European Food Safety Authority

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SCIENTIFIC OPINION

Calcium phosphinate as a source of calcium added for nutritional purposes to food supplements[1]

Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food

(Question No EFSA-Q-2006-279)

Adopted on 6 April 2009

PANEL MEMBERS

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SUMMARY

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

The present opinion deals only with the safety of calcium phosphinate as a source of calcium and the bioavailability of calcium from this source. The safety of calcium itself, in terms of amounts that may be consumed, is outside the remit of this Panel.

Calcium phosphinate should be used according to the petitioner as a mineral supplement in a liquid and a solid form for oral administration.

The petitioner mentioned reports in the literature on the elimination of phosphinate, according to which there is no metabolism of the anion (phosphinate).

[1] For citation purposes: Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food on calcium phosphinate as a source of calcium added for nutritional purposes to food supplements following a request from the European Commission. *The EFSA Journal* (2009) 1054, 1-11.

The bioavailability of calcium from calcium phosphinate is likely to be similar to that of calcium from other soluble sources.

Based on the proposed daily supplementation of up to 2500 mg/day for the use of calcium phosphinate in liquid and solid form, the Panel calculated an exposure to 589 mg calcium/day and 1911 mg phosphinate/day, the latter corresponding to 32 mg phosphinate/kg bw/day for a 60 kg person.

To evaluate the toxicity of the anion (phosphinate), the petitioner selected sodium phosphinate as reference substance, but only reported data on the acute toxicity in rats and mice. Further toxicity data on phosphinate were not provided.

The Panel concludes that due to the lack of toxicological data on phosphinate, the safety of calcium phosphinate as a source of calcium cannot be assessed.

Key words:

Food supplements, calcium phosphinate, CAS Registry Number 7789-79-9.

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BACKGROUND AS PROVIDED BY THE 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 phosphinate 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 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 phosphinate added for nutritional purposes in food supplements.

ACKNOWLEDGEMENTS

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

ASSESSMENT

1. Introduction

The present opinion deals only with the safety of calcium phosphinate as a particular source of calcium to be used in food supplements and the bioavailability of calcium from this source.

The safety of calcium itself, in terms of amounts that may be consumed, is outside the remit of this Panel.

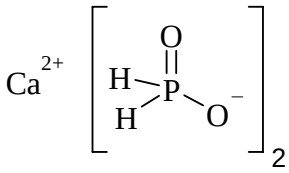
2. Technical data

2.1. Chemistry

Calcium phosphinate is an inorganic compound with a CAS Registry Number 7789-79-9.

Synonyms are calcium hypophosphite, phosphinic acid calcium salt, calcii phosphinas, calcium phosphinicum, calcium hypophosphorosum.

The molecular weight of calcium phosphinate is 170.1 g/mol, the formula is $Ca(PH_2O_2)_2$ and the molecular structure is presented below.



Phosphinate does not seem to occur in nature.

2.2. Specifications

The petitioner indicates that calcium phosphinate is available in two forms, in a solid as well as in a liquid form. Calcium phosphinate contains at least 98.0 % and not more than 100.5% $Ca(PH_2O_2)_2$ (Deutscher Arzneimittel-Codex, 2000). Calcium phosphinate is a colourless, shiny crystal or a white, crystalline powder; almost odourless.

The purity test is conducted in accordance with the Deutscher Arzneimittel-Codex, 1997. An additional purity determination method is undertaken using Atomic Absorption spectroscopy. This method allows quantitative detection of all metals and also phosphorus (Holleman *et al.*, 1985).

The pH value (50 g/L in H_2O) is 6.7-7.5.

Thermal decomposition occurs at temperatures > 300 ^oC.

Specifications provided by the petitioner include lead, silver, mercury, copper, iron and cobalt < 20 ppm and arsenic < 10 ppm. Calcium phosphinate is easily soluble in water, slightly soluble in glycerol (85%) and practically insoluble in ethanol and diethyl ether (DAC, 1997).

The Panel notes that according to Commission Regulation (EC) No 629/2008, the maximum levels of lead, mercury and cadmium in food supplements as sold should be 3.0 mg/kg, 0.1 mg/kg and 1 mg/kg, respectively.

2.3. Manufacturing process

The petitioner indicates that for reasons of patent law, the company has until now not been supplied with any information about the manufacture and the corresponding process controls of calcium phosphinate.

No further details on the manufacturing process of calcium phosphinate have been provided by the petitioner.

2.4. Methods of analysis in food

The petitioner indicates that the analytical method available for the determination of calcium phosphinate is described in the DAC (2000), and is based on redox titration.

Quantitative analysis is carried out by determining the calcium in the finished product via Atomic Absorption (AA) spectroscopy (SALUS). Determination of the anion would only be possible to a limited extent, since phosphorus compounds occur in foodstuffs and dietary supplements in many and varied forms and interfere with the determination. For this reason, the petitioner argued that a phosphinate determination is not conducted.

The petitioner indicates that from the technological point of view it can be assumed that calcium phosphinate – due to the manufacturing process - is present in the finished product in the desired concentration.

A method for analysis of phosphinate in food was not provided by the petitioner.

2.5. Reaction and fate in foods to which the source is added

The petitioner refers to a wide variety of reports on the stability of calcium phosphinate preparations used in food supplements (Prugnaud, 1973; Zuniga, 1975; Gregoire and Mouls, 1971).

The petitioner indicates that there is no known negative effect on foodstuffs due to the addition of calcium phosphinate.

Because of the almost neutral pH-value (pH = 6.7 – 7.5) of calcium phosphinate solutions, the petitioner does not expect any negative effect on the intestinal milieu in humans, nor any effect on the absorption of other nutrients.

2.6 Case of need and proposed uses

According to the petitioner commercially available calcium mineral preparations usually contain calcium gluconate, calcium lactate, calcium lactogluconate and especially calcium carbonate.

The petitioner indicated that calcium phosphinate should be used as a mineral supplement for the supportive and preventive treatment of calcium deficiency because of its good solubility and bioavailability (Gregoire and Mouls, 1971).

The petitioner intends to use calcium phosphinate liquid and solid form for oral administration.

The petitioner proposed a dose of up to 2500 mg/day for the use of calcium phosphinate in liquid and solid form.

2.7. Information on existing authorisations and evaluations

For calcium, in 1993 the SCF established the Population Reference Intakes (PRI) of 700 mg/day (range 400-1200 mg/day depending on age and physiological status (SCF, 2003). More recent reports (IOM, 1997; D-A-CH, 2000; AFSSA, 2001) include the attainment of peak bone mass during childhood, adolescence and young adulthood in their calculations. The Adequate Intakes (AI) and recommended daily intakes (RDA) thus derived are generally higher than the PRI. They are between 500 and 800 mg calcium per day for children up to the age of 7 years, 1200 to 1300 mg per day for older children and adolescents and 900 to 1200 mg calcium per day for adults.

The SCF allocated a Tolerable Upper Intake Level (UL) of 2500 mg calcium/person/day as a nutrient (SCF, 2003).

2.8 Exposure

The petitioner proposed a daily dose of up to 2500 mg/day for the use of calcium phosphinate in liquid and solid form. Such a supplementation would give a calculated exposure to 589 mg calcium/day and 1911 mg phosphinate/day, the latter corresponding to32 mg phosphinate/kg bw/day for a 60 kg person.

Since phosphinate is not naturally occurring in the diet there is no additional exposure from that source.

3. Biological and toxicological data

3.1. Absorption, distribution, metabolism and excretion

Calcium phosphinate is a salt, which is present in almost completely dissociated form in the aqueous milieu. Therefore, the petitioner gives a separate toxicological evaluation of the anion and the cation.

The petitioner mentioned reports in the literature on the elimination of phosphinate, according to which there is no metabolism of the anion (phosphinate) which is eliminated exclusively via renal excretion (Rhodehamel *et al,* 1990).

3.2 Toxicological data

To evaluate the toxicity of the anion (phosphinate), the petitioner selected sodium phosphinate as reference substance.

The petitioner reported an LD_{50} of 7.64 g/kg bw in rats (EG Safety Data Sheet, 2005). The petitioner also indicated that mice injected intraperitoneally with sodium phosphinate demonstrated an LD_{50} of 1.6 g/kg bw (Rhodehamel *et al,* 1990).

No other toxicological data were provided by the petitioner.

4. Discussion

The Panel noted that calcium phosphinate is easily soluble in water. Calcium phosphinate is expected to dissociate before absorption and to be readily absorbed in the intestine. The Panel concludes that the bioavailability of calcium from calcium phosphinate is similar to that of calcium from of other soluble sources.

The petitioner mentioned reports in the literature on the elimination of phosphinate, according to which there is no metabolism of the anion (phosphinate) which is eliminated mainly via renal excretion (Rhodehamel *et al,* 1990). However, the toxicological data reported in this review (intraperitoneally LD50s value of 1600 mg/kg bw with sodium hypophosphite) did not allow to characterize the hazard of phosphinate.

The petitioner proposed a daily dose of up to 2500 mg/day for the use of calcium phosphinate in liquid and solid form. Such a supplementation would give a calculated exposure to 589 mg calcium/day and 1911 mg phosphinate/day, the latter corresponding to 32 mg phosphinate/kg bw/day for a 60 kg person.

Since phosphinate is not naturally occurring in the diet there is no additional exposure from that source.

CONCLUSIONS

The present opinion deals only with the safety of calcium phosphinate as a particular source of calcium and the bioavailability of calcium from this source added for nutritional purposes to food supplements.

Calcium phosphinate is easily soluble in water and is expected to dissociate before absorption in the intestine. The bioavailability of calcium from calcium phosphinate is likely to be similar to that of calcium from other soluble calcium sources.

The Panel concludes that due to the lack of adequate toxicological data on phosphinate, the safety of calcium phosphinate as a source of calcium cannot be assessed.

DOCUMENTATION PROVIDED TO EFSA

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GLOSSARY / ABBREVIATIONS

AI	Adequate Intake
ANS	Scientific Panel on Food Additives and Nutrient Sources added to Food
bw	body weight
CAS	Chemical Abstract Service
EC	European Commission
EFSA	European Food Safety Authority
IOM	Institute of Medicine
NOAEL	No-Observed-Adverse-Effect Level
RDA	Recommended Daily Intake
SCF	Scientific Committee on Food
UL	Tolerable Upper Intake Level