



## Dermatology Reports

<https://www.pagepress.org/journals/index.php/dr/index>

eISSN 2036-7406



**Publisher's Disclaimer.** E-publishing ahead of print is increasingly important for the rapid dissemination of science. **Dermatology Reports** is, therefore, E-publishing PDF files of an early version of manuscripts that undergone a regular peer review and have been accepted for publication, but have not been through the copyediting, typesetting, pagination and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear on a regular issue of the journal.

E-publishing of this PDF file has been approved by the authors.

*Please cite this article as:*

*Prakoewa CRS, Damayanti D, Anggraeni S, et al. Indonesian pineapple allergen extract for skin prick test as an alternative diagnostic tool in atopic dermatitis. Dermatol Rep 2025 [Epub Ahead of Print] doi: 10.4081/dr.2025.10004*

 © the Author(s), 2025  
Licensee [PAGEPress](https://www.pagepress.org/), Italy

Submitted 28/03/24 - Accepted 30/08/25

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.  
All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

## **Indonesian pineapple allergen extract for skin prick test as an alternative diagnostic tool in atopic dermatitis**

Cita Rosita Sigit Prakoeswa, Damayanti Damayanti, Sylvia Anggraeni, Menul Ayu Umborowati, Mochammad Ayyub Arachman, Trisniartami Setyaningrum

Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

**Correspondence:** Prof. Cita Rosita Sigit Prakoeswa, MD, PhD, Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital, Prof. Dr. Moestopo Number 47, Surabaya, 60286, East Java, Indonesia.

E-mail: [cita-rosita@fk.unair.ac.id](mailto:cita-rosita@fk.unair.ac.id)

**Key words:** skin prick test; pineapple; sensitive skin; human and health.

**Contributions:** CRSP, study design, funding acquisition, data interpretation, review, and revision; DD, study design, data collection and interpretation, writing – original draft; SA, MAU, and TS, study design, data collection and interpretation, review, and revision; MAU, study design, data collection and interpretation, review, and revision; MAA, study design, data collection, analysis and interpretation, review, and revision. All authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

**Conflict of interest:** the authors have no conflict of interest to declare.

**Ethics approval and consent to participate:** this study was approved by the ethics committee of Dr. Soetomo General Academic Hospital (1837/KEPK/II/2020). All patients provided written informed consent to participate.

**Availability of data and materials:** the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Funding:** this study was funded by Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

**Acknowledgments:** we gratefully thank Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, and other parties that supported this research.

## **Abstract**

Several fruits have been identified as allergens and potential triggers for exacerbations of atopic dermatitis (AD). This study evaluated pineapple allergy and sensitization among adult patients with AD and examined the diagnostic accuracy of a locally produced pineapple allergen extract in skin prick tests (SPTs).

A total of 30 adult patients with AD, with a mean age of  $36.07 \pm 10.81$  years, were enrolled in the study. Firstly, SPT was performed using a standard pineapple allergen extract manufactured by Astromed<sup>®</sup> (Astromed Inc., West Warwick, Rhode Island, USA). Subsequently, a second SPT was carried out with the pineapple allergen extract produced by Teaching Industry Allergen Dr. Soetomo General Academic Hospital, Universitas Airlangga (Surabaya, Indonesia). Data were analyzed for diagnostic test accuracy and agreement. The local pineapple SPT had a sensitivity of 33.33% and a specificity of 100%. The test exhibited a positive predictive value (PPV) of 100%, whereas the negative predictive value (NPV) was 93.10%. The agreement between the standard SPT and the local SPT was statistically significant, exhibiting moderate concordance ( $p=0.002$ ). The Indonesian pineapple allergen extract for SPT can serve as an alternative diagnostic tool to assess pineapple allergy and sensitization in AD patients.

## **Introduction**

Atopic dermatitis (AD) is a chronic inflammatory dermatological condition that is increasingly prevalent across numerous nations. In high-income countries, it is well-documented that up to 20% of children and 10% of adults have AD.<sup>1</sup> Other atopic diseases that mostly accompany AD are asthma, allergic rhinitis, urticaria, and allergic conjunctivitis in patients or in their family history.<sup>2</sup> Atopic diseases run in over 70% of AD patients' families.<sup>3</sup>

The multidimensional model of AD encompasses genetic susceptibility – most notably mutations in the filaggrin gene, though this is not the sole genetic factor – as well as a range of environmental influences. These include the “Western diet” (high in sugar and polyunsaturated fatty acids), urban living, higher education levels, low exposure to ultraviolet radiation, air pollution, hard water, and elevated household hygiene standards.<sup>1,3</sup> These factors, when combined with genetic factors, will cause a shift in the immunological phenotype, which may increase the chances of developing AD.<sup>3</sup>

A clear association was observed between AD, food sensitivity, and food allergy, particularly in children. Food allergens are thought to be one of the triggers of AD exacerbations, despite growing evidence that AD causes food allergy and not the other way around. The context of AD and food allergy interaction is further complicated by the fact that various endotypes of food allergy, including non-IgE-mediated and mixed endotypes, have also been linked to AD exacerbations or morbidity.<sup>1</sup>

An accurate medical history and physical examination are necessary for the diagnosis of allergies. Skin prick tests (SPTs) are advised to identify specific IgE to important causal allergens, such as inhalants, foods, venoms, medications, and occupational allergens, if the clinical information suggests type I (immediate type) allergy. A serum-specific IgE test or a challenge with the causative allergen may be required when the SPT result is unclear or does not match the clinical history.<sup>4</sup>

Cow's milk and egg whites are the top two foods that cause food allergies in kids. However, a South Korean survey study found that fruit was the most frequent type of food that triggers allergy reactions in children under the age of six.<sup>5</sup> Adults also have a high chance of developing allergies to fruits and vegetables. Several fruits have been identified as sources of allergy due to their specific properties or cross-reactivity with other properties. Fruit allergies are increasing at an uncertain rate.<sup>6</sup> According to a systematic review, the prevalence of reported allergy to any fruit in adults ranged from 0.4% to 3.5%, with less than 1% for specific fruits.<sup>7</sup>

Pineapple is a tropical and subtropical fruit widely consumed around the world. It contains bromelain, a group of protein-digesting enzymes (proteases) found in various parts of the pineapple plant, including the stem, fruit, and leaves.<sup>8</sup> Bromelain is recognized as a potential allergen in some individuals and its concentration varies by variety and growth conditions. Studies suggest that environmental factors, such as soil type and climate, can affect bromelain levels, potentially leading to differences between Indonesian- and internationally grown pineapples. A study of AD patients in Indonesia found that 5.26% (3 out of 57) had sensitization to the pineapple allergen.<sup>2</sup> This study aimed to assess pineapple allergy and sensitization among adult AD patients and measure the accuracy of local pineapple allergen extract for SPT compared to the internationally available standard allergen extract.

## **Materials and Methods**

### ***Study design***

This diagnostic study recruited adult AD patients from the Dermatologic Allergy-Immunology Division outpatient clinic of Dr. Soetomo General Academic Hospital (Surabaya, Indonesia). It was approved by the institution's ethics committee (1837/KEPK/II/2020).

The study was conducted for 2 months at the end of 2020, using purposive sampling. Patients with AD who were 20 years of age or older, in generally good health at the time of the study, and who had agreed to participate were recruited. Patients who were pregnant, suffered from other chronic diseases, experienced acute exacerbation of AD, had tested positive for COVID-19, and had consumed antihistamines, corticosteroids, antidepressants, beta-blockers, or angiotensin-converting enzyme (ACE) inhibitors in the last 2 weeks prior to the study were excluded.

### ***Skin prick test protocol***

The study's subjects completed the necessary history-taking for the research. The SPT was done in 2 encounters, one week apart. On the first encounter, the subject underwent SPT with standard pineapple allergen extract by Astromed® (Astromed Inc., West Warwick, Rhode Island, USA), and on the second encounter, the pineapple allergen extract used for the SPT was produced by the Teaching Industry Allergen Dr. Soetomo General Academic Hospital, Airlangga University. The tests were done on the volar side of the arms, and the skin reaction was evaluated 15-20 minutes after the test. The edges of the induration were marked with a pen and transferred onto translucent tape. The translucent tape was then placed on millimeter paper, and the lesion's diameter was measured. The SPT was considered positive when the diameter exceeded 3 mm from the negative control.

### ***Statistical analysis***

The data were gathered and analyzed with Microsoft Excel (Microsoft Corp., USA) for test accuracy and IBM SPSS Statistics for Windows Ver. 26 (IBM Corp., USA) for agreement between variables. Cohen's  $\kappa$  was used to assess agreement, with p-values <0.05 considered statistically significant.

### **Results**

This study involved 30 adult patients who had been diagnosed with AD. The subjects consisted of 10 males and 20 females. The mean age for the subjects was  $36.07 \pm 10.81$  years (Table 1) and they were healthcare workers (53.33%), office workers (33.33%), university students (6.67%), entrepreneurs (3.33%), and housewives (3.33%). Among the subjects, one patient reported a history of pineapple allergy.

Three patients (10%) got positive results from the standard pineapple SPT. One out of the 3 patients had a history of pineapple allergy. Meanwhile, one positive result (3.33%) was observed in local pineapple SPT in a patient with no prior history of pineapple allergy (Figure 1). The results are shown in Table 2. The sensitivity of local pineapple SPT was 33.33%, and the specificity was 100%. The local pineapple SPT had a positive predictive value (PPV) of 100%, while the negative predictive value (NPV) was 93.10%.

The agreement between standard SPT, local SPT, and the history of pineapple allergy can be found in Table 3. The agreement between standard SPT and history of pineapple allergy, as well as local SPT, was statistically significant with moderate agreement for both analyses. Meanwhile, there was no agreement between the local SPT and the history of pineapple allergy. In the SPT examination, no adverse events occurred in any patient.

## Discussion

The skin prick test is a widely used procedure to confirm sensitization in IgE-mediated allergic diseases, such as urticaria, AD, asthma, rhino-conjunctivitis, anaphylaxis, and food and drug allergies. This diagnostic method is indicated for suspected type 1 (immediate type) allergies. The test involves pricking the skin with a small amount of allergen extract and observing for the development of a wheal and flare reaction. This method is widely regarded as a valuable diagnostic tool for allergic diseases. Its simplicity, safety, accuracy, and cost-effectiveness make it highly favorable in the field of diagnosis.<sup>9</sup>

The participants in this study had an average age of  $36.07 \pm 10.81$  years, which aligns with Ismayani's findings, who reported that most research subjects fell within the age range of 21-40 years.<sup>10</sup> The study by Nopriyati also stated that the majority of the respondents were around 17-35 years old.<sup>11</sup> Furthermore, a significant proportion of female participants (66.7%) was observed in this study, consistent with previous epidemiological studies indicating a higher prevalence of AD among females compared to males, with a ratio ranging from 1:27 to 2:1.<sup>12</sup> Although allergies were generally more common among males, there was an increase in incidence among females after puberty or equivalent rates as males. It should be noted that hormonal changes can influence IgE levels during the menstrual cycle, which may contribute to the development of post-pubertal allergies.<sup>13</sup>

To ensure the accuracy of diagnostic tests, it is crucial to carefully evaluate the clinical relevance of IgE-mediated sensitizations. Positive skin-prick test results may not always indicate allergies and can be influenced by factors such as dermographism or false-positive reactions to negative controls. Therefore, clinicians must consider the patient's allergy history, clinical manifestations, and other relevant allergy tests in conjunction with SPT results when diagnosing allergies. The importance of comprehensive history-taking is demonstrated in this study, in which a subject with a prior pineapple allergy had a positive SPT result consistent with their clinical history. According to research by Nugroho *et al.*, there is a significant correlation (80% clinical relevance) between a history of pineapple allergy and skin prick test results in patients with AD.<sup>14</sup> This highlights the significance of thorough patient assessment in initiating an accurate diagnosis.<sup>4</sup>

Due to the high cost and limited availability of imported allergen extracts for skin prick tests, a local allergen was used as an alternative in Indonesia. This allowed the SPT to be conducted without relying solely on costly imported materials.<sup>15</sup> In this research, two types of SPT were utilized: the standard SPTs that are internationally recognized and the locally produced SPT at Dr. Soetomo General Academic Hospital, Airlangga University. The international standards for SPT are widely accepted as the gold standard for allergen examination.

This study aimed to compare the results of new locally produced allergen extracts (pineapple) with their imported counterparts. The findings indicated that both local and standard SPTs yield comparable clinical relevance values, demonstrating the effectiveness of local SPT. The sensitivity of the new local allergens was 33.3%, while the specificity was 100%. Comparable results were obtained for homemade and standard food allergen extracts in a Danish study, showing higher mean sensitivity (84% and 73%, respectively) but lower specificity (38% and 37%, respectively). Interestingly, the homemade peach extract demonstrated a high sensitivity of 94%, whereas the Allergy Laboratories Copenhagen extract had a sensitivity of only 19%.<sup>16</sup> A similar study conducted by Lubis *et al.* had reported sensitivity and specificity values for fruit skin prick tests. This study's findings reported a sensitivity of 30% and a specificity of 82%,<sup>17</sup> consistent with previous research on fruit allergens, which suggested that commercially available extracts may have reduced protein content due to manufacturing processes.<sup>18</sup>

The local pineapple skin prick test showed a high PPV of 100% and an NPV of 93.10%, while the prevalence of fruit allergy ranged between 0.1% and 4.3%. There was significant agreement between the standard SPT, history of pineapple allergy, and local SPT, with moderate agreement ( $\kappa=0.474$ ). Similarly, Anggraeni *et al.* examined the correlation of skin prick test results using new local and imported allergen extracts. The highest correlation was  $\kappa=0.502$  for house dust mite allergens, indicating moderate agreement between the two types of extracts. On the other hand, there was only a fair correlation ( $\kappa=0.225$ ) with shrimp extracts, suggesting lower agreement in SPT results when using these allergen extracts from different sources.<sup>19</sup>

These findings suggest that the new locally sourced allergen extract should be considered an alternative diagnostic tool rather than imported ones.

## **Conclusions**

Based on our study findings, the Indonesian pineapple allergen extract for SPT can serve as an alternative diagnostic tool to assess pineapple allergy and sensitization in patients with AD.

## References

1. Papapostolou N, Xepapadaki P, Gregoriou S, Makris M. Atopic Dermatitis and Food Allergy: A Complex Interplay. What We Know and What We Would Like to Learn. *J Clin Med* 2022;11.
2. Rismauli NF, Barakbah J. Retrospective Study of Skin Prick Test in Atopic Dermatitis Patients at DermatoVenereology Outpatient Clinic of Dr. Soetomo General Hospital Surabaya During 2007-2012. *Berkala Ilmu Kesehatan Kulit dan Kelamin* 2016;27:9-16.
3. Domínguez O, Plaza AM, Alvaro M. Relationship Between Atopic Dermatitis and Food Allergy. *Curr Pediatr Rev* 2020;16:115-22.
4. Ansotegui IJ, Melioli G, Canonica GW, et al. IgE allergy diagnostics and other relevant tests in allergy, a World Allergy Organization position paper. *World Allergy Organ J* 2020;13:100080.
5. Chang LS, Chang HY, Yang YH, et al. Allergen Tests of Fruit Sensitization Involving Children with Allergic Diseases. *Children* 2022;9:470.
6. Thongkhom R, Oncham S, Sompornrattanaphan M, Laisuan W. Banana anaphylaxis in Thailand: case series. *Asia Pac Allergy* 2020;10:e4.
7. Zuidmeer L, Goldhahn K, Rona RJ, et al. The prevalence of plant food allergies: A systematic review. *J Allergy Clin Immunol* 2008;121:1210-8.e4.
8. Liang J, Xu J, Pan J, et al. Identification of the Main Allergenic Proteins in High Hydrostatic Pressure Pineapple Juice and Assessing the Influence of Pressure on their Allergenicity. *Int J Food Prop* 2015;18:2134-44.
9. Bignardi D, Comite P, Mori I, et al. Allergen-specific IgE: comparison between skin prick test and serum assay in real life. *Allergol Select* 2019;3:9-14.
10. Ismayani. Hubungan Gejala Klinis dengan Hasil Tes Cukit Kulit pada Pasien dengan Rinitis Alergi di RSUP H. Adam Malik Medan [The Relationship Between Clinical Symptoms and Skin Prick Test Results in Patients with Allergic Rhinitis at H. Adam Malik General Hospital, Medan]. Medan: Universitas Sumatera Utara; 2017.
11. Nopriyati N, Antonius CS, Thaha HMA, et al. Skin Prick Test Profile: A Retrospective Study. *Berkala Ilmu Kesehatan Kulit dan Kelamin* 2022;34:189-96.
12. Munthaha MIA, Widayati RI, Afriliana L, Candra A. Characteristics of Atopic Dermatitis in Puskesmas (Public Health Center) Masaran 1 Sragen Regency. *DIMJ* 2021;10:27-34.
13. Leffler J, Stumbles P, Strickland D. Immunological Processes Driving IgE Sensitisation and Disease Development in Males and Females. *Int J Mol Sci* 2018;19:1554.

14. Nugroho WT, Ervianti E, Zulkarnain I, et al. Characteristics of Atopic Dermatitis Patients who Underwent Skin Prick Test. *Berkala Ilmu Kesehatan Kulit dan Kelamin*. 2022;34:10-4.
15. Anggraeni S, Umborowati MAD, Endaryanto A, Prakoeswa CRS. Correlation between Skin Prick Test and Specific IgE of Local Mites Allergen in Atopic Dermatitis Patients: an Indonesian Study. *CMUJ Nat Sci* 2022;21.
16. Terlouw S, van Boven FE, Borsboom-van Zonneveld M, et al. Homemade Food Allergen Extracts for Use in Skin Prick Tests in the Diagnosis of IgE-Mediated Food Allergy: A Good Alternative in the Absence of Commercially Available Extracts? *Nutrients* 2022;14:475.
17. Lubis A, Barlianto W, Endaryanto A, Harsono A. Compatibility of Clinical Manifestation with Skin Prick Test Result and Food Provocation Test in Food Cross Reaction. *Berkala Ilmu Kesehatan Kulit Dan Kelamin* 2017;29:106-16.
18. Gupta M, Cox A, Nowak-Węgrzyn A, Wang J. Diagnosis of Food Allergy. *Immunol Allergy Clin North Am* 2018;38:39-52.
19. Anggraeni S, Prakoeswa CRS, Endaryanto A, Damayanti D, et al. The Accuracy of Indonesian New Local Skin Prick Test (SPT) Allergen Extracts as Diagnostic Tool of IgE-mediated Atopic Dermatitis. *Indian J Forensic Med Toxicol* 2021;15.

**Table 1.** Sample characteristics.

Characteristics	Total	Percentage
<b>Gender</b>		
Female	20	66.67
Male	10	33.33
<b>Age</b>		
Mean $\pm$ SD, years	36.07 $\pm$ 10.81	

SD, standard deviation.

**Table 2.** Results of standard and local pineapple SPT.

		Standard pineapple SPT		Total (%)
		Positive (%)	Negative (%)	
Local pineapple SPT	Positive	1 (3.33)	0 (0)	1 (3.33)
	Negative	2 (6.67)	27 (90)	29 (96.67)
Total		3 (10)	27 (90)	30 (100)

SPT, skin prick test.

**Table 3.** Agreement between the history of suspected pineapple allergy and test results.

Cohen's $\kappa$ agreement	$\kappa$	p
History of pineapple allergy and local SPT	-.034	.851
History of pineapple allergy and standard SPT	.474	.002*
Local and standard pineapple SPT	.474	.002*

SPT, skin prick test; \*Statistically significant.

**Figure 1.** Patients with a positive SPT result.

