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Effects of daily food processing on allergenicity

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ABSTRACT

Daily food processing has the potential to alter the allergenicity of foods due to modification of the physico-chemical properties of proteins. The degree of such modifications depends on factors such as processing conditions, type of food considered, allergenic content, etc. The impact of daily food processing like boiling, roasting, frying or baking on food allergenicity have been extensively studied. The influence of other thermal treatments such as microwave heating or pressure cooking on allergenicity has also been analyzed. Non-thermal treatment such as peeling impacts on the allergenic content of certain foods such as fruits. In this review, we give an updated overview of the effects of daily processing treatments on the allergenicity of a wide variety of foods. The different variables that contribute to the modification of food allergenicity due to processing are also reviewed and discussed.

KEYWORDS

boiling; food allergy; food processing; IgE-reactivity; peanut allergy; roasting

Introduction

Foods can be subjected to different processing treatments to improve organoleptic properties according to culinary traditions or to make foods suitable for a determined way of consumption. Thermal processing methods such as boiling, frying or roasting are frequently applied to certain foods prior consumption, to improve suitability for specific applications. Baking, pressure cooking or microwave heating represent additional food processing methods (Verhoeckx et al., 2015). Non-thermal food processing such as peeling is applied to certain foods. Such processing methods may alter the biochemical characteristics of proteins or generate chemical reactions within the food matrix components. Importantly, food allergenicity can be variably affected by the type and conditions of the processing method applied, the specific chemical structure of a given protein or its allergenic features (Jimenez-Saiz et al., 2015). In addition, the allergenic pattern of sensitization of a specific study population of allergic patients is an important factor to consider while analyzing the effects of processing on food allergenicity (Maleki, 2004).

The many factors that can contribute to the impact of processing on the allergenicity of foods have generated a very active area of research. This review gives an overview of the effects of daily processing methods on the allergenicity of different foods with a focus on the different variables that may contribute to allergenic modification during food processing (Figure 1). Certain industrial treatments based on food processing methods under research and their impact on food allergenicity have been considered.

Food processing and allergenicity

Food processing has the potential to alter the allergenicity of foods in several ways. The degree of such modifications depends on

different factors such as the type of processing applied (i.e. thermal or non-thermal), the processing conditions, time, environment etc. The type of food, its structure and its allergenic content are also key factors that play an important role on the effects of food processing. In that regard, it has been found that some food allergens are labile to certain food processing methods. Most of the plant food allergens homolog to the major birch allergen Bet v 1 have been shown to be less resistant to thermal processing than other types of allergens. Bet v 1 homologs have the potential to unfold and to lose IgE-binding conformational epitopes upon specific thermal treatments (Mills et al., 2009; Sathe, Teuber, and Roux, 2005). Those IgE conformational epitopes comprise elements of native tertiary structure that have the potential to be lost after certain food processing (Mills and Mackie, 2008). Other allergens, however, have a high resistance to food processing. That is the case for allergens belonging to the prolamin superfamily, which includes 2S albumins such as Ara h 2 in peanut or Ana o 3 in cashew. Lipid transfer proteins (LTPs) belong to the prolamin superfamily, and are characterized by a high resistance to denaturation. The structure of those allergens is characterized by a conserved scaffold stabilized by a network of disulphide bonds necessary to keep the tridimensional protein structure. The compact structure of such allergens enriched in α -helices has been found to be key to keep their stability to processing as well as resistance to enzymatic degradation, variations in pH, etc (Mills et al., 2009).

At IgE epitopes level, theoretically, conformational epitopes are more labile to certain processing methods than linear epitopes. Conformational epitopes are associated to secondary protein structure and are more likely to be disrupted under harsh conditions of food processing or by enzymatic hydrolysis. Interestingly, several studies have demonstrated that food processing can act in a way that can mask or unmask determined

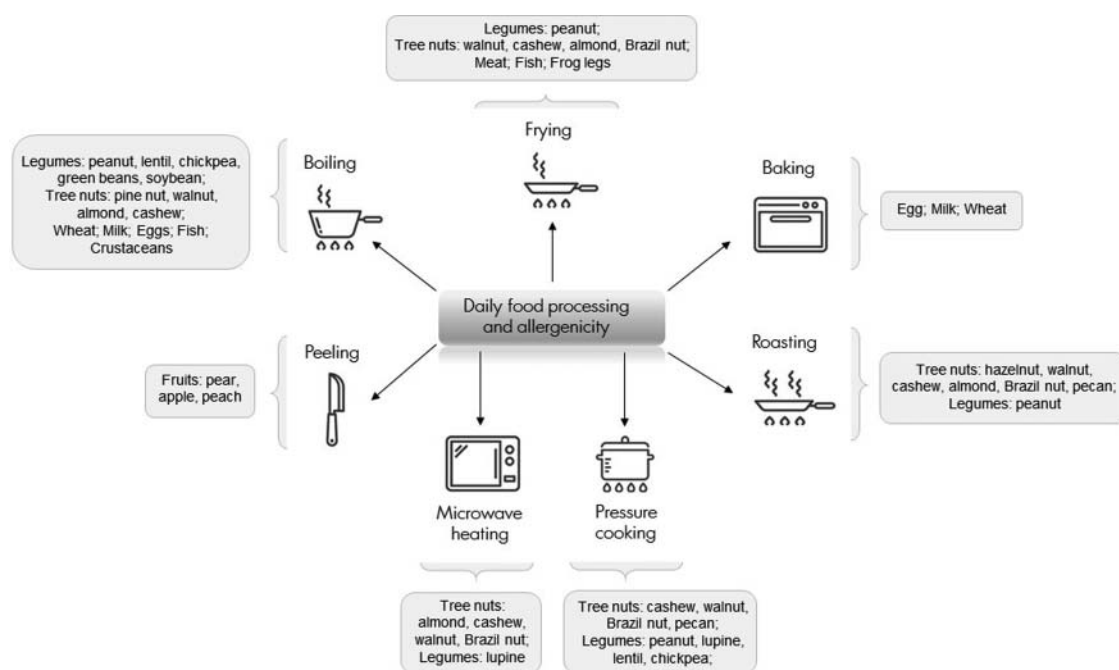


Figure 1. Overview of the types of daily food processing methods and foods included in this review.

IgE epitopes within the same allergen. Certain conditions of food processing have been shown to be able to expose portions of the amino acids sequence, previously buried, which can generate neoallergens, thus increasing the allergenicity of a given food. Therefore, the modifications that a given protein is subjected to during food processing can contribute not only to the disruption of certain IgE epitopes but also to their alteration, to mask, or unmask them, with a potential impact on the increase or decrease of allergenicity (Sathe, Teuber, and Roux, 2005; Mills and Mackie, 2008).

Food processing can also lead to a wide variety of biochemical reactions among the different components of foods. Foods are complex mixtures of proteins, sugars, fats, water, etc, and such biochemical reactions have the potential to modify the allergenicity of foods. One of these reactions is the Maillard reaction, which implicates modifications of amino groups of proteins by reducing sugars. The Maillard reaction has been found to play a key role for the increase of allergenicity of certain allergens in roasted peanut (Maleki, 2004).

Peeling and allergenicity

Certain fruits such as **peach, apple or pear** have shown to induce more frequent and severe allergic reactions in sensitized subjects when they are consumed with the peel. A study found that more than 40% of patients with allergy to pear and apple tolerated the pulp but reacted to the peel (Fernandez-Rivas and Cuevas, 1999). Another study evaluated the frequency of tolerance to the pulp of peach in children with a history of reactions after ingestion and/or contact with peach. In more than 90% of the subjects, pulp tolerance was confirmed (Boyano-Martinez et al., 2013). Peel and pulp composition in many fruits belonging to the *Rosaceae* family (to which the above-mentioned fruits belong) is different. Peel is rich in protein content and important allergens such as LTP are mainly located in this part

of the fruit. Ahrazem et al., (2007) found a 250-fold increase in the content of LTP from peach (Pru p 3) in peel compared with pulp, confirming previous studies (Carnes et al., 2002). Tissue localization of Pru p 3 by MALDI-MSI analysis indicated that this allergen is almost exclusively localized in the peel and external parts of the pulp in close contact with the peel (Cava-torta et al., 2009). Similar distribution was found for the LTP from apple Mal d 3 (Marzban et al., 2005). Therefore, it has been proposed that the mechanical or chemical (treatment with 10% NaOH at 70°C, during 30–60 s) peeling of these fruits can be a potential strategy to reduce the content of these specific allergens, with a potential benefit for subjects specifically sensitized to them (Brenna et al., 2004; Bernna et al., 2005; Primavesi et al., 2006).

Boiling and allergenicity

Boiling is used to process a wide variety of foods before consumption. Studies on the effects of boiling on allergenicity have been carried out in several foods such as legumes, nuts, wheat, eggs, milk, fish, or crustaceans (Figure 1, Table 1).

Legumes like **lentils, green beans, or chickpeas** are usually subjected to extensive boiling upon consumption. Several studies have shown that boiling treatment has little effect on allergens from lentils, chickpeas (Cuadrado et al., 2009; Martinez San Ireneo et al., 2000; Ibanez Sandin et al. 1999), green beans (Asero et al., 2001; Pastorello et al., 2010; Kasera et al., 2013) or peas (Sanchez Monge et al., 2004; Bogdanov et al., 2016). Even the inhalation of the boiling vapors of these legumes has been reported to be able to produce allergic reactions in sensitized patients (Vitaliti et al., 2012; Kalogeromitros et al., 1996; Pascual et al., 1999). Other legumes allergens such as **soybean** have also been found to be resistant to boiling, tested as whole protein extract (Son et al., 2000). However, when individual allergens from soybean were analyzed, more variable results

Table 1. Effects of boiling on IgE reactivity / antigenicity of specific food allergens sources.

Boiling				
	Allergen	Conditions	IgE reactivity / antigenicity*	Ref.
Peanut	Ara h 2, 6, 7	100°C, 6 h	↓	Turner et al. 2014
	Ara h 2	100°C, 15 min	↓	Zhang et al., 2016
	Ara h 1	100°C 15 min	↓	Blanc et al. 2011
	PE	100°C, 1 h	~↓	Cabanillas et al. 2012
Soybean	PE	100°C, 12 h	↓	Tao et al. 2016
	PE	—	=	Son et al. 2000
	Gly m Bd 30K (P34)	100°C, 1 h (in Tris-HCl)	↓	Wilson et al., 2008
	Gly m 7	—	=	Riascos et al. 2016
Lentil	PE	100°C, up to 1 h	= (~↓)	Cuadrado et al. 2009
Chickpea	PE	100°C, up to 1 h	= (~↓)	Cuadrado et al. 2009
Green bean	PE	100°C, 20 min	=	Asero et al. 2001
	LTP	100°C, 15 min	=	Pastorello et al. 2010
Pea	31 kDa allergen	100°C, up to 1 h	=	Kasera et al. 2013
	PE	30 min	=	Sanchez Monge et al. 2004
Pine nut	Pin p 1	100°C, 2 h	=	Cabanillas et al. 2016
Almond	PE	100°C, 5 and 10 min	=	Su et al. 2004
Cashew	Ana o 1, 2, 3	100°C, 10 min	~↓	Venkatachalam et al. 2008
Wheat	LTP	100°C, **	↓	Pastorello et al. 2007
	α-amylase/trypsin family and gliadins	100°C, **	=	Pastorello et al. 2007
	Tri a 36	10 min	=	Baar et al. 2012
Milk	PE	100°C, 2h	↓	Shandilya et al. 2013
Egg	PE	100°C (in water)	=	Liu et al. 2013
	PE	100°C (in tea solution)	↓	Liu et al. 2013
Fish (pilchard)	Parvalbumins	95°C, 20 min	= (~↓)	Kuehn et al. 2010
	PE	95°C, 20 min	↑	Van der Ventel et al. 2011
(pomfret)	PE	90°C, 10 min (in PBS)	↓	Chatterjee et al. 2006
(hilsa)	PE	90°C, 10 min (in PBS)	↓	Chatterjee et al. 2006
(mackerel)	PE	90°C, 10 min (in PBS)	=	Chatterjee et al. 2006
(bhetki)	PE	90°C, 10 min (in PBS)	= (~↑)	Chatterjee et al. 2006
Crustacean (shrimp)	Tropomyosin	10 min	~↑	Liu et al., 2010b
	Lit v 3	5 min	=	Ayuso et al. 2008
	PE	15 min (in PBS)	↑	Carnes et al 2007
(lobster)	PE	15 min (in PBS)	↑	Carnes et al 2007
(crab)	PE	20 min (in PBS)	↑	Abramovitch et al. 2013
(prawn)	PE	20 min (in PBS)	↑	Abramovitch et al. 2013

*IgE reactivity / antigenicity measured by different techniques and conditions (more detailed information in the text and in specific references). Legend: ↑; ↓; ~↑; ~↓, are a symbolic representation of the global effect of the specific treatment on IgE-reactivity / antigenicity of a given food (=, similar; ↑, increase; ↓, decrease; ~↑, slight increase; ~↓, slight decrease). PE: protein extract.

**time of boiling in this study was specified as: wheat flour was added to cold water, heated to reach boiling temperature and immediately removed from the heat.

were found. Wilson et al, found that the antigenicity of the soybean allergen Gly m Bd 30K (or P34) decreased with increased times of boiling (Wilson, Martinez-Villaluenga, and de Mejia, 2008). A recent study in which a new allergen from soybean was described (Gly m 7), found that this new allergen was resistant to boiling (Riascos et al., 2016).

Other legumes such as **peanuts** are consumed in boiled form only in some countries such as China, while roasting or frying are typical thermal treatments for peanuts in the U.S. or Europe. Interestingly, in spite of the fact that the consumption of peanut in China and the U.S. is similar, the prevalence of peanut allergy seems to be significantly higher in the U.S. than in China (Beyer et al., 2001). In contrast, the prevalence of peanut allergy in the Chinese-American population seems to be similar to the prevalence of the general U.S. population (Beyer et al., 2001). Therefore, differences in genetics of the populations seem not to be a key factor for the discrepancies in the prevalence of peanut allergy observed. Thus, it has been suggested that the method of processing of peanut may result in chemical and functional modifications in the peanut proteins with a direct impact on their allergenic properties.

Boiling processing of peanuts has caught attention over the years since studies carried out in 2001 showed that this processing method could modify the allergenicity of peanuts, by decreasing it (Beyer et al., 2001). In more recent years, several studies have tried to understand the effect of boiling on specific peanut allergens. Some of these studies have concluded that during boiling low molecular weight peanut allergens such as Ara h 2, Ara h 6, and Ara h 7 are transferred from the seed to cooking water, which can explain the decrease in content of these specific allergens in the seeds after boiling (Turner et al., 2014; Mondoulet et al., 2005). Other peanut allergens such as Ara h 1 seems to be also affected by boiling (Blanc et al., 2011). Mechanisms such as modification of the structure of allergens or even aggregation have been proposed to operate during boiling of peanuts (Comstock et al., 2016; Zhang et al., 2016). Extensive boiling up to 12 hours has been recently found to lead to a decrease of the IgE-binding capacity of peanut allergen, while their capability to stimulate T cells was retained (Tao et al., 2016).

Tree nuts are not commonly subjected to boiling, however, experimentally some studies have investigated the impact of

boiling on the IgE-binding resistance of purified allergens from certain tree nuts. For instance, the major pine nut allergens Pin p 1 (2S albumin from *Pinus pinea*) showed high resistance to boiling up to 2 hours (Cabanillas et al., 2016). Another allergen from pine nut, Pin k 2 (vicilin from *Pinus koraiensis*), also has been found to be highly resistant to thermal processing (Zhang et al., 2016). Another study showed that the antigenicity of walnut and almond proteins remained stable after boiling for 5 and 10 minutes (Su et al., 2004). In the same study, similar stability of the antigenicity of cashew proteins was found, however in another study that used specific antibodies against the main cashew allergens Ana o 1, Ana o 2, and Ana o 3, a decreased detection of those allergens could be found after boiling cashew for 10 minutes. Interestingly, authors found that the lower detection of the mentioned allergens was due to transfer of part of them to the cooking water (Venkatachalam et al., 2008).

Wheat. A study population of wheat allergic patients from Italy and Denmark had same symptoms with raw and cooked (boiled) wheat when double-blind placebo-controlled food challenges (DBPCFC) were performed (Scibilia et al., 2006). *In vitro*, the IgE-reactivity to the three Osborne protein fractions containing wheat allergens (albumin/globulin, gliadins and glutenins) was similar in cooked and raw wheat for most of the patients' sera. However, some differences could be found at the level of individual allergens. LTP from wheat showed a decreased IgE-binding capacity in heated wheat when some of the wheat allergic patients sera were tested. Other allergens such as the ones belonging to the α -amylase/trypsin family or gliadins maintained their IgE-reactive capacity after heating (Pastorello et al., 2007). Allergens from the glutenin fraction, such as Tri a 36, have been also shown to be resistant to boiling (Baar et al., 2012).

For **milk**, boiling for 2 hours decreased the intensity of the bands corresponding to whey proteins α -lactalbumin, β -lactoglobulin, and lactoferrin. Serum albumin had a higher resistance (Nowak-Węgrzyn and Fiocchi, 2009). In a mouse model of milk allergy, boiling and sterilization of cow and buffalo milk led to a decrease of allergenicity, measured as cell-mediated and humoral responses (Shandilya et al., 2013). However, baking at specific processing conditions, has been demonstrated to induce tolerance to baked products containing milk in clinical trials with milk allergic patients (Nowak-Węgrzyn et al., 2008).

Other foods such as **eggs** contain heat-resistant allergens such as ovomucoid and heat-labile allergens such as ovalbumin. A study in 2013 showed *in vitro* and in a mouse model of egg allergy that egg subjected to water boiling did not modify its allergenicity. However, a traditional Chinese boiling method (boiling in tea solution) was able to reduce partially the IgE-binding properties of specific egg allergens and allergic symptoms in egg sensitized mice (Liu et al., 2013). Another study focused on purified ovalbumin subjected to boiling for 10 minutes. Irreversible changes of the secondary protein structure could be found, those changes lead to activation of different T cell subpopulations with a shift to Th1 responses and reduction in allergenicity (Golias et al., 2012). However, as in the case of milk, another daily processing method of eggs (baking) has been demonstrated to be capable to induce tolerance in egg allergic patients (Lemon-Mule et al., 2008).

Fish. The effect of boiling on fish allergenicity has been shown to be species dependent and also dependent on the specific allergens to which fish allergic patients are sensitized (Chatterjee et al., 2006). The allergen parvalbumin is the major allergen in several fish species, being one of the most heat-resistant allergens, which also shows resistance to enzymatic digestion (Cai et al., 2010; Griesmeier et al., 2010; Liu et al., 2010a). Parvalbumins are localized in white muscles of lower vertebrates. Gal c 1 is the parvalbumin of codfish, one of the best studied fishes in relation to fish allergy (Tsabouri et al., 2012). Boiling has been found to have little effect on the extraction and serological detection of parvalbumin in several fish species (Kuehn et al., 2010). Using a mouse model of fish allergy, it was found that cooked fish (pilchard) extract induced higher levels of specific IgE than raw extract. Authors hypothesized that the effect could be due to an enrichment of parvalbumin, which was a major allergen in the protein remaining after cooking (van der Ventel et al., 2011). In spite of the high thermal resistance of fish allergens such as parvalbumin, other fish allergens have been described to be thermolabile. In a study of Indian fish species, it was found that allergens from two fish species (pomfret and hilsa) were sensitive to boiling, while two other species (mackerel and bhetki) showed allergenic resistance to the same thermal processing method (Chatterjee et al., 2006).

In the case of **crustacean**, such as shrimp, lobster, crab, prawn, or crawfish, the allergen tropomyosin has been found to be an important and highly resistant allergen to boiling. The IgE-binding capacity of tropomyosin purified from boiled shrimp was found to be even higher than tropomyosin isolated from raw shrimp (Liu et al., 2010b). Other major shrimp allergens such as the myosin light chain Lit v 3 has also shown high resistance to boiling (Ayuso et al., 2008). Using whole protein extracts from raw and boiled shrimps and two types of lobsters, it was found that the wheal sizes in SPT in allergic patients and their specific IgE levels were significantly higher for boiled than raw protein extracts (Carnes et al., 2007). Similar increase in IgE-reactivity was found in protein extracts from boiled crab and boiled prawn using ELISA, western blot and basophil activation test (Abramovitch et al., 2013). Table 1 summarizes the effects of boiling on IgE-reactivity / antigenicity of specific food allergen sources.

Baking and allergenicity

Baking treatment and its effects on allergenicity have caught attention due to studies that have shown that baked foods such as **eggs or milk** might be better tolerated by certain allergic patients. The high temperatures reached during baking and the interaction of allergens with food during the baking process, can reduce exposure of specific allergenic epitopes or generate chemical interactions of specific allergen with proteins in the food matrix. For those reasons, baking may have a higher impact on the modification of egg and milk allergy than boiling (Leonard et al., 2015). In clinical trials, it has been found that around 70% children allergic to milk or egg, were able to tolerate baked milk or egg and incorporate baked products into their diets. After 3 months of consuming baked milk or egg, increased levels of specific IgG4 antibodies against specific milk

or egg allergens and decreased skin prick test (SPT) wheals size were found (Lemon-Mulé et al., 2008; Nowak-Węgrzyn et al., 2008).

For **wheat**, the effects of baking on the allergenicity have been also analyzed. Previous studies showed that baking may induce a higher resistance to digestion of certain wheat allergens, keeping their immunological active form when they reach the gut mucosa. However, the effect of baking on other wheat allergens such as α -amylase inhibitors has been demonstrated to act in a way that decreases its IgE-binding capacity (Simonato et al., 2001). More recent studies have confirmed the decreased IgE-binding capacity of certain wheat allergens after baking (de Gregorio et al., 2009). Interestingly, the decrease in IgE-reactivity of certain wheat allergens after bake heating may explain why most of the patients suffering from bakers' asthma (which involves respiratory symptoms after exposure to raw wheat flour) can tolerate the ingestion of thermal processed foods based on wheat (Armentia et al., 2009; Simonato et al., 2001).

Frying and allergenicity

The effects of frying on allergy have been studied in foods derived from animal origin such as beef meat or fish and plant origin such as peanut or tree nuts (Figure 1, Table 2).

Concerning **beef meat**, frying seems to have certain impact on reducing the IgE-reactive capacity of beef proteins, however several α -Gal containing allergens could be still found after frying beef for 20 minutes when compared with the raw form (Apostolovic et al., 2014).

For **fish**, a study showed that the parvalbumin from carp resisted conditions of fish frying in oil at 180°C for a time of 8 minutes, detected by novel developed antibodies against parvalbumins (Bublin et al., 2015). In a study analyzing Indian fish species, the effect of frying over fish allergenicity was dependent on the fish species considered and the specific IgE sensitization of the fish allergic patients included in the study (Chatterjee et al., 2006). Fumes generated while frying fish have been demonstrated to have the potential to elicit allergic reactions in fish allergic patients

(Crespo et al., 1995). Therefore, the allergenicity of fish after frying seems to be persist, however frying can have a variable impact on allergenicity depending on the fish species and/or the allergic sensitization of a determined fish allergic patient.

The allergenicity of other foods from animal origin such as **frog legs** has been described to persist after frying, being able to produce severe allergic reactions as reported by Hilger et al., 2002. α -Parvalbumin was found to be the allergen involved in the described case of severe IgE-mediated anaphylaxis after the consumption of fried frog legs. Interestingly, the report was the first which implicates a key role of parvalbumin in allergic reactions outside fish species (Hilger et al., 2002).

In foods from plant origin, the effects of frying on allergenicity have been studied in **peanut** and **tree nuts** mainly. Conflicting results have been obtained when analyzing the allergenicity of fried peanut. Previous studies found that frying was able to decrease the IgE-reactivity of peanut proteins (Beyer et al., 2001), however later studies have not found major differences in the allergenicity of fried peanut when compared with raw peanut (Schmitt et al., 2010; Cabanillas et al., 2012; Verhoeckx et al., 2015). In the case of tree nuts such as cashew, almond, walnut or Brazil nut, the antigenicity of their proteins was found to remain stable after frying in vegetable oil at 191°C for 1 minute (Su et al., 2004; Sharma, Roux, and Sathe, 2009). Table 2 summarizes the effects of frying on IgE-reactivity / antigenicity of specific food allergen sources.

Roasting and allergenicity

Roasting is a thermal processing method that involves heating of foods under dry conditions in pans or roasters. Roasting can reach temperatures up to 200°C. Foods such as nuts and seeds are usually subjected to this thermal processing method (Figure 1, Table 3). In the case of **peanut**, this nut is normally consumed roasted in the U.S. or Europe. An extensive investigation on the effects of roasting on peanut allergenicity has been carried out in the last years, since it was suggested that roasting was able to increase the allergenicity of peanut (Maleki

Table 2. Effects of frying on IgE reactivity / antigenicity of specific food allergen sources.

Frying				
Allergen	Conditions	IgE reactivity / antigenicity*	Ref.	
Beef meat	α -Gal containing allergens	80°C, 20 min	$\sim\downarrow$	Apostolovic et al. 2014
Fish	Parvalbumin	180°C, 8 min	=	Bublin et al. 2015
(carp)	PE	Temperature N.I., 5 min	$\downarrow$	Chatterjee et al. 2006
(pomfret)	PE	Temperature N.I., 5 min	$\downarrow$	Chatterjee et al. 2006
(hilsa)	PE	Temperature N.I., 5 min	=	Chatterjee et al. 2006
(mackerel)	PE	Temperature N.I., 5 min	= ($\sim\uparrow$)	Chatterjee et al. 2006
(bhetki)	PE	Temperature N.I., 5 min	=	Hilger et al. 2002
Frog legs	Parvalbumin	N.I.	=	Beyer et al. 2001
Peanut	PE	5 or 10 min	$\downarrow$	Cabanillas et al. 2012
	PE	fried commercial brand	= ($\sim\downarrow$)	Schmitt et al. 2010
		160°C, 50 min	=	Su et al. 2004
Cashew	PE	191°C, 1 min	= ($\sim\downarrow$)	Su et al. 2004
Almond	PE	191°C, 1 min	=	Su et al. 2004
Walnut	PE	191°C, 1 min	= ($\sim\downarrow$)	Su et al. 2004
Brazil nut	PE	191°C, 2 min	=	Sharma, Roux, and Sathe 2009

*IgE reactivity / antigenicity measured by different techniques and conditions (more detailed information in the text and in specific references). Legend: $\uparrow$; $\downarrow$; $\sim\uparrow$; $\sim\downarrow$, are a symbolic representation of the global effect of the specific treatment on IgE-reactivity / antigenicity of a given food (=, similar; $\uparrow$, increase; $\downarrow$, decrease; $\sim\uparrow$, slight increase; $\sim\downarrow$, slight decrease). PE: protein extract. N.I.: Not indicated

Table 3. Effects of roasting on IgE reactivity / antigenicity of specific food allergen sources.

		Roasting		
Allergen	Conditions	IgE reactivity / antigenicity*		Ref.
Peanut	PE	roasted commercial brand	↑	Maleki et al. 2000
	PE	170°C, 20 min	↑	Beyer et al. 2001
	Ara h 1	roasted commercial brand	↑	Mondoulet et al. 2005
	Ara h 2	roasted commercial brand	↑	Mondoulet et al. 2005
	Ara h 2	—	↑	Kim et al. 2013
	Ara h 8	roasted commercial brand	↑	Petersen et al. 2014
Hazel nut	Oleosins	roasted commercial brand	↑	Schwager et al. 2017
	PE	140°C, 40 min	↓	Hansen et al. 2003
Walnut	PE	144°C, time N.I.	↓	Worm et al. 2009
	PE	160°C, 30 min and 177°C, 12 min	=	Su et al. 2004
Cashew	PE	180°C, 20 min	=	Downs et al. 2016b
	Ana o 1, 2, 3	200°C, 15 min	~↑	Venkatachalam et al. 2008
Almond	PE	180°C, 15 min	=	de Leon et al. 2003
	PE	160°C, 30 min; 177°C, 12 min	=	Su et al. 2004
Brazil nut	PE	180°C, 15 min	=	de Leon et al. 2003
	PE	Up to 160°C, 30 min; up to 177°C, 12 min	=	Sharma, Roux, and Sathe 2009
Pecan	PE	180°C, 15 min	=	de Leon et al. 2003
	PE	137°C, 30 min; 148°C, 30 min; 160°C, 30 min; 168°C, 12 min; 176°C, 12 min	=	Venkatachalam et al. 2006

*IgE reactivity / antigenicity measured by different techniques and conditions (more detailed information in the text and in specific references). Legend: ↑; ↓; ~↑; ~↓, are a symbolic representation of the global effect of the specific treatment on IgE-reactivity / antigenicity of a given food (=, similar; ↑, increase; ↓, decrease; ~↑, slight increase; ~↓, slight decrease). PE: protein extract. N.I.: Not indicated

et al., 2000; Beyer et al., 2001). At a molecular level, it has been demonstrated that allergens from roasted peanut have higher capacity to bind peanut-specific IgE from the sera of peanut allergic patients than raw, boiled or fried peanut (Maleki et al., 2000; Beyer et al., 2001; Mondoulet et al., 2005). The chemical reactions that occur during roasting seem to play a pivotal role in the increased capacity of peanut allergens to bind serum peanut-specific IgE. One of the reactions that has been implicated in the increase is the Maillard reaction. This reaction is a non-enzymatic chemical reaction that occurs during roasting that implies modifications of amino groups of proteins by reducing sugars that generate glycated proteins named advanced glycation end (AGE) adducts (Maleki et al., 2000). The high temperatures reached during roasting would facilitate the reaction. This chemical reaction has been shown to have the potential to increase the IgE-binding capacity of peanut allergens such as Ara h 1, Ara h 2 (Maleki et al., 2000; Kim et al., 2013). Recently a higher IgE-binding capacity of the peanut allergens oleosins has been described in roasted peanut (Schwager et al., 2017). Furthermore, roasting has the potential to increase the function of Ara h 2 as a trypsin inhibitor, which theoretically can protect itself and other peanut allergens from trypsin degradation (Maleki et al., 2000; Maleki et al., 2003). Higher resistance to gastric and pancreatic enzymes after roasting were also found in Ara h 8 (Petersen et al., 2014). The chemical reactions during roasting have been also found to be able to produce higher IgE crosslinking capacity of Ara h 1 and degranulation of effector cells of allergy (Vissers et al., 2011).

The above-mentioned studies have shown that roasted peanut allergens seem to have an increased capacity to bind pre-formed peanut-specific IgE, in the elicitation phase of the allergic response than other forms of peanut. However, less information is available regarding the role of the chemical modifications in roasted peanut allergens in the initial phase of allergy, named sensitization phase, where an immunological priming towards an allergic response takes part. Some studies

have found that allergens with glycosylated / carbohydrate structures can be recognized by dendritic cells (DCs) through specific type of receptors, increasing the allergen uptake by DCs, and T_H2 response induction (Hilmenyuk et al., 2010; Royer et al., 2010). The peanut allergen Ara h 1 is naturally glycosylated and can activate human monocyte-derived dendritic cells (MDDCs) through recognition by the C-type lectin receptor DC-SIGN to induce T_H2 differentiation. When Ara h 1 was chemically deglycosylated, however, the allergen lost its T_H2-skewing capacity (Shreffler et al., 2006). Recently, it was found that sensitization of peanut allergens by DCs may occur by interaction with the receptor for AGE (RAGE). The study showed that RAGE interacts with AGE-modified rAra h 1, but failed to bind rAra h 1 without AGE modifications (Mueller et al., 2013).

Interestingly in tree nuts such as **hazelnut**, the effect of roasting has been found to depend on the specific pattern of allergic sensitization of the patients. Two clinical studies involving patients from northern parts of Europe with birch pollen and hazelnut allergy found that roasting at 140°C decreased the allergenicity of hazelnut by challenging with DBPCFC. In both studies the elicited doses were higher for roasted hazelnut compared to the raw form. SPT and basophil activation and degranulation tests were reduced with roasted hazelnut (Hansen et al., 2003; Worm et al., 2009). The patients considered in both studies were allergic to birch pollen and their hazelnut allergy could be explained in a context of birch pollen-related hazelnut allergy. In fact, one of the studies found that all patients considered were sensitized to the hazelnut allergen Cor a 1.04 which is a homolog of the birch pollen allergen Bet v 1 (Hansen et al., 2003). It is known that Bet v 1 homologs have the common feature of being heat-labile. Therefore, roasting could have specifically decreased the IgE-binding and IgE-crosslinking properties of the hazelnut allergen to which this study populations from northern regions of Europe were mainly sensitized to (Cor a 1). But it could be different with other hazelnut allergens, since in

the study patients did not have specific IgE to the more heat-resistant hazelnut LTP allergen Cor a 8 (Hanzen et al. 2003). Therefore, the reduction of hazelnut allergenicity due to roasting in those study populations seem to be due to the specific pattern of sensitization to Bet v 1 homologs, which is characteristic for populations of North Europe. The effects of roasting on hazelnut allergenicity in other study populations with different allergenic sensitization patterns could have given different results. In fact, in a more recent study in which hazelnut allergy was analyzed in 3 different European regions (Denmark, Switzerland, and Spain), it was found that all Spanish patients considered reported symptoms to roasted hazelnut, which correlated to a pattern of sensitization to the hazelnut allergen Cor a 8, a heat-stable LTP. Spanish patients also had higher sensitization to Cor a 9 (a seed storage protein). However, only one third of the patients from Denmark and Switzerland reacted to roasted hazelnut and they had a predominance in sensitization to Cor a 1, homolog of Bet v 1 (Hansen et al., 2009). The resistance of Cor a 8 to different heat treatments such as roasting (at 140°C) has been demonstrated in other studies using sera from patients sensitized to this allergen (Pastorello et al., 2002).

In other tree nuts such as **walnut**, previous studies found that the antigenicity of walnut proteins remained stable to different conditions of roasting (Su et al., 2004). A recent study analyzed the effects of roasting on walnut at 132°C or 180°C for 5, 10, or 20 minutes using mass spectrometric analysis. Authors found that walnut allergens are affected differently by roasting. Proteins such as 2S albumin or LTP had little changes in their abundance after roasting, however the mature 7S globulin and 11S globulin was significantly higher detected after roasting at 180°C for 20 minutes (Downs et al., 2016a). Same authors observed a decrease in walnut protein solubility after dry roasting at 180°C, 20 minutes. However, both soluble and insoluble protein fractions showed similar pattern of IgE-reactivity using sera from walnut allergic patients (Downs, et al., 2016b).

For **cashew**, stability to roasting at 200°C for 15 minutes or even an increased allergen content was found by western blot

using antibodies against the main cashew allergens (Ana o 1, Ana o 2, and Ana o 3) or when samples were roasted at 180°C for 15 minutes (Venkatachalam et al., 2008; de Leon et al., 2003).

Other tree nuts such as **almond**, **pecan** or **Brazil nut** showed stability of antigenicity after roasting (Sharma, Roux, and Sathe, 2009; Venkatachalam et al., 2006; Su et al., 2004). The stability of the IgE-binding proteins from Brazil nut and almond were confirmed using sera from patients sensitized to tree nuts (de Leon et al., 2003). Table 3 summarizes the effects of roasting on IgE-reactivity / antigenicity of specific food allergen sources.

Pressure cooking and allergenicity

Pressure cooking involves a sealed pot with a valve for the control of the pressure inside. Domestic pressure cookers are designed to cook at a maximum operating pressure of around 1 atmosphere (atm) (equivalent to ~1 bar or ~15 psi), with a maximum cooking temperature of ~121°C. Several studies have analyzed the effect of pressure cooking on the allergenicity of foods. Some of those studies have focused on the operating conditions of domestic pressure cookers (Su et al., 2004; Venkatachalam et al., 2008; Sharma, Roux, and Sathe 2009), while others have investigated the effect of higher pressure and temperature only able to be reached with food grade tabletop autoclaves (Cabanillas et al., 2014; Cabanillas et al., 2015) (Figure 1, Table 4).

For **tree nuts** such as cashew, Venkatachalam et al., found that cashew allergens had high stability to a wide variety of treatments. Interestingly, although highly stable, cashew allergens Ana o 1, Ana o 2 and Ana o 3 seemed to be affected at some extent only by pressure cooking at 121°C, 15 psi for 20 minutes (Venkatachalam et al., 2008). The same treatment in combination with a pre-treatment of γ -irradiation had an impact on the decrease of cashew antigenicity (Su et al., 2004). For almond or Brazil nut, however, the antigenicity remained stable to such processing methods (Su et al., 2004; Venkatachalam et al., 2002; Sharma, Roux, and Sathe 2009). In the case of walnut or pecan, pressure cooking at 121°C, 15 psi for 30 minutes seemed to cause a decrease in antigen detection (Su

Table 4. Effects of pressure cooking on IgE reactivity / antigenicity of specific food allergen sources.

Pressure cooking				
	Allergen	Conditions	IgE reactivity / antigenicity*	Ref.
Cashew	Ana o 1, 2, 3	121°C, 15 psi, 30 min	↓	Venkatachalam et al. 2008
	PE	121°C, 15 psi, 30 min	↓	Su et al. 2004
Almond	PE	121°C, 15 psi, 30 min	=	Venkatachalam et al. 2002
	PE	121°C, 15 psi, 30 min	=	Su et al. 2004
Brazil nut	PE	121°C, 15 psi, 30 min	=	Su et al. 2004
	PE	121°C, 15 psi, 30 min	= (∼↓)	Sharma, Roux, and Sathe 2009
Pecan	PE	121°C, 15 psi, 30 min	∼↓	Venkatachalam et al. 2006
Walnut	PE and Jug r 4	138°C, 2.8 atm (37 psi), 15 and 30 min	↓	Cabanillas et al. 2014
Peanut	PE and Ara h 1, 2, 3, 6	138°C, 2.8 atm (37 psi), 15 and 30 min	↓	Cabanillas et al. 2012; 2015
Lupine	PE	138°C, 2.8 atm (37 psi), 15 and 30 min	↓	Alvarez-Alvarez et al. 2005
Lentil	PE	138°C, 2.8 atm (37 psi), 15 and 30 min	↓	Cuadrado et al. 2009
Chickpea	PE	138°C, 2.8 atm (37 psi), 15 and 30 min	↓	Cuadrado et al. 2009

*IgE reactivity / antigenicity measured by different techniques and conditions (more detailed information in the text and in specific references). Legend: ↑; ↓; ~↑; ~↓, are a symbolic representation of the global effect of the specific treatment on IgE-reactivity / antigenicity of a given food (=, similar; ↑, increase; ↓, decrease; ~↑, slight increase; ~↓, slight decrease). PE: protein extract.

et al., 2004; Venkatachalam et al., 2006). In another study performed in walnut, harsh conditions of pressure and temperature: autoclaving at 2.8 atm (37 psi), 138°C for 15 or 30 minutes, were found to lead to fragmentation of proteins that went along with a reduced IgE-binding and IgE crosslinking capacity. The results were confirmed by different *in vitro* and *in vivo* techniques (Cabanillas et al., 2014).

For **peanut** and other legumes such as **lupine**, **lentil** or **chickpea** similar effects of IgE-binding reduction were found when autoclaving conditions of 2.8 atm (37 psi), 138°C for 15 or 30 minutes were applied to these legumes (Cuadrado et al., 2009; Cabanillas et al., 2015; Alvarez-Alvarez et al., 2005). The combination of pressure and heat at specific conditions during autoclaving, has been found to lead to protein fragmentation that seems to resemble the effects of certain enzymes on protein extracts (Kulis et al., 2012). Interestingly, other food treatments that involve high pressure and low temperature did not have the same effect as autoclave conditions (Cabanillas et al., 2014; Husband et al., 2011). Therefore, the combination of heat and pressure during autoclaving seems to be key for protein degradation and potential decrease in IgE-reactivity. For the mentioned decrease, a potential loss of protein solubility can be the responsible for the decrease of IgE-reactivity of those foods. However, recent studies have demonstrated that extensive protein solubilization of the pressure/heat-treated food material renders the same profile of protein degradation with a decreased capacity to bind IgE from allergic patients' sera (Cabanillas et al., 2015). Table 4 summarizes the effects of pressure cooking on IgE-reactivity / antigenicity of specific food allergen sources.

Microwave heating and allergenicity

Heating through microwaves ovens is reached after interaction of microwaves and the medium by volumetric dissipation of electromagnetic energy in form of heat. Microwaves travel through the lossy medium producing an increase of the medium temperature. This heating property has made microwave ovens to be widespread used around the world for home food thermal processing (Feng, Yin, and Tang, 2012). Microwaves have the potential to alter the native structure of proteins and therefore might potentially have an impact on the ability of certain proteins to be recognized by IgE of sensitized subjects (Jimenez-Saiz et al., 2015). Several studies have analyzed the

capacity of microwave ovens to modify the allergenicity of certain foods (Figure 1, Table 5). **Lupines** subjected to microwave heating for 30 min at 750 and 900 W in water were found to present minimal changes in the IgE-binding profile of lupine proteins (Alvarez-Alvarez et al., 2005). In other foods such as **wheat**, microwave heating at 70, 200, and 500 W up to 5 minutes, did not decrease the IgE-reactivity of wheat gliadin (Leszczynska et al., 2003). In **tree nuts** such as almond, cashew or walnut, the protein profile and antigenicity of certain proteins remained stable after several thermal processing treatments including microwave heating at 500 W for 1 or 3 minutes (Su et al., 2004) confirming previous results for almond (Venkatachalam et al., 2002). The stability to microwave heating of cashew allergens to even more strong conditions (1000 W for 2 minutes) was further demonstrated using monoclonal antibodies against main cashew allergens Ana o 1, Ana o 2, and Ana o 3 (Venkatachalam et al., 2008). Other tree nuts such as Brazil nut has also shown immunogenic stability to microwave heating (Sharma, Roux, and Sathe, 2009). Table 5 summarizes the effects of microwave heating on IgE-reactivity / antigenicity of specific food allergen sources.

Discussion and conclusion

Daily processing has the potential to modify the allergenicity of foods due to numerous physico-chemical modifications that may be induced during processing in the complex matrixes that constitute foods. The extent of such modifications and its impact on allergenicity depends on factors such as type, conditions, and time of the processing method applied or the physical, chemical, and allergenic properties of the food itself.

In the present article, we have reviewed the effects of daily processing methods on the allergenicity of several foods. Some processing methods have a direct impact on the allergenic properties of certain foods, while others have been found to have little or no effect on food allergenicity (Figure 2). Non-thermal processing such as peeling seems to be effective in decreasing the content of specific allergens such as LTP in certain fruits belonging to the *Rosaceae* family (Bernna et al., 2005; Primavesi et al., 2006). This effect may constitute a benefit in the future for subjects with specific sensitization to LTP from *Rosaceae* family fruits. Daily processing of boiling has been found to potentially decrease the content of peanut

Table 5. Effects of microwave heating on IgE reactivity / antigenicity of specific food allergen sources.

Microwave heating				
	Allergen	Conditions	IgE reactivity / antigenicity*	Ref.
Cashew	Ana o 1, 2, 3	1000 W, 2 min	=	Venkatachalam et al. 2008
	PE	500 W, 3 min	=	Su et al. 2004
Almond	PE	500 W, 3 min	=	Su et al. 2004
	PE	50% power, 3 min	=	Venkatachalam et al. 2002
Walnut	PE	500 W, 3 min	=	Su et al. 2004
Brazil nut	PE	500 W, 3 min	=	Sharma, Roux, and Sathe 2009
Lupine	PE	900 W, 30 min	=	Alvarez-Alvarez et al. 2005
Wheat	Gliadin	500 W, 5 min	=	Leszczynska et al. 2003

*IgE reactivity / antigenicity measured by different techniques and conditions (more detailed information in the text and in specific references). Characters: = ; ↑; ↓; ~↑; ~↓, are a symbolic representation of the global effect of the specific treatment on the IgE-reactivity / antigenicity of a given food (= , similar; ↑, increase; ↓, decrease; ~↑, slight increase; ~↓, slight decrease). PE: protein extract.

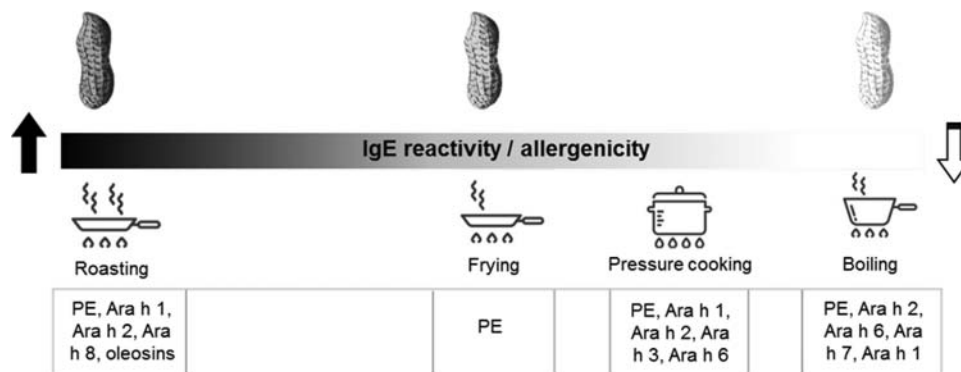


Figure 2. Schematic representation of the effects of different daily processing treatments on the allergenicity of peanut.

allergens Ara h 2, Ara h 6, and Ara h 7, due to transfer of those allergens to the cooking water (Turner et al., 2014; Mondoulet et al., 2005) (Figure 2). Baking of eggs or milk has been also found to alter the allergenic potential of those foods, by decreasing it (Lemon-Mulé et al., 2008; Nowak-Węgrzyn et al., 2008). However, other treatments, such as roasting has the ability to chemically modify certain allergens from peanut in the way that they can bind increased levels of specific IgE from allergic subjects (Maleki et al., 2000; Petersen et al., 2014) (Figure 2). On the other hand, processing treatments such as microwave heating has been found to have little effect on food allergenicity. The effects frying or pressure cooking on food allergenicity are variable and need further research.

Most studies evaluated the capacity of processed foods to bind specific IgE from allergic patients, through *in vitro* methods such as IgE-western blot or IgE-ELISA. However, there is an increased necessity for more physiologically relevant assays, since alterations in the IgE-binding properties of processed food proteins not always correlate with alteration in allergenicity. Assays, such as basophil activation tests or SPT, in which the IgE-cross linking capacity of processed food allergens are analyzed, are closer to the real effect that processing may produce in food allergenicity. In addition, clinical trials in which DBPCFC (the gold standard for food allergy diagnosis) are performed would give the definitive answer of the potential of a processing method to alter the allergenicity of a specific food.

Importantly, the study of the effects of processing on food allergenicity has been mainly focused in the evaluation of processed allergens to bind preformed IgE from allergic patients (Verhoeckx et al., 2015). However, the potential of processed foods to modify the immunological priming towards an allergic response, which takes place in the sensitization phase of allergy, has caught less attention and has been evaluated only in recent years (Hilmenyuk et al., 2010; Mueller et al., 2013). The potential alterations of processing in the chemical composition of certain food proteins, may increase the recognition of such proteins by DC through specific receptors, increasing uptake and potentially leading to a T_H2 response. More studies would be necessary in the future to evaluate the effects of processing in the sensitization phase of allergy.

Finally, food processing research would benefit from a higher standardization of the experimental conditions and

methods used to evaluate their impact on allergenicity. This review has highlighted the highly variable experimental conditions applied for a given processing treatment. The variances make it sometimes difficult to compare studies and to draw conclusions. Studies that aim to assess the effect of daily food processing on allergenicity should experimentally analyze conditions that ideally resembles the ones used for a given method in daily life. If the aim is to assess experimental conditions beyond the ones used in daily life, more variability may be expected. However, the field of research of food processing and allergenicity would benefit from a higher experimental standardization.

Overall, this review has shown that several complex factors impact on the alteration of the allergenicity of foods due to daily food processing. That complexity requires a careful evaluation of the experimental conditions of the processing method applied, the analysis of the physico-chemical and allergenic properties of the food under study, and a careful characterization of the allergic study populations used. Some daily processing methods have been shown to be effective in decreasing the content of specific allergens in certain foods, which may open a future path for hypoallergenic food development or pave the way the use of specifically processed foods for tolerance induction. Other treatments, however, have the capacity to increase the allergenicity of certain foods. Future research will hopefully increase our knowledge about the effects of processing on the properties of allergenic food sources.

Conflict of interests

Authors declare no conflict of interest.

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References

- Abramovitch, J. B., S. Kamath, N. Varese, C. Zubrinich, A. L. Lopata, R. E. O'Hehir, and J. M. Rolland. 2013. IgE reactivity of blue swimmer crab (*Portunus pelagicus*) Tropomyosin, Por p 1, and other allergens; cross-reactivity with black tiger prawn and effects of heating. *PLoS One* 8: e67487.
- Ahrazem, O., L. Jimeno, G. López-Torrejón, M. Herrero, J. L. Espada, R. Sánchez-Monge, O. Duffort, D. Barber, and G. Salcedo. 2007. Assessing allergen levels in peach and nectarine cultivars. *Annals of Allergy, Asthma & Immunology* 99:42–47.
- Alvarez-Alvarez, J., E. Guillamón, J. F. Crespo, C. Cuadrado, C. Burbano, J. Rodríguez, C. Fernández, and M. Muzquiz. 2005. Effects of extrusion, boiling, autoclaving, and microwave heating on lupine allergenicity. *Journal of Agricultural and Food Chemistry* 53:1294–98.
- Apostolovic, D., T. A. Tran, C. Hamsten, M. Starkhammar, T. Cirkovic Velickovic, and M. van Hage. 2014. Immunoproteomics of processed beef proteins reveal novel galactose- α -1,3-galactose-containing allergens. *Allergy* 69:1308–15.
- Armentia, A., A. Díaz-Perales, J. Castrodeza, A. Dueñas-Laita, A. Palacin, and S. Fernández. 2009. Why can patients with baker's asthma tolerate wheat flour ingestion? Is wheat pollen allergy relevant? *Allergol. Immunopathol. (Madr)* 37:203–04.
- Asero, R., G. Mistrello, D. Roncarolo, S. Amato, and R. van Ree. 2001. String bean-induced anaphylaxis. *Allergy* 56:259–60.
- Ayuso, R., G. Grishina, L. Bardina, T. Carrillo, C. Blanco, M. D. Ibáñez, H. A. Sampson, and K. Beyer. 2008. Myosin light chain is a novel shrimp allergen, Lit v 3. *Journal of Allergy and Clinical Immunology* 122:795–802.
- Baar, A., S. Pahr, C. Constantin, S. Scheibhofer, J. Thalhamer, S. Papadopoulos, N. G. Giavi, C. Ebner, A. Mari, S. Vrtala, and R. Valenta. 2012. Molecular and immunological characterization of Tri a 36, a low molecular weight glutenin, as a novel major wheat food allergen. *The Journal of Immunology* 189:3018–25.
- Bernna, O. V., C. Pomei, V. Pravettoni, L. Farioli, and E. A. Pastorello. 2005. Production of hypoallergenic foods from apricots. *Journal of food science* 70:S38–41.
- Beyer, K., E. Morrowa, X. M. Li, L. Bardina, G. A. Bannon, A. W. Burks, and H. A. Sampson. 2001. Effects of cooking methods on peanut allergenicity. *Journal of Allergy and Clinical Immunology* 107:1077–81.
- Blanc, F., Y. M. Vissers, K. Adel-Patient, N. M. Rigby, A. R. Mackie, A. P. Gunning, N. K. Wellner, P. S. Skov, L. Przybylski-Nicaise, B. Ballmer-Weber, L. Zuidmeer-Jongejan, Z. Szépfalusi, J. Ruinemans-Koerts, A. P. Jansen, H. Bernard, J. M. Wal, H. F. Savelkoul, H. J. Wichers, and E. N. Mills. 2011. Boiling peanut Ara h 1 results in the formation of aggregates with reduced allergenicity. *Molecular Nutrition & Food Research* 55:1887–94.
- Bogdanov, I. V., Z. O. Shenkarev, E. I. Finkina, D. N. Melnikova, E. I. Rumynskiy, A. S. Arseniev, and T. V. Ovchinnikova. 2016. A novel lipid transfer protein from the pea *Pisum sativum*: Isolation, recombinant expression, solution structure, antifungal activity, lipid binding, and allergenic properties. *BMC Plant Biology* 16:107.
- Boyano-Martínez, T., M. Pedrosa, T. Belver, S. Quirce, and C. García-Ara. 2013. Peach allergy in Spanish children: Tolerance to the pulp and molecular sensitization profile. *Pediatric Allergy and Immunology* 24:168–72.
- Brenna, O. V., E. A. Pastorello, L. Farioli, V. Pravettoni, and C. Pompei. 2004. Presence of allergenic proteins in different peach (*Prunus persica*) cultivars and dependence of their content on fruit ripening. *Journal of Agricultural and Food Chemistry* 52:7997–8000.
- Bublin, M., M. Kostadinova, J. E. Fuchs, D. Ackerbauer, A. H. Moraes, F. C. Almeida, N. Lengger, C. Hafner, C. Ebner, C. Radauer, K. R. Liedl, A. P. Valente, and H. Breiteneder. 2015. A cross-reactive human single-chain antibody for detection of major fish allergens, parvalbumins and identification of a major IgE-binding epitope. *PLoS One* 10: e0142625.
- Cabanillas, B., J. F. Crespo, S. J. Maleki, J. Rodríguez, and N. Novak. 2016. Pin p 1 is a major allergen in pine nut and the first food allergen described in the plant group of gymnosperms. *Food Chemistry* 210:70–77.
- Cabanillas, B., C. Cuadrado, J. Rodríguez, J. Hart, C. Burbano, J. F. Crespo, and N. Novak. 2015. Potential changes in the allergenicity of three forms of peanut after thermal processing. *Food Chemistry* 183:18–25.
- Cabanillas, B., S. J. Maleki, J. Rodríguez, H. Cheng, S. S. Teuber, M. L. Wallowitz, M. Muzquiz, M. M. Pedrosa, R. Linacero, C. Burbano, N. Novak, C. Cuadrado, and J. F. Crespo. 2014. Allergenic properties and differential response of walnut subjected to processing treatments. *Food Chemistry* 157:141–47.
- Cabanillas, B., S. J. Maleki, J. Rodríguez, C. Burbano, M. Muzquiz, M. A. Jiménez, M. M. Pedrosa, C. Cuadrado, and J. F. Crespo. 2012. Heat and pressure treatments effects on peanut allergenicity. *Food Chemistry* 132:360–66.
- Cai, Q. F., G. M. Liu, T. Li, K. Hara, X. C. Wang, W. J. Su, and M. J. Cao. 2010. Purification and characterization of parvalbumins, the major allergens in red stingray (*Dasyatis akajei*). *Food Chemistry* 122:64–69.
- Carnes, J., E. Fernandez-Caldas, M. T. Gallego, A. Ferrer, and J. Cuesta-Herranz. 2002. Pru p 3 (LTP) content in peach extracts. *Allergy* 57:1071–75.
- Carnés, J., A. Ferrer, A. J. Huertas, C. Andreu, C. H. Larramendi, and E. Fernández-Caldas. 2007. The use of raw or boiled crustacean extracts for the diagnosis of seafood allergic individuals. *Annals of Allergy, Asthma & Immunology* 98:349–54.
- Cavatorta, V., S. Sforza, G. Mastrobuoni, G. Pieraccini, S. Francese, G. Moneti, A. Dossena, E. A. Pastorello, and R. Marchelli. 2009. Unambiguous characterization and tissue localization of Pru P 3 peach allergen by electrospray mass spectrometry and MALDI imaging. *Journal of Mass Spectrometry* 44:891–97.
- Chatterjee, U., G. Mondal, P. Chakraborti, H. K. Patra, and B. P. Chatterjee. 2006. Changes in the allergenicity during different preparations of pomfret, hilsa, bhetki and mackerel fish as illustrated by enzyme-linked immunosorbent assay and immunoblotting. *International Archives of Allergy and Immunology* 141:1–10.
- Comstock, S. S., S. J. Malekik, and S. S. Teuber. 2016. Boiling and frying peanuts decreases soluble peanut (*arachis hypogaea*) allergens Ara h 1 and Ara h 2 but does not generate hypoallergenic peanuts. *PLoS One* 11:e0157849.
- Crespo, J. F., C. Pascual, C. Dominguez, I. Ojeda, F. M. Muñoz, and M. M. Esteban. 1995. Allergic reactions associated with airborne fish particles in IgE-mediated fish hypersensitive patients. *Allergy* 50:257–61.
- Cuadrado, C., B. Cabanillas, M. M. Pedrosa, A. Varela, E. Guillamón, M. Muzquiz, J. F. Crespo, J. Rodríguez, and C. Burbano. 2009. Influence of thermal processing on IgE reactivity to lentil and chickpea proteins. *Molecular Nutrition & Food Research* 53:1462–68.
- de Gregorio, M., A. Armentia, A. Díaz-Perales, A. Palacín, A. Dueñas-Laita, B. Martín, G. Salcedo, and R. Sánchez-Monge. 2009. Salt-soluble proteins from wheat-derived foodstuffs show lower allergenic potency than those from raw flour. *Journal of Agricultural and Food Chemistry* 57:3325–30.
- de Leon, M. P., I. N. Glaspole, A. C. Drew, J. M. Rolland, R. E. O'Hehir, and C. Suphioglu. 2003. Immunological analysis of allergenic cross-reactivity between peanut and tree nuts. *Clinical & Experimental Allergy* 33:1273–80.
- Downs, M. L., J. L. Baumert, S. L. Taylor, and E. N. Mills. 2016a. Mass spectrometric analysis of allergens in roasted walnuts. *Journal of Proteomics* 142:62–69.
- Downs, M. L., A. Simpson, A. Custovic, A. Semic-Jusufagic, J. Bartra, M. Fernandez-Rivas, S. L. Taylor, J. L. Baumert, and E. N. Mills. 2016b. Insoluble and soluble roasted walnut proteins retain antibody reactivity. *Food Chemistry* 194:1013–21.
- Feng, H., Y. Yin, and J. Tang. 2012. Microwave drying of food and agricultural materials: Basics and heat and mass transfer modeling. *Food Engineering Reviews* 4:89–106.
- Fernandez-Rivas, M., and M. Cuevas. 1999. Peels of Rosaceae fruits have a higher allergenicity than pulps. *Clinical & Experimental Allergy* 29:1239–47.
- Golias, J., M. Schwarzer, M. Wallner, M. Kverka, H. Kozakova, D. Srutkova, K. Klimesova, P. Sotkovsky, L. Palova-Jelinkova, F. Ferreira, and L. Tuckova. 2012. Heat-induced structural changes affect OVA-antigen

- processing and reduce allergic response in mouse model of food allergy. *PLoS One* 7:e37156.
- Griesmeier, U., M. Bublin, C. Radauer, S. Vázquez-Cortés, Y. Ma, M. Fernández-Rivas, and H. Breiteneder. 2010. Physicochemical properties and thermal stability of Lep w 1, the major allergen of whiff. *Molecular Nutrition & Food Research* 54:861–69.
- Hansen, K. S., B. K. Ballmer-Weber, D. Lüttkopf, P. S. Skov, B. Wüthrich, C. Bindslev-Jensen, S. Vieths, and L. K. Poulsen. 2003. Roasted hazelnuts—allergenic activity evaluated by double-blind, placebo-controlled food challenge. *Allergy* 58:132–38.
- Hansen, K. S., B. K. Ballmer-Weber, J. Sastre, J. Lidholm, K. Andersson, H. Oberhofer, M. Lluch-Bernal, J. Ostling, L. Mattsson, F. Schocker, S. Vieths, and L. K. Poulsen. 2009. Component-resolved in vitro diagnosis of hazelnut allergy in Europe. *Journal of Allergy and Clinical Immunology* 123:1134–41.
- Hilger, C., F. Grigioni, L. Thill, L. Mertens, and F. Hentges. 2002. Severe IgE-mediated anaphylaxis following consumption of fried frog legs: Definition of alpha-parvalbumin as the allergen in cause. *Allergy* 57:1053–58.
- Hilmenyuk, T., I. Bellinghausen, B. Heydenreich, A. Ilchmann, M. Toda, S. Grabbe, and J. Saloga. 2010. Effects of glycation of the model food allergen ovalbumin on antigen uptake and presentation by human dendritic cells. *Immunology* 129:437–45.
- Husband, F. A., T. Aldick, I. Van der Plancken, T. Grauwet, M. Hendrickx, I. Skypala, and A. R. Mackie. 2011. High-pressure treatment reduces the immunoreactivity of the major allergens in apple and celeriac. *Molecular Nutrition & Food Research* 55:1087–95.
- Ibanez Sandin, D., M. Martinez San Ireneo, E. Alonso Lebrero, T. Laso Borrego, F. Marañón Lizana, and E. Fernández-Caldas. 1999. Specific IgE determinations to crude and boiled lentil (*Lens culinaris*) extracts in lentil-sensitive children and controls. *Allergy* 54:1209–14.
- Jiménez-Saiz, R., S. Benedé, E. Molina, and I. López-Expósito. 2015. Effect of processing technologies on the allergenicity of food products. *Critical reviews in food science and nutrition* 55:1902–17.
- Kalogeromitros, D., M. Armenaka, I. Galatas, O. Capellou, and A. Katsarou. 1996. Anaphylaxis induced by lentils. *Annals of Allergy, Asthma & Immunology* 77:480–82.
- Kasera, R., A. B. Singh, S. Lavasa, K. Nagendra, and N. Arora. 2013. Purification and immunobiochemical characterization of a 31 kDa cross-reactive allergen from *Phaseolus vulgaris* (kidney bean). *PLoS One* 8: e63063.
- Kim, J., J. Y. Lee, Y. Han, and K. Ahn. 2013. Significance of Ara h 2 in clinical reactivity and effect of cooking methods on allergenicity. *Annals of Allergy, Asthma & Immunology* 110:34–38.
- Kuehn, A., T. Scheuermann, C. Hilger, and F. Hentges. 2010. Important variations in parvalbumin content in common fish species: A factor possibly contributing to variable allergenicity. *International Archives of Allergy and Immunology* 153:359–66.
- Kulis, M., I. Macqueen, Y. Li, R. Guo, X. P. Zhong, and A. W. Burks. 2012. Pepsinized cashew proteins are hypoallergenic and immunogenic and provide effective immunotherapy in mice with cashew allergy. *Journal of Allergy and Clinical Immunology* 130:716–23.
- Lemon-Mulé, H., H. A. Sampson, S. H. Sicherer, W. G. Shreffler, S. Noone, and A. Nowak-Węgrzyn. 2008. Immunologic changes in children with egg allergy ingesting extensively heated egg. *Journal of Allergy and Clinical Immunology* 122:977–83.
- Leonard, S. A., J. C. Caubet, J. S. Kim, M. Groetch, and A. Nowak-Węgrzyn. 2015. Baked milk- and egg-containing diet in the management of milk and egg allergy. *Journal of Allergy and Clinical Immunology Pract* 3:13–23.
- Leszczynska, J., A. Łacka, J. Szmraj, J. Lukamowicz, and H. Zegota. 2003. The effect of microwave treatment on the immunoreactivity of gliadin and wheat flour. *European Food Research and Technology* 217:387–91.
- Liu, G. M., N. Wang, Q. F. Cai, T. Li, L. C. Sun, W. J. Su, and M. J. Cao. 2010a. Purification and characterization of parvalbumins from silver carp (*Hypophthalmichthys molitrix*). *Journal of the Science of Food and Agriculture* 90:1034–40.
- Liu, G. M., H. Cheng, J. B. Nesbit, W. J. Su, M. J. Cao, and S. J. Maleki. 2010b. Effects of boiling on the IgE-binding properties of tropomyosin of shrimp (*Litopenaeus vannamei*). *Journal of Food Science* 75:T1–5.
- Liu, X., B. S. Feng, X. Kong, H. Xu, X. Li, P. C. Yang, and Z. Liu. 2013. Food-cooking processes modulate allergenic properties of hen's egg white proteins. *International Archives of Allergy and Immunology* 160:134–42.
- Maleki, S. J. 2004. Food processing: Effects on allergenicity. *Current Opinion in Allergy and Clinical Immunology* 4:241–45.
- Maleki, S. J., S. Y. Chung, E. T. Champagne, and J. P. Raufman. 2000. The effects of roasting on the allergenic properties of peanut proteins. *Journal of Allergy and Clinical Immunology* 106:763–68.
- Maleki, S. J., O. Viquez, T. Jacks, H. Dodo, E. T. Champagne, S. Y. Chung, and S. J. Landry. 2003. The major peanut allergen, Ara h 2, functions as a trypsin inhibitor, and roasting enhances this function. *Journal of Allergy and Clinical Immunology* 112:190–95.
- Martinez San Ireneo, M., M. D. Ibáñez Sandín, E. Fernández-Caldas, F. Marañón Lizana, M. J. Rosales Fletes, and M. T. Laso Borrego. 2000. Specific IgE levels to *Cicer arietinum* (Chick pea) in tolerant and non-tolerant children: Evaluation of boiled and raw extracts. *International Archives of Allergy and Immunology* 121:137–43.
- Marzban, G., H. Puehringer, R. Dey, S. Brynda, Y. Ma, A. Martinelli, and F. Altmann. 2005. Localisation and distribution of the major allergens in apple fruits. *Plant Science* 169:387–94.
- Mills, E. N., and A. R. Mackie. 2008. The impact of processing on allergenicity of food. *Current Opinion in Allergy and Clinical Immunology* 8:249–53.
- Mills, E. N., A. I. Sancho, N. M. Rigby, J. A. Jenkins, and A. R. Mackie. 2009. Impact of food processing on the structural and allergenic properties of food allergens. *Molecular Nutrition & Food Research* 53:963–69.
- Mondoulet, L., E. Paty, M. F. Drumare, S. Ah-Leung, P. Scheinmann, R. M. Willemot, J. M. Wal, and H. Bernard. 2005. Influence of thermal processing on the allergenicity of peanut proteins. *Journal of Agricultural and Food Chemistry* 53:4547–53.
- Mueller, G. A., S. J. Maleki, K. Johnson, B. K. Hurlburt, H. Cheng, S. Ruan, J. B. Nesbit, A. Pomés, L. L. Edwards, A. Schorzman, L. J. Deterding, H. Park, K. B. Tomer, R. E. London, and J. G. Williams. 2013. Identification of Maillard reaction products on peanut allergens that influence binding to the receptor for advanced glycation end products. *Allergy* 68:1546–54.
- Nowak-Węgrzyn, A., K. A. Bloom, S. H. Sicherer, W. G. Shreffler, S. Noone, N. Wanich, and H. A. Sampson. 2008. Tolerance to extensively heated milk in children with cow's milk allergy. *Journal of Allergy and Clinical Immunology* 122:342–47.
- Nowak-Węgrzyn, A., and A. Fiocchi. 2009. Rare, medium, or well done? The effect of heating and food matrix on food protein allergenicity. *Current Opinion in Allergy and Clinical Immunology* 9:234–37.
- Pascual, C. Y., J. Fernandez-Crespo, S. Sanchez-Pastor, M. A. Padial, J. M. Diaz-Pena, F. Martin-Muñoz, and M. Martin-Esteban. 1999. Allergy to lentils in Mediterranean pediatric patients. *Journal of Allergy and Clinical Immunology* 103:154–58.
- Pastorello, E. A., L. Farioli, A. Conti, V. Pravettoni, S. Bonomi, S. Iametti, D. Fortunato, J. Scibilia, C. Bindslev-Jensen, B. Ballmer-Weber, A. M. Robino, and C. Ortolani. 2007. Wheat IgE-mediated food allergy in European patients: Alpha-amylase inhibitors, lipid transfer proteins and low-molecular-weight glutenins. Allergenic molecules recognized by double-blind, placebo-controlled food challenge. *International Archives of Allergy and Immunology* 144:10–22.
- Pastorello, E. A., V. Pravettoni, L. Farioli, L. Primavesi, J. Scibilia, M. Piantanida, A. Mascheri, and A. Conti. 2010. Green bean (*Phaseolus vulgaris*): A new source of IgE-binding lipid transfer protein. *Journal of Agricultural and Food Chemistry* 58:4513–16.
- Pastorello, E. A., S. Vieths, V. Pravettoni, L. Farioli, C. Trambaioli, D. Fortunato, D. Lüttkopf, M. Calamari, R. Ansaloni, J. Scibilia, B. K. Ballmer-Weber, L. K. Poulsen, B. Wüthrich, K. S. Hansen, A. M. Robino, C. Ortolani, and A. Conti. 2002. Identification of hazelnut major allergens in sensitive patients with positive double-blind, placebo-controlled food challenge results. *Journal of Allergy and Clinical Immunology* 109:563–70.
- Petersen, A., S. Rennert, S. Kull, W. M. Becker, H. Notbohm, T. Goldmann, and U. Jappe. 2014. Roasting and lipid binding provide allergenic and proteolytic stability to the peanut allergen Ara h 8. *Biological Chemistry* 395:239–50.

- Primavesi, L., O. V. Brenna, C. Pompei, V. Pravettoni, L. Farioli, and E. A. Pastorello. 2006. Influence of cultivar and processing on cherry (*Prunus avium*) allergenicity. *Journal of Agricultural and Food Chemistry* 54:9930–35.
- Riascos, J. J., S. M. Weissinger, A. K. Weissinger, M. Kulis, A. W. Burks, and L. Pons. 2016. The seed biotinylated protein of soybean (Glycine max): A boiling-resistant new allergen (Gly m 7) with the capacity to induce IgE-mediated allergic responses. *Journal of Agricultural and Food Chemistry* 64:3890–900.
- Royer, P. J., M. Emara, C. Yang, A. Al-Ghoul, P. Tighe, N. Jones, H. F. Sewell, F. Shakib, L. Martinez-Pomares, and A. M. Ghaemmaghami. 2010. The mannose receptor mediates the uptake of diverse native allergens by dendritic cells and determines allergen-induced T cell polarization through modulation of IDO activity. *The Journal of Immunology* 185:1522–31.
- Sanchez-Monge, R., G. Lopez-Torrejón, C. Y. Pascual, J. Varela, M. Martin-Esteban, and G. Salcedo. 2004. Vicilin and convicilin are potential major allergens from pea. *Clinical & Experimental Allergy* 34:1747–53.
- Sathe, S. K., S. S. Teuber, and K. H. Roux. 2005. Effects of food processing on the stability of food allergens. *Biotechnology Advances* 23:423–29.
- Schmitt, D. A., J. B. Nesbit, B. K. Hurlburt, H. Cheng, and S. J. Maleki. 2010. Processing can alter the properties of peanut extract preparations. *Journal of Agricultural and Food Chemistry* 58:1138–43.
- Schwager, C., S. Kull, J. Behrends, N. Röckendorf, F. Schocker, A. Frey, A. Homann, W. M. Becker, and U. Jappe. 2017. Peanut oleosins associated with severe peanut allergy - Importance of lipophilic allergens for comprehensive allergy diagnostics. *Journal of Allergy and Clinical Immunology*. [pii: S0091-6749(17)30417-7]. <https://doi.org/10.1016/j.jaci.2017.02.020>.
- Scibilia, J., E. A. Pastorello, G. Zisa, A. Ottolenghi, C. Bindslev-Jensen, V. Pravettoni, E. Scovena, A. Robino, and C. Ortolani. 2006. Wheat allergy: A double-blind, placebo-controlled study in adults. *Journal of Allergy and Clinical Immunology* 117:433–39.
- Shandilya, U. K., R. Kapila, R. M. Haq, S. Kapila, and V. K. Kansal. 2013. Effect of thermal processing of cow and buffalo milk on the allergenic response to caseins and whey proteins in mice. *Journal of the Science of Food and Agriculture* 93:2287–92.
- Sharma, G. M., K. H. Roux, and S. K. Sathe. 2009. A sensitive and robust competitive enzyme-linked immunosorbent assay for Brazil nut (*Bertholletia excelsa* L.) detection. *Journal of Agricultural and Food Chemistry* 57:769–76.
- Shreffler, W. G., R. R. Castro, Z. Y. Kucuk, Z. Charlop-Powers, G. Grishina, S. Yoo, A. W. Burks, and H. A. Sampson. 2006. The major glycoprotein allergen from *Arachis hypogaea*, Ara h 1, is a ligand of dendritic cell-specific ICAM-grabbing nonintegrin and acts as a Th2 adjuvant in vitro. *The Journal of Immunology* 177:3677–85.
- Simonato, B., G. Pasini, M. Giannattasio, A. D. Peruffo, F. De Lazzari, and A. Curioni. 2001. Food allergy to wheat products: The effect of bread baking and in vitro digestion on wheat allergenic proteins. A study with bread dough, crumb, and crust. *Journal of Agricultural and Food Chemistry* 49:5668–73.
- Son, D. Y., B. R. Lee, D. W. Shon, K. S. Lee, K. M. Ahn, S. Y. Nam, and S. I. Lee. 2000. Allergenicity change of soybean proteins by thermal treatment. *Korean Journal of Food Science and Technology* 32:959–63.
- Su, M., M. Venkatachalam, S. S. Teuber, K. H. Roux, and S. K. Sathe. 2004. Impact of γ -irradiation and thermal processing on the antigenicity of almond, cashew nut and walnut proteins. *Journal of the Science of Food and Agriculture* 84:1119–25.
- Tao, B., K. Bernardo, P. Eldi, N. Chegeni, M. Wiese, A. Colella, A. Kral, J. Hayball, W. Smith, K. Forsyth, and T. Chataway. 2016. Extended boiling of peanut progressively reduces IgE allergenicity while retaining T cell reactivity. *Clinical & Experimental Allergy* 46:1004–14.
- Tsabori, S., M. Triga, M. Makris, D. Kalogeromitros, M. K. Church, and K. N. Priftis. 2012. Fish and shellfish allergy in children: Review of a persistent food allergy. *Pediatric Allergy and Immunology* 23:608–15.
- Turner, P. J., S. Mehr, R. Sayers, M. Wong, M. H. Shamji, D. E. Campbell, and E. N. Mills. 2014. Loss of allergenic proteins during boiling explains tolerance to boiled peanut in peanut allergy. *Journal of Allergy and Clinical Immunology* 134:751–53.
- van der Ventel, M. L., N. E. Nieuwenhuizen, F. Kirstein, C. Hikuam, M. F. Jeebhay, I. Swoboda, F. Brombacher, and A. L. Lopata. 2011. Differential responses to natural and recombinant allergens in a murine model of fish allergy. *Molecular Immunology* 48:637–46.
- Venkatachalam, M., E. K. Monaghan, H. H. Kshirsagar, J. M. Robotham, S. E. O'Donnell, M. S. Gerber, H. H. Roux, and S. K. Sathe. 2008. Effects of processing on immunoreactivity of cashew nut (*Anacardium occidentale* L.) seed flour proteins. *Journal of Agricultural and Food Chemistry* 56:8998–9005.
- Venkatachalam, M., S. S. Teuber, W. R. Peterson, K. H. Roux, and S. K. Sathe. 2006. Antigenic stability of pecan [*Carya illinoensis* (Wangenh.) K. Koch] proteins: Effects of thermal treatments and in vitro digestion. *Journal of Agricultural and Food Chemistry* 54:1449–58.
- Venkatachalam, M., S. S. Teuber, K. H. Roux, and S. K. Sathe. 2002. Effects of roasting, blanching, autoclaving, and microwave heating on antigenicity of almond (*Prunus dulcis* L.) proteins. *Journal of Agricultural and Food Chemistry* 50:3544–48.
- Verhoeckx, K. C., Y. M. Vissers, J. L. Baumert, R. Faludi, M. Feys, S. Flanagan, C. Herouet-Guicheney, T. Holzhauser, R. Shimojo, N. van der Bolt, H. Wichers, and I. Kimber. 2015. Food processing and allergenicity. *Food and Chemical Toxicology* 80:223–40.
- Vissers, Y. M., M. Iwan, K. Adel-Patient, P. Stahl Skov, N. M. Rigby, P. E. Johnson, P. Mandrup Müller, L. Przybylski-Nicaise, M. Schaap, J. Ruinemans-Koerts, A. P. Jansen, E. N. Mills, H. F. Savelkoul, and H. J. Wichers. 2011. Effect of roasting on the allergenicity of major peanut allergens Ara h 1 and Ara h 2/6: The necessity of degranulation assays. *Clinical & Experimental Allergy* 41:1631–42.
- Vitaliti, G., I. Morselli, V. Di Stefano, A. Lanzafame, M. La Rosa, and S. Leonardi. 2012. Urticaria and anaphylaxis in a child after inhalation of lentil vapours: A case report and literature review. *Italian Journal of Pediatrics* 38:71.
- Wilson, S., C. Martinez-Villaluenga, and E. G. de Mejia. 2008. Purification, thermal stability, and antigenicity of the immunodominant soybean allergen P34 in soy cultivars, ingredients, and products. *Journal of Food Science* 73:T106–14.
- Worm, M., S. Hompes, E. M. Fiedler, A. K. Illner, T. Zuberbier, and S. Vieths. 2009 Jan. Impact of native, heat-processed and encapsulated hazelnuts on the allergic response in hazelnut-allergic patients. *Clinical & Experimental Allergy* 39 (1):159–66.
- Zhang, W., Q. Zhu, T. Zhang, Q. Cai, and Q. Chen. 2016. Thermal processing effects on peanut allergen Ara h 2 allergenicity in mice and its antigenic epitope structure. *Food Chemistry* 212:657–62.
- Zhang, Y., W. X. Du, Y. Fan, J. Yi, S. C. Lyu, K. C. Nadeau, and T. H. McHugh. (2016). Identification, characterization, and initial epitope mapping of pine nut allergen Pin k 2. *Food Research International* 90:268–274.