Meeting

Dried Miracle Berry (DMB®) Discussion Paper

Committee Paper for Discussion - ACNFP/159/06.

Advisory Committee For Novel Foods and Processes.

Application for Authorisation of Dried Miracle Berry (DMB®) as a Novel Food.

Application number RP1351.

Issue

An application has been received under the novel food authorisation process (regulation 2015/2283 as retained in UK law) for dried miracle berry (DMB®).

The Committee is asked to advice on whether the available data provides an adequate basis for a risk assessment, and whether the novel food is safe and not nutritionally disadvantageous under the proposed use and use levels.

Background

1. In November 2021, the FSA received the submission for dried miracle berry from Baïa Food Co (Spain). The novel food consists of pitted fruits of *Synsepalum dulcificum*, dried and referred to as dried miracle berry (DMB). It is often consumed for the presence of the substance Miraculin. It serves as a functional food, food supplement taken before consumption of sour foods for palatability (taste modifier).

2. This food has not previously been commercialised in Europe but eaten in other regions of the world. This application has an EFSA opinion (2021) clearing its safety for consumption. This is provided in Annex D for information.

3. The application dossier is attached as Annex A, the annexes to the dossier attached as Annex B and subsequent information requested ahead of the review in Annex C. All annexes contain confidential information. Please note, the dossier (Annex A) contains data in blue colour in parts. These are updates made to the application by the applicant.

This Application Identification

4. This food belongs to the *Synsepalum dulcificum* species and is indigenous to the tropical forest regions of Western Africa. The novel food in this application is farmed in Ghana. The dried pulp and skin is referred to miracle berry, and dried miracle berry in this application (DMB®).

Production Process

5. The berry is harvested by hand from mature cultivated plants then sorted for the first time at cultivation site. It is then transported by land to the factory, washed, sorted, mechanically pitted, skin and pulp processed into juice/puree then dried. The resulting dried cake can further be milled into a powder and stored before export.

6. The production process is described in detail (Annex B: annex 1), flow chart provided (Annex B: annex 21), HACCP provided outlining associated hazards and their mitigation (Annex B: annex 22). GMP certificates have been provided following a request for further information [Annex C: (Quality certificates folder)].

Composition

7. The applicant has provided analytical data for five batches selected within a period of 3 years (2017-2019), concluding that their analysis indicates that their product consistently meets the proposed specifications for the novel food. They also include literature search to retrieve compositional information (Annex A: p24-31). All the Certificates of Analysis are provided in Annex B: Annex 3.

8. They have reported the heavy metal analysis for arsenic, cadmium, mercury and lead generated by inductively coupled plasma mass spectrometry (ICPMS). The results reported were within limits set in relevant Regulation (Annex A: p15-16).

9.Polycyclic aromatic hydrocarbons (PAH) analysis was provided (Annex A: p16), method used was Gas Chromotography coupled to Mass Spectroscopy (GC-MS).

10. The applicant stated that Pesticides, dioxins, furans and PCBs were compliant with the relevant Regulation across 4 different batches. Following a request for further information, a table summarising this including analytical reports of the certification for the laboratories used can be found in Annex C: Compositional data, with pesticides undetected and the latter within acceptable limits (Annex A: p17).

11. Analytical Mycotoxin analysis has been provided with the applicant stating that five batches were tested with levels under the limit of detection of the method used (UFCL) and below the EC safety standard (Annex A: p17-18)

12. The applicant conducted microbial analysis and conclude the microbes tested (E.coli, Staphylococcus, Salmonella spp., Clostridium perfrigens, sulphitereducing clostridia, faecal coliforms and total total Enterobacteriaceae) were within acceptable safety limits. They also state the HACCP and BRC standards in place reduces the potential growth of microorganisms which could alter quality and safety of the product (Annex A: p18-19).

Stability

13. The applicant states the product remained stable under normal conditions for 2 years in a 24-month shelf-life study (Annex A: p32-33 and Annex B: Annex 6). They also performed stability tests to temperature and pH to determine conditions at which the taste modifying molecule, miraculin, was denatured and consequently deactivated (Annex B: Annex 7).

Specification

14. The applicant has provided specification of the novel food with the parameters chosen based on nutritional properties, labelling and the main biologically active markers. Exact methods used has been reported showing compliance up to date of minimum durability under standard conditions (Annex A: p35).

History of Use

15. The applicant reports that miraculin, a substance found within the miracle berry, is marketed in a number of countries outside the EU, in different forms such as fresh berries, miraculin chewing gums, seasonings etc. (Annex A: p37) with complete literature reports of published data showing no concern to human safety from consumption (Annex A: p46-49 and Annex B: Annex 8 and 15).

Proposed Use and Intake

16. The applicant states the target population for this novel food is the general population except pregnant women and children since there is not sufficient information for this group of people and that it will be labelled accordingly.

17. The food is to be used as a supplement in different forms i.e., as an ingredient in food supplements or directly as a food supplement consisting of the dried fruit. The novel food is not intended to replace another food.

18. The dosage is recommended as 0.1g-0.3g per serving. Recommended maximum intake is 0.9g/day distributed in three servings per day before main meals. It will be the basis for oral formulations e.g., powders, granules, tablets, lozenges, liquids and gels.

19. The anticipated intake of the food is that of an ingredient in food supplements at of 100mg-300mg per serving (15mg/kg of body weight) and there in no combined intake from another source to be considered.

Absorption, distribution, metabolism and excretion

20. The applicant states the novel food is primarily made up of carbohydrates (7090%), ashes (3-6%), proteins (5-6%) as well as micronutrients whose fate in the body is well established. They however emphasise that miraculin (a type of glycoprotein), its main characteristic component comprising of approximately 2% of DMB, can be up to 1/3 of the total proteins. In-vitro stability assay to analyse digestibility of protein performed by the applicant shows miraculin follows normal metabolism of glycoproteins. Complete report in Annex B: Annex 9.

Nutritional information

21. Section 2.9 in the dossier (Annex A) gives a brief summary on this information. However, a full analysis is found in section 2.4.3 (Annex A: p21-32).

The novel food is not intended to replace or substitute any existing food. No novel production process is applied. It is not expected that any part of the process within the manufacturing chain prior to consumption affects the bioavailability of nutrients. Proximate analysis and characterisation of parameters for DMB has been provided with methods used specified (Annex B: appendix B2) and Certificates of Analysis (Annex B: Annex 3 and 4).

22. Minerals were analysed from five independent batches using Inductively Coupled Plasma Mass spectroscopy (ICP-MS) with data presented as mg/kg of product.

23. Fatty acids are also analysed in five different batches using Gas Chromography Flame Ionisation Detector (GC-FID). Linoleic and linolenic are most abundant polyunsaturated fat, palmitic acid for saturated fatty acids and oleic for the monounsaturated fat.

24. The applicant states that the miracle fruit has a substantial amount of polyphenols and tannins with three batches analysed. Method used is Spectrophotometry.

25. The applicant also states that no method to quantify miraculin has previously been standardized for food analysis. They have therefore developed a procedure with the initial method as electrophoresis method combined with Coomassie staining. Four batches were analysed with results expressed as total miraculin (µg of miraculin per mg of DMB) and as the percentage of total miraculin %w/w (Annex A p25-28). Certificates of Analysis are presented in Annex B: Annex 5.

26. The applicant states that from the composition analysis, there is no relevant presence of antinutritional factors. Following consideration to nutrition and health, it is suggested that due to the nature of the novel food’s flavour enhancing attribute, there might be a conscious use to change perception of taste influencing food choice, with the potential to impact health status,. However, this is difficult to predict as it will vary from person to person (Annex A: p40)

Toxicological information

27. A list of all toxicological studies are presented in a table (Annex B: Appendix B14). The applicant reports on acute toxicity with a certified report provided (Annex B: Annex 10) and concludes neither mortality nor any other systemic sign nor behavioural changes were observed in the animals studied.

28. A genotoxicity report has also been provided (Annex B: Annex 11 and Annex A: p41-43) from a bacterial reverse mutation study conducted. The applicant concluded that the novel food can be considered not mutagenic or promutagenic due to a lack of dose-response in all treatments.

29. In-vivo mammalian erythrocyte micronucleus test and in vitro mammalian cell micronucleus tests were reported (Annex B: Annex 12 and Annex A: pg4344). The applicant concludes that Dried Miracle Berry powder does not affect the production of circulating erythrocytes. Moreover, it did not cause statistically or biologically significant reproducible increases in the frequency of micro nucleated mouse lymphomaL5178Y $TK^{+/-}$ 3.7.2 C cells in the performed experiments with/without metabolic activation. It was concluded the novel food was not genotoxic.

30. A sub-chronic toxicity test carried out on rats for 90 consecutive days at a total dose of 2000mg/Kg/day resulted in no systemic toxicological alterations on either health, behaviour, growth, development, functional capacity, morphology and lifespan. The applicants also state that taking into consideration on the dosage administered to the rats, a No Adverse Effect Level (NOAEL) of 2000mg/kg/day could be established. A complete report can be found in Annex B: Annex 13 and Annex A: p45.

31. The applicant conducted literature review on human studies (Annex B: Annex 19) including a sensory study of the novel food carried out on healthy young adults with a high sweetness perception reported after 5-10 minutes and no health concerns reported. A complete report is attached in Annex B: Annex 14. The applicant has also provided data on published sensory studies on human exposure to the novel food (Annex B: annex 15 and Annex A: p47-49) reporting on the same findings and including other published animal studies (Annex A**:** p49-50 and Annex B: Annex 16).

32. Following a request for further information from the Secretariat a summary table of toxicology studies mentioned in the dossier has now been provided (Annex C: Toxicology folder). The applicant concludes that “the novel food is safe for use as or in a food supplement at the maximum intake level of 0.7 g/day for the target population, i.e., adults excluding pregnant and lactating women.”

Allergenicity

33. The applicant has considered the allergenicity potential of the novel food particularly with respect to miraculin, source, production process and available

information on cross reactivity. There were no published reports on allergic reactions.

34. They however report on data proposing cross reactivity between latex produced by species of this family (palaquium species) and latex from Hevea Brasiliensis that can be severe (Costa et al 2001) as well as that between latex and fruit food allergens (latex fruit syndrome). A protein analysis, sequence homology analysis and cross reactivity with food allergens has been investigated and reported in

Annex A: p52-54 and Annex B: Annex 17. The applicant also mentions the novel food tested positive for peanut allergens and states that they will continue investigating, although it is relatively difficult to establish the criteria for the study.

Committee Action Required

- The Committee is asked whether the available data provide a satisfactory basis for evaluating the safety of this novel food ingredient?
- If so, the Committee is asked whether it is content to recommend approval of the novel food as an ingredient to be added to the range of foods specified?
- If not, the Committee is asked to indicate what additional data would be required?

ACNFP Secretariat April 2023

Annexes

Annex A - Request for further information

Annex B - The applicants response

Annex C - Response Annexes

Annex D - EFSA Opinion