National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Steviol glycosides in food

Exposure scenarios and health effect assessment

RIVM Letter Report 350121001/2011
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Colofon

M.J. Tijhuis
D. Wapperom
G. Wolterink
C.H.M. van Oosterhout
E.H.M. Temme
J.D. van Klaveren
H. Verhagen
H.P. Fransen

Contact:
Heidi Fransen
CVG
heidi.fransen@rivm.nl

This investigation has been performed by order and for the account of the Dutch Food and Consumer Product Safety Authority, within the framework of 9.4.20 'sweeteners'

Abstract

Steviol glycosides in food: exposure scenarios and health effect assessment

Market introduction of products sweetened with steviol glycosides (extracts from the Stevia plant), as recently authorized by the European Committee, is not likely to create a serious health problem in the Netherlands. However, extreme consumers of products sweetened with steviol glycosides may exceed the acceptable daily intake (ADI).

The potential future exposure of children in the Netherlands to steviol glycosides is explored by means of scenarios. These comprised observational intake data from the DNFCS-young children (aged 2 to 6 years), the EC list of food products that are authorized to contain steviol glycosides and the maximum permitted levels for these products. Besides a worst case scenario, a 10% market share scenario was calculated. In this scenario, dietary exposure to steviol glycosides in children aged 2 to 6 years was 1.7 mg/kg bodyweight per day at the 95th percentile (expressed as steviol equivalents) and the ADI (4 mg/kg bodyweight per day) was exceeded by 0.3% of the children. The most important contributors to exposure to steviol glycosides in children were water-based flavoured drinks.

From a literature study on health effects it was concluded that little data exist on interactive effects of sweeteners, but from what is available interactive adverse effects are not expected.

It is advised to monitor exposure to all sweeteners, so that potential problems in the future can be foreseen and acted upon.

Keywords:
stevia, steviol glycosides, sweetener, food, exposure, scenario, health effect

Rapport in het kort

Steviol glycosiden in voedingsmiddelen: blootstellingsscenarios en beoordeling van gezondheidseffecten

Het gebruik van steviol glycosiden (extracten van de Stevia plant) als zoetstof in voedingsmiddelen is recent goedgekeurd door de Europese Commissie. De marktintroductie van deze producten zal waarschijnlijk niet leiden tot een gezondheidsprobleem in Nederland. Echter, extreme gebruikers van producten die gezoet worden met steviol glycosides zouden de ADI kunnen overschrijden.

De potentiële toekomstige blootstelling van Nederlandse kinderen aan steviol glycosides is bekeken met behulp van scenarios. Hiervoor zijn consumptiedata uit de VCP-jonge kinderen (van 2 tot 6 jaar), de EC lijst met maximaal toegestane hoeveelheden en de producten waarin stevia is toegestaan gebruikt. Naast een 'worst case' scenario zijn ook scenarios met marktaandelen berekend. Bij het 10% marktaandeel scenario was de blootstelling van kinderen aan steviol glycosiden 1.7 mg/kg lichaamsgewicht per dag op het 95^{e} percentiel en de ADI van 4 mg/kg lichaamsgewicht per dag werd overschreden door 0.3% van de kinderen. Limonades en frisdranken droegen het meest bij aan de blootstelling.

Uit een literatuurstudie naar de gezondheidseffecten van steviol glycosiden werd geconcludeerd dat er weinig informatie beschikbaar is over effecten die optreden in combinatie met andere zoetstoffen. Echter, op basis van de aanwezige informatie worden geen nadelige effecten verwacht.

Monitoring van de blootstelling aan zoetstoffen wordt geadviseerd, zodat potentiële problemen in de toekomst tijdig gesignaleerd en voorkomen kunnen worden.

Trefwoorden: stevia, steviol glycosiden, zoetstof, voeding, scenario

Contents

List of abbreviations

ADI	Acceptable Daily Intake
ANS panel	Panel on Food Additives and Nutrient Sources Added to Food
bw	body weight
DNFCS	Dutch National Food Consumption Survey
EC	European Commission
EFSA	European Food Safety Authority
EXPOCHI	Individual food consumption data and exposure assessment studies for children
GRAS	Generally Recognized As Safe
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD50	median Lethal Dose for 50% of subjects
MPL	Maximum Permitted Level
NEVO	Nederlands Voedingsstoffenbestand
NOAEL	No Observed Adverse Effect Level

1 Introduction

1.1 Background

The quest for sugar-replacers, driven by the obesity epidemic, is expanding. Policy makers support the development of new energy-reduced products. Consumers to whom "naturalness" appeals are forming an increasingly large segment. These developments are likely to have resulted in the increased attention for 'Stevia-based' sweeteners, which are allowed in the European supermarkets as of December 2011. This letter report deals with this new exposure and its possible health consequence for the Dutch population.

The source of these sweeteners is the plant *Stevia rebaudiana* Bertoni, which occurs naturally in South America. Legally, two uses of stevia are distinguished:
1) use of stevia in the form of the plant, dried leaves and crude extracts, which are considered novel foods and fall under EC Regulation 258/97.
In 2000, the placing on the market of *Stevia rebaudiana* Bertoni plants and dried leaves as a novel food or novel food ingredient under EC Regulation 258/97 of the European Parliament and of the Council was refused (EG, 2000).
Use in this form is not the topic of this letter report.
2) use of stevia in the form of purified extracts from the plant. These extracts, steviol glycosides, exhibit enormous sweetness, about 200-300 times more than regular sugar. The major types of steviol glycosides are stevioside and rebaudioside A. Steviol glycosides have been proposed to be used as food additives and as such fall under EC Regulation 1333/2008.

Until recently, the use of steviol glycosides as a food additive was not allowed in the EU as the toxicological data were considered to be insufficient to assess their safety. In 2007 and 2008 three applicants requested the authorization of steviol glycosides for use as sweetener. In 2010 and early 2011, EFSA performed a safety evaluation and exposure assessment (EFSA, 2010) and a second, revised, exposure assessment (EFSA, 2011). Hereafter, the Commission drafted a proposal amending annex II of Regulation 1333/2008 (a list of food additives approved for use in foods and their conditions of use) by adding steviol glycosides as additive E960 (EC, 2011). Formal adoption of the regulation by the Commission was given on November 11th 2011, marked by its publication in the Official Journal of the European Communities (EC, 2011). Taking into account a 20-day period for the regulation to enter into force, foods sweetened with steviol glycosides could be sold on the market from December 2nd 2011 on.

Besides the major forms stevioside and rebaudioside A, there are other forms of steviol glycosides that exist in small amounts. The EFSA opinion and EC authorization procedure deal with a total of 7 steviol glycosides, expressed as steviol equivalents, of at least 95% purity (as specified by JECFA (2008)). The steviol glycosides produced by the three applicants that were mentioned before are comprised of 95% or more stevioside and/or rebaudioside A.

1.2 Aim

The official adoption of the use of steviol glycosides in foods will change the exposure of the Dutch population to stevioside and rebaudioside A. In order to anticipate on what is coming, an exposure assessment for the Dutch situation is warranted. The aim of the current letter report is to assess the potential consequences in terms of exposure and effects, based on the currently available knowledge. This investigation has been performed within the framework of question 9.4.20 of the Dutch Food and Consumer Safety Authority.

1.3 Approach and outline

The food products that are authorized to contain steviol glycosides are described in EU legislation and this is the basis for our exposure assessment for the Netherlands. We will start with a worst case approach and continue with more realistic scenarios based on market predictions available from the United States. The outcome of the exposure calculations will be compared with the ADI. The available data on possible health effects will also be considered, including the potential interactive effects when steviol glycosides are used in combination with other sweeteners and nutrients.

In the following chapters we will first describe the historical and currently authorised use of stevia as a sweetener (chapter 2). In chapter 3 the exposure assessment is described and chapter 4 contains the health effect assessment. The findings will be discussed and placed into context in chapter 5. We end with conclusions and recommendations in chapter 6.

2 Stevia: historical and currently EC-authorized use

2.1 Historical perspective

The original place of growth of the *Stevia rebaudiana* Bertoni plant is Paraguay. The plant has a history of use in several South American countries to sweeten a.o. medicines and tea. The plant was first described in detail in 1899, but it was not untill 1931 that the origin of the sweet taste, the steviol glycosides, were isolated (Bridel and Lavielle, 1931).

2.2 Proposed use of steviol glysosides & evaluation by EFSA

In the EU, attention for steviol glycosides as sweeteners was renewed in 2007 and 2008 by applications to EFSA from three petitioners. Two applied for use as a sweetener in foodstuffs such as drinks, desserts, yoghurts, confectionary, cakes, biscuits and pastries, sauces, toppings, spread, cereals, canned fruits and jams. The other petitioner applied for uses and use-levels reflecting basically the current authorisation of aspartame under the Directive 94/35/EC (EFSA, 2010).

Steviol glycosides have been the subject of safety evaluations by SCF and JECFA since the 1980's. For a while the available data was judged to be insufficient to assess their safety. In 2004 JECFA established a temporary ADI of 2 mg/kg bw per day (expressed as steviol equivalents), which was revised to 4 mg/kg bw per day (expressed as steviol equivalents) in 2009 (JECFA, 2009) and confirmed by EFSA in 2010 (EFSA, 2010).

To investigate if consumers were likely to be exposed to steviol glycosides above the ADI, EFSA perfomed an exposure assessment (EFSA, 2010). In the assessment, maximum permitted use levels (MPLs) as proposed by the three petitioners were used in all proposed products (or product groups) for the exposure calculations. It was concluded that under these worst-case scenarios the ADI was likely to be exceeded by both children and adults.

Based on these results, the European Commission proposed revised MPLs and EFSA performed a revised exposure assessment (EFSA, 2011). Use levels were removed (for 15 categories, mostly 'desserts and similar products'), reduced (for 16 categories, by a factor 1.5-3), unchanged (for 12 categories), or newly included (3 categories).

After the second exposure assessment, the ADI was still likely to be exceeded in adults and children, but to a lower extent than in the first exposure assessment. The main contributors to steviol glycoside exposure were non-alcoholic flavoured drinks, in both children and adults.

2.3 EC authorized use of steviol glycosides

EC specifically recognized that despite revised uses, the conclusion of the revised exposure assessment remained the same, namely that for high-level consumers (both adults and children), the ADI can be exceeded. As the main contributors to the total anticipated exposure are the non-alcoholic flavoured drinks, EC requested a final adjustment in this group before authorization: to lower the maximum permitted level from 198-240 mg/l steviol equivalents to 80 mg/l steviol equivalents.

However, other differences exist between the included products in the revised exposure assessment by EFSA (EFSA, 2011) and the final EC Regulation 1131/2011 (EC, 2011):

- Dilutables (syrups) are now included (in the category 'Flavoured drinks').
- The group 'Smoked, dried, fried, fermented, and/or salted fish and fish products including molluscs, crustaceans, and echinoderms' was excluded.
- Furthermore, the following new food categories were added in the regulation:
  - Decorations, coatings and fillings;
  - Other confectionery, including breath refreshening microsweets: only cocoa, milk, dried fruit or fat based sandwich spreads, energy-reduced or with no added sugar;
  - Fine bakery wares (only essoblaten - wafer paper);
  - Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products;
  - Potato-, cereal-, flour- or starch-based snacks;
  - Processed nuts;
  - Desserts excluding products covered in category 1, 3 and 4: only energy-reduced or with no added sugar.

In the regulation (EC, 2011) it was stated that the actual use of steviol glycosides will be monitored. If deemed necessary, EFSA will be asked to perfom a new refined exposure assessment that takes the real use into account.

2.4 Use of steviol glycosides before EC authorization

Products containing rebaudioside A and stevioside were on the market in the Netherlands before the current authorization. They were available through the internet and via reform houses, under the notion that they were 'for external use only'.

Worldwide, use of steviol glycosides is authorized in among others: Japan (where it has been the main non-sucrose sweetener for over 40 years), China, Russia, South Korea, Brazil, Paraguay, Argentina, Indonesia, Slovakia, Mexico, Senegal, Thailand, Israel, Australia & New Zealand, United States, and Switzerland (for some recipes) (Geuns, 2010). Examples of products that include steviol glycosides are: soft drinks, dairy drinks, yoghurt, chewing gum, and tabletop sweeteners.

Although the Asian stevia market is large and has a long history, recent experience in the United States may be more relevant for the European situation. In December 2008, the US FDA approved the use of rebaudioside A in US food and beverages by granting it GRAS status. In the first eight months of 2009, Mintel's Global New Products Database (GNPD) monitored the launch of more than 110 US food, drink and healthcare products made with stevia (http://www.mintel.com/press-centre/press-releases/397/stevia-market-to-break-100-million-this-year). A succesfull introduction was the Tropicana Trop50® drink with sugar and stevia as sweeteners. Another product is for example a yoghurt sweetened with stevia and sugar.

In France, the use of highly purified rebaudioside A has been evaluated and authorized since August 2009 under a two year window in advance of full EU approval (AFFSA, 2009; France, 2009, 2010). Therefore, some products have already been available on the French market for the past 2 years, such as soft drinks and syrups.

For the development of products containing stevia extracts, large companies have started working together with smaller companies. For example, an alliance was formed between PepsiCo and Whole Earth Sweetener Company (a subsidiary of Merisant), specializing in 'Pure Via™' stevia products (http://www.purevia.com/Purevia/). Also, an alliance was formed between the Coca Cola Company and Cargill, a food and beverage innovater that has developed the sweetener Truvia® and products containing it (http://www.cargill.com/food/na/en/products/sweeteners/specialty-sweeteners/truvia/). The sweetener is used in for example soft drinks, juices,

water, ice cream and chocolate. In France this alliance has led to the production of a type of Fanta containing rebaudioside A.

2.5 Expected market consequence of EC authorization

Market and consumer intelligence provider Mintel predicted as a core trend for 2011 that sugar and stevia will be used in conjunction to achieve an overall lower sugar content in new products.

Leatherhead Food Research states that rebaudioside A accounts for 21% of the total US intense sweetener market in their market report "The global market for intense sweeteners" (April 2010). The US grew to a share of 85% of the global stevia market just 16 months after FDA approval. Globally, the share of stevia to the intense sweetener market went to 14%, coming from 1% in 2007 http://www.foodnavigator-usa.com/Business/Natural-sweeteners-could-take-a-quarter-of-market-share-Report. According to the report "Sugar, Sugar Substitute, and Sweetener Trends in the U.S." (September 2011) by Packaged Facts, stevia's share in the total sugars and sweeteners market is thought to rise from 1.8% in 2010 to 9.1% in 2011. The report states that stevia use is also expected to explode in Europe after approval (http://www.foodnavigator-usa.com/Market/Stevia-market-share-to-explode-in-2011-says-report).

The considerations on market development mentioned above are taken into account in the scenario development in the next chapter. These numbers reflect the market shares for steviol glycosides as a commodity. Further on in our exposure assessment, however, for practical reasons we will use them as the percentage of consumptions per product group that is sweetened with steviol glycosides.

2.6 Use of steviol glycosides in combination with other sweeteners

Steviol glycosides are mainly combined with sugar, not other intense sweeteners. In products containing more than 8% sugar (i.e. 8 g/100 g), such as soft drinks with sugar, steviol glycosides can reduce the amount of sugar with 30-50%. A potential full replacement of sugar is possible in products with less than 5% sugar. The higher the stevia dosage, the more need for taste modifiers, because of bitterness and lingering of taste at high dosages. Also, in certain products bulking substitutes need to be used, as stevia itself cannot provide bulking. By only replacing part of the sugar the need for taste modification and bulking substitution is limited. These developments offer the opportunity for a new line of products. Coca-cola® for example introduced Fanta Still® in France,

which is sweetened with steviol glycosides and 7% sugar. In this way the company can label their product with both the addition of stevia extracts and a 30% less sugar claim. Cost and supply aspects are not a reason to refrain from the use of steviol glycosides (VMT, 2011).

3 Exposure assessment by means of scenarios

3.1 Rationale and basic approach for new exposure assessment

The reason for this exposure assessment is twofold:

1) An exposure assessment specific to the situation in the Netherlands is lacking; Here we use data from the Dutch National Food Consumption Survey, containing Dutch products.
2) The exposure assessment performed by EFSA was extremely worst case. We are able to refine the exposure assessment by 1) using more detailled food codes and thus create more realistic product groups, excluding products that will not contain stevia; and 2) using different scenarios, going from a worst case scenario with full substitution of all products containing sugar or other sweeteners to scenarios using a substitution of 25% or 10% of the products.

3.2 Methods

Consumption data

We used the Dutch National Food Consumption Survey (DNFCS)-Young Children 2005/2006 (Ocké et al., 2008), which contains detailed information on the food consumption of 1,279 children in the age of 2 to 6 years. Parents (or caretakers) of the children were selected from representative consumer panels. Survey data was collected by means of a written general questionnaire and through two-day food records. Dieticians entered the data from the diaries into the EPIC-Soft computer program (Slimani et al., 2000).

Linking of consumption data and EC maximum levels of use

From the food consumption data, products were selected that
1) are sweetened with either sugar or an artificial sweetener at this moment and
2) fall into a food group in which steviol glycosides will be allowed, as indicated by the EC-list with maximum permitted use levels (see appendix A).
The selection was based on EPIC Soft food groups that contain products from the EC list and detailed food codes (NEVO, 2006) in these groups (see appendix B). Products that cannot or will not contain steviol glycosides, because it is not allowed or the product does not contain sugar/sweetener, were excluded (see appendix B). The selected NEVO codes were linked to the EC categories with maximum levels.

Some assumptions were made in the selection and linking process:

- for all non-diluted syrups, a dilution of 1:6 was assumed;
- the NEVO codes for prepared tea and prepared coffee include sugar. It was assumed that in each cup of 125 g one lump of sugar was used (5 g), this quantity was divided by 200 to take the relative sweetness of stevia into account and be able to link this quantity to the maximum level for stevia-based table top sweeteners;
- no distinction was made between several similar groups with the same maximum use levels: the groups 'Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EC', 'Extra jam and extra jelly as defined by Directive 2001/113/EC' and 'Other similar fruit or vegetable spreads (only dried-fruit based sandwich spreads)' were combined, the groups 'Cocoa and chocolate products as covered by Directive 2000/35/EC' and 'Other confectionery (only cocoa or dried fruit based)' were combined; and the groups 'Tabletop sweeteners in liquid form', 'Tabletop sweeteners in powder form' and 'Tabletop sweeteners in tablets' were combined;
- the consumed quantity of granulated sugar (NEVO code 377) was divided by 200 to link it to the maximum level for table top sweeteners, other table top sweeteners were linked 1:1.

Also, one product was not used in the DNFCS-young children ('Fine bakery wares: essoblaten') and one category was excluded because the necessary information was not readily available from the survey ('Decorations, coating and fillings').

Exposure calculations

The dietary exposure to steviol glycosides was estimated using the observed individual mean (OIM) method as implemented in version 7.0 of the Monte Carlo Risk Asessement (MCRA) programme (de Boer and van der Voet, 2007).
In short, based on the two-day food records of 1,279 children from the survey, all relevant consumed foods (selected NEVO codes) were multiplied with the maximum permitted level of steviol glycosides in their food group and summed over food groups per day per individual. This way, per consumption day (N=2,558), the amount of steviol glycoside that is consumed scenario-wise was calculated. This amount was divided by the individuals' body weight in kg.

A more refined usual intake modelling approach by using the BBN[1] (betabinomial-normal)-module was tested. However, this approach could not be applied because the data did not show a lognormal distribution after transformation.

Scenarios

We used three different scenarios, varying from worst-case (scenario 1) to more realistic (scenario 2 and 3).

- Scenario 1: "worst-case". In this scenario it is assumed that all selected foods contain steviol glycosides, at the maximum permitted level.
- Scenario 2 and 3: "market share scenarios". The market share prediction was based on developments in the US intense sweetener market, where stevia's share in the total sugars and sweeteners market is thought to have risen to 10% at the end of 2011 (see paragraph 2.5). We here take account of 2 market shares: 10% and 25%, the latter taking into account that the market share in the EU may be different and/or may increase in time.
  - Scenario 2: "market share 25%". Consumption amounts were linked randomly with stevia containing or non-stevia containing foods, with probabilities proportional to market shares of 25%.
  - Scenario 3: "market share 10%". Consumption amounts were linked randomly with stevia containing or non-stevia containing foods, with probabilities proportional to market shares of 10%.

In scenario 2 and 3, 100% brand loyality for all food groups was assumed. This means that when the consumption of one person from a food group is linked to a steviol glycosides containing product, it was assumed that all other consumed products that may contain steviol glycosides within this food group, will contain steviol glycosides. The same applied for non-steviol glycosides consumed products.

The uncertainty in the intake assessments was quantified using the bootstrap approach (generating 100 food consumption and 100 concentration bootstrap samples). The resulting 95% confidence interval around the different percentiles

[1] Usually, for substances exerting a chronic toxic effect, the usual intake is calculated. For long-term exposure the within-person variation (the variation between the exposure on the two days of one individual) should be subtracted from the total variation in the calculated exposures. The within-person is of no relevance when estimating the long-term exposure, as, in the long run the variation in exposure between different days of one individual will level out. To this aim the betabinomial-normal model (BBN) can be used, but only in case that the transformed intake distribution is a normal distribution.

of exposure indicates the degree of uncertainty (Efron, 1979; Efron and Tibshirani, 1993).

3.3 Results

Dietary intake, as categorized according to the EC food groups, is shown in Table 2. It can be seen that contribution to total intake is highest for the flavoured drinks, most notably water-based. Flavoured drinks were also consumed most often, e.g. water-based flavoured drinks were consumed on 84% of the consumption days. The lowest number of consumption days was found for a.o. breakfast cereals. Children in the DNFCS-young children did consume breakfast cereals, but only two of them were included in the EC categories and could therefore contain steviol glycosides.

Table 1 lists the percentiles of dietary exposure to steviol glycosides in children. In scenario 1 ("worst case") median exposure (p50) of the population is lower than the ADI of 4.0 mg/ kg bw/ day. However, almost 40% of the population exceeds this value. Exposure at the 99th percentile is over two times higher than the ADI.

In scenario 2 ("market share 25%") and 3 ("market share 10%"), the highest relative decrease in exposure is observed at the 50th percentile. Median exposure is 7 times lower in scenario 2 and decreases to zero in scenario 3 compared to scenario 1 ("worst-case"). In the highest percentiles, exposure estimates decrease on average with a factor 2 (scenario 2) and 2.5 (scenario 3) compared to the results of scenario 1. In scenario 3, 0.3% of the population exceeds the ADI. This percentage increases to 2.6% in the scenario 3.

Table 1 Dietary exposure to steviol glycosides (in mg/kg bw/day, as steviol equivalents) in children aged 2 to 6 years in the Netherlands for three scenarios*

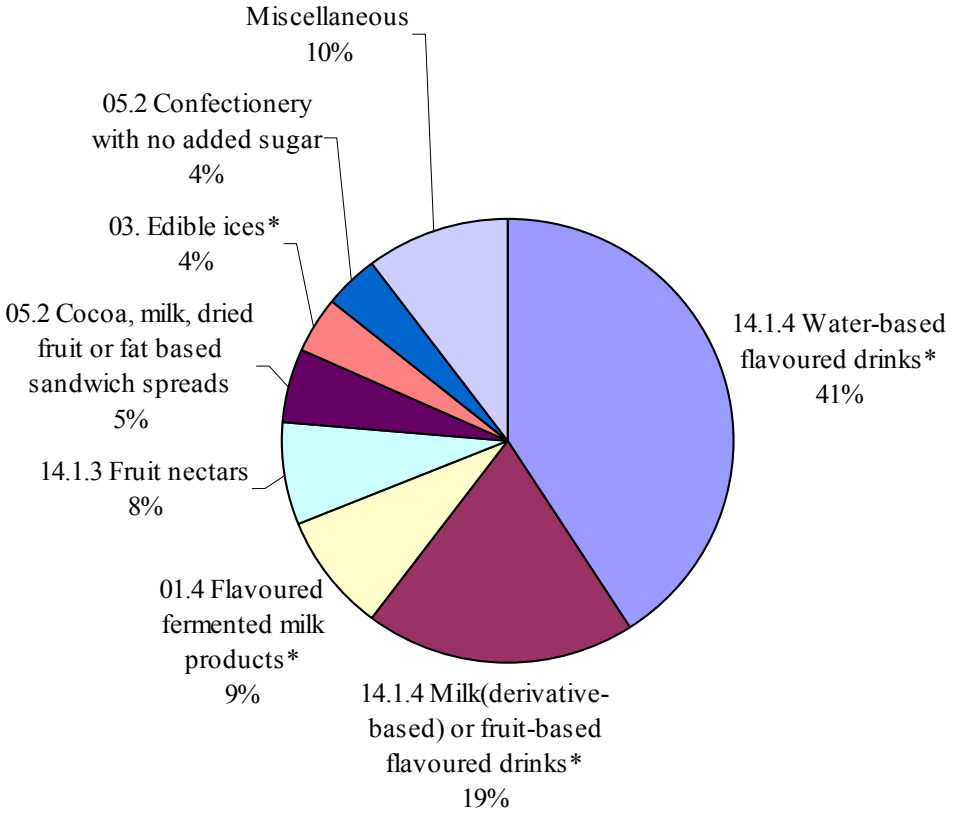
Percentile	Scenario 1 "Worst-case"	Scenario 2 "Market share 25%"	Scenario 3 "Market share 10%"
50	3.4 (3.3-3.5)	0.5 (0.4-0.5)	0.0 (0.0-0.0)
95	6.6 (6.3-7.0)	3.2 (3.0-3.6)	1.7 (1.7-2.1)
97.5	7.7 (7.2-8.4)	4.1 (3.6-4.5)	2.3 (2.3-3.0)
99	9.3 (8.5-11.3)	5.6 (4.5-5.5)	3.2 (3.0-4.2)
% exceeding ADI	37.5 (35.0-40.0)	2.6 (1.8-3.8)	0.3 (0.3-1.3)

* Point estimate is based on actual data; data between brackets represent the 95% confidence interval around the percentiles of exposure, based on the bootstrap method.

Table 2 Dietary intake of products containing steviol glycosides (according to the EC food groups categories) in children aged 2 to 6 years in the Netherlands

		Consumption		
EC-category number	EC group	Mean* (g)	P95 (g)	Days (%)
01.4	Flavoured fermented milk products including heat treated products.	55	206	46
03.	Edible ices	13	70	21
04.2.2	Fruit and vegetables in vinegar, oil, or brine (only sweet-sour preserves of fruit and vegetables)	1	0	3
04.2.4.1	Fruit and vegetable preparations excluding compote	10	57	15
04.2.5.2	Jams, jellies, and marmalades and sweetened chest nut puree	2	13	9
05.2	Other confectionery including breath refreshening microsweets (cocoa, milk, dried fruit or fat based sandwich spreads)	10	40	49
05.2	Other confectionery including breath refreshening microsweets	7	30	46
05.2	Other confectionery including breath refreshening microsweets (cocoa- or dried-fruit-based)	4	21	26
05.3	Chewing gum	0	0	4
06.3	Breakfast cereals	0	0	0
11.4.1/2/3	Tabletop sweeteners (liquid, powder and tablets)	0	0	19
12.5	Soups and broths	7	0	5
12.6	Sauces (except soybean sauce)	6	37	32
12.6	Soybean sauce	0	0	4
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal	0	0	0
14.1.4	Flavoured drinks (water-based)	330	881	84
14.1.4	Flavoured drinks (milk(-derivative) or fruit juice-based)	159	573	52
14.1.4	Flavoured drinks (soy-based)	5	0	2
14.1.3	Fruit nectars and vegetable nectars and similar products	50	300	19
15.1	Potato-, cereal-, flour- or starch-based snacks	4	25	19
15.2	Processed nuts	0	0	1
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms	0	1	28
17.2	Food supplements supplied in a liquid form	0	0	15
	Sugar	2	12	22

*Mean of 2 days for total population



*energy reduced or with no added sugar.

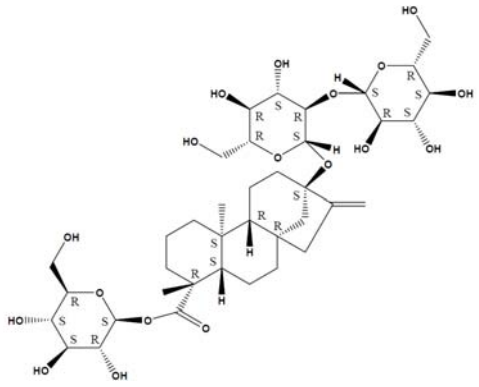
Figure 1 Main contributors of total dietary exposure of steviol glycosides in children aged 2 to 6 years in the Netherlands (Scenario 1).

The most important contributors to steviol glycoside exposure in children in the worst-case scenario are shown in Figure 1. Water-based flavoured drinks contributed to more than 40% of the total exposure. Other important contributors were milk(-derivative) or fruit juice-based flavoured drinks (19%), flavoured fermented milk products including heat treated products (9%), and fruit or vegetable nectars and similar products (8%). In the two other scenarios similar results were observed.

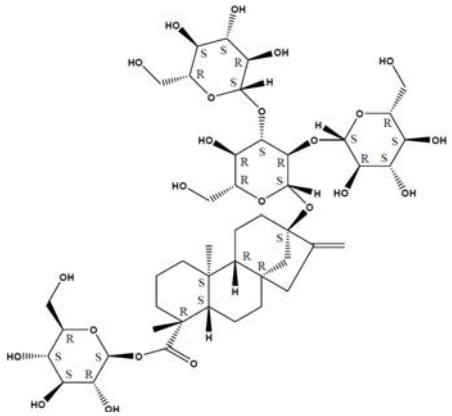
4 Health effects assessment

The toxicology of steviol glycosides has been evaluated by the Scientific Committee on Food (SCF, 1984, 1989, 1999), JECFA (JECFA, 2000, 2005a, b, 2007, 2008, 2009) and EFSA (EFSA, 2010). The following summary of the toxicology of steviol glycosides is predominantly based on the EFSA evaluation.

Steviol glycosides are natural constituents of the plant *Stevia rebaudiana* Bertoni. The steviol glycosides that are used as sweeteners are mixtures that contain predominantly stevioside and/or rebaudioside A. The structures of stevioside and rebaudioside are depicted in Figure 2.



Stevioside



Rebaudioside A

Figure 2 Molecule structures of stevioside and rebaudioside A

4.1 Toxicokinetics

Toxicokinetic studies with stevioside and rebaudioside A in animals and humans have shown that after oral administration these compounds are poorly absorbed from the gastrointestinal tract. However, the steviol glycosides are hydrolysed by the microflora in the colon. The resulting metabolite steviol is subsequently absorbed to a large extent; the remainder is excreted in the faeces. The absorbed steviol is conjugated with glucuronic acid to form steviol glucuronide. In humans the glucuronide is excreted primarily via the urine (whereas in rats the primary route of excretion is the bile). Apart from steviol glucuronide, no other steviol metabolites could be detected in the urine of humans.

4.2 Toxicology

Rebaudioside A and stevioside show similar toxicokinetics and metabolism in humans (and rats). Therefore, EFSA and JECFA concluded that the results of toxicological studies on either stevioside or rebaudioside A could be used for the risk assessment of steviol glycosides.

The acute toxicity of stevioside is low. Acute oral toxicity studies in mice, rats and hamsters indicated an LD50 of >15 g/kg bw.

Steviol glycosides have been tested in subchronic studies in rats at doses up to 50000 mg/kg feed, equivalent to 2500 mg/kg bw/day, and in a chronic carcinogenicity study at doses up to 25000 mg/kg feed, equal to 967 mg/kg bw/day. In subchronic and carcinogenicity studies no adverse effects of stevioside and rebaudioside A were found. Also, there are no indications for a carcinogenic effect of these compounds. In some of these studies, and also in the 2-generation reproductive toxicity study, reduced body weight gains, accompanied by decreased feed consumption and feed conversion efficiency were observed in the treatment groups. EFSA considered that the effects on body weight were related to lower palatability and lower nutritional value of feed containing the steviol glycosides and were not considered adverse. Stevioside and rebaudioside A were tested in a range of genotoxicity tests. Evidence of their genotoxicity, in vitro or in vivo, was not found (EFSA, 2010).

4.3 ADI

The results of studies on the reproductive and developmental effects of steviol glycosides showed no adverse effects. The NOAEL in the 2-year carcinogenicity study in the rat was 2.5% stevioside (95.6% purity) equal to 967 mg stevioside/kg bw/day (corresponding to approximately 388 mg steviol

equivalents/kg bw/day). This was the highest dose tested. Both JECFA and EFSA established an ADI of 4 mg/kg bw/day, expressed in steviol equivalents, on the basis of this NOAEL of 967 mg stevioside/kg bw/day using a 100-fold uncertainty factor.

4.4 Health effect studies in humans

Several studies with steviol glycosides have been performed in humans. In acute or repeated dose studies with stevioside or rebaudioside no effects on glucose homeostasis were observed in individuals with normal glucose tolerance or type-1 or type-2 diabetes mellitus and no effects on blood pressure were observed in normotensive and hypotensive individuals (Barriocanal et al., 2008; Maki et al., 2008a; Maki et al., 2008b).

Some in vitro and in vivo studies suggest that stevioside may have immunostimulating effects and modulatory activities on inflammation. However, EFSA (EFSA, 2010) considered that these effects had not been demonstrated in a robust and reproducible way, but that the effects of steviol glycosides on the immune system deserve more in depth examination. Should the immune-stimulating effects of steviosides be confirmed, they may raise concern regarding the use of steviosides in some sub-groups of the population, particularly for individuals suffering from auto-immune diseases or inflammation of the gastrointestinal tract.

4.5 Interactions

As part of the present evaluation, we searched PubMed and other sources for evidence of (the lack of) interactions between steviol glycosides and nutrients, vitamins, drugs and other food components, in particular other sweeteners. We used (combinations of) the search terms *stevia, steviol, rebaudioside* and nutrient, vitamin, sweetener, saccharin, cyclamate, aspartame, sucralose, acesulfame K, drug, pharmaceutical, medicin. The search yielded very little useful information.

Incubation of stevioside with individual water soluble B vitamins and vitamin C was reported not to change the levels of these nutrients (Kroyer, 1999). The stability of the sweeteners in aqueous solutions of stevioside with other individual low-calorie sweeteners, i.e. saccharin, cyclamate, aspartame, acesulfame and neohesperidin dihydrochalcone, was investigated. No interactions between individual sweeteners were found in the course of thermal treatment at 80ºC for up to 4 hours as well as for over 4 months of incubation at room temperature (Kroyer, 1999). No specific information on the interaction

with nutrients and vitamins *in vivo* is available. In some repeated dose studies in animals with high doses of steviosides decreases in body weight gain were observed. However, this was considered to be a result of poor palatability and lower nutritional value of the feed, rather than to a specific effect of steviosides.

Overall, there is little information on the interaction of steviosides with nutrients, vitamins and other sweeteners. There is no indication that adverse effects may occur when steviosides are administered in combination with other sweeteners (EFSA, 2010).

4.6 Beneficial effects

It is expected that the substitution of sugars in food with steviol glycosides will result in a reduced caloric intake in humans. As such it may help to counteract the current obesity epidemic in the western world. The current scientific literature gives no indication that the intake of steviol glycosides as a result of its use as a food additive has any other effect that could be considered beneficial in humans.

4.7 Reported side effects

An internet search yielded some information on reported side effects of the use of stevia (WebMD, 2011). People using stevia have reported bloating or nausea, dizziness, muscle pain and numbness via internetsites. However, the reliability of these reports is not clear.

5 Discussion

Our exposure scenarios show intakes at the 95th percentile ranging from 1.7 to 6.6 mg steviol glycosides (expressed as steviol equivalents) per kg bw/day between the different scenarios. The ADI for steviol glycosides is 4 mg steviol glycosides (expressed as steviol equivalents) per kg bw/day.

These results are in line with the results of a study by Renwick *et al*. (Renwick, 2008) which found an exposure of 1.7 mg/kg bw/day for high consumer children (p90-p97.5). In that study, exposure to steviol glycosides was based on observed exposure for aspartame derived from national individual intake surveys. The calculation method assumes that steviol glycosides will be used in a comparable pattern and to a comparable extent as the existing sweeteners.

Compared to the results of the exposure assessments performed by EFSA (EFSA, 2010, 2011), our calculations result in lower exposures. Our approach for the exposure assessment was different from the approach used by the EFSA ANS panel. The first difference is that we specifically look at the situation in the Netherlands and thus only use data from the Dutch National Food Consumption Survey. The second difference is that the ANS panel used the EXPOCHI food classification and we use a more detailed classification. We started with a wide classification in food groups like 'dairy products' and 'soups', based on the EPIC-Soft classification that is also used in the DNFCS (Ocké et al., 2008). After this first selection, we used the detailed NEVO codes (NEVO, 2006). Using these codes we were able to exclude products that are not sweetened by sugar or sweetener at this moment, e.g. plain yoghurt and milk, assuming that these products will not be sweetened with steviol glycosides in the future. Only products that are now sweetened with sugar or sweetener are included for the analysis.

After their first exposure assessment (EFSA, 2010), EFSA requested the removal of certain categories proposed for use. Removal and recalculation did not dramatically improve the outcome of the exposure assessment (EFSA, 2011). The Regulation (EC, 2011) names under point 3: "Despite the revised uses, the conclusion was very similar, namely that both in adults and children the ADI can be exceeded for high level consumers". However, in the regulation, categories emerged that were not in EFSA's revised exposure assessment. It is not clear how the final categories and MPLs were decided upon.

Of special relevance in this letter report, for the children, are the dilutable drinks. These were not intented to be included in the EFSA exposure assessment, but the EXPOCHI data did not allow separation between dilutables and other drinks. Despite the exclusion of dilutables in the water-based flavoured drinks category by EFSA, they do appear in EU legislation.

In our report, results of usual intake calculations, based on the OIM (Observed Individual Mean) method were presented. The mean value for an individual still contains a considerable amount of within-individual variation. The distribution of observed individual means has a larger variance than the true usual intake. As a consequence, the exposure estimates in the higher percentiles will most likely be overestimated. Further research regarding usual intake modelling is commissioned by EFSA and adressed in the ETUI project (van der Voet and van Klaveren, 2010).

In our study, a 100% brand loyality was used, which can be considered worst case, as people will not always consume the same brand. Also, in the exposure assessment, MPLs were used, as stated in the EC legislation. These MPLs appear to be realistic levels, i.e. using this level will not result in overly sweet products. However, it is likely, that steviol glycosides will be used in combination with other sweeteners, most likely sugar. For example, replacing 30% of sugar by steviol glycosides will result in a product which can be labeled as 'light'. Our market-share scenarios (25%, 10% of consumption moments – tied by brand loyalty) take into account the fact that not all products in which steviol glycosides may be used, will contain steviol glycosides. An additional step would be to take both a market share of less than 100% and the use of steviol glycosides in combination with other sweeteners into account, as in the example of the light soda. In the future, when products sweetened with steviol glycosides are actually on the market, actual consumption levels can be used in exposure calculations.

From our exposure calculations using the different scenarios with market shares of 10%, 25% and 100%, it was seen that the ADI was exceeded by respectively 0.3%, 2.6%, or 32% of the children. In light of the above considerations, i.e. a conservative modeling method and a substitution of all sugar even in the lowest exposure scenario, it is expected that children will not exceed the ADI in the near future. However, should steviol glycosides in the future be added to an increasingly large percentage of products, the ADI may be exceeded. This also applies to other intense sweeteners and therefore, the use of intense sweeters

should be monitored. It may be wise, when using a lot of "light" or "no sugar" products, to use different types of sweeteners to avoid exceeding the ADI for any one, especially since children have lower weights and thus more easily reach the ADI.

The major contributors to steviol glycoside intake in the EFSA exposure assessment were soft drinks. Therefore, the EC demanded a reduction in the use level for flavoured drinks. A group with high consumption of soft drinks in the Netherlands are the young adults. Despite the lowering of the MPL, it is relevant to elaborate about the potential future exposure to steviol glycosides in this group. From the DNFCS-young adults (19-30 years) can be seen that mean consumption of the group 'Carbonated drinks, softdrinks, isotonic drinks and diluted drinks' was 383 ml/day. If all these drinks would be sweetened with Stevia, exposure would be 31 mg (in steviol equivalents). Based on an average adult of 60 kg, this would result in an exposure to steviol glycosides of 0.5 mg/kg bw/day. The 90^{th} percentile of consumption was 983 ml/day, resulting in an exposure of 1.3 mg/kg bw/day. This exposure is still well below the ADI of 4. In the study of Renwick it was also seen that the exposure estimates for children were 1.5 fold higher than those of adults (Renwick, 2008).

6 Conclusions and recommendations

Introduction of products that are sweetened with steviol glycosides at the levels proposed by the EC is not likely to create a serious health problem in the Netherlands. In our 10% market share scenario, a very small percentage of the population exceeded the ADI. This may be reduced to zero percent when
1) more refined methods for measuring usual intake can be used and
2) when actual concentration levels instead of maximum permitted levels will be used. However, there is no actual exposure to steviol glycosides yet and we do not know exactly how industry will use the permitted concentration levels in their products. Therefore, it is advised that both policy makers and industry monitor exposure to sweeteners, so that potential problems in the future can be foreseen and acted upon.

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Appendix A: List of authorized use of steviol equivalents

From: Commission Regulation (EU) NO 1131/2011 of 11 November 2011 amending Annex II to Regulation (EC) No 1333/2008 of the European Parliament and of the Council with regard to steviol glycosides. Official Journal of the European Communities. 12.11.2011, L295/206 - L295/211.

EC category number	EC Group	Maximum level (steviol equivalents, mg/l or mg/kg)	EC restrictions/exception
01.4	Flavoured fermented milk products including heat treated products	100	only energy-reduced products or with no added sugar
03.	Edible ices	200	only energy-reduced or with no added sugar
04.2.2	Fruit and vegetables in vinegar, oil, or brine	100	only sweet-sour preserves of fruit and vegetables
04.2.4.1	Fruit and vegetable preparations excluding compote	200	only energy-reduced
04.2.5.1	Extra jam and extra jelly as defined by Directive 2001/113/EC	200	only energy-reduced jams, jellies and marmalades
04.2.5.2	Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EC	200	only energy-reduced jams, jellies and marmalades
04.2.5.3	Other similar fruit or vegetable spreads	200	only dried-fruit-based sandwich spreads, energy-reduced or with no added sugar
05.1	Cocoa and chocolate products as covered by Directive 2000/36/EC	270	only energy-reduced or with no added sugar
05.2	Other confectionery including breath refreshening microsweets	270	only cocoa or dried fruit based, energy reduced or with no added sugar
	Other confectionery including breath refreshening microsweets	330	only cocoa, milk, dried fruit or fat based sandwich spreads, energy-reduced or with no added sugar
	Other confectionery including breath refreshening	350	only confectionery with no added sugar

	microsweets		
	Other confectionery including breath refreshening microsweets	2000	only breath-freshening micro-sweets, with no added sugar
	Other confectionery including breath refreshening microsweets	670	only strongly flavoured freshening throat pastilles with no added sugar
05.3	Chewing gum	3300	only with no added sugar
05.4	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4	330	only confectionery with no added sugar
	Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.5	270	only cocoa or dried fruit based, energy reduced or with no added sugar
06.3	Breakfast cereals	330	only breakfast cereals with a fibre content of more than 15%, and containing at least 20% bran, energy reduced or with no added sugar
07.2	Fine bakery wares	330	only essoblaten - wafer paper
09.2	Processed fish and fishery products including molluscs and crustaceans	200	only sweet-sour preserves and semi preserves of fish and marinades of fish, crustaceans and molluscs
11.4.1	Table Top Sweeteners in liquid form	QS	
11.4.2	Table Top Sweeteners in powder form	QS	
11.4.3	Table Top Sweeteners in tablets	QS	
12.5	Soups and broths	40	only energy-reduced soups
12.6	Sauces	120	except soy-bean sauce (fermented and non-fermented)
	Sauces	175	only soy-bean sauce (fermented and non-fermented)
13.2	Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)	330	
13.3	Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)	270	

14.1.3	Fruit nectars as defined by Council Directive 2001/112/EC and vegetable nectars and similar products	100	only energy-reduced or with no added sugar
14.1.4	Flavoured drinks	80	only energy-reduced or with no added sugar
14.2.1	Beer and malt beverages	70	only alcohol-free beer or with an alcohol content not exceeding 1,2% vol.; 'Bière de table/Tafelbier/Table beer' (original wort content less than 6%) except for 'Obergäriges Einfachbeer'; beers with a minimum acidity of 30 milli-equivalents expressed as NaOH; Brown beers of the 'oud bruin' type
14.2.8	Other alcoholic drinks including spirits with less than 15% of alcohol and mixtures of alcoholic drinks with non-alcoholic drinks	150	
15.1	Potato-, cereal-, flour- or starch-based snacks	20	
15.2	Processed nuts	20	
16.	Desserts excluding products covered in category 1, 3 and 4	100	only energy-reduced or with no added sugar
17.1	Food supplements supplied in a solid form including capsules and tablets and similar forms	670	
17.2	Food supplements supplied in a liquid form	200	
17.3	Food supplements supplied in a syrup-type or chewable form	1800	

QS = Quantum Satis

Appendix B: List of NEVO-codes in EC food group classification

For dietary supplements, NES-codes are presented (Buurma-Rethans et al., 2008).

01.4 Flavoured fermented milk products including heat treated products

276 Chocolate custard - dairy cream milk
282 Custard vanilla -dairy cream milk
284 No-fat yoghurt with fruit
477 No-fat vanilla custard
736 Vanilla pudding
767 Chocolate mousse
863 Full cream milk yoghurt with fruit
912 Pudding raspberries with currant sauce
915 Chocolate pudding with cream sauce
917 Cottage cheese - low-fat with fruit
931 Cottage cheese - no-fat with fruit
938 Semolina pudding with red currant sauce
1008 Dairy dessert with cream (averaged)
1720 Custard dairy cream milk several flavours
1721 Low-fat yoghurt/vanilla custard
1722 Semolina porridge
1791 Whipped cream from spray can
1957 Whipping cream custard
2241 Breaker yoghurt snack
2242 Breaker cottage cheese snack
2244 Yoghurt cream with fruit
2247 Cottage cheese yoghurt with fruit
2248 Danoontje cottage cheese with fruit
2267 Optimel no-fat custard with sweeteners
2269 Pudding light
2270 Chocolate mousse light
2310 Becel pro.activ yoghurt product
5007 Low-fat custard
5008 Low-fat fruit yoghurt
5044 Pudding like baverois, chipolata
5428 Straciatelli yoghurt
5438 Mona cream pudding with fruit
6003 Albert Heijn yoghurt/cottage cheese dessert (fortified children's dessert)
6003 Albert Heijn yoghurt/cottage cheese dessert (fortified children's dessert)
6004 Campina yoghurt & custard
6027 Cottage cheese fruit full cream
6036 Danoontje Prince chocolate/milk dessert
6051 Melkan children's cottage cheese
6086 Campioentje yoghurt dessert
6089 Campina soft & light custard dessert
6090 Nestlé pyjama porridge
6091 Campina double custard flip
6092 Friesche Vlag Bollino custard (with chocolate sprinkles)

03. Edible ices

303 Dairy ice cream - vanilla
485 Dairy ice cream/vanilla cornet
1474 Water pop/lolly
2250 Ice Festini
2251 Chocolate-coated dairy ice cream
6096 Ice Wicky fruit
6240 Ice with thin chocolate layer
6241 Staciatella ice
6242 Ice on stick with fruit layer

04.2.2 Fruit and vegetables in vinegar, oil, or brine

131 Gherkins - pickled/bottled
144 Silver-skin onions - sweet pickled/bottled
850 Mixed vegetables, sweet/sour
1161 Cucumber - pickled slices
1454 Beetroot – pickled

04.2.4.1 Fruit and vegetable preparations, excluding compote

179 Apple puree canned/bottled
181 Dates preserved
440 Ginger in syrup - canned
538 Rhubarb puree
1182 Apple puree without sugar canned/bottled
1396 Rhubarb puree, home-made with sugar
6068 Breaker fruit

04.2.5.1 Extra jam and extra jelly as defined by Directive 2001/113/EC
04.2.5.2 Jam, jellies and marmalades and sweetened chestnut puree as defined by Directive 2001/113/EC
04.2.5.3 Other similar fruit or vegetable spreads (only dried-fruit based sandwich spreads)

445 Jam - household quality
457 Rose hip jam
484 Jam - low sugar
807 Jam - no added sugar

05.1 Cocoa and chocolate products as covered by Directive 2000/35/EC
05.2 Other confectionery (only cocoa or dried fruit based)

431 Chocolate bar - milk
432 Chocolate bar - plain
487 Mars candy bar
524 M&M's chocolate
525 Milky Way candy bar
526 Bounty candy bar
528 Snickers candy bar
570 Nuts candy bar
621 M&M's chocolate with peanuts
717 Chocolate bar milk with nuts
845 Twix candy bar
929 Chocolate bar - milk without sugar
1450 Chocolate bar – plain without sugar

1508 Chocolate praline
2266 Chocolate bar - white
5479 Chocolate bar – milk/butterscotch
5488 Raisins in milk chocolate wrap
5489 Chocolate filled with fruit
5491 Chocolate bar plain with nuts
5494 Chocolate frogs/mice

05.2 Other confectionery (only cocoa, milk, dried fruit or fat based sandwich spreads)

436 Chocolate hazelnut spread
444 Chocolate spread - plain
1311 Chocolate sprinkles (averaged)
1962 Chocolate sprinkles - milk
1963 Chocolate sprinkles - plain
1964 Chocolate spread - milk
6094 St John's bread paste
6256 Chocolate paste coconut

05.2 Other confectionery

450 Acid drop
453 Peppermint
461 Toffees
482 Foam sweets
520 Liquorice Dutch-style - salted
522 Liquorice Dutch-style sweet
523 Stophoest cough drops
750 Marshmallows
751 Liquorice English-style
1256 Marzipan
1389 Liquorice Dutch-style (averaged)
2292 Boiled sweets, no added sugar
5495 Toffee with chocolate
5496 Nougat
5498 Sweet liquorice lollipop
5499 Liquorice with peppermint
6064 Wine gums (revised nevo 2006)
6095 Wine gums, light

05.2 Other confectionery (only breath-freshening microsweets)

Not included

05.2 Other confectionery (only strongly flavoured freshening throat pastilles)

Not included

05.3 Chewing gum

446 Chewing gum
447 Chewing gum, no sugar

05.4 Decorations, coatings and fillings, except fruit based fillings covered by category 4.2.4
Decorations, coatings and fillings, expect fruit based fillings covered by category 4.2.5

Not included

06.3 Breakfast cereals

591 Kellogg's All Bran
5015 Molenaar multigrain cereal

07.2 Fine Bakery wares (only essoblaten – wafer paper)

Not included

09.2 Processed fish and fishery products including mollusks and crustaceans

Not included

11.4.1 Tabletop sweeteners in liquid form
11.4.2 Tabletop sweeteners in powder form
11.4.3 Tabletop sweeteners in tablets

644 Coffee, ready to drink
645 Tea, ready to drink
1088 Natrena tablet
1089 Natrena liquid drop
1592 Saccharine tablet
1593 Aspartame/acesulfame tablet
1594 Saccharine/cyclamate tablet
1596 Aspartame powder
1597 Aspartame/acesulfame powder
5570 Cappuccino, instant (ready to drink)
5572 Herbal tea, sweetened (ready to drink)

12.5 Soups and broths

797 Soup vegetables-based dried packet (prepared)
798 Soup meat-based dried packet (prepared)
800 Soup vegetable-based canned (prepared)
801 Soup meat-based - canned (prepared)
802 Soup legume-based - canned (prepared)
803 Soup main course - canned (prepared)
5643 Soup not specified canned
5644 Soup not specified dried packet (prepared)

12.6 Sauces (except soy-bean sauce)

428 Barbecue sauce
437 Cocktail sauce 25% oil
451 Mayonnaise 80% oil
454 Piccalilly
458 Dressing French 25% oil
462 Tomato ketchup
465 Salad cream 25% oil
466 Salad cream 35% oil
539 Fruit sauce for pudding
540 Chocolate sauce for pudding
548 Schaschlik sauce
549 Sauce curry 25% oil
584 Curry ketchup
616 Peanut sauce - ready to serve
729 Dressing French 40% oil
844 Salad dressing natural without oil

1260 Yoghurt-based dressing 25% oil
1517 Packet sauce <3% fat prepared
1518 Packet sauce >3% fat prepared
1524 Tomato sauce, ready to eat - bottled
1803 Oriental sauce, ready to eat - bottled
1913 Peanut sauce/sate sauce, home-made
1938 Peanut sauce, packet (prepared)
2083 Mayonnaise with olive oil
5416 Oven delicious mix
5582 Sate sauce - low-fat milk, no fat
5583 Sate sauce - low-fat milk-water, no fat
5584 Sate sauce – water-based, no fat
5595 Chicken Tonight sauce
5599 Salad dressing Yofresh
6017 Warm sauce liquid ready to serve <12% fat
6018 Honey & mustard dressing
6023 Warm sauce liquid ready to serve >=12% fat
6025 Packet sauce dry approx. 10% fat (<3g fat prepared)
6044 Sauce, dried sachet, 30g (>3g fat prepared)
6049 Remia frites lijn (5% oil)
6050 Mayonnaise light 35% oil
6066 Garlic sauce 20% oil
6067 Dressing 13% fat
6251 Worcester sauce

12.6 Sauces (only soy-bean sauce)

1213 Soy sauce - salty
1215 Soy sauce – sweet

13.2 Dietary foods for special medical purposes defined in Directive 1999/21/EC (excluding products from food category 13.1.5)

Not included

13.3 Dietary foods for weight control diets intended to replace total daily food intake or an individual meal (the whole or part of the total daily diet)

5363 Herbalife powder
5364 Herbalife milkshake with low-fat milk

14.1.3 Fruit nectars

385 Fruit drink redberry
1463 Fruit drink/two or more fruits
1878 Roosvicee Multivit fruit drink
6019 Wicky fruit drink
6020 Wicky fruit drink light
6040 Coolbest light Vitaday original fruit drink
6043 Fruit drink light not fortified approx 7g CHO
6063 Surango multi vitamin nectar light
6097 Robinsons fruit shoot drink

14.1.4 Flavoured drinks

272 Full cream chocolate milk
273 No-fat chocolate milk
395 Cola soft drink with caffeine

400	Soft drink without caffeine
414	Tonic soft drink
417	Lemon squash
425	Rivella whey drink - light
463	Fruit drink concentrate - bottled
479	Buttermilk with fruit
497	Roosvicee rose hip syrup, various flavours
498	Roosvicee rose hip syrup ferro
500	Roosvicee rose hip syrup laxo
657	Yoghurt drink
738	Roosvicee diet rose hip syrup
862	Milkshake
863	Yoghurt with fruit
1294	Taksi whey drink
1294	Whey drink Taksi
1381	Alpro milk soy - natural fresh
1464	Low-fat chocolate milk
1510	Alpro milk soy Ca+
1521	Lemon squash light
1522	Soft drink, light without caffeine
1523	Cola light, soft drink with caffeine
1602	Alpro milk soy - several flavours
1655	Fruit juice - concentrated
1662	Spontin lemon/orange syrup - can
1807	Spontin syrup other flavours - can
1810	Karvan Cévitam fruit syrup - can
1813	Yakult
1832	Yoghurt drink - Vifit fruit
1833	Optimel no-fat yoghurt with fruit/vanilla with sweeteners
1834	Optimel yoghurt drink with sweeteners
1880	Roosvicee rose hip syrup calcium orange/mango
1881	Roosvicee rosehip syrup Multivit wild fruit/peaches
1882	Roosvicee Lessini light
1953	Alpro Yofu soja per 100 ml
1970	Chocomel light – low-fat chocolate milk with sweeteners
2023	Yoki yoghurt drink, with sweeteners
2037	Biomild milk drink peaches with sweeteners
2039	Yoki yoghurt drink
2041	AA Isotone sports drink
2042	AA High Energy, sports drink
2052	Milk & Fruit drink – strawberry-cherry/mango
2053	Milk & Fruit drink - orange
2079	Hero Fruitontbijt breakfast drink p 100 ml
2086	Ice tea
2087	Ice tea light
2088	Ice tea with sugar and sweetener
2134	Dubbelfrisss lemon squash
2135	Vruchtenfris/Tintelfruit lemon squash
2136	Dubbelfrisss lemon squash - light
2137	Vrfris/Tintelfruit lemon squash -light
2138	Spa&Fruit lemon squash
2139	Spa&Fruit lemon squash, light
2140	Sap&Fruit Vitamins lemon squash
2141	Spa&Fruit light clear water with sweeteners
2146	Appelsientje Vitamientje red/wild fruits

2218 Extran Energy sports drink
2219 Extran Refresh sports drink
2220 Taksi whey drink with sweeteners
2245 Vitalinea yoghurt no-fat, with fruit & sweeteners
2253 Vifit yoghurt drink fruit - light
2254 Yoghurt drink - with sweetener
2255 Fristi yoghurt drink - with sweetener
2256 Yomild yoghurt drink fruit
2257 Goede Morgen breakfast drink
2258 Actimel drink natural
2259 Milk & Fruit light
2261 Alpro Groeidrink milk soy-
2265 Yakult light
2287 Fruit syrup, sugar & sweetener
2288 Fruit syrup, sugar & sweetener, added vitamin C
2289 Fruit syrup - light
2291 Fruit juice concentrate - added vitamin C
5047 Lagona (Aldi) multi-vitamin 12 fruit nectar
5319 Fruit King tropical fruit juice
5321 ACE vitamin drink (averaged)
5323 Roosvicee multivit drink + sweetener
5324 Solevita multivit drink + sweetener
5325 Dr. Siemer multivit light + sweetener
5327 Sisi Fruitmania
5342 McDonald milkshake
5425 Instant chocolate low-fat powdered milk
6000 Campina yoghurt flip
6001 Campina custard flip
6002 Wicky fruitzacht red fruit with vitamin BCE
6007 C1000 fruit syrup 10-15 mg vitamin C
6008 Albert Hijn/Kruidvat fruit syrup 25-30
6009 Super/Fruitfris cassis fruit syrup (15-20 mg vitamin C)
6010 Raak/First Quality syrup, sugar & sweetener
6011 Fruit juice concentrate >65g CHO/100g
6015 Frisdrank sugar+sweetener 5-<7 g CHO/100g (not fortified)
6022 Albert Heijn syrup, sugar & sweetener
6024 Roosvicee Stralendfris
6029 Frisdrank sugar+sweetener 2-<5g CHO/100 g (not fortified)
6030 Solevita multi vitamin light nectar
6031 Sisi Fruitmania peach or lemon (vit C+)
6032 Roosvicee Spongebob
6034 Campina fruit milk
6035 Bi-Yo low-fat yoghurt drink without sweeteners
6041 Fruxano en Goldhorn Multivitamin 12 fruit nectar light
6060 Wicky fruitzacht peache vitamin ACE
6061 Melkan Topvit (yoghurt drink light fortified)
6087 Campioentje yoghurt drink
6088 Danone Dora drink
6099 Aldi ACE vitamin drink
6100 Caprisonne multvitamin
6102 Spa &Tea fruit flavoured
6103 Solevita tea & fruit
6104 Wicky ice tea
6105 River Power drink

6106 Provamel bio soya choco drink
6204 Syrup 2288 diluted
6205 Syrup 1882 diluted
6206 Syrup 2287 diluted
6207 Syrup 6022 diluted
6214 Syrup 6010 diluted
6215 Syrup 6007 diluted
6216 Fruit juice concentrate 6011 diluted
6220 Syrup 463 diluted 1 on 4
6221 Syrup 463 diluted 1 on 7
6222 Syrup 463 diluted (averaged)
6223 Syrup 497 diluted
6224 Karvan Cevitam syrup 1810 diluted
6227 Fruit juice concentrate 1655 diluted
6228 Syrup 6008 diluted
6229 Syrup 2289 diluted
6230 Multivit syrup 1881 diluted
6243 Instant chocolate prepared with full cream milk
6244 Instant chocolate Nesquik plus chocolate flavour prepared with low-fat milk
6245 Instant chocolate prepared with no-fat milk
6248 Syrup 6009 diluted
6249 Instant chocolate Nesquik no added sugar, prepared with low-fat milk

14.2.1 Beer and malt beverages

Not included

14.2.8 Other alcoholic drinks including spirits with less than 15% of alcohol and mixtures of alcoholic drinks with non-alcoholic drinks

Not included

15.1 Potato-, cereal-, flour- or starch-based snacks

122 Crisps
617 Ringlings cocktail snacks
618 Nibbits cocktail snacks
619 Wokkels cocktail snacks
620 Potato crisps straws - salted
1505 Crisps - light
1937 Crisps tortilla plain
2163 Bugles maize crisps
2173 Crisps based on potato flour
5469 Chipitos cocktail snacks

15.2 Processed nuts

205 Mixed nuts and raisins
546 Peanuts – coated

16. Desserts excluding products covered in category 1, 3 and 4

Not included

17.1 Food supplements supplied in a solid form including capsules and tablets and similar forms

1001 Vitamine A/D Davitamon AD (tablet)
1022 Vitamine A/D Optimax Kinder vitamine A, D en C (tablet)

1026 Multivtamine Kruidvat Multi-vit. voor kinderen
1027 Multivitamine Trekpleister voor kinderen
1045 Vitamine A/D Kruidvat
1074 Vitamine A/D Davitamon AD (aquosum)
3002 Multivit./min. Hema Multitotaal (tablet 50% ADH)
3026 Multivit./min. Orthica Dino-multi
3052 Multivit./min. Hema Jip en Janneke Multi Totaal
3053 Multivit./min. Centrum Junior
3054 Multivit./min. Davitamon Junior (dragee/kauw)
3056 Multivit./min. Davitamon Compleet
3065 Multivit./min. Bloem Kind&Balans (kauwtablet)
3066 Multivit./min. Hema Kind Multi Totaal (kauw)
3069 Multivit./min. Optimax kinder
3070 Multivit./min. Nature's Plus Animal Parade Kinder
3100 Multivit./min. Trekpleister Multi A-Z kind (kauw)
3101 Multivit./min. Kruidvat Multi A-Z kinderen (kauw)
3126 Multivit./min. DA Multi voor kinderen framboos
3140 Multivit./min. Kruidvat Multi vit. & min. (dragee)
3172 Multivit./min. SuperTed multivitamines & ijzer
3175 Multivit./min. Dagravit totaal 30
3210 Calcium/vit. D Orthica Dino-calcium
4029 Vitamine C Orthica Dino-C
4065 Vitamine C Trekpleister
4067 Vitamine C Kruidvat C-60 suikervrij
4069 Vitamine D Etos
4102 Vitamine C Dagravit (kauw)
4103 Vitamine C Roter C-50
4140 Vitamine C Kruidvat C60 sinaasappelsmaak
4143 Vitamine D Davitamon D (tablet)
4144 Vitamine D Kruidvat (tablet/kauwtablet)
4153 Vitamine D Trekpleister tablet
4180 Vitamine D DA kinderen (tablet)
5001 Fluor Zyma / Novartis / Fluor Kruidvat
6014 Calcium/vit. D Kruidvat Kalk-vitamine D3
8017 Probiotica Orthiflor Junior (Orthica)
10026 Multivit./min. Etos Multi Kind Alles in 1
10035 Vitamine A/D Trekpleister
10052 Multivitaminen Yoyabears
10061 Multivit./min. Multi Gummies for Kids
10062 Multivit./min. Funcio Optimum Health (met aminoz.)
10064 Multivit./min. Samenw. Apoth. voor kinderen (kauw)
10065 Multivit./min. Lucovitaal Multi+ Kids omega 3-6 sv
10068 Multivit./min. Gezond en Wel Multisprong
10070 Vitamine C Etos C-250
90001 Multivit./min. Dagravit Junior 30 (dragee)
100028 Multivit./min. KidVits Now foods
100029 Vitamine C Nova Vitae poeder

17.2 Food supplements supplied in a liquid form

2021 Multivitamine Dagravit titaak 8 (liquid)
1026 Multivtamine Kruidvat Multi-vit. voor kinderen
1045 Vitamine A/D Kruidvat
1070 Vitamine B2 riboflavin/nicotin 25/25 mg apotheek
1073 Vitamine A/D Davitamon AD (olie)

1074 Vitamine A/D Davitamon AD (aquosum)
3069 Multivit./min. Optimax kinder
4047 Vitamine K Davitamon K (olie)
4068 Vitamine D Etos (druppels)
4145 Vitamine D Davitamon D (aquosum)
4146 Vitamine D Davitamon D (olie)
4150 Vitamine D DA kinderen (waterbasis)
4151 Vitamine D Kruidvat druppels voor kinderen
4152 Vitamine D Trekpleister druppels voor kinderen
4181 Vitamine E/tocoferol 25 mg apotheek
5083 IJzerpreparaat Ferrofumaraat 20 mg/ml (vloeib.)
7001 Visoliecapsules El Mare v/h kind (met teunisbl.)
7002 Visoliecapsules Eye Q (Springfield)
7003 Visoliecapsules MorEPA mini-junior
7005 Visolie met vitamines Optimax Kinder omega (olie)
7007 Visoliecapsules Triomar for kids
7009 Visoliecapsules Sunwell krachtige visolie kind
7011 Visoliecapsules Ameu 500mg (LichtwerPharma/Cynarus
8068 Multivit./min. Floradix kindervital (Salus)
10037 Visoliecapsules Kruidvat omega 3 en 6
10049 Vitamine D etalpha (Leo Pharma)
10050 Paardenmelkpoeder
10063 Vitamine D Samenwerkende Apothekers (olie)
10066 Visoliecapsules Nutrilite Amway
10069 Visoliecapsules Eye Q (Springfield)
10025 Visoliecapsules Omega Combi-3 Junior Distrib.care
10026 Visoliecapsules Eskimo-3 Omega-3 FuncioMed
10027 Multivit./min. ADHD-Norm AOV

17.3 Food supplements supplied in a syrup-type or chewable form

Not included

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Rijksinstituut voor Volksgezondheid en Milieu
Postbus 1 | 3720 BA Bilthoven
www.rivm.nl