Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and materials in Contact with Food on a request from the Commission related to

Calcium Sulphate as a mineral substance in foods intended for the general population

Question N° EFSA-Q-2003-237

Adopted on 7 October 2004

SUMMARY

The Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food has been asked to evaluate the use of calcium sulphate as a mineral substance in foods intended for the general population.

Calcium sulphate is an approved food additive (E 516). It was evaluated by the Scientific Committee on Food in 1990 and was allocated an Acceptable Daily Intake not specified.

In December 2003 the Panel evaluated the use of calcium sulphate added for specific nutritional purposes in foods for particular nutritional uses and concluded that this use is not of concern from the safety point of view.

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The petitioner’s proposed use is in water and water based beverages. The intake of calcium sulphate from this proposed use is estimated to be from 531mg (375 mg of sulphate and 156 mg of calcium) to 1062 mg (750 mg of sulphate and 312 mg of calcium) per person per day. This intake is well below the tolerable upper intake level of 2500 mg/person/day for calcium established for adults by the SCF in 2003. The Panel does not anticipate that the additional intake of sulphate in waters would result in any adverse effects.

If calcium sulphate was to be used as a mineral substance in foods other than water and water based beverages a “worst case” scenario would be that the intake of calcium from calcium sulphate could approach the tolerable upper intake level of 2500 mg calcium per person per day proposed by the SCF, corresponding to an intake of about 8000 mg calcium sulphate per person per day, which would mean a daily intake of about 6000 mg
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sulphate ion per person. High bolus intakes of sulphate ion may lead to gastrointestinal discomfort in some individuals.

In human studies the bioavailability of calcium from calcium sulphate in mineral waters is comparable to that from milk and the sulphate anion does not affect the urinary excretion of calcium. Although no studies were available in humans, based on animal studies the bioavailability in humans of calcium from calcium sulphate in other foods is not expected to differ from that of already permitted calcium sources in foods for particular nutritional uses.

The Panel concluded that use of calcium sulphate as a mineral substance in foods intended for the general population is not of safety concern.

KEY WORDS
Calcium sulphate; E 516; CAS Registry number: 7778-18-9; CAS Registry number: 10101-41-4

BACKGROUND
Calcium sulphate as a source of calcium added for specific nutritional purposes in foods for particular nutritional uses has been evaluated by the European Food Safety Authority (EFSA) Scientific Panel on Food Additives, Flavourings, Processing Aid and Materials in Contact with Food. In its opinion of December 10, 2003 the Panel concluded that calcium sulphate, as a source of calcium for use in foods for particular nutritional purposes was not of concern from the safety point of view (EFSA, 2003).

The European Community legislation on foods for particular nutritional uses and food supplements specify for certain categories of nutritional substances the substances that may be added for nutritional purposes. In November 2003 the European Commission adopted a legislative proposal that would harmonised the addition of vitamins and minerals to foods in general. In the course of the discussion concerning the proposal the Commission was asked to include calcium sulphate as a nutrient source in the proposal.

TERMS OF REFERENCE
The European Commission requests that the European Food Safety Authority extend the evaluation of calcium sulphate in foods for particular nutritional uses to the use of calcium sulphate as a mineral substance in foods intended for the general population.
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ASSESSMENT
The use of calcium sulphate as a mineral substance in foods intended for the general population is not anticipated to differ significantly from the use of calcium sulphate added for specific nutritional purposes in foods for particular nutritional uses and from the use as a food additive. Therefore the assessment makes use of and reiterates parts of the previous assessment made by the panel on the use of calcium sulphate in foods for particular nutritional uses.

CHEMISTRY
Calcium sulphate, the calcium salt of sulphuric acid appears in two forms: as anhydrite with a chemical formula CaSO$_4$, molecular mass of 136.14 and CAS Registry Number 7778-18-9 or as a dihydrate with the chemical formula CaSO$_4$$ \cdot$2H$_2$O, a molecular mass of 172.18 and CAS Registry Number 10101-41. It exists either as odourless white crystals or crystalline powder. When dissolved both salts dissociate to calcium and sulphate ions. Calcium sulphate is of limited solubility in water. The following evaluation covers both calcium sulphate and calcium sulphate dihydrate.

SPECIFICATIONS
According to the petitioner, the purity criteria for calcium sulphate, as shown by the analysis of calcium sulphate dihydrate, comply with the specifications for the substance used as a food additive (E 516) in Commission Directive 2000/63/EC amending Directive 96/77/EC laying down specific purity criteria on food additives other than colours and sweeteners, with JECFA specifications (JECFA, 1975), and with those of the European Pharmacopoeia (third edition) (Ph. Eur.3, 1996).

CASE OF NEED AND PROPOSED USES
According to the petitioner, calcium sulphate is one of the three soluble inorganic compounds able to enrich drinks with calcium. Two other salts are calcium carbonate and calcium chloride. Calcium carbonate and calcium sulphate are of limited solubility in water. Use of a well-balanced mixture of these salts enables higher concentrations of calcium to be achieved in a product.

According to the petitioner, calcium sulphate is intended to be used in waters and water based beverages at a level of 354.2 mg/l providing 250 mg/l of sulphate and 104.2 mg/l of calcium. This level complies with the guidance level for sulphate in Directive 98/83/EC on drinking water. It is also in line with the WHO guidelines for water quality (1996) set on the taste perception threshold for sulphate by human beings.
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For comparison, the intended level of use is 4 to 5 times lower than that in certain natural mineral waters available on the marked in the European Union.

EXPOSURE

The intake of calcium sulphate from the proposed use can be estimated to be from 531mg (375 mg of sulphate and 156 mg of calcium) to 1062 mg (750 mg of sulphate and 312 mg of calcium) per person per day taking into account the level indicated by the petitioner and assuming that the normal daily water intake is 1.5 l to 3 l per person (25-50 ml per kg body weight for a person with a body mass of 60 kg) and that these drinks comprise the sole daily fluid intake. This intake is well below the tolerable upper intake level of 2500 mg for calcium established for adults by the SCF (SCF, 2003).

Although not the intention, as stated by the petitioner, it can not be excluded that calcium sulphate could be used as a mineral substance in foods other than water and water based beverages. In addition it may also be used as a food additive. As a “worst case” scenario, if intake of calcium from calcium sulphate approached the tolerable upper intake level of 2500 mg calcium per person per day corresponding to an intake of 8003 mg calcium sulphate per person per day this would amount to a daily intake of 6003 mg sulphate ion per person.

EXISTING AUTHORISATIONS AND EVALUATIONS

The use of calcium sulphate as a food additive was evaluated by SCF in 1990 and calcium sulphate was allocated an Acceptable Daily Intake (ADI) not specified (SCF, 1990). At that time the Committee evaluated several cations and anions and established a group ADI not specified, although extensive systematic toxicological studies have not been carried out with the individual ions. The Committee considered that these ions were constituents of the major electrolytes in all biological materials from animal and plant origin and therefore occurred naturally in foodstuffs. Therefore, the Committee was of the opinion that no safety problems were likely to arise, provided the contribution from food intake did not disturb the homeostatic mechanisms controlling the electrolyte balance of the body.

Calcium sulphate has also been evaluated by JECFA several times and allocated an ADI not specified. In the latest evaluation ADIs not specified were also allocated to the calcium and sulphate ions (JECFA, 1986). The sulphate ion has also been evaluated
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several times by JECFA in connection with its evaluation of sodium sulphate. In the latest evaluations an ADI not specified was allocated to sodium sulphate (JECFA 2000, 2002).

**TOXICOLOGICAL DATA**

No data on toxicological aspects were submitted.

In its evaluation of the sulphate ion, JECFA states, that the few available studies in experimental animals do not raise concern about the toxicity of sodium sulphate. Sodium sulphate is also used clinically as a laxative. In clinical trials using 2-4 single doses of up to 4500 mg sodium sulphate decahydrate per person (9000 – 18000 mg per person) only occasional loose stools were reported. These doses correspond to 2700 - 5400 mg sulphate ion. The sulphate absorbed remains in the extracellular fluid and is rapidly excreted via the kidneys (JECFA 2000, 2002).

In one study where sodium sulphate (18000 mg as the decahydrate) was administered orally to five human volunteers as either single doses corresponding to 8 g anhydrous salt (5400 mg sulphate ion) or as four equally divided hourly doses, the 72-hour urinary recovery of free sulphate was 53.4% and 61.8%, respectively. The single bolus doses produced diarrhoea while the divided doses caused only mild or no diarrhoea (Cocchetto and Levy 1981).

**ANIMAL DATA ON ABSORPTION OF CALCIUM FROM CALCIUM ENRICHED DIETS**

In order to compare bioavailability of calcium from different sources young male rats (7-10 animals/group) were fed *ad libitum* on a basal diet to which was added one of a number of calcium sources (carbonate, chloride, hydroxide, sulphate, oxide, lactate, acetate or propionate or yeast) to provide 0.25% calcium with a dietary Ca to P ratio of 1:2 for 4 consecutive weeks. Calcium seemed to be equally available from all sources based on growth response, efficiency of utilization of diet, apparent absorption of Ca, Ca in serum and Ca in femur (Ranhotra *et al*., 1980).

**HUMAN DATA ON ABSORPTION OF CALCIUM FROM CALCIUM-RICH MINERAL WATERS AND OTHER FOODS**

The bioavailability of calcium from mineral water containing calcium sulphate was studied in 15 lactose intolerant male individuals and compared to that from milk. In eight of 15 subjects, there was a higher level of calcium absorption from mineral water than from milk. Bioavailability was similar in five of 15 subjects. The bioavailability of
Calcium absorption from milk was greater than that from mineral water in two of 15 subjects (Harpern et al., 1991).

Calcium bioavailability from natural calcium and sulphate rich mineral water was compared with that from milk in nine healthy young women. Calcium absorption was measured in the fasting state with a dual-label stable isotope technique. Fractional absorption rates were $25.0 \pm 6.7\%$ (mean $\pm$ SD) from milk and $23.8 \pm 4.8\%$ ($p>0.05$) from mineral water. No significant difference was found in the excretion of calcium, or in the excretion of the two stable calcium isotopes. It was concluded that calcium from the calcium- and sulphate-rich mineral water was as well absorbed and retained as that from milk, and no calciuric effect of sulphate was found (Couzy et al., 1995).

No data were available on the bioavailability of calcium sulphate as a mineral substance in foods other than water and water based beverages. However, because absorption of calcium in the intestine requires that it is in a soluble form or bound to soluble organic molecules the bioavailability of calcium sulphate and calcium sulphate dihydrate is not expected to be significantly different from that of calcium chloride and calcium carbonate, respectively. Calcium chloride and calcium carbonate are already permitted as source of calcium in foods for particular nutritional uses and in food supplements.

**DISCUSSION**

A single feeding study in rats indicates no difference in calcium bioavailability from a diet with added calcium sulphate or other calcium sources.

The human studies indicate that the bioavailability of calcium from calcium sulphate in mineral waters is comparable to that from milk and that the sulphate anion does not affect the urinary excretion of calcium. Although human studies were not available, the bioavailability of calcium from calcium sulphate in other foods is not expected to differ from that of already permitted calcium sources in foods for particular nutritional uses.

The intake of calcium sulphate from the proposed use can be estimated to be from 531mg (375 mg of sulphate and 156 mg of calcium) to 1062 mg (750 mg of sulphate and 312 mg of calcium) per person per day. This intake is well below the tolerable upper intake level of 2500 mg/person/day for calcium established for adults by the SCF (2003). The Panel does not anticipate that the additional intake of sulphate in waters would result in any adverse effects.

If calcium sulphate is used as a mineral substance in foods other than water and water based beverages a “worst case” scenario would be that the intake of calcium from
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calcium sulphate could approach the tolerable upper intake level of 2500 mg calcium per person per day corresponding to an intake of 8003 mg calcium sulphate per person per day. This would amount to a daily intake of 6003 mg sulphate ion per person. JECFA states, that the few available studies in experimental animals do not raise concern about the toxicity of the sulphate ion in sodium sulphate. Sodium sulphate is used clinically as a laxative. In clinical trials using 2-4 single oral doses of up to 4500 mg sodium sulphate decahydrate per person (9000 – 18000 mg per person) only occasional loose stools were reported. These doses correspond to 2700 - 5400 mg sulphate ion per person. High bolus dose intake of sulphate ion may lead to gastrointestinal discomfort in some individuals.

Given the previous evaluations of the calcium and sulphate ions and calcium sulphate as a food additive (JECFA, 1986, 2002; SCF, 1990), a toxicological evaluation of calcium sulphate was not needed for the present opinion.

CONCLUSIONS AND RECOMMENDATIONS

The Scientific Panel on Food Additives, Flavourings, Processing Aids and Material in Contact with Food concluded calcium sulphate, as a mineral substance in foods intended for the general population is not of concern from the safety point of view.

DOCUMENTATION PROVIDED TO EFSA


Letter from the European Commission to the Chairman of the Scientific Committee on Food on “Evaluation of a number of substances added for specific nutritional purposes in foods for particular nutritional uses” dated 03/12/2002, Brussels. SCF/CS/ADD/NUT/50.

Additional submissions related with the dossier on calcium sulphate submitted by IDACE in February 2003:

- Letter Additional information on calcium sulphate: Answers to the questions 1,2, and 3 concerning the specification, intended use levels and intake estimates,
- Copy Chemische Fabrik Lehrte: Chemical analysis,
- Copy Specification Danone Group Beverages Ingredients, Mineral Salts, Appendices.

Additional submissions related with the dossier on calcium sulphate submitted by Danone-company in February 2003 consisting of the following scientific publications:
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- Calcium bioavailability from calcium- and sulphate-rich mineral water, compared with milk, in young adult women. Couzy, F. et al., 1995.
- Absorbability of the calcium in a high-calcium mineral water. Heaney, R.P. et al., 1994
- A release of the WHO dedicated to sulphates in general: Sulphate (without name of the author, date, publication details).

REFERENCES


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**SCIENTIFIC PANEL/COMMITTEE MEMBERS**
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