FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

Supporting document 1

Risk and technical assessment report – Application A1108

Rebaudioside M as a New Steviol Glycoside Intense Sweetener

Executive summary

Rebaudioside M is similar in chemical structure and sweetness intensity to other currently permitted steviol glycosides. The production of rebaudioside M preparations, analytical methods, specifications and stability are similar to other steviol glycosides. Rebaudioside M occurs naturally in the leaves of the stevia plant at much lower concentrations than several other steviol glycosides so specific concentration and purification steps are required to produce preparations containing high concentrations of rebaudioside M.

As for other steviol glycosides, rebaudioside M is hydrolysed completely to steviol by gut microflora. The existing acceptable daily intake (ADI) for steviol glycosides of 0–4 mg/kg bodyweight, which is expressed on the basis of steviol, is therefore applicable to rebaudioside M.

Rebaudioside M-containing preparations are intended for use in the same food categories and at the same use-levels already permitted for other steviol glycoside products. FSANZ has previously conducted a dietary exposure assessment using the current permissions for steviol glycosides and therefore no dietary exposure assessment was necessary for this Application.

It is concluded that the use of rebaudioside M as a food additive in accordance with the current permissions for steviol glycosides raises no public health and safety concerns.

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1 Introduction

FSANZ received an application from PureCircle seeking approval for rebaudioside M (Reb M) to be added to the permitted steviol glycosides that comprise the food additive intense sweetener, steviol glycosides (INS 960). Steviol glycosides are permitted to be added to a variety of food categories in Schedule 1 of Standard 1.3.1. The specifications for steviol glycosides in the relevant monographs in Standard 1.3.4 do not list Reb M.

1.1 Objectives of the Assessment

As there are no permissions for Reb M to be added to food as a steviol glycoside intense sweetener any application to amend the Code to permit the use of this sweetener requires a pre-market assessment.

The objectives of this risk and technical assessment are to:

- determine whether the proposed purpose is clearly stated and that Reb M achieves its technological function in the quantity and form proposed to be used as a food additive

- evaluate any potential public health and safety concerns that may arise from the use of Reb M as a food additive.

2 Food Technology Assessment

2.1 Steviol glycosides; chemical structures and properties

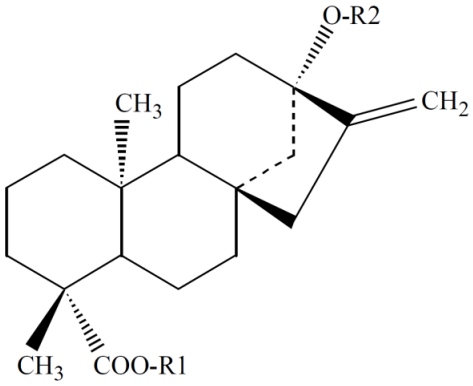
2.1.1 Chemical structure and composition

The purified extract of the leaves of *Stevia rebaudiana* contain at least ten different well identified glycosides of steviol, referred to as steviol glycosides. Each of the glycosides contains steviol as a common central component of its molecular structure and different sugar moieties forming the glycoside. There are four main steviol glycosides present in typical preparations: stevioside, rebaudioside A, rebaudioside C and dulcoside A. Stevioside and rebaudioside A generally comprise around 80% of the extract. The other six minor glycosides present generally constitute less than 5% of the total extract. Rebaudioside M (abbreviated as Reb M, also sometimes referred to as rebaudioside X) is naturally present at very low levels in typical steviol glycoside preparations. Reb M has been identified at levels of between 0.02-0.2% in commercial steviol preparations containing at least 95% total steviol glycosides (i.e. meeting the current JECFA[1] steviol glycoside specification: FAO 2010). Figure 1 below illustrates the chemical structure of the steviol skeleton and includes the structures of the related R (sugar moiety, glycoside) compounds of each common steviol glycoside, including the addition of Reb M. Ten of these steviol glycosides are listed in the JECFA Chemical and Technical (CTA) Assessment, which does not include Reb M. However, the JECFA specification (and hence the list of steviol glycosides in the Code and their conversion factors to calculate steviol equivalents) lists only nine. Rebaudiosides E and M are not included. Figure 2 provides a more detailed, full chemical structure of Reb M.

The Applicant has two Reb M preparations of different purity; one that contains greater than 95% Reb M, and the other less pure product which contains greater than 50% Reb M (as well as other steviol glycosides).

[1] Joint FAO/WHO Expert Committee on Food Additives

Both preparations meet the general JECFA specification for steviol glycosides of containing greater than 95% steviol glycosides (that is the total of different steviol glycosides).



Compound name	**R1**	**R2**
Steviol	H	H
Steviolbioside	H	*β*-Glc-*β*-Glc(2→1)
Stevioside	*β*-Glc	*β*-Glc-*β*-Glc(2→1)
Rubusoside	*β*-Glc	*β*-Glc
Rebaudioside A	*β*-Glc	*β*-Glc-*β*-Glc(2→1) | *β*-Glc(3→1)
Rebaudioside B	H	*β*-Glc-*β*-Glc(2→1) | *β*-Glc(3→1)
Rebaudioside C (dulcoside B)	*β*-Glc	*β*-Glc-*α*-Rha(2→1) | *β*-Glc(3→1)
Rebaudioside D	*β*-Glc-*β*-Glc(2→1)	*β*-Glc-*β*-Glc(2→1) | *β*-Glc(3→1)
Rebaudioside E	*β*-Glc-*β*-Glc(2→1)	*β*-Glc-*β*-Glc(2→1)
Rebaudioside F	*β*-Glc	*β*-Glc-*β*-Xyl(2→1) | *β*-Glc(3→1)
Dulcoside A	*β*-Glc	*β*-Glc-*α*-Rha(2→1)
Rebaudioside M	***β*-Glc-*β*-Glc(2→1)** **|** ***β*-Glc(3→1)**	***β*-Glc-*β*-Glc(2→1)** **|** ***β*-Glc(3→1)**

Glc, Xyl and Rha represent, respectively, glucose, xylose and rhamnose sugar moieties

Figure 1: Chemical structures of the common steviol glycosides including Reb M, showing the basic steviol skeleton and R groups [from the JECFA Chemical and Technical Assessment for steviol glycosides (FAO 2007), modified to incorporate Reb M].

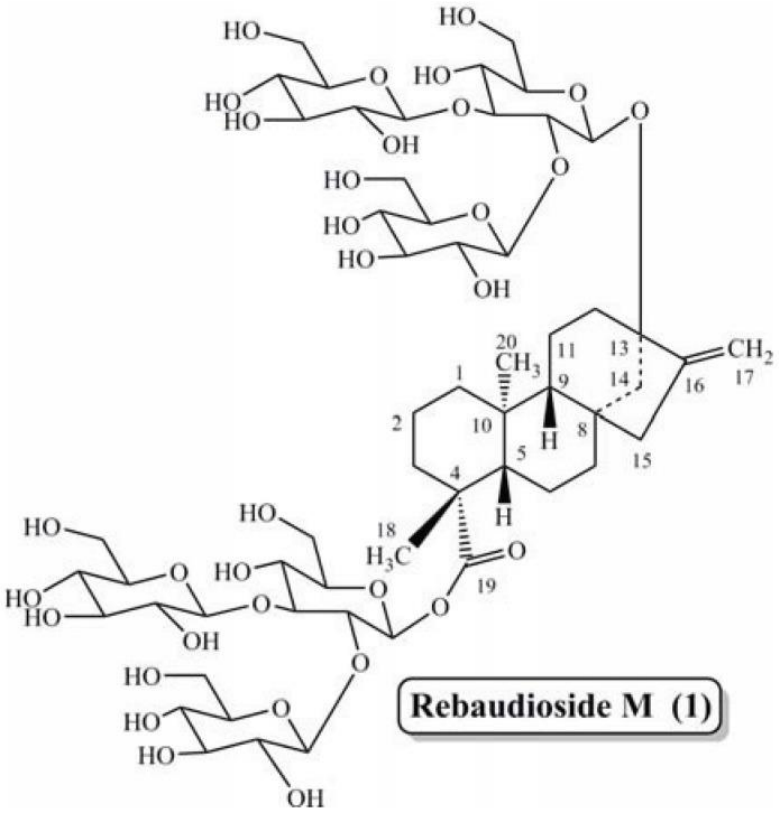


Figure 2: Chemical structure of Reb M, copied from an open access online source (Prakash et al 2014a).

2.2 Manufacturing methods for Reb M

The Application contains a schematic of the production process to produce their Reb M preparations. It is provided as Figure 3.

The production process occurs in a similar way to that described for the general production of steviol glycosides from solvent extraction from crushed stevia leaves, as outlined in the Chemical and Technical Assessment (CTA) of steviol glycosides for JECFA (FAO 2007). This was also summarised in FSANZ's Risk and Technical Assessment Report for Application A1037 – Steviol Glycosides: Increase in Permitted Use Levels (FSANZ 2011) and the Food Technology Report (Attachment 4) of the Draft Assessment Report for Application A540 – Steviol Glycosides as Intense Sweeteners (FSANZ 2008).

Crushed stevia leaves are extracted using hot water. The extract is purified using ion-exchange chromatography along with other purification steps including filtration and crystallisation. The Applicant explains that manipulating these steps (their propriety intellectual property) allows them to selectively produce crystalline products containing a high concentration of Reb M.

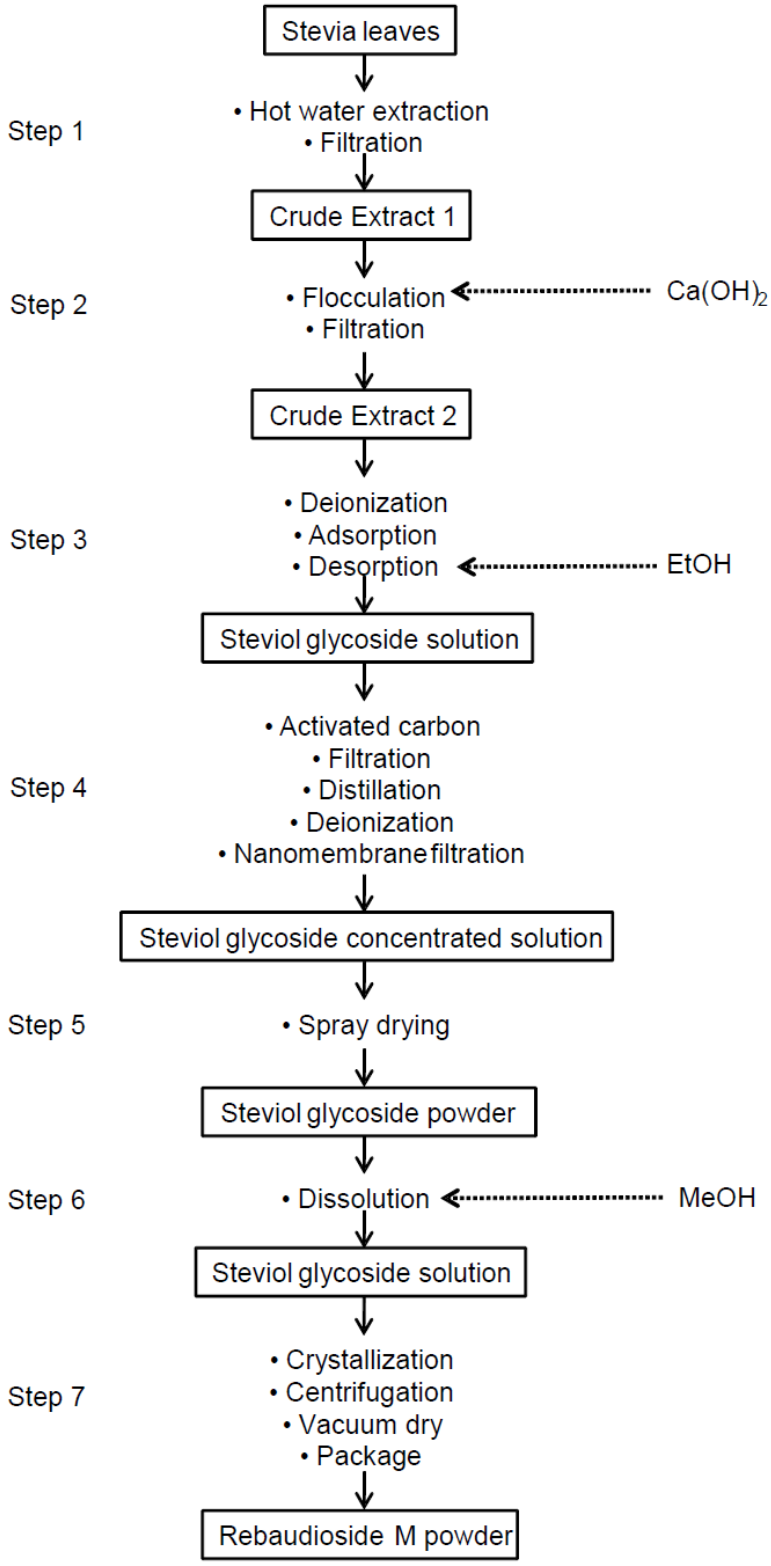
2.3 Reb M claimed advantages

The Applicant claims that their Reb M preparations provides both an increased sweetness potency (so allowing greater amounts of sugar to be replaced by steviol glycosides) and a superior flavour profile compared to other steviol glycosides (specifically mentioned the most common and abundant glycoside being rebaudioside A, Reb A).

Two reports were provided in the Application to support these claims. Sensory studies were conducted on products containing Reb M preparations (80% and 95% purity) and compared to those containing Reb A, aspartame and sucrose to the same sweetness intensity (sucrose equivalents). Studies were conducted in water, phosphoric acid and citric acid solutions to replicate different flavoured drink media, carbonated and non-carbonated. Blends of different mixtures of the sweeteners were also used. The over-riding conclusion relevant to this assessment was that the sensory perception of Reb M preparations were considered to be between that of aspartame (most similar to sucrose) and Reb A (least similar to sucrose) for nearly all attributes. Reb M preparations had slightly lower scores on negative sensory attributes of liquorice taste and aftertaste, bitter taste and aftertaste and sweetness linger compared to Reb A. Reb M preparations also scored slightly higher on sweetness compared to Reb A.

2.4 Analytical methods

There have been analytical methods available for the detection and quantification of steviol glycosides in food since preparations of steviol glycosides have been commercialised and permitted as intense sweetener food additives. These have been based on High Performance Liquid Chromatography (HPLC). Such analytical methods were mentioned in FSANZ's assessment of Application A1037 (FSANZ 2011). That report referred to the European Food Safety Authority (EFSA) scientific opinion on steviol glycosides in 2010 (EFSA 2010). Two HPLC analytical methods have been published (Geuns et al 2008, Gardana et al 2010). Such methods should be readily adaptable for the analysis of Reb M in foods and beverages.



$Ca(OH)_2$, calcium hydroxide; EtOH, ethanol; MeOH, methanol.

Figure 3 Schematic of the production process to produce rebaudioside M preparations, taken from the Application.

2.5 Specifications of steviol glycosides

The JECFA specification for steviol glycosides lists nine specific steviol glycosides but Reb M is not included (JECFA, 2010). The definition notes that the steviol glycosides are obtained via solvent extraction from the leaves of the stevia plant (specifically *Stevia rebaudiana* Bertoni). This is also the case for Reb M.

The JECFA specifications (Combined Compendium of Food Additive Specifications) are a primary source of specifications in Standard 1.3.4 – Identity and Purity of the current Code (and section S3-2 in Schedule 3 (Identity and Purity) of the revised Code). There are no known specifications for Reb M in other primary or secondary sources in Standard 1.3.4 of the current Code (or section S3-2 and S3-3 of the revised Code). Therefore, a specification is required for Reb M in the Schedule in Standard 1.3.4 of the current Code (and a new specification within Schedule 3 of the revised Code), until such a time as the JECFA steviol glycosides specifications include Reb M, or when any other source of specifications (monographs in clause 2 or 3) in Standard 1.3.4 of the current Code (or sections S3-2 and S3-3 of the revised Code) covers Reb M.

2.6 Specifications of Reb M

The Application contains the Applicant's specifications and levels of purity for their commercial preparations of Reb M (95% and 50% Reb M). The preparations comply with the JECFA steviol glycosides specification requirement that at least 95% of the preparation consists of steviol glycosides The Reb M preparations meet the other JECFA requirements as detailed in Table 1, except that Reb M preparations are only slightly soluble[2] in water compared to other steviol glycosides which are freely soluble in water. Solubility in water is not a suitable criterion for a specification so the difference will not be addressed in the proposed specification. This information along with appearance is appropriate in technical data but not specifications. However, food manufacturers will need to be aware of it to ensure they can incorporate the sweetener into their food matrix.

Table 1: Specifications of Reb M preparations compared to JECFA steviol glycosides specifications

Parameter	JECFA Steviol glycosides specifications	Reb M preparations
Total steviol glycosides on dried basis	Not less than 95%[2]	Not less than 95%[1]
Description	White to light yellow powder	conforms
Solubility	Freely soluble in water	Slightly soluble
pH (1% solution)	4.5-7.0	conforms
Total ash	Not more than 1%	conforms
Loss on drying	Not more than 6% (2 hours at 105°C)	conforms
Residual solvents	Not more than 200 mg/kg methanol	conforms
	Not more than 5,000 mg/kg ethanol	conforms
Arsenic	Not more than 1 mg/kg	conforms
Lead	Not more than 1 mg/kg	conforms

Notes:

1. Total steviol glycosides to include any of the ten listed steviol glycosides: steviolbioside, stevioside, rubusoside, rebaudioside A, rebaudioside B, rebaudioside C, (dulcoside B), rebaudioside D, rebaudioside E, rebaudioside F, dulcoside A, and rebaudioside M.
2. Total steviol glycosides to include any of the nine listed steviol glycosides: steviolbioside, stevioside, rubusoside, rebaudioside A, rebaudioside B, rebaudioside C, (dulcoside B), rebaudioside D, rebaudioside E, rebaudioside F, and dulcoside A.

[2] The crystalline form of Reb M has a water solubility of 0.1 g/100 mL at 25 °C (Prakash et al 2014b).

2.6 Conversion factor for Reb M to calculate steviol equivalents

Since the risk assessment indicated that all steviol glycosides are completely converted to steviol in animals and humans, the ADI is expressed in terms of steviol equivalents (JECFA uses the term 'expressed as steviol'). This allows for any variability in the individual glycosides in mixtures of steviol glycoside extracts (e.g. different ratios of stevioside/ rebaudioside) to be taken into account. Therefore, conversion factors are needed to convert the different steviol glycosides to steviol.

The conversion factor used in the current Code in subclause 5(3) of Standard 1.3.1 (and subsection 1.3.1 – 4(7) in the revised Code) to convert all the different steviol glycosides to steviol equivalents is related to the ratio of the molecular weights of the steviol to the steviol glycoside.

The molecular weight of steviol is 318.45 g/mol while that of Reb M is 1291.3 g/mol (provided in the Application), so the ratio is 318.45/1291.3, which gives a conversion factor of 0.25 (two significant figures).

This conversion factor needs to be added into the Table to subclause 5(3) of Standard 1.3.1 of the current Code (and subsection 1.3.1-4(7) of the revised Code) as part of the draft variations to the Code as an outcome of this Application.

2.7 Stability of Reb M in food

The Application contains a number of specific studies designed to test the stability of Reb M preparations and to determine if it is similar to the stability for characterised steviol glycosides (FAO 2007). JECFA concluded that steviol glycosides are thermally and hydrolytically stable for use in foods and acidic beverages under normal processing and storage conditions.

The submitted Reb M stability studies evaluated stability under normal and exaggerated storage conditions, and at a range of temperatures and pH. The results indicated that the stability of Reb M is similar to other steviol glycosides.

2.8 Food technology conclusion

The food technology assessment concludes that Reb M is similar to other currently permitted steviol glycosides. The production of Reb M preparations, analytical methods, specifications and stability can be considered like other steviol glycosides. It occurs naturally in the leaves of the stevia plant at much lower concentrations than the more common steviol glycosides so specific concentration and purification steps are required to produce preparations containing high concentrations of Reb M. Studies by the Applicant have supported the claim that Reb M has a similar sweetness and flavour profile compared to other steviol glycosides. It is noted that the water solubility of Reb M is lower than other steviol glycosides so food manufacturers may need to check its solubility in their products.

3 Hazard Assessment

3.1 Background

3.1.1 Previous FSANZ assessments

FSANZ conducted a hazard assessment for steviol glycosides as part of the assessment of Application A540 – Steviol Glycosides as Intense Sweeteners (FSANZ 2008).

FSANZ established an ADI of 0–4 mg/kg bodyweight (bw), expressed as steviol equivalents, derived by applying a 100-fold safety factor to the no observed adverse effect level (NOAEL) of 970 mg/kg bw/day of stevioside (equivalent to 383 mg/kg bw/day steviol) in a 2-year rat carcinogenicity study.

For Application A1037 – Steviol Glycosides: Increase in Permitted Use Levels, toxicological and other relevant data published since the FSANZ (2008) assessment were considered. The additional data raised no concerns regarding the safety of steviol glycosides and did not indicate a need to change the ADI (FSANZ 2011).

3.1.2 Assessments by other agencies

As summarised in FSANZ (2011), JECFA and EFSA each established an ADI for steviol glycosides of 0–4 mg/kg bw (expressed as steviol).

In 2013, the current Applicant submitted to the US FDA a Generally Recognized as Safe (GRAS) notice for steviol glycosides with Reb M as the principal component (>50% of its total steviol glycosides content). The proposed use was as a general purpose sweetener in foods excluding meat and poultry products and infant formula, at levels determined by Good Manufacturing Practice (GMP), as well as use as a table top sweetener. The US FDA had no questions regarding this GRAS notice (USFDA 2013).

3.2 Evaluation of Submitted Data

The Applicant submitted several studies and reviews that were published after the most recent FSANZ assessment of steviol glycosides (FSANZ 2011). One study on Reb M relevant for hazard assessment is available: an *in vitro* study investigating the hydrolysis of Reb M and other steviol glycosides to steviol by human gut microflora. The remaining submitted studies are on other steviol glycosides or steviol glycoside preparations, however only two of these studies (both repeat-dose toxicity studies) were considered potentially relevant for the hazard assessment of steviol glycosides. These studies are also evaluated below.

3.2.1 Absorption, metabolism and excretion

The hydrolysis of the steviol glycosides rebaudioside A, B, D, M, and steviolbioside to steviol was evaluated *in vitro* using human faecal homogenates from healthy donors. Incubations were carried out in triplicate at 37 °C under anaerobic conditions. Separate incubations were conducted with pooled faecal homogenates from male and female donors (n = 3/sex). Each set of incubation experiments was conducted twice. Rebaudioside A, B, and D were evaluated at concentrations of 0.2 and 2.0 mg/mL. Rebaudioside M and steviolbioside were evaluated only at a concentration of 0.2 mg/mL because these compounds precipitated out of solution at higher concentrations. Incubation time-courses were 0, 4, 8, 24, and 48 h (rebaudioside B and D) or 0, 8, 16, and 24 h (rebaudioside A and M and steviolbioside). The extent of hydrolysis of each compound was based on the amount of steviol generated over the course of the incubation periods. A liquid chromatography/mass spectrometry (LC/MS) method was used for the quantification of steviol in incubation mixtures.

Results for rebaudioside A and M incubated at a concentration of 0.2 mg/mL are shown in Table 2. After 8 h of incubation, the extent of hydrolysis of rebaudioside A and M was 52-101% and 46-91%, respectively. Complete hydrolysis of both rebaudioside A and rebaudioside M was evident after 16 h incubation with faecal homogenate samples from both sexes.

Table 2: Formation of steviol from incubation of rebaudioside A and M in pooled male and female faecal homogenate samples

Steviol glycoside	Incubation time (h)	Males		Females	
		Percent hydrolysed to steviol[a]		Percent hydrolysed to steviol	
		M1	M2	F1	F2
Reb A	8	52	77	94	101
	16	99	98	100	107
	24	97	98	98	104
Reb M	8	46	83	91	82
	16	116	107	108	109
	24	115	108	107	108

Abbreviations: F1, female faecal homogenate samples #1; F2, female faecal homogenate samples #2; M1, male faecal homogenate samples #1; M2, male faecal homogenate samples #2.
[a] Percent hydrolysed to steviol was calculated based on the theoretical maximum concentration of steviol that could be formed from nominal complete hydrolysis. Each value is the mean of three replicates. Results are for incubations conducted at a rebaudioside concentration of 0.2 mg/mL.

At a concentration of 0.2 mg/mL, hydrolysis of rebaudioside B and D to steviol was essentially complete after 24 h and 8 h incubation, respectively, however the extent of hydrolysis was lower at a 10-fold higher substrate concentration of 2 mg/mL. The yield of steviol from steviolbioside (tested at 0.2 mg/mL only) was consistently lower than 100% (77–82% hydrolysis to steviol after 24 h incubation) (Purkayastha et al 2014).

3.2.2 Sub-chronic toxicity

Three studies investigating the sub-chronic toxicity of steviol glycosides were submitted and are summarised below.

Male Sprague-Dawley rats (28-days old, 8 per group) were administered stevioside (purity 97%) in drinking water for 12 weeks at target dose levels of 0, 15, or 1500 mg/kg bw/day. An additional group was administered stevioside (15 mg/kg bw/day) together with inulin (15 mg/kg bw/day) in drinking water for the same period. Animals were monitored for clinical signs of toxicity throughout the experiment. Food and fluid intakes were recorded daily and bodyweights were recorded weekly. Haematological and serum chemistry parameters were analysed at the start and end of the study period. Organ weights were measured at necropsy; however, macro- and microscopic evaluations were not conducted.

Mean stevioside doses calculated from drinking water consumption were 14 and 1491 mg/kg bw/day for the low and high dose stevioside groups, respectively, and 13 mg/kg bw/day for the group receiving stevioside and inulin. No mortality or clinical signs of toxicity were observed for any of the animals. During the final 6-weeks of the study period, average bodyweight gain and food intake of animals in the high-dose stevioside group were 41% (statistically significant: $p < 0.05$) and 85% ($p < 0.01$) of the control mean, respectively.

At the high dose there were statistically significant ($p < 0.001$) decreases in blood glucose (59% of control), alkaline phosphatase (47%), acid phosphatase (46%), and tartrate-resistant acid phosphatase (TRAP, 22%). TRAP levels were also decreased ($p < 0.01$) in the low-dose stevioside group (56% of control) and in the stevioside + inulin group (52%).

At the high dose, creatinine ($p < 0.01$), bilirubin ($p < 0.01$) and urea ($p < 0.001$) were 1.6, 1.9 and 3.8-times the control mean, respectively. There were also increases in cholesterol, low-density lipoprotein, and high-density lipoprotein ($p < 0.001$) compared to controls, however total lipid levels were unaffected. There were no statistically significant changes in alanine aminotransferase or aspartate aminotransferase for any dosed group.

There were no statistically significant differences in any haematology parameters in the low-dose stevioside group or in the stevioside + inulin group compared to controls. In the high-dose stevioside group, mean corpuscular volume was decreased (89% of control; $p < 0.05$), while haemoglobin, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration (MCHC) were increased (1.3, 1.3 and 1.4-times the control mean, respectively; $p < 0.05$).

Animals in the low-dose stevioside group or in the stevioside + inulin group did not show any statistically significant differences in bodyweight-relative organ weights compared with controls. In the high dose group, bodyweight-relative weights of testes and epididymis ($p < 0.001$), kidney, and brain tissues ($p < 0.05$) were increased, while relative liver weights were decreased ($p < 0.01$) (Awney et al 2011).

The findings from the Awney et al study are discussed in Section 3.3 – Discussion.

In a 28-day study, Sprague-Dawley rats (10 animals/sex/group; 6 weeks old) were administered a control diet and either rebaudioside D at dietary concentrations to give target dose levels of 500, 1000, or 2000 mg/kg bw/day, or rebaudioside A at a dietary concentration providing a target dose of 2000 mg/kg bw/day. Purities of rebaudiosides D and A were 93.5 and 98.9%, respectively. All animals were observed twice daily for mortality and moribundity and clinical examinations were performed daily. Bodyweights and food consumption were recorded weekly. Motor activity data and a functional observational battery (FOB) were recorded for all animals during study week 3. Blood samples were collected for haematology and serum chemistry evaluations from all animals on the day of the scheduled necropsy (study day 28). Necropsies were conducted on all animals, and selected organs were weighed. Selected tissues were examined microscopically from all animals in the control group, the high-dose rebaudioside D group and the rebaudioside A group.

Mean intakes of rebaudioside D at each of the target dose levels were calculated to be 506 and 495, 1027 and 1012, and 2042 and 2016 mg/kg bw/day for males and females, respectively. For rebaudioside A, achieve intakes were estimated to be 2034 and 1965 mg/kg bw/day for males and females, respectively.

There were no deaths or test-article related signs of toxicity. The authors concluded that there were no test article-related effects on any of the toxicological endpoints investigated, however the focus of this paper was on studies investigating the absorption and metabolism of rebaudioside D and detailed toxicological data were not presented (Nikiforov et al 2013).

3.3 Discussion

Previous studies have confirmed that steviol glycosides such as stevioside and rebaudioside A are poorly absorbed following oral administration, but they are hydrolysed by gut microflora to steviol, which is well absorbed. For the present Application, an *in vitro* study shows that Reb M is hydrolysed completely to steviol by gut microflora (Purkayastha et al 2014) consistent with the results of similar studies conducted on stevioside and rebaudioside A (e.g. Gardana et al 2003; evaluated in FSANZ 2008). As such, the existing toxicological database for stevioside and rebaudioside A, upon which the ADI for steviol glycosides was established, supports the safety of Reb M.

A sub-chronic repeat-dose toxicity study on stevioside (Awney et al 2011) reported findings that are not consistent with the results of previous studies on stevioside or other steviol glycosides. The authors concluded that adverse effects were associated with a stevioside dose of 1500 mg/kg bw/day, the highest dose used in the study. Critical reviews of the study were subsequently published in the same journal and a number of potential flaws and inconsistencies in the study were noted (Carakostos 2012; Waddell 2011). For example, anomalous haematology parameters were observed for control rats which would be consistent with extreme anaemia. However, no signs of anaemia or other indicators of ill health were reported for any of the animals during the study.

Awney et al (2011) suggested that decreased TRAP values observed in their study may indicate stevioside-related adverse effects on bone metabolism, however Carakostas (2012) stated that the colorimetric measurement method used by the investigators was less reliable than methods currently in use and that the assay is not specific to enzyme activity in bone. In response, the lead study author stated that a confirmatory study investigating the effect of stevioside on serum TRAP activity will be conducted using the most recent methodology (Awney 2012). No subsequent study has been found in the published literature. Finally, it is noted that the high-dose of stevioside administered to animals in this study of 1500 mg/kg bw/day exceeds the dose of 970 mg/kg body weight/day which was the NOAEL for stevioside based on the results of a 2-year study (Toyoda et al 1997). It is therefore concluded that the study by Awney et al raises no concerns regarding the safety of steviol glycosides and does not indicate a need to change the ADI.

3.4 Conclusion

As for other steviol glycosides, Reb M is hydrolysed completely to steviol by gut microflora. The existing ADI for steviol glycosides of 0–4 mg/kg bw, which is expressed on the basis of steviol, is therefore applicable to Reb M.

4 Dietary Exposure Assessment

Reb M-containing preparations are intended for use in the same food categories and at the same use-levels already permitted for other steviol glycoside products. FSANZ has previously conducted a dietary exposure assessment using the current permissions for steviol glycosides (FSANZ 2011). No dietary exposure assessment was therefore necessary for this Application.

5 Risk Characterisation

The use of Reb M as a food additive in accordance with the existing permissions for steviol glycosides raises no public health and safety concerns.

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