Allergen Data Collection - Update:

Kiwi Fruit *(Actinidia chinensis)*

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Kiwi Fruit (Actinidia chinensis)

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Abstract

First reports of allergic reactions to kiwi fruit occurred relatively late in 1981, when this exotic fruit was becoming more common in nutrition in western countries. The prevalence of kiwi fruit allergy seems to be low in food allergic individuals. Nevertheless IgE mediated reactions after ingestion of kiwi fruit can be most severe, as shown by several cases of anaphylactic shocks. Belonging to the latex- associated fruit- allergens, kiwi is involved in so-called oral allergy syndrome which is reflected by high frequencies of kiwi allergy in birch pollen and latex sensitive patients. This review represents data on prevalence, symptoms, and cross- reacting allergens in tabular form. The molecular biological and allergenic properties of the two major kiwi allergens (Actinidin Act c 1 and a 43-kDa-Allergen) are summarized. (Internet Symposium on Food Allergens 2000, 2(Suppl.2):1-11)

Contents

1 Prevalence of Kiwi Fruit Allergy

Country / Subjects	Sensitivity to	References
France, Pierre Benite a) 580 patients with adverse reactions to food b) 60 cases of anaphylaxis (study period 1984-92)	a) kiwi fruit 11% b) kiwi fruit 3.3%	Andre et al. 1994
France, Toulouse 142 food allergic children	kiwi fruit 2.8% (Labial food challenge)	Rance & Dutau 1997
Germany 136 latex allergic patients	kiwi fruit 16% (RAST inhibition)	Brehler et al. 1997
Germany 30 patients with birch pollen associated fruit allergy	kiwi fruit 77% (EAST)	Möller et al. 1997b
Italy, Florence 54 episodes of food-dependent anaphylaxis in 44 children (age of 1 month to 16 years) (from 1994-1996)	kiwi fruit 5.6%	Novembre et al. 1998
Italy, Florence 15 spina bifida patients with latex allergy	kiwi fruit 27% (SPT), 0% (RAST)	Bernardini et al. 1999
Italy, Genoa 132 pollen and food sensitive patients	kiwi fruit 4.4% (incidents of hypersensitivity)	Troise et al. 1992
Japan 171 birchpollen allergic patients	kiwi fruit 3.5% (RAST)	Yamamoto et al. 1995
Spain, Gran Canaria 142 food allergic adults	kiwi fruit 9.9% (Clinical symptoms)	Castillo et al. 1996
Spain, Madrid 29 plant-derived food allergic patients	kiwi fruit 41% (SPT)	Diez-Gomez et al. 1999
Switzerland, Zurich 402 food allergic adults	kiwi fruit and apple 1.5%	Wüthrich 1993
Switzerland, Zurich 383 food allergic patients (study period 1990-94)	kiwi fruit 5.5%	Etesamifar & Wüthrich 1998
Turkey, Ankara 61 hospital employees, 40 atopic children	kiwi fruit 22 subjects (specific Serum-IgE)	Saraclar Y et al. 1998
USA 33 latex allergic patients with associated food allergy	kiwi fruit 17% (Skin Prick Test)	Beezhold et al. 1996
USA, Long Beach, CA 137 patients with latex allergy	kiwi 12.2% (convincing history after ingestion)	Kim & Hussain 1999

2 Symptoms of Kiwi Fruit Allergy

Symptoms & Case Reports	References
systemic reactions anaphylaxis (2, 3, 6, 7, 11, 13), severe generalized symptoms (1) cutaneous symptoms angioedema (13), contact urticaria (5), localized pruritic reaction (4), rhinitis (9), urticaria (4, 9, 13) gastrointestinal symptoms dysphagia (4), itching of mouth and throat (9), oral allergy syndrome* (10, 11, 13), oral and pharyngeal hypersensitivities (8), acute pancreatitis (12), swelling of lips (9), vomiting (4) * symptoms, which could be involved in oral allergy syndrome: local symptoms as intra-oral and lip-irritation, angioedema and systemic symptoms as rhino-conjunctivitis, urticaria-angioedema, asthma, and anaphylaxis	(1) Fine 1981 (2) Falliers 1983 (3) Freye 1989 (4) Garcia et al. 1989 (5) Veraldi & Schianchi-Veraldi 1990 (6) Novembre et al. 1995 (7) Shimizu & Morikawa 1995 (8) Yamamoto et al. 1995 (9) Möller et al. 1997b (10) Arai et al. 1998 (11) Fahlbusch et al. 1998 (12) Gastaminza et al. 1998 (13) Diez-Gomez et al. 1999

3 Diagnostic Features

Parameters / Subjects	Outcome	References
IgE and Clinical Symptoms 22 kiwi allergic patients	Patients with severe clinical symptoms to kiwi fruit had moderately elevated IgE levels to kiwi fruits, whereas those with mild localized symptoms had no detectable IgE to kiwi fruits	Gall et al. 1994
IgE and Clinical Symptoms 3 case reports of kiwi hypersensitivity reactions without elevated specific serum IgE- levels	(1) localized pruritic reaction, dysphagia, vomiting and urticaria (RAST 0.35 AEU/mL) (2) anaphylaxis after kiwi ingestion (RAST 0.87 kU/L) (3) gastrointestinal symptoms (RAST <0.35 kU/L)	(1) Garcia et al. 1989 (2) Fahlbusch et al. 1998 (3) Möller et al. 1998
Symptoms during Prick Test 6 kiwi allergic patients	2 of 6 patients had systemic allergic symptoms during prick by prick testing with kiwi pulp	Huertas et al. 1999

4 Composition of Kiwi Fruit

Distribution of Nutrients

Nutrients: Content per 100 g		
Energy 217 kJ (51 kcal)	Iron 800 µg	**Carbohydrates**
Water 83.8 g	Phosphorus 30 mg	Sucrose 1250 mg
Protein 1.0 g	Chloride 65 mg	Glucose 4490 mg
Lipid 0.6 g		Fructose 3540 mg
Carbohydrate 9.3 g	**Vitamins**	
Organic acids 1.5 g	Carotene 370 µg	**Organic acids**
Fiber 3.9 g	Vitamin B1 17 µg	Malic acid 500 mg
Minerals 0.7 g	Vitamin B2 50 µg	Citric acid 990 mg
	Nicotinamide 410 µg	Oxalic acid traces
Minerals	Vitamin C 20-300 µg	Salicylic acid 320 µg
Sodium 4 mg		
Potassium 295 mg		
Magnesium 25 mg		
Calcium 40 mg		

Ref: Deutsche Forschungsanstalt für Lebensmittelchemie, Garching bei München (ed), **Der kleine "Souci-Fachmann-Kraut" Lebensmitteltabelle für die Praxis**, WVG, Stuttgart 1991

5 Allergens of Kiwi Fruit

Proteins / Glycoproteins	**Allergen Nomenclature**	**References**
Actinidin (30 kDa)	Act c 1	Pastorello et al. 1998
43-kDa Allergen	Act c 2 *	Möller et al. 1997a
41-kDa Allergen (Putative chitinase)		Diaz-Perales et al. 1999
Allergens: 13, 22, 30, 67 kDa		Möller et al. 1997b
Allergens: 10-12 kDa, 20-25 kDa		Voitenko et al. 1997
Allergens: 12, 17, 24, 28 kDa		Pastorello et al. 1996, 1998
Allergens: 23, 30, 43, 80, 92 kDa		Fahlbusch et al. 1998
12 Allergens: 15-94 kDa		Rudeschko et al. 1998

* proposed name not yet listed in WHO/IUIS Allergen Nomenclature

5.1 Sensitization to Kiwi Fruit Allergens

Country / Subjects	Sensitivity to	References
Germany, Hamburg 22 kiwi allergic patients	67-kDa Allergen 55% 43-kDa Allergen 68% 30-kDa Allergen 19% 22-kDa Allergen 31% 13-kDa Allergen 9% (SDS-PAGE / immunoblot)	Möller et al. 1997b
Germany, Jena 9 kiwi allergic patients	92-kDa Allergen 22% 80-kDa Allergen 44% 43-kDa Allergen 44% 30-kDa Allergen 89% 23-kDa Allergen 56% (SDS-PAGE / immunoblot)	Fahlbusch et al. 1998
Italy, Milan 30 kiwi allergic patients	30-kDa Allergen (Act c 1) 100% 22-, 24-, 28-, 32-, 38-, and 41-kDa Allergens in 30 to 50% 12-, 14-, 17-, 20-, and 64-kDa Allergens in <30% (SDS-PAGE / immunoblot)	Pastorello et al. 1996

5.2 Properties of Actinidin

5.2.1 Molecular Biological Properties

Actinidin					References
Allergen Nomenclature Act c 1					(1) Larsen & Lowenstein 1998
Isoallergens and Variants Sequence variation in 2 kiwi varieties (1)					(1) Naylor et al. 1989
Molecular Mass Mr 30 kDa					(1) Pastorello et al. 1998
Isoelectric Point pI 3.5 (1, 2)					(1) Fahlbusch et al. 1998 (2) Pastorello et al. 1998
Amino Acid Sequence, mRNA, and cDNA					(1) Carne & Moore 1978 (2) Praekelt et al. 1988 (3) Podivinsky et al. 1989 (4) Keeling et al.1990 (5) Fahlbusch et al. 1998 (6) Pastorello et al. 1998
Act c 1					
SWISS-PROT:	P00785				
GenBank:	X16466	X13013	X13139	X57551	
PIR:	TAGB	S02728	S02729		
Amino acids	254 aa (1)	1-15 (5)	P* (6)		
mRNA	1370 bp (3)	1138 bp (2)	809 bp (2)		
cDNA				634 bp (4)	
* 5 partial sequences from tryptic digest (6)					
recombinant Actinidin expression in tabacco (1)					(1) Paul et al. 1995
3D-Structure X-ray studies (1) complex with inhibitor (2)					(1) Baker 1980 (2) Varughese 1992

Posttranslational Modifications Disulfide bonds: 3 disulfide bonds (1) Glycosylation: No glycosylation by lectin binding (2) No glycosylation by periodic acid-Schiff stain (3)	(1) SWISS-PROT: P00785 (2) Fahlbusch et al. 1998 (3) Pastorello et al. 1998
Biological Function enzyme: thiol-protease, EC 3.4.22.14 specificity close to papain (1)	(1) Baker et al. 1980
Sequence Homology Actinidin has a similar structure to Der p 1, the major allergen of house dust mite (*Dermatophagoides pteronyssinus*) (1)	(1) Tropham et al. 1994

5.2.2 Allergenic Properties

Actinidin	**References**
Frequency of Sensitization IgE-binding to Act c 1 in 19 to 100% of patients (1)	(1) see 5.1 Sensitization to Kiwi Fruit Allergens

5.3 Properties of 43-kDa-Allergen

5.3.1 Molecular Biological Properties

43-kDa-Allergen	**References**
Allergen Nomenclature Act c 2 (proposed name)	(1) Möller et al. 1997a
Molecular Mass Mr 43 kDa	(1) Möller et al. 1997a
Isoelectric Point pI 6.9	(1) Möller et al. 1997a
Amino Acid Sequence N-terminus: 1-17 AKEDP(G/P)*NKFARIGALV	(1) Möller et al. 1997a
Posttranslational Modifications Glycosylation: {alpha}-fucose moieties in 43-kDa protein by lectin binding from *Aleuria aurantia* (SDS-PAGE immunoblot) (1)	(1) Fahlbusch et al. 1998

5.3.2 Allergenic Properties

43-kDa-Allergen	**References**
Frequency of Sensitization IgE-binding to 43-kDa allergen in 44 to 68% of patients (1)	(1) see 5.1 Sensitization to Kiwi Fruit Allergens

6 Isolation & Preparation

Extract / Purified Allergens	Methods	References
Protein Extract	fresh fruit homogenized in acetone (-40°C), precipitates washed, filtered, lyophylized and water extracted	Möller et al. 1997a
Protein Extract	comparison of extraction buffers: phosphate- buffered saline and borate- buffered saline	Voitenko et al. 1997
Protein Extract	fresh fruit homogenized in phosphate buffer saline, centrifuged and dialyzed	Fahlbusch et al. 1998
Protein Extract	fresh fruit homogenized in phosphate buffer, centrifuged and dialyzed	Pastorello et al. 1998
Actinidin	covalent chromatography (thiol-disulfide interchange)	Thomas et al. 1995
43-kDa-Allergen (Act c 2)	IEC, SDS-PAGE / electroelution	Möller et al. 1997a
30-kDa-Allergen (Act c 1)	IEC purification	Fahlbusch et al. 1998
30-kDa-Allergen (Act c 1) and 17, 24, 28-kDa Allergens	IEC purification	Pastorello et al. 1998

7 Cross-Reactivities

Cross-Reacting Allergens	Subjects / Methods	References
Kiwi Fruit hazelnuts, rye grain	2 kiwi allergic patients (RAST inhibition)	Seifert et al. 1988
Kiwi Fruit hazelnuts, poppy seeds, sesame seeds, rye grain	8 patients with food / pollen allergy (immunoblot inhibition)	Vocks et al. 1993
Kiwi Fruit birch, grass and, mugwort pollen, apple, potato	2 kiwi allergic patients (1) 3 kiwi allergic patients (2) (RAST inhibition)	(1) Gall et al. 1990 (2) Gall et al. 1994
Kiwi Fruit 60 kDa mugwort allergen (Art v 1)	patients with food / pollen allergy (RAST inhibition)	Heiss et al. 1996
Kiwi Fruit latex	3 and 4 kiwi and latex allergic patients (RAST inhibition)	Brehler et al. 1997
Kiwi Fruit *potentially cross- reactive latex allergen: Hev b 5	Hev b 5, an acidic 16-kDa allergen in latex from Hevea brasiliensis with pI=3.5 shows a high degree of homology in the amino acid sequence (47% sequence identity) to an acidic protein from kiwi fruit*	Akasawa et al. 1996
Kiwi Allergens a) timothy pollen, b) birch pollen	Pooled serum and 6 sera from kiwi allergic patients: a) Inhibition of IgE- binding to 22, 38, and 41 kDa kiwi allergens by timothy pollen extract; b) Inhibition of IgE- binding to 14, 22, 24, 38, and 41 kDa kiwi allergens by birch pollen extract (immunoblot inhibition)	Pastorello et al. 1996
Kiwi Allergens (43, 67 kDa) birch pollen (68-kDa-Allergen), apple (67-kDa-Allergen), carrot, celery	7 kiwi allergic patients (immunoblot inhibition)	Möller et al. 1997b
Kiwi Allergens (10-12 kDa) birch pollen	15 birch pollen allergic patients (immunoblot inhibition)	Voitenko et al. 1997

Kiwi Fruit (23-92 kDa) birch pollen, birch pollen carbohydrates	2 kiwi allergic patients: 23-, 43-, 80-, and 92-kDa kiwi allergens were inhibited by birch pollen extract (immunoblot inhibition) Inhibition of IgE- binding to kiwi extract by birch pollen carbohydrates (proteinase-K digested birch pollen, ELISA inhibition)	Fahlbusch et al. 1998
Kiwi Allergens (43, 67 kDa) avocado, banana, latex	5 kiwi allergic patients (immunoblot inhibition)	Möller et al. 1998
Kiwi Fruit (15-94 kDa) birch, timothy, rye, and mugwort pollen	22 kiwi allergic patients (immunoblot inhibition)	Rudeschko et al. 1998
Kiwi Allergen (41 kDa) avocado allergen (Prs a 1, chitinase class I), latex extract	Pooled serum from latex- fruit allergic patients: Inhibition of IgE- binding to 41-kDa kiwi allergen by Prs a 1 from avocado and by latex extract (immunoblot inhibition)	Diaz-Perales et al. 1999

* not proven by inhibition-tests

Unique Allergens	Subjects / Methods	References
Kiwi Fruit / Birch Pollen 30-kDa allergen not cross-reactive to birch pollen extract	1 kiwi allergic patient with and 1 without birch pollen allergy, respectively (immunoblot inhibition)	Fahlbusch et al. 1998
Kiwi Fruit latex	Children with atopic dermatitis: cross inhibition between kiwi and latex <25% in 12 latex sensitized patients (latex and avocado 100%); no significant difference in sensitization to kiwi in 12 latex sensitized children and 20 children without specific latex IgE (RAST, RAST inhibition)	Tucke et al. 1999

8 Posttranslational Modifications

Modification	Methods	References
Carbohydrate Structures Specific binding to carbohydrate epitopes by 5 out of 7 sera from kiwi allergic patients	Preincubation of kiwi extract with periodate in order to destroy carbohydrate structures: 15 to 80% reduction of IgE- binding (EAST)	Fahlbusch et al. 1998
Carbohydrate Structures Specific binding to carbohydrate epitopes by 4 out of 5 sera from kiwi allergic patients	Preincubation of sera with proteinase-K digested kiwi extract to obtain cross- reactive carbohydrates: IgE (EAST inhibition)	Fahlbusch et al. 1998
Carbohydrate Structures {alpha}-fucose moieties in 35-, 43-, 50-, 60-, 80-, and 92-kDa proteins	Immunodection by lectin binding from *Aleuria aurantia* (SDS-PAGE immunoblot)	Fahlbusch et al. 1998
Asparagine-linked Glycans in 41-kDa kiwi allergen	Detection of complex asparagine- linked glycans by class I and II chitinase- specific mAb (rabbit); IgE- binding by pooled serum from latex- fruit allergic patients (SDS-PAGE immunoblot)	Diaz-Perales et al. 1999

9 Stability of Kiwi Allergens

Treatment	Effects	References
Kiwi Fruit heat: 40, 60, 80, and 90°C (microwave) 3 kiwi-allergic patients	Prick-test: decrease of activity with increasing temperature, 90°C: complete loss of activity in 2 patients	Gall et al. 1993

10 References

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Common Abbreveations

2D	two-dimensional
3D	three-dimensional
aa	amino acid(s)
Ab	antibody
Act c 1, 2	nomenclature of kiwi fruit allergens *(Actinidia chinensis)*
Bos d 4, 5, 6, 7, 8	nomenclature of cow's milk allergens *(Bos domesticus)*
C	concentration of N,N'-methylenbisacrylamide (crosslinker)
CAST	cellular antigen stimulation test
CICBAA	Cercle d'Investigations Cliniques et Biologiques en Allergologie Alimentaire (France)
CIE	crossed immunoelectrophoresis
CNBr	cyanogen bromide
cIEF	capillary isoelectric focussing
CLA	cutaneous lymphocyte antigen
CLIE	crossed line immunoelectrophoresis
CRIE	crossed radioimmunoelectrophoresis
Cor a 1	nomenclature of hazel pollen allergens *(Corylus avellana)*
Cyn d 1	nomenclature of bermuda grass pollen allergens *(Cynodus dactylus)*
DBPCFC	double-blind, placebo-controlled food challenge
DNA	deoxyribonucleic acid
EAST	enzyme allergosorbent test
EC	enzyme classification system
EDTA	ethylenediaminetetraacetic acid, disodium salt
ELISA	enzyme linked immunosorbent assay
EW	egg white
Fuc	fucose
Gad c 1	nomenclature of baltic cod allergen *(Gadus callarias)*
Gal	galactose
Gal d 1, 2, 3, 4	nomenclature of egg white allergens *(Gallus domesticus)*
GlcN	glucosamine
GlcNAc	N-acetylglucosamine
Gly m 1, 2, 3	nomenclature of soybean allergens *(Glycine max)*
HLA	human leucocyte antigen
Hol l 1	nomenclature of sweet velvet grass allergens *(Holcus lanatus)*
HPLC	high performance liquid chromatography
HR	Histamine Release
IEC	ion exchange chromatography
IEF	isoelectric focussing
Ig	immunoglobulin
IL	interleukin
INF-gamma	interferon-gamma
Lol p 1	nomenclature of rye grass allergens *(Lolium perenne)*
LTA4	leukotriene A4
LTB4	leukotriene B4

LTC4	leukotriene C4
LY	lysozyme
Man	mannose
Mal d 1, 3	nomenclature of apple fruit allergens *(Malus domestica)*
MALDI-MS	matrix-assisted laser-induced desorption/ionization mass spectrometry
MAST	multiple allergen sorbent test
MHC	major histocompatibility complex
Mr	molecular mass
NeuNAc	N-acetylneuraminic acid
NMR	nuclear magnetic resonance (spectroscopy)
OA	ovalbumin
OAS	oral allergy syndrome
OM	ovomucoid
Ory s 1	nomenclature of rice allergens *(Oryza sativa)*
OT	ovotransferrin
PAGE	polyacrylamide gel electrophoresis
PBMC	peripheral blood mononuclear cells
PBS	phosphate buffered saline
Phl p 1	nomenclature of timothy grass allergens *(Phleum pratense)*
pI	isoelectric point
PCA	passive cutaneous anaphylaxis (test)
PCR	polymerase chain reaction
PVDF	polyvinyliden difluoride
PVPP	polyvinyl polypyrrolidone
RAST	radioallergosorbent test
RBL cells	rat basophil leukaemia cells
RIEP	radioimmunoelectrophoresis
RNA	ribonucleic acid
RT	room temperature
SAFT	skin application food test
SDS	sodium dodecylsulfate
SEC	size exclusion chromatography
SPT	skin prick test
T	total acrylamide concentration
TCC	T-cell clone
TCL	T-cell line
TGF-beta-1	transforming growth factor beta-1
TH	thermolysin
TNF-alpha	tumor necrosis factor alpha
TR	trypsin
Tris	tris-(hydroxymethyl)aminomethane
Xyl	xylose