Black tea and improvement of attention: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006

Dominique Turck, Jean-Louis Bresson, Barbara Burlingame, Tara Dean, Susan Fairweather-Tait, Marina Heinonen, Karen-Ildico Hirsch-Ernst, Inge Mangelsdorf, Harry J. Mcardle, Androniki Naska, et al.

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 17 April 2018

doi: 10.2903/j.efsa.2018.5266

Black tea and improvement of attention: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), Dominique Turck, Jean-Louis Bresson, Barbara Burlingame, Tara Dean, Susan Fairweather-Tait, Marina Heinonen, Karen Ildico Hirsch-Ernst, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Kristina Pentieva, Yolanda Sanz, Anders Sjödin, Martin Stern, Daniel Tomé, Henk Van Loveren, Marco Vinceti, Peter Willatts, Ambroise Martin, Sean (JJ) Strain and Alfonso Siani

Abstract

Following an application from Unilever NV, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Ireland, 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 black tea and improvement of attention. The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence. The food proposed by the applicant as the subject of the health claim is black tea. The Panel considers that black tea characterised by its content of tea solids, caffeine and L-theanine, which is the subject of the health claim, is sufficiently characterised in relation to the claimed effect. The claimed effect proposed by the applicant is 'improves attention'. The Panel considers that improvement of attention is a beneficial physiological effect. Three human intervention studies provided by the applicant show an effect of black tea on attention under the conditions of used proposed by the applicant. The applicant proposed that the claimed effect depends on the concerted action of two substances, caffeine and L-theanine, both of which are present in black tea. The Panel considers that the effect of black tea on attention observed in the three human intervention studies provided by the applicant can be explained by its caffeine content. The Panel concludes that a cause and effect relationship has been established between the consumption of black tea and improvement of attention. The Panel considers that the effect of black tea on attention can be explained by its caffeine content. The following wording reflects the scientific evidence: 'Owing to its caffeine content, black tea improves attention'. In order to obtain the claimed effect, 2–3 servings of black tea providing at least 75 mg of caffeine in total should be consumed within 90 min.

Keywords: Black tea, attention, caffeine, L-theanine, health claim

Requestor: Competent Authority of Ireland following an application by Unilever NV

Question number: EFSA-Q-2017-00606

Correspondence: nda@efsa.europa.eu

Panel members: Jean Louis Bresson, Barbara Burlingame, Tara Dean, Susan Fairweather-Tait, Marina Heinonen, Karen Ildico Hirsch-Ernst, Inge Mangelsdorf, Harry McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Kristina Pentieva, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Daniel Tomé, Dominique Turck, Hendrik Van Loveren, Marco Vinceti and Peter Willatts.

Acknowledgements: The Panel wishes to thank the members of the Working Group on Claims: Jean-Louis Bresson, Susan Fairweather-Tait, Marina Heinonen, Ambroise Martin, Harry McArdle, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Sean (JJ) Strain, Hendrik Van Loveren and Peter Willatts, for the preparatory work on this scientific output.

Suggested citation: 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 SJJ and Siani A, 2018. Scientific Opinion on the black tea and improvement of attention: evaluation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006. EFSA Journal 2018;16(5):5266, 17 pp. https://doi.org/10.2903/j.efsa.2018.5266

ISSN: 1831-4732

The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.

Summary

Following an application from Unilever NV, submitted for authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of Ireland, 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 black tea and improvement of attention.

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 functions of the nervous system, including psychological functions.

The food proposed by the applicant as the subject of the health claim is black tea. The Panel considers that the food, black tea characterised by its content of tea solids, caffeine and L-theanine, which is the subject of the health claim, is sufficiently characterised in relation to the claimed effect.

The claimed effect proposed by the applicant is 'improve attention'. The proposed target population is 'adults in the general population'. The Panel considers that improvement of attention is a beneficial physiological effect.

The three human intervention studies provided by the applicant showed an effect of black tea on attention under the conditions of use proposed by the applicant (a cumulative amount of 1,040 mg of tea solids, delivering at least 90 mg of caffeine and 36 mg of L-theanine consumed within a time period of up to 90 min).

The applicant proposed that the claimed effect depends on the concerted action of two substances, caffeine and L-theanine, both of which are present in black tea. The Panel notes that a claim related to caffeine and increased attention has already been evaluated with a positive outcome. Five human intervention studies addressed the effects of caffeine plus L-theanine vs caffeine alone on attention. The Panel considers that these studies do not show an effect of caffeine and L-theanine on attention separate to that of caffeine alone, and that the mechanism of action for L-theanine on attention proposed by the applicant is speculative. The Panel also considers that it is well established that caffeine increases attention in healthy adult individuals of both sexes at doses of at least 75 mg, and that cumulative doses of caffeine consumed over a period of 90 min are likely to exert similar effects on attention as the same dose of caffeine consumed on a single occasion. The Panel, therefore, considers that the effect of black tea on attention observed in the three human intervention studies provided by the applicant can be explained by its caffeine content.

On the basis of the data provided, the Panel concludes that a cause and effect relationship has been established between the consumption of black tea and improvement of attention.

The Panel considers that the effect of black tea on attention can be explained by its caffeine content.

The Panel also considers that these conclusions could not have been reached without the study claimed as proprietary by the applicant.

The following wording reflects the scientific evidence: 'Owing to its caffeine content, black tea improves attention'.

In order to obtain the claimed effect, 2–3 servings of black tea providing at least 75 mg of caffeine in total should be consumed within 90 min. The target population is adults in the general population.

Table of contents

1. Introduction

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

Regulation (EC) No 1924/2006[1] 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: black tea and improvement of attention.

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

Information provided by the applicant

Food/constituent as stated by the applicant

According to the applicant, the food for which the health claim is made is 'black tea prepared from the leaves of *Camellia sinensis* (L.) Kuntz. Black tea is characterised by its tea solids content and the levels of two key constituents, caffeine and L-theanine'.

Health relationship as claimed by the applicant

According to the applicant, the claimed effect relates to: 'improves attention. Attention (claimed effect) is "a state of focused awareness on a subset of the available perceptual information" as defined by the American Psychological Association. The concept of attention is an umbrella term; it entails a number of distinct but related cognitive processes. Attention is measured as performance on validated and standardized psychometric tests, with improvements demonstrated in terms of increased accuracy (i.e. more correct responses) and/or decreased reaction times (i.e. faster responses)'.

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

The applicant claims that the claimed effect depends on the concerted action of caffeine and L-theanine present in black tea. 'Caffeine is known to affect neurotransmission in general, by antagonizing adenosine receptors, and to have secondary effects on specific neurotransmitters which are involved in cognitive function. L-theanine can bind to receptors and transporters involved in neurotransmission, which are involved in cognitive function'.

[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.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: 'black tea improves attention'.

Specific conditions of use as proposed by the applicant

According to the applicant, the target population for the intended health claim is adults in the general population. Consumption of black tea containing at least a cumulative amount of 1,040 mg of tea solids, delivering at least 90 mg of caffeine and 36 mg of L-theanine consumed within a time period of up to 90 min is proposed. According to the applicant, this equates to 2–3 servings of black tea (based on internal Unilever analyses of tea content).

Upon a request from EFSA to reconsider the scientific evidence submitted for the substantiation of the claim in the context of a claim on caffeine and attention at doses of at least 75 mg per serving which has already been assessed by EFSA with a positive outcome (EFSA NDA Panel, 2011), the applicant replied that in the current application, the claimed effect was demonstrated following consumption of black tea containing at least a cumulative amount of 1,040 mg of tea solids, delivering at least 90 mg of caffeine and 36 mg of L-theanine consumed within a time period of up to 90 min. This amount can typically be provided by 2–3 servings of black tea. This cumulative benefit is not supported by the conditions of use of the positive opinion for caffeine.

Data provided by the applicant

Health claim application on black tea and improvement of attention 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 functions of the nervous system, including psychological functions are outlined in a specific EFSA guidance (EFSA NDA Panel, 2012).

The application contains data claimed as confidential: unpublished consumer research, unpublished compositional data of a range of Unilever black teas, results of from the unpublished study by Giesbrecht et al. (2012); results from the unpublished meta-analysis by Giesbrecht and Rowson (2016) (specified in details in Confidentiality Decision).

The application contains data claimed as proprietary: Giesbrecht et al. (2012) unpublished study report, Rao and Nobre (2007), unpublished study report and unpublished meta-analysis by Giesbrecht and Rowson (2016).

3. Assessment

3.1. Characterisation of the food/constituent

The food proposed by the applicant as the subject of the health claim is 'black tea prepared from the leaves of *Camellia sinensis* (L.) Kuntz'. According to the applicant, black tea is characterised by its tea solids content and by the content of caffeine and L-theanine, the two constituents identified by the applicant as being responsible for the claimed effect.

Caffeine and L-theanine can be measured in foods by well-established methods.

The Panel considers that the food, black tea characterised by its content of tea solids, caffeine and L-theanine, which is the subject of the health claim, is sufficiently characterised in relation to the claimed effect.

[2] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific and technical guidance for the preparation and presentation of an application for authorisation of a health claim (revision 1). EFSA Journal 2011;9(5):2170, 36 pp. https://doi.org/10.2903/j.efsa.2011.2170

[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

3.2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is 'improvement of attention'. The proposed target population is 'adults in the general population'.

Attention (concentration), defined as a cognitive construct, refers to the ability to attend to, select and use incoming sensory information. There are two broad categories of attention. Selective attention is the ability to concentrate on one task or source of information to the exclusion of others. Sustained attention (vigilance) is the ability to concentrate over a period of time. The increase, maintenance or reduced loss of selective attention, sustained attention, or both, is considered to be a beneficial physiological effect.

Various valid psychometric tests can be used to assess changes in either selective attention (e.g. visual selective search tests and categorical search attention tests) or sustained attention (e.g. continuous performance tasks, rapid visual information processing tasks, and visual or auditory vigilance tasks), whereas standardised attention test batteries allow a comprehensive assessment of the full spectrum of attention by using sets of tests. Accuracy and reaction time/speed of response measures should be considered together in order to assess performance of attention tests and control for speed-accuracy trade-off (EFSA NDA Panel, 2012).

There are a number of tests which can be used to measure attention in research settings, including the Attention Switching Task, Attention Network Test, Intersensory Attention Tasks, Stroop Colour-Word Test, Choice Reaction Task, Match to Sample Visual Search, Rapid Visual Information Processing (RVIP) Task, Sustained Attention to Response Task, Digit Vigilance Reaction Time Task, Choice Reaction Time Task and Cued Attention Task.

The Panel considers that improvement of attention is a beneficial physiological effect.

3.3. Scientific substantiation of the claimed effect

The applicant performed a literature search in PubMed and Psych Info with the following key words: "tea", in combination with "attention", "concentration" or "alertness" [Title/Abstract] "theanine" AND "caffeine", in combination with "attention", "concentration" or "alertness" [Title/Abstract]. The search was limited to peer-reviewed articles, written in English, in healthy human adults. Hand searches were also performed.

The applicant identified 13 published and one unpublished human intervention studies, and one published and one unpublished meta-analyses of human intervention studies, as being pertinent to the claim.

The Panel noted that an application on 'black tea from *Camellia sinensis* and helps to focus attention' submitted by the same applicant had already been evaluated with an unfavourable outcome (EFSA NDA Panel, 2008). The Panel also noted that an unpublished study report by Rao and Nobre (2007) describing a human intervention study on black tea which was evaluated in the context of that application (EFSA NDA Panel, 2008) was not submitted with the present application. Upon a request from EFSA to justify this omission, the applicant explained that the study does not meet the current EFSA guidance for reporting of unpublished studies, but acknowledged that the study could be pertinent to the claim and re-submitted the study report.

Among the 15 human intervention studies provided, three studies included an intervention arm with black tea for which either the content of tea solids and L-theanine (Durlach, 1998; Durlach et al., 2002), or the content of tea solids, caffeine and L-theanine (Kahathuduwa et al., 2017) was not reported. The Panel considers that, in these studies, black tea was not sufficiently characterised in relation to the claimed effect and considers that no conclusions can be drawn from these intervention arms for the substantiation of the claim. In one study already provided with the previous application (Rao and Nobre, 2007, unpublished, claimed as proprietary), it is unclear whether the study beverages were or were not black tea, and therefore whether they comply with the characterisation of the food that is the subject of the claim.

Two studies (Hindmarch et al., 1998, 2000) included outcome measures of critical flicker fusion (CFF) and choice reaction time (CRT) for which no measures of response accuracy were obtained. One study (Durlach et al., 2002) assessed performance on the key-press task, which is a type of CRT task in which reaction time, but not accuracy, was measured. Upon a request from EFSA to consider whether tests of CFF and CRT are measures of attention, the applicant commented that there is a close link between attention and alertness, and that the findings of these studies are supportive. The Panel acknowledges the association between alertness and attention. However, the Panel notes that,

whereas alertness can be measured by psychometric tests which determine reaction time (e.g. CRT), both accuracy and reaction time should be considered together when assessing performance on attention tests in order to control for speed-accuracy trade-off (EFSA NDA Panel, 2012). Therefore, the Panel notes that no objective measures of attention were obtained in any of these three studies (Hindmarch et al., 1998, 2000; Durlach et al., 2002) and considers that no conclusions can be drawn from them for the scientific substantiation of the claim.

The remaining human intervention studies investigated the effects of either black tea (n = 3) or caffeine and L-theanine combinations from sources other than black tea (n = 9) on measures of attention.

Human intervention studies on black tea

Three of the human intervention studies provided (described in the two publications/reports) investigated the effects of black tea characterised by its content of tea solids, caffeine and L-theanine on measures of attention (De Bruin et al., 2011; Giesbrecht et al., 2012, unpublished study report claimed as proprietary by the applicant).

Two randomised, double-blind, placebo-controlled, cross-over, two-period, intervention studies are reported in one publication (De Bruin et al., 2011).

The first study included 26 healthy volunteers (mean age 30.7 ± 11.2 years; 20 females) who were regular caffeine consumers. No power analysis was reported. The authors stated that the sample size was loosely based on previous observational tea studies. Participants abstained from caffeinated foods for 15 h before visiting the laboratory. After completing baseline attention tests, participants consumed one 200 mL beverage, followed by a second 200 mL beverage 50 min after the first. Beverages were either black tea (providing 520 mg of tea solids, 50 mg of caffeine and 23 mg of L- theanine per serving; cumulative amount of 1,040 mg tea solids, 100 mg caffeine and 46 mg L-theanine) or placebo (i.e. coloured and tea-flavoured water). The black tea was prepared by pouring 235 mL of boiled, de-ionised water onto a PG Tips tea bag. The tea was passively infused for 60 s after which the teabag was removed and allowed to drip over the cup for 3 s. The 200 mL of the infusion was then poured and served in a fresh cup. The placebo was prepared by adding 10 mg caramel colour, 10 μL red food colour, 7 mg tea flavour, 150 mg oak tannin and 150 mg grapeseed tannin powders to 200 mL boiled, de-ionised water. The authors noted that the placebo tea flavours and colours have no known effects on cognitive performance. Interventions were allocated using a Latin square design such that the order of the beverages was counterbalanced across participants, with visits separated by 6–14 days.

Attention performance was measured at baseline and after each serving using two standardised tasks: the Attention Switching Task and the Intersensory Attention Task.

The Attention Switching Task measured ability to shift attention between different stimuli displayed on a screen. Participants had to respond to even numbers when the font colour was purple and vowels when the font colour was red. The font colour (and therefore the task) was switched every three trials in a predictable manner. The Intersensory Attention Task measured ability to attend to stimuli presented in the visual and auditory modalities. On each trial, an auditory cue instructed participants to attend to either the auditory or visual modality. This was followed by the presentation of stimuli in either the auditory modality or the visual modality (unisensory), or both modalities (intersensory), and participants had to report whether the stimuli were the same or different.

The proportion of correct responses and reaction times on the attention tests were analysed using a 2 × 2 mixed model analysis of covariance (ANCOVA) with a repeated-measures covariance structure. Subjects were modelled as a random effect, and treatment (black tea or placebo) and session were used as within-subject factors. Baseline scores and treatment order were included as covariates.

On the Attention Switching Task, participants were significantly more accurate after consuming black tea compared to placebo ($F_{1,22.4} = 12.0$; $p = 0.002$), but reaction times did not differ significantly. The Panel considers that increased accuracy with no increase in reaction time can be interpreted as an improvement in attention. On the Intersensory Attention Task, participants were more accurate in the black tea condition on both the auditory ($F_{1,79.7} = 14.2$, $p < 0.001$) and visual ($F_{1,63.7} = 5.2$, $p < 0.03$) intersensory subtasks, and had faster reaction times on the visual intersensory subtask ($F_{1,18.6} = 4.7$, $p = 0.043$), but not on the auditory-attention subtask.

In the second study with a similar design, 32 healthy volunteers (mean age 30.3 ± 10.1 years; 15 females) who were regular caffeine consumers and had abstained from caffeinated foods for 15 h, consumed three 200 mL servings of a beverage administered at 40-min intervals over the course of 80 min. Each serving contained either black tea (cumulative amount of 1,140 mg tea solids, 90 mg caffeine and 36 mg L-theanine) or placebo. Methods for the allocation of interventions and washout

periods were as in study one. Sample size was reported to be based on the results of study one. The Panel notes that no details of a power analysis were provided.

The tea was prepared by pouring 190 mL of boiled, de-ionised water onto a Lipton Yellow Label tea bag. The tea was passively infused for 90 s, after which the tea bag was removed and allowed to drip over the cup for 3 s. A quantity of 10 mL of water at room temperature was added. The placebo was prepared by matching colour and flavour with the tested back tea as in study one.

Participants were assessed on the Attention Switching and Intersensory Attention Tasks at baseline and after each serving. Results were analysed as in study one. Accuracy on the Attention Switching Task was significantly greater after black tea compared to placebo ($F_{1,28.9} = 8.53$, $p = 0.007$), but there were no significant differences in reaction time. Performance on the Intersensory Attention Tasks showed no significant effects of black tea compared to placebo.

The Panel notes that these two studies with a similar design showed a consistent effect of black tea on attention when attention performance was assessed using the Attention Switching Task. The Panel also notes that effects of black tea on attention when using Intersensory Attention Tasks were inconsistent between the studies, with the first study showing a significant effect of black tea on attention and the second study showing no effect compared to placebo. The Panel considers, however, that these two studies taken together support an effect of black tea on attention, and that the effect is observed for 2–3 servings of black tea consumed over 50–80 min providing a cumulative dose of tea solids, caffeine and L-theanine of about 1 g, 90–100 mg and 36–46 mg, respectively.

Giesbrecht et al. (2012, unpublished, claimed as proprietary) reported on a randomised, four-period, cross-over, placebo-controlled, double-blind study of the effects of black tea consumption on attention. A total of 40 healthy regular caffeine consumers (mean age 26.1 ± 8.5 years; 20 females) were recruited. Participants were instructed to refrain from food and beverages containing caffeine or L-theanine in the 24 h prior to testing.

At each test session, participants consumed two servings of a beverage (200 mL each) separated by an interval of 75 min. The beverages were:

a) regular strength tea (cumulative amount of 1,224 mg tea solids, 100 mg caffeine and 38 mg L-theanine);
b) 1.5 strength tea (cumulative amount of 1,704 mg tea solids, 150 mg caffeine and 57 mg L-theanine);
c) double strength tea (cumulative amount of 2,126 mg tea solids, 200 mg caffeine and 76 mg L-theanine);
d) placebo (deionised water with food grade colours and flavours, 0 mg caffeine and 0 mg L-theanine).

Each participant received all four beverages (each beverage on a different testing day, four testing days in total per participant) in a balanced order achieved with a Williams square design for 40 participants. Testing days were separated by 7 ± 2 days and the study duration for each participant was approximately 5 weeks.

The primary outcome was accuracy on the Attention Switching Task. A power analysis based on the results by De Bruin et al. (2011) estimated that a sample of 32 participants was necessary to detect a difference in accuracy of 1.6% with a power of 0.90 and an alpha of 0.05. Allowing for a dropout rate of 20% and considering the study design, 40 subjects were recruited for the study. The Attention Switching Task was performed according to the protocol reported by De Bruin et al. (2011).

The secondary outcome was performance on the Attention Network Test (ANT), which measures three different components of attention (Alerting, Orienting and Executive Control) within a single task. On each trial, participants are required to indicate the direction of a central arrow which is surrounded by flanker arrows. Each trial is preceded by one of four possible cue conditions.

The attention tasks were administered at baseline, 40 min after the first serving of the beverage, and 35 min after the second serving.

Intention-to-treat (ITT) analyses were conducted on all participants who received at least one test beverage. Per protocol (PP) analyses excluded participants on medical grounds, non-compliance with the protocol or on the basis of extreme results in cognitive tasks. No participants were excluded from data analyses because of missing data. No formal imputation was performed in the event of excluded or missing data. There were no drop outs and no missed visits.

Data were evaluated with linear mixed models. The model included all main effects and interactions between treatment, session, test type (three levels) and correct response (2: respond/withhold). Baseline response and order of testing were included as covariates. The primary response was based

on a contrast comparing the interventions corresponding to 0 cups and 2 cups of tea. Adjusted p-values were reported with the adjustment made using the Tukey–Kramer correction to reflect the number of comparisons being performed.

ITT analyses on the Attention Switching Task showed that regular strength black tea significantly reduced reaction time ($t_{111} = 2.64$, $p = 0.046$), but had no effect on accuracy as compared to placebo ($t_{111} = 2.06$, $p = 0.174$). The Panel considers that a reduction in reaction time with no reduction in accuracy can be interpreted as an improvement in attention. Compared to placebo, 1.5 strength black tea did not significantly reduce reaction time ($t_{111} = 2.03$, $p = 0.165$), but did improve accuracy ($t_{111} = 3.94$, $p = 0.0008$). Double strength black tea compared to placebo significantly reduced reaction time ($t_{111} = 4.14$, $p = 0.0003$) and increased accuracy ($t_{111} = 4.55$, $p < 0.0001$).

In dose–response ITT analyses, a significant linear dose–response effect for accuracy (increased) and reaction time (decreased) was observed across beverages with increasing doses of tea solids, caffeine and L-theanine ($p < 0.0001$). Similar results were obtained in PP analyses.

ITT analyses on the ANT showed that all three black tea beverages increased accuracy compared to placebo ($t_{111} = 4.44 – 4.55$, $p < 0.0001$), but did not differ significantly from each other. There was a significant linear dose–response effect ($F_{1,260.3} = 25.1$, $p < 0.0001$). All three doses of black tea significantly reduced reaction times compared to placebo ($t_{111} = 4.87 – 6.70$, $p < 0.0001$), and there was a significant linear dose–response effect ($F_{1,116.6} = 52.5$, $p < 0.0001$). Similar results were obtained in PP analyses.

The Panel considers that this study shows an effect of black tea on attention, and that the effect is observed for two servings of black tea consumed over 75 min providing a cumulative dose of tea solids, caffeine and L-theanine of 1,224 mg, 100 mg and 38 mg, respectively.

Meta-analyses of human intervention studies

One published (Camfield et al., 2014) and one unpublished meta-analysis (Giesbrecht and Rowson, 2016) were provided.

Camfield et al. (2014) conducted a meta-analysis including seven studies on the effect of a combination of caffeine and L-theanine on Attention Switching, Multisensory Attention Tasks and RVIP. The Panel notes that five of these studies were provided with the application (Haskell et al., 2008; Owen et al., 2008; Einöther et al., 2010; Giesbrecht et al., 2010; De Bruin et al., 2011) and two studies were not included in the application because the treatment involved epigallocatechin gallate and not caffeine or L-theanine (Scholey et al., 2012; Wightman et al., 2012). The analysis for Attention Switching included five studies of which three (Owen et al., 2008; Einöther et al., 2010; Giesbrecht et al., 2010) investigated the effect of a combination of caffeine and L-theanine in product matrixes different from black tea compared to placebo. The analysis for Multisensory Attention Tasks included three studies of which one (Einöther et al., 2010) investigated the effect of a combination of caffeine and L-theanine in product matrixes different from black tea. All of the studies in the analysis for RVIP investigated the effect of a combination of caffeine and L-theanine in product matrixes different from black tea. The Panel considers that no conclusions can be drawn from this meta-analysis for the scientific substantiation of a claim on black tea.

The applicant also submitted an unpublished meta-analysis (Giesbrecht and Rowson, 2016) pooling the results of the studies evaluating the consumption of two or three cups of black tea versus placebo on the Attention Switching Task (two studies by De Bruin et al., 2011 in one publication; Giesbrecht et al., 2012, unpublished). The Panel considers that no information is provided by this meta-analysis for the substantiation of the claim in addition to the information provided in the individual studies on black tea described above.

Conclusions of human intervention studies on black tea

The Panel considers that, overall, the three human intervention studies provided by the applicant (two studies by De Bruin et al., 2011 in one publication; Giesbrecht et al., 2012, unpublished) show an effect of black tea on attention under the conditions of use proposed by the applicant.

Mechanism of action

The applicant proposed that the claimed effect depends on the concerted action of two substances, caffeine and L-theanine, both of which are present in black tea. Caffeine has a structure that is similar to adenosine, which is a central nervous system neuromodulator. When adenosine binds to its receptors, neural activity slows down. Caffeine binds to the same receptors, and when this occurs it prevents adenosine from binding and thus slowing neural activity. Some of these receptors occur in

the striatum, which explains the ability of caffeine to enhance motor activity, as well as general neural activity (Ferre, 2010). Caffeine also affects the dopaminergic system (Ferre et al., 1997), which is involved in the control of attention. The Panel notes that the effects of caffeine on the central nervous system and consequent influence on the control of attention are well established (Niehlig et al., 1992; McLellan et al., 2016).

With regard to the possible effects of L-theanine on the central nervous system, the applicant noted that L-theanine can cross the blood–brain barrier (Kimura and Murata, 1971; Terashima et al., 1999), and hypothesised that L-theanine may compete with endogenous amino acids for transport into the brain, and may modulate the activity of neurotransmitters involved in attention processes, including glutamate, glycine and gamma-aminobutyric acid (GABA) (Nestler et al., 2009; Chapter 5). Such modulation could occur by L-theanine binding to a variety of receptors and blocking signal transduction between neurons (Nedergaard et al., 2002; Kam and Nicoll, 2007). L-Theanine may indirectly affect neurotransmitter concentrations by interfering with the availability of their precursors, and thus affect cognition. The Panel notes that the proposed mechanism of action for L-theanine is speculative, and that no evidence was provided on the effects of L-theanine on attention.

The Panel notes that a claim related to caffeine and increased attention has already been evaluated with a positive outcome (EFSA NDA Panel, 2011). The Panel took into account that the evidence provided by consensus opinions/reports and by the majority of the studies submitted for the scientific substantiation of the claim showed good consensus on the role of caffeine in increasing attention, measured by a range of psychometric tasks, in healthy individuals of both sexes, at doses of at least 75 mg. In this context, the applicant was requested to explain how the claim on black tea which is the subject of the present application is different from the claim on caffeine that has been already evaluated by the Panel (EFSA NDA Panel, 2011). The applicant argued that the conditions of use for that claim indicate that, in order to bear the claim, a product should contain at least 75 mg of caffeine per serving, which is not the case of black tea. In addition, the applicant explained that the present application refers to a cumulative amount of 1,040 mg of tea solids, delivering at least 90 mg of caffeine and 36 mg of L-theanine consumed within a time period of up to 90 min, an amount which can typically be provided by 2–3 servings of black tea, and that this cumulative benefit is not supported by the conditions of use of the positive opinion for caffeine. Finally, the applicant argued that the application was on a food (black tea) and not on a particular constituent, that the effect of black tea on attention is due to the combination of caffeine and L-theanine (the latter contributing to the claimed effect) and that other tea constituents could also contribute (e.g. epigallocatechin gallate (EGCG)), although the evidence there was currently limited.

The Panel notes that caffeine has a plasma half-life of about 4 h with range of about 2–8 h, and that the kinetics of caffeine are linear up to very high (~ 500 mg) doses (EFSA NDA Panel, 2015). In this context, the Panel considers that cumulative doses of caffeine consumed over a period of 90 min are likely to exert similar effects on attention that the same dose of caffeine consumed on a single occasion.

EFSA informed the applicant that, among the human studies submitted, eight assessed effects of caffeine and L-theanine on attention in a different product matrix than black tea, and that although no conclusions could be drawn from these studies for the substantiation of the claim on black tea, they could provide evidence that caffeine and L-theanine in combination have a greater effect on attention than caffeine alone to support a claim on black tea rather than on caffeine. In reply, the applicant explained that the focus of the studies provided was on the combination of caffeine and L-theanine as only the combination is found in black tea, and that no selection was made on whether the studies also investigated the effects of caffeine and L-theanine vs caffeine or L-theanine alone. The applicant acknowledged that some of the studies provided did not allow differentiating between the effects of caffeine and L-theanine in combination and in isolation but did not search for or provide additional evidence in this respect.

As explained in the Scientific and technical guidance to applicants (EFSA NDA Panel, 2017), it is the duty of the applicant to provide all the available scientific data (including data in favour and not in favour, published and unpublished) which are pertinent to the health claim in order to demonstrate that the health claim is substantiated by the totality of the scientific data. In its evaluation, the NDA Panel may use data which are not included in the application if they are considered pertinent to the claim. However, the NDA Panel should not be required to undertake any additional literature reviews, to assemble or process data in order to evaluate the application. As such, the application should be comprehensive and complete. Therefore, the Panel assessed whether black tea (or the combination of caffeine and L-theanine which characterises black tea) has an effect on attention over and above the

effect that could be expected by its caffeine content on the basis of the studies that have been provided in the application (i.e. whether L-theanine contributes to the claimed effect).

Among the studies provided which investigated the effects of caffeine and/or L-theanine on attention but did not use black tea as the intervention, two investigated the effects of caffeine and L-theanine in combination but not the effects of caffeine alone (Einöther et al., 2010; Giesbrecht et al., 2010) and two did not report on between-group statistical comparisons for the caffeine plus L-theanine vs the caffeine interventions (Haskell et al., 2008; Kelly et al., 2008). The Panel considers that no conclusions can be drawn from these studies with respect to the effects of the combination of caffeine and L-theanine vs caffeine alone on attention.

Five additional human intervention studies addressed the effects of caffeine plus L-theanine vs caffeine alone on attention (Rao and Nobre, 2007; unpublished, claimed as proprietary; Owen et al., 2008; Foxe et al., 2012; Dodd et al., 2015; Kahathuduwa et al., 2017).

In a randomised, four-period, cross-over, placebo-controlled study already provided with the previous application, Rao and Nobre (2007, unpublished, claimed as proprietary) investigated the effects of caffeine and L-theanine consumption on attention. A total of 20 healthy volunteers (aged between 18 and 35 years, 10 females) were recruited. The study beverages (tea base) contained, per cup, 49 mg caffeine and 49 mg L-theanine (CT-high), 49 mg caffeine and 23 mg L-theanine (CT-low), 49 mg caffeine and no L-theanine (C), and 5.27 mg of L-theanine and no caffeine (placebo). The Panel notes that the nature of the tea base was not specified.

Participants were asked to refrain from drinking beverages containing caffeine, including coffee, tea, cola or other soft drinks, chocolate (including any chocolate products) on the day of the experiment prior to arrival at the laboratory. Three cups of the test beverages were ingested over 80 min, each administration being separated by 40-min intervals. Each session lasted approximately 3 h. The respective cumulative doses for the study beverages were 147 mg caffeine and 147 mg L-theanine (CT-high), 147 mg caffeine and 69 mg L-theanine (CT-low), 147 mg caffeine with no L-theanine (C), and 16 mg L-theanine and no caffeine (placebo). The order of experimental conditions was counterbalanced between participants.

Attention performance was measured with five standardised tasks: Flanker Interference Task (FLA), Attentional Blink Task (AB), Cued Spatial Orienting Task (CUED), Visual Oddball Task and Auditory Oddball Task. The series of five tasks were performed successively in a block, with a total of three blocks per session. The first block was administered 40 min after consuming the first drink, the second block 40 min after consuming the second drink, and the third block 50 min after consuming the third drink.

In the FLA task, participants were significantly more accurate in the CT-high ($F_{1,19}$) = 4.952, p = 0.038), CT-low ($F_{1,19}$ = 13.052, p = 0.002) and C ($F_{1,19}$ = 11.027, p = 0.004) conditions compared to placebo, but the three caffeine-containing conditions did not differ from each other. There were no significant differences involving reaction time. There were no significant differences between conditions in performance on the AB task. In the CUED task, there was a significant main effect of condition, but individual comparisons between the three caffeinated conditions and placebo were not reported. There were no significant differences for reaction time. In the Visual Oddball Task, participants were more accurate in the C ($F_{1,19}$ = 8.358, p = 0.009) and CT-high ($F_{1,19}$ = 5.835, p = 0.026) conditions compared to placebo, but performance in the CT-low and placebo conditions did not differ significantly, and there were no significant differences involving reaction time. In the Auditory Oddball Task, accuracy was significantly higher in all the caffeinated conditions compared to placebo, but comparisons between the caffeine plus L-theanine and caffeine alone conditions were not reported. There were no significant differences for reaction time.

The Panel considers that this study does not show an effect of the combination of caffeine and L-theanine above the effect of caffeine alone on attention.

Dodd et al. (2015) carried-out a randomised, four-period, cross-over, placebo-controlled, double-blind study with 24 healthy participants (mean age 21.8 years) consuming two capsules providing a cumulative dose of (a) 75 mg caffeine, (b) 50 mg L-theanine, (c) 75 mg caffeine and 50 mg L-theanine and (d) placebo. Participants attended four study visits separated by at least 48 h. Attention tests administered at each study visit included Serial 3 subtractions, Serial 7 subtractions, RVIP, Choice Reaction Time and Stroop Colour-Word Test. Attention performance was examined with a mixed model ANCOVA, and significant effects or interactions ($p < 0.05$) were further explored with Bonferroni-corrected pairwise comparisons. There were no significant differences between the caffeine and caffeine plus L-theanine treatments on any attention measure.

The Panel considers that this study does not show an effect of the combination of caffeine and L-theanine above the effect of caffeine alone on attention.

Foxe et al. (2012) carried-out a randomised, four-period, cross-over, placebo-controlled, double-blind study with 21 healthy participants (mean age 26 years) consuming one 200 mL serving containing (a) 50 mg caffeine, (b) 100 mg L-theanine, (c) 50 mg caffeine and 100 mg L-theanine, and (d) placebo. Participants attended four study visits separated by an average of 4 days. The order of treatment across days was randomised and counterbalanced across participants The Sustained Attention to Response Inhibition Task (SART) was administered at each study visit. SART omission errors, commission errors and reaction times were examined with Generalised Linear Mixed Models in which treatment order, caffeine, L-theanine and the interaction of Caffeine x L-Theanine were fitted as fixed effects, and subject was included as a random effect. There were no significant differences between the caffeine and caffeine plus L-theanine treatments on any attention measure.

The Panel considers that this study does not show an effect of the combination of caffeine and L-theanine above the effect of caffeine alone on attention.

Owen et al. (2008) carried-out a randomised, three-period, cross-over, placebo-controlled, double-blind study with 27 healthy participants (mean age 28.3 years) consuming one 250 mL serving containing (a) 50 mg caffeine, (b) 100 mg L-theanine and (c) 50 mg caffeine and 100 mg L-theanine. Participants attended three study visits separated by at least 7 days. Attention at each study visit was measured by RVIP and Attention Switching tests administered twice at 60 min and 90 min post-ingestion. Attention scores were examined with a mixed model analysis of variance (ANOVA). There were no significant treatment effects for the RVIP test, but there was a significant treatment x time interaction for number of correct responses on the Attention Switching Test. At 60 min post-ingestion, the number of correct responses was significantly higher in the caffeine and L-theanine intervention compared to the caffeine intervention ($p < 0.001$), but at 90 min post-ingestion the number of correct responses was significantly higher in the caffeine intervention compared to the caffeine and L-theanine intervention ($p < 0.01$).

The Panel notes the contradictory results for the caffeine and L-theanine treatment compared to the caffeine treatment. The Panel considers that this study does not show an effect of the combination of caffeine and L-theanine above the effect of caffeine alone on attention.

Kahathuduwa et al. (2017) carried-out a randomised, five-period, cross-over, placebo-controlled, open-label study with 20 healthy male volunteers (mean age 21.9 years) consuming one 150 mL serving of (a) caffeine (160 mg), (b) L-theanine (200 mg), (c) caffeine (160 mg) and L-theanine (200 mg) combined (all in water), (d) black tea and (e) placebo (water). The Panel notes that the caffeine and L-theanine content of the black tea dose was not reported. Each subject was given five treatments in five consecutive days with order of test determined by a Latin Square design.

Simple visual reaction time (SVRT) and recognition visual reaction time (RVRT) tasks were administered at baseline and again from 30 min until 1 h post-consumption. The RVRT task was a type of go/no go task in which participants were required to respond to only one of the two stimuli. Reaction time was measured in both tasks, but accuracy was measured only in the RVRT task. An auditory odd-ball task was also administered during which auditory event-related potentials (ERPs) were recorded. The ERP is an electrophysiological measure of cortical activity in which the N2 negative wave occurring 200 ms after stimulus onset is related to covert (internal) orienting of attention towards relevant information, and increased selective attention is identified by a greater amplitude in the N2 component. Because the baseline correction for averaged waveforms was not possible owing to technical limitations, the N2-P300 peak to peak amplitude was obtained by measuring the amplitude difference between the N2 and the P300 peaks.

RVRT reaction time and accuracy data were examined in a time x treatment two-way within-subject ANOVA model. The Panel notes that no statistical comparisons between the L-theanine and caffeine plus L-theanine treatments were reported for either RVRT reaction time or accuracy. A one-way ANOVA on post-dose N2-P300 amplitudes showed a significant treatment effect ($F_{4,76} = 13.96$, $p < 0.001$), and N2-P300 amplitudes were significantly greater in the caffeine plus L-theanine treatment compared to the caffeine treatment ($t = 3.20$, $p = 0.005$).

The Panel considers that this study shows an effect of the combination of caffeine and L-theanine above the effect of caffeine alone on an electrophysiological measure of attention.

The Panel notes that four studies (Rao and Nobre (2007, unpublished; Owen et al., 2008; Foxe et al., 2012; Dodd et al., 2015) did not show an effect of the combination of caffeine and L-theanine above the effect of caffeine alone on measures of attention performance, and that one study (Kahathuduwa et al., 2017) reported improved performance on one electrophysiological measure of attention with the caffeine plus L-theanine intervention compared to caffeine alone. No study showed an effect on behavioural measures of attention performance.

The Panel considers that these studies do not show an effect of caffeine and L-theanine on attention above the effect of caffeine alone, and that the mechanism of action for L-theanine on attention proposed by the applicant is speculative. The Panel also considers that it is well established that caffeine increases attention in healthy adult individuals of both sexes at doses of at least 75 mg (EFSA NDA Panel, 2011), and that cumulative doses of caffeine consumed over a period of 90 min are likely to exert similar effects on attention as the same dose of caffeine consumed on a single occasion owing to the pharmacokinetics of caffeine (EFSA NDA Panel, 2015). Therefore, the effect of black tea on attention observed in the three human intervention studies provided by the applicant (two studies by De Bruin et al., 2011 in one publication; Giesbrecht et al., 2012, unpublished) can be explained by its caffeine content.

Weighing of the evidence

In weighing the evidence, the Panel took into account that the consumption of 2–3 servings of black tea (containing a cumulative amount of at least 1,040 mg of tea solids, 90 mg of caffeine and 36 mg of L-theanine) within a time period of up to 90 min consistently improved attention in three human intervention studies (two studies by De Bruin et al., 2011 in one publication; Giesbrecht et al., 2012; unpublished). The Panel also took into account that it is well established that caffeine increases attention in healthy adult individuals of both sexes at doses of at least 75 mg (EFSA NDA Panel, 2011), that cumulative doses of caffeine consumed over a period of 90 min are likely to exert similar effects on attention as the same dose of caffeine consumed on a single occasion owing to the pharmacokinetics of caffeine (EFSA NDA Panel, 2015) and that no evidence was provided that L-theanine in tea has an effect on attention beyond the effect of caffeine. Therefore, the effect of black tea on attention observed in the three human intervention studies provided by the applicant (two studies by De Bruin et al., 2011 in one publication; Giesbrecht et al., 2012, unpublished) can be explained by its caffeine content.

The Panel concludes that a cause and effect relationship has been established between the consumption of black tea and improved attention.

The Panel considers that the effect of black tea on attention can be explained by its caffeine content. The Panel also considers that these conclusions could not have been reached without the study by Giesbrecht et al. (2012) claimed as proprietary by the applicant.

3.4. Panel's comments on the proposed wording

The Panel considers that the following wording reflects the scientific evidence: 'Owing to its caffeine content, black tea improves attention'.

3.5. Conditions and restrictions of use

In order to obtain the claimed effect, 2–3 servings of black tea providing at least 75 mg of caffeine in total should be consumed within 90 min.

The target population is adults in the general population.

4. Conclusions

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

- the food/constituent, black tea characterised by its content of tea solids, caffeine and L-theanine, which is the subject of the health claim, is sufficiently characterised in relation to the claimed effect.
- the claimed effect proposed by the applicant is 'improvement of attention'. The target population proposed by the applicant is 'adults in general population'. Improvement of attention is a beneficial physiological effect.
- a cause and effect relationship has been established between the consumption of black tea and improvement of attention.
- the following wording reflects the scientific evidence: 'Owing to its caffeine content, black tea improves attention'.
- in order to obtain the claimed effect, 2–3 servings of black tea providing at least 75 mg of caffeine in total should be consumed within 90 min. The target population is adults in the general population.

Steps taken by EFSA

Health claim application on 'black tea' and 'improvement of attention' pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (Claim serial No: 0461_IE). Submitted by Unilever N.V., Weena 455, 3013 AL Rotterdam, The Netherlands.

1) This application was received by EFSA on 27/7/2017.
2) The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.
3) The scientific evaluation procedure started on 24/10/2017.
4) On 15/11/2017, 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 27/11/2017 and was restarted on 7/12/2017, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
5) On 17/1/2018, 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 6/2/2018 and was restarted on 14/2/2018, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
6) During its meeting on 17/4/2018, the NDA Panel, having evaluated the data, adopted an opinion on the scientific substantiation of a health claim related to black tea and improvement of attention.

References

Camfield DA, Stough C, Farrimond J and Scholey AB, 2014. Acute effects of tea constituents L-theanine, caffeine, and epigallocatechin gallate on cognitive function and mood: a systematic review and meta-analysis. Nutrition Reviews, 72, 507–522.

De Bruin EA, Rowson MJ, Van Buren L, Rycroft JA and Owen GN, 2011. Black tea improves attention and self-reported alertness. Appetite, 56, 235–240.

Dodd FL, Kennedy DO, Rigby LM and Haskell-Ramsay CF, 2015. A double-blind, placebo-controlled study evaluating the effects of caffeine and L-theanine both alone and in combination on cerebral blood flow, cognition and mood. Psychopharmacology (Berl), 232, 2563–2576.

Durlach PJ, 1998. The effects of a low dose of caffeine on cognitive performance. Psychopharmacology (Berl), 140, 116–119.

Durlach PJ, Edmunds R, Howard L and Tipper SP, 2002. A rapid effect of caffeinated beverages on two choice reaction time tasks. Nutritional Neuroscience, 5, 433–442.

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2008. Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies on a request from Unilever PLC and Unilever NV on the scientific substantiation of a health claim related to black tea from *Camellia sinensis* and help focus attention. EFSA Journal 2008;906, 1–10.

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2011. Scientific Opinion on the substantiation of health claims related to caffeine and increased fat oxidation leading to a reduction in body fat mass (ID 735, 1484), increased energy expenditure leading to a reduction in body weight (ID 1487), increased alertness (ID 736, 1101, 1187, 1485, 1491, 2063, 2103) and increased attention (ID 736, 1485, 1491, 2375) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. EFSA Journal 2011;9(4):2054, 29 pp. https://doi.org/10.2903/j.efsa.2011.2054

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2012. Guidance on the scientific requirements for health claims related to functions of the nervous system, including psychological functions. EFSA Journal 2012;10(7):2816, 13 pp. https://doi.org/10.2903/j.efsa.2012.2816

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2015. Scientific Opinion on the safety of caffeine. EFSA Journal 2015;13(5):4102, 120 pp. https://doi.org/10.2903/j.efsa.2015.4102

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

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, Valueña 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

Einöther SJL, Martens VEG, Rycroft JA and De Bruin EA, 2010. L-Theanine and caffeine improve task switching but not intersensory attention or subjective alertness. Appetite, 54, 406–409.
Ferre S, 2010. Role of the central ascending neurotransmitter systems in the psychostimulant effects of caffeine. Journal of Alzheimer's Disease, 20, S35–S49.
Ferre S, Fredholm BB, Morelli M, Popoli P and Fuxe K, 1997. Adenosine-dopamine receptor-receptor interactions as an integrative mechanism in the basal ganglia. Trends in Neuroscience, 20, 482–487.
Foxe JJ, Morie KP, Laud PJ, Rowson MJ, De Bruin EA and Kelly SP, 2012. Assessing the effects of caffeine and theanine on the maintenance of vigilance during a sustained attention task. Neuropharmacology, 62, 2320–2327.
Giesbrecht T and Rowson MJ, 2016 (unpublished). Black tea and attention: meta-analysis.
Giesbrecht T, Rycroft JA, Rowson MJ and De Bruin EA, 2010. The combination of L-theanine and caffeine improves cognitive performance and increases subjective alertness. Nutritional Neuroscience, 13, 283–290.
Giesbrecht T, Mulder T, van der Meer N and Rowson M, 2012 (unpublished study report, updated 2017). Black tea improves attention and self-reported alertness in a dose-dependent manner.
Haskell CF, Kennedy DO, Milne AL, Wesnes KA and Scholey AB, 2008. The effects of L-theanine, caffeine and their combination on cognition and mood. Biological Psychology, 77, 113–122.
Hindmarch I, Quinlan PT, Moore KL and Parkin C, 1998. The effects of black tea and other beverages on aspects of cognition and psychomotor performance. Psychopharmacology (Berl), 139, 230–238.
Hindmarch I, Rigney U, Stanley N, Quinlan P, Rycroft J and Lane J, 2000. A naturalistic investigation of the effects of day-long consumption of tea, coffee and water on alertness, sleep onset and sleep quality. Psychopharmacology (Berl), 149, 203–216.
Kahathuduwa CN, Dassanayake TL, Amarakoon AT and Weerasinghe VS, 2017. Acute effects of theanine, caffeine and theanine–caffeine combination on attention. Nutritional Neuroscience, 20, 1–9.
Kam K and Nicoll R, 2007. Excitatory synaptic transmission persists independently of the glutamate-glutamine cycle. Journal of Neuroscience, 27, 9192-200.
Kelly SP, Gomez-Ramirez M, Montesi JL and Foxe JJ, 2008. L-Theanine and caffeine in combination affect human cognition as evidenced by oscillatory alpha-band activity and attention task performance. The Journal of Nutrition, 138, 1572S–1577S.
Kimura R and Murata T, 1971. Influence of alkylamides of glutamic acid and related compounds on the central nervous system. I. Central depressant effect of theanine. Chemical and Pharmaceutical Bulletin, 19, 1257–1261.
McLellan TM, Caldwell JA and Lieberman HR, 2016. A review of caffeine's effect on cognitive, physical and occupational performance. Neuroscience and Behavioral Reviews, 71, 294–312.
Nedergaard M, Takano T and Hansen AJ, 2002. Beyond the role of glutamate as a neurotransmitter. Nature Reviews Neuroscience, 3, 748–755.
Nestler EJ, Hyman SE and Malenka RC, 2009. *Molecular Neuropharmacology: A Foundation for Clinical Neuroscience*, 2nd Edition. McGraw-Hill, New York.
Niehlig A, Daval JL and Debry G, 1992. Caffeine and central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. Brain Research Review, 17, 139–170.
Owen GN, Parnell H, De Bruin EA and Rycroft JA, 2008. The combined effects of L-theanine and caffeine on cognitive performance and mood. Nutritional Neuroscience, 11, 193–198.
Rao A and Nobre K 2007 (proprietary data, unpublished study report), The effects of theanine on attentional processes in the human brain. The 5th report to Unilever R&D.
Scholey A, Downey LA, Ciorciari J, Pipingas A, Nolidin K, Finn M, Wines M, Catchlove S, Terrens A, Barlow E, Gordon L and Stough C, 2012. Acute neurocognitive effects of epigallocatechin gallate (EGCG). Appetite, 58, 767–770.
Terashima T, Takido J and Yokogoshi H, 1999. Time-dependent changes of amino-acids in the serum, liver, brain and urine of rats administered with theanine. Bioscience, Biotechnology and Biochemistry, 63, 615–618.
Wightman EL, Haskell CF, Forster JS, Veasey RC and Kennedy DO, 2012. Epigallocatechin gallate, cerebral blood flow parameters, cognitive performance and mood in healthy humans: a double-blind, placebo-controlled, crossover investigation. Human Psychopharmacology, 27, 177–186.

Abbreviations

AB	Attentional Blink Task
ANCOVA	analysis of covariance
ANOVA	analysis of variance
ANT	Attention Network Test
CFF	critical flicker fusion
CRT	choice reaction time
CUED	Cued Spatial Orienting Task
EGCG	epigallocatechin gallate
ERP	event-related potential
$F_{(xx,xx)}$	F distribution$_{(\text{degrees of freedom})}$

FLA	Flanker Interference Task
GABA	gamma-aminobutyric acid
ITT	intention-to-treat
NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies
PP	per protocol
RVIP	Rapid Visual Information Processing
RVRT	recognition visual reaction time
SART	Sustained Attention to Response Inhibition Task
SVRT	simple visual reaction time