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Curcumin and normal functioning of joints: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006

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Abstract

Following an application from Suomen Terveystuote Oy, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Finland, 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 curcumin and normal functioning of joints. The food that is proposed as the subject of the health claim is curcumin. The Panel considers that curcumin is sufficiently characterised. The claimed effect proposed by the applicant is 'normal functioning of joints by reducing the biomarkers of inflammation'. The target population proposed by the applicant is the general population. Upon a request from EFSA to clarify whether the claimed effect is related to the normal function of joints or rather to the reduction of inflammation, the applicant did not address this issue in the reply. The Panel assumes that the claimed effect refers to the maintenance of joint function. The Panel considers that maintenance of joint function is a beneficial physiological effect. The Panel considers that no conclusions can be drawn from 15 human intervention studies conducted in patients with osteoarthritis or rheumatoid arthritis and from one study in obese subjects on serum cytokines for the scientific substantiation of the claim. In the absence of evidence for an effect of curcumin on the normal function of joints in humans, the results of the human studies on curcumin pharmacokinetics, safety and mechanistic studies, the animal studies and the *in vitro* studies submitted by the applicant cannot be used as a source of data for the scientific substantiation of the claim. The Panel concludes that a cause and effect relationship has not been established between the consumption of curcumin and maintenance of joint function.

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Keywords: curcumin, diferuloylmethane, joints, health claim

Requestor: Competent Authority of Finland following an application by Suomen Terveystuote Oy

Question number: EFSA-Q-2016-00856

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Summary

Following an application from Suomen Terveystuote Oy, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Finland, 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 curcumin and normal functioning of joints.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.

The general approach of the NDA Panel for the evaluation of health claims applications is outlined in the EFSA general guidance for stakeholders on health claim applications and the guidance on the scientific requirements for health claims related to guidance on the scientific requirements for health claims related to bone, joints, skin and oral health.

The food that is proposed as the subject of the health claim is curcumin. The Panel considers that curcumin, which is the subject of the health claim, is sufficiently characterised.

The claimed effect proposed by the applicant is 'normal functioning of joints by reducing the biomarkers of inflammation'. The target population proposed by the applicant is the general population. Upon a request from the European Food Safety Authority (EFSA) to clarify whether the claimed effect is related to the normal function of joints or rather to the reduction of inflammation, the applicant did not address this issue in the reply. In the absence of clarification from the applicant and taking into account the proposed wording for the claim, the Panel assumes that the claimed effect refers to the maintenance of joint function. The Panel considers that maintenance of joint function is a beneficial physiological effect.

The applicant identified 16 human intervention studies on the effects of curcumin on 'markers' of joint function as being pertinent to the claim. The Panel notes that 11 studies were performed in patients with knee osteoarthritis, two were performed in patients with osteoarthritis and clinical manifestations in many joints, and two were conducted in patients with rheumatoid arthritis. The Panel considers that no conclusions can be drawn from these 15 human intervention studies conducted in patients with osteoarthritis or rheumatoid arthritis for the scientific substantiation of the claim. Another human intervention study conducted in obese subjects assessed the effects of curcumin in combination with bioperine on 12 of serum cytokines; joint function was not assessed. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The Panel considers that, in the absence of evidence for an effect of curcumin on the normal function of joints in humans, the results of the human studies on curcumin pharmacokinetics, safety and mechanistic studies ($n = 15$), the animal studies ($n = 12$) and the *in vitro* ($n = 12$) studies submitted by the applicant cannot be used as a source of data for the scientific substantiation of the claim. The Panel considers also that no conclusions can be drawn from 25 narrative reviews for the scientific substantiation of the claim.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of curcumin and maintenance of joint function.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1924/2006¹ 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).

1.2. Interpretation of the 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: curcumin and normal functioning of joints.

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of curcumin, a positive assessment of its safety, nor a decision on whether curcumin 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.

2. Data and methodologies

2.1. Data

2.1.1. Information provided by the applicant

2.1.1.1. Food/constituent as stated by the applicant

According to the applicant, the food for which the health claim is made is curcumin. Curcumin is a general product that is separated from turmeric (*Curcuma longa* L., *Curcuma domestica*). Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone and zingiberone), sugars, proteins and resins. Curcumin is a lipophilic polyphenol that is nearly insoluble in water but is quite stable in the acidic pH of the stomach. It may make up 2–5% of the total spice in turmeric. Commercial curcumin contains three major components: diferuloylmethane (82%), demethoxycurcumin (15%) and bisdemethoxycurcumin (3%), together referred to as curcuminoids.

2.1.1.2. Health relationship as claimed by the applicant

According to the applicant, the claimed effect relates to: 'normal functioning of joints by reducing the biomarkers of inflammation. This helps to preserve the normal functioning and alleviate possible inflammations in the joints and joint cartilage'. The outcome measures used to assess the relationship between curcumin and normal functioning of joints were 'standardized tools such as the WOMAC scale'.

¹ 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.

2.1.1.3. Mechanism by which the food/constituent could exert the claimed effect as proposed by the applicant

According to the applicant, curcumin acts as an antioxidant and reduces the biomarkers of inflammation.

2.1.1.4. Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: 'curcumin contributes to the normal functioning of joints'.

2.1.1.5. Specific conditions of use as proposed by the applicant

According to the applicant, the target population for the intended health claim is the general population. At least 500 mg is recommended as an effective dose. Pregnant women should avoid using curcumin.

2.1.2. Data provided by the applicant

Health claim application on consumption of curcumin and normal function of joints pursuant to Article 13.5 of Regulation 1924/2006, presented in a common and structured format as outlined in the Scientific and technical guidance for the preparation and presentation of applications for authorisation of health claims.²

As outlined in the General guidance for stakeholders on health claim applications,³ it is the responsibility of the applicant to provide the totality of the available evidence.

2.2. Methodologies

The general approach of the NDA Panel for the evaluation of health claims applications is outlined in the EFSA general guidance for stakeholders on health claim applications (EFSA NDA Panel, 2016).

The scientific requirements for health claims related to bone, joints, skin and oral health are outlined in a specific EFSA guidance (EFSA NDA Panel, 2012).

3. Assessment

3.1. Characterisation of the food/constituent

The food that is proposed by the applicant as the subject of the health claim is curcumin.

Curcumin, a hydrophobic polyphenol, is the principal constituent extracted from dried rhizomes of *C. longa* L. (turmeric), synonym of *C. domestica* Valetton. It is also known as diferuloylmethane, with a chemical formula (1*E*,6*E*)-1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione, a molecular formula C₂₁H₂₀O₆, and a molecular weight of 368.39 g/mol.

Together with demethoxycurcumin and bis-demethoxycurcumin, curcumin belongs to the chemical group of curcuminoids. Curcumin is obtained by solvent extraction of turmeric, i.e. the ground rhizomes of natural strains of *C. longa*. In order to obtain a concentrated curcumin powder, the extract is purified by crystallisation (EFSA ANS Panel, 2010).

Curcumin is used as a colouring agent by the food industry and it is known under food additive E-code number E 100.

The Panel considers that curcumin, which is the subject of the health claim, is sufficiently characterised.

3.2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is 'normal functioning of joints by reducing the biomarkers of inflammation'. The target population proposed by the applicant is the general population.

² EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Turck D, Bresson J-L, Burlingame B, Dean T, Fairweather-Tait S, Heinonen M, Hirsch-Ernst KI, Mangelsdorf I, McArdle HJ, Naska A, Neuhäuser-Berthold M, Nowicka G, Pentieva K, Sanz Y, Sjödin A, Stern M, Tomé D, Van Loveren H, Vinceti M, Willatts P, Martin A, Strain JJ, Heng L, Valtuena Martinez S and Siani A, 2017. Scientific and technical guidance for the preparation and presentation of a health claim application (Revision 2). EFSA Journal 2017;15(1):4680, 31 pp. <https://doi.org/10.2903/j.efsa.2017.4680>

³ EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016. General scientific guidance for stakeholders on health claim applications. EFSA Journal 2016;14(1):4367, 38 pp. <https://doi.org/10.2903/j.efsa.2016.4367>

Upon a request from EFSA to clarify whether the claimed effect is related to the normal function of joints or rather to the reduction of inflammation, the applicant did not address this issue in the reply. The applicant explained that the outcome measures used to assess the relationship between curcumin and normal functioning of joints were standardised tools such as the WOMAC scale.

In the absence of clarification from the applicant and taking into account the proposed wording for the claim, the Panel assumes that the claimed effect refers to the maintenance of joint function.

Possible outcomes related to joint function include mobility, stiffness and (dis)comfort (e.g. pain). For example, validated protocols and procedures under well-defined testing conditions using appropriate goniometers have been used to assess the mobility of different joints (e.g. knee, ankle); validated questionnaires could be used for the assessment of joint stiffness and (dis)comfort. For self-reported outcome measures, adequate blinding of subjects is particularly important (EFSA NDA Panel, 2012).

The Panel considers that maintenance of joint function is a beneficial physiological effect.

3.3. Scientific substantiation of the claimed effect

The applicant performed a literature search with the use of the following key words: 'curcumin,' 'curcumin joints,' 'curcumin inflammation,' and later, 'curcumin osteoarthritis'. Details on the literature searches were not provided. The Panel notes that no information was provided how the studies were selected.

The applicant identified 16 human intervention studies on the effects of curcumin on 'markers' of joint function as being pertinent to the claim. The Panel notes that 11 studies were performed in patients with knee osteoarthritis (Chopra et al., 2004; Kuptniratsaikul et al., 2009, 2014; Belcaro et al., 2010, 2014; Kertia et al., 2012; Pinsornsak and Niempoog, 2012; Madhu et al., 2013; Henrotin et al., 2014; Nakagawa et al., 2014; Panahi et al., 2014), two were performed in patients with osteoarthritis and clinical manifestations in many joints (Kulkarni et al., 1991; Appelboom et al., 2014), and two were conducted in patients with rheumatoid arthritis (Deodhar et al., 1980; Chandran and Goel, 2012).

In order to explain why the results of these 15 human intervention studies conducted in patients with osteoarthritis or rheumatoid arthritis could be extrapolated to the target population for the claim (i.e. the general population), the applicant argued that biomarkers of inflammation are 'connected' to joint health, and that the reduction in markers of inflammation shown in patients with osteoarthritis has also been observed *in vitro* and in healthy subjects, so that the results obtained with curcumin in patients with osteoarthritis could be extrapolated to the general population. The applicant also argued that one study (Henrotin et al., 2014) showed that curcumin reduced serum concentrations of peptide of the alpha-helical region of type II collagen (Coll2-1), which suggests that curcumin could reduce cartilage matrix degradation, that this is supported by the *in vitro* observation that curcumin inhibits matrix metalloproteinase-a (MMP-a) production by chondrocytes, and that this 'ought to work similarly with non-osteoarthritis population'.

The Panel considers that, as specified in EFSA's guidance (EFSA NDA Panel, 2012), 'the available scientific evidence does not establish that results obtained in patients with osteoarthritis (degenerative arthrosis) relating to the treatment of symptoms of this disease [...] can be extrapolated to the target population for the claim (subjects without the disease). This is because normal cells and tissues are genetically (gene expression) and functionally different from osteoarthritic cells and tissues, and therefore may respond differently to interventions with exogenous substances. In addition, the mechanisms involved in the onset and/or progression of osteoarthritis are largely unknown, so that it cannot be established that an intervention which has an effect on the progression of the disease (in patients with osteoarthritis), would also have an effect on its onset (subjects without the disease)'. Also, "studies on subjects with arthritis of various origins (rheumatoid arthritis, [...]) and which relate to the treatment of symptoms of the disease cannot be considered for the scientific substantiation of health claims on joint function in the general population'.

The Panel considers that no conclusions can be drawn from these 15 human intervention studies conducted in patients with osteoarthritis or rheumatoid arthritis for the scientific substantiation of the claim targeted for the general population.

Another human intervention study (Ganjali et al., 2014) conducted in obese subjects assessed the effects of curcumin in combination with bioperine on 12 serum cytokines; joint function was not assessed. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The Panel considers that, in the absence of evidence for an effect of curcumin on the normal function of joints in humans, the results of the human studies on curcumin pharmacokinetics, safety

and mechanistic studies (n = 15), the animal studies (n = 12) and the *in vitro* (n = 12) studies submitted by the applicant cannot be used as a source of data for the scientific substantiation of the claim. The Panel considers also that no conclusions can be drawn from 25 narrative reviews for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of curcumin and maintenance of joint function.

4. Conclusions

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

- the food/constituent, curcumin, which is the subject of the health claim, is sufficiently characterised.
- the claimed effect proposed by the applicant is 'normal functioning of joints'. The target population proposed by the applicant is the general population. Maintenance of joint function is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of curcumin and maintenance of joint function.

Steps taken by EFSA

Health claim application on 'curcumin' and 'normal functioning of joints' pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 000856_0451_FI). Submitted by Suomen Terveysravinto Oy, PL 146, 33101, Tampere, Finland.

- 1) This application was received by EFSA on 19/12/2016.
- 2) The scientific evaluation procedure started on 13/1/2017.
- 3) On 18/1/2017, 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. The scientific evaluation was suspended on 11/2/2017 and was restarted on 21/2/2017, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- 4) On 20/1/2017, EFSA received the applicant's reply (which was made available to EFSA in electronic format on 20/1/2017).
- 5) During its meeting on 4/4/2017, the NDA Panel, having evaluated the data, adopted an opinion on the scientific substantiation of a health claim related to curcumin and normal functioning of joints.

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Abbreviations

Coll2-1	peptide of the alpha-helical region of type II collagen
MMP-a	matrix metalloproteinase-a
NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index