European Food Safety Authority

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SCIENTIFIC OPINION

Inability to assess the safety of calcium-enriched yeast added for nutritional purposes as a source of calcium in food supplements, based on the supporting dossiers [1]

Scientific Statement of the Panel on Food Additives and Nutrient Sources added to Food (ANS)

(Question No EFSA-Q-2005-096, EFSA-Q-2005-200)

Adopted on 4 June 2009

PANEL MEMBERS

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[1] For citation purposes: Scientific Statement of the Panel on Food Additives and Nutrient Sources added to Food on the inability to assess the safety of calcium-enriched yeast added for nutritional purposes as a source of calcium in food supplements, based on the supporting dossiers, following a request from the European Commission. *The EFSA Journal* (2009) 1119, 1-7.

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The European Community legislation lists nutritional substances that may be used for nutritional purposes in certain categories of foods as sources of certain nutrients.

The Commission has received a request for the evaluation of calcium-enriched yeast added for nutritional purposes to food supplements. The relevant Community legislative measure is:

- Directive 2002/46/EC of the European Parliament and of the Council on the approximation of the laws of the Member States relating to food supplements[2].

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority to provide a scientific opinion, based on its consideration of the safety and bioavailability of calcium-enriched yeast added to food supplements.

[2] OJ L 183, 12.7.2002, p.51.

STATEMENT

1. Introduction

Following a request from the European Commission to the European Food Safety Authority (EFSA), the Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to provide a scientific opinion on the safety of calcium-enriched yeast added for nutritional purposes as a source of calcium in food supplements and on the bioavailability of calcium from this source.

This statement is based on the information on calcium-enriched yeasts provided by two petitioners.

2. Summary of the information provided in the supporting dossiers on calcium-enriched yeasts

Calcium-enriched yeasts are derived from cultures of specified strains of *Saccharomyces cerevisiae* grown in the presence of calcium chloride. Fermentation takes place at a specified temperature and pressure for defined periods of time. This is followed by increasing the temperature to kill the yeast. The cell wall is ruptured enzymatically to release the contents which are then spray dried.

According to one of the petitioners, calcium in calcium-enriched yeast is naturally integrated by the growing yeast into its own structure and occurs, therefore, in the way calcium would be present in any food material. The other petitioner described calcium-enriched yeast as "a complex of proteins, peptides and amino acids, resulting from the hydrolysis of *Saccharomyces cerevisiae*, which are bound to calcium".

One of the petitioners states that during fermentation in the presence of calcium, a specific strain of *Saccharomyces cerevisiae* produces specific calcium compounds, the metabolic fate and the biological distribution of which are similar to those of other sources of calcium in the diet.

No specific chemical identity (name, CAS Registry Number, molecular weight) was provided by either petitioner, and the two petitioners name their products differently. One of the petitioners stated that "the integration will be chemically multi-formatted by the organism and therefore, its chemical name, formula, chemical family and CAS Registry Number is undefined".

The analytical techniques which have been used to characterise the formation of a bound calcium-yeast complex are Fourier Transform Infrared (FTIR) Spectroscopy, a comparative elemental analysis for carbon, hydrogen, and nitrogen (C:H:N analysis) and X-ray Photoelectron Spectroscopy (XPS).

Chemical and microbiological specifications have been provided by both petitioners. Calcium-enriched yeast is described by one of the petitioners as a cream powder, and as an off-white powder by the other. Both petitioners describe the source as soluble in water. The total content of calcium in the products from the different petitioners is in the range of 5-5.8%. The remaining 95% of the material is made up of enzymatically-ruptured yeast cells.

The manufacturing process was described in detail by one petitioner and more briefly by the other.

Calcium-enriched yeast was stated by the petitioners to be used as an ingredient in tablets, caplets, capsules, chewable tablets, effervescent powders and liquids that are food supplements. Calcium-enriched yeast is described by one petitioner as used in a tablet product, which contains 60 mg of calcium, of which 5 mg is from calcium-enriched yeast. The proposed daily intake of this product is 2-6 tablets, resulting in a maximum calcium daily intake of 360 mg, of which 30 mg of calcium is derived from calcium-enriched yeast. The other petitioner indicates that the supplements containing calcium-enriched yeast are intended to provide in the range of 4-65 mg calcium/day.

The petitioners state that calcium from calcium-enriched yeasts is more bioavailable than calcium from other sources, and is absorbed in the gut in a similar way as calcium from food.

Some studies comparing the absorption of calcium-enriched yeast with other sources of calcium (unpublished Vinson, 1986; Vinson *et al.*, 1987) were provided by one of the petitioners. Vinson (1986, unpublished) reported a study comparing calcium absorption from three different calcium sources (calcium carbonate, calcium gluconate and calcium-enriched yeast). The sources were administered sequentially to the subjects (18-29 years old, n= 8) as a single dose containing 500 mg of calcium. Calcium-enriched yeast was administered to all eight subjects, while calcium carbonate and calcium gluconate were administered to four of the eight subjects, respectively. Calcium excretion was then measured over a 24-hour period post-dosing, using a 24-hour urine sample. The authors concluded that calcium from calcium-enriched yeast was more efficiently absorbed than calcium from either calcium carbonate or calcium gluconate, as judged by higher urinary excretion of calcium following administration of calcium-enriched yeast than after the other two sources.

In another similar study, Vinson *et al.* (1987) compared the bioavailability of calcium from calcium gluconate and from calcium-enriched yeast, by measuring calcium excretion over a 24-hour period post-dosing, using a 24-hour urine sample. The two sources were administered sequentially to the same group of four male volunteers (20-29 years old), using a one-week wash out period between the first and the second treatment. The authors reported a greater-than three-fold increase in calcium excretion over a 24-hour period when calcium-enriched yeast was given, compared with when calcium gluconate was given.

Based on these studies, the petitioner claims that calcium from calcium-enriched yeast is more bioavailable than calcium from inorganic calcium salts or calcium amino acid chelates. A-description of the specifications of the calcium-enriched yeast used in the studies of Vinson *et al.* has been provided by this petitioner.

No toxicological data were provided on calcium-enriched yeasts.

3. Assessment

The Panel notes that *Saccharomyces cerevisiae* has a qualified presumption of safety (EFSA, 2008) but considers that this presumption of safety might not be applicable to the specific conditions of culture of the yeasts in the presence of a high quantity of calcium.

According to one of the petitioners, fermentation in the presence of calcium chloride within eukaryotic cells will produce calcium compounds not otherwise defined, but with a metabolic fate and biological distribution similar to those of other sources of calcium in the diet.

According to the same petitioner, the difference in the C:H:N ratio between the starter yeast and the calcium-enriched yeast supports the hypothesis that changes within the yeast due to

the incorporation of calcium into the internal structure of the yeast may have modified the overall composition of the yeast. However, the Panel considers that the C:H:N analysis is not relevant to compare the starter yeast and the calcium-enriched yeast and that such a difference in the C:H:N ratio would not in any case provide a clear evidence of incorporation of calcium or change in the structure of the yeast.

The same petitioner also stated that the XPS spectra submitted suggest ionic bonding, with the calcium ions showing an oxidation state of calcium (Ca^{2+}). The Panel considers that the XPS spectra provided can give some information on the crystallinity of calcium-enriched yeast, but do not provide a significant contribution to its chemical characterisation.

According to the other petitioner, the differences between the FTIR spectra of calcium-enriched yeast and the starter yeast reference spectrum suggest changes in composition and structure within the yeast. The Panel considers that the FTIR spectra provided do not demonstrate the existence of coordinate bonds between calcium and the yeast biomass.

According to the petitioners calcium-enriched yeast is safe. Although not explicitly stated in the dossiers the argument for the safety of calcium-enriched yeast appears to be based on calcium being a normal constituent of the diet, and the long history of use of *Saccharomyces cerevisiae* in fermented food and beverages. The assumption is that provided there is no overload of normal metabolic pathways, fermentation within eukaryotic cells will produce calcium compounds with a metabolic fate and biological distribution similar to those of other sources of calcium in the diet.

The Panel considers that the petitioners have insufficiently chemically characterised their products and therefore have not demonstrated that calcium from calcium-enriched yeast has a metabolic fate and biological distribution similar to that of other sources of calcium in the diet.

The Panel notes that both petitioners have stated that calcium from calcium-enriched yeast is bioavailable and is absorbed in the gut in a similar way as calcium from food; while one petitioner states that calcium from calcium-enriched yeast is more bioavailable than calcium from inorganic calcium salts or calcium amino acid chelates. Studies in human volunteers, comparing the absorption of calcium-enriched yeast with other sources of calcium (unpublished Vinson, 1986; Vinson *et al.*, 1987), have shown a higher urinary excretion of calcium in the 24 hours after administration of calcium-enriched yeast than after administration of calcium gluconate or calcium carbonate. This finding was interpreted by the authors as providing evidence of greater bioavailability of calcium from the enriched yeast product, and the Panel concurs with this interpretation.

Based on the information provided by one of the petitioners, the Panel notes that the calcium-enriched yeast used in the Vinson studies (unpublished Vinson, 1986; Vinson *et al.*, 1987) appears to be similar to one of the calcium-enriched yeasts under consideration in this statement. The Panel therefore concludes that calcium could be expected to be bioavailable from this calcium-enriched yeast. In the absence of further information from the other petitioner, the Panel is unable to extrapolate this conclusion on bioavailability to the other calcium-enriched yeast under consideration.

The Panel notes that neither safety data nor suitable supporting references were provided to support the assumption of safety of the calcium-enriched yeasts under consideration.

CONCLUSIONS

The Panel concludes that calcium could be expected to be bioavailable from one of the calcium-enriched yeast under consideration. The Panel concluded that the bioavailability of the other calcium-enriched yeast cannot be assessed due to the lack of an appropriate dossier.

The Panel also concludes that due to the lack of appropriate dossiers supporting the use of calcium-enriched yeast in food supplements, the safety of the calcium-enriched yeasts under consideration cannot be assessed.

Key words:

Food supplements, calcium, calcium chloride, yeast-transformed calcium, calcium-enriched yeast.

DOCUMENTATION PROVIDED TO EFSA

1. Technical dossier, 2005a. Dossier on calcium-enriched yeast (calcium-enriched *Saccharomyces cerevisiae*) proposed for addition to Annex II of Directive 2002/46/EC of the European Parliament and of the Council Relating to Food Supplements. March 2005. Submitted by Nature's Own Limited, UK.
2. Technical dossier, 2005b. Dossier on Bio-transformed calcium proposed for addition to Annex II of Directive 2002/46/EC of the European Parliament and of the Council Relating to Food Supplements. Original submission June 2005; revised versions January 2008 and November 2008. Submitted by Higher Nature Ltd, UK.

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GLOSSARY / ABBREVIATIONS

ANS	Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS)
CAS	Chemical Abstracts Service
EC	European Commission
EFSA	European Food Safety Authority
FTIR	Fourier Transform Infra Red
XPS	X ray Photoelectron Spectroscopy