SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 25 October 2017

doi: 10.2903/j.efsa.2017.5059

Statement on the safety of taxifolin-rich extract from Dahurian Larch (*Larix gmelinii*)

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, Alfonso Siani, Anders Sjödin, Martin Stern, Daniel Tomé, Marco Vinceti, Peter Willatts, Karl-Heinz Engel, Rosangela Marchelli, Annette Pöting, Morten Poulsen, Josef Schlatter, Wolfgang Gelbmann and Henk van Loveren

Abstract

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to carry out a supplementary safety assessment for taxifolin by considering also those population groups which were originally excluded at the request of the applicant (i.e. infants, young children and children up to 9 years) for the food categories set out in the application, and by taking into the extension of use of taxifolin from yogurt to a wider range of dairy products. In 2016, the EFSA NDA Panel adopted the Scientific Opinion on the safety of taxifolin-rich extract from Dahurian Larch (*Larix gmelinii*) as a novel food ingredient in non-alcoholic beverages, yogurts, chocolate confectionery and food supplements pursuant to Regulation (EC) No 258/97. In order to address the present mandate, an intake assessment was carried out by taking into account all population groups (including now also children below 9 years of age) and by considering the food intended categories for which the applicant provided maximum use levels of taxifolin. Intakes were estimated for all age groups of the general population. The highest 95th percentile intakes per kg bw per day among all population groups are 0.94 and 1.54 mg, respectively, derived for toddlers. Noting that the no-observed-adverse effect level (NOAEL) of the subchronic study was 1,500 mg/kg body weight (bw), the resulting margin of exposure (MOE) would be almost 1,000. For adults weighing 70 kg, the MOE to the combined intake from fortified foods and food supplements would be about 772. For adolescents, taking into account a default mean body weight of 61 kg, the MOE to the combined intake (including 100 mg from food supplements) would be about 627. The Panel considers that these MOEs are sufficient. The Panel concludes that the NF food, taxifolin-rich extract from Dahurian Larch, is safe under the proposed conditions of use.

Keywords: Taxifolin, (2*R*,3*R*) *trans*-dihydroquercetin, 2,3-dihydroquercetin, Dahurian Larch, novel food, ingredient

Requestor: European Commission following the provision of additional information by Ametix JSC

Question number: EFSA-Q-2017-00554

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 J McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Kristina Pentieva, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Daniel Tomé, Dominique Turck, Henk van Loveren, Marco Vinceti and Peter Willatts.

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, Siani A, Sjödin A, Stern M, Tomé D, Vinceti M, Willatts P, Engel K-H, Marchelli R, Pöting A, PoulsenM, Schlatter J, Gelbmann W and van Loveren H, 2017. Statement on the safety of taxifolin-rich extract from Dahurian Larch (*Larix gmelinii*). EFSA Journal 2017;15(11):5059, 8 pp. https://doi.org/10.2903/j.efsa.2017.5059

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 Dietetic Products, Nutrition and Allergies (NDA) was asked to carry out a supplementary safety assessment for taxifolin by considering also those population groups which were originally excluded at the request of the applicant (i.e. infants, young children and children up to 9 years) for the food categories set out in the application, and by taking into the extension of use of taxifolin from yogurt to a wider range of dairy products.

On 13 December 2016, the EFSA NDA Panel adopted the Scientific Opinion on the safety of taxifolin-rich extract from Dahurian Larch (*Larix gmelinii*) as a novel food ingredient in non-alcoholic beverages, yogurts, chocolate confectionery and food supplements pursuant to Regulation (EC) No 258/97[1] (EFSA NDA Panel et al., 2016). In order to address the present mandate, an intake assessment was carried out by taking into account all population groups (including now also children below 9 years of age) and by considering the food intended categories for which the applicant provided maximum use levels of taxifolin. The intended food categories for the extended proposed use of taxifolin were allocated to corresponding food categories of the EFSA Comprehensive Food Consumption Database (EFSA, 2011) which is based on data from EU Member States' dietary surveys. Mean and high intakes (i.e. 95th percentile) were estimated for 'all subjects' for all age groups of the general population by using individual data of that data base and assuming that all foods of the intended food categories contain taxifolin at the maximum proposed use levels.

The highest mean and 95th percentile intakes per kg bw per day among all population groups are 0.94 and 1.54 mg, respectively, derived for toddlers. Noting that the NOAEL of the 90-day subchronic study was 1,500 mg/kg body weight (bw), the resulting margin of exposure (MOE) to the 95th percentile intake estimate for toddlers would be almost 1,000. For adults weighing 70 kg, the MOE to the combined intake from fortified foods and food supplements would be about 772. For adolescents, taking into account a default mean body weight of 61 kg, the MOE to the combined intake (including 100 mg from food supplements) would be about 627. The Panel considers that these MOEs are sufficient.

The Panel concludes that the NF food, taxifolin-rich extract from Dahurian Larch, is safe under the proposed conditions of use.

[1] Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients**.** *OJ L 43, 14.2.1997, p. 1–6.*

Table of contents

1. Introduction

1.1. Background

On 13 December 2016, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) adopted the Scientific Opinion on the safety of taxifolin-rich extract from Dahurian Larch (*Larix gmelinii*) as a novel food ingredient in non-alcoholic beverages, yogurts, chocolate confectionery and food supplements pursuant to Regulation (EC) No 258/97[1] (EFSA NDA Panel, 2016).

The request for the supplementary assessment followed the comments raised by some Member States at the Standing Committee regarding the potential for exposure of the excluded population subgroups (i.e. infants, young children and children up to 9 years) to taxifolin from the consumption of food products containing taxifolin. Their concerns stem from the fact that although the use of taxifolin has been assessed by the European Food Safety Authority (EFSA) to be safe for the intended uses set out in the application, in real life situations, it would be difficult to ensure that those products (e.g. chocolate, yogurt, non-alcoholic beverages) will not be consumed by the excluded subgroups of the population. Consequently, an exposure and safety assessment is needed for these subgroups. In addition, the applicant requested to expand the use of taxifolin to all types of dairy products, not just yogurts and submitted an extended intake estimate to cover other dairy products.

1.2. Terms of Reference as provided by the European Commission

Consequently, EFSA was asked to update the former dietary exposure and safety assessment for taxifolin in order to consider:

1) The groups of the population which were excluded in the application of taxifolin as a novel food ingredient in the context of Regulation (EC) No 258/97, namely, infants, young children, and children up to nine years of age for all food products in the application (i.e. non-alcoholic beverages, yogurt and chocolate confectionary).
2) All groups of the population for all types of dairy products.

2. Data and methodologies

2.1. Data

The assessment of the safety of taxifolin at the extended uses for all groups of the general population is based on supplementary information to original novel food (NF) application (i.e. Dossier 'Taxifolin') provided by the applicant, the EFSA Comprehensive Food Consumption Database (EFSA, 2011) and the scientific opinion on the safety of taxifolin (EFSA NDA Panel, 2016).

2.2. Methodologies

The assessment follows the methodology set out in Commission Recommendation 97/618/EC of 29 July 1997 concerning the scientific aspects and the presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients and the preparation of initial assessment reports under Regulation (EC) No 258/97 of the European Parliament and of the Council.

3. Assessment

On 13 December 2016, the EFSA NDA Panel adopted the Scientific Opinion on the safety of taxifolin-rich extract from Dahurian Larch (*Larix gmelinii*) as a novel food ingredient in non-alcoholic beverages, yogurts, chocolate confectionery and food supplements pursuant to Regulation (EC) No 258/97[1] (EFSA NDA Panel, 2016). The maximum use levels proposed by the applicant were 0.02 g/L for non-alcoholic beverages, 0.02 g/kg for yogurts and 0.07 g/kg for chocolate confectionery. The maximum proposed daily intake of taxifolin from food supplements was 100 mg/day. According to the applicant, taxifolin was intended for the general population from the age of 9 years onwards with the exception of its use for food supplements which are not intended for children of below 14 years of age. For estimating intakes of taxifolin by the target population, the applicant used the summary statistics of the EFSA Comprehensive Food Consumption Database (EFSA, 2011). The approach applied by the applicant included several conservative elements as outlined in the EFSA Opinion (estimating all 'flavoured fermented milk and dairy products' as a whole food category instead of 'yogurt', assessing 'consumers

only' and summing up the high percentile consumption of each food category for deriving the high percentiles for the total intake from all categories). In 2016, the Panel considered that the highest dose tested in the 90-day subchronic rat study, i.e. 1,500 mg/kg bodyweight (bw) per day, was the no-observed-adverse effect level (NOAEL) of this study (Tselyico, 2016 – unpublished study report). The Panel concluded that the margins of exposure (MOEs) of this NOAEL and the estimated intake of taxifolin from the intended food uses (including 100 mg taxifolin/ day from supplements) were 660 for adults consuming 158 mg/day and 460 for adolescents consuming 146 mg/day, respectively. The Panel concluded that the NF, taxifolin-rich extract from Dahurian Larch, is safe under the proposed conditions of use (EFSA NDA Panel, 2016).

In order to address the present mandate, an intake assessment was carried out by taking into account all population groups (including now also children below 9 years of age) and by considering the food intended categories for which the applicant provided maximum use levels of taxifolin.

3.1. Anticipated intake/extent of use

Different from the original application assessed in 2016, the applicant intends to use taxifolin in the category 'dairy' not only for yogurts, but for a wider range of dairy products as presented in Table 1. This table contains also intended maximum use levels of taxifolin for these products. It is noted that the intended uses and use levels of taxifolin in chocolate confectionery and non-alcoholic beverages remain unchanged from the original application. The Panel also notes that taxifolin has been authorised for its use in food supplements excluding children younger than 14 years with and limited to an intake of 100 mg/day.

3.1.1. Intake from fortified foods

Table 1: Proposed uses and use levels for taxifolin

Food products	Applicant's assumptions of the fat content in the products (%)	Use of taxifolin in % by fat mass	Maximum use levels proposed by the applicant
Cowmilk yogurt, plain	10	0.02	0.020 g/kg
Cowmilk yogurt with fruits	10	0.02	0.020 g/kg
Kefir	3.2	0.025	0.008 g/kg
Buttermilk	2	0.025	0.005 g/kg
Dried milk	26	0.02	0.052 g/kg
Cream	30	0.025	0.070 g/kg
Sour cream	20	0.025	0.050 g/kg
Cheese	45	0.02	0.090 g/kg
Butter	82	0.02	0.164 g/kg
Chocolate confectionery	35	0.02	0.070 g/kg
Non-alcoholic beverages	–	–	0.020 g/L

The intended food categories for the extended proposed use of taxifolin were allocated to corresponding food categories (Table 2) of the EFSA Comprehensive Food Consumption Database (EFSA, 2011) which is based on data from EU Member States' dietary surveys.

Table 2: Extended intended uses and use levels for the NF as a food ingredient

Food category used for the EFSA Comprehensive Data Base	Use levels
Unflavoured fermented milk products, including natural unflavoured buttermilk (excluding sterilised buttermilk) non heat-treated after fermentation	0.020 g/kg
Flavoured fermented milk products including heat-treated products	0.020 g/kg
Dehydrated milk	0.052 g/kg
Cream and cream powder	0.070 g/kg
Cheese and cheese products	0.090 g/kg
Unripened cheese	0.090 g/kg
Ripened cheese	0.090 g/kg

Food category used for the EFSA Comprehensive Data Base	Use levels
Whey cheese	0.090 g/kg
Processed cheese	0.090 g/kg
Fats and oils essentially free from water (excluding anhydrous milkfat)	0.164 g/kg
Cocoa and Chocolate products	0.070 g/kg
Fruit juices as	0.020 g/L
Vegetable juices	0.020 g/L
Fruit nectars and vegetable nectars and similar products	0.020 g/L
Flavoured drinks with sugar	0.020 g/L
Flavoured drinks with sweetener	0.020 g/L

Mean and high intakes (i.e. 95th percentile) were estimated for 'all subjects' for all age groups of the general population by using individual data of that data base and assuming that all foods of the intended food categories contain taxifolin at the maximum proposed use levels. The ranges of the estimated mean and high intakes (in mg/kg bw per day) among the individual EU dietary surveys for the various population groups are presented in Table 3.

Table 3: Intake estimates for taxifolin on the basis of proposed uses and use levels

Population group	Range of means (mg/kg bw per day)	Range of high intakes (95th percentile)[(a)] (mg/kg bw per day)
Infants (up to 1 year)	0.12–0.34	0.32–0.74
Toddlers (1–3 years)	0.34–0.94	0.74–1.54
Other children (4–9 years)	0.28–0.73	0.66–1.47
Adolescents (10-17 years)	0.19–0.39	0.36–0.76
Adults (18–64 years)	0.09–0.22	0.24–0.52
Elderly (> 64 years)	0.05–0.17	0.13–0.32

bw: body weight.
(a): Based on surveys with > 60 consumers

The highest mean and highest 95th percentile intakes per kg bw per day among all population groups are 0.94 and 1.54 mg, respectively, derived for toddlers.

3.1.2. Combined intake from fortified foods and food supplements

Considering the highest 95th percentile intake for adults from fortified food (i.e. 0.52 mg/kg bw per day) and a default bodyweight of 70 kg for an adult (EFSA Scientific Committee, 2012), the combined taxifolin intake from fortified foods (36 mg) and from food supplements (100 mg), is estimated at 136 mg/day.

When considering the highest 95th percentile intake for adolescents from fortified food (i.e. 0.76 mg/kg bw per day) and a default mean body weight of 61 kg for adolescents of 14–18 years (EFSA Scientific Committee, 2012), combined taxifolin intake from fortified foods (46 mg) and from food supplements (100 mg), results to 146 mg taxifolin intake per day. The Panel notes that in its Opinion from 2016 a lower default body weight (45 kg, i.e. P5 according to EFSA Scientific Committee, 2012) was considered for the target group of adolescents between 14 and 18 years of age accounting for the use of consumption data of adolescents between 10 and 17 years of age and thus included children below 14 years of age with a lower food intake per person and lower body weight.

Also, the intake estimate for taxifolin from fortified food for adolescents of the present evaluation is based on consumption data of the population group between 10 and 17 years of age, but on per kg bw base and thus includes consumption data for younger children below 14 years with higher food intake per kg bw than adolescents from 14 years onwards. Therefore, multiplying the default body weight of 61 kg for adolescents from 14 years onwards with food consumption data on a per kg bw base from the population group 10–17 years of age, is considered conservative.

4. Discussion

The highest intake estimate per kg bw intake of taxifolin per day from fortified foods among all groups of the general population is derived for toddlers (1–3 years) and children of 4–9 years of age at approximately 1.5 mg/kg bw per day. Noting that the NOAEL of the 90-day subchronic study (Tselyico, 2016 – unpublished study report) was 1,500 mg/kg bw, the resulting MOE would be about 1,000 for these age groups. The MOE for infants and for children between 10 and 13 years of age would be approximately 2000.

For adults weighing 70 kg, the MOE to the combined intake from fortified foods and food supplements would be about 770. For adolescents, taking into account a default body weight of 61 kg (mean body weight for adolescents aged 14–18 years as suggested by EFSA Scientific Committee (2012)), the MOE to the combined intake (including 100 mg from food supplements) would be about 630.

The Panel considers that these MOEs are sufficient.

5. Conclusions

The Panel concludes that the NF food, taxifolin-rich extract from Dahurian Larch, is safe under the proposed conditions of use.

Documentation provided to EFSA

1) Letter from the European Commission to the European Food Safety Authority with the request to carry out a supplementary dietary exposure and safety assessment to L-ergothioneine. Ref. Ares(2017)3243708, dated 28/6/2017.
2) Supplementary information from the applicant including information on extended uses and a revised intake estimate.

References

EFSA (European Food Safety Authority), 2011. 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 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 H, Naska A, Neuhäuser-Berthold M, Nowicka G, Pentieva K, Sanz Y, Siani A, Sjödin A, Stern M, Tomé D, Vinceti M, Willatts P, Engel K-H, Marchelli R, Pöting A, Poulsen M, Schlatter J, Turla E and van Loveren H, 2016. Scientific opinion on the safety of safety taxifolin-rich extract from Dahurian Larch (*Larix gmelinii*) as a novel food pursuant to Regulation (EC) No 258/97. EFSA Journal 2017;15(1):4682, 16 pp. https://doi.org/10.2903/j.efsa.2017.4682

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

Tselyico SS, 2016. Unpublished study report. 90-day sub-chronic toxicity study of Lavitol (dihydroquercetin) in white Wistar rats with a 4-week recovery period. Project No: 211447. Ametis JSC. 16 May 2015.

Abbreviations

bw	body weight
MOE	margin of exposure
NDA Panel	EFSA Panel on Dietetic Products, Nutrition and Allergies
NF	novel food
NOAEL	no-observed-adverse effect level
P5	5th percentile