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Review

Food processing and allergenicity

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ABSTRACT

Food processing can have many beneficial effects. However, processing may also alter the allergenic properties of food proteins. A wide variety of processing methods is available and their use depends largely on the food to be processed.

In this review the impact of processing (heat and non-heat treatment) on the allergenic potential of proteins, and on the antigenic (IgG-binding) and allergenic (IgE-binding) properties of proteins has been considered. A variety of allergenic foods (peanuts, tree nuts, cows' milk, hens' eggs, soy, wheat and mustard) have been reviewed.

The overall conclusion drawn is that processing does not completely abolish the allergenic potential of allergens. Currently, only fermentation and hydrolysis may have potential to reduce allergenicity to such an extent that symptoms will not be elicited, while other methods might be promising but need more data. Literature on the effect of processing on allergenic potential and the ability to induce sensitisation is scarce. This is an important issue since processing may impact on the ability of proteins to cause the acquisition of allergic sensitisation, and the subject should be a focus of future research. Also, there remains a need to develop robust and integrated methods for the risk assessment of food allergenicity.

1. Introduction

Food allergy describes the adverse health effects in which immunological mechanisms are involved (allergic reactions) that can be induced in sensitised subjects following dietary exposure to relevant allergens in food. Food allergy is an important health problem (Sampson, 2004), and estimates of its prevalence in Europe are commonly in the region of 0.1–3.2% for adults and 0.1–5.7% for children. However, the extent to which the prevalence of food allergy has increased in line with other forms of atopic disease is not clear (Nwaru et al., 2014).

Most cases of food allergy are associated with a limited range of products. Previously the most commonly allergenic foods were considered to be cows' milk, hens' eggs, peanuts, tree nuts, soy, wheat, shellfish and fish (the 'big 8') (Hefle et al., 1996; Young et al., 1994). More recently, in Europe, that list has been expanded in number to 14: cereals containing gluten, crustaceans, molluscs, eggs, fish, peanuts, tree nuts, soybeans, milk, celery, mustard, sesame, lupin and sulphur dioxide (Commission-Directive 2006/142/EC). It is apparent, however, that the extent to which allergy is associated with particular foods varies with time and geography, with changing dietary habits and preferences, the introduction of new

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foods, the way in which food is prepared, and the age at which foodstuffs are first introduced into the diet (Hourihane, 1998; Lucas et al., 2004).

In common with other forms of allergic disease, food allergy develops in two phases. In the first phase susceptible subjects are immunologically primed to specific food proteins resulting in allergic sensitisation. Such sensitisation may be acquired following dietary exposure to food proteins, or possibly via other routes of exposure (including inhalation and skin contact). If sensitised subjects subsequently encounter sufficient levels of the inducing allergen(s) in the diet then an allergic reaction may be elicited. The symptoms of such reactions vary considerably and can range from mild, local and transient effects to systemic anaphylaxis that is potentially fatal (Perry and Pesek, 2013; Sicherer and Sampson, 2014; Sicherer and Wood, 2013).

By definition, allergy results from the elicitation of a specific immune response. The most common immunological mechanism implicated in the acquisition of sensitisation to food proteins is the elaboration of IgE antibodies. However, non-IgE-mediated cellular immune responses are also important in some forms of food allergy (Johnston et al., 2014; Kimber and Dearman, 2002; Sicherer and Sampson, 2014). The primary focus of this article is on IgE-mediated food allergy.

Although many uncertainties remain, there have been important advances in characterisation of some of the factors that influence the acquisition of sensitisation to food proteins and the development of food allergy. Among the important variables are the inherent allergenic potential of food proteins, the timing, duration, extent and route of exposure to food allergens, and heritable and acquired susceptibility factors (Kimber and Dearman, 2002; Sicherer and Sampson, 2014). Some intriguing questions that remain unanswered are the factors that maintain operational tolerance to foods and food proteins, and the events and immunological processes through which tolerance is broken and sensitisation is acquired.

There remains a need to understand in greater detail differences between proteins with respect to their inherent allergenic potential, and the properties that confer on proteins the ability to induce sensitisation. It is known, for instance, that protein function (including enzymatic activity), stability (including resistance to proteolytic digestion) and glycosylation patterns can affect both immunogenic and allergenic potential (Huby et al., 2000). However, in the case of food allergy there is an additional dimension that must be considered; the impact of food processing, and of the food matrix, on allergenic potential (Jiménez-Saiz et al., 2014; Lepski and Brockmeyer, 2013; Mills et al., 2009; Nowak-Wegrzyn and Fiocchi, 2009). The types of processing that have been implicated in influencing allergenic properties are: heating (thermal processing), fermentation including endogenous enzymatic hydrolysis, enzymatic and acid hydrolysis, physical treatments (such as high pressure processing or extrusion), the use of preservatives, changes in pH, or combinations of any two or more of these (EFSA, 2014, Mills and Mackie, 2008, Thomas et al., 2007).

In the context of this report it is important to appreciate that food processing can potentially impact on different aspects of food allergy, and it is necessary to distinguish clearly between these. A draft scientific opinion on the evaluation of allergenic foods and food ingredients for labelling purposes published recently by EFSA made the point as follows: '*Most studies available report on the IgE-binding capacity of processed foods rather than on their allergenicity, whereas systematic investigations on the effects of food processing on allergenicity are scarce*' (EFSA, 2014).

While it is clear that consideration of the influence of processing on not only the antigenic integrity/IgE-binding capacity of allergenic proteins, but also the ability to induce sensitisation is important, it must be acknowledged that addressing the latter is not without difficulty. Currently what is required is the use of well conducted and controlled animal studies in which the inherent allergenic potential of processed and unprocessed foods can be compared (Kroghsbo et al., 2014b).

In this report the impact of processing on antigenic and allergenic integrity of proteins (IgG and IgE antibody binding, respectively), and the ability of foods to elicit allergic reactions will be considered, together with potential effects on sensitisation where relevant data for the latter are available. For the purposes of this article we have chosen not to base our review solely on a consideration of what are normally considered to be the most common allergenic foods, although most are included. The foods evaluated were selected on the basis of the availability of relevant literature and the various forms of processing to which they are normally subjected. Those reviewed are: peanuts, tree nuts, cows' milk, hens' eggs, soy, wheat and mustard.

2. Influence of processing on the antigenic integrity and allergenicity of food proteins

For the purposes of this article it is necessary to clarify definitions and terminology. This is because food processing can potentially affect two aspects of the allergenic properties of proteins, as follows:

(a) In most investigations it is the impact of processing on the integrity of epitopes recognised by IgG antibodies or IgE antibodies that has been reported. Such changes are of potential importance because they will influence the ability of antibodies to bind to the modified protein, and in the case of IgE antibody binding this may result in an altered capacity to elicit an allergic reaction.
(b) Much less commonly the impact of processing on the ability of food proteins to induce allergic sensitisation has been investigated. Here, in the case of IgE-mediated food allergy, the question addressed is whether processing has impacted on the capacity of a protein to stimulate the production of IgE antibody.

To distinguish effectively between these two types of effects it is important to adopt for this article clear definitions that will avoid confusion. The definitions summarised below are not necessarily intended to be universally applicable, or to take the place of definitions that are commonly employed elsewhere. Rather, the intention is to adopt working definitions that will provide clarity in considering the influence of processing on the allergenic properties of food proteins. These are as follows:

2.1. General definitions

Food allergy*: an adverse reaction to food that is mediated through immunological mechanisms. Such reactions can be provoked in sensitised subjects following dietary exposure to relevant allergens in food.*

Allergic sensitisation: *the process of specific immunological priming through which heightened sensitivity (sensitisation) to food proteins is acquired.*

Allergenicity or allergenic potential: *the potential of a material to cause sensitisation and allergic reactions, frequently associated with IgE antibody.*

IgG or IgE antibody binding capacity: *an altered ability of IgG antibody (also antigenic integrity) or IgE antibody (also allergenic integrity) to bind to epitopes, respectively.*

Immunogenicity: *the ability of a material to elicit an immune response.*

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