Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to a notification from AAC on wheat-based maltodextrins pursuant to Article 6 paragraph 11 of Directive 2000/13/EC

(Request N° EFSA-Q-2004-091)

(adopted on 19 October 2004)

SUMMARY

Information is provided by the applicant on wheat starch hydrolysates, particularly on maltodextrins concerning their preparation, analysis and potential effects in coeliac disease and cereal allergy. It is stated that maltodextrins based on wheat starch are not likely to trigger adverse reactions. This statement is based on the description of the manufacturing process which includes protein removal by active carbon treatment. The evidence of non-allergenicity of wheat starch maltodextrin provided includes information on the safe use of wheat starch-based gluten-free diet in coeliac disease which is indirectly relevant to the topic. Similar information on wheat allergy is missing. Nitrogen analysis showed residual nitrogen compounds in maltodextrins from wheat starch. Trace amounts (1-40 mg/kg) of residual intact gliadin as well as peptides arising from degradation of gluten were found by mass spectrometry in wheat starch maltodextrins. Traces were also found by ELISA analysis for gluten. Additional information is given on preliminary results of specific T cell function testing in coeliac disease and on immunoprinting based on sera from patients with bakers' allergy. Finally, two studies planned into coeliac disease and into wheat allergy are outlined from which relevant information can be expected by the end of 2006.

Wheat-based maltodextrins may contain low levels of proteins, peptides or fragments thereof. It is not known at which levels of intake wheat-based maltodextrins would cause allergic reactions in cereal allergic individuals. Based on the data provided by the applicant the Panel is unable to predict the likelihood of adverse reactions in cereal allergic individuals. Nevertheless, taking into account the levels of wheat proteins reported to cause allergic reactions in severe allergic individuals, the Panel considers that it is not very likely that this product will cause a severe allergic reaction in the majority of cereal allergic individuals. More clinical information is needed with regard to the effects of wheat-based maltodextrins in cereal allergy. Appropriate clinical studies applying best clinical and laboratory practice should be carried out.

For coeliac disease, assessment of the evidence provided indicates that wheat-based maltodextrins are unlikely to cause an adverse reaction in individuals with coeliac disease provided that the provisional value of gluten considered by Codex Alimentarius for foods rendered gluten-free (currently 200 mg/kg) is not exceeded.

KEY WORDS

Wheat starch hydrolysates, maltodextrins, coeliac disease, food allergy.

BACKGROUND

In November 2003, the European Parliament and the Council adopted Directive 2003/89/EC[1] amending Directive 2000/13/EC, as regards indication of the ingredients present in foodstuffs.

Annex IIIa of the Directive specifies a list of ingredients that are known to trigger allergic reactions or intolerances for which no labelling exemptions are allowed. Whenever the listed ingredients or their derivatives are used in the production of foodstuffs, they must be labelled.

Article 1, paragraph 11 of the Directive establishes a procedure allowing for temporary labelling exemption of derivatives from ingredients listed in Annex IIIa for which it has been scientifically established that it is not possible for them to cause adverse reactions. In accordance with this provision, submissions of request for temporary labelling exemption were notified to the Commission before 25 August 2004. The Commission shall, not later than 25 November 2004, and after consultation with the European Food Safety Authority, adopt a list of those ingredients which shall be temporarily excluded from Annex IIIa, pending the final results of the notified studies, or at the latest until 25 November 2007. Therefore, the European Food Safety Authority is asked to provide scientific opinions on the submissions in accordance with the present terms of reference.

TERMS OF REFERENCE

In accordance with Article 29 (1) (a) of Regulation (EC) N° 178/2002, the European Commission requests the European Food Safety Authority to evaluate the scientific data submitted by AAC in the framework of the procedure laid down for temporary labelling exemptions in Article 6 paragraph 11 of Directive 2000/13/EC. On the basis of that evaluation, EFSA is requested to issue an opinion on the information provided, and particularly, pending the final results of the studies undertaken, to consider the likelihood of adverse reactions triggered in susceptible individuals by the consumption of the following ingredients/substances used under the conditions specified by the applicant: wheat-based maltodextrins.

ASSESSMENT

Since wheat is relevant both as a source of epitopes known to elicit coeliac disease and as a source of allergens eliciting wheat allergy (NDA, 2004), it is fully justified to investigate wheat products, namely wheat starch hydrolysates (WSH) for their potential to induce coeliac disease or wheat allergy.

The applicant comes to the conclusion that based on wheat based maltodextrins' history of safe use and based on the available analytical data, these substances are not likely to trigger adverse reactions. Furthermore, the applicant lists completed and ongoing experimental and clinical studies.

The following evidence is presented by the applicant in support of the statement given above.

[1] Directive 2003/89/EC of the European Parliament and of the Council amending Directive 2000/13/EC as regards indication of the ingredients present in foodstuffs. OJ L 308. 25.11.2003, p. 15.

1. Manufacturing process

The data provided show that in the preparation process of wheat starch hydrolysates (isolation, conversion, purification, preservation, blending) the code of good practice is observed including HACCP principles. The maximum protein content of maltodextrins is 0.5%. However, by the different purification steps, in particular the active carbon treatment, proteins and other nitrogen containing compounds are removed. Analytical data on the protein content are not given. It is made clear from analytical data that all samples tested contained trace amounts of proteins and peptides (1-40 mg/kg). This included native gliadin (see below for analytical data).

2. Characterisation of the product

Maltodextrins are used for confectionery, sauces and soups, and for dietetic foods.

A study analysing dietary exposure to gluten from wheat starch hydrolysates is currently being conducted by TNO Nutrition and Food Research (The Netherlands). This study is designed to collect data from The Netherlands, Italy and Ireland and it is expected to be completed by December 2004. It is unclear how much the study will be able to answer the central question, namely the potential effect of wheat hydrolysates in coeliac disease and in wheat allergy.

3. Evidence of non-allergenicity

3.1 History of non-allergenicity of the product

A large literature review gives partly redundant information on wheat protein analysis and effects in coeliac disease and wheat allergy. Wheat starch hydrolysates are not being dealt with in this literature review directly.

In a study on coeliac disease, wheat starch-based gluten-free diet was compared to naturally gluten-free diet in 76 adult coeliac patients (Collin *et al.*, 2004). The authors showed gluten contamination up to the level of 200 mg/kg of diet in both dietary groups. The long-term mucosal recovery of the patients was good in both groups. By this and other studies it has been shown that wheat starch derived gluten-free products still containing trace amounts of gluten are safe for children and adults with coeliac disease. The authors came to the conclusion that a gluten threshold of 100 mg/kg of food "can safely be set". Although the paper is not directly devoted to the use of maltodextrins in coeliac disease, the evidence given is relevant to the application.

Another study submitted concerns wheat allergy in children and adults (Moneret-Vautrin *et al.*, 2003). Most of the paper is not directly relevant to the use of wheat starch hydrolysates in wheat allergy. However, provocation tests using 1 mg-19.99 g of wheat protein have been used as part of the diagnostic procedure. It is not made clear how the figures reported for wheat proteins relate to the quantities of wheat flour used for provocation tests. The results given cannot be used as dose-response information with general validity. The authors' conclusion that "threshold doses of wheat flour in wheat flour allergics were globally higher than those considered risk levels for coeliac disease, seeming to indicate that a wheat starch-based diet could be safe for allergic patients" is not sufficiently based on the evidence presented.

Based on the literature review submitted no adverse reactions has been reported on wheat starch hydrolysates in coeliac disease and wheat allergy. However, most of the evidence provided is indirect and inconclusive and potentially misleading.

3.2 Laboratory-based tests

Using nitrogen analysis (Kjeldahl) residual nitrogen compounds were analysed in wheat starch and wheat starch hydrolysates. A wide range of calculated protein content based on Kjeldahl nitrogen x 6.25 is shown for different samples (0.15-0.38%) of the commercial product taking dry substance into account as well as the fact that phospholipids are the main source of wheat starch nitrogen. The true protein content is much lower than the figures given above. Protein nitrogen represents only 30% of total nitrogen in wheat starch. HPLC amino acid determination showed that the true protein content of wheat starch hydrolysates was less than 100 mg/kg (detection level of HPLC). This was also true for four samples of maltodextrins tested.

Further evidence is provided using R5 ELISA and Western blot analysis. While in wheat starchs up to 243 mg/kg gluten were found, there was no detected gluten level higher than 3.1 mg/kg (detection limit) in glucose and dextrose samples and in three maltodextrin samples. One out of four maltodextrin samples showed a positive response at 4.5 mg/kg gluten. Therefore the conclusion is justified that the gluten/gliadin epitope QQPFP was absent in most wheat starch hydrolysates with the exception of one maltodextrin sample where it was shown as a trace just above detection limit.

A large and exhaustive body of evidence on quantitative and qualitative protein and peptide content of wheat starch hydrolysates was provided. Twenty-one samples (14 wheat glucose syrups, 3 crystalline dextrose, 4 maltodextrins) were studied by a highly refined methodology based on a detailed purification scheme and different applications of mass spectrometry. The limit of detection for gliadin was 1 mg/kg. The recovery of gliadin by the method was 86%. It was found that all samples contained some level of residual intact gliadin as well as peptides arising from degradation of gluten in the range of 1-40 mg/kg. Protein composition was slightly variable. It was observed that specific peptides from well-defined regions of gliadins and glutenins were shown relatively resistant to hydrolysis as indicated by a summary table on 21 single samples.

The data submitted contain preliminary data and an outline for studies on specific T cell reactivity. Specific monoclonal ELISA has not been published yet and is not standardized. Therefore all results should be evaluated with caution. This is particularly true for the T cell assay which did not give any indication of T cell reactive peptides in four wheat starch hydrolysate samples. It also applies to the monoclonal ELISA indicating a very low protein level for a mixed sample. A clear significance of the findings submitted with regard to coeliac disease cannot be stated. There seems to be no relevance with regard to wheat allergy.

Immunoblotting data based on sera from five patients with bakers' asthma were included. Three wheat starch samples were investigated but no maltodextrins were tested. In a preliminary study there was no reactivity observed of sera with one commercial sample of glucose syrup and two subfractions. It cannot be concluded that these negative reactions are representative.

3.3 Proposed clinical studies

3.3.1 Coeliac disease

This is the outline of a well-designed clinical study on the effects of wheat starch hydrolysates in coeliac disease. Study duration is August 2004 to December 2006. The protocol is based on a double-blind placebo control design on 90 coeliac patients. It randomizes into a glucose syrup/maltodextrin/placebo group for a duration of 24 weeks. The decisive information is expected from small intestinal biopsy with histological examination. Relevant information can be expected from the design given, provided the study can be realized as indicated.

3.3.2 Wheat allergy

A study protocol is given for the study of wheat starch hydrolysates in wheat allergy. However, at present diagnosis of patients included is not based on double-blind placebo-controlled food challenge (DBPCFC). This is a deficiency of the protocol. The study is based on investigation of prick test, serology and DBPCFC based on different doses of wheat starch hydrolysates (0.9/7/20 g) of glucose syrup, maltodextrin and placebo. Clinical evaluation is appropriate. However, the study protocol seems preliminary. It is not stated how many children and adults shall be included. Twenty sera from wheat allergic patients and ten sera from pollen allergic and ten sera from non-atopic controls are proposed to enter the serological part of the study. Provided diagnosis at study entry is based on DBPCFC and provided that the decisive DBPCFC part of the study can be carried out appropriately (Taylor *et al.*, 2004), conclusive information can be expected from the study outline given.

CONCLUSIONS AND RECOMMENDATIONS

1. Wheat-based maltodextrins may contain low levels of proteins, peptides or fragments thereof. It is not known at which levels of intake wheat-based maltodextrins would cause allergic reactions in cereal allergic individuals. Based on the data provided by the applicant the Panel is unable to predict the likelihood of adverse reactions in cereal allergic individuals. Nevertheless, taking into account the levels of wheat proteins reported to cause allergic reactions in severe allergic individuals, the Panel considers that it is not very likely that this product will cause a severe allergic reaction in the majority of cereal allergic individuals. More clinical information is needed with regard to the effects of wheat-based maltodextrins in cereal allergy. Appropriate clinical studies applying best clinical and laboratory practice should be carried out.

2. For coeliac disease, assessment of the evidence produced indicates that wheat-based maltodextrins are unlikely to cause an adverse reaction in individuals with coeliac disease provided that the provisional value of gluten considered by Codex Alimentarius for foods rendered gluten-free (currently 200 mg/kg) is not exceeded.

DOCUMENTATION PROVIDED TO EFSA

Dossier submitted by Association des Amidonneries de Céréales de l'Union européenne (AAC) to the European Commission pursuant to Article 6 paragraph 11 of Directive 2000/13/EC as amended by Directive 2003/89/EC, 14 June 2004.

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ACKNOWLEDGEMENT

The Scientific Panel on Dietetic Products, Nutrition and Allergies wishes to thank Elide Pastorello, Martin Stern, and Jean-Michel Wal for their contributions to the draft opinion.