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Immunoglobulin E binding capacity to various types of Korean soy sauces among children sensitized to wheat and soybean

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Abstract

Background: Soy sauce (SS) is made from soy or a mix of soybean and wheat proteins. With the rise in global consumption of Korean SS, understanding the allergenicity of its different types is essential.

Objective: This study is the first to evaluate whether the immunoglobulin E binding capacity (IgE^+) in children sensitized to soybeans or wheat varies by SS types.

Methods: Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and an enzyme-linked immunosorbent assay (ELISA) using pooled and individual sera were performed with three SS types. Inhibition ELISA was performed using SS concentrate, extracts of wheat, and soybean.

Results: Guk-SS showed very faint protein bands, on SDS-PAGE. ELISA (pooled sera, n = 36) indicated that all groups had the lowest IgE^+ to Guk-SS. In individual ELISA, patients sensitized to both wheat and soybeans (WS; n = 4) showed significantly higher IgE^+ to all SS types (Yangjo > Jin > Guk) than those sensitized to wheat (W; n = 3) or Soy (S; n = 3) alone. The W group had IgE^+ similar to the control group for Guk and Jin-SS, while the S group showed slightly higher IgE^+ to Yangjo-SS. When soybean was used as an inhibitor, the IgE^+ to Yangjo-SS and Jin-SS was inhibited by more than 50% (Yangjo > Jin). In contrast, wheat exhibited only subtle inhibition of both SS (< 20%). Converse showed similar results.

Conclusion: For pediatric patients sensitized to wheat, it is suggested that Korean SS be carefully introduced at home. For patients sensitized to soybeans, it is safest to try Guk-SS before attempting other types.

Key words: soy sauce, wheat hypersensitivity, soybean hypersensitivity, IgE-mediated allergy, food hypersensitivity

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Introduction

Korean soy sauce (SS) is a seasoning used in many countries, with Meju commonly used as a main ingredient.[1] To create Meju commercially, soybeans that have undergone high temperature and pressure with pulverized and roasted wheat are commonly used together.[1,2] Therefore, it is rare to find Korean SS without soybeans and wheat as raw materials, but diverse food processing[3-5] could alter the allergenicity of soybean and wheat.[3,6-8] Since soybean and wheat are the major causative factors of immunoglobulin E (IgE)-mediated food allergy (FA) in children,[9,10] it is essential to elucidate these allergenicity changes to inform proper diet guidance.[11]

In addition to fermentation, heat treatment and filtration could induce diverse changes in the antigenicity of SS.[2,11,12] Gly m 4 (pathogenesis-related protein, 17 kDa), among the major soybean allergens that cross-react with birch pollen,[13] was not detected in fermented soy products. Contrastingly, Gly m 6 (glycinin, 11S globulin, 20–40 kDa)[14] is a storage protein whose Immunoglobulin E binding capacity (IgE^+) is increased upon exposure to heat[5,13] and is among the main allergenic components in children with soybean allergy.[15] Gly m 8 (2S albumin, 28 kDa) has been recently shown to be the major allergen in severe pediatric soybean allergy; further, it is stable to the digestion.[16] However, its allergenicity changes upon exposure to heat or fermentation remain unclear. Regarding wheat, glutenin is known to be relatively stable for food processing, but potentially losing its allergenicity;[17,18] a previous study on fermented Japanese SS reported the absence of IgE-binding wheat proteins in patients with wheat allergy.[12]

There are numerous types of Korean SS; however, they could be broadly divided into three types: Guk-SS, which is manufactured by soaking Meju in normal saline, fermenting, and boiling the filtered extract; Yangjo-SS, which is processed with defatted soy flour, wheat, and alcohol; and Jin-SS, which is a mixture of acid-hydrolyzed SS and Yangjo.[1] Allergic responses to different types of Korean SS could be influenced by variations in fermentation and processing, as well as the immunological characteristics of patients with soybean or wheat allergy. There have been no studies on allergenicity differences across different types of Korean SS. Moreover, the clinical reactivity of patients with wheat and soybean allergy to Korean SS remains unclear.

This study aims to evaluate soybean and wheat allergenicity variations across different types of Korean SS. Additionally, we strive to investigate whether pediatric patients sensitized to soybean or wheat exhibit different IgE^+ according to the type of Korean SS.

Methods

Patients and sera

Between January 2018 and January 2021, we identified all children referred to Ajou University Hospital (Suwon, Korea) for examination of suspected wheat or soybean allergic reactions. Among them, we examined patients aged < 10 years who had undergone ImmunoCAP assays (Thermo Fisher Scientific, Waltham, MA, USA) for both soybean and wheat serum-specific IgE (sIgE) concentrations, and had agreed on the further use of sera at the time of sampling. Immunological findings were classified into three groups as follows: WS (soybean sIgE > 0.70 & wheat sIgE > 0.70); S (soybean sIgE > 0.70 & wheat sIgE ≤ 0.35); W (soybean sIgE ≤ 0.35 & wheat sIgE > 0.70); Control (soybean sIgE ≤ 0.35 & wheat sIgE ≤ 0.35). The interval between 0.35–0.7 kU/L represents an equivocal zone where sensitization status may not be definitively established. In our study, individuals within this range were excluded to maintain a clear distinction between sensitized and non-sensitized groups. If the concentration result is reported as < 0.05, it is interpreted as 0.01. The sera of the participants were stored at -20°C until further testing. The clinical characteristics of the participants were collected from medical records and via telephone interviews with parents. The study protocol was approved by the Institutional Review Board of Ajou University Medical Center (AJOUIRB -KS-2023-248). Informed consent for study participation was obtained from the parents of all participants.

Preparation of concentrates and extracts

Three types of SS were purchased from the local market: Guk-SS (Sampyo, Gukganjang-for soup and vegetable®), Jin-SS (Sampyo, Jinganjang-gold F3®), and Yangjo-SS (Sampyo, Yangjoganjang-501®) to obtain protein extracts. (**Figure 1**). Without any specific extraction process, SS samples were directly used for SDS-PAGE and ELISA experiments. Initially, the protein content in SS was too low to perform the experiments. Therefore, to get suitable protein concentration, samples were concentrated by centrifugation at 14,000 rpm for 45 min using a centrifugal filter (Amicon® Ultra 0.5 mL, MW cutoff: 3 kDa). Soybean and wheat flour were purchased from a local store, and crude extracts were prepared using the following processes. 200 g of soybean was blended by Waring blender with 1 x phosphate buffered saline (PBS, pH 7.4; 1:4 w/v) solution and stirred overnight at 4°C. Extracts were centrifuged at 14,000 rpm for 1 h at 4°C, and then supernatants were defatted using cold petroleum ether (1:1 v/v) seven times for a duration of 10 minutes. After dialyzing against 1 x PBS solution in a dialysis membrane bag (pore size cutoff: 3.5 kDa) for more than 48 h at 4°C, the extract was filtered by a syringe filter (0.22-µm) and freeze-dried. To get wheat crude extract, wheat flour was added to 1 x PBS (1:10 w/v) and extracted for 24 h at 4°C and centrifuged at 12,000 rpm for 20 min. The supernatant was dialyzed against PBS in a cellophane tube (pore size cutoff: 6000-8000 Da) for 48 h. Then the sample was centrifuged once again at 12,000 rpm for 20 min, filtered by a syringe filter (0.2-µm), and freeze-dried. Protein concentrations were measured according to the Bradford assay (Bio-Rad, Hercules, CA, USA) using a microplate reader.

Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE)

For SDS-PAGE, the SS concentrates were measured by column concentration at 14,000 rpm for 45 minutes. Yangjo-SS and Jin-SS were prepared at a protein contents of 15 µg/mL. Given the relatively low protein contents of Guk-SS, it required to be mixed with 12.5 µL of sample buffer (Koma Biotech) and heated at 100°C for 10 minutes. Subsequently, the marker (SeeBlue® plus2, Invitrogen, San Diego, CA, USA) and SS concentrates were loaded onto a 4%–20% Tris-Glycine gradient gel (Koma Biotech) and electrophoresed at 100 V for 2 h and 30 min. Subsequently, protein bands were observed after staining.

ELISA (enzyme-linked immunosorbent assay) and inhibition ELISA

To assess IgE^+ with different types of SS, we conducted an initial ELISA using pooled sera, followed by individual ELISA analysis according to specific groups. Additionally, we performed inhibition ELISA to evaluate cross-reactivity among wheat, soybean, and various types of SS. The ELISA method employed in this study was as follows: In the ELISA assay, 96-well microplates (Corning Incorporated, USA) were coated with 5 µg/mL of each sample (soybean, wheat, Yangjo-SS, and Jin-SS) in coating buffer and incubated overnight at 4°C. Following five washes with

Product types	 **(a)**	 **(b)**	 **(c)**
Major ingredients	Meju	Acid-hydrolyzed soy sauce 70% Yangjo soy sauce 30%	Defatted soy flour, wheat flour and alcohol
Processing	Meju is prepared by soaking soybeans in salt water; steaming them at high temperature and pressure; adding wheat roasted and grinded. Then, mix and ferment.	Acid hydrolyzed soy sauce is made by decomposing defatted soybean with hydrochloric acid; adding sodium bicarbonate	Obtain lysate liquid of defatted soybean; adding wheat flour to lysate liquid; culturing and separating the fermented soy sauce

Figure 1. The representative types of Korean soy sauces. (a) Guk-SS (Sampyo, Gukganjang-for soup and vegetable®); (b) Jin-SS (Sampyo, Jinganjang-gold F3®); (c) Yangjo-SS (Sampyo, Yangjoganjang-501®).

0.05% phosphate-buffered saline solution (PBST), the plates were blocked with 200 μL of blocking buffer (10% fetal bovine serum in PBS) for 2 h at room temperature (RT). Subsequently, 100 μL of the antibody-antigen mixture (equally mixed pooled/individual sera diluted 1:10 in blocking buffer) and serially diluted inhibitors (0, 0.1, 1, 10, and 100 μg/mL) were added to the wells and incubated for 2 h at RT. In each inhibition ELISA, soybean, wheat, Yangjo-SS, Jin-SS, and fetal bovine serum were used as inhibitors, representing the major allergenic ingredients and SS types to evaluate cross-reactivity. Serial dilutions of inhibitors were added to determine the extent to which IgE^+ was reduced. After washing the microplate wells with 0.05% PBST, 100 μL of the working detector (a mixture of horseradish peroxidase and biotinylated anti-human IgE, diluted to 1:1,000) was added to each well and incubated at RT for 1 h. Next, the wells were reacted with 100 μL of TMB (3,3′,5,5′-tetramethylbenzidine; BD PharMigen) substrate solution. The reaction was stopped with 2N H_2SO_4; moreover, the optical densities (OD) were measured at 450 nm using a microplate reader (iMark™ Microplate Absorbance Reader, Bio-Rad). The percentage of inhibition by each inhibitor, to measure the relative cross-reactivity of each inhibitor, was calculated using the following formula: [((OD control - OD sample) / OD control) × 100%]. The analysis was conducted with the assistance of advanced data processing techniques provided by ChatGPT (version based on GPT-4 architecture), a language model developed by OpenAI.

Results

Clinical and immunological characteristics of the participants

We included 20 subjects (WS = 9; wheat and soybean sensitizer, S = 6; soybean sensitizer, W = 5; wheat sensitizer) and 9 controls with available serum samples and clinical information (**Table 1**). The median age of the subjects was 23.0 months (range: 5–119 months). Among the WS group, 6 individuals had tried both wheat and soybean, but only one (WS-8) was able to tolerate both. This 67-month-old girl, who had previously experienced anaphylaxis to wheat, successfully passed wheat oral food challenges during regular follow-ups. In the S group, 2 individuals tried soybean, and both exhibited clinical allergic symptoms. In the W group, no one had tried wheat before. One patient (WS-4) had a history of SS, soybean, and wheat consumption. This 69-month-old girl has had an elimination diet for soybean and wheat since 7 months but was accidentally exposed to wheat at the age of 7 and 12 months, which led to the development of whole-body urticaria. At the age of 24 months, she consumed SS and soybean paste without experiencing allergic symptoms.

Table 1. Clinical and immunological characteristics of the participants. (n = 29)

Group-No.	Sex	Age (m)	Total IgE	Wheat-sIgE	Soy-sIgE	Clinical history related to food allergy		
						Allergy to	Tolerable to	Never tried before
WS-1	F	13	188	1.23	9.72	Soybean		Wheat
WS-2	F	28	763	35.7	13.0	Wheat		Soybean
WS-3	F	22	571	37.5	15.1	Wheat	Tofu	Soya milk
WS-4*	F	69	1877	11.6	22.4	Wheat, soybean	Soy sauce	
WS-5*	M	47	604	22.1	20.9		Wheat	Soybean
WS-6	F	37	1088	30.9	15.2	Wheat	Soya milk, tofu	
WS-7	M	24	686	23.7	10.1	Wheat, soybean		
WS-8*	F	67	916	5.81	12.1		Wheat (previously anaphylaxis), soybean	
WS-9*	F	119	890	5.06	10.7	Wheat, soybean		
S-1	M	14	68	0.11	0.78			Wheat, soybean
S-2*	M	22	96	0.30	3.44	Soybean		Wheat
S-3	M	6	40	0.01	1.73			Wheat, soybean
S-4	M	6	111	0.08	1.56			Wheat, soybean
S-5*	F	35	204	0.09	7.67			Wheat, soybean
S-6*	F	16	120	0.25	4.79	Soybean	Wheat	
W-1	M	7	58	0.80	0.01			Wheat, soybean
W-2*	F	7	201	23.0	0.15			Wheat, soybean
W-3*	M	6	381	1.29	0.25			Wheat, soybean
W-4*	M	5	135	1.54	0.01			Wheat, soybean
W-5	F	15	37	1.08	0.01		Tofu	Wheat
C-1	M	8	< 2	0.01	0.01			Wheat, soybean
C-2	F	4	< 2	0.01	0.01			Wheat, soybean
C-3	F	14	4	0.01	0.01		Wheat	Soybean
C-4	F	3	4	0.01	0.01		Wheat, soybean	
C-5	F	13	5	0.01	0.01	None		Both tried
C-6	M	4	5	0.01	0.01			Wheat, soybean
C-7	M	4	6	0.01	0.01			Wheat, soybean
C-8	M	3	7	0.01	0.01			Wheat, soybean
C-9	M	8	7	0.01	0.01			Wheat, soybean

WS, wheat and soybean sensitizer; S, soybean sensitizer; W, wheat sensitizer
*Sufficient additional sera were collected for individual ELISA

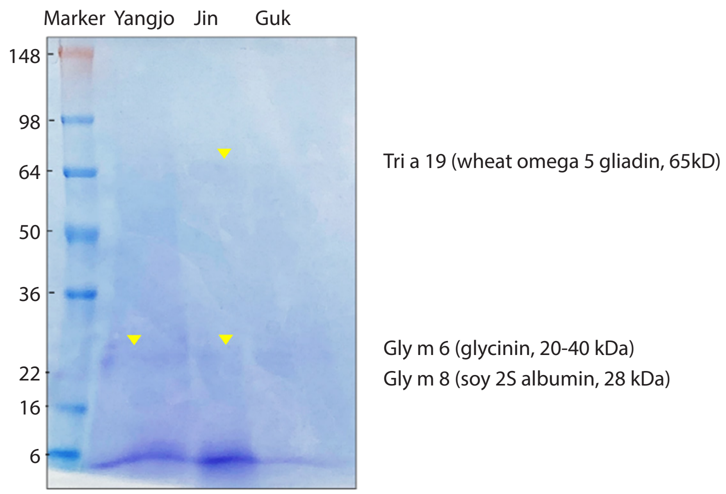

Figure 2. Protein bands observed in different types of soy sauce concentrates.

Protein bands observed in each soy sauce

The concentrations of SS extracts were as follows: Yangjo-SS, 1.2 mg/mL; Guk-SS, 0.3 mg/mL; and Jin-SS, 2.1 mg/mL. SDS-PAGE revealed differences in the distribution and density of protein bands according to the type of SS. Generally, SS exhibited faint proteins and was more significantly dim in those from Guk-SS. Yangjo- and Jin- SS showed protein bands corresponding to 28 kDa (2S albumin, Gly m 8, 28 kDa; glycinin, Gly m 6, 20-40 kDa). Jin-SS showed a faint protein band corresponding to 65 kDa (Tri a 19, wheat omega-5 gliadin) in addition to 22 kDa. (**Figure 2**).

IgE-binding capacity to each soy sauce

ELISA results for pooled sera show that the WS group exhibited significantly higher IgE^+ to all types of SS compared with both the control group and the blank. The IgE^+ of S and W is similar to that of the control or blank. Across all SS, Guk-SS showed the lowest level of IgE^+ (**Figure 3**).

Individual ELISA results revealed that all four WS exhibited significantly higher IgE^+ to all types of SS compared with the cases of W and S each. Contrastingly, the IgE^+ in all cases of W and S to Guk-SS and Jin-SS were similar to those in the control group. Notably, cases of S showed a slightly higher IgE^+ for Yangjo-SS than the control group. Contrastingly, the IgE^+ to all types of SS was similar between the cases of W and the control group (**Figure 4**).

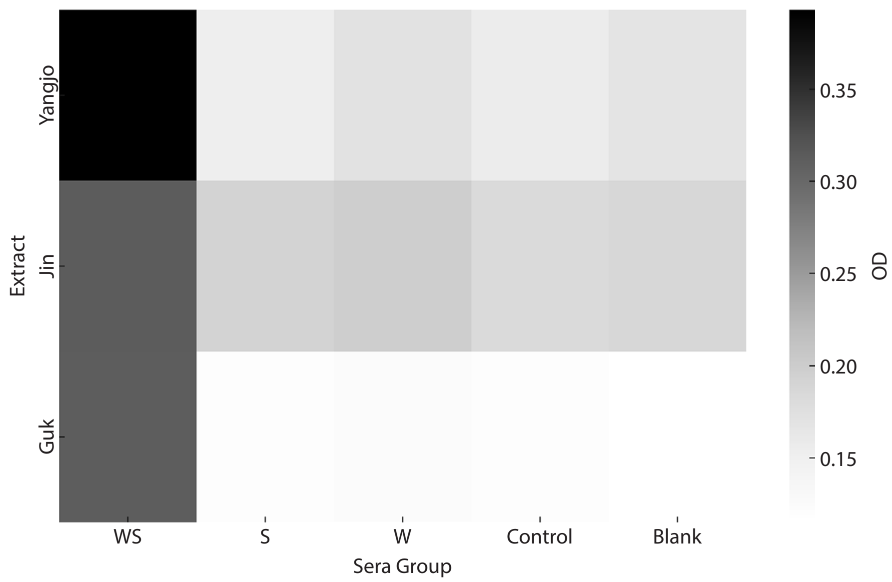

Figure 3. Grayscale heatmap of ELISA results for pooled sera groups with soy sauce concentrates.

OD, optical densities; WS, wheat and soybean sensitizer; W, wheat sensitizer; S, soybean sensitizer (> 0.70 kU/L).

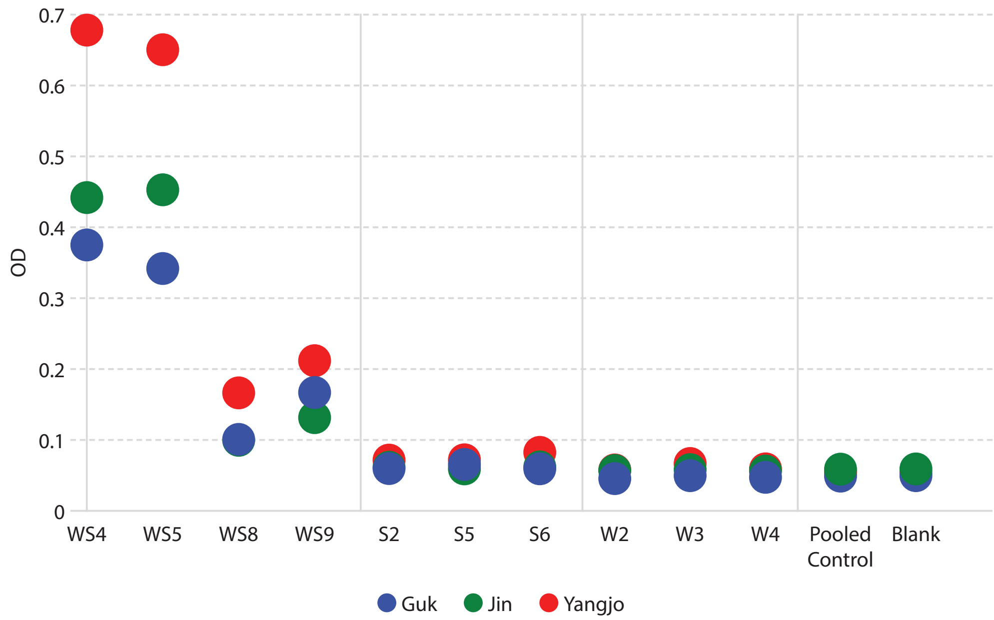

Figure 4. Immunoglobulin E binding capacity of ELISA results for individual sera with soy sauce concentrates.
OD, optical densities; WS, wheat and soybean sensitizer; W, wheat sensitizer; S, soybean sensitizer (> 0.70 kU/L).

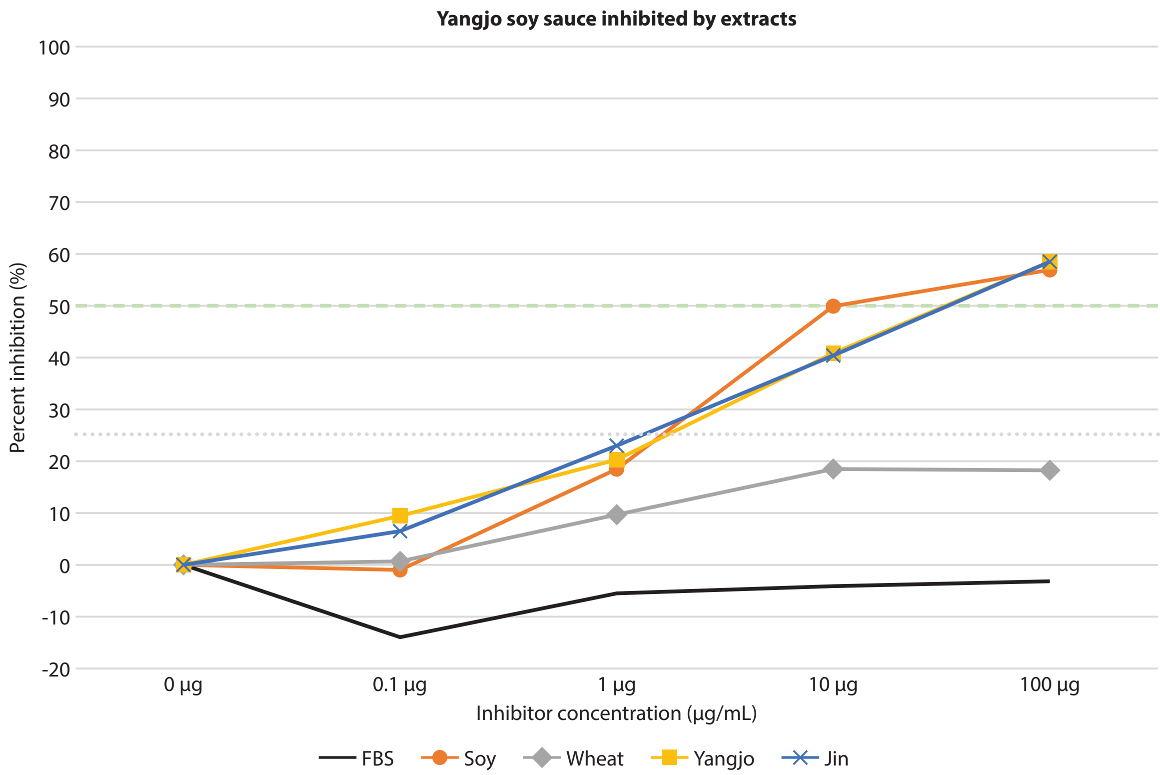

Figure 5-1. Immunoglobulin E enzyme-linked immunosorbent assay inhibition of Yangjo soy sauce concentrate using wheat, soybean extracts, Yangjo, Jin concentrates, and FBS. The IC50 values for Soybean, Yangjo and Jin were 9.87 ug/mL, 56.15 µg/mL, and 57.25 µg/mL, respectively. The IC25 values for Jin and Yangjo were 2.04 µg/mL and 3.05 µg/mL, respectively. FBS, fetal bovine serum.

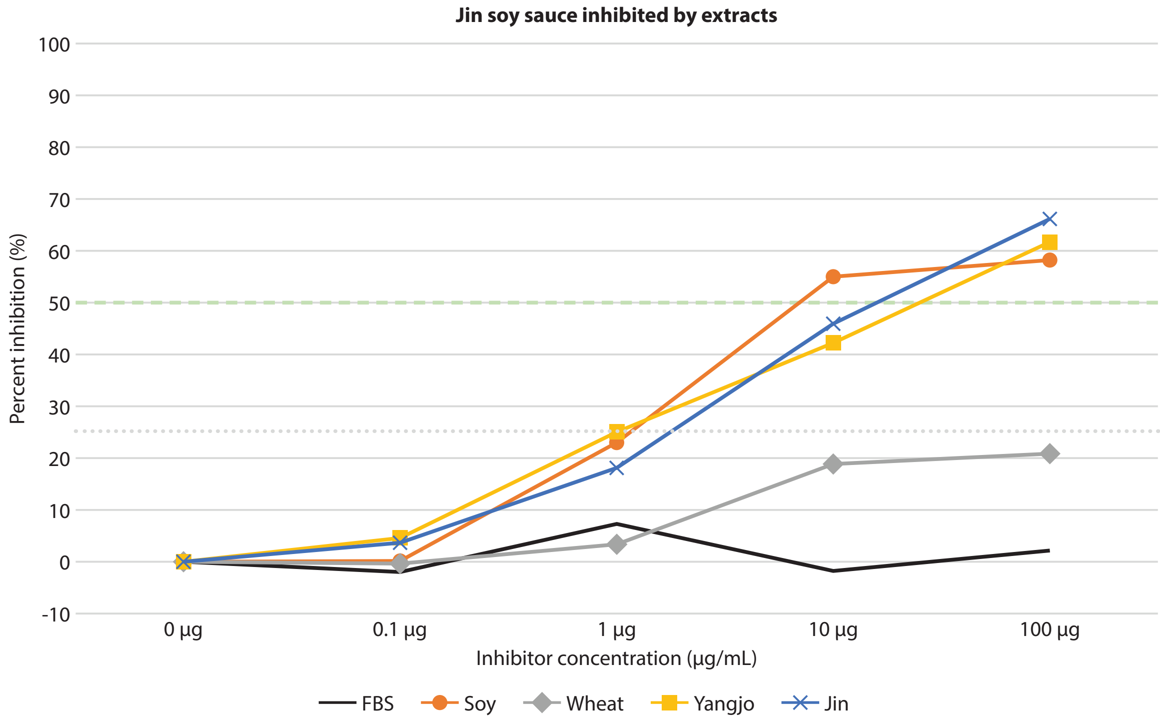

Figure 5-2. Immunoglobulin E enzyme-linked immunosorbent assay inhibition of Jin soy sauce concentrate using wheat, soybean extracts, Yangjo, Jin concentrates, and FBS. The IC50 values for Soybean, Jin and Yangjo were 4.46 µg/mL, 27.56 µg/mL, and 46.00 µg/mL, respectively. The IC25 values for Yangjo and Jin were 1.00 µg/mL and 3.21 µg/mL, respectively. FBS, fetal bovine serum.

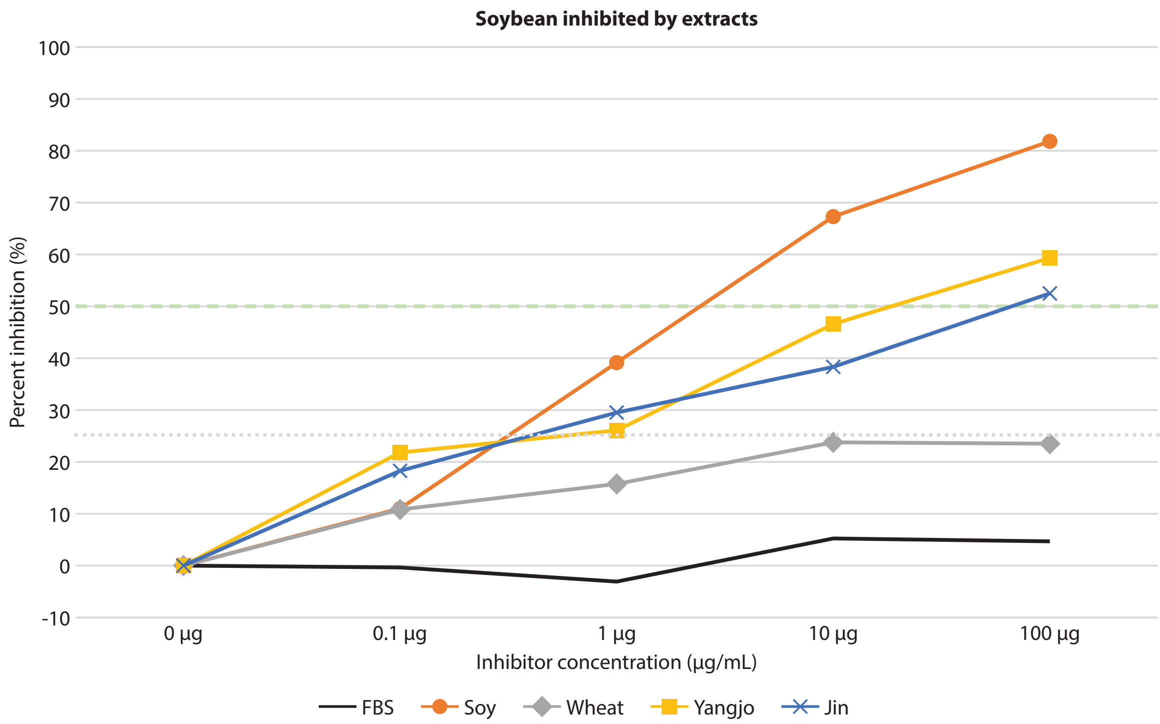

Figure 5-3. Immunoglobulin E enzyme-linked immunosorbent assay inhibition of soybean extract using soybean, wheat extracts, Yangjo, Jin concentrates, and FBS. The IC50 values for soybean, Yangjo, and Jin were 4.46 ug/mL, 33.71 µg/mL, and 84.42 ug/mL. The IC25 values for Jin and Yangjo were 0.63 ug/mL and 0.78 µg/mL µg/mL, respectively. FBS, fetal bovine serum.

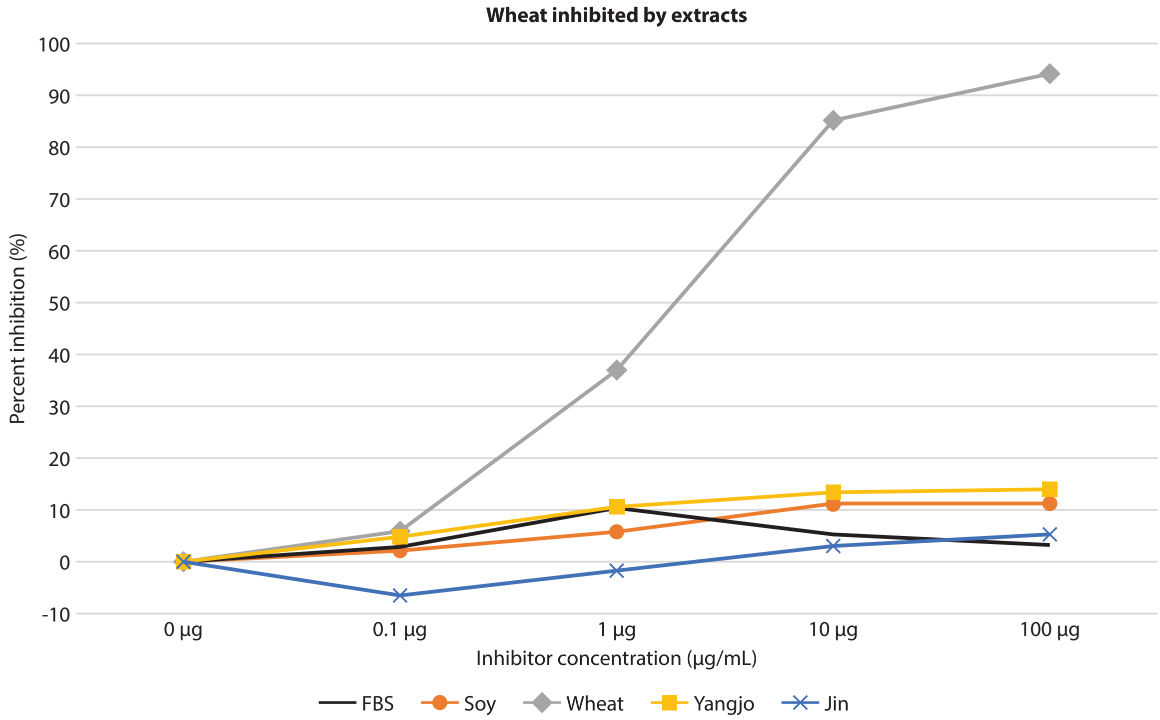

Figure 5-4. Immunoglobulin E enzyme-linked immunosorbent assay inhibition of wheat extract using wheat, soybean extracts, Yangjo, Jin concentrates, and FBS. The IC50 value for wheat was 1.51 µg/mL. FBS, fetal bovine serum.

Cross-reactivity between various soy sauces, soybean, and wheat

Competitive IgE ELISA inhibition revealed that the soybean is a potent inhibitor of Yangjo-SS (IC50: 9.87 ug/mL). The IC25 value of Jin-SS with Yangjo-SS (IC25: 2.04 ug/ml; IC50: 57.25 ug/mL) indicates that it has moderate cross-reactivity, requiring higher concentration for inhibition but still has some inhibitory potency (**Figure 5-1**). Soybean is also a potent inhibitor of Jin-SS, as indicated by the IC50 value of 4.46 ug/mL, suggesting a significant cross-reactivity. Yangjo-SS showed moderate cross-reactivity to Jin-SS, reflected by their IC25 values of 1.00 µg/mL, and demonstrated initial inhibitory effects at lower concentrations (**Figure 5-2**). Yangjo-SS and Jin-SS extracts showed moderate cross-reactivity to Soybean, with IC50 values of 33.71 µg/mL and 84.42 µg/mL, respectively, but had initial inhibitory effects at lower concentrations, reflected by their IC25 values of 0.78 µg/mL for Yangjo-SS and 0.63 µg/mL for Jin-SS (**Figure 5-3**). Conversely, we observed no cross-reactivity between wheat and all types of SS (**Figure 5-4**).

Discussion

This study provides insights into the allergenicity and cross-reactivity of various types of Korean SS with major allergenic ingredients, soybean, and wheat. Worldwide, previous studies have investigated the major allergenic components responsible for soybean and wheat allergies, leading to the identification of allergen components that remain stable after exposure to heat and mechanical processing.[9,19] However, there have been scarce studies on the clinical characteristics of SS allergy, particularly research using serum samples.[20]

The allergenicity of wheat and soybean proteins in SS are altered through various food processing techniques. Our results showed that IgE$^+$ of Yangjo-SS and Jin-SS partially inhibited by soybeans, with IC50 values of 33.71 µg/mL and 84.42 µg/mL, respectively. This indicates that soybean allergens are likely preserved during the processing of these SS. The substantial cross-reactivity of soybeans with Yangjo-SS and Jin-SS highlights the potential risk for individuals with soybean allergies when consuming these products. Further, Yangjo-SS showed a strong IgE$^+$ in the pooled sera of patients sensitized to both wheat and soybean. From individual ELISA, patients especially sensitized to soybean showed significant IgE$^+$ to Yangjo-SS. Liquid chromatography-mass spectrometry (LC-MS/MS) would be further required to obtain more precise information about the proteins that bind to IgE in these patients,[7,21] but we could not conduct this analysis given the low protein concentrations in all types of SS. Interestingly, our study found insignificant cross-reactivity between wheat and the various types of SS. For patients with wheat allergies, this finding is reassuring, suggesting that certain types of SS might be safer options. However, the minimal cross-reactivity should be interpreted with caution, and further studies are needed to confirm these results across a larger cohort. Studies on Japanese SS could not detect soybean and wheat proteins, suggesting that there is no significant level of allergenicity.[2,12,21-23] Given the diversity in SS manufacturing methods worldwide,[24,25] our findings, which differ from those in Japan, hold significant clinical relevance for patients globally who consume Korean SS.

The varying IgE^+ observed in different patient groups underscore the heterogeneity in allergic responses, which, theoretically, could only be confirmed through oral challenge tests. The WS group exhibited significantly higher IgE^+ to all SS types compared to the control group, indicating a heightened sensitivity. In contrast, the IgE^+ for the W and S groups were similar to the control group, except for a slight increase in IgE^+ to Yangjo-SS in the S group. The elevated IgE^+ observed in the WS group may be attributed to their higher sIgE levels to both wheat and soy, a finding not observed in the S and W groups with comparatively lower sIgE levels. This finding suggests that patients with multiple food allergies may be at greater risk when consuming fermented soy products, even if they are primarily allergic to one component. Notably, Guk-SS, whose protein concentration was far lower than others, had no significant levels of allergenicity. Guk-SS is considered the preferred SS choice for the WS group. Yet, differential response highlights the importance of personalized dietary recommendations and suggests that not all SS pose the same risk for all patients.

This study provides a comprehensive analysis of the allergenicity and cross-reactivity of different types of Korean SS. Future research should focus on expanding the cohort size, exploring the molecular mechanisms underlying the observed cross-reactivity, and investigating other types of food processing that might alter allergenicity. Additionally, the development of standardized guidelines for SS consumption in allergic individuals would be beneficial, providing clear recommendations to healthcare providers and patients alike.

This study has a few limitations. While it provides meaningful insights into the allergenicity of Korean SS, future research with larger sample sizes and clearer clinical histories could enhance the generalizability of the findings. Additionally, the low protein concentrations in SS limited the use of molecular techniques such as LC-MS/MS. Advanced research employing optimized protein extraction methods could help identify specific allergenic proteins, offering deeper insights into IgE-binding variations. Such research would refine dietary recommendations for allergic individuals and guide safer food manufacturing practices. Nonetheless, our findings contribute to more tailored dietary guidance for children diagnosed with both soybean and wheat allergies, particularly those who have previously restricted all types of SS from their diets.

In conclusion, pediatric patients with wheat allergies can cautiously explore any type of SS at home. Guk-SS is the only type of SS considered for home trial among children who are potentially allergic to both soybeans and wheat. Guk-SS is recommended as the first choice for children with soybean allergies, with Jin-SS as a secondary option to be used with caution. Yangjo-SS should be limited due to its higher allergenicity.

Conflict of interest disclosure

The authors declare no conflicts of interest regarding the publication of this study.

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Author contributions

- J.L., P.G., and S.L. contributed to the conception and design of the study, figure editing, manuscript drafting, and critical revision of the manuscript.
- J.L., S.Y., and P.G. contributed to the data analysis of the study.
- J.L., P.G., K.J., and S.L. revised and approved the final version of the manuscript.
- J.L., P.G., S.Y., and S.L. contributed to the acquisition and interpretation of the data and provided critical revisions.
- The manuscript has been read and approved by all authors, meeting the requirements for authorship as stated, and each author believes the manuscript represents honest work.

References

1. Lee DY, Chung SJ, Kim KO. Sensory characteristics of different types of commercial soy sauce. Journal of the Korean Society of Food Culture. 2013;28(6):640-50.
2. Magishi N, Yuikawa N, Kobayashi M, Taniuchi S. Degradation and removal of soybean allergen in Japanese soy sauce. Mol Med Rep. 2017;16(2):2264-8.
3. Franck P, Moneret Vautrin DA, Dousset B, Kanny G, Nabet P, Guenard-Bilbaut L, et al. The allergenicity of soybean-based products is modified by food technologies. Int Arch Allergy Immunol. 2002;128(3):212-9.
4. Dos Santos ALS, Dos Santos PPB, de Almeida Amaral G, Soares EC, de Oliveira ESCA, de Souza SVC. Effect of thermal processing on the antigenicity of allergenic milk, egg and soy proteins. J Food Sci Technol. 2022;59(7):2617-28.
5. Pi X, Liu J, Sun Y, Ban Q, Cheng J, Guo M. Heat-induced changes in epitopes and IgE binding capacity of soybean protein isolate. Food Chem. 2023;405(Pt A):134830.
6. Xia J, Zu Q, Yang A, Wu Z, Li X, Tong P, et al. Allergenicity reduction and rheology property of Lactobacillus-fermented soymilk. J Sci Food Agric. 2019;99(15):6841-9.
7. Hsiao JT, Chen KH, Sheu F. Determination of the soybean allergen Gly m 6 and its stability in food processing using liquid chromatography-tandem mass spectrometry coupled with stable-isotope dimethyl labelling. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2022;39(6):1033-46.
8. Pi X, Yang Y, Sun Y, Cui Q, Wan Y, Fu G, et al. Recent advances in alleviating food allergenicity through fermentation. Crit Rev Food Sci Nutr. 2022;62(26):7255-68.
9. Ballmer-Weber BK, Holzhauser T, Scibilia J, Mittag D, Zisa G, Ortolani C, et al. Clinical characteristics of soybean allergy in Europe: a double-blind, placebo-controlled food challenge study. J Allergy Clin Immunol. 2007;119(6):1489-96.
10. Lee SC, Kim SR, Park KH, Lee JH, Park JW. Clinical features and culprit food allergens of Korean adult food allergy patients: A cross-sectional single-institute study. Allergy Asthma Immunol Res. 2019;11(5):723-35.
11. Diez-Simon C, Eichelsheim C, Mumm R, Hall RD. Chemical and sensory characteristics of soy sauce: A review. J Agric Food Chem. 2020;68(42):11612-30.
12. Kobayashi M, Hashimoto Y, Taniuchi S, Tanabe S. Degradation of wheat allergen in Japanese soy sauce. Int J Mol Med. 2004;13(6):821-7.
13. Mittag D, Vieths S, Vogel L, Becker WM, Rihs HP, Helbling A, et al. Soybean allergy in patients allergic to birch pollen: clinical investigation and molecular characterization of allergens. J Allergy Clin Immunol. 2004;113(1):148-54.

14. Adachi A, Horikawa T, Shimizu H, Sarayama Y, Ogawa T, Sjolander S, et al. Soybean beta-conglycinin as the main allergen in a patient with food-dependent exercise-induced anaphylaxis by tofu: food processing alters pepsin resistance. Clin Exp Allergy. 2009;39(1):167-73.
15. Holzhauser T, Wackermann O, Ballmer-Weber BK, Bindslev-Jensen C, Scibilia J, Perono-Garoffo L, et al. Soybean (Glycine max) allergy in Europe: Gly m 5 (beta-conglycinin) and Gly m 6 (glycinin) are potential diagnostic markers for severe allergic reactions to soy. J Allergy Clin Immunol. 2009;123(2):452-8.
16. Briceno D, Hendriks L, Breedveld A, Savelkoul HFJ, Jansen A, Teodorowicz M, et al. Soy gly m 8 sige has limited value in the diagnosis of soy allergy in peanut ara h 2-sensitized adults. Int Arch Allergy Immunol. 2023;184(8):767-75.
17. Gao H, Jorgensen R, Raghunath R, Nagisetty S, Ng PKW, Gangur V. Creating hypo-/nonallergenic wheat products using processing methods: Fact or fiction? Compr Rev Food Sci Food Saf. 2021;20(6):6089-115.
18. Liu, M., Dai, S., Yin, L., Huang, Z., & Jia, X. Wheat gluten deamidation: structure, allergenicity and its application in hypoallergenic noodles. Journal of the Science of Food and Agriculture. 2024;104, 2477-83.
19. Klemans RJ, Knol EF, Michelsen-Huisman A, Pasmans SG, de Kruijf-Broekman W, Bruijnzeel-Koomen CA, et al. Components in soy allergy diagnostics: Gly m 2S albumin has the best diagnostic value in adults. Allergy. 2013;68(11):1396-402.
20. Sugiura K, Sugiura M. Soy sauce allergy. J Eur Acad Dermatol Venereol. 2010;24(7):852-5.
21. Li H, Byrne K, Galiamov R, Mendoza-Porras O, Bose U, Howitt CA, et al. Using LC-MS to examine the fermented food products vinegar and soy sauce for the presence of gluten. Food Chem. 2018;254:302-8.
22. Moriyama T, Yano E, Suemori Y, Nakano K, Zaima N, Kawamura Y. Hypoallergenicity of various miso pastes manufactured in Japan. J Nutr Sci Vitaminol (Tokyo). 2013;59(5):462-9.
23. Katz Y, Gutierrez-Castrellon P, Gonzalez MG, Rivas R, Lee BW, Alarcon P. A comprehensive review of sensitization and allergy to soy-based products. Clin Rev Allergy Immunol. 2014;46(3):272-81.
24. Choi UK, Jeong YS, Kwon OJ, Park JD, Kim YC. Comparative study of quality characteristics of Korean soy sauce made with soybeans germinated under dark and light conditions. Int J Mol Sci. 2011; 12(11):8105-18.
25. Kobayashi M. Immunological functions of soy sauce: hypoallergenicity and antiallergic activity of soy sauce. J Biosci Bioeng. 2005;100(2):144-51.