encompass genetic, immunological, mass

spectrometry, and dual-ELISA techniques; management approaches include probiotic interventions, extrusion processing, and enzymatic hydrolysis, while gene editing and combined-technique applications represent future directions. Collectively, multidimensional strategies—promoting hypoallergenic varieties, optimizing diagnostic protocols, and strengthening clinical management—must be implemented to advance relevant technologies, thereby balancing soy's nutritional benefits against allergenic risks to safeguard child health.

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