European Food Safety Authority

EFSA Journal 2012;10(7):2773

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to Wheat Polar Lipid Extract and protection of the skin against dehydration pursuant to Article 13(5) 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 Extraction Purification Innovation France, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of France, 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 Wheat Polar Lipid Extract and protection of the skin against dehydration. The Panel considers that Wheat Polar Lipid Extract is sufficiently characterised. The claimed effect is "contributes to improve skin hydration". The target population proposed by the applicant is healthy adults with skin dryness. The Panel considers that protection of the skin against dehydration is a beneficial physiological effect. The applicant identified one published and two unpublished human intervention studies as being pertinent to the health claim. The Panel considers that no conclusions can be drawn from one uncontrolled pilot study, nor from one study which was not carried out with the food which is the subject of the claim. In weighing the evidence, the Panel took into account that one human intervention study reported an effect of consumption of Wheat Polar Lipid Extract on transepidermal water loss and skin water-holding capacity, but that the outcome of the study lacked plausibility given the limitations in the study design, and that the evidence provided in support of a mechanism was weak. The Panel concludes that a cause and effect relationship has not been established between the consumption of Wheat Polar Lipid Extract and protection of the skin against dehydration. © European Food Safety Authority, 2012

KEY WORDS

Wheat Polar Lipid Extract, skin barrier, transepidermal water loss, TEWL, skin dehydration, health claims.

[1] On request from the Competent Authority of France following an application by Extraction Purification Innovation France, Question No EFSA-Q-2011-01122, adopted on 22 June 2012.

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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, 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 for the preparatory work on this scientific opinion.

Suggested citation: EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to Wheat Polar Lipid Extract and protection of the skin against dehydration pursuant to Article 13(5) of Regulation (EC) No 1924/2006. EFSA Journal 2012;10(7):2773. [11 pp.]. doi:10.2903/j.efsa.2012.2773. Available online: www.efsa.europa.eu/efsajournal

SUMMARY

Following an application from Extraction Purification Innovation France, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of France, 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 Wheat Polar Lipid Extract and protection of the skin against dehydration.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence and including a request for the protection of proprietary data.

The food constituent that is the subject of the health claim is Wheat Polar Lipid Extract. The Panel considers that Wheat Polar Lipid Extract is sufficiently characterised.

The claimed effect is "contributes to improve skin hydration". The target population proposed by the applicant is healthy adults with skin dryness caused, for instance, by weather conditions such as hot, cold or windy weather, low environmental humidity, or excessive cleansing. The Panel considers that protection of the skin against dehydration is a beneficial physiological effect.

The applicant identified one published and two unpublished (claimed as proprietary by the applicant) human intervention studies as being pertinent to the health claim.

The published study did not use the food which is the subject of the claim but rather another commercial product. The Panel notes that the information provided on the composition was insufficient to establish that this other product complies with the specifications of the food constituent which is the subject of the health claim, and considers that no conclusions can be drawn from this study for the scientific substantiation of a product-specific claim related to Wheat Polar Lipid Extract.

The two unpublished studies used the food product which is the subject of the claim. One of these two studies was a pilot study which reported on a one arm (no control group) intervention with the Wheat Polar Lipid Extract product in 20 female volunteers. The Panel considers that no conclusions can be drawn from this uncontrolled pilot study for the scientific substantiation of the claim.

The other unpublished study was a placebo-controlled, double-blind intervention in which 60 healthy Caucasian women (aged 30-60 years) were randomised to consume 30 mg/d Wheat Polar Lipid Extract (providing 1.8 mg/d ceramides and 15 mg/d DGDG; n=20), a wheat oil product (n=20) or placebo (mainly maltodextrin and dicalcium phosphate; n=20) for 60 days. The primary endpoint was water holding capacity. Secondary endpoints were skin elasticity, skin smoothness, skin roughness, skin wrinkles, and a measure of the water barrier function of the skin, the trans-epidermal water loss (TEWL). The Panel considers that measures of TEWL can be used as scientific evidence for a claim on protection of the skin against dehydration and that measures of the water-holding capacity of skin may be used as supportive evidence. Measures were taken at baseline and at three time points (days 15, 30 and 60). Following a request by EFSA for a re-analysis of the data, the applicant provided an analysis using RM-ANOVA followed by a Tukey-Kramer multiple-comparisons post-test. Results were provided for absolute differences from baseline, and for percent changes from baseline. When absolute differences were used, a significant effect of treatment ($p=0.0003$) but no significant effect of time or treatment x time interaction was reported for TEWL, whereas significant effects of treatment and time (both $p<0.0000$) but no significant effect of treatment x time interaction were reported for skin water-holding capacity. When calculations were based on percent changes from baseline, significant effects for treatment ($p=0.0006$), time ($p=0.0038$) and treatment x time interaction ($p=0.0296$) were reported for TEWL, and significant effects for treatment, time and treatment x time interaction (all $p<0.0000$) were reported for skin water-holding capacity.

The Panel notes that this study reported an effect of treatment with Wheat Polar Lipid Extract on one directly pertinent outcome measure (i.e. TEWL) and one supportive outcome measure (i.e. water holding capacity). However, the Panel also notes that the design of this study would have greatly limited the possibility of detecting an effect of Wheat Polar Lipid Extract on skin hydration as the dose of ceramides and DGDG provided by Wheat Polar Lipid Extract is only a small fraction (about 10 %) of the quantity which would be consumed in the background diet by subjects eating typical amounts of wheat-derived food products. Therefore, the Panel considers that the outcome of the study lacks plausibility given the limitations in the design of the study.

The applicant proposed three possible mechanisms by which Wheat Polar Lipid Extract might exert the claimed effect. The Panel considers that the evidence provided in support of a mechanism is weak.

In weighing the evidence, the Panel took into account that one human intervention study reported an effect of consumption of Wheat Polar Lipid Extract on TEWL and skin water-holding capacity, but that the outcome of the study lacked plausibility given the limitations in the study design, and that the evidence provided in support of a mechanism was weak.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Wheat Polar Lipid Extract and protection of the skin against dehydration.

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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, Article 13(5) of this Regulation lays down provisions for the addition of claims (other than those referring to the reduction of disease risk and to children's development and health) which are based on newly developed scientific evidence, or which include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3).

According to Article 18 of this Regulation, an application for inclusion in the Community list of permitted claims referred to in Art 13(3) 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 17/10/2011.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence and including a request for the protection of proprietary data.
- On 27/10/2011, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- The applicant provided the missing information on 18/11/2011.
- On 23/11/2011, EFSA sent another request to the applicant to provide missing information.
- The applicant provided the missing information on 01/12/2011.
- The scientific evaluation procedure started on 10/12/2011.
- On 01/03/2012, the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application. The clock was stopped on 12/03/2012 and restarted on 27/03/2012, in compliance with Art. 18(3) of Regulation (EC) No 1924/2006.
- On 30/03/2012, EFSA received the requested information as submitted by the applicant.
- On 22/06/2012, the NDA Panel, having evaluated the data submitted, adopted by written procedure an opinion on the scientific substantiation of a health claim related to Wheat Polar Lipid Extract and protection of the skin against dehydration.

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: Wheat Polar Lipid Extract and protection of the skin against dehydration.

[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.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of Wheat Polar Lipid Extract, a positive assessment of its safety, nor a decision on whether Wheat Polar Lipid Extract 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.

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address: Extraction Purification Innovation France SARL, 3 rue de Préaux, 02130 Villers-sur-Fère, France.

The application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006.

Food/constituent as stated by the applicant

According to the applicant, the food constituent for which the claim is made is Wheat Polar Lipid Extract containing specific polar lipids including ceramides (6±2 %) and digalactosyldiglycerides (DGDG) (54±10 %). A daily consumption of 30 mg/day provides 1.8 mg of ceramides and 15 mg of DGDG.

Health relationship as claimed by the applicant

According to the applicant, human *stratum corneum* lipids contain 50 % ceramides, which play a key role in maintaining skin hydration and skin barrier function. The applicant further claims that ingested ceramides are absorbed by the intestine and distributed to body tissues, including skin, where the compounds produced by the digestion of the ceramides are metabolised in the epidermis for *de novo* synthesis of skin lipids implicated in water retention and skin barrier function.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "Contributes to improve skin hydration".

Alternative wordings proposed: "Contributes to improve skin moisturization", "Helps act against skin dryness", "Helps to improve dry skin condition".

Specific conditions of use as proposed by the applicant

According to the applicant, the recommended daily dose of Wheat Polar Lipid Extract is 30 mg/day, which provides 1.8 mg of ceramides and 15.0 mg of DGDG, for at least two consecutive weeks, in the evening before going to sleep.

The target population is healthy adults with skin dryness caused, for instance, by weather conditions such as hot, cold or windy weather, low environmental humidity, or excessive cleansing.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is Wheat Polar Lipid Extract.

Wheat Polar Lipid Extract is a powder composed of more than 95 % polar lipids obtained from wheat (*Triticum aestivum*) by a specified extraction process. The extract consists of glycosyl ceramides and ceramides (6±2 %), digalactosyldiglycerides (DGDG) (54±10 %), phospholipids (27±5 %), monogalactosyldiglycerides (MGDG) (7±2 %), and glycosylated sterols (7±2 %). These constituents can be analysed in foods by established methods. Information pertaining to the manufacturing process, batch-to-batch variability, and stability has been provided by the applicant.

The Panel considers that the food constituent, Wheat Polar Lipid Extract, which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect is "contributes to improve skin hydration". The target population proposed by the applicant is healthy adults with skin dryness caused, for instance, by weather conditions such as hot, cold or windy weather, low environmental humidity, or excessive cleansing.

The skin is the outer barrier of the body and provides protection from water loss, pathogens, and oxidative and UV-induced damage.

An impairment of the permeability barrier function of the skin leads to water loss from the *stratum corneum* and to skin dehydration. Symptoms associated with skin dehydration include roughness with visible scaling and flaking, itching, and reduced resistance to shearing forces. Maintenance (i.e. reduced loss) of the permeability barrier function of the skin protects the skin against dehydration.

The Panel considers that protection of the skin against dehydration is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

The applicant performed a literature search in Pubmed, ScienceDirect, Blackwell Synergy, Wiley InterScience, Mary Ann Liebert, Scirus, IBIDS, SciFinder Scholar, Pascal and SCOPUS. The inclusion criteria for selecting pertinent publications were studies in healthy subjects (adults 18-65 years old) using lipids derived from wheat origin or a constituent containing at least sphingolipids or glycosphingolipids, studies on oral intake of sphingolipids or glycosphingolipids, and studies assessing skin moisturisation and/or skin barrier function. Studies were excluded if they were carried out in subjects with dermatological disease (including atopic dermatitis, psoriasis), used complex constituents composed of sphingolipids but associated with other components diverging from the composition of Wheat Polar Lipid Extract (e.g. vitamins, collagen and polyphenols), were concerned with topical or subcutaneous applications of ceramides, or addressed the improvement of skin recovery after skin disorders. On the relationship between the constituent and the claimed effect, the following terms were used alone or in combination: [wheat OR ceramide OR sphingolipid OR wheat oil OR wheat flour] AND [skin OR hydration OR moisturization OR epidermis OR fibroblast OR keratinocyte OR TEWL OR dry skin OR barrier functions OR smooth OR rough OR wrinkles]. With respect to constituent absorption, metabolism and tissue distribution, the following terms were used alone or in combination: [lipid OR glycolipid OR galactolipid OR sphingolipid OR ceramide] AND [absorption OR intestinal absorption OR metabolism OR intestinal uptake]. These terms were associated or not with [skin OR blood OR plasma OR dermis OR epidermis] and [dietary intake OR oral intake]. The following terms were also used: [lipid OR glycolipid OR galactolipid OR sphingolipid OR ceramide] AND [ceramidase OR sphingomyelinase OR hydrolysis OR enzyme]. The time period was from May 2008 to September 2010. One human study was excluded by the applicant because it used a wheat lipid extract in an oil form.

The applicant identified one published and two unpublished (claimed as proprietary by the applicant) human intervention studies as being pertinent to the health claim.

The published study by Boisnic and Branchet (2007) did not use the food which is the subject of the claim but rather another commercial product. The applicant was invited to provide a rationale on how this study could be pertinent for a product-specific claim on Wheat Polar Lipid Extract. In reply, the applicant indicated that both products (i.e. Wheat Polar Lipid Extract and the product used in the study) have similar characteristics with regards to the source of extraction and the respective amounts of glycosyl ceramides, ceramides, and DGDG. The Panel notes that the information provided on the composition was insufficient to establish that the product used in the study complies with the

specifications of the food constituent which is the subject of the health claim. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of a product-specific claim related to Wheat Polar Lipid Extract.

The two unpublished studies (Quaglini and Marzatico, 2006; Marzatico, 2010) used the food product which is the subject of the claim. The pilot study by Quaglini and Marzatico (2006, unpublished, claimed as proprietary by the applicant) described a one arm (no control group) intervention with the Wheat Polar Lipid Extract product in 20 female volunteers, aged 30-50 years. The Panel considers that no conclusions can be drawn from this uncontrolled pilot study for the scientific substantiation of the claim.

The other study report by Marzatico (2010, unpublished, claimed as proprietary by the applicant) was a placebo-controlled, double-blind intervention in which 60 healthy Caucasian women (aged 30-60 years) were randomised to consume 30 mg/d Wheat Polar Lipid Extract (providing 1.8 mg/d ceramides and 15 mg/d DGDG; n=20), a wheat oil product (n=20) or placebo (mainly maltodextrin and dicalcium phosphate; n=20) for 60 days. A base cream (claimed to be without any effect) was furnished to all volunteers for topical application during the intervention. Power calculations were based on measurements of water holding capacity in the pilot study (Quaglini and Marzatico, 2006, unpublished). The primary endpoint was water holding capacity (called "hydration" or "moisturization" in the application) measured by the Corneometer® method which assesses changes in dielectric capacitance. Secondary endpoints were skin elasticity (using a Cutometer®), skin smoothness, skin roughness, skin wrinkles (all three measured by Visioscan VC 98®) and a measure of the water barrier function of the skin, trans-epidermal water loss (TEWL), using a Tewameter® (based on the principle of open chamber measurement). The Panel considers that measures of TEWL can be used as scientific evidence for a claim on protection of the skin against dehydration, and that measures of the water-holding capacity of skin may be used as supportive evidence. Measures were taken at baseline and at three time points (days 15, 30 and 60). There were no drop-outs in any study group. Following a request by EFSA for a re-analysis of the data, the applicant provided an analysis using RM-ANOVA followed by a Tukey-Kramer multiple-comparisons post-test. Results were provided for absolute differences from baseline and for percent changes from baseline. When absolute differences were used, a significant effect of treatment ($p=0.0003$) but no significant effect of time or treatment x time interaction was reported for TEWL, whereas significant effects of treatment and time (both $p<0.0000$) but no significant effect of treatment x time interaction were reported for skin water-holding capacity. When calculations were based on percent changes from baseline, significant effects for treatment ($p=0.0006$), time ($p=0.0038$) and treatment x time interaction ($p=0.0296$) were reported for TEWL, and significant effects for treatment, time and treatment x time interaction (all $p<0.0000$) were reported for skin water-holding capacity.

The Panel notes that the design of this study would have greatly limited the possibility of detecting an effect of Wheat Polar Lipid Extract on skin hydration as the dose of ceramides and DGDG provided by Wheat Polar Lipid Extract is only a small fraction (about 10 %) of the quantity which would be consumed in the background diet by subjects eating typical amounts of wheat-derived food products. The applicant was invited to comment on the plausibility of the effect, taking into account the recommended dose. In reply, the applicant indicated that "the usual intake of bread in the French population is 130 g/day (CREDOC, 2001), thus an additional consumption of on average 15 g of bread/day leads to an increased intake of 11 %". The applicant also argued that not only "the amount of bread consumed, but also the lipid composition of wheat, the wheat processing, the bread-making and baking processes highly modify the content and absorption of polar lipids". The applicant also stated that "because they are not processed, the bound polar lipids (ceramides and DGDG) provided in a food supplement present a highest bioavailability to the body than the one supplied by wheat or wheat flour". The applicant concluded that "it was estimated that the amount of polar lipid provided by Wheat Polar Lipid Extract could be provided by an additional consumption of 15 g of bread. However, in reality to have the same physiological effect, the required bread consumption is much larger than those indicated on only the basis of the concentration of ceramides and DGDG". The

Panel notes that the applicant did not provide evidence to substantiate these statements but rather provided references on the amount of lipids in wheat flour streams (Prabhasankar and Haridas Rao, 1999), on digestion of polysaccharides (Englyst, 1985), on the role of polar lipids in bread baking (Pomeranz, 1987) and on retrogradation/resistant starch (Bird, 2000; Pomeranz, 1987; Sajitala, 2006).

The Panel notes that this study reported an effect of treatment with Wheat Polar Lipid Extract on one directly pertinent outcome measure (i.e. TEWL) and one supportive outcome measure (i.e. water holding capacity). However, the Panel considers that the outcome of the study lacks plausibility given the limitations in the design of the study.

The applicant proposed three possible mechanisms by which the Wheat Polar Lipid Extract might exert the claimed effect: (a) after absorption the ceramides transfer to the epidermis without any metabolic conversion; (b) metabolites of the ceramides are distributed to the epidermis after their reconstruction in the skin; and/or (c) metabolites *per se* promote ceramide production. The applicant provided animal and *in vitro* studies on the digestion and bioavailability of ceramides (Andersson et al., 1995, 1996; Fukami et al., 2010; Nilsson, 1969; Nilsson and Duan, 1999; Ohlsson et al., 1998; Schmelz et al., 1994; Ueda et al., 2009). The Panel considers that the evidence provided in support of a mechanism is weak.

In weighing the evidence, the Panel took into account that one human intervention study reported an effect of consumption of Wheat Polar Lipid Extract on TEWL and skin water-holding capacity, but that the outcome of the study lacked plausibility given the limitations in the study design, and that the evidence provided in support of a mechanism was weak.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Wheat Polar Lipid Extract and protection of the skin against dehydration.

CONCLUSIONS

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

- The food constituent, Wheat Polar Lipid Extract, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect is “contributes to improve skin hydration”. The target population proposed by the applicant is healthy adults with skin dryness caused, for instance, by weather conditions such as hot, cold or windy weather, low environmental humidity, or excessive cleansing. Protection of the skin against dehydration is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of Wheat Polar Lipid Extract and protection of the skin against dehydration.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on Wheat Polar Lipid Extract and protection of the skin against dehydration pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0315_FR). October 2011. Submitted by Extraction Purification Innovation France SARL.

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GLOSSARY / ABBREVIATIONS

DGDG	digalactosyldiglycerides
MGDG	monogalactosyldiglycerides
TEWL	transepidermal water loss