SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to molybdenum and contribution to normal amino acid metabolism (ID 313) and protection of DNA, proteins and lipids from oxidative damage (ID 341) pursuant to Article 13(1) of Regulation (EC) No 1924/2006[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to molybdenum and contribution to normal amino acid metabolism and protection of DNA, proteins and lipids from oxidative damage. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food constituent that is the subject of the health claims is molybdenum, which is a well recognised nutrient and is measurable in foods by established methods. The Panel considers that molybdenum is sufficiently characterised.

Contribution to normal amino acid metabolism

The claimed effect is "for amino acids (including uric acid) metabolism". The target population is assumed to be the general population. The Panel considers that contribution to normal amino acid metabolism is a beneficial physiological effect.

Molybdenum functions as a cofactor for some enzymes in humans, such as sulphite oxidase, xanthine oxidase (XO) and aldehyde oxidase, which are involved in sulphur amino acid metabolism and purine metabolism.

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[1] On request from the European Commission, Question No EFSA-Q-2008-1100, EFSA-Q-2008-1128, adopted on 09 July 2010.

[2] Panel members: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Monika Neuhäuser-Berthold, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Daniel Tomé, Hendrik van Loveren and Hans Verhagen. Correspondence: nda@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank for the preparatory work on this scientific opinion the members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Albert Flynn, Ines Golly, Marina Heinonen, Hannu Korhonen, Martinus Løvik, Ambroise Martin, Hildegard Przyrembel, Seppo Salminen, Yolanda Sanz, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren and Hans Verhagen. The members of the Claims Sub-Working Group on Cardiovascular Health/Oxidative Stress: Antti Aro, Marianne Geleijnse, Marina Heinonen, Ambroise Martin, Wilhelm Stahl and Henk van den Berg.

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The Panel concludes that a cause and effect relationship has been established between the dietary intake of molybdenum and contribution to normal sulphur amino acid metabolism. However, the evidence provided does not establish that inadequate intake of molybdenum leading to impaired sulphur amino acid metabolism occurs in the general EU population.

Protection of DNA, proteins and lipids from oxidative damage

The claimed effect is "antioxidant activity". The target population is assumed to be the general population. The Panel considers that protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.

No references have been provided from which conclusions for the scientific substantiation of the claimed effect could be drawn.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the dietary intake of molybdenum and the protection of DNA, proteins and lipids from oxidative damage.

Conditions and possible restrictions of use

The Panel considers that in order to bear the claim, a food should be at least a source of molybdenum as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population is the general population.

KEY WORDS

Molybdenum, antioxidant, oxidative damage, DNA, lipids, proteins, amino acids, health claims.

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006[4] submitted by Member States contains main entry claims with corresponding conditions of use and literature for similar health claims. EFSA has screened all health claims contained in the original consolidated list of Article 13 health claims which was received by EFSA in 2008 using six criteria established by the NDA Panel to identify claims for which EFSA considered sufficient information had been provided for evaluation and those for which more information or clarification was needed before evaluation could be carried out[5]. The clarifications which were received by EFSA through the screening process have been included in the consolidated list. This additional information will serve as clarification to the originally provided information. The information provided in the consolidated list for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the claims is molybdenum, which is a well recognised nutrient and is measurable in foods by established methods. Molybdenum occurs naturally in foods and is authorised for addition to foods (Annex I of the Regulation (EC) No 1925/2006[6] and Annex I of Directive 2002/46/EC[7]). This evaluation applies to molybdenum naturally present in foods and those forms authorised for addition to foods (Annex II of the Regulation (EC) No 1925/2006 and Annex II of Directive 2002/46/EC).

The Panel considers that the food constituent, molybdenum, which is the subject of the health claims, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Contribution to normal amino acid metabolism (ID 313)

The claimed effect is "for amino acids (including uric acid) metabolism". The Panel assumes that the target population is the general population.

The Panel considers that contribution to normal amino acid metabolism is a beneficial physiological effect.

2.2. Protection of DNA, proteins and lipids from oxidative damage (ID 341)

The claimed effect is "antioxidant activity". The Panel assumes that the target population is the general population.

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[4] Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.
[5] Briefing document for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims: http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf
6 Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. OJ L 404, 30.12.2006, p. 26–38.
7 Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements. OJ L 183, 12.7.2002, p. 51–57.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the protection of body cells and molecules (such as DNA, proteins and lipids) from oxidative damage.

Reactive oxygen species (ROS) including several kinds of radicals are generated in biochemical processes (e.g. respiratory chain) and as a consequence of exposure to exogenous factors (e.g. radiation, pollutants). These reactive intermediates damage biologically relevant molecules such as DNA, proteins and lipids if they are not intercepted by the antioxidant network which includes free radical scavengers such as antioxidant nutrients.

The Panel considers that protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

3.1. Contribution to normal amino acid metabolism (ID 313)

Molybdenum functions as a cofactor for some enzymes in humans, such as sulphite oxidase, xanthine oxidase (XO) and aldehyde oxidase, which are involved in sulphur amino acid metabolism and purine metabolism (IoM, 2001). Observations of molybdenum deficiency have been limited to genetic defects that interfere with the molybdenum cofactor's ability to activate molybdoenzymes and to one case of feeding molybdenum-free total parenteral nutrition. Human dietary deficiency of molybdenum has not been reported (Eckhert, 2006).

The Panel concludes that a cause and effect relationship has been established between the dietary intake of molybdenum and contribution to normal sulphur amino acid metabolism. However, the evidence provided does not establish that inadequate intake of molybdenum leading to impaired sulphur amino acid metabolism occurs in the general EU population.

3.2. Protection of DNA, proteins and lipids from oxidative damage (ID 341)

Molybdenum functions as a cofactor for some enzymes in humans, such as sulphite oxidase, xanthine oxidase (XO) and aldehyde oxidase, which are involved in sulphur amino acid and purine metabolism (IoM, 2001). None of these enzymes are recognised as belonging to the antioxidant defence system. Dietary deficiency of molybdenum has not been documented. In acquired molybdenum deficiency, uric acid levels are lowered owing to low XO activity. Uric acid can act *in vivo* as a radical scavenger (IoM, 2001). However, XO can also produce superoxides, contributing to increased oxidative damage.

The references provided for the scientific substantiation of this claim were general reviews and textbook information on molybdenum metabolism, function, toxicity and dietary intake in the US, but no specific data on ROS scavenging and/or protection of cells or molecules against ROS-induced damage were submitted.

The Panel considers that a cause and effect relationship has not been established between the dietary intake of molybdenum and the protection of DNA, proteins and lipids from oxidative damage.

4. Panel's comments on the proposed wording

4.1. Contribution to normal amino acid metabolism (ID 313)

The following wording reflects the scientific evidence: "Molybdenum contributes to normal sulphur amino acid metabolism".

5. Conditions and restrictions of use

5.1. Contribution to normal amino acid metabolism (ID 313)

The Panel considers that in order to bear the claim a food should be at least a source of molybdenum as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. Tolerable Upper Intake Levels have been established for molybdenum in children, adolescents and adults (SCF, 2000).

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituent, molybdenum, which is the subject of the health claims, is sufficiently characterised.

Contribution to normal amino acid metabolism (ID 313)

- The claimed effect is "for amino acids (including uric acid) metabolism". The target population is assumed to be the general population. Normal amino acid metabolism is a beneficial physiological effect.
- A cause and effect relationship has been established between the dietary intake of molybdenum and contribution to normal sulphur amino acid metabolism.
- The evidence provided does not establish that inadequate intake of molybdenum leading to impaired sulphur amino acid metabolism occurs in the general EU population.
- The following wording reflects the scientific evidence: "Molybdenum contributes to normal sulphur amino acid metabolism".

Protection of DNA, proteins and lipids from oxidative damage (ID 341)

- The claimed effect is "antioxidant activity". The target population is assumed to be the general population. Protection of DNA, proteins and lipids from oxidative damage may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the dietary intake of molybdenum and the protection of DNA, proteins and lipids from oxidative damage.

Conditions and possible restrictions of use

- In order to bear the claim, a food should be at least a source of molybdenum as per Annex to Regulation (EC) No 1924/2006. Such amounts can be easily consumed as part of a balanced diet. The target population is the general population.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2008-1100, EFSA-Q-2008-1128). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The full list of supporting references as provided to EFSA is available on: http://www.efsa.europa.eu/panels/nda/claims/article13.htm.

REFERENCES

Eckhert CD, 2006. Other trace elements. In : Modern nutrition in health and disease, tenth edition. Shils ME, Shike M, Ross AC, Caballero B, Cousins RJ (eds). Lippincott Williams and Wilkins, Philadelphia, 338-350.

IoM (Institute of Medicine), 2001. Dietary Reference Intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium and zinc. National Academy Press, Washington D.C.

SCF (Scientific Committee on Food), 2000. Opinion on the Tolerable Upper Intake Level of Molybdenum.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods[8] (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

a) the role of a nutrient or other substance in growth, development and the functions of the body; or

b) psychological and behavioural functions; or

c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

(i) based on generally accepted scientific evidence; and

(ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13 (1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD[9]

Foods are commonly involved in many different functions[10] of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

[8] OJ L12, 18/01/2007
[9] The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.
[10] The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

(a) the claimed effect of the food is beneficial for human health,

(b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),

(c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,

(d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to

describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.

- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.

- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.
- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.
- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.
- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Main entry health claims related to molybdenum, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
313	Molybdenum	For amino acids (including uric acid) metabolism.	To support an optimal amino acid metabolism, It supports normal cells function, It supports normal growth, Component of enzymes needed in metabolism.
	Conditions of use - 20-50 mcg. Must meet minimum requirements for use of the claim "source of [name of vitamin/s] and/or [name of mineral/s]" as per Annex to Regulation 1924/2006. - Group: Erwachsene, amount: 10 bis 50 Mikrogramm (µg), upper limit: 100 Mikrogramm (µg).		
ID	**Food or Food constituent**	**Health Relationship**	**Proposed wording**
341	Molybdenum	Antioxidant activity	-Antioxidant. -Protects cells from ageing. -Important for nitrogen metabolism.
	Conditions of use - Food supplement with 120 µg of molybdenum in the daily dose		

GLOSSARY AND ABBREVIATIONS

DNA	Deoxyribonucleic acid
ROS	Reactive oxygen species
XO	Xanthine oxidase