



EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to “Appl’In® polyphenolic apple extract powder (*Malus domestica*)” and reduction of post-prandial glycaemic responses pursuant to Article 13(5) of Regulation (EC) No 1924/2006

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to “Appl’In[®] polyphenolic apple extract powder (*Malus domestica*)” and reduction of post-prandial glycaemic responses pursuant to Article 13(5) of Regulation (EC) No 1924/2006¹

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

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following an application from Diana Naturals 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 was asked to deliver an opinion on the scientific substantiation of a health claim related to “Appl’In[®] polyphenolic apple extract powder (*Malus domestica*)” and reduction of post-prandial glycaemic responses. The food constituent, Appl’In[®] polyphenolic apple extract powder (*Malus domestica* Borkh.) containing at least 5 % phloridzin, is considered to be sufficiently characterised in relation to the claimed effect. The Panel considers that reduction of post-prandial glycaemic responses (as long as post-prandial insulinaemic responses are not disproportionately increased) may be a beneficial physiological effect. The applicant provided one published and two unpublished human studies, three animal studies and two *in vitro* studies as pertinent to the claim. The Panel notes that the food used in one human study did not comply with the specifications of the food which is the subject of the claim and considers that no conclusion can be drawn from this study for the scientific substantiation of the claim. In two other human studies, post-prandial blood glucose concentrations were measured but not insulin responses. The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of the claim. The Panel concludes that a cause and effect relationship has not been established between the consumption of Appl’In[®] and reduction of post-prandial glycaemic responses. © European Food Safety Authority, 2011

KEY WORDS

Apple, polyphenolic extract, phloridzin, post-prandial glycaemic response, health claim.

¹ On request from the Competent Authority of France following an application by Diana Naturals, Question No EFSA-Q-2011-00190, adopted on 14 September 2011.

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SUMMARY

Following an application from Diana Naturals, 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 was asked to deliver an opinion on the scientific substantiation of a health claim related to Appl'In® polyphenolic apple extract powder and reduction of post-prandial glycaemic responses.

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 which is the subject of the claim, is Appl'In®, a polyphenolic extract powder of apple, standardised for its content in phloridzin, which is proposed by the applicant to be the active ingredient. The Panel considers that the food Appl'In® polyphenolic apple extract powder (*Malus domestica* Borkh.) containing at least 5 % phloridzin, which is the subject of the claim, is sufficiently characterised in relation to the claimed effect.

The claimed effect proposed by the applicant relates to the reduction of post-prandial glycaemic responses. The target population proposed for the claim is healthy women in the general population willing to reduce their glycaemic response. The Panel considers that reduction of post-prandial glycaemic responses (as long as post-prandial insulinaemic responses are not disproportionately increased) may be a beneficial physiological effect.

The applicant provided one published and two unpublished human intervention studies, three animal studies and two *in vitro* studies as pertinent to the claim.

The food used in one human intervention study did not comply with the specifications of the food which is the subject of the claim. The Panel considers that no conclusion can be drawn from this study for the scientific substantiation of the claim.

In two other human intervention studies, post-prandial blood glucose concentrations were measured but not insulin responses. The Panel considers that no conclusions can be drawn from these studies for the scientific substantiation of the claim.

Animal and *in vitro* studies were provided on the effect of phloridzin on glucose transport and absorption. The Panel considers that human studies are required for the substantiation of a claim, and that evidence provided in animal and *in vitro* studies is not sufficient to predict the occurrence of an effect of apple polyphenol extract powder consumption on reduction of post-prandial glycaemic responses in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Appl'In® and reduction of post-prandial glycaemic responses.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1924/2006⁴ 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 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 04/03/2011.
- 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 10/03/2011, 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 26/04/2011.
- The scientific evaluation procedure started on 30/04/2011.
- During the meeting on 14/09/2011, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to Appl'In® polyphenolic apple extract powder and reduction of post-prandial glycaemic responses.

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(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: "Appl'In® polyphenolic apple extract powder (*Malus domestica*)" and reduction of post-prandial glycaemic responses.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of "Appl'In®", a positive assessment of its safety, nor a decision on whether "Appl'In®" 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.

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. Official Journal of the European Union OJ L 404, 30.12.2006. Corrigendum OJ L 12, 18.1.2007, p. 3–18.

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: Diana Naturals BP15, 35560 ANTRAIN (France).

The application includes a request for the protection of proprietary data in accordance with Article 21 of Regulation (EC) No 1924/2006 for two unpublished study reports (Mireaux and Schmitt, 2007, unpublished; Schmitt and Mireaux, 2008, unpublished).

Food/constituent as stated by the applicant

According to the applicant, the food constituent for which the claim is made is “Appl'In®”, polyphenolic apple extract powder (*Malus domestica*)”.

Health relationship as claimed by the applicant

According to the applicant, an intake of 25 mg of Appl'In® per gram of sucrose leads to a reduction in the incremental area under the curve for blood glucose levels over 2 hours in females with a BMI between 20 and 28.3 kg/m². The action of Appl'In® on glucose metabolism is proposed to be mainly due to its content in phloridzin. Phloridzin is a strong inhibitor of the transport of glucose in the intestine (Ehrenkranz et al., 2005). Less glucose reaches the blood stream, decreasing the glycaemic response after glucose intake.

Wording of the health claim as proposed by the applicant

The applicant proposes the following wording: “Appl'In® contributes to decrease glycaemic response in women”.

Specific conditions of use as proposed by the applicant

The target population proposed by the applicant is healthy women in the general population willing to reduce their glycaemic response.

The applicant proposes that the daily quantity and pattern of consumption required to obtain the claimed effect is 25 mg of Appl'In® per gram of sucrose to be consumed with or added to a snack (food or drink), as the unpublished clinical trial was carried out with this dose.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent which is the subject of the claim is Appl'In®.

Appl'In® is a fine powder of a polyphenolic extract from apple (*Malus domestica* Borkh.), soluble in water (85 to 95 % at a 10 % concentration), which is proposed to be used in capsules or tablets or added to foods or drinks. The specified total polyphenol content is 80 % of the final product expressed as catechin equivalents based on light absorption at 280 nm. The Panel notes that this method is not specific for polyphenols because other compounds such as proteins and nucleic acids will also be included in the quantification, thus leading to an overestimation of the actual polyphenol content. However, the Panel considers that, given the standardised manufacturing process and the final standardisation on the phloridzin content, this method is acceptable as an additional standardisation tool.

The major polyphenol constituents of Appl'In® are identified and quantified by HPLC so that the product can be standardised as having at least 5 % phloridzin, which is claimed to be the active component. Stability of Appl'In® has been tested.

In addition to polyphenols, the extract contains 4.8 % proteins, 4.0 % sugars, 4.5 % dietary fibre, of which 2.8 % is soluble fibre and 1.8 % insoluble fibre, and 150 mg sodium per 100 g, and has an energy content of 46 kcal/100 g. The analyses of four batches were provided and establish the reproducibility of the manufacturing process.

The Panel considers that the food, Appl'In® polyphenolic apple extract powder (*Malus domestica* Borkh.) containing at least 5 % phloridzin, which is the subject of the claim, is sufficiently characterised in relation to the claimed effect.

2. Relevance of the claimed effect to human health

The claimed effect is “contributes to decrease glycaemic response in women”. The target population proposed by the applicant is women in the general population willing to reduce their glycaemic response.

Elevation of blood glucose concentrations after consumption of a food and/or meal is a normal physiological response which varies in magnitude and duration and may be influenced by the chemical and physical nature of the food or meal consumed, as well as by individual factors (Venn and Green, 2007). Decreasing post-prandial glycaemic responses may be beneficial to individuals with, for example, impaired glucose tolerance as long as post-prandial insulinaemic responses are not disproportionately increased. Impaired glucose tolerance is common in the general population of adults.

The Panel considers that the reduction of post-prandial glycaemic responses (as long as post-prandial insulinaemic responses are not disproportionately increased) may be a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

The applicant searched 10 databases using different combinations of terms. The use of defined inclusion and exclusion criteria led to the identification of one pertinent published human study (Johnston et al., 2002). Two other unpublished human studies claimed as proprietary by the applicant were also provided as being pertinent to the application (Mireaux and Schmitt, 2007, unpublished; Schmitt and Mireaux, 2008, unpublished) as well as three animal studies and two *in vitro* studies (Besnard et al., 2008; Ikumi et al., 2008; Katsuno et al., 2007; Pajor et al., 2008; Takii et al., 1997).

The study by Johnston et al. (2002) was a single-blind, randomised, cross-over study in which nine subjects consumed, in a random order, a single dose (400 mL) of a control beverage, of a clear apple juice and of a cloudy apple juice in fasting conditions. Beverages were standardised to contain the same amount of sugars but differed in their phloridzin content. The Panel notes that the pectin content in the apple juice, which could have an impact on the claimed effect (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2010), was not reported. The Panel notes that the product used in this study does not comply with the specifications of the product that is the subject of the claim, and considers that no conclusion can be drawn from this study for the scientific substantiation of the claim.

The study by Mireaux and Schmitt (2007, unpublished) was a pilot, single-blind, placebo-controlled, cross-over study which investigated the effects of a single dose of 1.25 g of Appl'In® (equivalent to 78 mg phloridzin, 1.25 g of talc were used as placebo) on post-prandial blood glucose concentrations in 10 healthy adults. Appl'In® and placebo were consumed either 30 min before or together with 50 g of glucose on a single occasion in fasting conditions. Blood glucose concentrations were determined

immediately before and up to 120 minutes after consumption of glucose. The Panel notes that insulin responses were not assessed. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The study by Schmitt and Mireaux (2008, unpublished) was a double-blind, placebo-controlled, cross-over study which investigated the effect of 250 mg of Appl'In® (equivalent to 14 mg phloridzin), 1.25 g of Appl'In® (equivalent to 70 mg phloridzin) or microcrystalline cellulose (placebo) in capsules, on post-prandial blood glucose concentrations in 18 adults (16 female). Appl'In® and placebo were consumed 15 min before administration of 50 g of sucrose, each on a single occasion, in fasting conditions. Blood glucose concentrations were determined before and up to 120 min after consumption of sucrose. The Panel notes that insulin responses were not assessed. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

Five animal and *in vitro* studies which assessed the effect of phloridzin on glucose transport and absorption (Besnard et al., 2008; Ikumi et al., 2008; Katsuno et al., 2007; Pajor et al., 2008; Takii et al., 1997), have been provided. The Panel considers that human studies are required for the substantiation of a claim, and that evidence provided in animal and *in vitro* studies is not sufficient to predict the occurrence of an effect of Appl'In® consumption on post-prandial glycaemic responses in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Appl'In® and reduction of post-prandial glycaemic responses.

CONCLUSIONS

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

- The food, Appl'In® polyphenolic apple extract powder containing at least 5 % phloridzin, which is the subject of the claim, is sufficiently characterised in relation to the claimed effect.
- The claimed effect proposed by the applicant relates to the reduction of the post-prandial glycaemic responses. The target population proposed for the claim is healthy women in the general population willing to reduce their glycaemic response. Reduction of post-prandial glycaemic responses (as long as post-prandial insulinaemic responses are not disproportionately increased) may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of Appl'In® and reduction of post-prandial glycaemic responses.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on “Appl'In® polyphenolic apple extract powder (*Malus domestica*)” and reduction of post-prandial glycaemic responses pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0296_FR). April 2011. Submitted by Diana Naturals.

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GLOSSARY / ABBREVIATIONS

BMI Body Mass Index

HPLC High performance liquid chromatography