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SCIENTIFIC OPINION

Opinion on the safety of Tahitian Noni® '*Morinda citrifolia* (noni) fruit puree and concentrate' as a novel food ingredient [1]

Scientific Opinion of the Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2007-181)

Adopted on 13 March 2009

PANEL MEMBERS

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SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to deliver a scientific opinion on the safety of *Morinda citrifolia* (Noni) fruit puree and concentrate' as a novel food ingredient.

Noni fruit puree manufactured according to the procedure described in this application is the same as the noni fruit material used to produce Tahitian Noni® Juice. Noni fruit concentrate is also made directly from noni fruit puree. The compositional data provided demonstrate that the manufacture of noni fruit concentrate results in an increase of the proportions of more hydrophilic components (carbohydrates, sugars, minerals) and in a decrease of the fat content. The Panel considers that the two steps involved in the production of the noni fruit concentrate (removal of the pulp by centrifugation and concentration by evaporation) are not expected to result in qualitative or quantitative compositional changes which might be of toxicological or nutritional relevance.

According to the applicant, the quantity of noni fruit puree or noni juice concentrate to be included in products will be equivalent to 30 mL of *Morinda citrifolia* fruit juice per serving. The highest estimate at the 97.5th percentile is 504 mL *Morinda citrifolia* fruit juice/day for adults, excluding Tahitian Noni® Juice. Adding the 97.5th percentile for consumption of Tahitian Noni® Juice by adults (120 mL/day) results in a total 97.5th percentile estimate of 624 mL *Morinda citrifolia* fruit juice/day. The average combined intake for adult males, from all sources, is estimated to be no more than 161 mL *Morinda citrifolia* fruit juice.

In children, the highest quantity estimated for any high consumer group is equivalent to 416 mL *Morinda citrifolia* fruit juice/day. Combining this with the high consumption (97.5th percentile)

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estimate of 132 mL Tahitian Noni® Juice/day by children provides a total of 548 mL *Morinda citrifolia* fruit juice/day. The highest average combined intake in children is estimated to be 169 mL *Morinda citrifolia* fruit juice/day.

In a previous opinion adopted in 2006, the Panel considered four case studies to investigate a possible association between the consumption of noni juice and hepatotoxicity. On the basis of the available toxicological information and against the background of the data provided on consumption of noni juice without the reporting of hepatotoxic effects, the Panel considered it unlikely that consumption of noni juice, at the observed levels of intake, induces adverse human liver effects. This would also apply to the anthraquinones potentially present in the commercially produced noni juice. The Panel concluded that there was no convincing evidence for a causal relationship between the acute hepatitis observed in the case studies reported and the consumption of noni juice.

Since then, the Panel has been made aware of five additional case reports on a possible association between the consumption of noni juice and hepatotoxicity, and one case report on the consumption of a non-specified noni preparation. The Panel noted that in most of the case studies reported the source of the noni product consumed remained unclear. While the Panel considers that available data are not sufficient to establish a causal relationship between the consumption of Noni Juice and hepatoxicity, the increasing number of case reports might indicate that some individuals have a particular sensitivity for hepatotoxic effects to noni fruit products.

The Panel concludes that '*Morinda citrifolia* (Noni) fruit puree and concentrate as novel food ingredients' under the specified conditions are considered safe for the general population. However the Panel considers that the increasing number of case reports might indicate that some individuals have a particular sensitivity for hepatotoxic effects to noni fruit products.

Key words: Morinda citrifolia, Tahitian Noni® Juice, noni puree, noni concentrate,

hepatotoxicity

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BACKGROUND AS PROVIDED BY THE COMMISSION

On 1 December 2006, Morinda Inc. submitted a request under Article 4 of the Novel Food Regulation (EC) N° 258/97 to the competent authorities of Belgium for placing on the market '*Morinda citrifolia* (Noni) fruit puree and concentrate as a novel food ingredient'.

On 21 March 2007, the competent authorities of Belgium forwarded to the Commission their initial assessment report, which had reached the conclusion that there are no reasons to believe that there is a risk for human health linked to the consumption of the fruit puree or concentrate within the expected consumption levels.

On 28 March 2007, the Commission forwarded the initial assessment report to the other Member States. Several of these Member States submitted additional comments or raised objections. The concerns of a scientific nature can be summarised as follows:

- A clear distinction should be made between noni puree and noni concentrate. Changes in concentrations of individual components during the production of the concentrate should be described. The compositions of noni puree and concentrate should be compared to that of the authorised noni juice.
- More details on the manufacturing process should be given.
- An approval to use noni fruit puree and fruit concentrate as food ingredients should only be given under the condition that there is no occurrence of anthraquinones in the fruit puree and fruit concentrate. The absence of lucidin and rubiadin must be substantiated by analysis (detection limit 10 μg/kg) and should be included in the specification.
- The dossier provides insufficient insight into the anticipated intake of the products following their inclusion in the proposed wide range of products. The intakes of sub-groups, in particular children, should be discussed.
- The use may reach higher levels than the 30 mL per day previously recommended for consumption of Tahitian Noni® Juice especially if products are used as ingredients in several food groups.
- Consumers should be recommended not to exceed daily doses of puree corresponding to 30 mL of squeezed juice.
- As the noni puree and concentrate will be available in a wide range of products, the intake levels could be considerably higher than considered in the EFSA opinion on noni juice, and therefore there should be sufficient reassurance that increasing the product range and the likely consumption of a number of the products by children do not give rise to hepatotoxicity.
- The risk assessment should include an estimate of the intake of the ingredients by children. The consumption should be monitored, with particular attention to children and adolescents.
- Given that noni fruit concentrate is obtained from a fraction of the puree, the compositions are different, and supplementary toxicological information would be desirable.
- The validity of the animal test referred to regarding the assessment of the allergenic potential is considered limited due to the fact that no information on the levels of the sensitising or challenging doses is presented. The difference in the composition of the puree and the concentrate including the protein content was noted.

In consequence, a Community Decision is now required under Article 7, paragraph 1 of Regulation (EC) No 258/97.

TERMS OF REFERENCE AS PROVIDED BY THE COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002, the European Food Safety Authority is asked to carry out the additional assessment for '*Morinda citrifolia* (Noni) fruit puree and concentrate' in the context of Regulation (EC) N° 258/97.

EFSA is asked to consider the elements of a scientific nature in the comments raised by the Member States (Annex 3).

When appropriate, EFSA is invited to take into account also the information and documents used for the 'Opinion on a request from the Commission related to the safety of noni juice (juice of the fruits of *Morinda citrifolia*)' (Request N° EFSA-Q-2005-236).

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ASSESSMENT

The product belongs to class 2, sub-category 2.2 (complex novel foods derived from sources which have not been genetically modified and which have no history of food use within the Community), as defined in the SCF recommendations concerning the assessment of novel foods (European Commission, 1997b). Accordingly, information related to the structured schemes I, II, III, IX, XI, XII, XIII has been submitted. In addition, the applicant also provided data related to scheme X (previous human exposure to the novel food or its source).

I. Specification of the novel food (NF)

According to results from routine quality control tests, the mean moisture content of M. citrifolia puree is 91.5 (± 0.97) g/100g (104 batches) and the pH is 3.81 (± 0.08).

Compositional data provided for M. citrifolia puree and M. citrifolia concentrate are shown in Table 1. They are based on analyses of 10 batches of M. citrifolia puree from 1996 (1), 1999 (1), 2005 (5), 2006 (2) and 2007 (1) and of 6 batches of M. citrifolia concentrate from 2002 (1), 2004 (2), 2005 (1) and 2006 (2).

Table 1. **Compositional data on *M. citrifolia* puree, *M. citrifolia* concentrate and Tahitian Noni Juice (TNJ)®**

	***M. citrifolia* PUREE**		***M. citrifolia* CONCENTRATE**		**Tahitian Noni® JUICE[(a)]**
	Mean	***SD***	***Mean***	***SD***	***Range***
Proximate					
Moisture (g/100g)	91.6	2.0	50.5	2.3	89 – 90
Protein (g/100g)	0.55	0.1	3.3	0.2	0.2 – 0.5
Fat (g/100g)	0.10	0.1	0.02	0.01	0.1 – 0.2
Ash (g/100g)	0.54	0.2	4.7	0.2	0.2 – 0.3
Total carbohydrates (g/100g)	7.2	1.9	41.5	2.2	9.0 – 11.0
Fructose (g/100g)	1.1	0.4	10.0	0.2	3.0 – 4.0
Glucose (g/100g)	1.3	0.4	10.2	0.6	3.0 – 4.0
Sucrose (g/100g)	< 0.1	-	< 0.1	-	< 0.1
Dietary fiber (g/100g)	2.0	0.3	2.9	1.0	0.5 -1.0
Energy (kJ/100g)	136	32	762	40	163-197
Vitamins					
Vitamin A (IU/g)	< 1	-	< 1	-	< 1
ß-Carotene (µg/g)	19.1	12.1	124	50	18-22 IU/100 g
Thiamin (mg/g)	< 0.02	-	< 0.02	-	0.003-0.01 mg/100g
Riboflavin (mg/g)	< 0.02	-	< 0.02	-	0.003-0.01 mg/100 g
Niacin (mg/g)	0.03	0.01	0.2	0.05	0.1-0.5 mg/100g
Vitamin B6 (mg/g)	< 0.02	-	< 0.02	-	0.04-0.13 mg/100g
Vitamin B12 (µg/g)	< 0.001	-	< 0.002	-	0.1-0.3 µg/100g
Vitamin C (mg/g)	1.1	0.8	1.3	0.5	3.0-25 mg/100 g
Vitamin E (µg/g)	11.0	6.6	52.4	34.1	0.25-1.0 IU/g
Folic acid (µg/g)	< 0.06	-	0.45	0.2	7.0-25.0 µg/100 g
Biotin (µg/g)	0.02	-	0.14	0.01	1.5–5.0 µg/100 g
Pantothenic acid (mg/g)	< 0.02	-	0.1	0.02	0.15-0.5 mg/100 g

Minerals					
Ca (mg/100g)	48.2	16.0	114	34	20-25
K (mg/100g)	214.3	56.9	2026	144	30-150
Na (mg/100g)	17.0	6.0	121	41	15-40
Mg (mg/100g)	26.1	8.3	152	20	3.0-12
P (mg/100g)	20.4	6.8	139	20	2.0-7.0
Fe (mg/100g)	0.7	0.06	26.1	7.5	0.1-0.3
Mo (mg/100g)	< 0.0004	-	< 0.0004	-	0.3-1.0
Amino acids					
Alanine (mg/100 g)	45	4	259	11	17 - 33
Arginine (mg/100g)	32	4	148	12	30 - 44
Aspartic acid (mg/100g)	80	8	409	26	30 - 77
Cystine (mg/100 g)	23	3	138	78	7 - 11
Glutamic acid (mg/100 g)	64	5	331	21	25 - 44
Glycine (mg/100 g)	36	4	150	15	10 - 22
Histidine (mg/100 g)	< 10	-	31	5	4 - 6
Isoleucine (mg/100 g)	29	1	136	12	7 - 11
Leucine (mg/100 g)	38	2	173	17	10 - 22
Lysine (mg/100 g)	25	4	79	13	7 - 11
Methionine (mg/100 g)	< 10	-	40	3	1 - 4
Phenylalanine (mg/100 g)	21	5	99	9	5 - 8
Proline (mg/100 g)	26	3	138	7	24 - 33
Serine (mg/100 g)	27	2	107	13	9 - 12
Threonine (mg/100 g)	27	3	104	0.1	8 - 11
Tryptophan (mg/100 g)	< 10	-	31	6	1 - 3
Tyrosine (mg/100 g)	25	3	123	1	6 - 11
Valine (mg/100 g)	36	3	165	12	10 - 22

(a) Values from SCF Opinion on Tahitian Noni® Juice, 2002; *SD* = standard deviation

Normalisation of the data given for *M. citrifolia* concentrate (moisture content 50.5 %) in Table 1 to the water content of *M. citrifolia* puree (91.5 %) reveals that the separation of the pulp from the puree and the concentration of the resulting juice results in increased contents of hydrophilic constituents, e.g. carbohydrates, proteins, minerals.

For some of the constituents listed in Table 1, the contents provided for *M. citrifolia* puree are outside the ranges given for TNJ®. However, such a comparison is hampered by the fact that the production of TNJ® involves the addition of other juices to the noni puree.

For heavy metals the following contents were reported as typical results of analyses: arsenic < 0.10 mg/kg; cadmium < 0.05 mg/kg; lead < 0.05 mg/kg; mercury < 0.025 mg/kg. On the basis of results from a pesticide screen (USFDA Pesticide Analytical Method 302), the following contents were provided: organophosphate compounds < 0.05 mg/kg; organonitrogen compounds < 0.5 mg/kg; organochlorine compounds < 0.2 mg/kg; N-methylcarbamate compounds < 0.1 mg/kg.

Mycotoxin analyses of *M. citrifolia* puree revealed no detectable presence of aflatoxin B1, B2, G1, and G2 (all Detection Limit, DL = 1.0 µg/kg), ochratoxin A (DL = 5.0 µg/kg), T-2 toxin (DL = 0.5 mg/kg), HT-2 toxin (DL = 0.5 mg/kg), diacetoxyscirpenol (DL = 1.2 mg/kg), neosolaniol (DL = 0.5 mg/kg), fusarenon X (DL = 0.5 mg/kg), deoxynivalenol (DL = 0.1 mg/kg), 15 acetyl-

DON (DL = 0.1 mg/kg), 3 acetyl-DON (DL = 0.1 mg/kg), nivalenol (DL = 0.5 mg/kg), zearalenone (DL = 100 µg/kg), fumonisin B1 (DL = 0.1 mg/kg), fumonisin B2 (DL = 0.1 mg/kg), and fumonisin B3 (DL = 0.1 mg/kg), or patulin (40µg/kg).

The applicant developed and validated an HPLC-UV method for the analysis of anthraquinones in *M. citrifolia* puree and concentrate. The limits of detection determined for 5,15-dimethylmorindol, lucidin, alizarin and rubiadin were 2.5, 50.0, 6.3 and 62.5 ng/mL, respectively. Spiking of *M. citrifolia* puree with 5,15-dimethylmorindol (0.1 – 0.3 µg/mL) revealed recoveries between 83 and 90 %. The amounts of 5,15-dimethylmorindol detected in five batches of *M. citrifolia* puree ranged from 0.19 to 0.20 µg/mL, those in five batches of *M. citrifolia* concentrate from 0.11 to 0.77 µg/mL. Lucidin, alizarin and rubiadin were not detected in the samples analyzed.

II. Effect of the production process applied to the NF

M. citrifolia puree is identical to the puree produced as the major ingredient of TNJ®. The fruits are harvested by hand. Seeds and skin are separated mechanically from the pureed fruits. After pasteurisation, the puree is packaged in aseptic containers and stored under cold conditions.

The *M. citrifolia* puree serves as starting material to prepare *M. citrifolia* concentrate. The puree is treated with food-grade pectinolytic enzymes (50-60 °C for 1-2 h) to break down the pectin and thus to aid in the separation of the juice from the pulp. The puree is heated to inactivate the pectinases and then immediately cooled. The juice is then separated from the pulp in a decanter centrifuge. After the juice is collected, it is heated to 93 °C for at least 1 second, as a pasteurisation step, prior to being concentrated in a double effect vacuum evaporator from a brix of 6 to 8 to a finished brix of 49 to 51.

The steps involved in the production of both *M. citrifolia* puree *and M. citrifolia* concentrate are standard procedures commonly applied in the manufacture of fruit juices.

III. History of the organism used as the source of the NF

Taxonomically, *Morinda citrifolia* L. (common name "Noni") belongs to the Rubiaceae family. It has a long tradition as a dye plant and has been traditionally used throughout Polynesia as a medicinal plant. Several ethnobotanical studies from tropical regions refer to raw or cooked *Morinda citrifolia* fruit as part of the diet of aboriginal populations of Polynesia and Australia. According to some references, the consumption was limited to famine due to the rather unpleasant taste and odour of the ripe fruits (SCF, 2002).

IX. Anticipated intake/extent of use of the NF

According to the applicant, the following types of products are intended to be formulated with *M. citrifolia* fruit puree and concentrate: Candy/confectionery, nutritional bars; powdered nutritional drink mixes; noni fruit juice concentrates blended with other ingredients; jams; syrups.

In the future the applicant intends to extend the product categories as follows: Concentrated fruit juice beverages; ice cream; yogurt; fruit smoothies; sorbet; jams and jellies (fruit preserves); pastry and pie filling; dessert topping; cookies and other baked goods; breakfast cereal; chutney; curry; marinade; sauces (such as barbecue); salsa; dressing; stuffing; meat breading/coating.

In the original application sales data for TNJ® had been used to calculate the total anticipated intake of concentrated noni juice and noni puree, including the noni puree in TNJ® that is equivalent to 313 mL *Morinda citrifolia* fruit juice/day.

Additionally, data from two consumer surveys have been provided. The first survey was conducted in October 2003 at a meeting of sales consultants and consumers of TNJ® from 17 countries in Copenhagen (1143 questionnaires; respondents from Sweden (325), Germany (302), Norway (204), Denmark (98), Hungary (95), Great Britain (41), Finland (22), The Netherlands (15), France (11), USA (10), others (20); 68% of the participants female and 38% male; average age 48 years). The average daily intake of TNJ® was about 50 mL/day. The majority had a daily intake between 30 and 90 mL; 0.7% consumed less than 30 mL and 7.6% more than 90 mL/day. There was no significant difference between the daily intakes of male (52.8 mL) and female (52.0 mL) participants. The average duration of TNJ® consumption was 26 months.

The second is an internet-based survey launched in 2004 (at the time of evaluation: 299 male and 271 female participants; average age 44 years). The average daily intakes of TNJ® by male and female consumers were 63.5 and 67.0 mL, respectively. 36.5% consumed 30-60 mL, 35.1% 60-90 mL, 22.6% 90-120 mL and 5.6 % >120 mL/day. The median duration time of TNJ® consumption was 14.7 months. About 60% of the participants had a history of TNJ® intake of less than one year.

Among European adult consumers, the average consumption is 58 mL TNJ®/day (97.5th percentile: 120 mL TNJ®/day). Among European children, the average consumption is 67 mL TNJ®/day (97.5th percentile: 132 mL TNJ®/day). The total number of children (< 19 yr) included in these surveys was 16, i.e. less than 1% of the total number of participants.

According to the applicant, the quantity of noni fruit puree or noni juice concentrate to be included in products will be equivalent to 30 mL of *Morinda citrifolia* fruit juice per serving (Table 2).

Table 2. **Maximum Per Serving Equivalents of M. citrifolia Fruit Ingredients**

Ingredient	Equivalent amounts per serving[(a)]
M. citrifolia Fruit Juice	30 mL
M. citrifolia Fruit Puree	26.5 g
M. citrifolia Fruit Concentrate	6 g

[(a)] based on % solids

With this per serving amount, the amount of *Morinda citrifolia* fruit juice equivalents per g serving was calculated for each intended food category (Table 3).

Table 3. **Quantity of Morinda citrifolia fruit juice equivalents per serving in intended food categories**

Product	Serving size (g)	*Morinda citrifolia* fruit juice equivalent (mL) / serving	*Morinda citrifolia* fruit juice equivalent (mL) / g serving
Candy/Confectionery			
- sugar confectionery	59	30	0.5
- chocolate confectionery	59	30	0.5
Nutritional bars ("other products category")	50	30	0.6
Powdered nutritional drink mixes (as "other beverages" dry weigh)	50	30	0.6

Low calorie carbonated beverages	240	30	0.1
Ice Cream & sorbet	85	30	0.4
Yogurt	225	30	0.1
Biscuits	50	30	0.6
Buns, cakes & pastries	50	30	0.6
Breakfast cereal (whole grain)	30	30	1.0
Jams and jellies (fruit preserves)	20	30	1.5
Sweet spreads, fillings and icings	85	30	0.4
Savoury sauces, pickles, gravies, and condiments	30	30	1.0

The per gram quantities were then applied to the total quantities of food consumed, by category, as reported in the UK NDNS of 1997 and 2000/2001, to calculate the estimated daily intake of *Morinda citrifolia* fruit juice equivalents (Table 4).

Table 4. **Estimated daily intake of M. citrifolia fruit juice equivalents (mL), Tahitian Noni® Juice excluded, based on UK National Diet and Nutrition Surveys**

Group	Age (yr)	mL/day	
		Mean	97.5%
Young males	4 - 6	78	294
	7 - 10	99	358
	11 - 14	102	416
	15 - 18	96	413
Young females	4 - 6	81	299
	7 - 10	87	321
	11 - 14	86	327
	15 - 18	73	307
Adult males	19 - 64	103	504
Adult females	19 - 64	92	406

The highest estimate for adult males at the 97.5th percentile is 504 mL *Morinda citrifolia* fruit juice/day, excluding TNJ®. Adding the 97.5th percentile for consumption of TNJ® by adults (120 mL/day), results in a total 97.5th percentile estimate of 624 mL *Morinda citrifolia* fruit juice/day. The average combined intake for adult males, from all sources, is estimated to be no more than 161 mL *Morinda citrifolia* fruit juice.

In children, the highest quantity estimated for any high consumer group is equivalent to 416 mL *Morinda citrifolia* fruit juice/day. Combining this with the high consumption (97.5th percentile) estimate of 132 mL TNJ®/day by children provides a total of 548 mL *Morinda citrifolia* fruit juice/day. The highest average combined intake in children is estimated to be 169 mL Morinda citrifolia fruit juice/day.

This type of intake methodology is generally considered to be "worst case" as a result of several conservative assumptions made in the consumption estimates. For example, it is often assumed that all food products within a food category contain the ingredient at the maximum specified level of use. In addition, it is well established that the length of a dietary survey affects the estimated consumption of individual users. Short-term surveys, such as the 4-day children's survey, may overestimate consumption of food products that are consumed relatively infrequently, particularly when weighted to 7 days (Gregory *et al*., 1995).

X. Information from previous human exposure to the NF or its source

TNJ® has been marketed for several years in a number of countries. According to data obtained in the USA for a 4-month period in 2002, an average number of approximately 300,000 one-litre bottles were sold per month.

According to data obtained in the USA for 2001, an average number of 46,603 people purchased TNJ® per month. 74% purchased 4 bottles per month. Assuming that the purchaser is the only consumer, this is equivalent to a daily consumption of 133 mL.

The manufacturer of TNJ® has compiled consumer complaint data relative to noni juice (EFSA, 2006).

The Panel requested from the applicant any additional consumption data and reports of adverse effects from active or passive surveillance for noni juice in general and in particular for noni products from Tahitian Noni International.

According to the information provided, the number of bottles of TNJ® sold between 1996 and 2006 amounts to more than 80 million. The applicant compiles complaint data sent to the company by consumers or other parties regarding TNJ®. They are catalogued regardless of the authenticity of the reported event, an actual diagnosis by a physician, or receipt of valid medical records. Up to January 2006, 304 health-related complaints were received from consumers. The categories were as follows: allergic reactions (71); diarrhoea (37); nausea (57); skin rash (42); and uncategorised (97).

Continuing post-market surveillance has revealed that from January 2006 to October 2008 the number of one litre-bottles of TNJ® sold was 26,491,314. During this period 117 health-related complaints were received from consumers. Similarly to the previous period, this corresponds to approximately one health-related complaint for every 225,000 bottles sold. The categories were as follows: allergic reactions (26); diarrhoea (14); nausea (27); skin rash (12); and uncategorised/unknown (38).

According to the applicant, another group of carbonated noni juice-containing products has been marketed internationally since March 2007, with more than 15 million cans (250 mL) sold. There have been 18 health-related complaints for these products. Eleven are reported as allergic reactions, with another three as nausea. The remaining are miscellaneous health complaints, none of which involves liver or hepatitis.

The applicant also provided information from searches of the data files of the United States Food and Drug Administration (FDA) adverse event reporting system (http://www.fda.gov/cder/aers/extract.htm). Reports in which noni juice or noni supplements are mentioned were listed in a summarising Table that also included the nature of the adverse events, demographic data and information on medications and supplements used.

According to this information, the FDA adverse event reporting system contained 12 US cases that mention noni juice or a noni supplement. None of the cases reports liver injury. In ten of the cases noni is described only as "concomitant" and in one case noni juice is described as "secondary suspect" along with medications taken.

The one case in which noni juice (from a different manufacturer) was described as primary suspect "drug" involved a patient treated with levetiracetam (an anti-epileptic drug). The adverse effects reported were convulsions and drug interaction.

XI. Nutritional information on the NF

The composition of TNJ® in terms of macronutrients, vitamins and minerals is comparable to the ranges known for other fruit juices. According to the SCF (2002), the compositional information

available does not indicate any detrimental effect arising from the consumption of the juice. For some of the constituents listed in Table 1, the contents provided for noni puree are outside the ranges given for TNJ®. However, the deviations are not considered nutritionally relevant by the Panel.

For noni concentrate the production process results in slight shifts of the proportions of constituents. According to the data provided in Table 1, the contents of hydrophilic components, such as proteins and carbohydrates are increased and the fat content is reduced. The Panel does not consider the changes reported to be of nutritional concern.

XII. Microbiological information on the NF

Pasteurisation (i.e. thermal inactivation of micro-organisms) and concentration (i.e. reduction of the water activity) are essential steps in the production of *M. citrifolia* puree and concentrate. If Good Agricultural Practices (GAP), Good Hygienic Practices (GHP) and Good Manufacturing Practices (GMP) are applied, the products are to be regarded as microbiologically safe.

XIII. Toxicological information on the NF

Noni puree manufactured according to the procedure described in this application is obtained in the same way as noni fruit puree used as material to produce TNJ®. The puree constitutes the major ingredient and is only blended with minor amounts of other fruit juices to result in TNJ®. Accordingly, the applicant has referred to the studies on acute, subacute and subchronic oral toxicity in rodents as well as studies on genotoxicity and allergenicity (SCF, 2002) and to the data from a safety study with humans (EFSA, 2006) provided for TNJ®.

In a study on developmental toxicity noni fruit puree was administered by gastric intubation to groups (n=12) of pregnant Sprague Dawley rats at doses of 1.72, 3.43 and 6.86 g/kg bw from day 0 until day 20 of gestation. A control group received water. On day 20 of gestation, one day before the expected delivery of pups, the dams were killed and their uteri removed for examination. According to the authors, there were no symptoms of toxicity in the pregnant rats. There was no difference between the control and any noni group in the number of live foetuses, resorptions, foetal weight and length, or skeletal abnormalities. No dead foetuses, gross external malformations, or internal organ defects were observed in any group (West et al. 2008).

In a study on possible oestrogenic activity (Müller et al., 2009) an aqueous extract of *Morinda citrifolia* fruits was administered by gavage daily for 3 consecutive days to groups (n = 8-9) of immature female Wistar rats at doses of 7.5, 75 and 750 mg/kg bw/day. One control group received water and an additional group was administered 17-alpha-ethynylestradiol (positive control for oestrogenicity). According to the authors, there were no statistically significant differences in relative uterus weights between the groups treated with the extract and the control group. Possible anti-oestrogenic activity was tested by treatment of three further groups receiving the same doses of fruit extract after treatment with 17-alpha-ethynylestradiol. An additional group was administered tamoxifen after 17-alpha-ethynylestradiol (positive control group for anti-oestrogenicity). There were statistically significant reductions in relative uterus weights at doses of 7.5 and 750 mg/kg which, according to the authors, indicated an anti-oestrogenic activity of the fruit extract. The Panel notes, however, that the differences were small and not dose-related. The fruit extract was also examined in a developmental toxicity study using rats. After administration from day 8 of gestation to day 21 of lactation at doses of 7.5, 75 and 750 mg/kg bw/day (number of animals per group not given), a decrease of 50 % on the parturition index and postimplantation losses index of 74 % differences compared with the control group were reported only at the lowest dose level. The body weight gain of dams exposed to different doses of *M. citrifolia* aqueous extract during pregnancy did not differ to control group. Likewise, the absolute

and relative masses of the liver, kidneys, adrenal glands, ovaries and uterus did not differ among the groups. Furthermore, since the tested fruit extract does not correspond to the products which are the subject of the present application, the Panel does not consider the findings of these studies relevant for the toxicological assessment of noni fruit puree and concentrate.

DISCUSSION

Noni fruit puree manufactured according to the procedure described in this application is the same as the noni fruit material used to produce TNJ®. Noni fruit concentrate is also made directly from noni fruit puree. The compositional data provided demonstrate that the manufacture of noni fruit concentrate results in an increase of the proportions of more hydrophilic components (carbohydrates, sugars, minerals) and in a decrease of the fat content. The Panel considers that the two steps involved in the production of the noni fruit concentrate (removal of the pulp by centrifugation and concentration by evaporation) are not expected to result in qualitative or quantitative compositional changes which might be of toxicological or nutritional relevance.

The applicant drew attention to the fact that for a noni fruit juice concentrate produced by an essentially similar process (in particular, involving mechanical removal of insoluble pulp from the puree and subsequent concentration of the resulting juice by thermal evaporation) substantial equivalence to the existing noni fruit ingredient from Tahiti has been established within the EU (FSA, 2006).

In a previous opinion the Panel considered four case studies (Millonig et al., 2005; Stadlbauer et al., 2005; Yüce et al., 2006) to investigate a possible association between the consumption of noni juice and hepatotoxicity (EFSA, 2006). On the basis of the available toxicological information and against the background of the data provided on consumption of noni juice without the reporting of hepatotoxic effects, the Panel considered it unlikely that consumption of noni juice, at the observed levels of intake, induces adverse liver effects in humans. This would also apply to the anthraquinones potentially present in the commercially produced noni juice. The Panel concluded that there was no convincing evidence for a causal relationship between the acute hepatitis observed in the case studies reported and the consumption of noni juice (EFSA, 2006).

Since then, the Panel has been made aware of five additional case reports on a possible association between the consumption of noni juice and hepatotoxicity (Matrana et al., 2007; Stadlbauer et al., 2008; Evira 2008; Juluri and Vuppulanchi, 2008), and one case report on the consumption of a non-specified noni preparation (López-Cepero Andrada et al., 2007). The Panel noted that in most of the case studies reported the source of the noni product consumed remained unclear. The Panel considers that available data are not sufficient to establish a causal relationship between the consumption of noni juice and hepatoxicity. However the Panel considers that the increasing number of case reports might indicate that some individuals have a particular sensitivity for hepatotoxic effects to noni fruit products.

Considering the broad spectrum of "noni juices" world-wide on the market, it becomes increasingly important to determine whether a product is in accordance with the specifications as described by the Scientific Committee on Food in its opinion on Tahitian Noni® juice (SCF, 2002).

CONCLUSIONS

The Panel concludes that '*Morinda citrifolia* (Noni) fruit puree and concentrate as novel food ingredients under the specified conditions are considered safe for the general population.

However the Panel considers that the increasing number of case reports might indicate that some individuals have a particular sensitivity for hepatotoxic effects to noni fruit products.

DOCUMENTATION PROVIDED TO EFSA

1. Application under Regulation (EC) N° 258/97 concerning novel foods and novel food ingredients concerning '*Morinda citrifolia* (Noni) fruit puree and concentrate' (Morinda Inc.).
2. Initial assessment report carried out by Belgium:
   Opinion of the Conseil Supérieur d'Hygiène: Initial assessment report concerning an authorization request for *Morinda citrifolia* (NONI): fruit puree and concentrate under Regulation EC 258/97
3. Member States' comments
4. Response to Member States Comments on the Belgian Assessment (by the applicant)

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