Review:

Legumes, Nuts, and Seeds:
Allergen Stability and Allergenicity of Processed Foods

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SUMMARY

Most severe allergic reactions, including fatal events, after ingestion of peanuts, soybeans and tree nuts have been reported. Allergens from legumes, nuts, and seeds are predominantly highly potent and stable to food processing. However, it is possible to alter the allergenicity potentially by various procedures. Heat treatments (dry heating, roasting, or baking) and enzymatic digestion affect the allergen structure. Although food processing usually induces at least partial loss of IgE-binding, the formation of neoallergens or release of cryptic IgE-binding epitopes can occur.

The present review reports the allergenic and IgE-binding potentials, respectively, of experimental food preparations involving heat and enzymatic treatments and of various food products including peanut and soybean flour, roasted peanuts and nuts, and edible oils. Events of allergic reactions due to inadvertant ingestion of "hidden" allergens in food products are also reported.

Available data lack systematic investigations of the allergenicity of foods throughout manufacturing processes from source to shelf-products. Especially products containing peanut, tree nuts, and seeds should be evaluated since they are commonly seen as "hidden" allergens in various processed foods.

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[Introduction] [Peanut] [Soybean] [Tree Nuts] [Sesame Seed] [Conclusions] [References] [Abbreviations]

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INTRODUCTION

The prevalence of food allergy in children younger than 3 years of age can be up to 8% and in adults can be about 2% (Sampson 1999). The most potent allergens of plant origin include legumes, nuts, and seeds. The frequencies of self-reported allergy to peanuts and tree nuts were about 0.4% in adults representative of the general population while the frequencies of self-reported allergy to pulses, soybean, and sesame seeds were about 0.04% (Table 1). Allergy to soybean is more frequently seen in young children while allergies to peanut and nuts are more frequent in children older than 3 years of age (Table 2). Children with a history of peanut anaphylaxis are not likely to develop tolerance to peanuts (Spergel et al. 2000). The most common symptoms of food allergy are gastrointestinal, cutaneous, and respiratory reactions. Anaphylactic reactions to foods are less frequent. However legumes, nuts, and seeds are commonly seen among foods inducing anaphylactic reactions (Table 3). Moreover, fatal cases of anaphylaxis after ingestion of peanut, pecan, cashew, soybean, hazelnut, and walnut have been reported (Yunginger et al. 1988, Sampson et al. 1992, Foucard & Malmheden Yman 1999, European Commission 1999).

Table 1: Allergy prevalences to legumes, nuts, and seeds in the general adult population of Great Britain (16420 men and women, > 15 years of age, interview survey) (Emmett et al. 1999)

Food	Prevalence
Tree Nuts	0.40 %
Peanuts	0.39 %
Pulses	0.04 %
Soybean	0.04 %
Sesame Seed	0.04%

Table 2: Allergy prevalences to legumes, nuts, and seeds in children and adolescents with DBPCFC- proven food allergy (Bock & Atkinson 1990)

Food	Children < 3 years (n=74)	Children 3-19 years (n=111)
Peanut	18 %	41 %
Nuts	2.7 %	21 %
Soybean	16 %	2.7 %
Pea	2.7 %	2.7 %

Table 4 shows the threshold concentrations to elicit symptoms after ingestion of the offending food as determined by double- blind, placebo controlled food challenge (DBPCFC). Threshold concentrations ranged from 2 mg to several grams of protein in the cited studies. They are strongly dependent on the patient's individual susceptibility and the allergenic potency of the particular food. However the percentage of children reacting to doses of less than 500 mg of peanut and soybean was 26% and 28%, respectively (Sicherer et al. 2000). According to Moneret-Vautrin et al. (1998) 25% of 50 peanut allergic individuals reacted to doses of less than 25 mg of peanut protein. Although allergic reactions to lower amounts can not be excluded, the lowest dose of legume, nut, or seed protein eliciting (objective) allergic symptoms in DBPCFC was 2 mg of peanut protein (Table 4).

Table 3: Frequency of legumes, nuts, and seeds in episodes of food-induced anaphylaxis

France (Andre et al. 1994)	Great Britain (Pumphrey & Stanworth 1996)	Spain (Novembre et al. 1998)	USA (Kemp et al. 1995)
Adults and Children (n=60)	**Adults and Children (n=90)**	**Children (<16 years) (n=44)**	**Adults (12-75 years) (n=89)**
Peanut 12 %	Peanut 47 %	Brazil Nut 6.8 %	Peanut 22 %
Mustard 3.3%	Brazil Nut 10 %	Hazelnut 2.3 %	Almond / Peach 5.6 %
Soybean 3.3%	Hazelnut 4.4 %	Peanut 2.3 %	Walnut / Pecan 4.5 %
Almond 1.7%	Pistachio 4.4 %	Pinefruit 2.3 %	Cashew 2.2 %
White Bean 1.7%	Almond 3.3 %	Chestnut 2.3 %	Brazil Nut 1.1 %
	Cashew 3.3 %		
	Walnut 3.3 %		

Table 4: Threshold concentrations for eliciting symptoms in DBPCFC

Allergen	Dose at first reaction	Amount of protein*	Reference
Cashew	500 mg and 8 g (dried food)	88 mg - 1.4 g	Bock et al. 1978
Hazelnut	1.4 g, 2.7 g, and 15.3 g **	168 mg, 324 mg, and 1.8 g **	Ortolani et al. 2000
Peanut	100 mg - 8 g (dried food)	26 mg - 2 g	Bock et al. 1978
Peanut	appr. 4 - 100 mg (peanut flour) (at 200 µg subjective symptoms)	2 - 50 mg (at 100 µg subjective symptoms)	Hourihane et al. 1997b
Peanut	<100 mg (in 25% of 50 patients) 100 - 1000 mg (62.5%) 1 - 7.1 g (12.5%)	<25 mg 25 - 250 mg 0.25 - 1.8 g	Moneret-Vautrin et al. 1998
Pecan	1 g (dried food)	93 mg	Bock et al. 1978
Pistachio	500 mg (dried food)	88 mg	Bock et al. 1978
Sesame Seed	100 mg - 10 g	18 mg - 1.8 g	Kanny et al. 1996
Sesame Seed	100 mg - 10 g	18 mg - 1.8 g	Kolopp-Sarda et al. 1997
Soybean	1 g - 8 g (dried food)	0.3 - 2.7 g	Bock et al. 1978
Soybean	500 mg and less (dried food)	150 mg	Sicherer et al. 2000

* calculated

** mean provocative doses in 3 clinical centers

Many food allergens are generally resistant to extremes of heat, pH and enzymatic degradation. Resistance to denaturation and degradation during food processing and passage through the digestive system enables the allergen to either sensitize the individual or to elicit an allergic reaction. With the exception of pollen associated food allergens such as the major allergens cross-reactive to Bet v 1, only a few plant-food allergens are labile and do not survive processing. Several legume, nut, and seed allergens have been identified and characterized (Table 5), but little is known about their stability and the allergenicity of processed foods determined under standardized conditions.

During food processing the allergenicity can be altered by various procedures such as storage time, prolonged washing, separation techniques, heating, and texturizing. Moreover, various chemical interactions during the food manufacture between natural food ingredients and food additives can occur. The allergenic potential may be unaffected or decreased or even increased by food processing. Physico-chemical methods may simply reduce the allergen content of a specific product by, for example, extraction, precipitation, or ultrafiltration. The molecular basis of allergen alteration is the inactivation or destruction of IgE-binding epitope structures or the formation of new epitopes or better accessibility of cryptic epitopes after denaturation of the native allergen. Heat treatment can induce the loss of the tertiary protein structure and induce aggregation of allergens affecting the conformational structure. In contrast, proteolytic or hydrolytic treatments affect the conformational structure as well as the linear amino acid sequence, which may destroy sequential IgE-binding epitopes.

The majority of available studies examined the impact of heating (dry heating, roasting, or baking) and enzymatic digestion on native foods or allergen extracts of native foods. For recent reviews on the alteration of allergenicity by food processing see Moneret-Vautrin 1998 and Hefle 1999. This review summarizes available data on the stability of peanut, soybean, nut (hazelnut), and sesame seed allergens during food processing.

Table 5: Characterized legume, nut, and seed allergens

Source	Species	WHO/IUIS Allergen Nomenclature*	Protein name / family	Molecular mass (kDa)
Legumes				
Peanut	*Arachis hypogaea*	Ara h 1 Ara h 2 Ara h 3 Ara h 4 Ara h 5 Ara h 6 Ara h 7	Vicilin Conglutin Glycinin Glycinin Profilin Conglutin-homologous Conglutin-homologous	63.5 17 60 37 ** 15 15 15
Soybean	*Glycine max*	- - - Gly m 3	Gly m Bd 30 K Glycinin beta-Conglycinin Profilin	34 58-62 42-76 14
Nuts				
Brazil nut	*Bertholletia excelsa*	Ber e 1	2S-Albumin	9
Hazelnut	*Corylus avellana*	Cor a 1.04 Cor a 2 *** Cor a 8 ***	Bet v 1 homologous Profilin Lipid-transfer Protein	17
English Walnut	*Juglans regia*	Jug r 1 Jug r 2	2S-Albumin Vicilin	 44
Seeds				
Oriental Mustard	*Brassica juncea*	Bra j 1	2S-Albumin	14.6
Yellow Mustard	*Sinapis alba*	Sin a 1	2S-Albumin	14.2
Rapeseed	*Brassica napus*	Bra n 1	2S-Albumin	15
Sesame Seed	*Sesamum indicum*	Ses i 1	2S-Albumin	10

* Allergen Nomenclature Sub-Committee 2001

** Partial sequence (calculated Mr from full length clone: 61 kDa; Kleber-Janke et al. 1999)

*** GeneBank; not listed in the official list of allergens

PEANUT ALLERGENS

The major peanut allergens recognized by more than 50% of peanut allergic individuals are named Ara h 1 (vicilin), Ara h 2 (conglutin- homologue protein), and Ara h 3 (glycinin) (see Table 5). Ara h 4 represents an isoallergen of Ara h 3 with an amino acid identitiy of 91% (Kleber-Janke et al. 2001). These allergens are seed storage proteins and their primary structure and major IgE-binding epitopes have been characterized. More recently three additional minor allergens Ara h 6 and Ara h 7 (both conglutin-homologue proteins) as well as the plant pan- allergen profilin (Ara h 5) have been described (Table 5) (for a recent overview see: Bannon et al. 2000).

Raw Peanuts
Doses of raw peanuts eliciting first allergic reactions in DBPCFC were tested by Moneret-Vautrin et al. (1998). In this study 25% of 50 peanut allergic patients reacted to less than 100 mg, 62.5% reacted to 100 to1000 mg, and 12.5% to cumulative doses of up to 7.1 g.

Peanut Flour
Eight peanut flours tested in RAST inhibition showed strong IgE-binding from a pooled serum of five

highly sensitized peanut allergic individuals (Nordlee et al. 1981). Five peanut flours showed no difference in IgE-binding to extracts from raw peanuts, while three flours showed significantly different slopes which could be due to different peanut varieties. Peanut shells showed only weak allergenic activity (Nordlee et al. 1981).

In DBPCFC with 14 peanut allergic patients a commercial peanut flour was tested at extremely low doses of 10 µg to 50 mg of peanut protein (Hourihane et al. 1997c). In one case a systemic reaction was observed at a provocation dose of 5 mg. In two cases milder objective symptoms were induced at doses of 2 mg and 50 mg, while in five other cases milder subjective symptoms were elicited at doses of 1 to 50 mg. Two allergic individuals who had objective symptoms at higher doses showed short-lived subjective symptoms at a dose as low as 100 µg. Another five peanut allergic individuals showed no symptoms after challenges with doses up to 50 mg (Hourihane et al. 1997c).

Heated Peanuts

Comparing oil-roasted and dry-roasted peanuts in RAST inhibition, Nordlee et al. (1981) found almost the same IgE-binding activities as for raw peanuts (RAST inhibition).

Using a pooled serum from five peanut allergic patients Keating et al. (1990) identified peanut allergens in plant edible oils which were used for roasting of peanuts (radio-immuno assay, RIA). After filtration and steam cleaning of the plant oil samples the allergen concentration could be reduced to approximately 0.1-1%.

No reduction of IgE-binding in RAST inhibition was observed after heating of peanut protein extracts and Ara h 1 and Ara h 2 at 100°C for up to 60 min (pooled serum from 10 patients with peanut allergy) (Burks et al. 1992). It should be noted that the extracts were prepared from roasted peanuts (13-16 min, 163-177°C).

Koppelman et al. (1999a) isolated Ara h 1 from ground peanuts heated for 15 min at temperatures between 20° and 140°C. No significant differences in IgE-binding potencies were observed in ELISA inhibition with a pooled serum from 8 peanut allergic individuals.

More recently Maleki et al. (2000) observed an increased IgE binding capacity of roasted peanuts from two different peanut varieties in comparison to raw peanuts (ELISA inhibition, pooled serum from 10 peanut allergic individuals). Thereafter, the purified allergens Ara h 1 and Ara h 2 were subjected to the Maillard reaction (modification of amino groups of proteins with reducing sugars). Such modified peanut allergens bound more IgE (approximately 90 fold increase) and were more resistant to heat and digestion by gastrointestinal enzymes than the native allergens. Therefore the Maillard reaction may contribute to enhancing the allergenic properties of roasted peanuts (Maleki et al. 2000).

Beyer et al. (2001) investigated the effects of dry roasting, boiling, and frying on the allergenicity of peanuts. The roasting was carried out at 170°C for 20 minutes, and frying was done for 5 min and 10 min to account for the difference in the size of two different peanut varieties. Boiled peanuts were cooked for 20 min in water (100°C). SDS-PAGE analysis showed that the protein fractions of fried and boiled peanuts were altered to a similar degree. The relative amount of Ara h 1 was reduced in the fried and boiled preparations compared with that in roasted peanuts, resulting in a markedly reduced potency of IgE binding in SDS-PAGE immunoblot. In contrast, amounts of Ara h 2 and an Ara h 3 fragment (14 kd) were similar in all three peanut preparations, while significantly less IgE binding to Ara h 2 and Ara h 3 was observed in fried and boiled peanuts. Only minimal amounts of Ara h 1 were determined in the cooking water of boiled peanuts.

Hydrolysis with Digestive Enzymes

By chewing of peanuts for 10 min, peanut allergens were released without any detectable degradation in SDS-PAGE immunoblot using sera from 10 peanut allergic patients (Becker 1997).

Burks et al. (1992) simulated digestive fluids by combining two successive enzymatic steps for digestion of peanut protein extracts from roasted peanuts. The first step simulated the gastric digestion (pepsin hydrolysis) while the second step simulated the duodenal digestion (trypsin, chymotrypsin, and intestinal mucosa peptidase). In RAST inhibition a 100 fold decrease of IgE-binding was observed (pooled serum from 10 patients with peanut allergy).

In similar digestion studies with peanut protein extracts from roasted peanuts, after peptic digestion for 2 h

several IgE-binding fragments were identified in SDS-PAGE immunoblot (Vieths et al. 1999). After subsequent digestion with pancreatic enzymes for 45 min the allergenic activity was strongly reduced. However, IgE reactive and allergenic peptides were still present as indicated by EAST and RBL cell mediator release assay of digested peanut extracts.

Astwood et al. (1996) observed a high stability of Ara h 2 (>60 min) against peptic hydrolysis (pH 1.2), while peanut lectin was stable for 8 min (IgE binding was not tested).

Becker (1997) demonstrated the high stability of Ara h 1 against pepsin digestion for 80 min with chewed peanut meal in the preparation.

After pepsin hydrolysis applying a higher enzyme-substrate ratio of 1:3 (treatment for 24 h and 48 h), Hong et al. (1999) observed complete loss of IgE-binding to peanut protein extracts (five peanut allergic patients, SDS-PAGE immunoblot). However, these pepsin digested peanut preparations were capable of T-cell proliferation. In vitro stimulation of PBMC (peripheral blood mononuclear cells) from 7 peanut allergic patients showed a significant T-cell proliferation slightly lower than by stimulation with native peanut protein extracts (Hong et al. 1999).

Peanut Allergens in Breast Milk

Vadas et al. (2001) investigated the ability of maternal dietary peanut protein to pass into breast milk during lactation. Samples of 23 lactating women were collected after each woman had consumed 50 g of dry roasted peanuts. Peanut protein was detected in 43% of subjects within 2 hours of ingestion and in 4% within 6 hours. The median peak peanut protein concentration in breast milk was 200 ng/mL (range, 120-430 ng/mL) as measured by ELISA. The major peanut allergens Ara h 1 and Ara h 2 were detected in SDS-PAGE immunoblot.

Peanut Butter

Spergel et al. (2000) performed open food challenges with peanut butter at cumulative doses between 0.15 to 15 mL. 19 of 33 children younger than 8 years of age with histories of peanut allergy reacted to oral challenges.

Four commercially available peanut butter samples showed an increased capacity of IgE-binding in RAST inhibition to crude raw peanut extract using a pooled serum from five highly sensitive peanut allergic patients (Nordlee et al. 1981).

Peanut Oil

Studies on the allergenicity and IgE-binding potency of peanut oil, respectively, revealed contrary results. Nordlee et al. (1981) analyzed peanut oil samples which demonstrated no inhibition of IgE-binding to raw peanut extracts in RAST inhibition. Moreover safe ingestion of total doses of 8 mL of refined peanut oil was demonstrated in DBPCFC with 10 peanut allergic individuals (Taylor et al. 1981).

Teuber et al. (1997) analyzed four commercial peanut oils which underwent different treatments. In dot-immunoblotting tests with a pooled serum from 17 nut and/or peanut allergic patients the IgE-binding capacities of the samples decreased in the following order: unrefined peanut oil (54°C maximum temperature of processing) > unrefined peanut oil (65-93°C) >> refined, bleached, and deodorized peanut oils (230-260°C). In dot-blotting 1 µg protein from each sample was applied. Unrefined oils contained about 10-11 µg/mL and refined oils contained about 3 and 5.7 µg/mL.

Hourihane et al. (1997a) tested the allergenicity of refined and unrefined peanut oils in DBPCFC with 60 peanut allergic patients. After challenge with refined peanut oil no symptoms were observed, while six patients experienced allergic reactions after ingestion of 1-10 mL of unrefined peanut oil (oral and throat itching, swelling of lips, wheeze). While SPT were negative for 11 peanut allergic patients, four positive reactions were elicited by challenge with 5 mL crude peanut oil in DBPCFC (Olszewski et al. 1998). Positive DBPCFC with doses of 5 to 15 mL of refined peanut oil could be demonstrated in 14 of 62 peanut allergic patients by Moneret-Vautrin et al. (1998). The symptoms were immediate reactions of the skin (facial erythema and pruritus, 6 cases) and respiratory tract (bronchospasm 1 case) as well as delayed respiratory (bronchospasm 1 case), cutaneous (labial oedema 1 case, eczema 3 cases, buccual itching and oral allergy syndrome 2 cases), and gastrointestinal symptoms (abdominal pain with nausea 2 cases). Infant food formulas containing peanut oil were reported to induce adverse reactions in four children with

atopic dermatitis (aged 4-13 months) (Moneret-Vautrin et al. 1994). Symptoms improved after eliminating peanut oil from the diet. All four children were positive in oral provocation tests with refined peanut oil and two had positive labial challenge tests. Skin tests were performed in one child (with positive result). Kull et al. (1999) studied 41 children with clinically relevant peanut allergy. A significantly higher frequency of allergic symptoms after consumption of peanuts was observed in children who were exposed to peanut oil containing vitamin A and D preparations than in children who were exposed to water-based vitamin preparations. No differences could be observed in the frequency of in vitro sensitization. In SPT protein extracts from refined peanut oil were not reactive, while extracts from unrefined peanut oil gave positive results in 15 of 41 children (Kull et al. 1999).

"Hidden" Peanut Allergens

Four cases of fatal anaphylaxis after ingestion of "hidden" peanut were reported by Yunginger et al. (1988). The fatal reactions occurred after ingestion of "two bites" of chili containing peanut butter, cake and a cookie containing peanuts, and a Vietnamese dish topped with slivered peanuts.

Three fatal anaphylactic reactions in adolescents between 8 and 16 years old with severe peanut allergy were reported to have occurred after ingestion of candy, cake, and a sandwich containing peanuts in different forms (Sampson et al. 1992). Another case of a near-fatal anaphylaxis in a 13 year old boy was induced by cookies.

Malmheden Yman et al. (1994) reported a case of anaphylaxis after inadvertent ingestion of peanut containing-cake.

Ingestion of a dry soup preparation containing undeclared peanut flour as a component of a flavouring ingredient caused a systemic allergic reaction in a 33-year old peanut sensitive woman. Approximately 45 mg peanut protein were ingested (McKenna et al. 1997).

Two cases of anaphylaxis after ingestion of pizza in a fast food restaurant were reported by Hogendijk et al. (1998). The pizza sauce contained peanut allergens.

Recurrent anaphylactic reactions after ingestion of Asian foods, chocolate products and bakery products containing peanuts were described by Borelli et al. (1999) in three patients with peanut allergy.

Two fatal reactions in adolescents with known peanut allergy occurred after ingestion of an "almond bun" with peanut flakes which were substituted for almond flakes (presumed co-factor: a cold beverage) and a self prepared beverage containing peanuts, respectively (Foucard & Malmheden Yman 1999). Additional four near-fatal allergic reactions were observed after ingestion of peanut butter, peanut paste, and candy.

Approximately 1% of 3704 peanut and nut allergic individuals experienced an allergic reaction to peanuts on a commercial airliner (American survey; Sicherer et al. 1999). In 32 of these 35 cases peanuts or peanut products were served during the flight. Allergic symptoms were induced after ingestion in 14 cases, by skin contact in 7 cases, and by inhalation in 14 cases.

Five of 17 commercial food products contained peanut protein without appropriate declaration on the label. The amounts ranged between 2 and 18 mg/kg of peanut protein as determined by a competitive ELISA with polyclonal antiserum (Holzhauser & Vieths 1999a).

SOYBEAN ALLERGENS

The major allergens from soybean are seed storage proteins: Gly m Bd 30K (30 kDa, formerly Gly m 1), glycinin (320-360 kDa, 6 subunits 58-62 kDa), and beta-conglycinin (140-180 kDa, 3 subunits 42-76 kDa) (for a recent overview see Besler et al. 2000). Further allergenic proteins are soybean profilin (Gly m 3, 14 kDa) and the Kunitz-trypsin-inhibitor (20 kDa). The major allergens from soybean shells are the inhalative allergens Gly m 1 (two isoallergens with 7 and 7.5 kDa) and Gly m 2 (8 kDa) (Besler et al. 2000). Recently, cross-reactivity between Bet v 1, the major birch pollen allergen, and a soy protein isolate has been reported, indicating the presence of a Bet v 1 related soybean allergen (Kleine-Tebbe et al. 2001).

Heated Soybeans

The IgE-binding properties of the 11S-, 7S-, and 2S-globulin fractions were studied by Shibasaki et al. (1980) after heating for 30 min at various temperatures. A slight increase of IgE-binding by the 2S-fraction was observed after heating to 80°C, while the IgE-binding potencies of the 11S- and 7S-fractions both decreased about 42-75% in RAST. Higher temperatures of 100° and 120°C reduced the IgE-binding potencies in all three fractions by about 39-83%.

In contrast, after heating at 100°C up to 60 min Burks et al. (1992) observed no significant decrease in IgE-binding of whole soybean protein extracts as well as 7S- and 11S-fractions and whey proteins (RAST inhibition; pooled serum from two patients with soybean allergy).

Müller et al. (1998) tested the IgE-binding potentials of boiled (100°C, 2 h) and raw soybeans in EAST and EAST inhibition. Three of six sera from soybean allergic patients had specific IgE against boiled soybean protein.

Microwave heating (700W, 25 min) of soybeans gave similar results (Vieths et al. 1995). In EAST nine of 15 soybean allergic patients had detectable specific serum IgE against heated soybean protein.

Hydrolysis with Digestive Enzymes

Digestion of soybean protein with gastric fluid and duodenal fluid was performed by Burks et al. (1992) using successive steps of peptic hydrolysis and hydrolysis with trypsin, chymotrypsin and intestinal mucosa peptidase. A 10 fold decrease in RAST inhibition was observed for digested soybean protein as compared to native soybean protein (pooled serum from two patients with soybean allergy).

Astwood et al. (1996) observed a high stability (>60 min) of beta-conglycinin (beta-subunit) and Kunitz-trypsin inhibitor against peptic digestion (pH 1.2). Soybean lectin was stable against peptic digestion for 15 min, while the alpha-subunit of beta-conglycinin and Gly m Bd30K were completely abolished after 2 min and 30 sec, respectively. No IgE-binding assays were performed in this study.

Processed Soybean Products

Herian et al. (1993) studied several soybean products in RAST inhibition of IgE-binding to a protein extract from raw soybeans (pooled serum from 7 soybean allergic patients). IgE-binding potentials of protein extracts decreased in the following order: soybean sprouts (approx. 70% max. inhibition), acid hydrolyzed soy sauce (40%), hydrolyzed soybean protein (40%), tofu (25-30%), tempeh (20%), miso (20%), mold-hydrolyzed soy sauce (10%). Self inhibition of raw soybeans was 70% max. inhibition. Therefore all investigated soybean products retained detectable IgE-binding activity.

The IgE-binding potential of soy milk, tofu, and texturized soybean protein was confirmed by Vieths et al. (1995) in EAST inhibition.

Soybean Lecithins

Severe systemic reactions occurred in three cases due to soybean lecithins which were contained as emulsifiers in parenteral lipid-emulsions (Weidmann et al. 1997).

Müller et al. (1998) detected three IgE-binding proteins with 27, 39, and 40 kDa in four out of six commercial soybean lecithins, whereas Awazuhara et al. (1998) identified a 31-kDa IgE-binding protein in soybean lecithins which had a protein content of 2.8 mg / 100 g.

Palm et al. (1999) performed a DBPCFC with soybean lecithins in a 4-year old boy. The ingested dose of 100 mg induced allergic symptoms of the skin (erythema) within one hour. The protein content of the soybean lecithin was 3.5 g / 100 g.

Using a pooled serum from 9 soybean allergic patients Paschke et al. (2001) detected two IgE-binding proteins with 35 and 37 kDa in soybean lecithins which were also present in a soybean protein isolate (SDS-PAGE immunoblot). An additional IgE-binding protein with 16 kDa was detected in all of the three investigated lecithin preparations. The protein contents of the soybean lecithins were between 173 and 202 mg / 100 g. Maximum inhibition of IgE-binding to native soybean protein by protein extracts from the lecithins were 54% to 84% with C_{50}-concentrations of 10-16 µg/mL (native soybean protein 0.3 µg/mL, EAST inhibition).

Soybean Oil

No adverse reactions occurred in DBPCFC with seven soybean allergic patients using two refined soybean oils and one cold-pressed soybean oil (Bush et al. 1985). A total dose of 15 mL of soybean oils was applied. The protein contents of the oils were not given in this study.

A patient treated with an infusion based on soybean oil for parenteral nutrition experienced an anaphylactic shock (Andersen et al. 1993).

In three unrefined soybean oils IgE-binding proteins with 53 and 58 kDa were detected while no IgE-binding to protein extracts from two refined soybean oils was observed using a pooled serum of 9 soybean allergic patients (SDS-PAGE immunoblot; Paschke et al. 2001). Protein contents were about 7-10 µg / 100 g (unrefined oils) and 2.5 and 2.7 µg / 100 g (refined oils), respectively. Maximum inhibition of IgE-binding to native soybean protein by protein extracts from unrefined oils was between 25% and 53%, while no inhibition was observed with refined oils (EAST inhibition).

"Hidden" Soybean Allergens

A case of fatal anaphylaxis in a 10-year old girl after ingestion of a pizza sausage fortified with soybean protein was reported by Yunginger et al. (1991). The girl was concomitantly sensitized to peanut and soybean (specific IgE).

Malmheden Yman et al. (1994) reported a case of fatal anaphylactic reaction after ingestion of a hamburger containing soybean additives (2.1% soybean protein) without appropriate labelling. Further allergic reactions occurred after ingestion of a kebab containing 7% soybean protein and crab sticks containing 0.5-0.9% undeclared soybean protein.

Severe anaphylactic reactions were described after ingestion of Spanish sausage products (chorizo, salchichon, mortadella, and boiled ham), doughnut and soup stock cubes all containing soybean proteins (skin test, RAST, bronchial and oral challenge) (Vidal et al. 1997).

Another case of anaphylaxis after ingestion of pizza containing soybean proteins was reported by Senne et al. (1998).

Foucard & Malmheden Yman (1999) described four fatal reactions in adolescents with known peanut allergy, who had an unknown soybean allergy at the same time. Reactions were induced by meat balls (with 3% soybean protein), a hamburger with unknown content of soybean, a hamburger with 2.2% soybean protein, and a kebab containing 7% soybean protein. Six other life-threatening allergic reactions were elicited by ice cream with soybean protein, meat balls, and soy sauce.

NUT ALLERGENS

In the present review the terms "nuts" or "tree nuts" include shell (nut) fruits of various botanical families. Specifically, almond, brazil nut, cashew nut, hazelnut, pecan nut, pistachio, and walnut are referred to as nuts or tree nuts. Unless stated otherwise, peanuts, chestnut, and coconuts are not included.

The major hazelnut allergen is the Bet-v-1-homologous protein Cor a 1 (17 kDa). Up to now four Cor a 1 isoforms have been identified in hazel pollen (Cor a 1.01, Cor a 1.02, and Cor a 1.03) and hazelnuts (Cor a 1.04). A 14-kDa hazelnut allergen is cross- reactive to birch profilin (Bet v 2) (for a recent overview see Besler et al. 2001b). Major walnut allergens are 2S-albumin Jug r 1 and vicilin Jug r 2 (44 kDa). Brazil nut contains the major allergen Ber e 1 a 2S-Albumin (9 kDa) (Table 5).

Heated Nuts

The allergens from hazelnut showed a high stability against heating (Wigotzki et al. 2000 b). No reduction of IgE binding was observed after heating of ground hazelnuts at 100°C for 90 min (dry heating oven) or after microwave heating (630 W, 10 min), respectively. IgE-binding was tested in immunoblot and EAST inhibition with sera from hazelnut allergic patients. The IgE binding potency decreased after conventional dry heating at temperatures above 100°C for 15 min. While the 18-kDa- and 14-kDa-allergens were detected after heating to 155°C, heating to more than 170°C resulted in loss of IgE-binding to the major allergens in SDS-PAGE immunoblotting. A minor allergen with <14 kDa was still detectable after heating up to 185°C (15 min).

In another study most patient's sera showed a strongly reduced IgE-binding to proteins from roasted hazelnut (Müller et al. 2000). The Bet v 1 related allergen Cor a 1.0401 was shown to be heat-labile. Its IgE-binding capacity was lost after heating at 140°C for 30 min. In contrast, high molecular mass bands (>40 kDa) and a low molecular mass allergen (12 kDa) appeared to be stable under these conditions (Müller et al. 2000).

Similarly, Schocker et al. (2000) identified non pollen-related heat-stable hazelnut allergens with molecular masses of 5-7, 8, and 9-10 kDa using sera from 2 patients with non-pollen associated hazelnut allergy and from 1 patient with IgE reactivity to both pollen and non-pollen associated hazelnut allergens. IgE-binding potencies of extracts from native and heated hazelnuts (roasted at 140°C for 40 min) were similar in EAST inhibition. There was no significant cross-reactivity between hazelnut and birch pollen extracts in immunoblot and EAST inhibition using the serum of a woman with severe allergic reactions to hazelnut. Hazelnut allergic individuals with related pollinosis were not sensitized against the low molecular mass hazelnut allergens.

Hydrolysis with Digestive Enzymes

A combination of hydrolysis with artificial gastric fluid (2 h) followed by hydrolysis with pancreatic enzymes (45 min) resulted in reduced IgE-binding of digested hazelnut proteins. The IgE-binding was less than 10% of IgE-binding potency of native protein extract (EAST with sera from hazelnut allergic individuals) (Vieths et al. 1999).

Wigotzki et al. (2000 a) investigated the stability of hazelnut protein extracts against various enzymes. Peptic hydrolysis for 60 min induced only a slight decrease in IgE-binding (max. EAST inhibition appr. 65%). Even after 240 min of peptic hydrolysis two of seven sera from hazelnut allergic subjects showed IgE-binding in SDS-PAGE immunoblot. Maximum EAST inhibition was about 40% as compared to native hazelnut extract (Wigotzki et al. 2000 a). In contrast, hydrolysis of hazelnut proteins with trypsin, elastase, and protease (from Tritirachium album) significantly decreased the IgE-binding potential after 30 min of treatment to a maximum inhibition value less than 30%. Hydrolysis of hazelnut proteins with pancreatin for 60 min also reduced the IgE-binding to < 30% maximum inhibition (Wigotzki et al. 2000 a).

Processed Nut Products

Wigotzki et al. (2001) investigated the IgE-binding potencies of commercially available products containing hazelnuts as indicated on the labels. A pooled serum from 13 hazelnut allergic patients was used. In general all processed nut products showed reduced IgE-binding. Ten times higher concentrations of 50%-inhibition (C_{50}-values) in EAST inhibition indicated reduced IgE-binding of protein extracts from two nougat chocolates as compared to native hazelnut extracts. Two nougat masses and two nougat-creams showed only 40% maximum inhibition. Protein extracts from five hazelnut chocolates showed a 6-25 times lower IgE-binding potency. A 17-fold decrease in C_{50}-value was observed with the protein extract from a hazelnut cookie as inhibitor. Two additional hazelnut cookie products did not produce a 50%-inhibition of IgE-binding. C_{50}-values of two hazelnut crackers were 16 and 23 times higher as compared to native hazelnut protein. The IgE-binding potential of a muesli bar was comparable to native hazelnut protein, while protein extracts from a cake containing hazelnut protein did not give a 50% inhibition in EAST (Wigotzki et al. 2001).

"Hidden" Nut Allergens

A fatal anaphylactic reaction in a 16-year old boy with known allergy to peanuts and pecan nuts after ingestion of a piece of cheesecake containing ground pecans in the crust was described by Yunginger et al. (1988).

Sampson et al. (1992) reported two fatal anaphylactic reactions after ingestion of candies containing cashew protein.

A chocolate which contained 0.2% hazelnut protein induced asthma after ingestion of a 3-6 g piece (from a Christmas calendar) (Malmheden Yman et al. 1994).

Malanin et al. (1995) described a girl who experienced an anaphylactic reaction after ingestion of cookies containing pecan nuts, but tolerated the ingestion of raw pecans. An exclusive reactivity to a 15 kDa neoallergen from heated pecans was demonstrated in the patient.

Using a Sandwich ELISA with rabbit-antibodies against hazelnut protein, amounts of hazelnut between 3.4 and 752 mg/kg could be detected in 15 of 26 samples of food products like chocolate spread, chocolate bar, chocolate cookie, muesli cookie, and cake, which were thought to be free of hazelnuts. A complaint sample of chocolate spread contained 4 g/kg undeclared hazelnut (Koppelman et al. 1999b).

A hazelnut-specific Sandwich ELISA based on polyclonal antisera was used to detect hazelnut protein between 2 and 421 mg/kg in 12 of 28 commercial food products without labelling of hazelnut (Holzhauser & Vieths 1999b).

Wensing et al. (2001) reported severe colic and itching of urticaria pigmentosa lesions in a 5-year old boy after eating bred with chocolate spread. Skin tests and RAST revealed a monosensitization to hazelnut. A sample of chocolate spread from the same production batch and 6 other samples from different production batches were analyzed for the presence of hazelnut protein by ELISA. All samples contained hazelnut protein at varying levels from 300 mg/kg to 5600 mg/kg.

SESAME SEED ALLERGENS

There are few studies on sesame seed allergens (for a recent overview see Besler et al. 2001a). Only recently a 2S albumin (10 kDa) has been described as the major sesame seed allergen named Ses i 1 (Pastorello et al. 2001). Using a serum from only one patient Asero et al. (1999) described allergens with 10 kDa, 15-20 kDa, and 30-67 kDa. A 25 kDa and a 14 kDa allergen were previously detected by Kolopp-Sarda et al. (1997).

Processed Foods
A 16-year old girl experienced an anaphylactic reaction after ingestion of a chocolate candy rolled in sesame seeds (Asero et al. 1999). Reportedly she ingested sesame seeds for the first time knowingly.

Sesame seed and oil masked in baked bread induced allergic reactions in a patient after DBPCFC (Stern & Wüthrich 1998).

Similarly, Pajno et al. 2000 performed a DBPCFC using baked bread containing masked sesame seeds, which induced allergic reactions in a sesame seed allergic individual.

"Hidden" Sesame Allergens
Malish et al. (1981) described four sesame allergic patients who experienced allergic reactions including anaphylaxis after ingestion of sesame seed products like hamburger, candy and salad with sesame oil.

Three anaphylactic reactions in sesame allergic patients occurred after ingestion of falafel burgers (Kägi & Wüthrich 1993). Falafel burgers are oriental specialities made from a wheat flour bun filled with chickpea balls. The ingredient eliciting adverse reactions, namely freshly ground sesame seeds, was contained in a white sauce.

Kanny et al. (1996) reported nine allergic events to sesame products including five anaphylactic reactions. Foods causing the symptoms were Lebanese sesame-rice-cake, bread and other pastry, Chinese food, pizza, "health" food, Turkish cake, and a hamburger sandwich.

An anaphylactic reaction in a 46-year old man after ingestion of sesame oil was described by Chiu et al. (1991).

Table 6: Stability of allergens from legumes, nuts, and sesame seed

Allergen	Heat Treatment	Enzymatic Hydrolysis
Peanut	stable	partially resistant
Soybean	partially stable	partially resistant
Tree Nuts	partially stable	partially resistant
Sesame Seed	stable	no information

CONCLUSIONS

Most allergens from legumes, nuts, and seeds are highly resistant to common treatments during food processing. The impact of heat and enzymatic treatments on the allergenicity are summarized in Table 6. Peanut allergens are not even stable to heating, but an increase in IgE-binding could be demonstrated in several studies. The example of peanut allergens indicates that the formation of neoallergens or the release of cryptic IgE-binding epitopes during food processing should be considered. Soybeans and tree nuts retained significant IgE-binding potencies after heat treatment. As mentioned before there are few studies on sesame seeds. The fact that sesame seeds masked in baked bread were capable of inducing allergic reactions indicates a high stability to heat treatment. Peanut, soybean, and tree nut allergens retain at least partially their IgE-binding potencies after treatment with gastrointestinal enzymes.

Usually refined, heated oils are not allergenic, while crude edible plant oils generally contain amounts of proteins which could induce allergic reactions (Hefle & Taylor 1999). Teuber et al. (1997) identified IgE-binding proteins in several gourmet nut oils including almond, hazelnut, macadamia, pistachio, walnut, and peanut oils. Recently refined peanut oil was demonstrated to induce allergic reactions in DBPCFC (Moneret-Vautrin et al. 1998).

Obviously there is a lack of information with respect to the allergenicity of processed foods. Future research should systematically characterize food products by various in-vitro and in-vivo methods such as DBPCFC, SPT, RAST, SDS-PAGE immunoblot, mediator release assays, and inhibition tests. The investigations should be based on well-characterized food products and their intermediates. Standardized manufacturing processes and reliable food specifications are mandatory. Evaluation of the allergenicity of processed foods must involve an appropriate number of patients clinically allergic to the native food allergen. Ideally patient cohorts should be recruited from various countries and represent child and adult population.

REFERENCES

- Allergen Nomenclature Sub-Committee, International Union of Immunological Societies (2001) **Allergen Nomenclature: List of allergens** *http://www.allergen.org/List.htm*
- Andersen HL, Nissen I (1993) **Presumed anaphylactic shock after infusion of Lipofundin** *Ugeskr Laeger 155(28):2210-1* (in Swedish)
- Andre F, Andre C, Colin L, Cacaraci F, Cavagna S (1994) **Role of new allergens and of allergens consumption in the increased incidence of food sensitizations in France** *Toxicology 93:77-83*
- Asero R, Mistrello G, Roncarolo D, Antoniotti PL, Falagiani P (1999) **A case of sesame seed-induced anaphylaxis** *Allergy 54(5):526-7*
- Astwood JD, Leach JN, Fuchs RL (1996) **Stability of food allergens to in vitro digestion** *Biotechnol 14:1269-73*
- Awazuhara H, Kawai H, Baba M, Matsui T, Komiyama A (1998) **Antigenicity of the proteins in soy lecithin and soy oil in soybean allergy** *Clin Exp Allergy 28:1559-1564*
- Bannon GA, Besler M, Hefle SL, Hourihane JO'B, Sicherer SH (2000) **Allergen data collection: Peanut** (*Arachis hypogaea*) *Internet Symposium on Food Allergens 2(2):87-122*
- Becker WM (1997) **Characterization of Ara h 1 by two- dimensional electrophoresis immunoblot and recombinant techniques: new digestion experiments with peanuts imitating the gastrointestinal tract** *Int Arch Allergy Immunol 113:118-21*
- Besler M, Helm R, Ogawa T (2000) **Allergen data collection - update: Soybean** (*Glycine max*) *Internet Symposium on Food Allergens 2(Suppl.3):1-35*
- Besler M, Hefle SL, Jensen-Jarolim E (2001a) **Allergen data collection: Sesame seed** (*Sesamum indicum*) *Internet Symposium on Food Allergens 3(2):93-102*
- Besler M, Koppelman S, Pumphrey R (2001b) **Allergen data collection - update: Hazelnut** (*Corylus avellana*) *Internet Symposium on Food Allergens 3(Suppl.1): 1-22*
- Beyer K, Morrow E, Li XM, Bardina L, Bannon GA, Burks AW, Sampson HA (2001) **Effects of cooking methods on peanut allergenicity** *J Allergy Clin Immunol 107:1077-81*
- Bock SA, Atkins FM (1990) **Patterns of food hypersensitivity during sixteen years of double-blind, placebo-**

controlled food challenges *J Pediatr 117:561-7*

● Bock SA, Lee WY, Remigio LK, May CD (1978) **Studies of hypersensitivity reactions to foods in infants and children** *J Allergy Clin Immunol 62:327-34*

● Borelli S, Anliker MD, Wuthrich B (1999) **Peanut anaphylaxis: the problem of hidden allergens** *Dtsch Med Wochenschr 124:1197-200* (in German)

● Burks AW, Williams LW, Thresher W, Connaughton C, Cockrell G, Helm RM (1992b) **Allergenicity of peanut and soybean extracts altered by chemical or thermal denaturation in patients with atopic dermatitis and positive food challenges** *J Allergy Clin Immunol 90(6 Pt 1):889-97*

● Bush RK, Taylor SL, Nordlee JA, Busse WW (1985) **Soybean oil is not allergenic to soybean-sensitive individuals** *J Allergy Clin Immunol 76(2 Pt 1):242-5*

● Chiu JT, Haydik IB (1991) **Sesame seed oil anaphylaxis** *J Allergy Clin Immunol 88:414-5*

● Emmett SE, Angus FJ, Fry JS, Lee PN (1999) **Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut allergy in other household members** *Allergy 54:380-5 (erratum 54:891)*

● European Commission (1998) **Reports on tasks for scientific cooperation. The occurrence of severe food allergies in the EU** *European Commission, Directorate-General III, Brussels*

● Foucard T, Malmheden Yman I (1999) **A study on severe food reactions in Sweden - is soy protein an underestimated cause of food anaphylaxis?** *Allergy 54:261-5*

● Hefle SL (1999) **Impact of processing on food allergens** *Adv Exp Med Biol 459:107-19*

● Hefle SL, Taylor SL (1999) **Allergenicity of edible oils** *Food Technol 53:62-70*

● Herian AM, Taylor SL, Bush RK (1993) **Allergenic reactivity of various soybean products as determined by RAST inhibition** *J Food Science 58:385-8*

● Hogendijk S, Eigenmann PA, Hauser C (1998) **The problem of hidden food allergens: two cases of anaphylaxis to peanut proteins concealed in a pizza sauce** *Schweiz Med Wochenschr 128:1134-7* (in French)

● Holzhauser T, Vieths S (1999a) **Indirect competitive ELISA for determination of traces of peanut** *(Arachis hypogaea)* **protein in complex food matrices** *J Agric Food Chem 47:603-11*

● Holzhauser T, Vieths S (1999b) **Quantitative Sandwich ELISA for the determination of traces of hazelnut** *(Corylus avellana)* **protein in complex food matrices** *J Agric Food Chem 47:4209-18*

● Hong SJ, Michael JG, Fehringer A, Leung DY (1999) **Pepsin- digested peanut contains T-cell epitopes but no IgE epitopes** *J Allergy Clin Immunol 104(2 Pt 1):473-8*

● Hourihane JO, Bedwani SJ, Dean TP, Warner JO (1997a) **Randomised, double blind, crossover challenge study of allergenicity of peanut oils in subjects allergic to peanuts** *BMJ 314:1084-8*

● Hourihane JO'B, Kilburn SA, Nordlee JA, Hefle SL, Taylor SL, Warner JO (1997b) **An evaluation of the sensitivity of subjects with peanut allergy to very low doses of peanut protein: a randomized, double- blind, placebo- controlled food challenge study** *J Allergy Clin Immunol 100:596-600*

● Kägi MK, Wüthrich B (1993) **Falafel burger anaphylaxis due to sesame seed allergy** *Ann Allergy 71:127-9*

● Kanny G, De Hauteclocque C, Moneret-Vautrin DA (1996) **Sesame seed and sesame seed oil contain masked allergens of growing importance** *Allergy 51:952-7*

● Keating MU, Jones RT, Worley NJ, Shively CA, Yunginger JW (1990) **Immunoassay of peanut allergens in food-processing materials and finished foods** *J Allergy Clin Immunol 86:41-4*

● Kemp SF, Lockey RF, Wolf BL, Lieberman P (1995) **Anaphylaxis. A review of 266 cases** *Arch Intern Med 155:1749-54*

● Kleber-Janke T, Crameri R, Appenzeller U, Schlaak M, Becker WM (1999) **Selective cloning of peanut allergens, including profilin and 2S albumins, by phage display technology** *Int Arch Allergy Immunol 119:265-74*

● Kleber-Janke T, Crameri R, Scheurer S, Vieths S, Becker WM (2001) **Patient-tailored cloning of allergens by phage display: peanut** *(Arachis hypogaea)* **profilin, a food allergen derived from a rare mRNA** *J Chromatogr B 756:295-305*

● Kleine-Tebbe J, Vieths S, Franke S, Jahreis A, Rytter M, Haustein UF (2001) **Severe allergic reactions to a dietary procuct containing soy protein due to IgE-mediated cross-reactivity and hypersensitivity to Bet v 1** *Allergo J 10:154-9* (in German)

● Kolopp-Sarda MN, Moneret-Vautrin DA, Gobert B, Kanny G, Brodschii M, Bene MC, Faure GC (1997) **Specific humoral immune responses in 12 cases of food sensitization to sesame seed** *Clin Exp Allergy 27:1285-91*

● Koppelman SJ, Bruijnzeel-Koomen CA, Hessing M, de Jongh HH (1999a) **Heat- induced conformational changes of Ara h 1, a major peanut allergen, do not affect its allergenic properties** *J Biol Chem 274:4770-7*

● Koppelman SJ, Knulst AC, Koers WJ, Penninks AH, Peppelman H, Vlooswijk R, Pigmans I, van Duijn G, Hessing M (1999b) **Comparison of different immunochemical methods for the detection and quantification of hazelnut proteins in food products** *J Immunological Methods 229:107-20*

● Kull I, Hallner E, Lilja G, Ohman-Johansson AC, Oman H, Wickman M (1999) **Peanut oil in vitamin A and D**

preparations: reactions to skin test and manifestation of symptoms *Pediatr Allergy Immunol 10:21-6*

- Malanin K, Lundberg M, Johansson SG (1995) **Anaphylactic reaction caused by neoallergens in heated pecan nut** *Allergy 50:988-91.*
- Maleki SJ, Chung SY, Champagne ET, Raufman JP (2000) **The effects of roasting on the allergenic properties of peanut proteins** *J Allergy Clin Immunol 106:763-8*
- Malish D, Glovsky MM, Hoffman DR, Ghekiere L, Hawkins JM (1981) **Anaphylaxis after sesame seed ingestion** *J Allergy Clin Immunol 67:35-8*
- Malmheden Yman I, Eriksson A, Everitt G, Yman L, Karlsson T (1994) **Analysis of food proteins for verification of contamination or mislabelling** *Food Agric Immunol 6:167-72*
- McKenna C, Klontz KC (1997) **Systemic allergic reaction following ingestion of undeclared peanut flour in a peanut-sensitive woman** *Ann Allergy Asthma Immunol 79:234-6*
- Moneret-Vautrin DA (1998) **Modifications of allergenicity linked to food technologies** *Allerg Immunol (Paris) 30:9-13*
- Moneret-Vautrin DA, Hatahet R, Kanny G (1994) **Risks of milk formulas containing peanut oil contaminated with peanut allergens in infants with atopic dermatitis** *Pediatr Allergy Immunol 5:184-8*
- Moneret-Vautrin DA, Rance F, Kanny G, Olsewski A, Gueant JL, Dutau G, Guerin L (1998) **Food allergy to peanuts in France - evaluation of 142 observations** *Clin Exp Allergy 28:1113-9*
- Müller U, Weber W, Hoffmann A, Franke S, Lange R, Vieths S (1998) **Commercial soybean lecithins: a source of hidden allergens ?** *Z Lebensm Unters Forsch A 207:341-351*
- Müller U, Lüttkopf D, Hoffmann A, Petersen A, Becker WM, Schocker F, Niggemann B, Altmann F, Kolarich D, Haustein D, Vieths S (2000) **Allergens in raw and roasted hazelnuts (*Corylus avellana*) and their cross-reactivity to pollen** *Eur Food Res Technol 212(1):2-12*
- Nordlee JA, Taylor SL, Jones RT, Yunginger JW (1981) **Allergenicity of various peanut products as determined by RAST inhibition** *J Allergy Clin Immunol 68:376-82*
- Novembre E, Cianferoni A, Bernardini R, Mugnaini L, Caffarelli C, Cavagna G, Giovane A, Vierucci A (1998) **Anaphylaxis in children: clinical and allergological features** *Pediatrics 101(4):e8*
- Olszewski A, Pons L, Moutete F, Aimone-Gastin I, Kanny G, Moneret-Vautrin DA, Gueant JL (1998) **Isolation and characterization of proteic allergens in refined peanut oil** *Clin Exp Allergy 28:850-9*
- Ortolani C, Ballmer-Weber BK, Hansen KS, Ispano M, Wüthrich B, Bindslev-Jensen C, Ansaloni R, Vannucci L, Pravettoni V, Scibilia J, Poulsen LK, Pastorello EA (2000) **Hazelnut allergy: A double- blind, placebo- controlled food challenge multicenter study** *J Allergy Clin Immunol 105:577-81*
- Pajno GB, Passalacqua G, Magazzu G, Barberio G, Vita D, Canonica GW (2000) **Anaphylaxis to sesame** *Allergy 55:199-201*
- Palm M, Moneret-Vautrin DA, Kanny G, Denery-Papini S, Fremont S (1999) **Food allergy to egg and soy lecithins** *Allergy 54:1116-7*
- Paschke A, Zunker K, Wigotzki M, Steinhart H (2001) **Determination of the IgE-binding activity of soy lecithin and refined and non-refined soybean oils** *J Chromatogr B 756:249-54*
- Pastorello EA, Varin E, Farioli L, Pravettoni V, Ortolani C, Trambaioli C, Fortunato D, Giuffrida MG, Rivolta F, Robino A, Calamari AM, Lacava L, Conti A (2001) **The major allergen of sesame seeds (*Sesamum indicum*) is a 2S albumin** *J Chromatogr B 756:85-93*
- Pumphrey RS, Stanworth SJ (1996) **The clinical spectrum of anaphylaxis in north-west England** *Clin Exp Allergy 26:1364-70*
- Sampson HA, Mendelson L, Rosen JP (1992) **Fatal and near-fatal anaphylactic reactions to food in children and adolescents** *N Engl J Med 327:380-384*
- Schocker F, Luttkopf D, Muller U, Thomas P, Vieths S, Becker WM (2000) **IgE binding to unique hazelnut allergens: identification of non pollen-related and heat-stable hazelnut allergens eliciting severe allergic reactions** *Eur J Nutr 39(4):172-80*
- Senne GE, Crivellaro M, Bonadonna P, Dama A, Mezzelani P, Passalacqua G (1998) **Pizza; an unsuspected source of soybean allergen exposure** *Allergy 53(11):1106-1107*
- Shibasaki M, Suzuki S, Tajima S, Nemoto H, Kuruome T (1980) **Allergenicity of major component proteins of soybean** *Int Arch Appl Immunol 61:441-448*
- Sicherer SH, Furlong TJ, DeSimone J, Sampson HA (1999) **Self- reported allergic reactions to peanut on commercial airliners** *J Allergy Clin Immunol 104:186-9*
- Sicherer SH, Morrow EH, Sampson HA (2000) **Dose- response in double- blind, placebo- controlled oral food challenges in children with atopic dermatitis** *J Allergy Clin Immunol 105:582-6*
- Spergel JM, Beausoleil JL, Pawlowski NA (2000) **Resolution of childhood peanut allergy** *Ann Allergy Asthma Immunol 85:473-6*
- Stern A, Wüthrich B (1998) **Non-IgE-mediated anaphylaxis to sesame** *Allergy 53:325-6*

- Taylor SL, Busse WW, Sachs MI, Parker JL, Yunginger JW (1981) **Peanut oil is not allergenic to peanut- sensitive individuals** *J Allergy Clin Immunol 68:372-5*
- Teuber SS, Brown RL, Haapanen LA (1997) **Allergenicity of gourmet nut oils processed by different methods** *J Allergy Clin Immunol 99:502-7*
- Vadas P, Wai Y, Burks W, Perelman B (2001) **Detection of peanut allergens in breast milk of lactating women** *JAMA 285:1746-8*
- Vidal C, Perez-Carral C, Chomon B (1997) **Unsuspected sources of soybean exposure** *Ann Allergy Asthma Immunol 79(4):350-2*
- Vieths S, Zagon J, Fischer K, Dehne LI, Bögl KW (1995) **Verarbeitungsbedingte Einflüsse auf das allergene Potential von Lebensmitteln. Die Sojaallergie als Modellbeispiel** *Lebensmittelchemie 49:29-31* (in German)
- Vieths S, Reindl J, Müller U, Hoffmann A, Haustein D (1999) **Digestibility of peanut and hazelnut allergens investigated by a simple in vitro procedure** *Eur Food Res Technol 209:379-88*
- Weidmann B, Lepique C, Heider A, Schmitz A, Niederle N (1997) **Hypersensitivity reactions to parenteral lipid solutions** *Support Care Cancer 5(6):504-5*
- Wensing M, Koppelman SJ, Penninks AH, Bruijnzeel-Koomen CA, Knulst AC (2001) **Hidden hazelnut is a threat to allergic patients** *Allergy 56:191-2*
- Wigotzki M, Schubert S, Steinhart H, Paschke A (2000a) **Effects of in vitro digestion on the IgE-binding activity of proteins from hazelnuts** *(Corylus avellana) Internet Symposium on Food Allergens 2:1-8*
- Wigotzki M, Steinhart H, Paschke A (2000b) **Influence of varieties, storage and heat treatment on IgE-binding proteins in hazelnuts** *(Corylus avellana) Food Agric Immunol 12:217-29*
- Wigotzki M, Steinhart H, Paschke A (2001) **Determination of the allergenicity of various hazelnut products by immunoblotting and enzyme allergosorbent test inhibition** *J Chromatogr B 756:239-48*
- Yunginger JW, Sweeney KG, Sturner WQ, Giannandrea LA, Teigland JD, Bray M, Benson PA, York JA, Biedrzycki L, Squillace DL, et al (1988) **Fatal food- induced anaphylaxis** *JAMA 260:1450-2*
- Yunginger JW, Nelson DR, Squillace DL, Jones RT, Holley KE, Hyma BA, Biedrzycki L, Sweeney KG, Sturner WQ, Schwartz LB (1991) **Laboratory investigation of deaths due to anaphylaxis** *J Forensic Sci 36:857-65*

[Summary] [Abbreviations]