

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to OPC PremiumTM and the reduction of blood cholesterol pursuant to Article 14 of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2, 3}

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following an application from GP International Holding B.V. submitted pursuant to Article 14 of Regulation (EC) No 1924/2006 via the Competent Authority of Germany, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver a scientific opinion on OPC PremiumTM and the reduction of blood cholesterol.

The scope of the application was proposed to fall under a health claim referring to reduction of a disease risk.

The food that is the subject of the health claim is OPC PremiumTM, which contains 40 mg oligomeric procyanidins (OPC) and 400 mg berry-blend per capsule. The manufacturing process has been described. The Panel notes that no constituent relevant to the claimed effect has been identified in the berry-blend for standardisation purposes. The Panel considers that the food, OPC PremiumTM, which is the subject of the health claim is not sufficiently characterised with respect to the berry blend, whereas the active constituent OPC extracted from grape (*Vitis vinifera*) seeds is sufficiently characterised.

The claimed effect is “reduces blood cholesterol and may therefore reduce the risk of cardiovascular disease”. The target population is males and females over 30 years of age. The Panel considers that lowering elevated blood LDL-cholesterol is beneficial to human health by decreasing the risk of coronary heart disease.

Among the 21 references provided, five report on animal and *in vitro* studies investigating outcomes unrelated to the claimed effect and 14 (four reviews) report on human studies on either substances

1 On request from GP International Holding B.V., Question No EFSA-Q-2009-00454, adopted on 15 October 2009.

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3 Acknowledgement: The Panel wishes to thank the members of the Working Group on Claims for the preparation of this opinion: 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.

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unrelated to the food/component that is the subject of the health claim and/or on health outcomes unrelated to the claimed effect.

In a randomised, double-blind, placebo-controlled human intervention study, the effect of a daily dose of 100 mg of grape seed procyanidin extract (GSE) on serum total and LDL-cholesterol was investigated over two months in 20 hypercholesterolaemic subjects compared to placebo. No significant differences between the GSE group and the placebo group were observed.

One animal study reported on bioavailability and safety of a red grape seed extract. The Panel notes that this study did not report on blood LDL-cholesterol.

In weighing the evidence, the Panel has taken into account the lack of a significant effect of GSE intake on blood LDL-cholesterol when administered to hypercholesterolaemic subjects for two months, and the lack of studies conducted with OPC PremiumTM or with OPC contained in OPC PremiumTM.

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

KEY WORDS

OPC PremiumTM, oligomeric procyanidins, berries, blood cholesterol, risk reduction, health claims.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1924/2006⁴ establishes rules governing the Community authorisation of health claims made on foods. Health claims shall be prohibited unless they comply with the general and specific requirements of that Regulation and are authorised in accordance with this Regulation and included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Article 14 of that Regulation lays 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 that Regulation, an application for authorisation shall be submitted by the applicant to the national competent authority of a Member State, who will make the application and any supplementary information supplied by the applicant available to European Food Safety Authority (EFSA).

STEPS TAKEN BY EFSA:

- The application was received on 04/03/2009.
- The scope of the application falls under disease risk reduction claim.
- During the completeness check⁵ of the application, the applicant was requested to provide missing information on 17/03/2009 and on 18/05/2009.
- The applicant provided the missing information on 15/05/2009 and on 08/06/2009.
- The application was considered valid by EFSA and the scientific evaluation procedure started on 15/06/2009.
- During the meeting on 15/10/2009, the NDA Panel, in the light of the overall data submitted adopted an opinion on OPC PremiumTM and the reduction of blood cholesterol.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16 of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA is requested to issue a scientific opinion on the information provided by the applicant concerning OPC PremiumTM and the reduction of blood cholesterol.

EFSA DISCLAIMER

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

It should also be highlighted that the scope and the proposed wording of the claim as considered by the EFSA in this opinion may be subject to changes pending the outcome of the authorisation procedure foreseen in Article 17 of Regulation (EC) No 1924/2006.

⁴ European Parliament and Council (2006). 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. Official Journal of the European Union OJ L 404, 30.12.2006. Corrigendum OJ L 12, 18.1.2007, p. 3–18.

⁵ In accordance with EFSA "Scientific and Technical guidance for the Preparation and Presentation of the Application for Authorisation of a Health Claim"

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address: GP International Holding B.V., Am Roda Ring 39, NL-6460 HA Kerkrade, the Netherlands.

Food/constituent as stated by the applicant

OPC PremiumTM. Each capsule contains: 40 mg OPC and 400 mg Berry-blend.

Health relationship as claimed by the applicant

High levels of LDL cholesterol are the most common risk factors for cardiovascular disease. There are scientific documentations on numerous risk factors such as high lipid / lipoprotein levels.

Wording of the health claim as proposed by the applicant

OPC have been shown to reduce blood cholesterol levels and may therefore reduce the risk of cardiovascular disease.

Specific conditions of use as proposed by the applicant

2 capsules per day orally with water at least 2 months.

ASSESSMENT

1. Characterisation of the food/constituent

The food that is the subject of the health claim is OPC PremiumTM, which contains 40 mg oligomeric procyanidins (OPC) and 400 mg berry-blend per capsule. The capsule also contains silicon dioxide (15.0 mg) and magnesium stearate (5.0 mg). The manufacturing process has been described.

OPC is extracted from grape (*Vitis vinifera*) seeds. According to the specifications, OPC contains minimum of 75% of procyanidins (gel permeation chromatography method) or 65% of procyanidins (Porter test), of which 22% are monomers, 20% dimers, and 56% trimers and tetramers. OPC also contains other phenolics including epicatechin-3-O-gallate and phenolic acids. The composition of the OPC has been assessed in batch to batch analyses (n=6). Analytical data on residual solvents, sulphuric ashes, heavy metals, and pesticides are given. No data are available regarding stability or bioavailability of OPC.

The berry blend in OPC PremiumTM consists of freeze-dried powder of bod bilberry (*Vaccinium uliginosum*, 35.4%), lingonberry (*Vaccinium vitis-idaea*, 35.4%), black currant (*Rubus nigrum*, 13.6%), aronia (*Aronia melanocarpa*, 5%), blueberry (*Vaccinium angustifolium*, 3.9%), pomegranate (*Punica granatum*, 2.7%), concord grape (*Vitis vinifera*, 1.4%), red raspberry (*Rubus idaeus*, 0.7%), sour cherry (*Prunus cerasus*, 0.7%), wild elderberry (*Sambucus nigra*, 0.5%), wild cranberry (*Vaccinium oxycoccus*, 0.4%), and black raspberry (*Rubus occidentalis*, 0.3%). Analytical data have been provided on the microbiological quality and residual heavy-metals. The Panel notes that no constituent relevant to the claimed effect has been identified in the berry-blend for standardisation purposes.

The Panel considers that the food, OPC PremiumTM, which is the subject of the health claim is not sufficiently characterised with respect to the berry blend, whereas the active constituent OPC extracted from grape (*Vitis vinifera*) seeds is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect is “reduces blood cholesterol and may therefore reduce the risk of cardiovascular disease”. The target population is males and females over 30 years of age.

Coronary heart disease (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, 2002). It has been shown that blood cholesterol can be decreased by drugs and by dietary and lifestyle changes.

The Panel considers that lowering elevated blood LDL-cholesterol is beneficial to human health as it may decrease the risk of coronary heart disease.

3. Scientific substantiation of the claimed effect

The applicant has identified a total of 21 references as being pertinent to the claimed effect. No details concerning the search strategy have been provided.

Among the 21 references provided, five report on animal and *in vitro* studies with outcomes unrelated to the claimed effect and 14 (four reviews) report on human studies with either substances unrelated to the food/component that is the subject of the health claim and/or with health outcomes unrelated to the claimed effect. Four of these describe the effects of pine bark extract, vegetable juice, various berries, or fruits and vegetables in general on the primary outcome measures blood pressure, plasma antioxidant capacity, platelet function, HDL cholesterol, and risk of coronary heart disease (Cao et al., 1998; Daucher et al., 2006; Erlund et al., 2008; Hosseini et al., 2001). A human study designed to investigate the postprandial effects of grape seed extract reported on other health outcomes than LDL-cholesterol lowering, such as LDL oxidation (Natella et al., 2002). The Panel considers that no scientific conclusions can be drawn from these references for the substantiation of the claimed effect.

In a randomised, double-blind, placebo-controlled human intervention study by Preuss et al. (2000), the effect of a daily dose of 100 mg of grape seed procyanidin extract (GSE) on serum total and LDL-cholesterol was investigated over two months in 20 hypercholesterolaemic subjects compared to placebo (10 subjects per group). No significant differences between the GSE group and the placebo group were observed. The Panel notes the small number of subjects, the lack of effect on either total or LDL-cholesterol concentrations and that no information is provided on how the GSE used in this study related to the OPC contained in OPC PremiumTM.

One animal study by Bagchi et al. (2000) reported on bioavailability and safety of a red grape seed extract. The Panel notes that this study did not report on blood LDL-cholesterol.

The Panel notes that no studies have been provided on the effect of the food (OPC PremiumTM) which is the subject of the health claim on LDL-cholesterol concentrations.

In weighing the evidence, the Panel has taken into account the lack of a significant effect of GSE intake on blood LDL-cholesterol when administered to hypercholesterolaemic subjects for two months, and the lack of studies conducted with OPC PremiumTM.

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

CONCLUSIONS

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

- The food, OPC Premium™, which is the subject of the health claim is not sufficiently characterised with respect to the berry blend, whereas the active constituent OPC extracted from grape (*Vitis vinifera*) seeds is sufficiently characterised.
- The claimed effect is “reduces blood cholesterol and may therefore reduce the risk of cardiovascular disease”. The target population is males and females over 30 years of age. The Panel considers that lowering elevated blood LDL-cholesterol is beneficial to human health as it may decrease the risk of coronary heart disease.
- A cause and effect relationship has not been established between the consumption of OPC Premium™ and the reduction of blood LDL-cholesterol concentrations.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on OPC Premium™ and the reduction of blood cholesterol pursuant to Article 14 of Regulation (EC) No 1924/2006 (Claim serial No: 0242_DE). June 2009. Submitted by GP International Holding B.V.

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GLOSSARY / ABBREVIATIONS

CHD	Coronary Heart Disease
GPC	Gel Permeation Chromatography
GSE	Grape Seed Extract
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
OPC	Oligomeric Procyanidins