

Allergen Data Collection - Update:

Soybean (*Glycine max*)

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Soybean (*Glycine max*)

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Abstract

Soybean is the most important nutrient of the legume family. Allergy to soybeans is common in food allergic children younger than 3 years of age. Adverse reactions caused by soybean formulas are seen in 14-35% of cow's milk allergic infants. In food allergic subjects with atopic dermatitis egg, milk, peanut, and soybean account for almost 90% of allergic reactions. The prevalence of soybean allergy in the general population is probably below 0.5%. Symptoms range from skin, gastrointestinal, and respiratory reactions to severe systemic reactions including anaphylaxis. There are several reports of inadvertent ingestions of soy protein which caused life-threatening allergic reactions. Fatal reactions to soybean have also occurred in peanut allergic individuals, whose sensitivity to soybean was not recognized previously.

Soybean products are used in the manufacture of foods with almost no limits, e.g. as a texturizer, emulsifier, or protein filler. Therefore it is a particularly hazardous hidden allergen in pastries, bakery products, infant foods, sausages, processed meats, and hamburgers. Fermented soybean products such as miso, tempeh, shoyu, and natto are potentially less allergenic than raw soybeans. However, even acid and mold-hydrolyzed soy sauce retain significant allergenic potencies. While soybean lecithins can induce allergic reactions, highly refined soybean oils are generally safe. Soybeans and its products should always be declared according to a list of the Codex Alimentarius Commission on mandatory labelling of prepackaged foods.

About 16 soybean allergens have been identified. Major ingestive allergens are the following water soluble proteins: Gly m Bd 30K (thiol-protease P34), the storage proteins glycinin and beta-conglycinin, and profilin (Gly m 3). Several sequential IgE-binding epitopes have been identified on Gly m Bd 30K, while studies with recombinant profilin fragments indicate the predominant role of conformational epitopes. On the other hand soybean hull proteins Gly m 1 and Gly m 2, and the Kunitz-trypsin inhibitor are involved in respiratory hypersensitivity reactions. Soybean dust has caused several epidemic incidents of asthma in soybean mill workers, harbour workers and animal feed workers as well as in bakers. In asthma, cross-reactivities between soy flour and wheat, rye, and barley flours could be observed. Although there is extensive in vitro cross-reactivity among various legumes, e.g. soybean, peanuts, peas, and beans, clinical reactivity is usually limited to a single legume source.

The present review summarizes data on prevalence, symptoms, diagnostic features, allergenic potencies of processed foods and transgenic soybeans, allergen sources, and infant formulas as well as molecular biological and allergenic properties of the major soybean allergens in tabular form.

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1 Prevalence of Soybean Allergy

1.1 General Population

Prevalences within the author's selected populations are listed. Those that are assigned randomly selected ("unselected") with numbers more than 500 may be regarded as representative of the "general population". Inclusion criteria may involve circumstances not related to atopic predisposition according to current knowledge.

Country / Subjects	Allergy / Sensitivity to	References
<i>Sweden (Göteborg, Uppsala, Västerbotten)</i> 1397 unselected adults, age of 20-44 years (study period 1991-92)	soybean 2% (RAST)	Björnsson et al. 1996

1.2 Subjects with Atopic or Other Diseases

Country / Subjects	Allergy / Sensitivity to	References
<i>Australia, Victoria</i> 100 cow's milk allergic children	soy milk 47% (parents reported)	Bishop et al. 1990
<i>Croatia, Zagreb</i> 35 animal feed workers	soybean 29% (SPT)	Zuskin et al. 1992
<i>Finland, Oulu</i> children with atopic dermatitis	soybean 2.8%, 5.0%, and 13% in patients < 1 year, 1-3 years, and 3-15 years of age (n=36, 40, 40) (SPT)	Hannuksela 1987
<i>France</i> 80 cases of food- related anaphylaxis (from 1993-97)	soy flour 2.5% (reported to CICBAA databank)	European Commission 1998
<i>France, Meuse</i> 742 agricultural workers	soybean dust 6.5% (SPT)	Maria et al. 1991
<i>France, Pierre Benite</i> a) 580 patients with adverse reactions to food b) 60 cases of anaphylaxis (study period 1984-92)	a) soybean 30% (RAST) b) soybean 3.3%	Andre et al. 1994
<i>France, Nancy and Toulouse</i> 544 food allergic children	soybean 1.2% (food challenge)	Rance et al. 1999
<i>Germany, Berlin</i> 107 children with atopic dermatitis	soybean 16% (n=45, DBPCFC)	Niggemann et al. 1999
<i>Germany, Bonn</i> 250 patients with suspected food allergy	soybean 10% (clinical history, oral challenge)	Mistereck et al. 1992
<i>Germany, Bonn</i> 150 children allergic to egg white, milk, cod fish, wheat, peanut and/or soybean	soybean 46% (RAST)	Liappis & Starke 1999
<i>Germany, Ulm</i> 24 legume-sensitive adults	soybean 21% (SPT, RAST)	Hagner et al. 1998
<i>Italy, Milano</i> 71 children with food intolerance	soybean 17% (oral challenge)	Bardare et al. 1988
<i>Italy, Milano</i> 704 atopic children	soybean 21% (SPT), from which 6% were DBPCFC-positive	Magnolfi et al. 1996
<i>Italy, Rome</i> 371 children with food allergy	soy 22% (RAST) soy 3% (positive challenge)	Giampietro et al. 1992

Italy, Rome 174 infants at risk for atopy	soybean 5% (RAST)	Bruno et al. 1995
Italy, Rome a) 505 children with food allergy b) 243 children at risk for atopy	a) soybean 6% (SPT) from which 19% had positive challenge b) soybean 6% (SPT) from which 1/14 were DBPCFC-positive	Bruno et al. 1997
Japan, Gifu, Nabu children with asthma and/or atopic dermatitis from Gifu (n = 167) and Nanbu (n = 146)	soybean 6.8% (Nanbu), 18% (Gifu) (RAST)	Agata et al. 1994
Japan, Tokyo 39 children with positive food challenge	soybean 10% (positive challenge)	Iwasaki et al. 1994
Japan, Tokushima 86 patients with atopic dermatitis	soybean 20% (SDS-PAGE immunoblot)	Ogawa et al. 1991
Netherlands 131 cases of food- induced anaphylaxis (from 1993-1997)	legumes (excluding peanut) 4.6% (survey, reported to the TNO Nutrition and Food Research Institute)	European Commission 1998
Netherlands, Rotterdam 91 patients with atopic dermatitis	soybean 1% (SAFT)	Oranje et al. 1992
Poland 163 food allergic infants	soybean 52% (RAST)	Hofman 1994
Spain, Cartagena patients with asthma (associated to asthma outbreak during the unloading of soybeans)	soybean 81% (SPT)	Navarro et al. 1993
Spain, Tarragona 15 atopic patients affected by a soybean asthma outbreak	soybean 87% (SPT)	Garcia-Ortega et al. 1998
South Africa, Cape Town 112 children with atopic dermatitis (age of 5 months to 13 years)	soybean 3.6% (questionnaire)	Steinman & Potter 1994
South Afrika, Johannesburg 22 workers exposed to soybean dust	soybean 36% (SPT) soybean 36% (RAST)	Roodt & Rees 1995
Sweden 61 cases of food- induced anaphylaxis (from 1994-1996)	legumes (excluding peanut) 23% (reported to the National Food Administration)	European Commission 1998
Sweden 55 cases of food- induced anaphylaxis (from 1994-1996)	legumes (excluding peanut) 27% (Hospital Reports)	European Commission 1998
Sweden, Linköping 76 healthy newborn babies (at 8 months)	soybean 6% (RAST) (0% at 3, 25, and 48 months)	Hattevig et al. 1984
Sweden, Malmö 20 cow's milk allergic infants	soybean in 35% (clinical history)	Jakobsson & Lindberg 1979
Sweden 60 severe allergic reactions caused by food	soybean, nuts and almonds >70%	Foucard et al. 1997
Switzerland, Zurich 402 food allergic adults (study period 1978-87)	soybean 1% (clinical history, diagnostic tests)	Wüthrich 1993
Switzerland, Zurich 383 food allergic patients (study period 1990-94)	soybean 9% (clinical history, diagnostic tests)	Etesamifar & Wüthrich 1998

Thailand, Bangkok cow's milk-sensitive children	soybean 17% (clinical history)	Harikul et al. 1995
Thailand 100 asthmatic children	soy 4% (SPT)	Kongpanichkul et al. 1997
UK a) 394 bread bakery and b) 77 cake bakery workers	soy a) 7%, b) 1% (SPT)	Smith & Smith 1998
UK, London 100 patients with food intolerance	soy 1% (repeated challenge)	Lessof et al. 1980
UK, Manchester 172 patients experienced anaphylactic reactions to foods (from 1994-1996)	legumes (excluding peanut) 2.3% (suspected cause of patients' worst reaction)	Pumphrey & Stanworth 1996
USA, Baltimore, MD 196 food-allergic patients with atopic dermatitis	soybean 28% (DBPCFC, n=111)	Sampson & Ho 1997
USA, Denver, CO a) 74 food allergic children (age of <3 years) b) 111 food allergic children (age of 3-19 years)	a) soybean 16% (DBPCFC) b) soybean 2.7% (DBPCFC)	Bock & Atkins 1990
USA, Durham, NC a) 113 food allergic children with atopic dermatitis b) 63 DBPCFC positiv children of a)	a) soybean 30% (SPT) b) soybean 8% (DBPCFC)	Sampson & McCaskill 1985
USA, Little Rock, AR 165 patients with atopic dermatitis	soybean 13% (SPT) from which 3/19 were DBPCFC-positive	Burks et al. 1998
USA, New Haven, CT 98 infants and children with multiple gastrointestinal allergies	soy and milk 62% soy and gluten 35% (clinical histroy)	Gryboski & Kocoshis 1980
USA, OH 148 respiratory-allergic children with reproduced symptoms after food challenge	soy formula 5% (oral challenge)	Ogle et al. 1980
USA, San Diego, CA cow's milk-sensitive infants	soybean 25%	Wilson & Hamburger 1988
USA, San Diego, CA 93 cow's milk-allergic children (<3.5 years)	soybean 14 % (DBPCFC, open challenge, or convincing history of an anaphylactic reaction)	Zeiger et al. 1999

2 Outgrowing / Persistence of Soybean Allergy

Country / Subjects	Allergy / Sensitivity to	References
Spain, Barcelona patients with asthma (associated to asthma outbreak during the unloading of soybeans, 1981-1987)	Soybean in 55% of patients with epidemic asthma and 6.0% of those with non-epidemic asthma (p<0.05) 8 years after outbreak (RAST, measurable levels in 1995 and 1989 almost identical)	Anto et al. 1999
USA Food allergic patients	soy, egg, milk, wheat, and peanut: 26% loss (after 1 year of onset, DBPCFC)	Sampson & Scanlon 1989
USA infants (mean age 8 weeks) with food protein-induced enterocolitis syndrome caused by soybean	soy in 2 of 8 (after 25 months)	Sicherer et al. 1998

3 Symptoms of Soybean Allergy

Symptoms & Case Reports	References
<p><u>systemic reactions</u> anaphylaxis (5, 7, 13, 15, 22), exercise-induced anaphylaxis (25), fatal reactions (12, 22)</p> <p><u>cutaneous symptoms</u> angioedema (6), atopic dermatitis (10, 23), eczema (23), itching (14), urticaria (6), urticarial contact dermatitis (24), in general (20)</p> <p><u>gastrointestinal symptoms</u> colitis (8, 18), diarrhea (1), enterocolitis (16), vomiting (1, 6) diffuse small bowel disease (8), in general (20)</p> <p><u>respiratory symptoms</u> allergic rhinitis (2, 10), asthma (1, 2, 3, 9, 11, 17, 19, 22), bronchospasm (14), dyspnea (6), laryngeal edema (14), pollinosis (2), wheeze (6, 14)</p> <p><u>other symptoms</u> hypotension, lethargy, and fever (1) food protein-induced enterocolitis syndrome (21)</p>	<p>(1) Virchow 1965 (2) Fries 1971 (3) Bush & Cohen 1977 (4) Whittington & Gibson 1977 (5) Moroz & Yang 1980 (6) Bush et al. 1985 (7) Stricker et al. 1986 (8) Richards et al. 1988 (9) Bush et al. 1988 (10) Burks et al. 1991 (11) Gonzalez et al. 1991 (12) Yunginger et al. 1991 (13) Patane et al. 1992 (14) Herian et al. 1990 (15) Andersen & Nissen 1993 (16) Burks et al. 1994 (17) Lavaud et al. 1994 (18) Machida et al. 1994 (19) Räsänen et al. 1994 (20) Magnolfi et al. 1996 (21) Sicherer et al. 1998 (22) Foucard & Malmheden Yman 1999 (23) Niggemann et al. 1999 (24) Ikeda et al. 2000 (25) Steurich & Feyerabend 2000</p>
<p>Percentage of Reactions cutaneous 68%, gastrointestinal 77%, respiratory 23% in 31 soybean-allergic patients with atopic dermatitis (1) cutaneous 58%, gastrointestinal 14%, both 28%, respiratory 0%, early reaction 57%, late reactions 43% in 7 soybean-allergic patients (2)</p>	<p>(1) Sampson & Ho 1997 (2) Niggemann et al. 1999</p>
<p>Threshold for Elicitation of Symptoms Amounts of soybeans inducing allergic symptoms ranged from 1 g to 8 g (estimated protein content: 0.3 - 2.7 g) (DBPCFC, 4 soybean allergic children) (1) Estimated amount of soy intake in 4 fatal cases: 1-10 g as hidden allergen (2) Amounts of soybean inducing symptoms: ≤ 500 mg in 28% (DBPCFC, 196 food allergic children with atopic dermatitis) (3)</p>	<p>(1) Bock et al. 1978 (2) Foucard & Malmheden Yman 1999 (3) Sicherer et al. 2000</p>

4 Diagnostic Features of Soybean Allergy

Parameters / Subjects	Outcome	References
<i>IgA and IgM</i> 5 patients with soy allergy (previously suffering from cow's milk allergy)	increased numbers of IgA- and IgM- containing cells (jejunal biopsy)	Perkkio et al. 1981
<i>IgE and IgD</i> 13 children with various intestinal diseases	increased levels of IgE and IgD antibodies specific for soybean agglutinin (and milk proteins) in basal and pancreozymin- stimulated duodenal fluid	Freier et al. 1983
<i>T-Cells</i> 7 cases of fatal soybean dust-induced asthma	reduced numbers of CD3+ and CD8+ T-cells in airways	Synek et al. 1996
<i>Ig-Classes</i> a) 12 soydust-asthmatic patients b) 23 asthmatic patients c) 32 non-allergic subjects	<u>positive results in patients (specific Ig):</u> a) IgE 100%, IgG 75%, IgG1 16.6%, IgG2 8.3%, IgG3 0%, IgG4 66.6%, IgA 25%, and IgM 25% b) IgE 4.3%, others negative c) IgE 0%, IgG 0%, IgG1 6.2%, IgG2 9.4%, IgG3 9.4%, IgG4 9.4%, IgA 6.2%, and IgM 6.2% <u>significant positive correlation:</u> for IgE and IgG4 in a) only	Codina et al. 1997a
a) <i>RAST and DBPCFC</i> b) <i>SPT and DBPCFC</i> food-allergic children with atopic dermatitis	a) predictive values of specific IgE > 0.35 kU/L positive predictive value 21% (50% for IgE > 65 kU/L) negative predictive value 95% b) predictive values of SPT (> 3 mm) positive predictive value 35% negative predictive value 84%	Sampson & Ho 1997
<i>SPT and DBPCFC</i> Children suspected of IgE-mediated symptoms to soybean	No significant differences in wheal sizes between individuals who were allergic or tolerant to soybean	Eigenmann & Sampson 1998
<i>IgE and DBPCFC</i> children with atopic dermatitis	a) Specific serum IgE in children with positive oral provocation: 7.4 kU/L negative oral provocation: 3.2 kU/L (no significant difference) b) predictive value of specific IgE > 0.35 kU/L positive predictive value 23% negative predictive value 100%	Niggemann et al. 1999

5 Composition of Soybeans

5.1 Distribution of Nutrients (in dried seeds)

Nutrients: Content per 100 g		
Energy 1364 kJ (322 kcal)	Vitamins	Thr 1490 mg
Water 8.5 g	Carotene 380 µg	Trp 450 mg
Protein 33.7 g	Vitamin E 1500 µg	Tyr 1250 mg
Lipids 18.1 g	Vitamin K 190 µg	Val 1760 mg
Carbohydrate 6.1 g	Vitamin B1 990 µg	
Minerals 4.7 g	Vitamin B2 520 µg	Carbohydrates
	Nicotinamide 2510 µg	Glucose 5 mg
Minerals	Pantothenic acid 1920 µg	Sucrose 6100 mg
Sodium 4 mg	Vitamin B6 1190 µg	
Potassium 1740 mg	Biotin 60 µg	Lipids
Magnesium 245 mg	Folic acid 230 µg	Palmitic acid 1580 mg
Calcium 255 mg		Stearic acid 590 mg
Manganese 3 mg	Amino Acids	Oleic acid 3790 mg
Iron 8.6 mg	Arg 2360 mg	Linolic acid 8650 mg
Copper 110 µg	His 830 mg	Linoleic acid 1000 mg
Zinc 1 mg	Ile 1780 mg	
Phosphorus 590 mg	Leu 2840 mg	Other
Chloride 7 mg	Lys 1900 mg	Lecithin 1.1-3.2 g
Iodine 6 µg	Met 580 mg	Purines 380 mg
Selenium 60 µg	Phe 1970 mg	

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

5.2 Protein Fraction

Proteins / Glycoproteins	Amount of total protein
<i>Sedimentation fractions</i>	
2S	20 %
7S (incl. beta-conglycinin 50%, cytochrome c, beta-amylase, lipoxygenase, hemagglutinins)	33 %
11S	33 %
15S	10 %
<i>Soluble fractions</i>	
globulins (salt-soluble)	90 %
albumins (water-soluble)	10 %
<i>Water-soluble fraction</i>	
glycinin (in 11S) and beta-conglycinin (in 7S)	>70 %
trypsin inhibitors (in 2S)	15 %
soybean vacuolar protein P34 (Gly m Bd 30K) (in 7S)	2-3% of seed proteins
<i>60%-Ethanol-soluble fraction</i>	
hydrophobic protein (Gly m 1.0101)	~ 20 mg / 100 g seeds

References: [Burks et al. 1991](#), [Samoto et al. 1994](#), [Kalinski et al. 1990](#), [Odani et al. 1987](#)

6 Allergens of Soybean

Proteins / Glycoproteins	Allergen Nomenclature	References
Soybean Hydrophobic Protein [7.5 / 7 kDa]	Gly m 1.0101, Gly m 1.0102	Gonzalez et al. 1995
Soybean Hull Protein [8 kDa]	Gly m 2	Codina et al. 1997b
Soybean Profilin [14 kDa]	Gly m 3	Rihs et al. 1999
Soybean Vacuolar Protein (Gly m Bd 30K) [30 kDa]	(formerly Gly m 1)*	Ogawa et al. 1991
Glycinin [subunits 58-62 kDa]		Djurtoft et al. 1991
alpha subunit of beta-Conglycinin [subunits 42-76 kDa]		Ogawa et al. 1995
Kunitz-trypsin Inhibitor [20 kDa]		Moroz & Yang 1980 , Burks et al. 1994b , Baur et al. 1996

* not in accordance with the official list (WHO/IUIS Allergen Nomenclature)

6.1 Sensitization to Soybean Allergens

Country / Subjects	Sensitivity to	References
Australia, North Ryde 8 peanut sensitive patients	soybean lectin: agglutinin (30 kDa) in all patients (RAST)	Barnett & Howden 1987
Denmark 10 soybean sensitive patients	Glycinin in 90% glycinin subunits in 100% (EAST)	Djurtoft et al. 1991
Germany, Bochum 14 soybean-sensitized asthmatic bakers	trypsin inhibitor in 86% lipoxidase in 43% lectin in 21% (RAST) 14 kDa / pI 8 allergen in 14% (2D-immunoblot)	Baur et al. 1996
Germany, Bochum 13 soybean-sensitized patients	profilin (Gly m 3) in 69% (immunoblot, EAST)	Rihs et al. 1999
Germany, Langen 6 soybean-allergic adults	10 proteins, major allergens: 39 and 50 kDa (SDS-PAGE / immunoblot)	Müller et al. 1998
Japan, Gunma 5 soybean sensitive children	2S > 7S > 11S fraction (RAST, allergenic potency: RAST inhibition)	Shibasaki et al. 1980
Japan, Nagano 30 soybean- sensitive patients (including 7 challenge positive patients)	whey fraction: 20 kDa and 58 kDa allergens globulin fraction: 26 kDa and 31 kDa allergens Monosensitization to 78 kDa allergen of globulin fraction in 2 challenge positive patients (SDS-PAGE immunoblot)	Awazuhara et al. 1997
Japan, Tokushima soybean-sensitized patients with atopic dermatitis	16 allergens, (14-97 kDa): 7S fraction: 10 allergens, Gly m Bd 30K in 65% alpha- subunit (beta- conglycinin) in 23%; 2S and whey fraction: 6 allergens (SDS-PAGE immunoblot)	Ogawa et al. 1991 Ogawa et al. 1995
Japan, Tokushima soybean-sensitized patients with atopic dermatitis	26 kDa allergen (Gly m Bd 28K) in 23% (SDS-PAGE immunoblot)	Ogawa et al. 1991 Tsuji et al. 1997
Spain, Barcelona 10 patients with asthma	soybean hull and dust extracts: minor allergens (21 to 42 kDa), major allergen < 14 kDa glycopeptide, pI < 6 (SDS- and IEF-PAGE immunoblot)	Rodrigo et al. 1990 Swanson et al. 1991
Spain, Barcelona 15 soybean-sensitized patients with asthma	2 nonoverlapping IgE binding patterns: a) in 73% 3 allergens : 8, 7.5 and 7 kDa (Gly m 2, Gly m 1.0101 and Gly m 1.0102) b) in 20% 1 allergen at 8.2-8.3 kDa and 4 allergens at 25-36 kDa (SDS-PAGE immunoblot)	Codina et al. 1999
Spain, Cartagena 32 patients with asthma	shell allergens of soy dust in 90%; major allergen of 8 kDa (RAST, immunoblot)	Gonzalez et al. 1991
Spain, Cartagena 20 patients with asthma sensitized to soy	Gly m 1.0101 / Gly m 1.0102 in 95% (EAST)	Gonzalez et al. 1992
Spain, Tarragona 13 patients with asthma sensitized to soy	5-6 kDa allergen in 62% 15.5-17 kDa allergen in 77% (SDS-PAGE / immunoblot)	Garcia-Ortega et al. 1998
UK, London 21 patients with wheat-induced asthma	21 kDa allergen in 100% 15 kDa allergen in 19% (SDS-PAGE / immunoblot)	Sandiford et al. 1995

USA, Little Rock, AR 8 Children with atopic dermatitis and soy allergy	7S and 11S protein fractions: increased specific serum IgE and IgG (ELISA)	Burks et al. 1988
USA, Little Rock, AR 8 Children with atopic dermatitis and soy allergy	crude soy extract and 7S fraction: increased specific IgE; whey and 11S: no significant difference in IgE-binding (EAST) 7S and 11S fraction detected by all sera (SDS-PAGE / immunoblot)	Burks et al. 1991
USA, Little Rock, AR 5 patients with atopic dermatitis and soy allergy	trypsin inhibitor in 1 patient (spec. IgE, immunoblot, EAST)	Burks et al. 1994b
USA, Little Rock, AR 2 soybean-allergic patients, 1 soybean- and peanut- allergic patient	17, 21, 26, and 45 kDa allergens (SDS-PAGE / immunoblot)	Eigenmann et al. 1996
USA, Little Rock, AR 4 patients with atopic dermatitis and soy allergy	20, 30-35, 50, and 65 kDa allergens (SDS-PAGE / immunoblot)	Helm et al. 1998
USA, Madison, WI 1 soybean-asthmatic patient	14.8, 17, 21, 48, 52, and 54.5 kDa allergens (SDS-PAGE / immunoblot)	Bush et al. 1988
USA, Madison, WI 7 soybean allergic adults	50-60 kDa allergens in 57% (patients with soy and peanut allergy) 20 kDa allergen in 29% (detected by monosensitized patients) 14 kDa allergen in 14% (SDS-PAGE / immunoblot)	Herian et al. 1990

6.2 Properties of Soybean Hydrophobic Protein (Gly m 1)

6.2.1 Molecular Biological Properties

Soybean Hydrophobic Protein	References
<p>Allergen Nomenclature</p> <p>a) Gly m 1.0101 (Gly mIA, S2) b) Gly m 1.0102 (Gly mIB, S1)</p>	(1) Larsen & Lowenstein 1998
<p>Isoallergens and Genetic Variants</p> <p>b) 2 isoforms by IEF-PAGE (1)</p>	(1) Gonzalez et al. 1992
<p>Molecular Mass a) 7.5 kDa b) 7.0 kDa</p>	(1) Gonzalez et al. 1992
<p>Isoelectric Point a) pI 6.8 b) pI 6.1-6.2</p>	(1) Gonzalez et al. 1992
<p>Amino Acid Sequence</p> <p>PIR: A29385</p> <p>a) N-terminal sequence of 42 aa (2) matching the sequence of hydrophobic seed protein, 80 aa (1) b) lacking N-terminal tripeptide (2)</p>	(1) Odani et al. 1987 (2) Gonzalez et al. 1995
<p>3D-Structure</p> <p>X-ray studies (1)</p>	(1) Baud et al. 1993
<p>Posttranslational Modifications</p> <p><u>Disulfide bonds</u> 4 disulfide bonds (1)</p> <p><u>Glycosylation:</u> carbohydrate detection (immunoblot) (2)</p>	(1) Odani et al. 1987 (2) Gonzalez et al. 1992
<p>Localization</p> <p>Predominantly located on seed surface; amounts vary among soybean cultivars, higher on dull-seeded phenotypes (SDS-PAGE, micro-sequencing) (1)</p> <p>Pattern of gene expression shows that Gly m 1 is synthesized in endocarp of inner ovary wall and is deposited on seed surface during development (in situ hybridization, RNA analysis) (1)</p>	(1) Gijzen et al. 1999

6.2.2 Allergenic Properties

Soybean Hydrophobic Protein	References
<p>Frequency of Sensitization</p> <p>IgE-binding to Gly m 1 in 95% of patients (1)</p>	(1) see 6.1 Sensitization to Soybean Allergens
<p>Allergenic Potencies</p> <p>IgE-binding inhibition of total soybean extract: 72% (a) and 76% (b) (EAST) Concentrations of 50%-inhibition: (a) lower concentrations as (b) (1)</p> <p>(a) Gly m 1.0101 (b) Gly m 1.0102</p>	(1) Gonzalez et al. 1992

6.3 Properties of Soybean Hull Protein (Gly m 2)

6.3.1 Molecular Biological Properties

Soybean Hull Protein	References
Allergen Nomenclature Gly m 2	(1) Larsen & Lowenstein 1998
Molecular Mass 8 kDa (SDS-PAGE)	(1) Codina et al. 1997
Isoelectric Point pI 6.0 (IEF-PAGE)	(1) Codina et al. 1997
Amino Acid Sequence PIR: A57106 N-terminal fragment, 20 aa (1)	(1) Codina et al. 1997
Sequence Homology N-terminal fragment: 71% homology with a storage protein from cotyledon of <i>Vigna radiata</i> (cow pea) and 64% with a "disease response protein" from <i>Pisum sativum</i> (green pea) (1)	(1) Codina et al. 1997

6.3.2 Allergenic Properties

Soybean Hull Protein	References
Frequency of Sensitization IgE-binding to Gly m 2 in 12 patients (RAST) and 5 patients (immunoblot) (1)	(1) see 6.1 Sensitization to Soybean Allergens

6.4 Properties of Soybean Profilin (Gly m 3)

6.4.1 Molecular Biological Properties

Soybean Profilin			References
Allergen Nomenclature Gly m 3			(1) Larsen & Lowenstein 1998
Isoallergens and Variants 2 isoforms differing in 3 aa substitutions (1)			(1) Rihs et al. 1999
Molecular Mass 14 kDa (SDS-PAGE)			(1) Rihs et al. 1999
Isoelectric Point pI 4.4 (2D-PAGE)			(1) Rihs et al. 1999
Amino Acid Sequence, mRNA, and cDNA			
Proteins	GmPRO 1*	GmPRO 2*	(1) Rihs et al. 1999
SWISS-PROT:	O65809	O65810	
GenBank:	AJ223982	AJ223981	
Amino Acids	131 (1)	131 (1)	
mRNA precursor	394 bp (1)		
cDNA precursor			
* 97.7% identity			
recombinant Profilin <u>Expression in <i>Escherichia coli</i>:</u> rGly m 3 (Profilin 1) (1) fragments: aa 1-65, 38-88, 50-131 (1)			(1) Rihs et al. 1999
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 identities 69% to 88% (1) Bet v 2 from birch pollen: aa sequence identity 73% (1)			(1) Rihs et al. 1999

6.4.2 Allergenic Properties

Soybean Profilin	References
Frequency of Sensitization IgE-binding to profilin in 69% of patients (1)	(1) see 6.1 Sensitization to Soybean Allergens
B-Cell Epitopes IgE binding to rGly m 3, inactive recombinant fragments (aa 1-65, 38-88, 50-131) indicating conformational epitopes (1) (a) SDS-PAGE / immunoblot (b) EAST / EAST inhibition	(1) Rihs et al. 1999

6.5 Properties of Soybean Vacuolar Protein (Gly m Bd 30 K)

6.5.1 Molecular Biological Properties

Soybean Vacuolar Protein	References																					
Allergen Nomenclature Gly m Bd 30 K	(1) Ogawa et al. 1991																					
Molecular Mass monomer: 34 kDa (1)*, 32 kDa (2)*, 30 kDa (SDS-PAGE) (3) oligomer: 3000 kDa (Gel filtration) (2) precursor: 46-47 kDa (1, 4) <hr/> *34 kDa polypeptide is processed during seedling growth to a 32 kDa polypeptide by the removal of an N-terminal decapeptide (1)	(1) Kalinski et al. 1990, 1992 (2) Ogawa et al. 1993 (3) Helm et al. 1998 (4) Ji et al. 1998																					
Isoelectric Point pI 4.5 (oligomer)	(1) Ogawa et al. 1993																					
Amino Acid Sequence, mRNA, and cDNA <table border="1"> <thead> <tr> <th>Proteins</th> <th>Gly m Bd 30K*</th> <th>P34*</th> </tr> </thead> <tbody> <tr> <td>SWISS-PROT:</td> <td></td> <td>P22895</td> </tr> <tr> <td>TrEMBL:</td> <td>O64458</td> <td></td> </tr> <tr> <td>GenBank:</td> <td>AB013289</td> <td>J05560</td> </tr> <tr> <td>Amino Acids</td> <td>379 (2)</td> <td>379 (1)</td> </tr> <tr> <td>mRNA precursor</td> <td></td> <td>1287 bp (1)</td> </tr> <tr> <td>cDNA precursor</td> <td>6675 bp (2)</td> <td></td> </tr> </tbody> </table> * Gly m Bd 30K and P34 are identical (Ogawa et al. 1995)	Proteins	Gly m Bd 30K*	P34*	SWISS-PROT:		P22895	TrEMBL:	O64458		GenBank:	AB013289	J05560	Amino Acids	379 (2)	379 (1)	mRNA precursor		1287 bp (1)	cDNA precursor	6675 bp (2)		(1) Kalinski et al. 1990, 1992 (2) Takano et al. 1995
Proteins	Gly m Bd 30K*	P34*																				
SWISS-PROT:		P22895																				
TrEMBL:	O64458																					
GenBank:	AB013289	J05560																				
Amino Acids	379 (2)	379 (1)																				
mRNA precursor		1287 bp (1)																				
cDNA precursor	6675 bp (2)																					
recombinant Protein <u>Expression in <i>Escherichia coli</i>:</u> Isolation of protein coding region from clone P34 by PCR technique, subcloned into pet-24(b)+ vector and expression in E.coli (2) <u>Expression in insect cells:</u> 46-, 34-, and 32-kDa forms (1)	(1) Ji et al. 1998 (2) Helm et al. 2000																					
Posttranslational Modifications <u>Glycosylation:</u> Carbohydrate composition: Man, GlcNAc, Fuc, and Xyl (3:2:1:1, molar ratio) (1) N-Glycosylation site: Asn-170 (mature protein) (1)	(1) Bando et al. 1996																					
Biological Function cysteine protease (papain superfamily)	(1) Kalinski et al. 1992																					
Sequence Homology Der p 1, a house dust mite allergen: 30% identity (1), 54% similarity (2)	(1) Ogawa et al. 1993 (2) Helm et al. 1998																					
Localization Seed protein storage vacuoles in soybean cotyledons (electron microscopic immunolocalization, mAb (1, 2), patients' IgE (2))	(1) Kalinski et al. 1992 (2) Helm et al. 1998																					
Other Properties Binding to alpha'- and alpha-subunits of beta-conglycinin (1) Binding of syringolides (which trigger defense responses) (2)	(1) Samoto et al. 1996 (2) Ji et al. 1998																					

6.5.2 Allergenic Properties

Soybean Vacuolar Protein		References															
<p>Frequency of Sensitization IgE-binding to Gly m Bd 30K in 65% of patients (1)</p>		(1) see 6.1 Sensitization to Soybean Allergens															
<p>B-Cell Epitopes IgE binding sites located on Gly m Bd 30K (the precursor sequence):</p> <table border="1"> <thead> <tr> <th>Peptides</th> <th>Positivity in Patients</th> </tr> </thead> <tbody> <tr> <td>aa 3-12 (synthetic peptide)</td> <td>+ (1), 67% (2)</td> </tr> <tr> <td>aa 100-110 (synthetic peptide)</td> <td>+ (1), 50% (2)</td> </tr> <tr> <td>aa 229-238 (synthetic peptide)</td> <td>+ (1), 58% (2)</td> </tr> <tr> <td>aa 299-308 (synthetic peptide)</td> <td>+ (1), 67% (2)</td> </tr> <tr> <td>aa 331-340 (synthetic peptide)</td> <td>+ (1), 75% (2)</td> </tr> </tbody> </table> <p>dot / immunoblot (SPOTs membrane technique)</p> <p>(1) 4 patients with soybean allergy (DBPCFC) (2) additional 8 patients with soybean allergy (DBPCFC)</p>		Peptides	Positivity in Patients	aa 3-12 (synthetic peptide)	+ (1), 67% (2)	aa 100-110 (synthetic peptide)	+ (1), 50% (2)	aa 229-238 (synthetic peptide)	+ (1), 58% (2)	aa 299-308 (synthetic peptide)	+ (1), 67% (2)	aa 331-340 (synthetic peptide)	+ (1), 75% (2)	(1) Helm et al. 1998 (2) Helm et al. 2000			
Peptides	Positivity in Patients																
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aa 331-340 (synthetic peptide)	+ (1), 75% (2)																
<p>Mutational Analysis of B-Cell Epitopes Critical aa residues for IgE binding identified by single site aa substitution:</p> <table border="1"> <thead> <tr> <th>Peptides</th> <th>aa Substitution</th> <th>Positivity in Patients</th> </tr> </thead> <tbody> <tr> <td rowspan="2">aa 100-110 (synthetic peptide)</td> <td>a) S105A</td> <td>a) 0% (1)</td> </tr> <tr> <td>b) K106A</td> <td>b) 0% (1)</td> </tr> <tr> <td rowspan="3">aa 331-340 (synthetic peptide)</td> <td>a) I315A</td> <td>a) 66% (1)</td> </tr> <tr> <td>b) Q316A</td> <td>b) 66% (1)</td> </tr> <tr> <td>c) R317A</td> <td>c) 33% (1)</td> </tr> </tbody> </table> <p>dot / immunoblot (SPOTs membrane technique)</p> <p>(1) 6 patients with soybean allergy (DBPCFC) and positive IgE-binding to non-mutated peptide</p>		Peptides	aa Substitution	Positivity in Patients	aa 100-110 (synthetic peptide)	a) S105A	a) 0% (1)	b) K106A	b) 0% (1)	aa 331-340 (synthetic peptide)	a) I315A	a) 66% (1)	b) Q316A	b) 66% (1)	c) R317A	c) 33% (1)	(1) Helm et al. 2000
Peptides	aa Substitution	Positivity in Patients															
aa 100-110 (synthetic peptide)	a) S105A	a) 0% (1)															
	b) K106A	b) 0% (1)															
aa 331-340 (synthetic peptide)	a) I315A	a) 66% (1)															
	b) Q316A	b) 66% (1)															
	c) R317A	c) 33% (1)															
<p>Alteration of Allergenicity <u>galactomannan treatment (Maillard reaction):</u> complete reduction of allergenicity (a) (1)</p> <p>(a) dot / immunoblot</p>		(1) Babiker et al. 1998															

6.6 Properties of Glycinin

6.6.1 Molecular Biological Properties

Glycinin	References																																				
Allergen Nomenclature none																																					
Molecular Mass 320-360 kDa (SEC) 6 subunits: 58-62 kDa each subunit: acidic polypeptide 31-45 kDa, basic polypeptide 18-20 kDa exception: acidic subunit A5 10 kDa	(1) Brooks & Morr 1985																																				
Isoelectric Point acidic subunits pI 4.8-5.5, basic subunits pI 6.5-8.5 (IEF-PAGE, 2D-PAGE) estimated values according to (1) and (2)	(1) Staswick et al. 1981 (2) Lei & Reeck 1987																																				
Amino Acid Sequence, mRNA, and cDNA																																					
<table border="1"> <thead> <tr> <th>Glycinin (subunits)</th> <th>G1 (5) (A1, BX)</th> <th>G2 (1) (A2, B1A)</th> <th>G3 (4) (A2, B1)</th> <th>G4 (3) (A4, A5, B3)</th> <th>G (2, 5) (A3, B4)</th> </tr> </thead> <tbody> <tr> <td>SWISS-PROT:</td> <td>P04776</td> <td>P04405</td> <td>P11828</td> <td>P02858</td> <td>P04347</td> </tr> <tr> <td>GenBank:</td> <td>M36686</td> <td>X15122</td> <td>X15123</td> <td>X02626</td> <td>M10962</td> </tr> <tr> <td>Amino Acids</td> <td>A1a: 287 BX: 180</td> <td>A2: 278 B1a: 180</td> <td>A: 275 B: 180</td> <td>A4: 257 A5: 97 B3: 185</td> <td>A3: 320 B4: 172</td> </tr> <tr> <td>mRNA precursor</td> <td colspan="2">1743 bp</td> <td colspan="2">1899 bp</td> <td>1786 bp</td> </tr> <tr> <td>cDNA precursor</td> <td colspan="2">4617 bp</td> <td colspan="3">3573 bp</td> </tr> </tbody> </table>	Glycinin (subunits)	G1 (5) (A1, BX)	G2 (1) (A2, B1A)	G3 (4) (A2, B1)	G4 (3) (A4, A5, B3)	G (2, 5) (A3, B4)	SWISS-PROT:	P04776	P04405	P11828	P02858	P04347	GenBank:	M36686	X15122	X15123	X02626	M10962	Amino Acids	A1a: 287 BX: 180	A2: 278 B1a: 180	A: 275 B: 180	A4: 257 A5: 97 B3: 185	A3: 320 B4: 172	mRNA precursor	1743 bp		1899 bp		1786 bp	cDNA precursor	4617 bp		3573 bp			(1) Staswick et al. 1984a (2) Fukazawa et al. 1985 (3) Momma et al. 1985 (4) Cho & Nielsen 1989 (5) Nielsen et al. 1989
Glycinin (subunits)	G1 (5) (A1, BX)	G2 (1) (A2, B1A)	G3 (4) (A2, B1)	G4 (3) (A4, A5, B3)	G (2, 5) (A3, B4)																																
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mRNA precursor	1743 bp		1899 bp		1786 bp																																
cDNA precursor	4617 bp		3573 bp																																		
recombinant Protein <u>Expression in <i>Escherichia coli</i>:</u> glycinin (A1aB1b and A2B1a) 57 kDa (1) glycinin (A1aB1b) with modified functional and nutritional properties (2) <u>Expression in Yeast:</u> site-directed mutagenesis of proglycinin (A1a,B1b) (3)	(1) Fukazawa et al. 1985 (2) Kim et al. 1990 (3) Katsube et al. 1998																																				
3D-Structure X-ray studies of recombinant proglycinin (1, 2)	(1) Gidamis et al. 1994 (2) Utsumi et al. 1996																																				
Posttranslational Modifications <u>Disulfide bonds</u> acidic and basic subunits linked by disulfide bond: A2 Cys-86 to B1a Cys-7 (1) <u>Glycosylation:</u> small glycosylated portion of glycinin (approx. 1%) (2) glycosylation of site-mutated proglycinin (4) <u>Phosphorylation:</u> in vitro phosphorylation of Ser-75 and Ser-117 (3)	(1) Staswick et al. 1984b (2) Lei & Reeck 1987 (3) Fouques et al. 1998 (4) Katsube et al. 1998																																				
Genetic Variants at least 5 variants (see Amino Acid Sequence) (1)	(1) Staswick et al. 1981																																				
Biological Function Seed storage protein (11S fraction)																																					

6.6.2 Allergenic Properties

Glycinin	References
<p><i>Frequency of Sensitization</i> IgE-binding to glycinin in 90% of patients (1, 3) to 11S-fraction (1, 2), acidic- and basic-subunit (a) (2) to acidic-subunits (A1a, A1b, A2, A3, and A4) (b) (3) to acidic-subunit (a) (4) (a) immunoblot (b) EAST</p>	<p>(1) see 6.1 Sensitization to Soybean Allergens (2) Burks et al. 1988 (3) Djurtoft et al. 1991 (4) Müller et al. 1998</p>
<p><i>B-Cell Epitopes</i> IgE-binding region on acidic chain from glycinin G1: aa 192-306 (GluC protease digest) (1) (a) SDS-PAGE / immunoblot</p>	<p>(1) Zeece et al. 1999</p>
<p><i>Allergenic Potencies</i> higher IgE-binding to acidic-subunit A4 than to A1a, A1b, A2, and A3 (EAST) (1)</p>	<p>(1) Djurtoft et al. 1991</p>
<p><i>Alteration of Allergenicity</i> <u>heat treatment:</u> soybeans cooked at 100°C for 2h: IgE-binding to stable acidic-subunit (immunoblot) (1)</p>	<p>(1) Müller et al. 1998</p>

6.7 Properties of beta-Conglycinin

6.7.1 Molecular Biological Properties

beta-Conglycinin	References																								
Allergen Nomenclature none																									
Molecular Mass 140-180 kDa 3 subunits (SEC, SDS-PAGE): alpha 76 kDa (2), 70 kDa (3), 57 kDa (1) alpha' 72 kDa (2), 57 kDa (1) beta 53 kDa (1), 42 kDa (1)	(1) Thanh & Shibasaki 1977 (2) Shattuck-Eidens & Beachy 1985 (3) Ogawa et al. 1995																								
Isoelectric Point pI alpha 4.90, alpha' 5.18, beta 5.66-6.00 (gel electrofocusing)	(1) Thanh & Shibasaki 1977																								
Amino Acid Sequence, mRNA, and cDNA <table border="1" data-bbox="113 707 922 981"> <thead> <tr> <th>beta- conglycinin (subunits)</th> <th>alpha</th> <th>alpha'</th> <th>beta</th> </tr> </thead> <tbody> <tr> <td>SWISS-PROT:</td> <td>P13916</td> <td>P11827</td> <td>P25974</td> </tr> <tr> <td>GenBank:</td> <td>X17698</td> <td>M13759</td> <td>S44893</td> </tr> <tr> <td>Amino Acids</td> <td>543 (1)</td> <td>577 (1)</td> <td>414 (3)</td> </tr> <tr> <td>mRNA precursor</td> <td colspan="3">1955 bp (4)</td> </tr> <tr> <td>cDNA precursor</td> <td></td> <td>3636 bp (2)</td> <td>3840 bp (3)</td> </tr> </tbody> </table>	beta- conglycinin (subunits)	alpha	alpha'	beta	SWISS-PROT:	P13916	P11827	P25974	GenBank:	X17698	M13759	S44893	Amino Acids	543 (1)	577 (1)	414 (3)	mRNA precursor	1955 bp (4)			cDNA precursor		3636 bp (2)	3840 bp (3)	(1) Schuler et al. 1982 (2) Doyle et al. 1986 (3) Harada et al. 1989 (4) Sebastiani et al. 1990
beta- conglycinin (subunits)	alpha	alpha'	beta																						
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recombinant Protein <u>Expression in <i>Arabidopsis thaliana</i>:</u> alpha' and beta subunits (3) <u>Expression in <i>Escherichia coli</i>:</u> non-glycosylated subunits and deletion mutants of alpha and alpha' (4) <u>Expression in petunia and tobacco plants:</u> alpha' and beta subunits (1) <u>SP6-derived expression plasmids:</u> non-glycosylated alpha and beta subunits (2)	(1) Chen et al. 1989 (2) Lelievre et al. 1992 (3) Hirai et al. 1995 (4) Maruyama et al. 1998																								
Posttranslational Modifications <u>Glycosylation:</u> carbohydrates: alpha and alpha' subunits contain 4 mol Man, 12 mol GlcN and beta subunit 6 mol Man, 2 mol GlcN(1) alpha and alpha': 2 carbohydrate moieties, beta chain: 1 carbohydrate moiety (1)	(1) Thanh & Shibasaki 1977																								
Biological Function Seed storage protein																									

6.7.2 Allergenic Properties

beta-Conglycinin	References
<p><i>Frequency of Sensitization</i> IgE-binding to 7S fraction (1) to alpha, alpha' and beta- subunits (2) to alpha-subunit in 23% of patients (3) no cross- reactivity to alpha'- and beta- subunits (3)</p>	<p>(1) see 6.1 Sensitization to Soybean Allergens (2) Burks et al. 1988 (3) Ogawa et al. 1995</p>
<p><i>B-Cell Epitopes</i> IgE-binding region on alpha- subunit: aa 232-383 (enzymatic digestion) (1) (a) SDS-PAGE / immunoblot</p>	<p>(3) Ogawa et al. 1995</p>

6.8 Properties of Kunitz-trypsin Inhibitor

6.8.1 Molecular Biological Properties

Kunitz-trypsin Inhibitor (KTI)	References																												
<i>Allergen Nomenclature</i> none																													
<i>Molecular Mass</i> 20 kDa (SDS-PAGE)	(1) Baur et al. 1996																												
<i>Isoelectric Point</i> pI ~4.5 (2D-PAGE)	(1) Baur et al. 1996																												
<i>Amino Acid Sequence, mRNA, and cDNA</i>																													
<table border="1"> <thead> <tr> <th>Kunitz-trypsin-inhibitor</th> <th>A</th> <th>B</th> <th>C</th> </tr> </thead> <tbody> <tr> <td>SWISS-PROT:</td> <td>P01070</td> <td>P01071</td> <td>P01070</td> </tr> <tr> <td>PIR:</td> <td>TISY</td> <td>TISYB</td> <td>TISYC</td> </tr> <tr> <td>GenBank:</td> <td>S45092</td> <td></td> <td></td> </tr> <tr> <td>Amino Acids (1)</td> <td>181</td> <td>181</td> <td>181</td> </tr> <tr> <td>mRNA precursor</td> <td colspan="3">1259 bp (2)</td> </tr> <tr> <td>cDNA precursor</td> <td colspan="3"></td> </tr> </tbody> </table>	Kunitz-trypsin-inhibitor	A	B	C	SWISS-PROT:	P01070	P01071	P01070	PIR:	TISY	TISYB	TISYC	GenBank:	S45092			Amino Acids (1)	181	181	181	mRNA precursor	1259 bp (2)			cDNA precursor				(1) Kim et al. 1985 (2) Jofuku et al. 1989
Kunitz-trypsin-inhibitor	A	B	C																										
SWISS-PROT:	P01070	P01071	P01070																										
PIR:	TISY	TISYB	TISYC																										
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Amino Acids (1)	181	181	181																										
mRNA precursor	1259 bp (2)																												
cDNA precursor																													
<i>recombinant Protein</i>																													
<u>Expression in tobacco plants:</u> all 3 variants (1)	(1) Jofuku & Goldberg 1989																												
<i>3D-Structure</i>																													
X-ray studies of complex with trypsin (1, 2)	(1) Sweet et al. 1974 (2) Song & Suh 1998																												
<i>Posttranslational Modifications</i>																													
<u>Disulfide bonds</u> 2 disulfide bonds: 39-86, 136-145 (1)	(1) Brown et al. 1966																												
<i>Genetic Variants</i>																													
3 variants (1)	(1) Kim et al. 1985																												
<i>Biological Function</i>																													
inhibition of trypsin active site: Arg-63 (KTI A) (1)	(1) Ozawa & Laskowski 1966																												
<i>Sequence Homology</i>																													
Lol p 11, a rye grass pollen allergen: 32% homology (1)	(1) van Ree et al. 1995																												

6.8.2 Allergenic Properties

Kunitz-trypsin Inhibitor (KTI)	References
<i>Frequency of Sensitization</i>	
IgE-binding to Kunitz-trypsin inhibitor in 86% of patients (1)	(1) see 6.1 Sensitization to Soybean Allergens

7 Isolation & Preparation

Extract / Purified Allergens	Methods	References
Hydrophobic protein (Gly m 1.0101)	60% ethanolic extract of seeds	Odani et al. 1987
Commercial and self-prepared extracts	absence of high Mr proteins in commercial extracts (SDS-PAGE immunoblot)	Herian et al. 1992
Gly m 1.0101, Gly m 1.0102	Purification by SEC / RP-HPLC	Gonzalez et al. 1992
Soybean trypsin inhibitor	Extraction from soy protein isolate with PBS for 4h at 4°C; Purification by gel filtration and electroelution	Burks et al. 1994b
Gly mBd 28K	Isolation from defatted soybean flakes using 5 chromatographic steps including immunoaffinity chromatography with a mAb	Tsuji et al. 1997
Soybean proteins	Soybeans frozen, ground (<-5°C) and extracted with PBS for 4h at 4°C Soybean lecithin extracted in a two phase aqueous / organic solvent system, purification of aqueous phase by gel chromatography	Müller et al. 1998
Soybean hull	grounded hulls: extraction with ammonium bicarbonate buffer (0.2 M, pH 7.9) overnight, centrifugation, dialysis and centrifugation	Morell et al. 1999

8 Cross-Reactivities

Cross-Reacting Allergens	Subjects / Methods	References
Soybean soybean (sensitivity in 90% of patients), peanut (90%), green pea (80%), lima bean (53%), string bean (43%)*	30 atopic children with suspected soybean allergy (Skin test)	Fries 1971
Soybean peanut, garden pea, and chick pea	15 peanut-sensitive patients (RAST-inhibition)	Barnett et al. 1987
Soybean allergen (17 kDa) green pea (17 kDa)	1 patient with asthma (immunoblotting)	Bush et al. 1988
Soybean soybean (sensitivity in 43% of patients), peanut (87%), green bean (22%), pea (26%), and lima bean (41%)*	69 legume-sensitive patients (SPT) (1) frequency of multiple sensitization: 4.9% (DBPCFC, 41 patients) (1) in vitro cross-reactivity did not correlate with clinical hypersensitivity (SDS-PAGE and dot / immunoblot) (2)	(1) Bernhisel-Broadbent & Sampson 1989 (2) Bernhisel-Broadbent et al. 1989
Soybean peanut	patient allergic to peanut and soy: 73% reduction of IgE-binding to peanut after adsorption of cross-reacting antibodies (ELISA)	Eigenmann et al. 1996
Soybean wheat, rye, and barley flours	21 patients with wheat-induced asthma (RAST inhibition)	Sandiford et al. 1995
Soybean wheat flour (sensitivity in 80% of patients), rye flour 66%, alpha-amylase of <i>Aspergillus oryzae</i> (Asp o 2) 33%*	14 soybean-sensitized asthmatic bakers (RAST)	Baur et al. 1996
Soybean peanuts and peas	4 peanut allergic and 2 pea allergic adults (RAST-inhibition)	Hagner et al. 1998

Soybean corn, rice, and peanut	soybean, corn, rice, and peanut allergic patients: significant inhibition of IgE- binding to soybean by corn, rice, and peanut (RAST inhibition)	Lehrer et al. 1999
Soybean Profilin Gly m 3 birch pollen profilin Bet v 2	Complete inhibition of IgE-binding to Bet v 2 by recombinant Gly m 3 (EAST inhibition, 2 soybean sensitive patients)	Rihs et al. 1999

* multiple sensitization (not proven by inhibition-tests)

Unique Allergens	Subjects / Methods	References
Soybean / Peanut 46 and 21 kDa allergens from soybean did not cross-react with peanut allergens; 46, 29, 25, 19, 17, 14, and 5 kDa allergens from peanut did not cross-react with soybean allergens	2 patients allergic to peanut and soy 3 patients allergic to peanut a) removal of cross-reacting antibodies from serum by soy- and peanut-affinity chromatography, respectively b) detection of unique IgE-binding proteins in SDS-PAGE immunoblot	Eigenmann et al. 1996

9 Stability of Soybean Allergens

Treatment	Effects	References
Soybean hull (Storage) (a) fresh, (b) stored, (c) stored and heated for 16 h	<u>IgE- and IgG4-binding:</u> stored > fresh extracts heated > untreated extracts (EAST inhibition) <u>heated to 80°C:</u> absence of several bands > 20 kDa absence of 1 major allergen (probably Gly m 2) 2 new IgE-binding bands of 10 and 15.3 kDa 1 new IgG4-binding band of 10 kDa as compared to RT, 37°C, 55°C treatment (SDS-PAGE immunoblot)	Codina et al. 1998
Soybean hull (Storage) fresh and glycerinated extracts: storage (30 days, -70°C to 4°C)	increase of positivities in SPT with all glycerinated extracts after 30 days of storage, loss of protein bands > 66 kDa for non-glycerinated extract stored at 4°C (SDS-PAGE)	Morell et al. 1999
Soybeans (Heat) microwave 700W, 25 min 15 soybean-allergic adults	<u>IgE-binding (EAST):</u> raw soybean: 15 sera heated soybean: 9 sera	Vieths et al. 1995
Soybeans (Heat) cooking 100°C, 2h 6 soybean-allergic adults	<u>IgE-binding (EAST):</u> raw soybean: 6 sera cooked soybean: 3 sera <u>max. inhibition of Ig-binding to heated soybean extract (EAST):</u> 39% by raw extract 89% by heated extract	Müller et al. 1998
Crude Soy Protein (Heat) heat 80°C and 120°C, 60 min	decrease in IgE-binding 80°C: no change in IgG-binding 120°C: decrease in IgG-binding (ELISA)	Burks et al. 1991
Crude Soy, 7S-, 11S-, and Whey Proteins (Heat) heat RT to 100°C, 5 to 60 min	no significant changes in IgE- and IgG-binding (2 patients with soybean allergy, EAST inhibition)	Burks et al. 1992
Soy Whey Proteins (Heat) heat 80°C and 120°C, 60 min	80°C: no change in IgE- and IgG-binding 120°C: decrease in IgE- and IgG-binding (ELISA)	Burks et al. 1991

<i>11S-, 7S- and 2S-Globulins (Heat)</i> heat 80°C, 100°C and 120°C, 30 min	80°C: 2S-globuline slightly increased, 11S and 7S reduced IgE-binding (42-75%) 100°C, 120°C: decreased IgE-binding for all fractions (39-83%) (RAST)	Shibasaki et al. 1980
<i>11S- and 7S-Globulins (Heat)</i> heat 80°C and 120°C, 60 min	80°C: decrease in IgE-binding; decrease (7S) and increase (11S) in IgG-binding 120°C: decrease in IgE- and IgG-binding (ELISA)	Burks et al. 1991
<i>Crude Soy Protein (Hydrolysis)</i> 2 step enzyme digestion a) pepsin and b) trypsin, chymotrypsin and intestinal mucosal peptidase digestion	50%-inhibition concentration: 10 fold increased for digested soy proteins (2 patients with soybean allergy, EAST inhibition)	Burks et al. 1992
<i>Crude Soy Protein (Hydrolysis)</i> enzyme digestion (2 proteases)	reduced IgE-binding (immunoblot)	Yamanishi et al. 1996
<i>Glycinin, beta-Conglycinin (Hydrolysis)</i> a) in vitro digestion with trypsin b) in vivo digestion of a processed soy ingredient in rats	a) beta-Conglycinin: decrease in immunoreactivity; Glycinin: 3-fold increase in immunoreactivity (ELISA, rabbit antibody) b) Glycinin and beta-conglycinin were digested rapidly, intact globulins disappeared from the gastrointestinal tract within 3 h; immunoreactive globulins in gut contents and associated with gut tissues in a semi-intact form, probably comprising proteolytic intermediates	Perez et al. 2000

10 Allergen Sources

Reported Adverse Reactions	References
<i>Several Food Products</i> Fatal anaphylaxis of a 10 year old girl sensitized to peanut and soy (RAST) after ingestion of sausage pizza fortified with soy protein (1) Symptoms after ingestion of tofu, soybean salat, soybean sprouts, and spring rolls (2) Baker's asthma induced by soy lecithin (Skin test, RAST, bronchial challenge) (3) Soy proteins in Spanish sausage products (chorizo, salchichon, mortadella, and boiled ham), doughnut and soup stock cubes (Skin test, RAST, bronchial and oral challenge) (4) Anaphylactic symptoms caused by pizza containing soy proteins (5) 4 fatal anaphylactic reaction in adolescents with known peanut allergy and unrecognized soybean allergy caused by meatballs with 3% soyprotein, hamburger (1 case soyprotein content unknown, other case 2.2% soyprotein), and kebab with 7% soyprotein (6) 6 life-threatening allergic reactions after ingestion of ice cream and meatballs with soy, and soysauce (6)	(1) Yunginger et al. 1991 (2) Misterek et al. 1992 (3) Lavaud et al. 1994 (4) Vidal et al. 1997 (5) Senne et al. 1998 (6) Foucard & Malmheden Yman 1999
<i>Hamburger, Kebab, Crab Stick</i> Fatal anaphylactic reaction after ingestion of a hamburger with added soyprotein (2.1%); 2 additional allergic reaction after ingestion of a kebab containing 7% soyprotein and a crab stick with 0.5-0.9% undeclared soyprotein	Malmheden Yman et al. 1994
<i>Tofu</i> Urticarial contact dermatitis in a 20 year old woman after contact with tofu (SPT, Immunoblot)	Ikeda et al. 2000
<i>Soy lecithins</i> Positive DBPCFC with 100 mg soy lecithins in a 4 year old boy, symptoms of erythematous rash on the jaws 1 h after ingestion	Palm et al. 1999
<i>Pharmaceuticals</i> Urticarial eruptions associated with lipid emulsions (1) Anaphylactic shock after infusion of soybean oil based preparation for parenteral nutrition (2) Systemic reactions (flush, dyspnea, tachycardia, hypotension, back pain) to a parenteral lipid emulsion, reexposure to parenteral solutions containing no soy lecithin emulsifier was tolerated (3)	(1) Buchman & Ament 1991 (2) Andersen & Nissen 1993 (3) Weidmann et al. 1997

Allergens in Soybean Products	Content / Products	References
Soybean Proteins 7 soybean-allergic adults (RAST inhibition)	<u>Inhibitory potency of IgE-binding to raw soybean proteins (max. Inhibition):</u> raw soybeans (70%), sprouts (70%) > acid- hydrolyzed sauce (40%), tofu (25-30%), hydrolyzed vegetable protein (40%), tempeh (20%), miso (20%) > mold-hydrolyzed sauce (10%)	Herian et al. 1993
Soybean Proteins 15 soybean-allergic adults (EAST inhibition)	<u>IgE-binding proteins in</u> soy-milk, tofu, textured soy-protein	Vieths et al. 1995
Soybean Proteins Patients with atopic dermatitis and high levels of IgE; Determination of IgG-binding to protein fractions (ELISA, immunoblot)	<u>IgG-binding proteins in</u> commercial margarines <u>not detected in</u> hypoallergenic magarine	Yokota et al. 1996
Soybean Proteins 30 soybean-allergic adults (immunoblot)	<u>IgE-binding proteins in</u> lecithins (31 kDa allergen) <u>protein contents:</u> soybean lecithin 2.8 mg / 100 g soybean oil 1.4 to 4.0 µg / 100 g	Awazuhara et al. 1998
Soybean Proteins 6 soybean-allergic adults (EAST, immunoblot)	<u>IgE-binding proteins in</u> 4/6 commercial lecithins: 27, 39, and 40 kDa allergens	Müller et al. 1998
Gly m Bd 30K Determination of Gly m Bd 30K (ELISA)	<u>high concentrations in</u> soy milk, tofu, kori-dofu, yuba, and in soybean protein isolate containing foods meat balls, beef croquettes, and fried chicken <u>low concentration in</u> kinako <u>not detected in</u> fermented foods (miso, shoyu, and natto)	(1) Tsuji et al. 1995
Gly m Bd 28K Determination of Gly m Bd 28K (ELISA)	<u>detected in</u> : soy milk, tofu, kori-tofu, yuba <u>not detected in</u> : fermented foods (miso, shoyu, and natto), meat ball, beef croquettes, and fried chicken (1)	(1) Bando et al. 1998

Reported Safe Products	References
Soybean Oil 6 commercial soybean oil samples: safe ingestion of total dose of 15 mL by 7 soybean allergic individuals (DBPCFC) (1)	(1) Bush et al. 1985
Pharmaceuticals tolerance to parenteral solutions containing no soy lecithin emulsifier (1)	(1) Weidmann et al. 1997

Allergen Depleted Products	Method	References
Soy Protein Isolate 90% removal of allergen Gly m Bd 30K (1)	salted out with Na ₂ SO ₄ , acidifying to pH 4.5 and centrifugation (1)	(1) Samoto et al. 1994
Soy Protein Isolate from a genetically mutated soybean (Tohoku 124): 99.78% removal of allergen Gly m Bd 30K (1)	salted out with Na ₂ SO ₄ , acidifying to pH 4.5 and centrifugation (1)	(1) Samoto et al. 1996b
Soybean Mutants lacking alpha and alpha' subunits of beta-conglycinin (1) lacking the 7S globulin (beta-conglycinin) subunits, alpha, alpha' and beta (2)	soybean mutation induced by gamma-ray irradiation (1) soybean variety produced by classical breeding techniques (2)	(1) Takahashi et al. 1996 (2) Hayashi et al. 1998

11 Soybean Protein in Infant Feed

Subjects	Feeding / Formula	References
328 children with a positive family history of allergy (15 years follow up)	Breast fed infants were found to have approximately one-half the incidence of atopy of cow's milk or soy based formula fed infants	Gruskay 1982
16 infants with congenital lactase deficiency (lactose malabsorption)	10 on soy-based formula 1 had allergic symptoms	Savilahti et al. 1983
101 newborn infants of atopic parents (total serum IgE)	development of atopic disease <u>breast-fed group:</u> 38% with IgE > 0.8 U/ml 12% with IgE < 0.8 U/ml <u>soy-fed group:</u> 33% with IgE > 0.8 U/ml 16% with IgE < 0.8 U/ml <u>cow's milk-fed group:</u> 90% with IgE > 0.8 U/ml 17% with IgE < 0.8 U/ml	Businco et al. 1983
97 breast fed and 124 non breast fed infants	development of atopic eczema <u>breast-fed group:</u> 22% (restricted maternal diet) 48% (no restricted maternal diet) <u>soy-fed group:</u> in 63% <u>cow's milk-fed group:</u> in 70% <u>casein hydrolysate-fed group:</u> in 21%	Chandra et al. 1989a
72 infants with family history of atopy (each group)	incidence of atopic eczema, wheezing, rhinitis, gastrointestinal symptoms, or colic <u>breast-fed group:</u> in 20% <u>soy-fed group:</u> in 37% <u>cow's milk-fed group:</u> in 36% <u>cow's milk whey hydrolysate-fed group:</u> in 7% <u>cumulative incidence of atopic disease:</u> breast-fed and whey hydrolysate-fed group < cow's milk and soy-formula fed group	Chandra et al. 1989b Chandra & Hamed 1991 Chandra 1997
20 cow's milk allergic infants	incidence of allergic symptoms: <u>2S protein fraction depleted soy milk</u> in 17% of infants	Marano et al. 1989

(a) 12 infants with protracted enteritis (b) 10 infants with atopic eczema	fed with lactose-free soy and beef hydrolysate based formula: improvement of symptoms in both groups, allergic symptoms in 1 (a) and 3 (b) infants who were previously fed with intact soy protein	Donzelli et al. 1990
21 infants with gastrointestinal symptoms of cow's milk and/or soy protein intolerance	fed with whey protein hydrolysate formula: improvement of symptoms	Merrit et al. 1990
40 atopic children	specific IgE against soy / beef collagen hydrolysate in 1 patient	Gortler & Urbanek 1990
43 patients with possible milk- and/or soy-protein enterocolitis	<u>cow's milk</u> 23% positive challenge <u>2 hydrolyzed soy protein isolates</u> a) 33% positive challenge b) 30% positive challenge	Burks et al. 1994
12 infants with adverse reactions to soy formula, whey hydrolysate, or casein hydrolysate (4)	infant formula composed of individual amino acids: no symptoms	Hill et al. 1995
analysis of 17 studies	<u>allergy to soy-based formula:</u> in 27% of patients (total incidences), 3% (DBPCFC) and 4% (positive challenge)	Cantani & Lucenti 1997

12 Allergenicity of Genetically Modified Soybeans

Product	References
<p><i>Transgenic Soybean / Pesticide resistant</i> <u>Aim:</u> glyphosate-tolerant soybeans (product Roundup Ready) <u>Modification:</u> Introduced enzyme: 5-enolpyruvylshikimate- 3-phosphate synthase enzyme derived from <i>Agrobacterium</i> sp. strain <u>Digestability:</u> introduced enzyme degrades readily in simulated gastric and intestinal fluids (2) <u>Allergenicity:</u> no discernible changes, either qualitatively or quantitatively, in composition of endogenous soybean allergens in either of the glyphosate- tolerant varieties analyzed (1)</p>	<p>(1) Burks & Fuchs 1995 (2) Harrison et al. 1996</p>
<p><i>Transgenic Soybean / Brazil nut protein</i> <u>Aim:</u> Improvement of nutritional quality <u>Modification:</u> Introduced allergen: methionine-rich 2S albumin from the Brazil nut (<i>Betholletia excelsa</i>) <u>Allergenicity:</u> All patients with positive reactions to brazil nut proteins were positive to the transgenic soybean (SPT, RAST, immunoblot) (Product withheld from the market by the company)</p>	<p>Nordlee et al. 1996</p>
<p><i>Transgenic Soybean / Corn proteins</i> <u>Aim:</u> Improvement of nutritional quality (amino acid composition) <u>Modification:</u> Introduced corn proteins: 10 kDa and HSZ <u>Allergenicity:</u> Both proteins did not bind IgE from sera of corn-reactive subjects (immunoblot)</p>	<p>Lehrer & Reese 1997</p>
<p><i>Transgenic Soybean / Oleic acid</i> <u>Modification:</u> transgenic soybean with an altered fatty acid profile <u>Allergenicity:</u> no difference in allergen content of wild-type and transgenic soybean extracts (RAST inhibition, immunoblot)</p>	<p>Lehrer & Reese 1997</p>
<p><i>Cultivar Tohoku 124</i> lacks alpha- and alpha'-subunits of conglycinin which bind allergen Gly m Bd 30K (1) and lacks Gly m Bd 28K (2)</p>	<p>(1) Samoto et al. 1996b (2) Samoto et al. 1997</p>

13 Food Allergen Labelling

Food Allergen	Labelling / Regulation Status	References
International Regulations Peanuts, soybeans and products of these	mandatory labelling of prepackaged food / advisory status (1)	(1) Codex Alimentarius Commission 1999
European Regulations Soybean and Soybean Products	labelling appropriate / recommendation (1)	(1) Bousquet et al. 1998

14 References

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Common Abbreviations

2D	two-dimensional
3D	three-dimensional
aa	amino acid(s)
Ab	antibody
Act c 1, 2	nomenclature of kiwi fruit allergens (<i>Actinidia chinensis</i>)
Ara h 1-7	nomenclature of peanut allergens (<i>Arachis hypogaea</i>)
Bos d 4, 5, 6, 7, 8	nomenclature of cow's milk allergens (<i>Bos domesticus</i>)
C	concentration of N,N'-methylenbisacrylamide (crosslinker)
CAST	cellular antigen stimulation test
CCD	cross-reactive carbohydrate determinants
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
CMA	cow's milk allergy
CRIE	crossed radioimmunoelectrophoresis
Cor a 1	nomenclature of hazel pollen allergens (<i>Corylus avellana</i>)
Cyn d 1	nomenclature of bermuda grass pollen allergens (<i>Cynodus dactylus</i>)
DBPCFC	double-blind, placebo-controlled food challenge
DEAE	diethylaminoethyl (cellulose) (anion exchanger)
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 (<i>Gadus callarias</i>)
Gal	galactose
Gal d 1, 2, 3, 4	nomenclature of egg white allergens (<i>Gallus domesticus</i>)
GlcN	glucosamine
GlcNAc	N-acetylglucosamine
Gly m 1, 2, 3	nomenclature of soybean allergens (<i>Glycine max</i>)
HLA	human leucocyte antigen
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 (<i>Lolium perenne</i>)
LTA4	leukotriene A4
LTB4	leukotriene B4
LTC4	leukotriene C4
LY	lysozyme
Man	mannose
Mal d 1, 2, 3	nomenclature of apple fruit allergens (<i>Malus domestica</i>)
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	ovomuroid
Ory s 1	nomenclature of rice allergens (<i>Oryza sativa</i>)
OT	ovotransferrin
PAGE	polyacrylamide gel electrophoresis
PBMC	peripheral blood mononuclear cells
PBS	phosphate buffered saline
Phl p 1	nomenclature of timothy grass allergens (<i>Phleum pratense</i>)
pI	isoelectric point
PCA	passive cutaneous anaphylaxis (test)
PCR	polymerase chain reaction
PVDF	polyvinylidene difluoride
PVPP	polyvinyl polypyrrolidone
RAST	radioallergosorbent test
RBL cells	rat basophil leukaemia cells
RIEP	radioimmuno-electrophoresis
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
TNF-alpha	tumor necrosis factor alpha
TR	trypsin
Tris	tris-(hydroxymethyl)aminomethane
Xyl	xylose