STATEMENT

ADOPTED: 24 October 2018

doi: 10.2903/j.efsa.2018.5485

Statement on the safety of D-ribose

EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA), Dominique Turck, Jacqueline Castenmiller, Stefaan De Henauw, Karen Ildico Hirsch-Ernst, John Kearney, Helle Katrine Knutsen, Alexandre Maciuk, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Carmen Pelaez, Kristina Pentieva, Alfonso Siani, Frank Thies, Sophia Tsabouri, Marco Vinceti, Tara Dean, Karl Heinz Engel, Marina Heinonen, Rosangela Marchelli, Monika Neuhäuser-Berthold, Morten Poulsen, Annette Pöting, Yolanda Sanz, Josef Rudolf Schlatter, Andrea Germini and Henk van Loveren

Abstract

In 2018, the EFSA NDA Panel adopted the Scientific Opinion on the safety of D-ribose as a novel food pursuant to Regulation (EU) 2015/2283 when used in a variety of food, concluding that D-ribose is safe for the general population at intake levels up to 36 mg/kg body weight (bw) per day, but that its safety at the intended uses and use levels as proposed by the applicant could not be established. Following a request from the European Commission, the EFSA NDA Panel was asked to carry out a supplementary safety assessment for D-ribose by considering the new proposed uses and use levels submitted by the applicant. In order to address the present mandate, an intake assessment was carried out based on individual data from the EFSA Comprehensive European Food Consumption Database. Intakes were estimated for all age groups of the general population. The resulting ranges for the mean and high-level estimated intakes of D-ribose for all the population groups, including the target population groups, did not exceed the acceptable level of intake for the general population previously defined, i.e. 36 mg/kg bw per day, except for one survey on adolescents where the mean and 95th percentile of the intake estimates were 8.6 and 39.4 mg/kg bw per day, respectively. The Panel concludes that the novel food, D-ribose, is safe under the new proposed conditions of use.

Keywords: ribose, D-ribose, novel food, ingredient, intake assessment

Requestor: European Commission following the provision of additional information by Bioenergy Life Science, Inc.

Question number: EFSA-Q-2018-00697

Correspondence: nda@efsa.europa.eu

Panel members: Dominique Turck, Jacqueline Castenmiller, Stefaan De Henauw, Karen Ildico Hirsch-Ernst, John Kearney, Helle Katrine Knutsen, Alexandre Maciuk, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Carmen Pelaez, Kristina Pentieva, Alfonso Siani, Frank Thies, Sophia Tsabouri, Marco Vinceti.

Suggested citation: EFSA NDA Panel (EFSA Panel on Nutrition, Novel Foods and Food Allergens), Turck D, Castenmiller J, De Henauw S, Hirsch-Ernst KI, Kearney J, Knutsen HK, Maciuk A, Mangelsdorf I, McArdle HJ, Naska A, Pelaez C, Pentieva K, Siani A, Thies F, Tsabouri S, Vinceti M, Dean T, Engel KH, Heinonen M, Marchelli R, Neuhäuser-Berthold M, Poulsen M, Pöting A, Sanz Y, Schlatter JR, Germini A and van Loveren H, 2018. Statement on the safety of D-ribose. EFSA Journal 2018;16(12):5485, 10 pp. https://doi.org/10.2903/j.efsa.2018.5485

ISSN: 1831-4732

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

Summary

Following a request from the European Commission, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) was asked to assess additional information on D-ribose by considering the new proposed uses and use levels provided by the applicant, and if necessary to update its Scientific opinion on the safety of D-ribose.

On 18 April 2018, the EFSA NDA Panel adopted the scientific opinion on the Safety of D-ribose as a novel food ingredient when added to a variety of foods (EFSA NDA Panel, 2018). In the scientific opinion, the Panel concluded that the novel food was safe for the general population at intake levels up to 36 mg/kg body weight (bw) per day, based on the no-observed-adverse-effect-level (NOAEL) of 3.6 g/kg bw per day derived from a subchronic toxicity study in Wistar rats (Griffiths et al., 2006) and an uncertainty factor of 100. In the opinion, the Panel had performed an intake assessment of the novel food (NF) based on the proposed use and use levels provided by the applicant and using individual-based data from the EFSA Comprehensive Food Consumption database. Based on the results of the intake assessment, the Panel considered that the safety of the NF at the intended uses and use levels as proposed by the applicant had not been established since the estimated intake of the novel food exceeded the acceptable level of intake in most of the population groups.

Based on the new proposed uses and use levels, a new intake assessment for D-ribose was performed by the Panel based on individual data from the EFSA Comprehensive European Food Consumption Database. The resulting ranges for the mean and high-level estimated intakes of D-ribose for all the population groups, including the target population groups, did not exceed the acceptable level of intake for the general population previously defined, i.e. 36 mg/kg bw per day, except for one survey on adolescents where the 95th percentile of the intake estimates was 39.4 mg/kg bw per day. However, the Panel notes that the intake estimates are based on conservative assumptions that all proposed food items consumed by an individual actually contain the novel food at the maximum proposed use levels. Therefore, the Panel considers the NF as safe, at the proposed use levels in all population groups.

The main source of intake of the novel food from the proposed uses were: fine bakery wares, the highest contributors in all population groups; milk drinks, high contributors in all population groups apart from infants; and sports, isotonic and energy drinks, which were high contributors in adolescents, adults and the elderly.

The Panel notes that food supplements containing D-ribose are already on the market in the European Union (EU). Their consumption may lead to an additional intake of D-ribose which is not possible to estimate precisely, due to the variability in the content of D-ribose in the supplements.

The Panel concludes that the NF, D-ribose, is safe under the new proposed conditions of use. However, if used in conjunction with food supplements containing D-ribose, the Panel noted that the acceptable level of intake (36 mg/kg bw per day) may be exceeded.

Table of contents

1. Introduction

1.1. Background and Terms of Reference as provided by the European Commission

1.1.1. Background as provided by the European Commission

On 18 April 2018, EFSA adopted the Scientific Opinion on the safety of D-ribose as a novel food ingredient in various foods (EFSA NDA Panel, 2018).

In that Scientific Opinion, EFSA concluded that, based on the existing data, the safety of the novel food at the intended uses and use levels as proposed by the applicant has not been established.

The applicant has now provided additional information. In consequence, the applicant is asking to review the additional information provided and, if necessary, update the Scientific Opinion on the safety of D-ribose as a novel food in various foods.

1.1.2. Terms of Reference as provided by the European Commission

In view of the above, the Commission requests EFSA to review the additional information provided by the applicant and, if necessary, to update the conclusions of the Scientific Opinion on D-ribose.

1.2. Interpretation of the terms of reference

The EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) interprets the mandate as the request

- to perform a new intake assessment of D-ribose based on the new proposed uses and use levels provided by the applicant, and
- to assess whether the safety of the novel food (NF) at the intended uses and use levels as proposed by the applicant can be established.

2. Data and methodologies

2.1. Data

The assessment of the safety of D-ribose at the new proposed uses and use levels is based on supplementary information to the original NF application provided by the applicant, on the EFSA Comprehensive Food Consumption Database[1] (EFSA, 2011a) and on the scientific opinion on the safety of D-ribose (EFSA NDA Panel, 2018). Information on the food supplements containing D-ribose introduced in the EU market was extracted from the Mintel Global New Products Database (GNPD).[2]

2.2. Methodologies

The assessment follows the methodology set out in the EFSA guidance on NF applications and the principles described in the relevant existing guidance documents from the EFSA Scientific Committee. The legal provisions for the assessment are laid down in Article 11 of Regulation (EU) 2015/2283 and in Article 7 of the Commission Implementing Regulation (EU) 2017/2469.

This assessment concerns only risk that might be associated with consumption of the NF under the proposed conditions of use, and is not an assessment of the efficacy of D-ribose with regard to any claimed benefit.

3. Assessment

On 18 April 2018, the EFSA NDA Panel adopted the scientific opinion on the safety of D-ribose as a NF ingredient when added to a variety of foods (EFSA NDA Panel, 2018). In the scientific opinion, the Panel concluded that the NF, is safe for the general population at intake levels up to 36 mg/kg body weight (bw) per day, based on the no-observed-adverse-effect-level (NOAEL) of 3.6 g/kg bw per day derived from a subchronic toxicity study in Wistar rats (Griffiths et al., 2006) and an uncertainty factor of 100. During the assessment, the Panel had performed an intake assessment of the NF based on the proposed use and use levels provided by the applicant and using individual-based data from the EFSA

[1] http://www.efsa.europa.eu/en/food-consumption/comprehensive-database
[2] http://www.mintel.com/global-new-products-database

Comprehensive Food Consumption database. Based on the results of the intake assessment, the Panel considered that the safety of the NF at the intended uses and use levels as proposed by the applicant had not been established since the estimated combined intake of the NF exceeded the acceptable level of intake in most of the population groups.

In order to address the present mandate, a new intake assessment is carried out by taking into account the new proposed uses and use level of D-ribose provided by the applicant.

3.1. Target population

The applicant specified that, as already proposed in the previous application for D-ribose, the target population for the consumption of the NF would be adults and adolescents above 14 years of age.

3.2. Proposed uses and use levels

In the additional information submitted, the applicant has removed some of the proposed uses included in the original application and reduced the maximum use levels of the remaining proposed uses. The new proposal for intended uses and use levels of D-ribose in foods provided by the applicant is summarised in Table 1.

Table 1: Summary of the individual proposed food-uses and use levels for D-ribose

Proposed use	Maximum use level (g/100 g)
Cereal bars	0.20
Fine bakery wares	0.31
Chocolate confectionery (excluding chocolate bars)	0.17
Milk drinks (excluding malts and shakes)	0.08
Sports, isotonic, and energy drinks	0.80
Meal replacement beverages	0.13
Meal replacement bars and energy bars	3.30
Hard and soft confectionery	0.20
Instant teas	0.23

3.3. Anticipated intake

3.3.1. Intake from the proposed uses of the NF

The applicant has provided an intake assessment based on the proposed uses and use levels, utilising the summary statistics published in the EFSA Comprehensive European Food Consumption Database (EFSA, 2011a). To perform the assessment, the applicant categorised the proposed uses according to the EFSA food classification system FoodEx at level 2 and 3 (EFSA, 2011b).

In the evaluation of the intake estimates for D-ribose a new intake assessment was performed by EFSA based on individual data from the EFSA Comprehensive European Food Consumption Database (EFSA, 2011a). The FoodEx codes and corresponding levels used for the intake assessment are reported in Appendix A. The resulting ranges of the estimated daily intake of D-ribose from the consumption of the foods to which D-ribose is proposed to be added, are reported in Table 2. For the proposed use in meal replacement beverages, it was not possible to identify a specific code in the FoodEx classification system. This was therefore not included in the assessment of intake; the uncertainty related to this issue is considered to result in a possible minor underestimation of the overall intake.

Table 2: Summary of the ranges of the estimated daily intake of D-ribose from its new proposed uses, based on individual data from the EFSA Comprehensive European Food Consumption Database

Estimated intake (mg/kg bw per day)	Infants (4–11 months)	Toddlers (12–35 months)	Children (3–9 years)	Adolescents (10–17 years)	Adults (18–64 years)	The elderly (≥ 65 years)
Mean	0.0–2.9 (11)	0.4–11.2 (14)	0.6–11.7 (19)	0.7–8.6 (18)	0.5–4.0 (19)	0.3–4.2 (18)
High-level (P95)	0.0–15.5 (10)	2.3–33.6 (12)	2.6–32.4 (19)	1.6–39.4 (17)	2.0–12.3 (19)	1.3–12.7 (18)

Between brackets the number of surveys considered per population group.

The Panel notes that the mean and high-level estimated intakes of D-ribose for all the population groups, including the target population groups, do not exceed the acceptable level of intake for the general population previously defined, i.e. 36 mg/kg bw per day, (EFSA NDA Panel, 2018) except for one survey on adolescents where the 95th percentile of the intake estimates was 39.4 mg/kg bw per day.

With regard to the main source of intake of the NF from the proposed uses, the Panel notes that fine bakery wares were the highest contributors in all population groups; milk drinks contributed to up to 40% of the intake of D-ribose in all population groups apart from infants; sports, isotonic and energy drinks were also high contributors in adolescents, adults and the elderly. The contributions of each food category to the intake of the different dietary surveys used in the assessment are reported in the supplementary material referred to in Appendix A.

3.3.2. Intake from other sources

The Panel notes that according to the EU Novel food catalogue[3] D-ribose was used in food supplements before 15 May 1997 and therefore its use in food supplement in the EU does not require a specific authorisation. A search performed in the Mintel GNPD for food supplements that have been introduced in the EU market or rebranded in the last 15 years, identified 10 products containing D-ribose. The intake of D-ribose from the recommended uses of these products ranged from 50 to 450 mg per day for the majority of the products, with two products going up to 2,000 and 2,500 mg per day, respectively. Consumption of 450 mg of D-ribose from food supplements is equivalent to an intake of 7.4 and 6.4 mg/kg bw per day for adolescents (14–18 years old) and adults, respectively (EFSA Scientific Committee, 2012). Consumption of 2,500 mg per day of D-ribose from food supplements is equivalent to an intake of 40.8 and 35.7 mg/kg bw per day for adolescents (14–18 years old) and adults respectively.

The Panel acknowledges that other food supplements are present on the market with recommended use leading to intakes of D-ribose > 2,500 mg per day.

4. Discussion

In its scientific opinion on D-ribose, the Panel concluded that the NF, is safe for the general population at intake levels up to 36 mg/kg bw per day, based on the NOAEL of 3.6 g/kg bw per day.

The intake assessment of D-ribose based on the new proposed uses and use levels indicated that the mean and high-level estimated intakes of D-ribose for all the population groups are below the acceptable level of intake except for one of the intake surveys. In adolescents in one country, the 95th percentile of the estimated intake slightly exceeds (39.4 mg/kg bw per day) the acceptable level of intake. However, the Panel notes that the intake estimates are based on conservative assumptions that all proposed food items consumed by an individual actually contain the novel food at the maximum proposed use levels. Therefore, the Panel considers the NF as safe, at the proposed use levels in all population groups.

The Panel notes that food supplements containing D-ribose are already on the market in the EU. Their consumption may lead to an additional intake of D-ribose which is not possible to estimate precisely, due to the variability in the content of D-ribose in the supplements. The combined intake of food products supplemented with D-ribose at the maximum proposed use levels and food supplements containing D-ribose may result in intakes in some population groups that exceed the

[3] https://ec.europa.eu/food/safety/novel_food/catalogue_en

acceptable level. The Panel also notes that the consumption of some of the food supplements currently on the market could, on its own, result in intakes of D-ribose higher than those considered safe in the EFSA opinion (EFSA NDA Panel, 2018).

5. Conclusions

The Panel concludes that the NF, D-ribose, is safe under the new proposed conditions of use. However, if used in conjunction with food supplements containing D-ribose, the Panel noted that the acceptable level of intake (36 mg/kg bw per day) may be exceeded.

Documentation provided to EFSA

1) Letter from the European Commission to the European Food Safety Authority with the request to review the additional information on D-ribose provided by the applicant and, if necessary, to update the conclusions of the Scientific Opinion on D-ribose. Ref. Ares(2018) 4530068 - 4/9/2018.
2) Additional information from the applicant including new proposed uses and use levels for d-ribose and a revised intake estimate. Ref. Ares(2018)4530068 - 4/9/2018.

References

EFSA (European Food Safety Authority), 2011a. Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment. EFSA Journal 2011;9(3):2097, 34 pp. https://doi.org/10.2903/j.efsa.2011.2097

EFSA (European Food Safety Authority), 2011b. Evaluation of the FoodEx, the food classification system applied to the development of the EFSA Comprehensive European Food Consumption Database. EFSA Journal 2011;9(3):1970, 27 pp. https://doi.org/10.2903/j.efsa.2011.1970

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, Siani A, Sjödin AM, Stern M, Tomé D, Vinceti M, Willatts P, Engel K-H, Marchelli R, Pöting A, Poulsen M, Schlatter JR, Germini A and Van Loveren H, 2018. Scientific opinion on the safety of D-ribose as a novel food pursuant to Regulation (EU) 2015/2283. EFSA Journal 2018;16(5):5265, 11 pp. https://doi.org/10.2903/j.efsa.2018.5265

EFSA Scientific Committee, 2012. Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579, 32 pp. https://doi.org/10.2903/j.efsa.2012.2579

Griffiths JC, Borzelleca JF and St Cyr J, 2006. Sub-chronic (13-week) oral toxicity study with D-ribose in Wistar rats. Food and Chemical Toxicology, 45, 144–152.

Abbreviations

bw	body weight
GNPD	Global New Products Database
NDA	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NF	novel food
NOAEL	no-observed-adverse-effect-level

Appendix A – Intake assessment

The intake assessment of D-ribose was performed with the data available in the EFSA Comprehensive European Food Consumption Database (Comprehensive database).

Since 2010, the Comprehensive database has been populated with national data on food consumption at a detailed level. Competent authorities in the European countries provide EFSA with data on the level of food consumption by the individual consumer from the most recent national dietary survey in their country (EFSA, 2011a). New consumption surveys added in the Comprehensive database were also taken into account in this assessment.

The food consumption data gathered by EFSA were collected by different methodologies and thus direct country-to-country comparisons should be interpreted with caution. Depending on the food category and the level of detail used for exposure calculations, uncertainties could be introduced owing to possible subjects' underreporting and/or misreporting of the consumption amounts. Nevertheless, the EFSA Comprehensive database represents the best available source of food consumption data across Europe at present.

Food consumption data from the following population groups: infants, toddlers, children, adolescents, adults and the elderly were used for the exposure assessment. For the present assessment, food consumption data were available from 38 different dietary surveys carried out in 22 European countries (Table A.1). Consumption records were codified according to the FoodEx classification system (EFSA, 2011b).

Table A.1: Population groups considered for the intake estimates of D-ribose

Population	Age range	Countries with food consumption surveys covering more than 1 day
Infants	4–11 months of age	Bulgaria, Germany, Denmark, Estonia, Finland, France, Italy, Latvia, Portugal, Spain, UK
Toddlers	12–35 months of age	Belgium, Bulgaria, Germany, Denmark, Estonia, Finland, France, Italy, Latvia, Netherlands, Portugal, Spain, UK
Children[(a)]	3–9 years of age	Austria, Belgium, Bulgaria, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Italy, Latvia, Netherlands, Portugal, Spain, Sweden, UK
Adolescents	10–17 years of age	Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Italy, Latvia, Netherlands, Portugal, Spain, Sweden, UK
Adults	18–64 years of age	Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Netherlands, Portugal, Romania, Spain, Sweden, UK
The elderly[(a)]	From 65 years of age and Older	Austria, Belgium, Germany, Denmark, Estonia, Spain, Finland, France, Hungary, Ireland, Italy, Latvia, Netherlands, Portugal, Romania, Sweden, UK
Pregnant women	–	Latvia, Portugal
Lactating women	–	Estonia, Greece

(a): The terms 'children' and 'the elderly' correspond, respectively, to 'other children' and the merge of 'elderly' and 'very elderly' in the Guidance of EFSA on the 'Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment' (EFSA, 2011a).

For the estimation of the intake the Panel considered the new uses proposed by the applicant as reported in Table 1. The intake of D-ribose was assessed based on the list of food categories provided by the applicant according to the FoodEx classification system, together with the proposed use levels (Table A.2).

Table A.2: FoodEx codes and levels and corresponding use levels for D-ribose used in the intake assessment performed with individual data from the EFSA Comprehensive European Food Consumption Database

Proposed use	FoodEx code	FoodEx level	Use levels (g/100 g)
Cereal bars	A.01.000220	3	0.20
Fine bakery wares	A.01.000252	2	0.31
Chocolate confectionery (excluding chocolate bars)	A.01.001295	3	0.17
	A.01.001296	3	
	A.01.001297	3	
	A.01.001299	3	
	A.01.001300	3	
	A.01.001301	3	
	A.01.001302	3	
	A.01.001303	3	
	A.01.001304	3	
	A.01.001305	3	
	A.01.001306	3	
	A.01.001308	3	
	A.01.001309	3	
Milk drinks (excluding malts and shakes)	A.01.000964	3	0.08
Sports, isotonic, and energy drinks	A.01.001767	3	0.80
Meal replacement beverages[(a)]	Not available	–	0.13
Meal replacement bars and energy bars	A.01.001766	3	3.30
Hard and soft confectionery	A.01.001311	3	0.20
	A.01.001313	3	
	A.01.001314	3	
	A.01.001315	3	
	A.01.001316	3	
	A.01.001317	3	
	A.01.001318	3	
	A.01.001319	3	
	A.01.001320	3	
	A.01.001321	3	
	A.01.001322	3	
	A.01.001323	3	
	A.01.001324	3	
	A.01.001325	3	
	A.01.001326	3	
Instant teas	A.01.001520	3	0.23
	A.01.001521	3	

(a): Specific code not available in the FoodEx classification system and therefore not included in the assessment of intake.

The contribution of each survey to the estimated intake for each population groups is reported in the excel file annexed to this opinion.