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EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of a health claim related to coffee C21 and reduction of spontaneous DNA strand breaks 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 coffee C21 and reduction of spontaneous DNA strand breaks 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 Tchibo GmbH, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Germany, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to coffee C21 and reduction of spontaneous DNA strand breaks. The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The food constituent that is the subject of the health claim is coffee C21, which is sufficiently characterised. The claimed effect is reduction of spontaneous DNA strand breaks, which may be a beneficial physiological effect. The target population proposed by the applicant is the general population. One human study on coffee C21 was not controlled adequately for confounding factors that may have affected the outcome. Four additional human studies investigated coffees other than coffee C21. Two of these had no control group and a third study did not assess spontaneous DNA strand breaks. No conclusions could be drawn from these human studies for the scientific substantiation of the claim. The fourth study did not show an effect of coffee compared to water on spontaneous DNA strand breaks. The evidence provided in animal and *in vitro* studies is not sufficient to predict the occurrence of an effect of coffee C21 consumption on the reduction of spontaneous DNA strand breaks in humans. The Panel concludes that a cause and effect relationship has not been established between the consumption of coffee C21 and a reduction in spontaneous DNA strand breaks.

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KEY WORDS

Coffee, C21, DNA strand break, comet assay, health claims.

¹ On request from the Competent Authority of Germany following an application by Tchibo GmbH, Question No EFSA-Q-2011-00783, adopted on 23 November 2011.

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SUMMARY

Following an application from Tchibo GmbH, submitted pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Germany, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver an opinion on the scientific substantiation of a health claim related to coffee C21 and reduction of spontaneous DNA strand breaks.

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

The food constituent that is the subject of the health claim is coffee C21. Coffee C21 is a blend of roasted coffee arabica (*Coffea arabica* L.) standardised by its concentrations of chlorogenic acids, trigonelline and *N*-methylpyridinium. Chlorogenic acids, trigonelline and *N*-methylpyridinium can be measured in ground and brewed coffee by established methods. The Panel considers that coffee C21, which is the subject of the health claim, is sufficiently characterised.

The claimed effect is “reduction of the amount of DNA strand breaks and of oxidative DNA damage in white blood cells”. The target population proposed by the applicant is the general population. The Panel considers that reduction of spontaneous DNA strand breaks may be a beneficial physiological effect.

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

One single-arm human intervention study investigated the effect of consuming coffee C21 on spontaneous DNA strand breaks in 35 healthy non-smoking male volunteers. The Panel notes that possible confounding factors (e.g. changes in body weight, the overall diet, or exposure to environmental factors) which may have affected spontaneous DNA strand breaks independently of coffee C21 intake throughout the study were not controlled adequately. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The remaining four human intervention studies provided by the applicant used coffee types which had a composition different from that of C21. Two of these were single-arm intervention studies. The Panel notes the absence of a control group and considers that no conclusions can be drawn from these uncontrolled studies for the scientific substantiation of the claim. The remaining two studies were randomised, cross-over trials in which subjects consumed 800 mL of either coffee or water for five consecutive days each. One of the studies did not report on spontaneous DNA strand breaks. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim. The second study used a coffee arabica for which the composition regarding chlorogenic acids, trigonelline and *N*-methylpyridinium was provided. No significant differences in spontaneous DNA strand breaks between the coffee and water interventions were reported. The Panel considers that this study does not show an effect of coffee with the reported composition on spontaneous DNA strand breaks.

The Panel considers that evidence provided in animal and *in vitro* studies is not sufficient to predict the occurrence of an effect of coffee C21 consumption on the reduction of spontaneous DNA strand breaks in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of coffee C21 and a reduction of spontaneous DNA strand breaks.

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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 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 07/06/2011.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.
- The scientific evaluation procedure started on 20/06/2011.
- On 14/07/2011, 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 25/07/2011 in compliance with Art. 18(3) of Regulation (EC) No 1924/2006.
- On 09/08/2011, EFSA received the requested information as submitted by the applicant and the clock was restarted.
- During the meeting on 23/11/2011, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to coffee C21 and reduction of spontaneous DNA strand breaks.

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: coffee C21 and reduction of spontaneous DNA strand breaks.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of coffee C21, a positive assessment of its safety, nor a decision on whether coffee C21 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 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.

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: Tchibo GmbH, Üherseering 18, D-22297 Hamburg, Germany.

Food/constituent as stated by the applicant

According to the applicant, the food constituent for which the claim is made is coffee C21, a blend of roast of pure coffee arabica (*Coffea arabica* L.), standardised by its content in caffeoyl quinic acids (chlorogenic acids), *N*-methylpyridinium and trigonelline.

Health relationship as claimed by the applicant

According to the applicant, consumption of coffee C21 leads to a significant reduction of the amount of DNA strand breaks and of oxidative DNA damage in white blood cells.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "Regular consumption of Coffee C21 contributes to the maintenance of DNA integrity in cells of the body".

Specific conditions of use as proposed by the applicant

The conditions of use proposed by the applicant are three large cups of coffee C21 (750 mL) per day. The target population proposed by the applicant is the general population.

ASSESSMENT

1. Characterisation of the food/constituent

The food that is the subject of the health claim is coffee C21.

Coffee brew is a mixture of compounds, including coffee constituents such as caffeine, caffeoyl quinic acids and trigonelline, together with compounds formed during roasting, such as *N*-methylpyridinium, nicotinic acid, nicotinamide and melanoidins (Lang et al., 2008).

Coffee C21 is a blend of roasted coffee arabica (*Coffea arabica* L.). The roasting is accomplished with regular coffee manufacturing roasters by applying heat to dry beans. Roasted ground coffee C21 is standardised by its concentrations of chlorogenic acids (also called caffeoyl quinic acids, polyphenols), trigonelline (alkaloid) and *N*-methylpyridinium (NMP, pyridine derivative). The concentrations of chlorogenic acids, trigonelline and the thermal degradation product NMP depend on the degree of roasting. The desired composition is obtained by blending different coffee roasts and by adjusting the roasting conditions (temperature and time). A decline of 6.6 % in caffeoyl quinic acids was reported during 45 months' storage at room temperature.

According to the applicant, standard filtered C21 coffee (i.e. 29.5 g in 600 mL water, prepared with a standard drip filter coffee machine) contains 580 mg/L chlorogenic acids, 265 mg/L trigonelline and 72 mg/L NMP, respectively.

Chlorogenic acids, trigonelline and NMP can be measured in ground and brewed coffee by established methods.

The Panel considers that the food, coffee C21, which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect is “reduction of the amount of DNA strand breaks and of oxidative DNA damage in white blood cells”. The target population proposed by the applicant is the general population.

Following EFSA’s request to clarify the claimed effect, the applicant indicated that the primary outcome measure to be used for the scientific substantiation of the health claim is the amount of “spontaneous” DNA strand breaks in freshly isolated (untreated) lymphocytes, measured by the comet assay as mean tail intensity (TI%).

Spontaneous DNA strand breaks normally occur during the DNA repair process but also represent DNA lesions induced by genetic or environmental factors (e.g. mutagenic or pro-oxidant chemicals, radiation). Such DNA strand breaks alter DNA properties, may induce anomalies during DNA replication and translation, and require repair for maintenance of cell functioning and survival.

The Panel considers that reduction of spontaneous DNA strand breaks may be a beneficial physiological effect.

3. Scientific substantiation of the claimed effect

The applicant performed a literature search in PubMed with the following terms: “coffee and DNA damage”, “coffee and DNA strand break(s)”, “coffee and Comet assay”, “caffeine and DNA damage and trial”, “chlorogenic acid and DNA damage and trial”, “trigonelline and DNA damage and trial”, “methyl pyridinium and DNA damage and trial” and “niacin and DNA damage and trial”. Five studies were excluded by the applicant because they did not report on measures of spontaneous DNA strand breaks, assessed the effect of age on sperm DNA damage, or used a high dose of niacin. The applicant identified five human intervention studies, one animal study and two *in vitro* studies as being pertinent to the health claim.

One single-arm human intervention study investigated the effect of consuming coffee C21 on spontaneous DNA strand breaks in 35 healthy non-smoking male volunteers (age 20-44 years) (Bakuradze et al., 2011). The 12-week study included a four-week run-in, a four-week intervention phase, and a four-week follow-up (wash-out). Subjects were asked to consume 750 mL of coffee C21 daily during the intervention phase, and the same amount of water instead during the run-in and follow up. Subjects were instructed to keep their usual diet and to avoid coffee and caffeinated products, foods and beverages rich in polyphenols, and dietary supplements for the entire duration of the study. Food records were completed by the subjects in the last week of each study phase and in the second week after the end of the study. At the beginning of each period and at the end of the study, blood samples were taken to measure spontaneous DNA strand breaks in lymphocytes by the comet assay (TI%). Within group differences between the study periods were assessed. Two subjects dropped out because of side effects related to the intervention (gastric symptoms and sleeplessness). Energy (and all macronutrient) intakes as well as body weight were reported to be significantly lower in the intervention phase than in the run-in phase. Follow-up values fell in between and were not significantly different from either phase, indicating that the study may have been temporally confounded by other factors. The Panel notes that possible confounding factors (e.g. changes in body weight, the overall diet, or exposure to environmental factors) which may have affected spontaneous DNA strand breaks independently of coffee C21 intake throughout the study were not controlled adequately. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The remaining four human intervention studies provided by the applicant (Bichler et al., 2007; Hoelzl et al., 2010; Misik et al., 2010; Steinkellner et al., 2005) used coffee types which had a composition different from that of C21. Two of these were single-arm intervention studies in eight (Bichler et al., 2007) and 10 (Steinkellner et al., 2005) subjects who consumed 600 mL or 1 L of coffee/day,

respectively, for five days. The Panel notes the absence of a control group and considers that no conclusions can be drawn from these uncontrolled studies for the scientific substantiation of the claim. The remaining two studies were randomised, cross-over trials in which 36 (Hoelzl et al., 2010) and 38 (Misik et al., 2010) subjects, respectively, consumed 800 mL of either coffee or water for five consecutive days each after a run-in phase, and with a wash-out period in between. One of the studies (Hoelzl et al., 2010) did not report on spontaneous DNA strand breaks. The Panel considers that no conclusions can be drawn from this study for the scientific substantiation of the claim. The second study (Misik et al., 2010) used a 100 % coffee arabica product which contained 2.44 % chlorogenic acids, 0.89 % trigonelline, and 0.0426 % NMP. Chlorogenic acid (125 mg/100 mL), caffeine (65 mg/100 mL) and NMP (3.1 mg/100 mL) concentrations were also measured in the brew (prepared by paper filtration) consumed by participants. No significant differences in spontaneous DNA strand breaks between the coffee and water interventions were reported in the study. The Panel considers that this study does not show an effect of coffee with the reported content of chlorogenic acids, trigonelline and NMP on spontaneous DNA strand breaks.

One animal study (Paur et al., 2010) investigated the effects of roasted coffee, and of the degree of roasting, on nuclear factor kappa B (NF- κ B) and nuclear factor-E2-related factor 2 (Nrf2)/electrophile response element (EpRE) activities in transgenic NF- κ B-luciferase and transgenic EpRE-luciferase mice, respectively. Two *in vitro* studies assessed the effects of differentially roasted coffee extracts on antioxidant activity, cellular reactive oxygen species, DNA damage, NAD(P)H-quinone oxidoreductase, γ -glutamylcysteine ligase, and glutathione reductase in HT-29/Caco-2 cells at 24-h incubation (Bakuradze et al., 2010), and on the Nrf2/antioxidant response element (ARE) pathway in human colon carcinoma cells (Boettler et al., 2011), respectively. The Panel considers that evidence provided in animal and *in vitro* studies is not sufficient to predict the occurrence of an effect of coffee C21 consumption on the reduction of spontaneous DNA strand breaks in humans.

The Panel concludes that a cause and effect relationship has not been established between the consumption of coffee C21 and a reduction of spontaneous DNA strand breaks.

CONCLUSIONS

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

- The food constituent, coffee C21, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect is “reduction of the amount of DNA strand breaks and of oxidative DNA damage in white blood cells”. The target population, as proposed by the applicant, is the general population. A reduction of spontaneous DNA strand breaks may be a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of coffee C21 and a reduction of spontaneous DNA strand breaks.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on coffee C21 and reduction of spontaneous DNA strand breaks pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0303_DE). June 2011. Submitted by Tchibo GmbH.

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GLOSSARY / ABBREVIATIONS

ARE	Antioxidant response element
DNA	Deoxyribonucleic acid
EpRE	Electrophile response element
NAD(P)H	Nicotinamide adenine dinucleotide phosphate
NF- κ B	Nuclear factor kappa B
NMP	<i>N</i> -methylpyridinium
Nrf2	Nuclear factor-E2-related factor 2
TI	Tail intensity