

SCIENTIFIC OPINION

Scientific Opinion on the modification of the authorisation of a health claim related to water-soluble tomato concentrate and helps to maintain a healthy blood flow and benefits circulation pursuant to Article 13(5) of Regulation (EC) No 1924/2006 following a request in accordance with Article 19 of the 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 Provexis Natural Products Limited submitted pursuant to Article 19 of Regulation (EC) No 1924/2006 via the Competent Authority of United Kingdom, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on a request for modification of the authorisation of a health claim related to water-soluble tomato concentrate and platelet aggregation. The modification concerns an extension of the authorised health claim to additional proposed conditions of use for powdered single-serve sachets, tablets, and capsules. The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence and/or including a request for the protection of proprietary data. The Panel considers that the food constituents, water-soluble tomato concentrate I and II (i.e., in powder sachets, tablets and capsules), which are the subject of the claim are sufficiently characterised. The results of one unpublished study showed that the three water-soluble tomato concentrate formulations reduced platelet aggregation as compared to the corresponding control and baseline values, with no significant differences between the three formulations. The Panel concludes that a cause and effect relationship has been established between the consumption of water-soluble tomato concentrate I and II (corresponding to the specifications provided by the applicant) and a reduction in platelet aggregation under the new conditions of use proposed by the applicant (i.e., consumed as powder, tablets or capsules). © European Food Safety Authority, 2010

KEY WORDS

Water soluble tomato concentrate, platelet aggregation, clotting time, adults, conditions of use, health claims.

¹ On request from Provexis Natural Products Limited, Question No EFSA-Q-2010-00809, adopted on 09 July 2010.

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SUMMARY

Following an initial application from Provexis Natural Products Limited, submitted in 2009 pursuant to Article 13(5) of Regulation (EC) No 1924/2006, and subsequently to the opinion adopted by the Panel on Dietetic Products, Nutrition and Allergies on a health claim related to the effects of water-soluble tomato concentrate (WSTC) I and II on the blood platelet activity, the Commission Decision was adopted on 17 December 2009 authorising a health claim related to “water-soluble tomato concentrate (WSTC) I and II helps maintain normal platelet aggregation, which contributes to healthy blood flow”.

In April 2010, Provexis Natural Products Limited submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 a request in accordance with Article 19 of the afore-mentioned Regulation for modification of the authorisation of the health claim related to water-soluble tomato concentrate (WSTC) I and II helps maintain normal platelet aggregation, which contributes to healthy blood flow.

The modification concerns an extension of the authorised health claim to additional proposed conditions of use for powdered single-serve sachets, tablets, and capsules.

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

As a consequence, the Panel on Dietetic Products, Nutrition and Allergies, in the present opinion, addresses only whether the conditions of use for the authorised claim could be extended to powdered single-serve sachets, tablets, and capsules.

The Panel considers that the food constituents, WSTC I and II (i.e., in powder sachets, tablets and capsules), which are the subject of the claim, are sufficiently characterised.

The Panel considers that the bioavailability of potentially active compounds in WSTC, when administered as powder, tablets or capsules, would not be different from that observed in other food matrices for which the health claim has been authorised (i.e., fruit juices, flavoured drinks or yogurt drinks) as long as these are easily dissolved in water.

One unpublished study addressed the acute effects of different forms of the tomato extract on platelet aggregation. The study was a double-blind placebo-controlled, randomised crossover design with three interventions (corresponding to 3 g WSTC I (syrup), WSTC II 150 mg (powder) produced at ambient temperature, and WSTC II 150 mg (powder) produced at 65°C) and one control. All test and control materials were administered in capsules with hydroxypropyl methylcellulose as food matrix together with 200 mL of water. The results showed that the three WSTC formulations reduced platelet aggregation (ADP agonist) as compared to the corresponding control and baseline values, with no significant differences between the three formulations. The responses to collagen 2 mg/L were also significant for all three formulations, whereas the response to collagen 5 mg/L was significant only for WSTC I. Thromboxane A₂ generation (measured by the concentration of the stable metabolite thromboxane B₂) was significantly reduced by the three formulations for ADP and both collagen concentrations. No changes were observed in plasma soluble P-selectin, a marker of platelet activation. This study indicated that the biological activity of both forms of WSTC (I and II) administered in capsules is comparable to equivalent doses provided in fruit juice.

The Panel concludes that a cause and effect relationship has been established between the consumption of water-soluble tomato concentrate (i.e., WSTC I and II corresponding to the specifications provided by the applicant) and the reduction in platelet aggregation under the new conditions of use proposed by the applicant (i.e., consumed as powder, tablets or capsules).

In order to achieve the claimed effect, 3 g WSTC I or 150 mg WSTC II as powder, tablets or easily dissolved capsules with at least 200 mL of liquid should be consumed daily. The target population is

adults between 35 and 70 years of age. The Panel considers that there is no basis to restrict the conditions of use to this age range in the adult population.

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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 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 13(5) of that Regulation lays down provisions for 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).

The same Regulation, as referred to in Article 19, also lays down provisions for modification, suspension and revocation of authorisations. The procedures laid down in Article 15 and 18 shall apply *mutatis mutandis*.

According to Article 18 of that Regulation, an application for the modification, suspension or revocation of authorisations of health claims included 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, who 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 22/04/2010.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence and/or including a request for the protection of proprietary data.
- The scientific evaluation procedure started on 30/04/2010.
- During the meeting on 09/07/2010, the NDA Panel, after having evaluated the overall data submitted, adopted an opinion on the scientific substantiation of a health claim related to water-soluble tomato concentrate and the reduction in platelet aggregation under the new conditions of use proposed by the applicant.

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 19 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: water-soluble tomato concentrate (WSTC I and II) and reduction of platelet aggregation.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of water-soluble tomato concentrate (WSTC I and II), a positive assessment of its safety, nor a decision on whether water-soluble tomato concentrate (WSTC I and II) 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 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.

INFORMATION PROVIDED BY THE APPLICANT

Applicant's name and address: Provexis Natural Products Limited, Thames Court, 1 Victoria Street, Windsor, Berkshire, SL4 1YB, United Kingdom.

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

Water-soluble tomato concentrate (WSTC) in two variant forms named WSTC I and its low-sugar derivative, WSTC II. WSTC is derived from ripe tomatoes, *Lycopersicon esculentum*, and is intended for use in fruit juices, fruit flavoured drinks, yoghurt drinks, and dietary supplements.

Health relationship as claimed by the applicant

Water-soluble tomato concentrate (WSTC) contains naturally occurring anti-platelet compounds which have been shown to suppress blood platelet activity in healthy people after consumption. Consuming WSTC reduces platelet aggregability, thereby maintaining the blood in a fluid and low-coagulable state. This helps to maintain healthy blood flow, by preventing micro-aggregates forming within the circulation, and by preventing the adherence of platelets to blood vessel walls or fatty plaques. Platelet function is not completely suppressed, and an appropriate level is maintained so that platelets can aggregate upon vascular injury. However after WSTC consumption, circulating platelets will be less responsive to activating factors, such as plasma VLDL or signals from inflammatory cells. This maintains the haemostatic balance required for a healthy vascular circulation.

Wording of the health claim as proposed by the applicant

Water-Soluble Tomato Concentrate (WSTC) I and II helps maintain normal platelet aggregation, which contributes to healthy blood flow.

Specific conditions of use as proposed by the applicant

The conditions of use associated with the authorised claim require the provision of information to the consumer stating that the beneficial effect is obtained with a daily consumption of 3g WSTC I or 150mg WSTC II in up to 250 ml of either fruit juices, flavoured drinks or yoghurt drinks (unless heavily pasteurised).

The applicant, Provexis Natural Products Limited, included human intervention data in the original dossier supporting the use of WSTC in other categories of foods, specifically dietary supplements, but inadvertently neglected to specifically request the inclusion of this format in the conditions of use. The applicant is now seeking to address this oversight and is requesting the formal extension of the approved conditions of use to include dietary supplements.

ASSESSMENT

The Panel has already issued an opinion on the scientific substantiation of a health claim related to water-soluble tomato concentrate (WSTC I and II) and platelet aggregation pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (EFSA, 2009). The Commission Decision was adopted on 17 December 2009 authorising a health claim related to “water-soluble tomato concentrate (WSTC) I and II helps maintain normal platelet aggregation, which contributes to healthy blood flow” (EC, 2009).

Therefore, the present opinion will only address whether the conditions of use for this claim could be extended to powdered single-serve sachets, tablets, and capsules.

1. Characterisation of the food/constituent

The applicant states that no modification has been introduced in the manufacturing process of the food constituents that are the subject of the health claim (i.e., WSTC I and II) in order to prepare the food forms to which the extension for the use of the claim is requested (i.e., powdered single-serve sachets, tablets and capsules).

The applicant also provides *in vitro* data suggesting that, when filled with WSTC I or II with or without common excipients, hard-shell capsule materials such as gelatine or hydroxypropyl methylcellulose (HPMC), as well as other vegetarian alternatives (e.g. Vegicaps) have good solubility characteristics allowing the capsules to absorb water and disintegrate quickly in the stomach environment.

The Panel considers that the food constituents, WSTC I and II (i.e., in powder sachets, tablets and capsules), which are the subject of the claim, are sufficiently characterised.

2. Relevance of the claimed effect to human health

See previous assessment of the EFSA NDA Panel (EFSA, 2009).

3. Scientific substantiation of the claimed effect

The Panel considers that the bioavailability of potentially active compounds in WSTC when administered as powder, tablets or capsules would not be different from that observed in other food matrices for which the health claim has been authorised (i.e., fruit juices, flavoured drinks or yogurt drinks) as long as these are easily dissolved in water.

As stated in the previous assessment (EFSA, 2009) the unpublished study by O’Kennedy et al. (2007) addressed the acute effects of different forms of the tomato extract on platelet aggregation. The study was a double-blind placebo-controlled, randomised crossover design with three interventions (corresponding to 3 g WSTC I (syrup), WSTC II 150 mg (powder) produced at ambient temperature, and WSTC II 150 mg (powder) produced at 65°C) and one control, with 45 healthy males and females 35-70 years old in each arm. All test and control materials were administered in capsules with hydroxypropyl methylcellulose as food matrix (i.e., Vegicaps) together with 200 mL of water. The results showed that the three WSTC formulations reduced platelet aggregation (ADP agonist) as compared to the corresponding control and baseline values, ranging from 13.5 to 17.2 %, with no significant differences between the three formulations. The responses to collagen 2 mg/L were also significant for all three formulations, whereas the response to collagen 5 mg/L was significant only for WSTC I. Thromboxane A₂ generation (measured by the concentration of the stable metabolite thromboxane B₂) was significantly reduced by the three formulations for ADP and both collagen concentrations. No changes were observed in plasma soluble P-selectin, a marker of platelet activation. This study indicated that the biological activity of both forms of WSTC (I and II) administered in capsules (i.e., Vegicaps) is comparable to equivalent doses provided in fruit juice.

The Panel concludes that a cause and effect relationship has been established between the consumption of water-soluble tomato concentrate (i.e., WSTC I and II corresponding to the specifications provided by the applicant) and the reduction in platelet aggregation under the new conditions of use proposed by the applicant (i.e., consumed as powder, tablets or capsules).

4. Panel's comments on the proposed wording

See previous assessment of the EFSA NDA Panel (EFSA, 2009) and Commission Decision dated 17 December 2009⁵.

5. Conditions and restrictions of use

The Panel considers that, in order to achieve the claimed effect, 3 g WSTC I or 150 mg WSTC II as powder, tablets or easily dissolved capsules with at least 200 mL of liquid should be consumed daily. The target population is adults between 35 and 70 years of age. The Panel considers that there is no basis to restrict the conditions of use to this age range in the adult population.

CONCLUSIONS

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

- The Panel considers that the food constituents, WSTC I and II (i.e., in powder sachets, tablets and capsules), which are the subject of the claim, are sufficiently characterised.
- A cause and effect relationship has been established between the consumption of water-soluble tomato concentrate (i.e., WSTC I and II corresponding to the specifications provided by the applicant) and the reduction in platelet aggregation under the new conditions of use proposed by the applicant (i.e., consumed as powder, tablets or capsules).
- In order to achieve the claimed effect, 3 g WSTC I or 150 mg WSTC II as powder, tablets or easily dissolved capsules with at least 200 mL of liquid should be consumed daily. The target population is adults between 35 and 70 years of age. The Panel considers that there is no basis to restrict the conditions of use to this age range in the adult population.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on water-soluble tomato concentrate (WSTC I and II) and helps to maintain a healthy blood flow and benefits circulation pursuant to Article 13(5) of Regulation (EC) No 1924/2006 following a request in accordance with Article 19 of the afore-mentioned Regulation (Claim serial No: 0282_UK). April 2010. Submitted by Provexis Natural Products Limited.

REFERENCES

- EFSA (European Food Safety Authority), 2009. Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific substantiation of a health claim related to water-soluble tomato concentrate (WSTC I and II) and platelet aggregation pursuant to Article 13(5) of Regulation (EC) No 1924/2006. The EFSA Journal, 1101, 1-15.
- O'Kennedy N, Crosbie L, Greyling A, de Bree A, Kroner CK, Arthur JA and Duttaroy AK, 2007. A randomised, controlled and double-blinded crossover study to compare the antiplatelet effects of three different formats of WSTC in healthy humans. REC No. 07/S0801/13.

⁵ Commission Decision of 17 December 2009 authorising a health claim on the effect of water-soluble tomato concentrate on platelet aggregation and granting the protection of proprietary data under Regulation (EC) No 1924/2006 of the European Parliament and of the Council (notified under document C(2009) 10113) (Text with EEA relevance). Official Journal of the European Union OJ L 336, 18.12.2009, p. 55–57.

GLOSSARY / ABBREVIATIONS

WSTC Water-Soluble Tomato Concentrate