

Letter to the Editor

Differences in the allergenicity of 6 different kiwifruit cultivars analyzed by prick-to-prick testing, open food challenges, and ELISA

To the Editor:

The prevalence of kiwifruit allergy appears to be increasing,¹ because the fruit's availability and consumption has risen since the early 1970s. Symptoms of kiwifruit allergy vary from mild oral symptoms to severe systemic reactions.² Studies investigating the allergenicity of different kiwifruit cultivars are scarce and mostly limited to *in vitro* evaluation, focusing on the common green and gold kiwifruits (Hayward and Hort16A, the latter marketed as Zespri Gold).^{3,4} The aim of this study was to determine the differences in allergenicity of 6 different kiwifruit cultivars *in vivo* by prick-to-prick-test (PPT) and food challenge (FC) and *in vitro* by IgE ELISA. The kiwifruit cultivars studied included those already on the market for a long time (Hayward, Hort16A), and those recently introduced (Summer 3373, Jintao) or likely to become available on the market in the future (Eriantha 96, Eriantha 114; see this article's Fig E1 in the Online Repository at www.jacionline.org).

Twenty-six Dutch and 11 Swiss patients (mean age $\pm$ SD, 30.1 $\pm$ 9.45 years; 86% female) were recruited from the outpatient clinic of the University Medical Center Utrecht and University Hospital Zurich, respectively. All patients had a convincing history of kiwifruit allergy as well as a positive PPT for the common green kiwifruit Hayward. The PPT test was performed in duplicate by using the pulp of 6 different fresh kiwifruit cultivars (2 each from 3 different species): *Actinidia deliciosa* cultivar Hayward and cultivar Summer 3373, *Actinidia chinensis* cultivar Hort16A and cultivar Jintao, and *Actinidia eriantha* cultivar Eriantha 96 and cultivar Eriantha 114. All kiwifruits except Hort16A were grown in the orchard of the Department of Agriculture and Environmental

Sciences (Udine, Italy). Hort16A was bought locally. In addition to the Hayward cultivar from Udine, we also bought Hayward locally for testing in the PPT. Skin prick tests (SPTs) with commercial extracts of the common green kiwifruit, birch pollen, grass pollen, mugwort pollen, and latex were performed (ALK-Abelló, Madrid, Spain).

All 11 Swiss patients underwent open FC with fresh Hayward (10, 20, and 50 g). In 11 Dutch patients, single-blind FC was performed with 2 kiwifruit cultivars: Hayward and Hort16A or Hayward and Summer 3373 (2, 10, 20, and 50 g). Doses were given at an interval of 30 minutes. The challenge was discontinued in case of objective symptoms or moderate or severe subjective symptoms that persisted for more than 45 minutes. Specific IgE binding to kiwifruit proteins was tested in IgE ELISA as described elsewhere.³

All patients were sensitized to Hayward kiwifruit by PPT and to 1 or more pollens (91% grass, 94% birch, 56% mugwort; see this article's Table E1 in the Online Repository at www.jacionline.org). In only 28% of the patients with kiwifruit allergy, SPT was positive with the commercial kiwifruit extract. Kiwifruit allergy for the common green kiwifruit Hayward was confirmed by FC in 11 of 11 Swiss and in 9 of 11 Dutch patients. The 2 Dutch patients who did not react to Hayward had a positive FC for Hort16A.

When performing PPT in the Dutch patients with kiwifruit allergy, significant differences ($P < .006$) were found between the means for the skin test reaction size for different cultivars (Fig 1, A). Hort16A and Summer 3373 had the lowest allergenicity in PPT and Hayward, Eriantha 96, and Eriantha 114 the highest. However, the absolute differences were small, and there was a large overlap in individual reactions. Findings were similar in the Swiss patients (Fig 1, B).

Single-blind FCs for Hayward versus Hort16A ($n = 8$) and for Hayward versus Summer 3373 ($n = 3$) were performed (Table I).

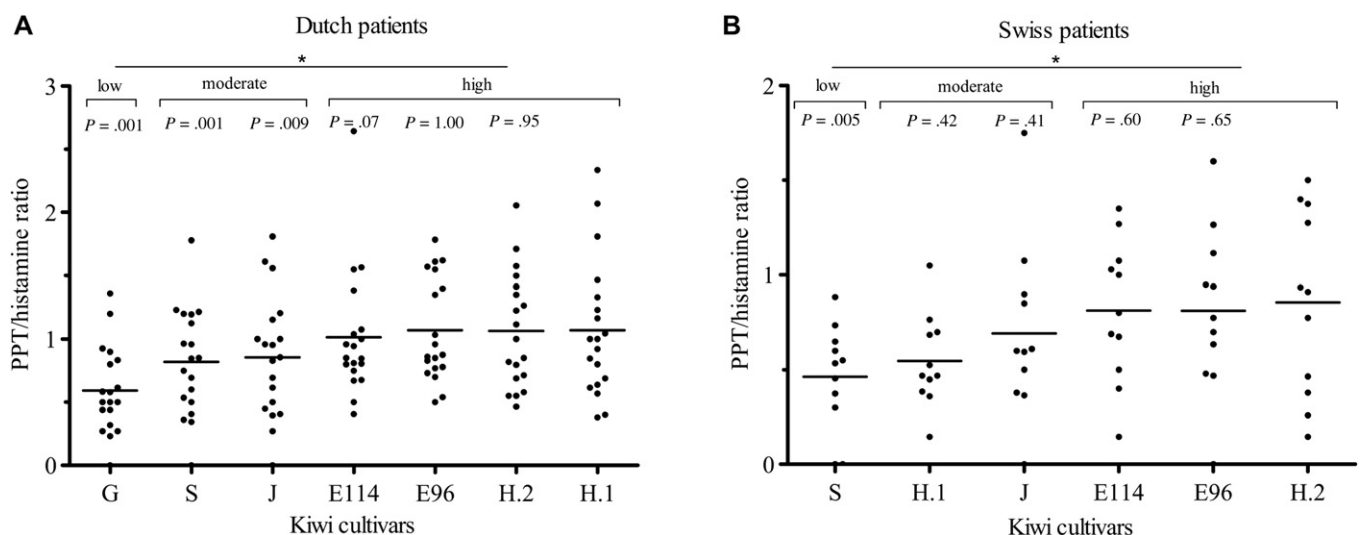


FIG 1. Scatter plot and mean of PPT in Dutch (A) and Swiss (B) patients with fresh kiwifruit. The low-allergenic cultivars are significantly different from the high-allergenic cultivars. The P values shown are from the comparison of each kiwifruit cultivar with Hayward. E96, Eriantha 96; E114, Eriantha 114; G, Hort16A; H.1, Hayward (obtained from Udine); H.2, Hayward (bought locally); J, Jintao; S, Summer 3373.

*Adjusted α with Bonferroni correction ($P < .006$).

TABLE I. Comparison of allergenicity by food challenge

ID	Food challenge Hayward	Food challenge Hort16A	Food challenge Summer 3373	Severity Hayward*	Severity Hort16A or Summer 3373*	Obj/subj symptoms Hayward†	Obj/subj symptoms Hort16A or Summer 3373†	Allergenicity‡
K7	OAS, E	OAS		Moderate	Mild	Objective	Subjective	H>G
K9	OAS	No symp		Mild	No symp	Subjective	No symp	H>G
K18	OAS, BL	No symp		Moderate	No symp	Objective	No symp	H>G
K22	OAS, TT, CO, DP, D, HE	OAS, ANG, CO		Severe	Moderate	Objective	Objective	H>G
K23	OAS, N	OAS		Moderate	Mild	Subjective	Subjective	H>G
K24	OAS, TT	OAS, TT		Moderate	Moderate	Subjective	Subjective	H=G
K25	No symp	OAS		No symp	Mild	No symp	Subjective	H<G
K26	No symp	OAS, TT		No symp	Moderate	No symp	Subjective	H<G
K3	OAS, HO, TT, CO, ANG, DI, P, PA		OAS	Severe	Mild	Objective	Subjective	H>S
K5	OAS, HE, R, I, CO, CR		OAS, HE	Moderate	Mild	Objective	Subjective	H>S
K13	OAS, ANG		OAS, ANG	Moderate	Moderate	Objective	Objective	H=S

ANG, Angioedema; BL, blisters; CO, conjunctivitis; CR, abdominal cramps; D, dysphonia; DI, diarrhea; DP, dyspnea; E, erythema; HE, headache; HO, hoarseness; I, itching; ID, patients' identification; N, nausea; No symp, no symptoms; OAS, oral allergy symptoms; Obj, objective; P, perspiring; PA, pale; R, rhinitis; Subj, subjective; TT, tightness of throat.

*Classification of symptoms in no reactivity, mild, moderate, and severe: mild, only OAS; moderate, symptoms of skin, mucous membranes, or gastrointestinal tract; severe, respiratory or cardiovascular symptoms.

†Classification of symptoms into subjective and objective.

‡Comparison of the allergenicity of the 2 kiwifruit cultivars tested, taking into account all 3 types of classifications (symptoms, classification into mild/moderate/severe, objective or subjective symptoms). G, Hort16A; H, Hayward; S, Summer 3373 kiwi.

Patients reacted to Hayward, Hort16A, and Summer 3373 with no symptoms (18%, 25%, 0%, respectively) or mild (9%, 38%, 67%), moderate (55%, 38%, 33%), or severe (18%, 0%, 0%) reactions. In contrast with Hayward, no severe reactions occurred with Hort16A or Summer 3373. Objective symptoms during FC occurred for Hayward in 54% (6/11), Hort16A in 13% (1/8), and Summer 3373 in 33% (1/3).

Overall the sera showed little IgE binding to the kiwifruit proteins as expressed in predominantly low OD values in IgE ELISA. In the Dutch sera, Hayward, Jintao, and Summer 3373 were the least frequently recognized cultivars (36%, 36%, and 40%, respectively), whereas Eriantha 114 was the most frequently recognized (68%). In Swiss sera, Jintao showed the lowest frequency (19%) compared with Hayward with the highest rate (82%). The other cultivars were recognized intermediately in the Swiss patients (Summer 3373, 45%; Eriantha 96 and Eriantha 114, both 55%).

So far, the allergenicity of kiwifruit cultivars has mainly been investigated *in vitro*.^{3,4} This study suggests there may be *in vivo* differences in allergenicity between the common green kiwifruit cultivar and other newly available kiwifruit cultivars. Hort16A was the least allergenic cultivar. This is in accordance with a small previous study in 3 children and 2 adults.⁵ In addition, we demonstrated a lower clinical reactivity of another more recently introduced cultivar: Summer 3373. However, differences in allergenicity of kiwifruit cultivars have to be interpreted with some caution, taking the individual patients' reactivity toward cultivars into account. Recently, a Spanish patient with anaphylaxis to gold kiwifruit was described.⁶ Interestingly, 2 patients from our study reacted to the gold kiwifruit in FC with mild/moderate symptoms, but not to green kiwifruit in FC. This has never been reported before.

Summarizing, our data show that PPT with fresh kiwifruit appears to be the most sensitive and least time-consuming test to assess allergenicity. In contrast, IgE ELISA and SPT with commercial kiwifruit extracts appear less sensitive. This is in agreement with a previous study.⁷ Actinidin, which accounts for about 50% of the total fruit protein, is an active protease that

may cause degradation of allergens in commercially available kiwifruit extracts.

The finding that Summer 3373 and the gold Hort16A kiwifruit may be less allergenic than the common green kiwifruit Hayward in some of the patients with kiwifruit allergy may offer these patients a safe way to reintroduce kiwifruit into their diets. However, further research in a larger patient population and further selection and breeding of less allergenic kiwifruit cultivars are needed.

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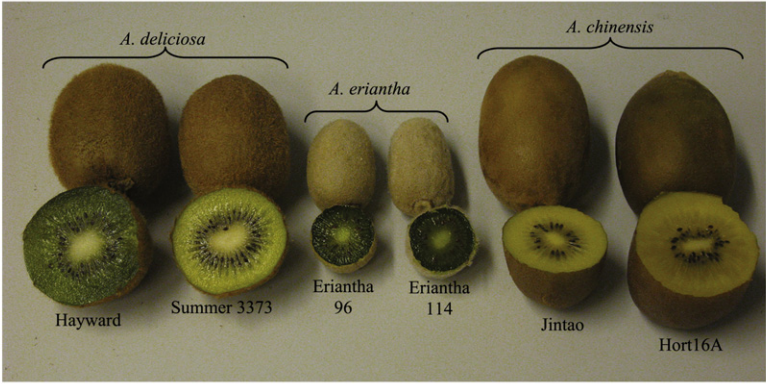
Species:	<i>A. deliciosa</i>	<i>A. eriantha</i>	<i>A. chinensis</i>
Cultivars:	<i>Hayward</i> : Most widely consumed kiwifruit in Europe <i>Summer 3373</i> : Early green fruit, volumes in Europe increasing fast	<i>Eriantha 96</i> : <i>A. eriantha</i> has been used in a number of crosses, some of the progeny from these may reach the market in 10 to 20 years <i>Eriantha 114</i> : <i>A. eriantha</i> has been used in a number of crosses, some of the progeny from these may reach the market in 10 to 20 years	<i>Jintao</i> : Is becoming more available in Europe <i>Hort16A</i> : Most widely available yellow cultivar in Europe at present
Species:			
Cultivars:			

FIG E1. Description and pictures of the different kiwifruit cultivars: Hayward, Summer 3373, Hort 16A, Jintao, Eriantha 96, and Eriantha 114.

TABLE E1. Clinical characteristics of patients with kiwifruit allergy

ID	Country	Age (y)	Sex	Symptoms kiwi	Positive SPT to pollen	SPT kiwi extract*	Food challenge Hayward
K1	NL	21	F	OAS, N, TT	G, MU	1.33	ND
K2	NL	40	F	OAS, CU	G, B	0	ND
K3	NL	41	F	OAS, D, TT	G, B, MU	0.83	OAS, H, TT, CO, ANG, DI, P, PA
K4	NL	41	F	OAS	G, B	0	ND
K5	NL	26	F	OAS	G, B	0	OAS, HE, R, I, CO, CR
K6	NL	33	M	OAS, TT	G, B	0.50	ND
K7	NL	27	F	OAS	G, B, MU	0.50	OAS, E
K8	NL	29	F	OAS, N	G, B, MU	0	ND
K9	NL	26	F	OAS, TT	G, B	0	OAS
K10	NL	24	F	OAS	B, MU	0	ND
K11	NL	25	F	OAS, R, TT	G	0.54	ND
K12	NL	29	M	OAS, TT	G, B	1.38	ND
K13	NL	43	F	OAS	G, B, MU	0	OAS, ANG
K14	NL	50	M	OAS, TT, DP	B	0	ND
K15	NL	26	F	OAS, CR, DI	B	0.33	ND
K16	NL	29	F	OAS, U, TT, CO	G, B	0	ND
K17	NL	33	F	OAS, TT, DP	G, B, MU	0	ND
K18	NL	22	F	OAS, U, I, A, TT	G, B, MU	0.83	OAS, BL
K19	NL	22	F	OAS	G, B, MU	0	ND
K20	NL	17	F	CU	G, B	0.25	ND
K21	NL	21	F	OAS, CU	G, B	0	ND
K22	NL	29	F	OAS, TT	ND	0	OAS, TT, CO, DP, D, HE
K23	NL	24	F	OAS	ND	0	OAS, N
K24	NL	22	F	OAS	ND	0	OAS, TT
K25	NL	51	F	OAS	ND	0	No symptoms
K26	NL	53	F	OAS	ND	0	No symptoms
KW1	CH	35	M	OAS	G, B, MU	0	OAS
KW2	CH	22	F	OAS	G, B	0	OAS
KW3	CH	20	F	OAS, CU	G, B, MU	0.4	OAS, ANG
KW4	CH	25	F	OAS	G, B, MU	0	OAS
KW5	CH	28	M	OAS, D, L	G, B, MU	0.27	OAS, DY
KW6	CH	55	F	OAS, DY	G, B	0	OAS, DY
KW7	CH	18	F	OAS	G, B, MU	0	OAS, ANG
KW8	CH	45	M	OAS, ANG	G, B, MU	0	OAS
KW9	CH	33	F	OAS	G, B, MU	0	OAS
KW10	CH	33	M	OAS	G, B, MU	0.47	OAS, SS
KW11	CH	24	F	OAS, BL	G, B, MU	0	OAS

A, Asthma; ANG, angioedema; B, birch; BL, blisters; CH, Switzerland; CO, conjunctivitis; CR, abdominal cramps; CU, contact urticaria; D, dysphonia; DI, diarrhea; DP, dyspnea; DY, dysphagia; E, erythema; F, female; G, grass; H, hoarseness; HE, headache; I, itching; ID, patients' characteristics; L, laryngeal edema; M, male; MU, mugwort; N, nausea; ND, not done; NL, The Netherlands; OAS, oral allergy symptoms; P, perspiring; PA, pale; R, rhinitis; SS, strong salivation; TT, tightness of throat; U, urticaria.

*SPT/histamine ratio.