Allergen Data Collection:

Sunflower Seed *(Helianthus annuus)*

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Abstract

Sunflower belongs to the family of Compositae. The whole seeds are used in breads and for garnishing bakery products or as livestock, bird, and poultry feed. Edible sunflower seed oils are ingredients of cooking and salad oils, and of margarine. Reportedly anaphylactic reactions have been elicited after ingestion of sunflower seeds, sunflower oil, and honey containing sunflower pollen.
About 10 different allergens from 10 to 67 kDa have been detected in sunflower seeds. Recently a 2S methionine-rich sunflower seed albumin (SSA) has been identified as a sunflower seed allergen. In pollen a 34 kDa protein (Hel a 1) and sunflower profilin (Hel a 2) were characterized as allergens.
The present allergen data collection summarizes data on prevalence, symptoms, allergen sources, stability and cross-reactivity of sunflower allergens and their molecular biological and allergenic properties in tabular form.
Sesquiterpene lactones occur in the glandular hairs of sunflower. These substances are not discussed in the present review, but are considered to be capable of inducing allergic contact dermatitis in sensitized individuals.
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Contents

1 Prevalence of Sunflower Seed Allergy

Prevalence data are based on different diagnostic procedures. While the prevalence of sensitization (sensitivity) can be estimated by SPT, RAST, and immunoblot, a clinical relevant sensitization (allergy) is evaluated by convincing history (anamnesis) or food challenge tests (ideally by DBPCFC).

1.1 Subjects with Atopic or Other Diseases

Country / Subjects	Incidences of Allergy / Sensitivity	References
Crotia, Zagreb 35 animal feed workers	sunflower seed 54% (SPT)	Zuskin et al. 1992
Italy, Genoa 132 pollen and food sensitive patients	sunflower seed 0.7% (incidents of hypersensitivity)	Troise et al. 1992
Israel, Tel-Aviv 112 patients with food allergy (onset after 10 years of age)	sunflower seed 78% (SPT, n=108) sunflower seed 35% (food challenge, n=71)	Kivity et al. 1994
Netherlands 131 cases of food-induced anaphylaxis (from 1993-1997)	sunflower seed 0.8% (survey, reported to the TNO Nutrition and Food Research Institute)	European Commission 1998
Spain, Gran Canaria 102 adults with symptoms after ingestion of specific foods	sunflower seed 9% (SPT, RAST)	Castillo et al. 1996
Spain, Madrid 355 food allergic children	sunflower seed 4.2% (SPT, RAST)	Crespo et al. 1995a
Spain, Madrid 29 plant-derived food allergic patients	sunflower seed 3.4% (SPT / RAST)	Diez-Gomez et al. 1999
Spain, Plasencia (Caceres) 262 patients with pollinosis	sunflower seed 4.5% (self-reported)	Garcia-Ortiz et al. 1995
Spain, Salamanca a) 84 mugwort sensitive patients without other pollen sensitizations b) 57 fruit allergic patients (age of 6-56 years, mean 21.5)	a) sunflower seed 13% honey 17% (RAST) b) sunflower seed 8.8% (clinical history)	a) Garcia-Ortiz et al. 1996 b) Garcia Ortiz et al. 1998
Sweden 61 cases of food-induced anaphylaxis (from 1994-1996)	sunflower seed 1.6% (reported to the National Food Administration)	European Commission 1998
Sweden, Stockhom 84 atopic patients with positive SPT to at least 1 common allergen	sunflower seed 21% (SPT) sunflower seed 3.6% (RAST)	Axelsson et al. 1994

Switzerland, Zurich 402 food allergic adults (study period 1978-87)	sunflower seed 0.2% (anamnesis, clinical relevance, diagnostic tests)	Wüthrich 1993

1.2 Associated Allergies

Country / Subjects	Allergy / Sensitivity	References
Spain, Madrid 52 children sensitized to sunflower seeds	pollen 90% (SPT)	Crespo et al. 1995b

2 Symptoms of Sunflower Seed Allergy

Symptoms & Case Reports	References
Systemic reactions anaphylaxis (1, 4, 5, 7, 8, 10, 11, 12, 15, 16) Symptoms of skin and mucous membranes angioedema (4, 15), facial angioedema (6, 9, 16), pruritus (4), rhinoconjunctivitis (6, 11, 14), urticaria (2, 4, 8, 11, 15), contact urticaria (13), generalized urticaria (6) Gastrointestinal symptoms abdominal pain (3, 9, 16), angioedema of lips and mouth (11), diarrhea (3, 6), laryngeal edema (6), nausea (4), oral itching (15), oral pruritus (11), vomiting (3, 4, 6, 8, 15) Respiratory symptoms asthma (14), chronic bronchial asthma (7), cough (6, 9, 16), dyspnoea (6, 8, 12), shortness of breath (2), wheeze (4) Other symptoms fever (15), hypotension (8, 15)	(1) Noyes et al. 1979 (2) Bernstein et al. 1982 (3) Bousquet et al. 1985 * (4) Halsey et al. 1986 (5) Stricker et al. 1986 (6) Fernández et al. 1993 * (7) Axelsson et al. 1994 (8) Iwaya et al. 1994 (9) Kanny et al. 1994 (10) Kivity et al. 1994 (11) Garcia Ortiz et al. 1995 (12) Fäh et al. 1995 (13) Duran et al. 1997 (14) Vandenplas et al. 1998 ** (15) Kelly et al. 2000 (16) Zitouni et al. 2000 * symptoms after ingestion of honey containing sunflower pollen ** sunflower seed dust
Onset of Symptoms Symptoms occured within 15 min in DBPCFC and within 1 h in open challenge in 2 sunflower seed allergic patients (1)	(1) Bernstein et al. 1982
Percentage of reactions Sunflower seed Oral pruritus in 67%, anaphylaxis in 33%, angioedema of lips/mouth in 33%, gastrointestinal symptoms in 25%, urticaria in 17%, and rhinoconjunctivitis in 8% of 12 patients with reported sunflower seed allergy (1) Sunflower pollen (honey) Itching in mouth in 52%, gastrointestinal symptoms in 17%, contact urticaria/angioedema in 9%, bronchial asthma in 30%, generalized urticaria in 9%, and anaphylaxis in 17% in 23 patients allergic to honey (2)	(1) Garcia Ortiz et al. 1995 (2) Bauer et al. 1996
Threshold for Elicitation of Symptoms Doses of 14.6 g of sunflower seeds elicited allergic symptoms in 2 sunflower seed allergic patients (DBPCFC and open challenge, respectively) (1) A dose of 5 mL sunflower seed oil induced allergic symptoms in a sunflower seed allergic patient (DBPCFC) (2)	(1) Bernstein et al. 1982 (2) Zitouni et al. 2000

3 Diagnostic Features of Sunflower Seed Allergy

Parameters / Subjects	Outcome	References
Route of Sensitization 4 patients with sunflower seed allergy	All 4 patients had kept cage birds fed on sunflower seeds and reacted at the first time of sunflower seed ingestion; therefore, the route of sensitization was probably by inhalation of airborne sunflower seed allergens	Axelsson et al. 1994
Augmentation Factors Simultaneous ingestion of acetylsalicylic acid: 39 year old patient with sunflower seed sensitivity (SPT, RAST)	Intense allergic reaction and shock after simultaneous ingestion of sunflower seeds and acetylsalicylic acid; ingestion of sunflower seeds and acetylsalicylic acids alone induced only milder symptoms or no symptoms, respectively	Moller & Paul 1996
SPT 12 patients with reported sunflower seed allergy	Positivity in SPT with a) commercial extract 8% b) fresh sunflower seeds 42%	Garcia Ortiz et al. 1995

4 Composition of Sunflower Seeds

4.1 Distribution of Nutrients

For other sunflower seed products see: USDA Nutrient Database

Nutrients: Content per 100 g		
Energy 2454 kJ (580 kcal) Water 6.6 g Protein 22.5 g Lipids 49.0 g Carbohydrate 12.3 g Fiber 6.3 g Minerals 3.3 g **Minerals** Sodium 2 mg Potassium 725 mg Magnesium 420 mg Calcium 100 mg Manganese 2.4 mg Iron 6.3 mg Copper 2.8 mg Zinc 5.2 mg Phosphorus 620 mg	**Vitamins** Vitamin B1 1900 µg Vitamin B2 140 µg Nicotinamide 4100 µg **Amino Acids** Arg 2200 mg His 630 mg Ile 1370 mg Leu 1710 mg Lys 890 mg Met 490 mg Phe 1260 mg Thr 910 mg Trp 310 mg Tyr 650 mg Val 1260 mg	**Lipids** Palmitic acid 3140 mg Stearic acid 2120 mg Oleic acid 13.4 g Linolic acid 29.7 g Linoleic acid 90 mg **Other** Salicylic acid 120 µg

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

5 Allergens of Sunflower Seed and Pollen

Seed Proteins / Glycoproteins	Allergen Nomenclature	References
2S Methionine-rich Protein [12 kDa]		Kelly & Hefle 2000
Allergen: 13.5 kDa		Iwaya et al. 1994
Allergen: 67 kDa		Zitouni et al. 2000
Allergens: 10.5, 13.5, 15.9, 16.7, 17.2, 22.7, 33.2, 43.6, and 48.9 kDa		Kelly et al. 2000

Pollen Proteins / Glycoproteins	Allergen Nomenclature	References
34-kDa Allergen	Hel a 1	Jiménez et al. 1994
Sunflower Profilin [15.7 kDa]	Hel a 2	Asturias et al. 1998
Allergen: 14 kDa		Ostroumov et al. 1979
Allergens: 14, 24, 25, 47, and 56 kDa		Fernández et al. 1993
Allergens: 24, 32, and 55 kDa		de la Hoz et al. 1994
Allergens: 14-102 kDa		Jiménez et al. 1994
Allergens: 17, 42, and 85 kDa		Astwood et al. 1995
Allergens: 30, 33, 54, 60, and 72 kDa		Bauer et al. 1996

5.1 Sensitization to Sunflower Allergens

Country / Subjects	Sensitivity to	References
Austria, Vienna / Bad Vöslau a) 23 patients allergic to honey b) 10 patients allergic to bee venom	Sunflower Pollen (honey extract): **Allergen** **a)** **b)** 30 / 33 kDa 48% 54 / 60 / 72 kDa 74% 46 / 54 / 69 kDa 70% (SDS-PAGE / immunoblot)	Bauer et al. 1996
Spain, Bilbao 14 patients with Compositae pollen allergy	Sunflower Pollen: **Allergen** 34 kDa 57% 43 kDa 57% 33 kDa 43% 76 kDa 43% 40 kDa 36% 102 kDa 36% 14, 18, 29, 47, 53, 58, 60, 63, 65, 81, and 86 kDa <30% (SDS-PAGE immunoblot)	Jiménez et al. 1994
Spain, Bilbao 121 patients sensitive to sunflower pollen	Sunflower pollen profilin 31% (specific IgE)	Asturias et al. 1998

Spain, Guadalajara / Madrid 20 patients with Compositae pollen allergy	Sunflower Pollen: **Allergen** 24 kDa 100% 25 kDa 95% 14, 47, and 56 kDa 75-80% <14, 18, and 20 kDa <50% (SDS-PAGE / immunoblot)	Fernández et al. 1993
Spain, Madrid 21 patients with sunflower pollen allergy	Sunflower Pollen: **Allergen** 24 kDa 85% 32 kDa 80% 55 kDa 92% 55 kDa 92% (RAST)	de la Hoz et al. 1994
USA, Lincoln, NE 5 sunflower seed allergic patients	Sunflower Seed: 16-17 kDa allergen in 40% (SDS-PAGE / immunoblot)	Kelly et al. 2000

5.2 Properties of 2S-Methionine-rich Protein (SSA)

5.2.1 Molecular Biological Properties

2S-Methionine-rich Protein			References
Allergen Nomenclature none			
Molecular Mass			(1) Kelly & Hefle 2000 (2) Kelly et al. 2000
	SDS-PAGE		
mature protein	12 kDa (2)		
immature protein	16-17 kDa (1)		
Isoelectric Point			(1) Kelly et al. 2000
	IEF-PAGE		
mature protein	pI 5.91 (1)		
immature protein	pI 5.35 (1)		
Amino Acid Sequence, mRNA, and cDNA			(1) Kortt et al. 1991
	SSA (precursor)	**SSA (mature protein)**	
SWISS-PROT:	P23110		
GenBank:	X56686		
PIR:			
Amino acids	141 residues (1)	103 residues (1)	
mRNA	600 bp (1)		
cDNA			
Gene			
Posttranslational Modifications Disulfide bonds: 4 intra-chain disulfide bonds (1)			(1) Egorov et al. 1996
Biological Function Family of 2S albumin seed storage proteins (1)			(1) Kortt et al. 1991

Sequence Homology 2S-Methionine-rich from Brazil nut: 34% aa identity (1) Conglutin-like protein from peanut (Ara h 2): 34% aa similarity (2)	(1) Kortt et al. 1991 (2) Stanley et al. 1997

5.2.2 Allergenic Properties

2S-Methionine-rich Protein	References
Frequency of Sensitization IgE-binding to immature protein in 40% of patients (1)	(1) see 7.1 Sensitization to Sunflower Seed Allergens

5.3 Properties of Sunflower Pollen Profilin (Hel a 2)

5.3.1 Molecular Biological Properties

Sunflower Profilin				References
Allergen Nomenclature Hel a 2				(1) Allergen Nomenclature Sub-Committee 2001
Isoallergens and Variants 3 isoforms differing in pI (1)				(1) Asturias et al. 1998
Molecular Mass 14.7 kDa (SDS-PAGE)				(1) Asturias et al. 1998
Isoelectric Point pI 4.41, 4.46, and 4.50 (Agarose-IEF)				(1) Asturias et al. 1998
Amino Acid Sequence, mRNA, and cDNA				(1) Asturias et al. 1998
Proteins				
SWISS-PROT:				
GenBank:	T31427	O81982	CAA75506	
Amino Acids	133 (1)	133 (1)	133 (1)	
mRNA precursor			402 bp (1)	
cDNA precursor				
recombinant Profilin Expression in *Escherichia coli*: rHel a 2 expressed as non-fusion form (1) 2 recombinant profilins as glutathione-S-transferase fusion-proteins (2)				(1) Asturias et al. 1998
Biological Function Binds to actin (1:1), affects structure of the cytoskeleton profilin family (1)				(1) SWISS-PROT
Sequence Homology 11 plant profilins: aa sequence identies 69% to 88% (1) Bet v 2 from birch pollen: aa sequence identity 73% (1)				(1) Rihs et al. 1999

5.3.2 Allergenic Properties

Sunflower Profilin	References
Frequency of Sensitization IgE-binding to profilin in 31% of patients (1)	(1) see 6.1 Sensitization to Sunflower Allergens

Allergenicity of Recombinant Proteins IgE binding capacity of rHel a 2 comparable to natural Hel a 2 (immunoblot inhibition, EAST inhibition) (1)	(1) Asturias et al. 1998

6 Isolation & Preparation

Extract / Purified Allergens	Methods	References
Protein extract from seeds	After the oil was squeezed out (hydraulic press) pressed sunflower seeds were extracted overnight with physiologic saline solution followed by centrifugation, ultracentrifugation, and sterile filtration	Axelsson et al. 1994
Protein extract from seeds	Seeds were ground and respectively extracted in either 0.01-M PBS (pH 7.4) or double-destilled water overnight with shaking at RT; followed by centrifugation, storage at -20°C	Kelly et al. 2000
Protein extract from seed oil	Extraction of oil with 0.05-M PBS (pH 6.5) with rocking for 24 h at 60°C; followed by centrifugation, dialysis of the aqueous phase and lyophilization	Zitouni et al. 2000
Protein extract from seeds, pollens and honey	Crushed seeds, pollens, and honey extracted with Coca's solution by stirring for 24 h at 4°C, followed by sterile filtration and lyophylization	Bousquet et al. 1985
Protein extract from pollens	Extraction by incubation of pollens in 0.05-M ammonium carbonate buffer for 7 h at 4°C followed by centrifugation, filtration, and lyophylization; storage at -20°C	Fernández et al. 1993
Protein extract from pollens	Extraction of pollens with 0.05-M ammonium carbonate buffer for 60 min at RT followed by centrifugation, dialysis, centrifugation, membrane filtration, and lyophylization	de la Hoz et al. 1994
Protein extract from pollens	Defatted pollen extracted with 0.1-M phosphate buffer (pH 8) by stirring for 24 h at 4°C; followed by centrifugation, membrane filtration, dialysis, sterile filtration, and lyophylization	Jiménez et al. 1994
Protein extract from honey	Honey suspended and extracted in water overnight at 4°C, followed by centrifugation, dialysis, and lyophylization, storage at -20°C	Bauer et al. 1996
2S Methionine-rich Protein (Seeds)	Extraction of albumins from washed, dried, and defatted raw sunflower seed meal; isolation of 2S methionine-rich protein by HPLC; followed by dialysis of fractions and lyophilization	Kelly & Hefle 2000
34-kDa Allergen (Hel a 1) (Pollen)	Purification from pollen extract by size exclusion chromatography followed by anion exchange chromatography	Jiménez et al. 1994
Sunflower Profilin (Pollen)	Isolation from pollen extract by affinity chromatography on poly-(L-prolin)- Sepharose column, followed by purification by anion exchange chromatography (MonoQ column) and size exclusion chromatography (Superdex column)	Asturias et al. 1998

7 Cross-Reactivities

Cross-Reacting Allergens	Subjects / Methods	References
Sunflower Pollen *(Pollen)* Compositae pollen	Maximal inhibition of 90% of IgE-binding to sunflower pollen extract by mugwort and marguerite pollen extract; less inhibition by golden rod, short ragweed, and dandelion pollen extracts (RAST inhibition); Inhibition of IgE-binding to sunflower pollen extract in immunoblot inhibition by mugwort, marguerite, and short ragweed pollen extract	Fernández et al. 1993
Sunflower Pollen *(Pollen)* Compositae pollen	Inhibition of IgE-binding to sunflower pollen extract by Ambrosia, Artemesia, and Crysanthemum pollen extracts (RAST inhibition, pooled serum)	Jiménez et al. 1994
Sunflower Pollen *(Pollen)* Compositae pollen, other plant pollen, and sunflower profilin	High cross-reactivity between recombinant Hel a 2 and profilins from mugwort, short ragweed, Bermuda grass, olive tree, *Mercuialis annua* pollen profilins (immunoblot inhibition, EAST inhibition, pooled serum)	Asturias et al. 1998
Sunflower Pollen *(Pollen, Camomile)* Mugwort pollen, dried *Martricaria chamomila*, honey containing 24% of sunflower pollen of total pollen	Inhibition of IgE-binding to extract of honey containing sunflower pollen by mugwort pollen and camomile extract (RAST inhibition, pooled serum from honey and camomile tea allergic patients)	Florido-Lopez et al. 1995
Sunflower Pollen *(Honey Bee)* Honey bee head extract, sunflower pollen (honey extract)	Inhibition of IgE-binding to extract form sunflower pollen honey by honey bee head extract (immunoblot inhibition, pooled sera from honey and/or honey bee venom allergic patients)	Bauer et al. 1996
Sunflower Seed / Pollen *(Pollen)* Mugwort pollen, sunflower pollen and seed	IgE-binding to mugwort pollen extract was inhibited by sunflower pollen about 50% and by sunflower seed extract about 28% (RAST inhibition, 1 patient allergic to mugwort pollen and sunflower seed)	Kanny et al. 1994
Sunflower Seed *(Pollen)* birch pollen, 35 kDa birch allergen, Bet v 1, and sunflower seed	IgE binding to sunflower seed extract inhibited by birch pollen extract (97% inhibition), 35 kDa birch allergen (40%) and Bet v 1 (28%) (EAST inhibition, pooled serum from 7 birch pollen allergic patients)	Wellhausen et al. 1996
Sunflower Seed *(Fruits)* Lychee fruit, sunflower seed	77% inhibition of IgE-binding to lychee extract by sunflower seed extract (RAST inhibition, 1 lychee fruit allergic patient)	Fäh et al. 1995

Unique Allergens	Subjects / Methods	References
Sunflower Seed / Pollen Sunflower seed, sunflower pollen, honey containing sunflower pollen	IgE-binding to sunflower pollen significantly inhibited by honey containing sunflower pollen; no IgE-binding to sunflower seeds (RAST, RAST inhibition, 1 patient allergic to sunflower pollen)	Bousquet et al. 1985

8 Stability of Sunflower Seed Allergens

Treatment	Effects	References
Sunflower Seeds *(Heat)* roasting	IgE-binding to protein extract of salted roasted sunflower seeds (3 patients with sunflower seed allergy)	Kelly et al. 2000
Sunflower Seed Oil *(Refining Steps)* steps of the refining process: a) crude pressed oil (expeller, chemical extraction), b) acidification and neutralization (85°C, 15 min), c) pregumming by centrifugation (10°C, 4 h), d) washing (85°C, 5 min), e) bleaching 85°C, 20 min), f) gumming by filtration (10°C, 5 h), and g) deodorization (220°C, 4 min, vacuum)	Protein content decreased after each refining step: a) to c) from 13.6 to 11.3 µg/mL, d) to g) from 2.75 to 0.22 µg/mL; SDS-PAGE showed 5 bands (67 to 145 kDa), amount of most abundant protein (67 kDa) decreased after each step, trace amounts in the refined oil Immunoblot: 67-kDa protein showed allergenic activity, faint bands at 114, 131, 132, and 145 kDa in crude oil (1 patient serum)	Zitouni et al. 2000

9 Allergen Sources

Reported Adverse Reactions	References
Food / Food additives After ingestion of sunflower seeds (1)	(1) see 2 Symptoms of Sunflower Seed Allergy
Sunflower Seeds in Foods Allergic reactions in a patient after ingestion of a fruit yoghurt containing sunflower seeds (SPT, RAST inhibition) (1)	(1) Fäh et al. 1995
Sunflower Seed Oil Allergic reactions to sunflower seed oil in a patient allergic to mugwort pollen and sunflower seed oil (SPT, single blinded oral challenge test with 5 mL oil) (1) Allergic reactions after ingestion of a meal containing sunflower oil and margarine in a sunflower seed allergic patient (2)	(1) Kanny et al. 1994 (2) Zitouni et al. 2000
Honey *(Sunflower Pollens)* Allergic reactions in a sunflower pollen allergic patient after ingestion of honey containing 30% sunflower pollen among total pollens (1) 50% of 20 patients with allergy to Compositae pollen experienced allergic symptoms after ingestion of sunflower honey (2) Allergic reactions after ingestion of honey containing 24% sunflower pollen among total pollen in 7 patients (clinical history, SPT, RAST) (3)	(1) Bousquet et al. 1985 (2) Fernández et al. 1993 (3) Florido-Lopez et al. 1995
Sunflower Seed *(Sunflower Pollens)* Allergic reactions to sunflower pollen concealed in a commercial preparation of peeled sunflower seeds in a 22-year old woman (RAST, open food challenge) (1)	(1) Rottem & Waisel 1998

Allergens in Sunflower Seed Products	Content / Products	References
Sunflower Seed Oil 1 patient with sunflower seed allergy	IgE-binding to 67-kDa in crude and refined oil; faint bands at 114, 131, 132, and 145 kDa in crude oil (SDS-PAGE immunoblot) Positive SPT to refined sunflower oil	Zitouni et al. 2000

Potential Sources	References
Transgenic Lupins Aim: improving the nutritive value of an important grain legume crop Modification: expression of the 2S methionine-rich sunflower seed albumin (SSA) stably transformed into narrow-leafed lupin (*Lupinus angustifolius* L.) Allergenicity: transferred protein is a known sunflower seed allergen which accounted for 5% of extractable seed proteins in transgenic lupins; allergenicity of transgenic lupin not tested (1)	(1) Molvig et al. 1997

Reported Safe Products	References
Sunflower Seed Oil * 2 patients with clinical relevant sunflower seed allergy: negative SPT (only 1 patient tested) and safe ingestion of up to 16 mL of refined and cold-pressed sunflower seed oil (open challenge, protein concentration of both oils: 2-8 µg/mL) (1)	(1) Halsey et al. 1986

* see also Reported Adverse Reactions

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