

# RISK MANAGEMENT FOR FOOD ALLERGENS IN CEREALS AND DERIVATIVES

ISABELA CRĂCIUN<sup>a</sup>, EMIL IGNAT<sup>a</sup>, ANGELA MĂRCULESCU<sup>a</sup>, MIHAELA BADEA<sup>a</sup>, LIVIU GACEU<sup>a</sup>,  
PATRIZIA RESTANI<sup>b</sup> and LUCA BUCCHINI<sup>c</sup>

<sup>a</sup> Romanian Society of Etnofarmacology Braşov,

<sup>b</sup> University of Milan, Italy, <sup>c</sup> Hylobates Consulting SRL, Rome, Italy,

<sup>a</sup> Larex Laboratory of Sibiu, Emiliana Laboratory of Sibiu, University Transilvania of Braşov

*Received January 28, 2010*

The present paper discusses about food allergy with particular attention to hazard identification and risk assessment of cereals allergy. To perform a risk characterization it is important to know the threshold level for clinical reactions. If threshold is not established, the risk assessment and management is difficult and labeling such as “May contain gluten” is unavoidable even if it can be used with or without reason. Unjustified warning declarations do not help the allergic individuals but create more confusion than guidance.

*Key words:* Cereals allergy; Risk assessment; Thresholds; Labeling.

## INTRODUCTION

Food allergy is defined as an adverse reaction to food, mediated by the immune system. Of greatest concern, it is IgE-mediated food allergy, in which the patient produces IgE antibodies to one or more proteins present in a specific food. Recent data indicate that around 3–4 % of the total population suffer from this type of food allergy, making it a significant public health problem, although the percentage at risk of a severe life-threatening reaction is considerably lower (even though it can not be easily estimated). It has been estimated that the amount of protein capable to provoke an objective allergic reaction ranges from a tenth of a milligram up to grams, and sometimes tens of grams; considerable individual variability exists among food-allergic individuals. However, these amounts are not defined for most allergenic foods.

More than 120 foods have been described as causing food allergies, but experts consider only few of them as responsible for public health concerns.

Among the foods most commonly involved in serious allergic reactions on worldwide bases there are: cereals containing gluten, milk, egg, tree nuts,

peanuts, soybeans and their derivatives, fish and crustaceous. Among cereals, wheat is the most frequently involved in adverse reactions such as Celiac disease and IgE-mediated wheat allergy both resulting from the malfunctioning of the immune system.

Allergies to other cereals (maize, sorghum, millet) are not common and are not related to reactions triggered by wheat, rye, barley and wheat.

Celiac disease is triggered by the gluten fraction of wheat or by the gluten-like proteins found in rye and barley. Some sensitive individuals may also react to oats. The gut reacts to the gluten and, due to a flattening of villi, loses its ability to absorb nutrients; symptoms include diarrhea as well as deficiencies in nutrients like minerals and vitamins. Symptoms can appear either in childhood, affecting growth and development, or in adulthood. As there is no therapy, subjects suffering from celiac disease have to avoid eating gluten for all their life.

However celiac disease does not cause the potentially fatal reactions like anaphylactic shock if gluten is accidentally eaten. Differently from celiac disease, IgE mediated allergy can be caused by sensitization to both gluten and other proteins.

Individuals with wheat allergy often react to closely related cereals like barley, rye and oats.

Diagnosis of allergy to cereal can be complicated by the fact that some tests, measuring serum antibodies, can detect grass pollens allergens.

### **RISK ASSESSMENT (RA) AND RISK MANAGEMENT FOR FOOD-ALLERGENS, FOOD BUSINESSES AND CATERING IN CEREALS AND DERIVATIVES**

Cereals containing prolamines (alpha-gliadin, ordeine, secaline, avenine) are molecules representing a hazard for some individuals. To this category belongs wheat, semolina, spelt, Bulgar, couscous, durum, barley, malt, kamut, faro, triticale which are better to be avoided.

Gluten-free grains suitable for the diet of celiac subjects and of some groups of allergic patients are amaranth, corn, potato, rice, sorghum, tapioca, millet and oats.

Managing allergen risks is a shared responsibility of all the stakeholders and requires a consistent approach across industry in order to be effective. The food industry and catering services must ensure that allergenic ingredients are declared and that accidental residual allergen levels are safe for the vast majority of allergic consumers. Health professionals diagnose and advice patients, who in turn must use the due care in their food and product choices, while regulators must balance the interests of all stakeholders and ensure compliance.

### **RISK COMMUNICATION AND CONSUMER PERCEPTION: FOOD ALLERGENS IN CEREALS AND DERIVATIVES**

Because of the uncertainties associated with food allergy and food allergens, current approaches to protect allergic consumers have focused on allergenic hazards rather than attempting to assess the risk. Thus legislation in several regions now makes mandatory the declaration of specified allergenic ingredients whenever present in a manufactured food. This approach is generally effective in managing the risk from ingredients present in meaningful quantities, although it is arguably unhelpful for minor ingredients added in minuscule amounts, for instance, because they are minor constituents in another ingredient. However, the risks associated with allergens do not arise only

from their use as ingredients. Allergenic constituents can be present through cross-contamination during manufacturing, or through their presence in raw materials. Since allergenic ingredients such as wheat, peanuts, milk and egg are used extensively in food industry, the “total” reduction of their traces is often not a practical proposition. This problem has led to the extensive use of precautionary labeling (such as “it may contain”). Allergic individuals dislike excessive precautionary labeling because they are not clear information and reduce their food choices. Aside from the impact on the allergic consumer, the hazard-based approach to allergen management can also cause problems to the food industry by requiring technological measures, which may go beyond what is necessary for the safety of allergic consumers.

Considering the problems of patients suffering from celiac disease and allergy to cereals, the use of “May contain gluten” should be limited to those cases where gluten traces cannot be avoided (in the case of celiac disease traces must be below 20–100 ppm).

### **THE EU LEGAL FRAMEWORK FOR FOOD ALLERGENS IN CEREALS AND DERIVATIVES: THE SITUATION IN ROMANIA CONCERNING IMPLEMENTATION AND CONTROLS. IMPLICATIONS FOR EXPORT**

The process of risk assessment is conventionally organized into four separate steps: hazard identification, hazard characterization, exposure assessment and risk characterization (FAO/WHO, 1995; FAO/WHO, 1997; Codex Alimentarius Commission, 2003).

This framework can be applied to food allergy. Thus, for food allergens, the hazard is implicitly identified insofar as it is the potential to cause an allergic reaction. However, despite the growing body of data becoming available, the hazard is poorly characterized, to the extent that amounts of allergen below which no one reacts cannot be defined currently. Thus, based on a review of the existing data, Taylor *et al.* (2002) concluded that “thresholds for common allergenic foods are finite, measurable and above zero. However, attempting to reach consensus on the threshold doses for peanut, egg, cows’ milk, fish, and mustard on the basis of the existing data would probably be premature”. The European Food

Safety Authority (EFSA, 2004) reached a similar conclusion more recently. Furthermore, the relationship between the dose of the allergenic food and the nature and severity of the response is even less well defined, and for ethical reasons, difficult in being established.

Allergic responses, in common with other adaptive immune responses, consist of two phases: sensitization and elicitation. The concept of thresholds can be applied to both phases. However, no international consensus has been reached on thresholds of sensitization to food proteins in human beings and in practice, the term “threshold” is only used in relation to the elicitation phase.

Food allergens differ from substances normally included in conventional toxicological risk assessments, insofar as they do not provoke reactions in the vast majority of the population. Many allergenic foods are part of the diet and significantly contribute to the nutrition. No imperative need therefore exists to identify a threshold below which sensitization would not occur. Systematic consideration of each element in risk assessment highlights the need to understand exposure in order to fully characterize the risk.

Based on available evidences, adverse reactions, including anaphylactic shock could be elicited at any dose level. For several reasons, the definition of a legal thresholds is critical: matrix, presence of more allergens in the same food and cross-reactivity.

According to new European Regulation tolerable daily intake of gluten for celiac subjects is 20 ppm for products including ingredients naturally free from gluten and 100 ppm for products including ingredients where gluten has been eliminated.

#### **LABELING IN CEREALS AND DERIVATIVES FOR ALLERGENS: EXAMPLES FOR ROMANIA AND EXPORT MARKETS**

To reply to the answer “How to label allergens?” Codex Alimentarius proposed in 1993 the “93” list, that was elaborated later in a final list where cereals containing gluten (wheat, rye, barley, oats, spelt) or their hybridized strains and products of these were included.

According to the CODEX suggestion and as a consequence of adverse reactions to cereals containing gluten, EU decided to include them in

the annex III-a of the food labeling directive (Directive 2003/89).

In Romania Directive 2003/89 was translated in a labeling law HG nr.751/2008.

Temporary exceptions to the labeling rule have been granted for some wheat derivatives: wheat based glucose syrup, dextrose, wheat maltodextrins, barley and cereals used in distillation.

In the case of unavoidable cross-contamination among allergens, a precautionary labeling could be useful because it intends to warn consumers on the possible presence of traces of “hidden” allergens. The precautionary labeling is usually in the form of “may contain traces of” and is not regulated by any legislation.

Some food products made in Romania are precautionary labeled.

#### **SPECIFIC ALLERGEN TESTING METHODS FOR CEREALS AND DERIVATIVES**

To obtain qualitative and quantitative data on food allergens and information on how to reduce the traces of these compounds in foodstuffs, different analytical methods have been developed to meet the requirements for food control. These methods are based on electrophoretic, immunochemical and chromatographic techniques with colorimetric or mass-spectrometric detection.

The allergic reaction occurs when specific IgE antibodies bind the specific allergen. The binding is mediated by a restricted area of the protein, named epitope, which can be (or not) “active” even after the protein has been modified or degraded during technological processing. Studies on the epitope characteristics as well as other molecular details such as molecular weight, primary/secondary and tertiary structure and glycosylation of the allergenic protein, are important objectives to better understand the mechanism of sensitization.

Allergens can be identified by immuno-blotting after gel-electrophoresis; further details can be obtained after a pre-fractionation of proteins by HPLC.

Alternatively, immunochemical methods based on specific antigen-antibody reaction (enzyme linked immunosorbent assay, ELISA) or polymerase chain reaction (PCR) can be used to identify and quantify traces of allergens in complex foods.

## ENZYME-LINKED IMMUNOSORBENT ASSAY– ELISA

ELISA is a biochemical technique used to detect the presence of an antibody or an antigen in a sample: the basis of the test is the antigen-antibody reaction.

This binding is detected thanks to the activity of an enzyme that converts a colorless substrate to a stained product.

ELISA can be used to detect either the presence of AgS or AbS in a sample, depending on how the test is designed.

The enzyme activity allows the detection of target proteins and their quantification.

ELISA is a useful and powerful method in estimating mg/g concentrations (ppm) of a target protein in samples such as cereal and food extracts.

ELISA is used to quantify of gliadins of gluten in gluten free products (bread, bakery products and snack) or raw material (rise flour, amaranth flour).

## CONCLUSIONS

Allergen risk management must balance the needs of several different groups with potentially divergent interests.

The most sensitive allergic individuals ideally need:

- a) the absolute assurance that a certain product is free from the allergenic compounds responsible for the clinical reactions.
- b) a wide number of “safe” foods.

This could in theory be achieved by the complete elimination of allergenic ingredients from food manufacturing, or specific manufacturing facilities.

However, most allergenic ingredients like cereal derivatives are a good source of nutrients and form a valuable part of the diet for the general population.

For patients suffering from celiac disease, the food which may contain traces of gluten must be correctly labeled and this is made relatively simple thanks to the defined legal limits.

On the other hands, there is no sufficient evidence about the relationship between the presence of allergen in traces and the clinical reactions and this fact makes very difficult the correct management of the problem.

## ACKNOWLEDGMENTS

*The authors are gratefully acknowledged for the financial support to the project nr: LLP-LdV/VETPRO/2009/RO/124, obtained by the Romanian Society of Ethnopharmacology.*

## REFERENCES

1. Bock, S.A., Lee, W.Y., Remigio, L.K., May, C.D., 1978. Studies of Hypersensitivity reactions to foods in infants and children. *J. AllergyClin. Immunol.* 62, 1327–1334
- Christie, L., Hine, J., Parker, J.G., Burks, A.W., 2003.
2. Food allergies in children affect nutrient intake and growth. *J. Amer. Diet Assoc.* 102(11), 1648–1651.
- R.W.R. Crevel , D. Briggs, S.L. Hefle, A.C. Knulst, S.L. Taylor.
3. Hazard characterization in food allergen risk assessment: The application of statistical approaches and the use of clinical data-Chung, S.Y., Butts, C.L., Maleki, S.J., Champagne, E.T., 2003.
4. Peanut allergenicity to the processes of maturation, curing, and roasting. *J. Agric. Food Chem.* 51 (15), 4273–4277.
5. Codex Alimentarius Commission, 2003. Draft Principles for the Risk Analysis of Foods Derived from Modern Biotechnology, at Step 8 of the Elaboration Procedure. ALINORM 03/34, Appendix II. Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme,
6. Food and Agriculture Organization, Rome. Available from <ftp://ftp.fao.org/codex/alinorm01/al0134ae.pdf>. Crevel, R.W.R., 2002.
7. Industrial dimensions of food allergy. *Biochem. Soc. Trans.* 30 (Pt 6), 941–944.Crump, K.S., 1984. An improved procedure for low-dose carcinogenic risk assessment from animal data.- *J. Environ. Pathol. Toxicol. Oncol.* 5,339–348.Edler, L., Poirier, K., Dourson, M., Kleiner, J., Mileson, B., Nordmann, H., Renwick, A., Slob, W., Walton, K., Wurtzen, G., 2002.
8. Mathematical modeling and quantitative methods. *Food Chem. Toxicol.* 40, 283–326.
9. European Food Safety Authority, 2004. EFSA Journal 32, 1–197, Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission relating to the evaluation of allergenic foods for labeling purposes. FAO/WHO, 1995.
10. Food chemistry 101 (2007). Recent developments in instrumental analysis for food quality-Andre Muller, Hans Steinhart.