European Food Safety Authority

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SCIENTIFIC OPINION

Assessment of the safety of vanadium-enriched yeasts added for nutritional purposes as a source of vanadium in food supplements and the bioavailability of vanadium from vanadium-enriched yeasts [1]

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

(Question No EFSA-Q-2005-171, EFSA-Q-2005-190)

Adopted on 13 May 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 assessment of the safety of vanadium-enriched yeast added for nutritional purposes as a source of vanadium in food supplements and the bioavailability of vanadium from vanadium-enriched yeasts following a request from the European Commission. *The EFSA Journal* (2009) 1084, 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 vanadium-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 vanadium-enriched yeast added for nutritional purposes 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 vanadium-enriched yeast added for nutritional purposes as a source of vanadium in food supplements and on the bioavailability of vanadium from this source.

This statement is based on the information on vanadium-enriched yeast provided by two petitioners.

2. Summary of the information provided in the supporting dossiers on vanadium-enriched yeast

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

Vanadium-enriched yeast has no specific chemical identity (name, CAS No., molecular weight) but is chemically defined in terms of its vanadium content, following culture of the yeast in the presence of ammonium vanadium oxide or ammonium vanadate. Both petitioners state that the vanadium content is not attributable to residual amounts of the vanadium sources, but to vanadium incorporated into the biological matrix of the yeast cell. One petitioner describes the vanadium to be 96.5 - 99.5% in the organic form, as determined by washing but neither petitioner provides further details on the nature of the incorporated vanadium.

Vanadium-enriched yeast is described by the petitioners as an off-white to tan powder with characteristic yeast odour. Both petitioners provided various data on the chemical and microbiological specifications for vanadium-enriched yeast. The petitioners indicate a vanadium content ranging from 1.0 to 1.2% of the source. The remaining is made up of enzymatically ruptured yeast cells. The loss on drying and the ash content are reported by both petitioners. Microbiological specifications are provided by both petitioners, but specifications for cadmium, lead and arsenic were only provided by one petitioner.

Additional information is given on the analytical methods used for the identification and characterisation of the source, its purity and the residual impurities of the end product. However, information on the chemical characterisation of the fermentation complexes was not provided. The petitioners also provided Fourier Transform Infrared Spectroscopy (FTIR) analysis spectra of samples of the starter yeast (as reference) and the vanadium-enriched yeast. A comparative elemental analysis for carbon, hydrogen, and nitrogen (C:H:N analysis) of the starter yeast and the vanadium-enriched yeast was provided by one petitioner.

The manufacturing process is adequately described by one of the petitioners. The other petitioner provided only brief details of the manufacturing process.

Analytical methods for analysis of vanadium-enriched yeast are based on determination of total vanadium by Atomic Absorption Spectroscopy (AAS).

The petitioners report that vanadium-enriched yeasts are stable in foods and food supplements for a minimum of three years, although no data were provided to support this statement by one petitioner.

One petitioner describes several products containing vanadium-enriched yeast, providing an intake of between 30 and 99 µg vanadium/day. According to the other petitioner, vanadium-enriched yeast is incorporated into supplements at levels providing a daily intake of vanadium between 5 µg and 25 µg.

No data were provided by either petitioner on the bioavailability of vanadium from vanadium-enriched yeast, other than a statement provided by one petitioner that vanadium from vanadium-enriched yeast "is more bioavailable than the vanadium source" (ammonium vanadium oxide) provided to the yeast strain during the production process. According to this petitioner, the metabolic fate and biological distribution of vanadium-enriched yeast is expected to be similar to that of other sources of vanadium in the diet, but no specific data were provided by either petitioner.

No toxicological data were provided on the vanadium-enriched yeasts under consideration.

One petitioner provided an overview of toxicity studies, including genotoxicity studies, on sodium metavanadate, sodium orthovanadate ammonium vanadate, vanadyl sulphate, bismaltolato oxo vanadium and vanadium pentoxide. The other petitioner states that no adverse evidence is available for vanadium-enriched yeast as part of the food chain. In relation to the yeast component of the source, one petitioner states that there is a long history of use of *Saccharomyces cerevisiae* in food preparation, and that *Saccharomyces cerevisiae* and the spent medium it is grown in is an approved animal feedstuff, with no observable toxic effects even at very high levels. The other petitioner notes that to the best of their knowledge, vanadium-enriched yeast has no impact on the intestinal milieu, and that since the yeast does not contain live yeast cells there is no risk of digestive colonisation following ingestion of a supplement containing vanadium-yeast.

3. Assessment

Vanadium-enriched yeasts are derived from cultures of specified strains of *Saccharomyces cerevisiae* in the presence of natural substrates and a source of vanadium (ammonium vanadium oxide or ammonium vanadate). The Panel notes that *Saccharomyces cerevisiae* has a qualified presumption of safety (EFSA, 2008a) 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 vanadium.

According to the petitioners, vanadium-enriched yeasts are safe. Although not explicitly stated in the dossiers, the argument for the safety of vanadium-enriched yeast appears to be based on vanadium 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 organic vanadium compounds, not further defined but with a metabolic fate and biological distribution similar to that of other sources of vanadium in the diet.

Further characterisation of the fermentation product was not provided.

One of the petitioners stated that the identification of the source may be ascertained by several fingerprinting parameters that include amino acid profiling and elemental analysis. According to this petitioner, the difference in the C:H:N ratio between the starter yeast (9.8:1.5:1) and the vanadium-enriched yeast (9.7:1.5:1) supports the hypothesis that changes within the yeast due to vanadium incorporation into the internal structure of the yeast may have modified the overall composition of the yeast. However, the Panel considers that such a difference in the C:H:N ratio would not in any case provide a clear evidence of vanadium incorporation or change in the structure of the yeast.

Both of the petitioners stated that the differences between the FTIR spectra of vanadium-enriched yeasts and the starter yeast reference spectrum suggest changes in composition and structure within the yeast. The Panel considers that the FTIR spectra do not demonstrate the existence of coordinate bonds between vanadium and the yeast biomass.

The Panel concludes that both petitioners have insufficiently chemically characterised the products and therefore have not demonstrated that vanadium from vanadium-enriched yeast has a metabolic fate and distribution similar to those of other sources of vanadium in the diet.

No data were provided by either petitioner on the bioavailability of vanadium from vanadium-enriched yeast. According to one petitioner, vanadium from vanadium-enriched yeast is more bioavailable than from ammonium vanadium oxide provided to the yeast strain during the manufacturing process. The Panel notes that it is not possible to assess the bioavailability of vanadium from vanadium-enriched yeast since neither data nor suitable supporting references were provided.

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

The Panel notes the conclusion of the EFSA Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) that a No Observed Adverse Effect Level (NOAEL) could not be derived from the available studies on vanadium compounds, neither from subacute/subchronic studies, in which adverse effects were observed on kidneys, spleen, lungs and blood pressure, nor from studies, in which developmental toxicity was seen in the offspring of rats. Therefore, a Tolerable Upper Intake Level (UL) for vanadium could not be derived (EFSA, 2004). The conclusions of the NDA Panel were based on the toxicity of the vanadium sources vanadyl sulphate, vanadium pentoxide, ammonium monovanadate and some other vanadium compounds.

The NDA Panel also concluded that vanadium has not been shown to be essential for humans.

The ANS Panel considers that these conclusions are relevant, not only for vanadium itself, but also for the vanadium sources (enriched yeasts) under consideration in the present opinion.

CONCLUSIONS

The Panel concludes that the safety of vanadium-enriched yeasts and the bioavailability of vanadium from these sources cannot be assessed on the basis of the dossiers supporting the use of vanadium-enriched yeasts in food supplements.

However, the Panel considers that the conclusions and risk characterisation in the opinion of the NDA Panel on vanadium (EFSA, 2004), based on the toxicity of the vanadium sources vanadyl sulphate, vanadium pentoxide, ammonium monovanadate and some other vanadium

compounds, are relevant, not only for vanadium itself, but also for the vanadium sources (vanadium-enriched yeasts) under consideration in the present opinion.

Key words:

Vanadium, ammonium vanadium oxide, ammonium vanadate, vanadium-enriched yeast, yeast, food supplements.

DOCUMENTATION PROVIDED TO EFSA

1. Technical dossier, 2005a. Bio-transformed Vanadium Proposed for Addition to Annex II of Directive 2002/46/EC of the European Parliament and of the Council Relating to Food Supplements. Submitted by Higher Nature Ltd UK. Original submission June 2005. Additional information submitted January 2008 and October 2008.
2. Technical dossier, 2005b. A request for consideration of the addition of Vanadium-enriched yeast (Vanadium-enriched *Saccharomyces cerevisiae)* to Annex II of the Food Supplements Directive (2002/46/EC). Submitted by Nature's Own Limited, UK. Original submission June 2005.

REFERENCES

EFSA (European Food Safety Authority), 2004. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Level of Vanadium. *The EFSA Journal* (2004) 33, 1-22.

EFSA (European Food Safety Authority), 2008. Opinion of the Scientific Panel on Biological Hazards on the maintenance of the list of QPS microorganisms intentionally added to food or feed. *The EFSA Journal* (2008) 923, 1-48.

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GLOSSARY / ABBREVIATIONS

AAS	Atomic Absorption Spectroscopy
ANS	Scientific Panel on Food Additives and Nutrient Sources added to Food (ANS)
AFC	Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food
CAS	Chemical Abstracts Service
EC	European Commission
EFSA	European Food Safety Authority
FTIR	Fourier Transform Infra Red
NDA	Scientific Panel on Dietetic Products, Nutrition and Allergies
NOAEL	No Observed Adverse Effect Level