SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to "L-tug lycopene" and reduction of blood LDL-cholesterol pursuant to Article 14 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

ABSTRACT

Following an application from Lycotec Ltd, submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to "L-tug lycopene" and reduction of blood low-density lipoprotein (LDL)-cholesterol. The food constituent that is the subject of the claim is L-tug lycopene (i.e. Lyc-O-Mato® embedded in fat-rich matrices by a manufacturing process claimed as proprietary and confidential by the applicant). The Panel considers that the food constituent, L-tug lycopene, which is the subject of the claim, is sufficiently characterised. The Panel considers that reduction of blood LDL-cholesterol concentrations is a beneficial physiological effect. A reduction in blood LDL-cholesterol concentrations reduces the risk of CHD. The Panel notes that the unpublished studies submitted to support the claim were exploratory in nature and insufficient information was provided to allow the scientific evaluation of these studies. The Panel concludes that a cause and effect relationship has not been established between the consumption of L-tug lycopene and reduction of blood LDL-cholesterol.

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KEY WORDS

L-tug lycopene, cholesterol, LDL-cholesterol, coronary heart disease, health claims

[1] On request from the Competent Authority of the United Kingdom following an application by Lycotec Ltd, Question No EFSA-Q-2014-00590, adopted on 6 February 2015.

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[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims: Carlo Agostoni, Jean-Louis Bresson, Susan Fairweather-Tait, Marina Heinonen, Ambroise Martin, Hildegard Przyrembel, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Sean (J.J.) Strain, Inge Tetens, Hendrik van Loveren, Hans Verhagen and Peter Willatts for the preparatory work on this scientific opinion.

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SUMMARY

Following an application from Lycotec Ltd, submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of the United Kingdom, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to "L-tug lycopene" and reduction of blood low-density lipoprotein (LDL)-cholesterol.

The scope of the application was proposed to fall under a health claim referring to disease risk reduction. The application included a request for the protection of proprietary data.

The food that is the subject of the health claim is L-tug lycopene (i.e. Lyc-O-Mato® embedded in fat-rich matrices by a manufacturing process claimed as proprietary and confidential by the applicant). The Panel considers that the food, L-tug lycopene, which is the subject of the health claim, is sufficiently characterised.

The claimed effect proposed by the applicant is "decreases blood cholesterol and triglycerides levels". Therefore, "L-tug lycopene" is the substance, "LDL-cholesterol" is the risk factor and "coronary heart disease" (CHD) is the human disease. The target population proposed by the applicant comprises "healthy adults who wish to lower their blood cholesterol levels". In reply to a request from the European Food Safety Authority (EFSA), the applicant confirmed that the health relationship proposed is related to lowering LDL-cholesterol concentrations, which decreases the risk of CHD. The Panel considers that reduction of blood LDL-cholesterol concentrations is a beneficial physiological effect. A reduction in blood LDL-cholesterol concentrations reduces the risk of CHD.

The applicant identified eight unpublished human intervention studies as pertinent to the claim.

The eight human intervention studies provided were conducted with L-tug lycopene in different food matrices, followed similar protocols, and, as indicated by the applicant, were exploratory in nature. The Panel notes that the information provided was insufficient to allow a scientific evaluation of the studies, and therefore EFSA requested that the applicant provide the full study reports. In reply, the applicant claimed that no additional information on the studies existed.

From the limited information available in the application, the Panel notes that the studies were not randomised and that some methodological aspects, such as the definition of primary outcome(s), power calculations, treatment of missing data, compliance or correction for multiplicity of outcomes, were not considered in the study reports, possibly because of the exploratory nature of these studies, as claimed by the applicant. The Panel also notes that, for one of the studies, a number of discrepancies exist between the version provided to EFSA and the published version, regarding the number of subjects included, the participant flow and the presence or absence of randomisation. The Panel considers that no conclusions can be drawn from these studies for the scientific evaluation of the claim.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of L-tug lycopene and reduction of blood LDL-cholesterol.

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BACKGROUND

Regulation (EC) No 1924/2006[4] harmonises the provisions that relate to nutrition and health claims, and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of this Regulation, are authorised in accordance with this Regulation, and are included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Articles 14 to 17 of this Regulation lay down provisions for the authorisation and subsequent inclusion of reduction of disease risk claims and claims referring to children's development and health in a Community list of permitted claims.

According to Article 15 of this Regulation, an application for authorisation shall be submitted by the applicant to the national competent authority of a Member State, which will make the application and any supplementary information supplied by the applicant available to the European Food Safety Authority (EFSA).

STEPS TAKEN BY EFSA

- The application was received on 27/08/2014.
- The scope of the application was proposed to fall under a health claim referring to disease risk reduction.
- The scientific evaluation procedure started on 07/11/2014.
- On 26/11/2014, the Working Group on Claims of the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application, and the clock was stopped on 04/12/2013, in compliance with Art. 18(3) of Regulation (EC) No 1924/2006.
- On 16/01/2015, EFSA received the requested information as submitted by the applicant and the clock was restarted.
- During its meeting on 06/02/2015, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related "L-tug lycopene" and reduction of blood LDL-cholesterol.

TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16(3) of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to "L-tug lycopene" and reduction of blood LDL-cholesterol.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of "L-tug lycopene", a positive assessment of its safety, nor a decision on whether "L-tug lycopene" is, or is not, classified as a foodstuff. 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 wording of the claim, and the conditions of use as proposed by the applicant may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 18(4) of Regulation (EC) No 1924/2006.

[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.

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address

Lycotec Ltd, 2nd Floor, The Platinum Building, St. John's Innovation Park, Cowley Road, Cambridge CB4 0WS, United Kingdom.

The application contains a request for the protection of the unpublished proprietary data study reports from Petyaev et al., in accordance with Article 21 of Regulation (EC) No 1924/2006.

Food as stated by the applicant

According to the applicant, the food for which this health claim is made is L-tug lycopene—a proprietary formulation of lycopene embedded in fat-based foods.

Health relationship as claimed by the applicant

According to the applicant, the claimed effect is "significantly and dose-dependently decrease blood cholesterol and triglycerides levels". Therefore, in this health claim application, L-tug lycopene is the substance, "LDL-cholesterol" is the risk factor and "coronary heart disease" (CHD) is the human disease.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "L-tug lycopene has been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease".

Specific conditions of use as proposed by the applicant

The applicant has proposed a daily intake of 7 mg L-tug lycopene. The target population proposed comprises healthy adults who wish to lower their blood cholesterol levels.

ASSESSMENT

1. Characterisation of the food

The applicant stated that the food that is the subject of the health claim is "L-tug lycopene".

L-tug lycopene is prepared from a lycopene-rich oleoresin extract obtained from ripe fruits of tomato (Lyc-O-Mato®, LycoRed, Beer Sheva, Israel), which is embedded in fat-based foods such as dark chocolate, olive oil, dairy butter and sunflower oil, following a manufacturing process described in the application which has been claimed as proprietary and confidential by the applicant.

The concentration of lycopene in the final food products is measured by high-performance liquid chromatography (HPLC). The Panel notes that L-tug lycopene cannot be distinguished from standard lycopene by HPLC.

The Panel considers that the food, L-tug lycopene (i.e. Lyc-O-Mato® embedded in fat-rich matrices by a manufacturing process claimed as proprietary and confidential by the applicant), which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is "decrease blood cholesterol and triglycerides levels". Therefore, in this health claim application, "L-tug lycopene" is the substance, "LDL-cholesterol" is the risk factor and "coronary heart disease" is the human disease. The target population proposed by the applicant comprises "healthy adults who wish to lower their blood cholesterol levels". In reply to a

request from the European Food Safety Authority (EFSA), the applicant confirmed that the health relationship proposed is related to lowering low-density lipoprotein (LDL)-cholesterol concentrations, which decreases the risk of CHD.

CHD is a leading cause of mortality and morbidity in European populations, with over 1.9 million deaths in the European Union and over 4.35 million deaths in Europe each year (Pedersen et al., 2005). Elevated blood cholesterol is an important modifiable risk factor in the development of CHD (WHO, 2002a, b). It has been shown that blood cholesterol concentrations can be decreased by drugs and by dietary and lifestyle changes (Ornish et al., 1998; Gordon, 2000; Denke, 2005; van Horn et al., 2008).

The Panel considers that reduction of blood LDL-cholesterol concentrations is a beneficial physiological effect. A reduction in blood LDL-cholesterol concentrations reduces the risk of CHD.

3. Scientific substantiation of the claimed effect

The applicant stated that, as L-tug lycopene is a recent innovation, only proprietary, unpublished studies were available. The applicant identified eight unpublished human intervention studies as pertinent to the claim (Petyaev et al., unpublished). One of these studies was published during the evaluation of the application (Petyaev et al., 2014).

The eight human intervention studies provided were conducted with L-tug lycopene in different food matrices, followed similar protocols, and, as indicated by the applicant, were exploratory in nature. The Panel notes that the information provided was insufficient to allow a scientific evaluation of the studies, and therefore EFSA requested that the applicant provide the full study reports. In reply, the applicant indicated that no additional information on the studies existed.

From the limited information available in the application, the Panel notes that the studies were not randomised and that some methodological aspects, such as the definition of primary outcome(s), power calculations, treatment of missing data, compliance or correction for multiplicity of outcomes were not considered in the study reports, possibly because of the exploratory nature of these studies, as claimed by the applicant. The Panel also notes that for one of the studies, a number of discrepancies exist between the version provided to EFSA (Petyaev et al., unpublished) and the published version (Petyaev et al., 2014) regarding the number of subjects included, the participant flow and the presence or absence of randomisation. The Panel considers that no conclusions can be drawn from these studies for the scientific evaluation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of L-tug lycopene and reduction of blood LDL-cholesterol concentrations.

CONCLUSIONS

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

- The food, L-tug lycopene (i.e. Lyc-O-Mato® embedded in fat-rich matrices by a manufacturing process claimed as proprietary and confidential by the applicant), which is the subject of the health claim is sufficiently characterised.

- The claimed effect is "lowering low-density lipoprotein (LDL)-cholesterol concentrations, which decreases the risk of coronary heart disease". The target population as proposed by the applicant comprises "healthy adults who wish to lower their blood cholesterol levels". Reduction of blood LDL-cholesterol concentrations is a beneficial physiological effect. A reduction in blood LDL-cholesterol concentrations reduces the risk of CHD.

- A cause and effect relationship has not been established between the consumption of L-tug lycopene and reduction of blood LDL-cholesterol concentrations.

DOCUMENTATION PROVIDED TO EFSA

1. Health claim application on "L-tug lycopene" and reduction of blood LDL-cholesterol concentration pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0427_UK). August 2014. Submitted by Lycotec Ltd.

REFERENCES

Denke MA, 2005. Diet, lifestyle, and nonstatin trials: review of time to benefit. American Journal of Cardiology, 96, 3–10.

Gordon DJ, 2000. Cholesterol lowering reduces mortality. The Statins. In: Cholesterol-lowering therapy. Evaluation of clinical trial evidence. Ed. Grundy SM. Marcel Dekker Inc., New Yori, NY, USA, 299–311.

Ornish D, Scherwitz LW, Billings JH, Brown SE, Gould KL, Merritt TA, Sparler S, Armstrong WT, Ports TA, Kirkeeide RL, Hogeboom C and Brand RJ, 1998; erratum in 1999. Intensive lifestyle changes for reversal of coronary heart disease. Journal of the American Medical Association, 280, 2001–2007; erratum, 281, 1380.

Petyaev IM, Dovgalevsky PY, Chalyk NE, Klochkov V and Kyle NH, 2014. Reduction in high pressure and serum lipids by lycosome formulation of dark chocolate and lycopene in prehypertension. Food Science and Nutrition, 2, 744–750.

Petyaev IM, Bashmakov YK, Kyle NH, Klochkov V and Thakur D, unpublished. Clinical development of L-tug lycopene as an LDL-cholesterol lowering agent – study report (including study protocol) of proprietary studies. Protocol number: DT 01-12-23-14.

Van Horn L, McCoin M, Kris-Etherton PM, Burke F, Carson JA, Champagne CM, Karmally W and Sikand G, 2008. The evidence for dietary prevention and treatment of cardiovascular disease. Journal of the American Dietetic Association, 108, 287–331.

ABBREVIATIONS

CHD	coronary heart disease
HPLC	high-performance liquid chromatography
LDL	low-density lipoprotein