

Editorial

Thermal processing and allergenicity of foods

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Many thousands of years ago, when humans decided to stop eating foods exclusively in their raw state and started cooking them, they certainly did not intend to reduce their allergenicity. Heat treatments were, and still are, used for increasing food qualities in terms of safety and storage ability by inactivation of microbes and toxins, in nutritional value through improvement of digestibility and in pleasure through improvements of appearance, texture, flavour, and taste.

In the past few years, consumers and the food industry have been facing the challenge of a rapid and substantial increase in food allergies characterized by an increase in the prevalence and also in the severity of the clinical manifestations. Additionally, there has been an increase in the number of foods incriminated in allergic reactions. Food allergy has thus become a major public health concern with important socioeconomic consequences.

It has been observed that food processing, and particularly thermal processing, could also reduce the allergenicity of some foods as an indirect effect and it has even been proposed that this might serve for a better management of the allergenic risk of foods.

The rationale is apparently quite simple. Heat treatments alter the structure of proteins, i.e. the allergenic constituents of a food and, as a consequence, alter their allergenic potential and therefore the allergenicity of the whole food. Although no clear and general relationship between the structure of a protein and its allergenicity has been established, this view assumes, albeit not explicitly, that allergenicity is an intrinsic property of a protein because of or strictly related to particular structural features. This view, however, does not take into account the qualitative and quantitative variability of the allergen repertoire of a whole food, the multiplicity of epitopes on a given allergen or the genetic/geographic variability of the immune response in atopic human beings.

Significant alterations in protein structure do occur during heat treatments, the nature and extent of such changes being dependent on the temperature and duration of the thermal processing as well as on the intrinsic characteristics of the protein and the physico-chemical conditions of its environment (e.g. pH). Typically loss of tertiary structure is followed by (reversible) unfolding, loss of secondary structure (55–70°C), cleavage of disulphide bonds (70–80°C), formation of new intra-/inter-molecular interactions, rearrangements of disulphide bonds (80–90°C) and the formation of aggregates (90–100°C) (1). These modifications reflect a progressive passage to a disorganized structure with denaturation of the proteins that adopt an unfolded, random-coil conformation. The denatured molecules associate to form aggregates and then gels resulting in a modification of the surface properties and an increase in size.

Besides those physical transformations, chemical modifications of the protein may also occur at high temperatures (100–125°C and higher). These may involve formation of covalent bonds between the lysine residues of a protein and other constituents of the food matrix leading to various adducts. Advanced glycation end-products, carboxymethyl lysine, malondialdehyde and 4-hydroxynonenal formed through protein–sugar interactions (i.e. by the Maillard reaction) and the cross-linking of oxidized lipid products with proteins are commonly found and may contribute to the formation of new immunologically reactive structures.

It appears that there are no general rules regarding the consequences of thermal treatment on allergenicity. Some allergens or, more properly, some allergenic foods, are described as heat stable (e.g. milk, egg, fish, peanuts, and products thereof), while others are considered partially stable (e.g. soya bean, cereals, celery, tree nuts, and their products) or labile (fruits of the Rosaceae family and

carrots) (2). In addition, thermal processing can create new allergenic epitopes as well as destroying existing epitopes (1, 3). Whether and how heat treatments may significantly alter the allergenicity of a food is thus a complex question (4).

Hansen et al. bring new insights in a comprehensive study presented in a previous issue of the journal. Using a series of tests including double-blind, placebo-controlled food challenge, skin prick tests, histamine release and *in vitro* studies on immunoglobulin (IgE) binding capacity, they provide an overview on the impact of roasting (i.e. 140°C for 40 min) on the allergenicity of purified/recombinant major allergens of hazelnut, i.e. Cor a 1.04 and Cor a 2 and on the overall allergenicity of the whole hazelnut. Moreover, they discuss the consequences of heat treatment in terms of safety assessment and management of the allergenic risk of foods containing hazelnuts or hazelnut products.

In the study population of patients allergic to birch pollen and to raw hazelnuts, Hansen et al. found that roasting significantly reduced the allergenicity of Cor a 1.04 and of hazelnuts. In contrast to what has been previously observed with Ara h 1 (5, 6), it appears that the apparent affinity of specific IgE, as measured by the 50% inhibition of enzyme allerge sorbent test (EAST), is decreased approximately 100-fold in roasted *vs* raw hazelnuts whereas IgE binding was increased approximately 90-fold in roasted *vs* raw peanuts. Interestingly, thermal treatment of peanuts at lower temperatures such as boiling (100°C) or frying (120°C), where heat-induced conformational changes take place but where the Maillard reaction is unlikely to occur, did not affect the allergenic properties of Ara h 1. This may explain why the prevalence of peanut allergy may depend on the dietary habits and type of cooking traditionally used in various populations of different countries (7).

Despite the significant reduction of allergenicity, Hansen et al. stressed that trace amounts of the residual protein that remain in the roasted hazelnuts can still bind IgE and elicit symptoms in highly sensitive patients and that a significant number of patients in the study population (ca. 30%) proved still to be clinically reactive.

This raises the important question of the clinical relevance of such a 'limited' reduction of allergenicity and of its significance and applicability in terms of risk management and protection of allergic consumers. This is linked to the more general question of threshold doses which is presently much debated. Taylor et al. (8) discussed the significance of 'low' concentrations of allergens and wondered when 'how much is too much'. A recent paper (9) has proposed a statistical approach to determine threshold levels from published data in the literature and then to derive an 'acceptable intake' for a given proportion of an allergic population (e.g. 90%), using a paradigm similar to that used in classical toxicology. Up to now, the recorded/calculated data show that a substantial part of the population reacts to

very low amounts of allergens, particularly those of the peanut, which appears even more important because patients with severe reactions react to lower threshold doses than patients with mild symptoms (10).

Hansen's paper also gives an illustration of the other issues to be addressed to provide reliable reassurance to allergic consumers, in particular: 1) will reducing the allergenicity of one or two major allergens mechanically reduce the allergenicity of the whole food? and 2) will the heterogeneity and variability in the genetic background of individuals and in environmental conditions induce differences in susceptibility?

As noted in Hansen's paper (4), individuals in northern and central Europe who are allergic to hazelnuts are almost exclusively sensitized to Bet v 1-related allergens that cross-react immunologically with birch pollen allergens, whereas allergic populations of Mediterranean countries are essentially sensitized to Cor a 8, which is a lipid transfer protein (LTP). Both types of protein are present in the same food, i.e. the hazelnut, but LTPs and Bet v 1 pollen-related allergens have different structural and physico-chemical features. Non-specific LTPs belong to a widespread family of plant proteins that share similar characteristics: they are heat-stable and resistant to proteolytic degradation by digestive enzymes, whereas Bet v 1-related allergens are altered during thermal treatments and quite rapidly and extensively hydrolysed by proteases. This makes a considerable difference to the everyday life of allergic patients and in the management of their allergy. 'True' food allergies to LTPs and to foods containing LTPs elicit more severe clinical manifestations than allergic reactions to the same foods due to pollen cross-reactive allergens and they require the compliance with a very strict diet which should avoid any product from food containing LTP. The same allergenic food may thus differently affect two distinct populations which are not sensitive to the same allergenic constituents of the food. Management of their condition would then require different specific measures adapted to the needs of the two groups to prevent or decrease the risk of severe allergic reactions.

In conclusion it is difficult to anticipate the effects on allergenicity of protein/food modifications because of thermal treatments and because of any (bio)technological process used in the food industry for production, storage and processing. Moreover, the impact may differ completely from one allergenic food constituent to another. As a consequence, depending on which allergenic constituent of the food is responsible for the sensitization, the process may be clinically relevant, i.e. have a beneficial impact, for some allergic individuals but not for others. It is therefore difficult to decide how extensive and how uniform or specific the product information, with respect to labelling of food allergens and products thereof, should be to provide a suitable warning and an appropriate means of prevention to the various subgroups of the allergic patients population.

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