

SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function pursuant to Article 13(5) of Regulation (EC) No 1924/2006¹

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

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ABSTRACT

Following an application from Gelita AG, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Germany, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function. The Panel considers that the food, VeriSol[®]P, which is the subject of the health claim, is sufficiently characterised. The claimed effect proposed by the applicant is “maintenance of skin health, as indicated by an increased skin elasticity and a reduction of wrinkles volume”. The target population proposed by the applicant is the general adult population. The Panel considers that a change in skin elasticity leading to an improvement in skin function is a beneficial physiological effect. The applicant presented two human studies, one animal study and one *in vitro* study as being pertinent to the health claim. No conclusions can be drawn from one of the two human studies as it did not assess a function of the skin. The second human study assessed a function, i.e. the water barrier function, of the skin, but did not show an effect on this function. In the absence of evidence for an effect on skin function in humans, the animal and *in vitro* studies cannot be used for the scientific substantiation of the claim. The Panel concludes that a cause and effect relationship has not been established between the consumption of VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function.

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KEY WORDS

VeriSol[®]P, collagen hydrolysate, skin elasticity, skin function, health claims

¹ On request from the Competent Authority of Germany following an application by Gelita AG, Question No EFSA-Q-2012-00839, adopted on 30 May 2013.

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SUMMARY

Following an application from Gelita AG, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Germany for authorisation of a health claim, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function.

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

The food that is the subject of the health claim is VeriSol[®]P, which is a collagen hydrolysate derived from porcine sources. The Panel considers that VeriSol[®]P is sufficiently characterised.

The claimed effect proposed by the applicant is “maintenance of skin health, as indicated by an increased skin elasticity and a reduction of wrinkles volume”. The target population proposed by the applicant is the general adult population. The Panel considers that a change in skin elasticity leading to an improvement in skin function is a beneficial physiological effect.

The applicant presented two human studies, one animal study and one *in vitro* study as being pertinent to the health claim.

In a randomised, double-blind, placebo-controlled study, 114 women received daily for eight weeks 2.5 g VeriSol[®]P or a placebo. The primary outcome of the study was the volume of eye wrinkles. Secondary outcomes were the contents of pro-collagen type I, elastin and fibrillin in suction blister biopsies. The Panel notes that this study did not assess a function of the skin, and considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

In another randomised, double-blind, placebo-controlled study, 69 women received daily for eight weeks 2.5 g VeriSol[®]P, 5 g VeriSol[®]P or a placebo. Primary outcomes of the study were skin elasticity and skin hydration. Secondary outcomes were transepidermal and transonychia water loss. In addition, skin roughness was assessed. The Panel considers that measures of transepidermal water loss can be used as scientific evidence for a function, i.e. the water barrier function, of the skin, and that measures of the water-holding capacity (hydration) of skin may be used as supportive evidence. There were no significant differences between the groups for transepidermal water loss or skin hydration at any time point. The Panel notes that this study did not show an effect on the water barrier function of the skin, and that no other function of the skin was measured.

One animal study in mice and one *in vitro* study in fibroblasts were provided. The Panel considers that in the absence of evidence for an effect of VeriSol[®]P on a change in skin elasticity leading to an improvement in skin function in humans, the animal and *in vitro* studies cannot be used for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function.

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BACKGROUND

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 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 Article 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 20/09/2012.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The application included a request for the protection of proprietary data.
- On 29/10/2012, during the validation process of the application, EFSA sent a request to the applicant to provide missing information.
- On 07/12/2012, EFSA received the missing information as submitted by the applicant.
- The scientific evaluation procedure started on 20/12/2012.
- On 28/02/2013, 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 06/03/2013, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- On 21/03/2013, EFSA received the requested information (which was made available to EFSA in electronic format on 19/03/2013) and the clock was restarted, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- During its meeting on 30/05/2013, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function.

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: VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function.

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 for the marketing of VeriSol[®]P, a positive assessment of its safety, nor a decision on whether VeriSol[®]P 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: Gelita AG, Uferstrasse 7, 69412 Eberbach, Germany.

The application includes a request for the protection of proprietary data for four unpublished studies (Oesser, 2010; Schunck, 2011; Westphal, 2012a, 2012b), in accordance with Article 21 of Regulation (EC) No 1924/2006.

Food/constituent as stated by the applicant

According to the applicant, specific collagen hydrolysates (either from bovine or porcine sources) which are produced under the brand names of VeriSol[®]B (from bovine sources) and VeriSol[®]P (from porcine sources).

Health relationship as claimed by the applicant

According to the applicant, the collagen hydrolysates (i.e. VeriSol[®]B and VeriSol[®]P) have an effect on the “maintenance of skin health”. This would be indicated by an increase in skin elasticity and a reduction of skin wrinkles volume. As the mechanism a contribution to normal collagen and elastin synthesis was proposed.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: “characteristic collagen peptide mixture (collagen hydrolysate) having a beneficial physiological effect on the maintenance of skin health, as indicated by an increased skin elasticity and a reduction of wrinkles volume, by contributing to a normal collagen and elastin synthesis”.

Specific conditions of use as proposed by the applicant

The applicant has proposed a daily intake of 2.5 g of the product. The target population is the general adult population.

ASSESSMENT

1. Characterisation of the food/constituent

The food that is the subject of the health claim is a collagen hydrolysate produced under the brand name of VeriSol[®]P.

The applicant proposed two distinct types of collagen hydrolysate, derived either from bovine (i.e. VeriSol[®]B) or porcine (i.e. VeriSol[®]P) sources. On the basis of the studies provided, the Panel considers that VeriSol[®]P is the subject of the health claim.

VeriSol[®]P is a mixture of collagen peptides produced by enzymatic hydrolysis of type I and type III collagen from pig skin gelatine. An overview of the manufacturing process, the typical amino acid profile, molecular weight distribution of the collagen peptides (mean 2.0±0.3 kDa), batch-to-batch variability and stability data were provided.

The Panel considers that the food, VeriSol[®]P, 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 “maintenance of skin health, as indicated by an increased skin elasticity and a reduction of wrinkles volume”. The target population proposed by the applicant is the general adult population.

During the validation and assessment of the application, EFSA informed the applicant that a change in skin structure contributing to the maintenance (i.e. reduced loss) of skin function might be considered a beneficial physiological effect provided that there is evidence that such changes in skin structure lead to changes in skin function (EFSA NDA Panel, 2012). The applicant was also informed that health claims on the maintenance of normal structure, hydration, elasticity or appearance of the skin do not necessarily refer to a particular physiological function of the skin as required by Regulation (EC) No 1924/2006; nor does a decrease in wrinkles, which may be related to the maintenance or improvement of skin structure/hydration/elasticity (EFSA NDA Panel, 2012). EFSA requested the applicant to indicate the function of the skin to which the health claim refers and the outcome measure(s) which would be appropriate for the assessment of the claim. In reply, the applicant indicated that the health claim refers to the mechanical and immune skin barrier function. However, the outcome measures proposed by the applicant focused solely on skin elasticity rather than immune barrier function. In addition, a number of putative mechanisms were indicated, such as an increased expression of extracellular matrix proteins. It was agreed that a change in skin elasticity is a beneficial physiological effect provided that it leads to an improvement in skin function.

The Panel considers that a change in skin elasticity leading to an improvement in skin function is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

The applicant performed a literature search in PubMed, the Cochrane database, Web of Science and Google using the search terms [(“collagen hydrolysate” AND “skin”), (“collagen hydrolysate” AND “dietary supplements” AND “skin”), (“collagen peptides” AND (“intake” OR “dietary supplements”) AND “skin”)]. Studies were included if they were performed with the specified collagen hydrolysates (i.e. VeriSol[®]B or VeriSol[®]P). No such published studies were identified.

The applicant presented two unpublished human intervention studies (Westphal, 2012a, 2012b), one unpublished animal study (Schunck, 2011) and one unpublished *in vitro* study (Oesser, 2010) as being pertinent to the health claim. All four studies were claimed as proprietary by the applicant.

In a randomised, double-blind, placebo-controlled study (Westphal, 2012b, unpublished), 114 women (mean age 55.6 years, age range 45-65) received daily for eight weeks 2.5 g VeriSol[®]P (n = 57) or a placebo (maltodextrin, n = 57). Inclusion criteria were female sex, 45-65 years of age, and skin phototype I to III (Fitzpatrick scale). The primary outcome of the study was the volume of eye wrinkles. Secondary outcomes were the contents of pro-collagen type I, elastin and fibrillin in suction blister biopsies which were taken from a subgroup of participants.

The Panel notes that this study did not assess a function of the skin, and considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

In a randomised, double-blind, placebo-controlled study (Westphal, 2012a, unpublished), 69 women (mean age 47.8 years, age range 35-55) received daily for eight weeks 2.5 g VeriSol[®]P (n = 23), 5 g VeriSol[®]P (n = 23) or a placebo (maltodextrin, n = 23). Inclusion criteria were female sex, 35-55 years of age, skin phototype I to IV (Fitzpatrick scale) and dry skin on forearms (according to self-assessment). Power calculations were based on a previous study (Segger et al., 2008). It was estimated that 20 subjects per group were required to achieve a power of 70 % for the primary outcomes of the study which were skin elasticity and skin hydration. Secondary outcomes of the study

were transepidermal (TEWL) and transonychia (TOWL) water loss. In addition, skin roughness was assessed. The Panel considers that measures of TEWL can be used as scientific evidence for a function, i.e. the water barrier function, of the skin, and that measures of the water-holding capacity (hydration) of skin may be used as supportive evidence. Test sites were the inner sides of both forearms. Measurements were taken at baseline and at weeks four and eight. Seven subjects dropped out of the study. Data on 68 subjects were taken into consideration for the analysis (one subject was excluded as only base-line data were available). Data were tested for normal distribution using the Kolmogorov-Smirnov test. Differences between groups were compared using one-way analysis of variance (ANOVA) for normally distributed data, or the Kruskal-Wallis test for non-normally distributed data. There were no significant differences between the groups for TEWL or skin hydration at any time point.

The Panel notes that this study did not show an effect on the water barrier function of the skin, and that no other function of the skin was measured.

One animal study (Schunck, 2011, unpublished) in hairless (i.e. SKH-1) mice was provided. VeriSol[®]P or a placebo were administered to 32 male mice for four weeks. Following UV-B light irradiation (in order to stimulate skin-ageing), skin hydration, skin elasticity and transepidermal water loss were measured.

One *in vitro* study (Oesser, 2010, unpublished) investigated gene expression of various extracellular matrix molecules (biglycan, decorin, versican and collagen type I), inflammatory cytokines (IL-1 β and IL-6) and matrix metalloproteinases (MMP-1 and MMP-13) in human primary dermal fibroblasts which were exposed to VeriSol[®]P.

The Panel considers that in the absence of evidence for an effect of VeriSol[®]P on a change in skin elasticity leading to an improvement in skin function in humans, the animal and *in vitro* studies cannot be used for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function.

CONCLUSIONS

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

- The food, VeriSol[®]P, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is “maintenance of skin health, as indicated by an increased skin elasticity and a reduction of wrinkles volume”. The target population proposed by the applicant is the general adult population. A change in skin elasticity leading to an improvement in skin function is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on VeriSol[®]P and a change in skin elasticity leading to an improvement in skin function pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0366_DE). September 2012. Submitted by Gelita AG.

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GLOSSARY/ABBREVIATIONS

ANOVA	Analysis of variance
TEWL	Transepidermal water loss
TOWL	Transonychial water loss