UKNHCC

UK Nutrition & Health Claims Committee

SCIENTIFIC OPINION

Scientific Opinion for the substantiation of a health claim on a single component of *Morus alba* (white mulberry) leaf extract and assisting healthy blood glucose levels pursuant to Article 14(1)(a) of retained Regulation (EC) No 1924/2006[1], as amended by the Nutrition (Amendment etc.) (EU Exit) Regulations 2019 and the Nutrition (Amendment etc.) (EU Exit) Regulations 2020

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Application ID 002UKNHCC

Requestor Ascarit UK

UKNHCC members

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Declarations of interest

Read the UKNHCC register of interests containing all declarations of interests made by members.

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Official observers[2]

Sarah Clarke (Welsh Government), Chika Edeh (Food Standards Scotland), Kerry Gribbin (Food Standards Agency Northern Ireland) and Debby Webb (Department of Health and Social Care)

Suggested citation

[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.

[2] The UKNHCC code of practice states that Official observers attend UKNHCC meetings to provide updates from their respective nations on science and policy matters of relevance whilst respecting UKNHCC independence.

UKNHCC (United Kingdom Nutrition and Health Claims Committee) 2023. Scientific Opinion for the substantiation of a health claim on a single component of *Morus alba* (white mulberry) leaf extract and assisting healthy blood glucose levels pursuant to Article 14(1)(a) of retained Regulation (EC) No 1924/2006, as amended by the Nutrition (Amendment etc.) (EU Exit) Regulations 2019 and the Nutrition (Amendment etc.) (EU Exit) Regulations 2020

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UKNHCC disclaimer

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of *Morus alba* (white mulberry) leaf extract, a positive assessment of its safety, nor a decision on whether *Morus alba* (white mulberry) leaf extract is, or is not, classified as a foodstuff. It should be noted that such an assessment is not foreseen in the framework of retained Regulation (EC) No 1924/2006[1], as amended by the Nutrition (Amendment etc.) (EU Exit) Regulations 2019 and the Nutrition (Amendment etc.) (EU Exit) Regulations 2020.

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 retained Regulation (EC) No 1924/2006[1] as amended by the Nutrition (Amendment etc.) (EU Exit) Regulations 2019 and the Nutrition (Amendment etc.) (EU Exit) Regulations 2020.

Claim type

Article 14(1)(a): Reduction of disease risk claim

Process undertaken by the UKNHCC

- The application was received by the UKNHCC on 5 August 2022 at which point the scientific evaluation process started
- On 19 August 2022, the scientific evaluation was suspended following the ‘stop the clock’ process to request additional information from the applicant
- On 4 September 2022, the UKNHCC received additional information and the scientific evaluation was restarted, in compliance with Article 16(1) of Regulation (EC) No 1924/2006
- During its meeting on 14 October 2022, the UKNHCC evaluated the evidence submitted by the applicant
- During its meeting on 25 November 2022, the UKNHCC discussed the scientific opinion
- Following the meeting, the final scientific opinion was agreed via email correspondence

Summary

Following an application from Ascarit UK, submitted for authorisation of a health claim pursuant to Article 14(1)(a) of retained Regulation (EC) No 1924/2006[1] as amended by the Nutrition (Amendment etc.) (EU Exit) Regulations 2019 and the Nutrition (Amendment etc.) (EU Exit) Regulations 2020 via the Competent Authority of Great Britain, the United Kingdom Nutrition and Health Claims Committee (UKNHCC) was asked to deliver an opinion on the scientific substantiation of a health claim that *Morus alba* (*M. alba*) leaf extract is “clinically proven in assisting healthy blood glucose levels”.

The scope of the application was proposed to fall under a health claim referring to disease risk reduction including, a request for the protection of proprietary data which was subsequently withdrawn.

The food that is the subject of the health claim is the single constituent *M. alba* (white mulberry) leaf extract.

The Committee considers that the food, *M. alba* leaf extract, is not sufficiently characterised in relation to the proposed claimed effect.

The claimed effect proposed by the applicant is that *M. alba* leaf extract is “clinically proven in assisting healthy blood glucose levels”. The proposed risk factor is raised blood glucose levels and the disease to which the risk is related is type 2 diabetes mellitus. The proposed target population is “type 2 diabetes mellitus patients”. This claimed effect does not fall within the scope of an Article 14(1)(a) health claim. As defined in Article 2(6) of Regulation (EC) No 1924/2006, a ‘reduction of disease risk claim’ means any health claim that states, suggests or implies that the consumption of a food category, a food or one of its constituents significantly reduces a risk factor in the development of a human disease. In line with the European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA), the Committee considers that health claims should be intended for the general (healthy) population. The Committee also considers that where a health claim relates to a function or effect which may be associated with a disease, subjects with the disease are not the target population for the claim (EFSA, 2021).

The Committee is unclear on the methods used in the literature review provided by the applicant and is therefore unable to assess whether the totality of evidence was provided for consideration. The applicant identified a total of 13 publications, including 3 randomised controlled trials (RCTs) (Lown et al, 2017; Thondre et al, 2021; Mudra et al, 2007), 1 uncontrolled intervention study (Chatterji & Fogel, 2018), 1 book (Bensky, 1993), 1 laboratory study (Asano et al, 2001), 1 consensus statement (Saudek et al, 2008), 3 non scientific publications (Lown, 2017; Drugs.com, 2022; Gordon-Seymour, 2021), 1 comparative methodological study (Gomyo et al, 2004), 1 factsheet (NIH, 2008) and 1 review paper (Thaipitakwong et al, 2018) which the applicant suggested as being pertinent to the claim.

Of the evidence identified by the applicant, two RCTs (Lown et al, 2017; Thondre et al, 2021) did not evaluate evidence for the substantiation of the claim. One RCT (Mudra et al, 2007) was a brief report and was considered to have a potentially high risk of bias. One uncontrolled study (Chatterji & Fogel, 2018) did not evaluate evidence for the substantiation of the claim. Five publications (Bensky, 1993; Asano et al, 2001; Saudek et al, 2008; Gomyo et al, 2004; NIH, 2008) did not report on the food and/or the claimed effect. Three publications (Lown, 2017; Drugs.com, 2022; Gordon-Seymour, 2021) were not scientific publications. One publication (Thaipitakwong et al, 2018) was a review paper on mulberry leaves and their potential effect on cardiometabolic risk. The Committee considers that no conclusions can be drawn from these publications for the substantiation of the claim.

On the basis of the information provided, the Committee concludes that a cause and effect relationship cannot be established between the consumption of *M. alba* leaf extract and the claimed effect. The Committee also concludes that no evidence has been provided on the link between the claimed effect and risk of developing type 2 diabetes mellitus.

Information provided by the applicant

Applicant name and address

Ascarit UK, Flat 5 Byron Court, 26 Exeter Road, London, NW2 4SH, England.

The application includes a request for the protection of proprietary data, which was subsequently withdrawn.

Food/constituent as stated by the applicant

The food that is the subject of the health claim is *M. alba* (white mulberry) which represents 50% of the content of Ascarit.

Health relationship as claimed by the applicant

According to the applicant, “The presence of morus alba significantly reduces the amount of glucose from control level to a lower level and significantly increased the insulin level from control level. In a clinical study, the ability of Ascarit to reduce glucose levels was tested. A single centre, un-blinded, prospective interventional study was conducted in Israel”.

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: “Clinically proven in assisting healthy blood glucose levels”.

Specific conditions of use as proposed by the applicant

No specific conditions of use for the food that is the subject of the claim, *M. alba,* were proposed by the applicant. Proposed conditions of use were provided for the supplement Ascarit. The proposed target population is type 2 diabetes mellitus patients.

Documentation provided

Health claim application on *Morus alba* (white mulberry) leaf extract and assisting healthy blood glucose levels pursuant to Article 14(1)(a) of retained Regulation (EC) No 1924/2006[1], as amended by the Nutrition (Amendment etc.) (EU Exit) Regulations 2019 and the Nutrition (Amendment etc.) (EU Exit) Regulations 2020. Application ID: 002UKNHCC. Submitted by Ascarit UK.

Assessment

1. Characterisation of the food/constituent

1.1. Following a request from the UKNHCC for clarification on the food that is the subject of the proposed health claim, the applicant confirmed that the food is *Morus alba* (*M. alba*) (white mulberry) leaf extract. No detailed compositional data, batch-to-batch variability or stability studies of *M. alba* leaf extract were provided by the applicant.

1.2. The applicant provided an overview of the manufacturing process of Ascarit, described as a multiple constituent supplement containing *M. alba* leaves, the leaves of *Urtica dioica (U. dioica)*, the bark of *Cinnamomum*, leaves of *Artemisia dracunculus (A. dracunculus)*, and *Taraxacum officinale* (*T. officinale*) L. root extract. According to the applicant "the leaves and flowers are cleaned and processed fresh (i.e.: while retaining their original color, shape, and turgor) with a combination of cutting, pressing, and heat extraction with brewing to maximize the extraction of plant products, including leaf latex. After this, the liquid was rapidly cooled to 20–30 degrees Celsius and then filtered. The root and bark components were cleaned and then processed using heat extraction followed by cooling. The mixed solution comprised (by weight percent of the total solution weight) 50% Morus, 20% Artemisia, 10% Urtica, 10% Cinnamomum, and 10% Taraxacum". The applicant requested that the composition and manufacturing process of Ascarit remain proprietary, but later withdrew this request.

1.3. The Committee considers that the food, *M. alba* leaf extract, which is the subject of the health claim, is not sufficiently characterised in relation to the proposed claimed effect.

2. Relevance of the claimed effect to human health

2.1. The applicant states that type 2 diabetes mellitus is a metabolic disorder characterised by raised blood glucose levels. Following a request from the UKNHCC for evidence on the characterisation of the relationship between the proposed risk factor (raised blood glucose levels) and the risk of the related disease (type 2 diabetes mellitus), the applicant submitted 3 studies (DCCT,

1995; Rohlfing et al, 2002; Swetha, 2014). The Diabetes Control and Complications Trial (DCCT) Research Group (1995) and Rohlfing et al (2002) both report on the DCCT which included patients with insulin dependent (type 1) diabetes mellitus rather than patients with type 2 diabetes mellitus (the disease to which the risk reduction claim is proposed). Swetha (2014) calculated the correlation between HbA1c (glycated haemoglobin) and various outcomes (fasting blood glucose, post prandial blood glucose and resting blood glucose) to assess their usefulness in monitoring glycaemic control in diabetic patients. The Committee considers that no evidence has been provided by the applicant to establish that there is a causal relationship between raised blood glucose levels and risk of developing type 2 diabetes, and whether raised blood glucose level is an independent predictor of type 2 diabetes mellitus.

2.2. Upon a request from the UKNHCC for information on the outcome, the outcome variable(s) and the methods of measurement proposed to assess the risk factor in human studies, the applicant provided some additional information. However based on the information provided, the Committee is unclear on the outcome proposed by the applicant and how it should be measured.

2.3. The claimed effect proposed by the applicant is “clinically proven in assisting healthy blood glucose levels”. The target population proposed by the applicant is patients with type 2 diabetes mellitus.

2.4. The Committee notes that the proposed target population of patients living with type 2 diabetes mellitus does not fall within the scope of an Article 14(1)(a) health claim as laid down in Regulation (EC) No 1924/2006. As defined in Article 2(6) of Regulation (EC) No 1924/2006, a ‘reduction of disease risk claim’ means any health claim that states, suggests or implies that the consumption of a food category, a food or one of its constituents significantly reduces a risk factor in the development of a human disease. In line with the European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA), the Committee considers that health claims should be intended for the general (healthy) population. The Committee also considers that where a health claim relates to a function or effect which may be associated with a disease, subjects with the disease are not the target population for the claim (EFSA, 2021).

2.5. The applicant proposed that two capsules of Ascarit, of which *M. alba* is a component, should be consumed 3 times per day 30 minutes before meals with water in order to achieve the claimed effect. No concentration, dose or duration of use was proposed by the applicant.

2.6. The Committee notes that a reduction in post-prandial blood glucose response may be considered a beneficial effect for individuals already living with impaired glucose tolerance, but the Committee considers that the proposed wording does not meet the criteria to be considered for an Article 14(1)(a) health claim nor

does it meet the population criteria for which a disease risk reduction claim can be made.

3. Scientific substantiation of the claimed effect

3.1. Upon request from the UKNHCC, the applicant was asked to provide details on the literature review to include authorship, objectives, eligibility criteria, full search strategy and each database searched. Very limited information was provided, therefore the Committee is unable to assess whether the totality of evidence was provided for consideration.

3.2. The applicant identified a total of 13 publications, including 3 randomised controlled trials (RCTs) (Lown et al, 2017; Thondre et al, 2021; Mudra et al, 2007), 1 uncontrolled intervention study (Chatterji & Fogel, 2018), 1 book (Bensky, 1993), 1 laboratory study (Asano et al, 2001), 1 consensus statement (Saudek et al, 2008), 3 non scientific publications (Lown, 2017; Drugs.com, 2022; Gordon-Seymour, 2021), 1 comparative methodological study (Gomyo et al, 2004), 1 factsheet (NIH, 2008) and 1 review paper (Thaipitakwong et al, 2018) which the applicant suggested as being pertinent to the claim.

3.3. Three publications were not peer-reviewed scientific papers: 1 article published in The Conversation (Lown, 2017) provided a brief summary of an RCT investigating the effects of mulberry extract on blood glucose and insulin responses in healthy volunteers over a 2 hour period; 1 publication (Drugs.com, 2022) provided an overview of *M. alba*; 1 publication (Gordon-Seymour, 2021) provided an overview of a supplement containing a proprietary mulberry leaf extract, 'Reducose®'. The Committee considers that no conclusions can be drawn from these publications as none evaluated evidence for the substantiation of the claim.

3.4. Reference to 1 book (Bensky, 1993) on Chinese Herbal Medicine was provided. No chapter information, page numbers or an excerpt from the book was submitted for the Committee to review, therefore it could not be evaluated.

3.5. One factsheet (NIH, 2008) summarising the Diabetes Control and Complications Trial and follow-up study did not evaluate evidence for the substantiation of the claim, therefore no conclusions could be drawn from this publication.

3.6. Three reports were submitted: 1 consensus statement (Saudek et al, 2008) reporting on the screening and diagnosis of diabetes; 1 review paper (Thaipitakwong et al, 2018) reporting on the potential effects of *M. alba* leaves on cardiometabolic risks; and 1 review paper (Gomyo et al, 2004) reporting on the effects of sex, age and BMI on screening tests for impaired glucose tolerance. One laboratory study (Asano et al, 2001), describing the isolation of

alkaloides of *M. alba* and their glycosidase inhibitory activities, did not evaluate evidence for the substantiation of the claim. The Committee considers that no conclusions can be drawn from these publications.

3.7. Three RCTs (Lown et al, 2017; Thondre et al, 2021; Mudra et al, 2007) considered participants randomised to mulberry leaf extract. Lown et al (2017) and Thondre et al (2021) were both double-blind, randomised, repeat measure, crossover trials evaluating the glycaemic response to a carbohydrate challenge with or without proprietary mulberry leaf extract (Reducose®) compared with placebo in healthy participants. The Committee considers that no conclusions can be drawn from these publications as they did not evaluate evidence for the substantiation of the claim. Mudra et al (2007) was a brief report summarising a randomised crossover study evaluating the glycaemic response of mulberry leaf extract or placebo in both healthy participants (10 participants) and participants with type 2 diabetes mellitus (10 participants). The Committee considers this study to potentially have a high risk of bias due to a lack of information reported on the randomisation process, potential deviations from the intended intervention and potential bias in the selection of the reported result.

3.8. One uncontrolled intervention study (Chatterji & Fogel, 2018) included participants with type 2 diabetes mellitus. Chatterji and Fogel (2018) evaluated the effects of a herbal composition of SR2004 (comprised of *M. alba* leaves, *U. dioica* leaves, the bark of *Cinnamomum*, *A. dracunculus* leaves and *T. officinale* root extract) on HbA1c weekly for 12 weeks and then at 24 weeks. The Committee considers that no conclusions can be drawn from this uncontrolled study that did not evaluate evidence for the substantiation of the claim.

3.9. In summary, the Committee considers that, based on the evidence submitted by the applicant, no conclusions can be drawn on the effect of *M. alba* leaf extract on blood glucose concentrations.

4. Weighing the evidence

4.1. In weighing the evidence, the Committee took account of 1 RCT (Mudra et al, 2007) from which conclusions could be drawn.

4.2. The Committee concludes that a cause and effect relationship cannot be established between the consumption of *M. alba* leaf extract and the claimed effect based on the evidence provided. The Committee also concludes that no evidence has been provided on the link between the claimed effect and risk of developing type 2 diabetes mellitus.

Conclusions

On the basis of the data presented by the applicant, the Committee concludes that:

- the food, *Morus alba* (white mulberry) leaf extract, which is the subject of the proposed health claim, is not sufficiently characterised in relation to the claimed effect

- the claimed effect in patients with type 2 diabetes mellitus does not comply with the criteria laid down in Regulation (EC) No 1924/2006. The proposed wording of the claim “clinically proven in assisting healthy blood glucose levels” does not meet the criteria to be considered for an Article 14(1)(a) health claim

- a cause and effect relationship cannot be established between the consumption of *Morus. alba* (white mulberry) leaf extract and the claimed effect and no evidence has been provided on the link between the claimed effect and risk of developing type 2 diabetes mellitus

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Abbreviations

DCCT	Diabetes Control and Complications Trial
DJN	1-deoxynojirimycin
EC	European Commission
EFSA	European Food Safety Authority
HbA1c	Glycated Haemoglobin
NDA	Panel on Dietetic Products, Nutrition and Allergies
RCT	Randomised Controlled Trial
UKNHCC	United Kingdom Nutrition and Health Claims Committee