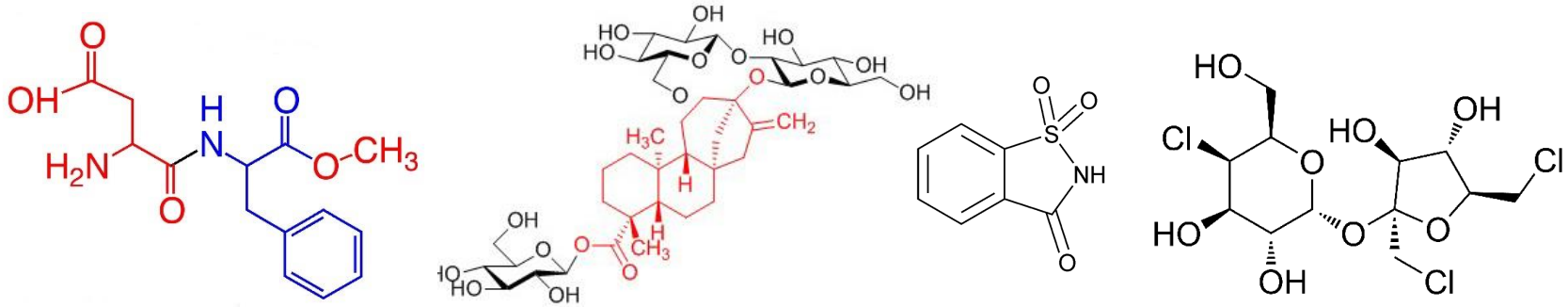
Intense (“artificial”) sweeteners

Sweet dreams or nightmares?



Dr Alan Barclay

Cert III(Commercial Cookery); BSc(Nutrition and Food Science); Grad Dip (Dietetics); PhD

Disclosure statement

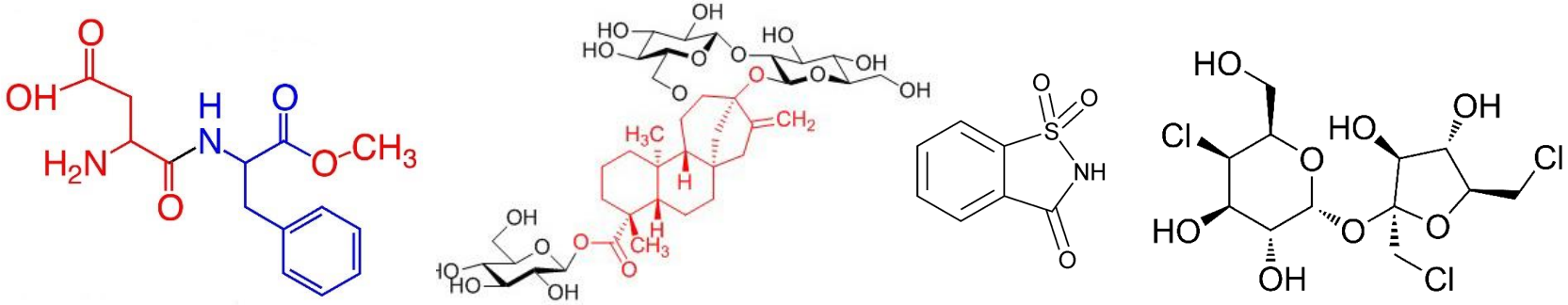
- Potential for conflict(s) of interest:
  - I am a consultant to Merisant Australia, the University of Sydney; the Glycemic Index Foundation and Kuisine.
- Relationships with commercial interests:
  - Speakers Bureau/Honoraria:

    AstraZeneca, C3, ConTech, DiabetesNSW, DiabetesSA, DiabetesQld, Fonterra, GPCE, ILSI, Nestle, Novo Nordisk, OmniInnovation, Roche, University of Sydney.

  - Other:

    Author/co-author of several books on carbohydrates (starches and sugars), the glycemic index and alternative sweeteners.

The headlines

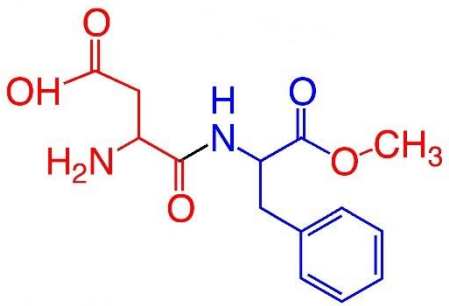


Compounds like saccharin are potent sweeteners, but new research suggests they could be a bitter pill for some gut microbes. Tobik/Shutterstock

Artificial sweeteners may contribute to diabetes, controversial study finds

By Kai Kupferschmidt | Sep. 17, 2014 , 1:15 PM

The Facts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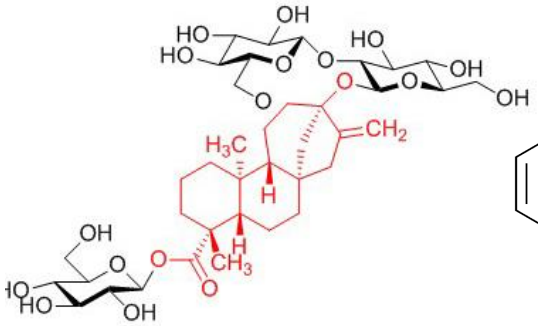
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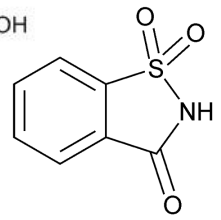
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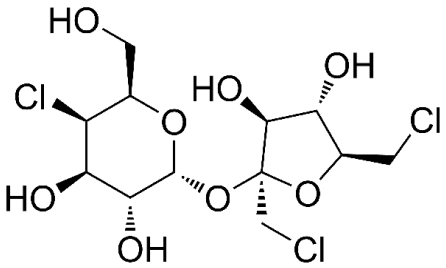
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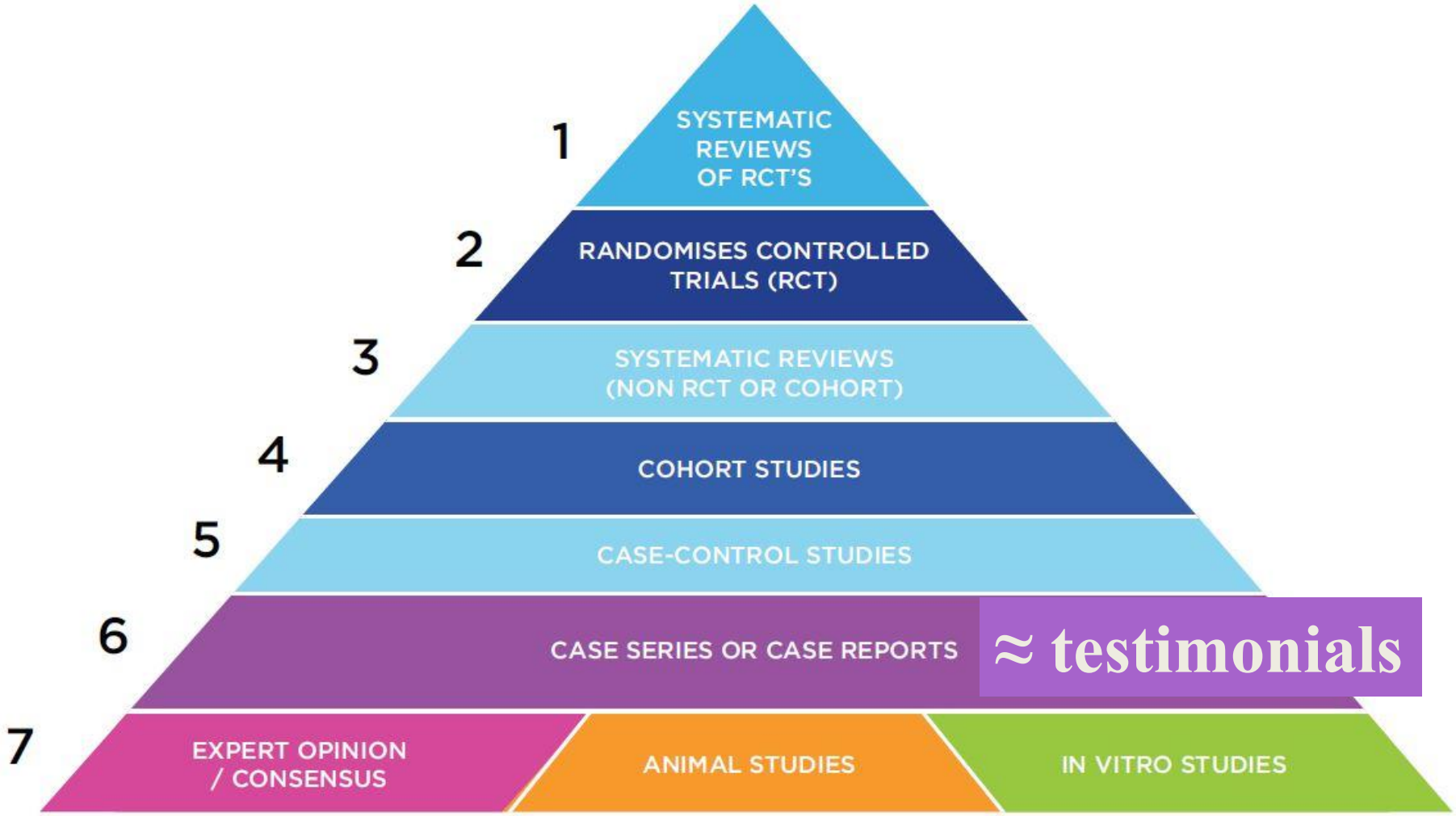
Scientific evidence hierarchy

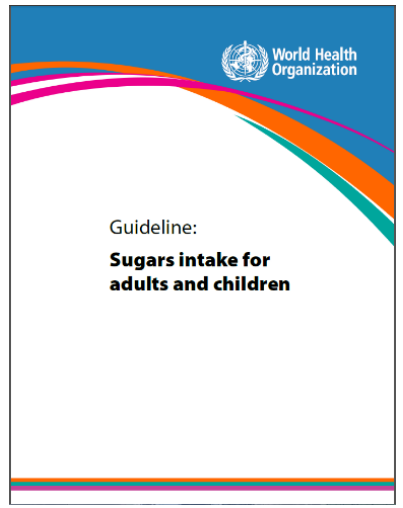


Sugars

World Health Organization (WHO) Sugars Classification

- **Monosaccharides and disaccharides =**

  fructose, galactose, glucose/dextrose, lactose, maltose sucrose



- **Total sugars** =

  naturally occurring in food (e.g., fruit and milk) + added sugars

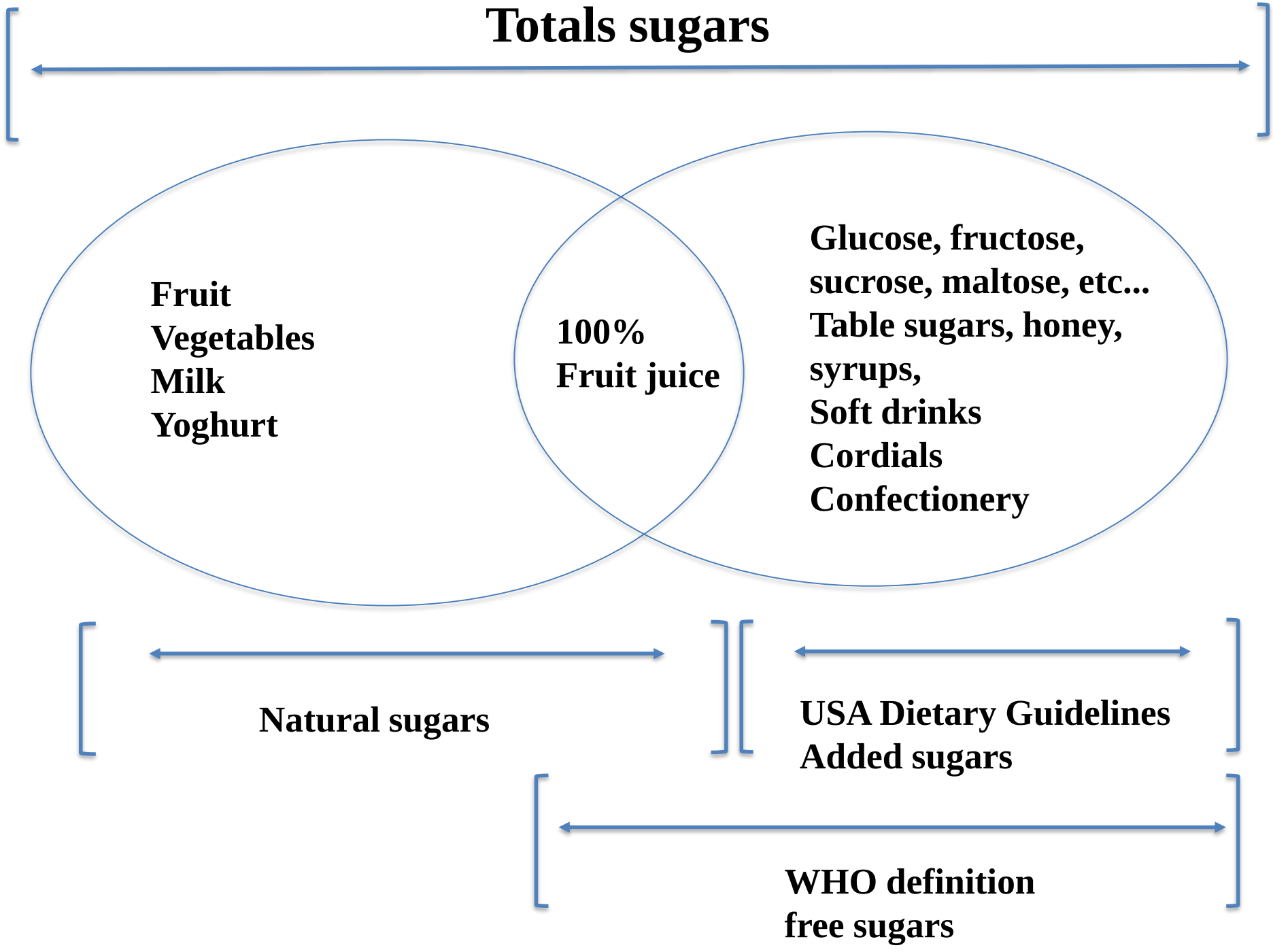
- **Added sugars =**

  added during processing and food preparation by food manufacturers, cooks or consumers

- **Free sugars** =

  added sugars + honey + syrups (agave, maple, rice, etc…) + fruit juice/concentrates

Guideline: Sugars intake for adults and children. World Health Organization, 2015

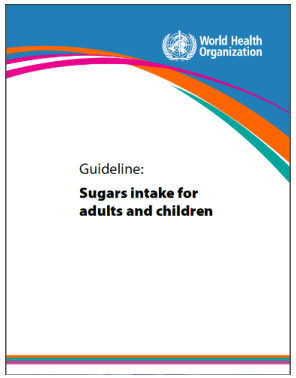

Totals sugars
Fruit
Vegetables
Milk
Yoghurt
100%
Fruit juice
Glucose, fructose,
sucrose, maltose, etc...
Table sugars, honey,
syrups,
Soft drinks
Cordials
Confectionery
Natural sugars
USA Dietary Guidelines
Added sugars
WHO definition
free sugars

2015 WHO Guideline:
Sugars intake for adults and children.

Recommendations:

- In both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of total energy intake (strong recommendation).

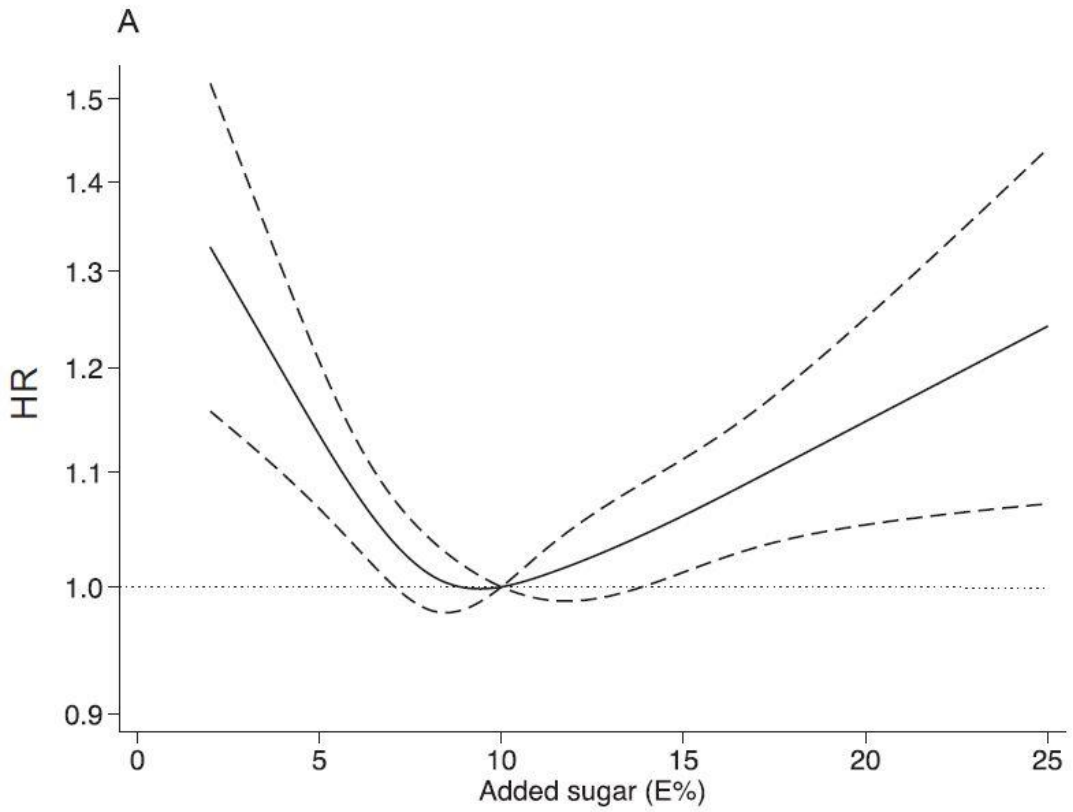
- WHO suggests a further reduction of the intake of free sugars to below 5% of total energy intake (conditional recommendation).



Guideline: Sugars intake for adults and children. Geneva: World Health Organization; 2015.

Association between free / added sugars intake and mortality

- Prospective cohort studies of ~50,000 middle aged (36-73 years) Swedes with ~ 20 years of follow-up time.
- 9,190 deaths.
- lowest mortality with added sugar intakes 7.5% - 10%E.
- Intakes >20%E were associated with a 30% increased mortality risk.
- Intakes <5%E had a 23% increase in risk.



Ramne et al; AJCN, 2019.

Do sugars cause weight gain in humans?

2013 WHO review of sugars and overweight/obesity

- SLR and meta-analysis of 30 RCTs and 38 cohort studies.
- ↓ intake of dietary sugars was associated with ↓ body weight (0.80 kg, 95% confidence interval 0.39 to 1.21; P<0.001) in adults;
- ↑ sugars intake was associated ↑ weight (0.75 kg, 0.30 to 1.19; P=0.001) in adults.
- No association between advice to reduce intake of dietary sugars and change in standardised BMI or BMI z score in children (0.09, 95%CI −0.14 to 0.32).
- Isoenergetic exchange of dietary sugars with other carbohydrates (e.g., starches) showed no change in body weight (0.04 kg, −0.04 to 0.13).

Te Morenga et al. BMJ 2013

2013 WHO review of sugars and overweight/obesity

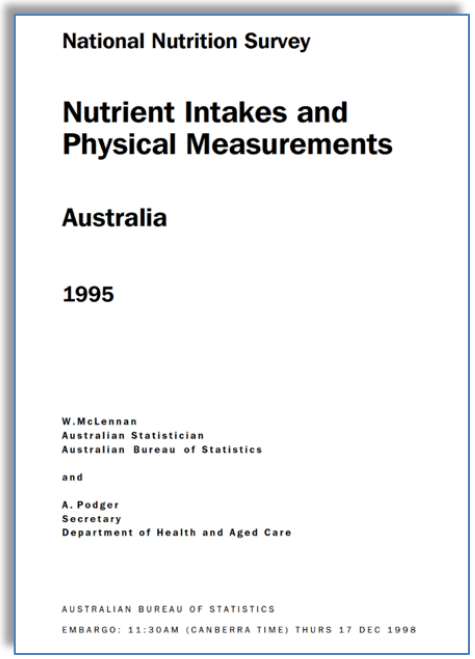
"*The data suggest that the change in body fatness that occurs with modifying intake of sugars results from an alteration in energy balance rather than a physiological or metabolic consequence of monosaccharides or disaccharides.*"

"*Owing to the multifactorial causes of obesity, it is unsurprising that the effect of reducing intake is relatively small.*"

Te Morenga et al. BMJ 2013

How much “sugar” are we consuming?

Macronutrient consumption in Australia 1995–2011/2


National Nutrition Survey

Nutrient Intakes and Physical Measurements

Australia

1995

W.McLennan
Australian Statistician
Australian Bureau of Statistics

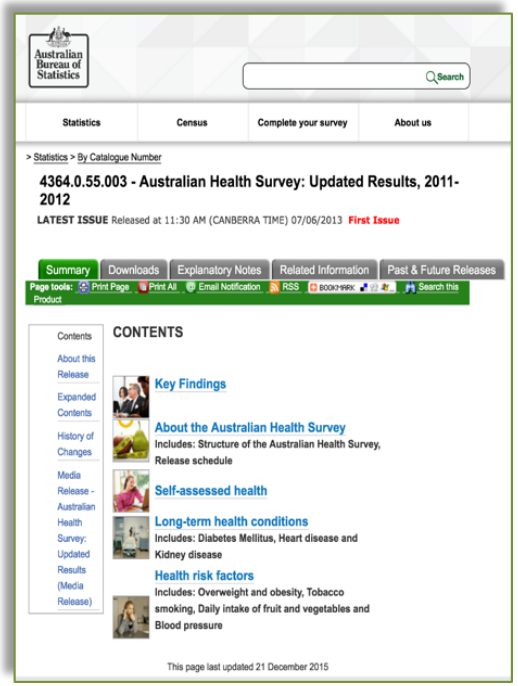
and

A. Podger
Secretary
Department of Health and Aged Care

AUSTRALIAN BUREAU OF STATISTICS

EMBARGO: 11:30AM (CANBERRA TIME) THURS 17 DEC 1998

~14,000 people
61% response rate
24 h recall


Australian Bureau of Statistics

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Statistics | Census | Complete your survey | About us

> Statistics > By Catalogue Number

4364.0.55.003 - Australian Health Survey: Updated Results, 2011-2012

LATEST ISSUE Released at 11:30 AM (CANBERRA TIME) 07/06/2013 First Issue

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Expanded Contents
History of Changes
Media Release - Australian Health Survey: Updated Results (Media Release)

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Key Findings

About the Australian Health Survey
Includes: Structure of the Australian Health Survey, Release schedule

Self-assessed health

Long-term health conditions
Includes: Diabetes Mellitus, Heart disease and Kidney disease

Health risk factors
Includes: Overweight and obesity, Tobacco smoking, Daily intake of fruit and vegetables and Blood pressure

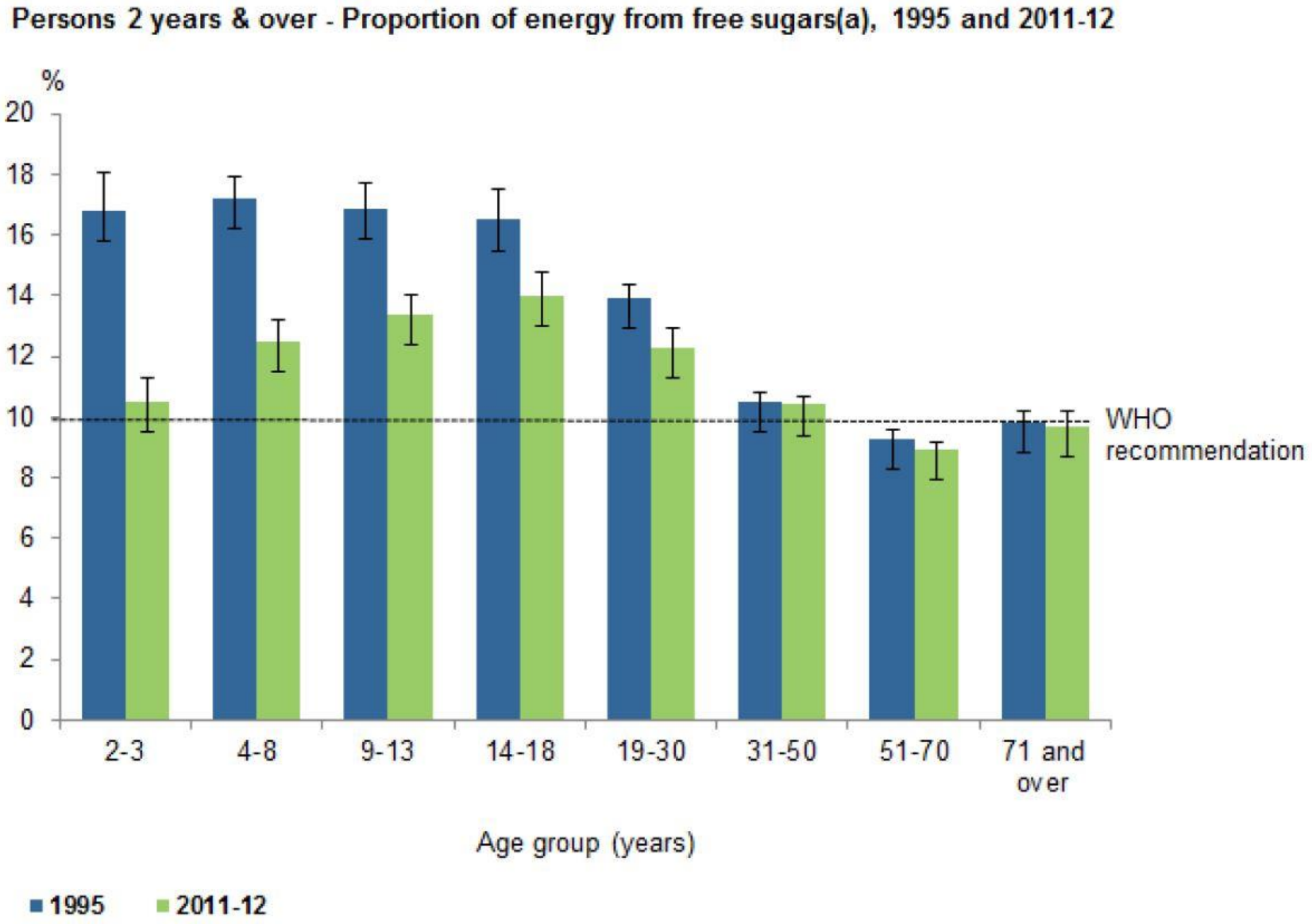
This page last updated 21 December 2015

~12,000 people
77% response rate
24 h recall

ABS. National Nutrition Survey. Com of Aust, 1998; ABS. Australian survey. Com of Aust, 2014.

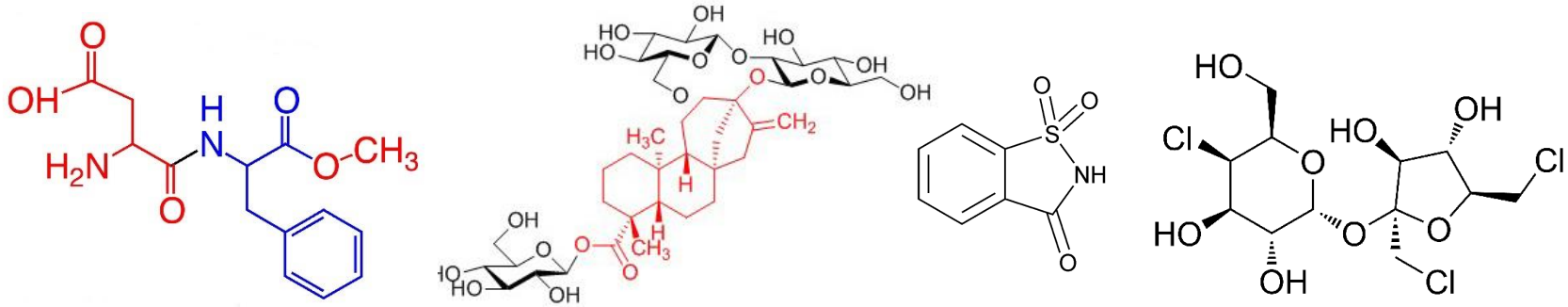
Aren’t we all having too much sugar?

Free sugars intake **(%E)**



ABS. Australian Health Survey: Consumption of Added Sugars. Com of Aust, 2017.

Intense (“Artificial”) sweeteners



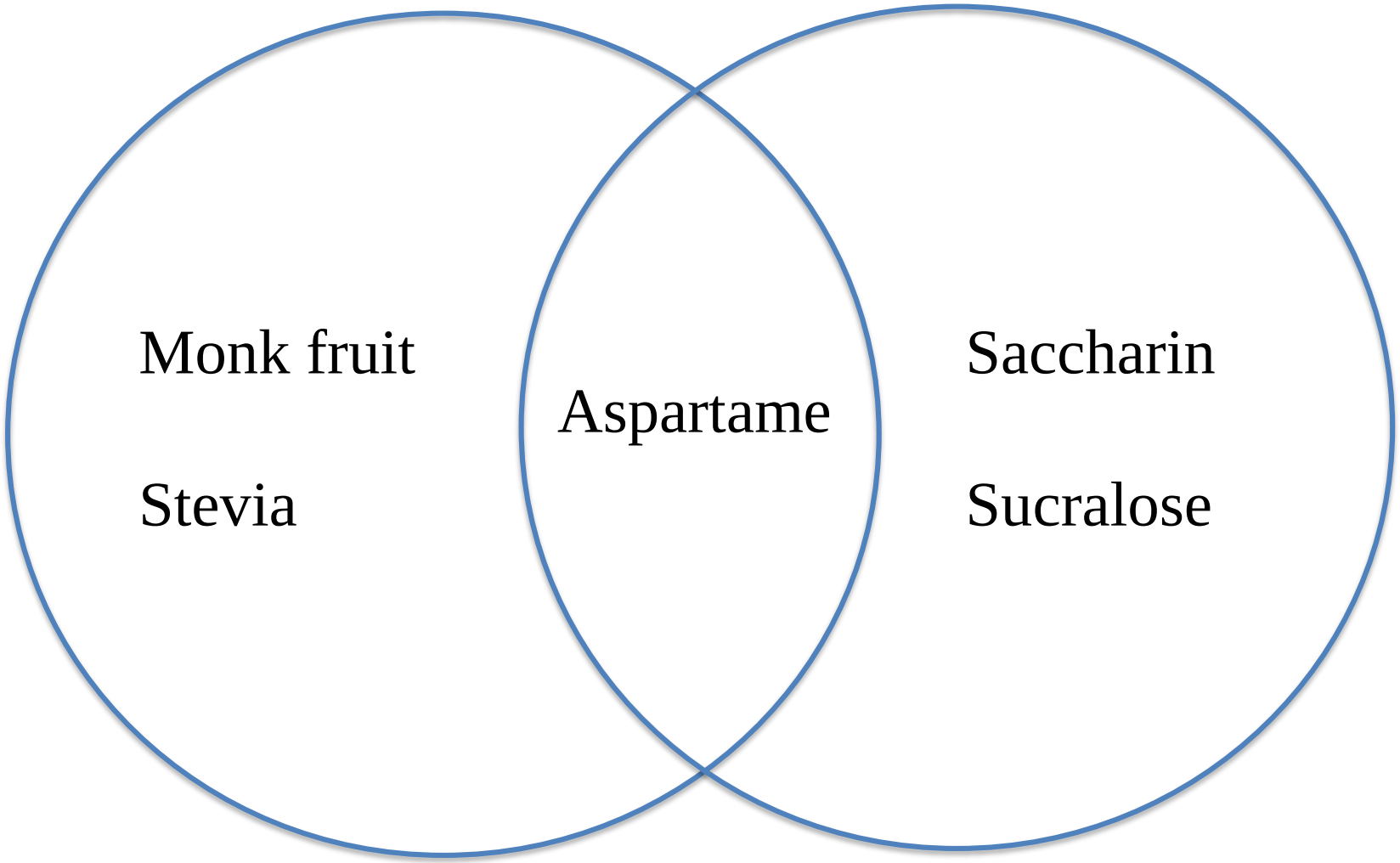
Intense sweeteners = non-nutritive / “Artificial” sweeteners

- Zero- or low-kilojoule alternatives to free and added sugars, such as table sugar, honey and syrups.
- 100s of times sweeter than sucrose, so only small amounts are used in foods and beverages.
- FSANZ has approved the use of: alitame, acesulfame potassium (Ace K), **aspartame**, advantame, cyclamate, neotame, **saccharin**, **steviol glycosides (“stevia”)**, **sucralose,** luo han guo **(**monk fruit) and thaumatin.
- Labelled low-calorie, low-kilojoule, non-caloric, non-nutritive, and diet.

http://www.foodstandards.gov.au/consumer/additives/intensesweetener/pages/default.aspx.

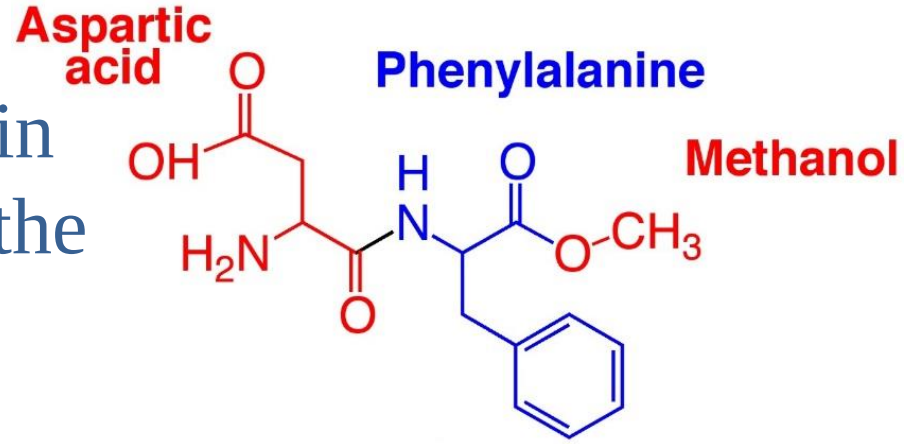
Intense sweeteners

“Natural” → “Artificial”



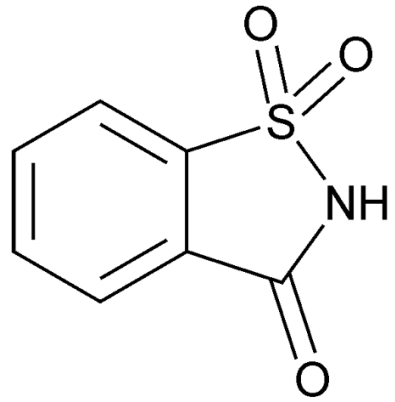
Aspartame

- Composed of two common amino acids: aspartic acid and phenylalanine.
- Produced via bacterial fermentation (*B thermoproteolyticus*) or through a chemical process.
- After swallowing, aspartame is rapidly (within a few minutes) and fully broken-down within the gastro-intestinal tract and is not detectable in blood.
- Methanol (10%) and the amino acids aspartic acid (45%) and phenylalanine (45%) are absorbed into the blood.



Saccharin

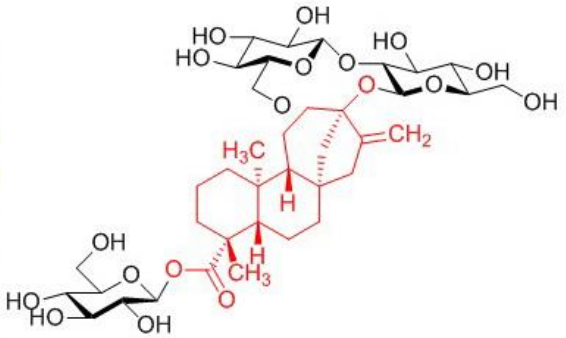
- Saccharin was discovered serendipitously by chemists in 1878.
- Usage peaked in World War 1 and II
- It is a coal tar derivative.



- Saccharin, and its salts ammonium saccharin, calcium saccharin, potassium saccharin and **sodium saccharin** have been used as sweetening agents in a selected range of foods and beverages for > 130 years.

“Stevia”

- Diterpenoids are a group of naturally occurring compounds, commonly found in plants - in particular vegetables, fruits, tea, and wine.
- Steviol glycosides, a family of diterpenoids (11 varieties identified to-date), are derived from the South American plant *Stevia rebaudiana Bertoni*, and are commonly known as “Stevia” around the globe.
- For human consumption, they are extracted from the Stevia rebaudiana Bertoni plant to 95%+ purity using a standardised process.



Stevia ≈ Steviol glycosides

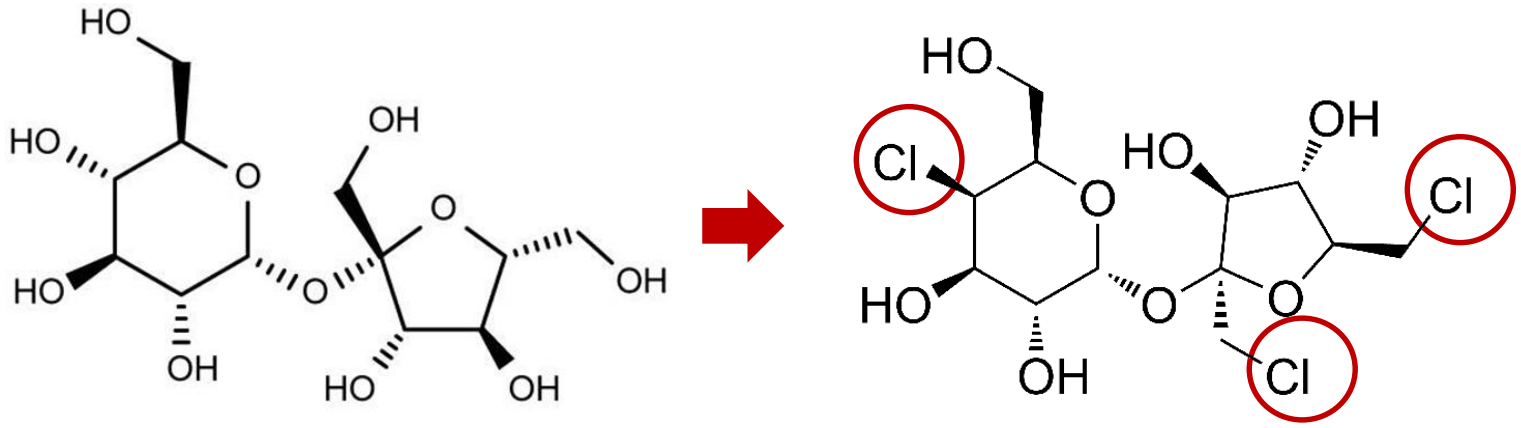
Trivial name	Formula	MW (g/mol)	Conversion factor X
Steviol	$C_{20}H_{30}O_3$	318.45	1.00
Stevioside	$C_{38}H_{60}O_{18}$	804.87	0.40
Rebaudioside A	$C_{44}H_{70}O_{23}$	967.01	0.33
Rebaudioside C	$C_{44}H_{70}O_{22}$	951.01	0.34
Dulcoside A	$C_{38}H_{60}O_{17}$	788.87	0.40
Rubusoside	$C_{32}H_{50}O_{13}$	642.73	0.50
Steviolbioside	$C_{32}H_{50}O_{13}$	642.73	0.50
Rebaudioside B	$C_{38}H_{60}O_{18}$	804.87	0.40
Rebaudioside D	$C_{50}H_{80}O_{28}$	1129.15	0.29
Rebaudioside E	$C_{44}H_{70}O_{23}$	967.01	0.33
Rebaudioside F	$C_{43}H_{68}O_{22}$	936.99	0.34

EFSA Journal 2010;8(4):1537

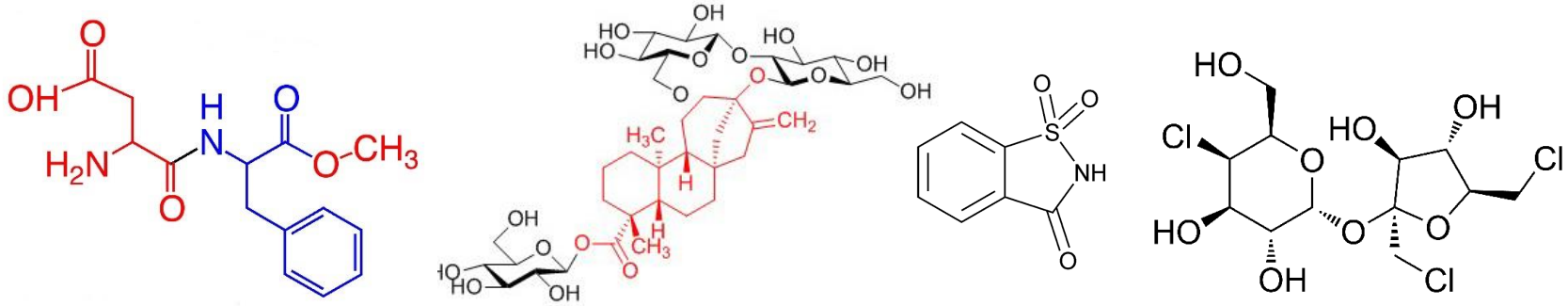
Sucralose

- Is a disaccharide made from sucrose.

- In a 5-step process, 3 of sucrose's hydroxyl groups are replaced with 3 atoms of chlorine.



Are intense sweeteners safe?



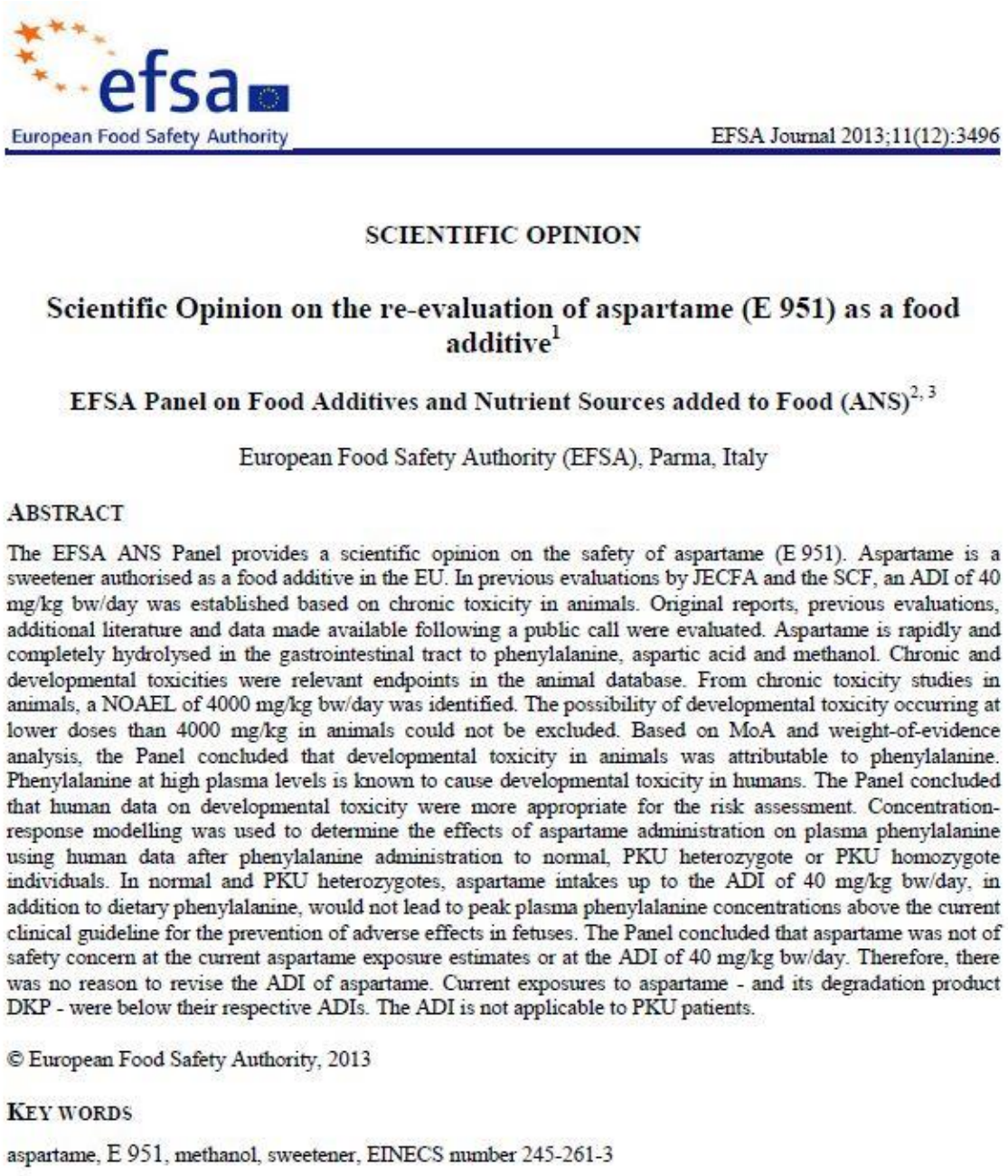
Acceptable daily intake (ADI)

- The ADI for humans is considered to be a level of intake of a substance that can be **consumed daily** over an **entire lifetime without any appreciable risk to health**.
- Calculated by dividing the overall No Observable Adverse Effect Level (NOEL) from animal studies by a safety factor (typically 100).
- The magnitude of the safety factor is selected to account for uncertainties in extrapolation of animal data to humans, variation between people, the completeness of the toxicological data base and the nature of any potential adverse effects.

Australian Government Department of Health, Canberra, 2015

Aspartame

- European Food S… ll toxicological, carcinogenicity, te… on aspartame and its metabolite… nans in 2013.
- In rat studies, th… mg aspartame/kg bw/day) produced… be of minimal toxicological sign…
- A dose-depende… 2000 and 4000 mg/kg bw/day co… ption was reported in one st…



efsa
European Food Safety Authority

EFSA Journal 2013;11(12):3496

SCIENTIFIC OPINION

Scientific Opinion on the re-evaluation of aspartame (E 951) as a food additive[1]

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The EFSA ANS Panel provides a scientific opinion on the safety of aspartame (E 951). Aspartame is a sweetener authorised as a food additive in the EU. In previous evaluations by JECFA and the SCF, an ADI of 40 mg/kg bw/day was established based on chronic toxicity in animals. Original reports, previous evaluations, additional literature and data made available following a public call were evaluated. Aspartame is rapidly and completely hydrolysed in the gastrointestinal tract to phenylalanine, aspartic acid and methanol. Chronic and developmental toxicities were relevant endpoints in the animal database. From chronic toxicity studies in animals, a NOAEL of 4000 mg/kg bw/day was identified. The possibility of developmental toxicity occurring at lower doses than 4000 mg/kg in animals could not be excluded. Based on MoA and weight-of-evidence analysis, the Panel concluded that developmental toxicity in animals was attributable to phenylalanine. Phenylalanine at high plasma levels is known to cause developmental toxicity in humans. The Panel concluded that human data on developmental toxicity were more appropriate for the risk assessment. Concentration-response modelling was used to determine the effects of aspartame administration on plasma phenylalanine using human data after phenylalanine administration to normal, PKU heterozygote or PKU homozygote individuals. In normal and PKU heterozygotes, aspartame intakes up to the ADI of 40 mg/kg bw/day, in addition to dietary phenylalanine, would not lead to peak plasma phenylalanine concentrations above the current clinical guideline for the prevention of adverse effects in fetuses. The Panel concluded that aspartame was not of safety concern at the current aspartame exposure estimates or at the ADI of 40 mg/kg bw/day. Therefore, there was no reason to revise the ADI of aspartame. Current exposures to aspartame - and its degradation product DKP - were below their respective ADIs. The ADI is not applicable to PKU patients.

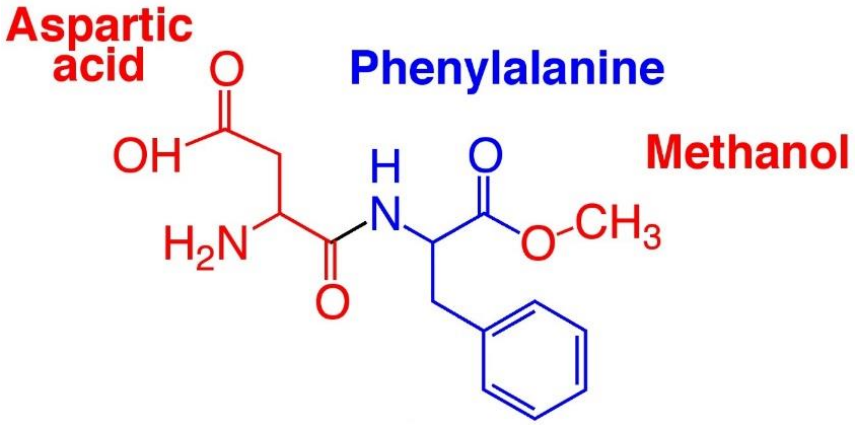
KEY WORDS

aspartame, E 951, methanol, sweetener, EINECS number 245-261-3

EFSA Journal 2013;11(12):3496

Aspartame

- Overall, the Panel derived a No Observable Adverse Effect Level (NOEL) of 4000 mg/kg bw/day from the four studies.
- In 1983, the United States Food and Drug Administration (FDA) set the ADI for aspartame at 50 mg/kg bw.
- In Australia, FSANZ established an ADI of 40 mg/kg bw/day.
- A 60 kg Australian would need to consume 60 sachets of a typical aspartame sweetener per day to exceed this.

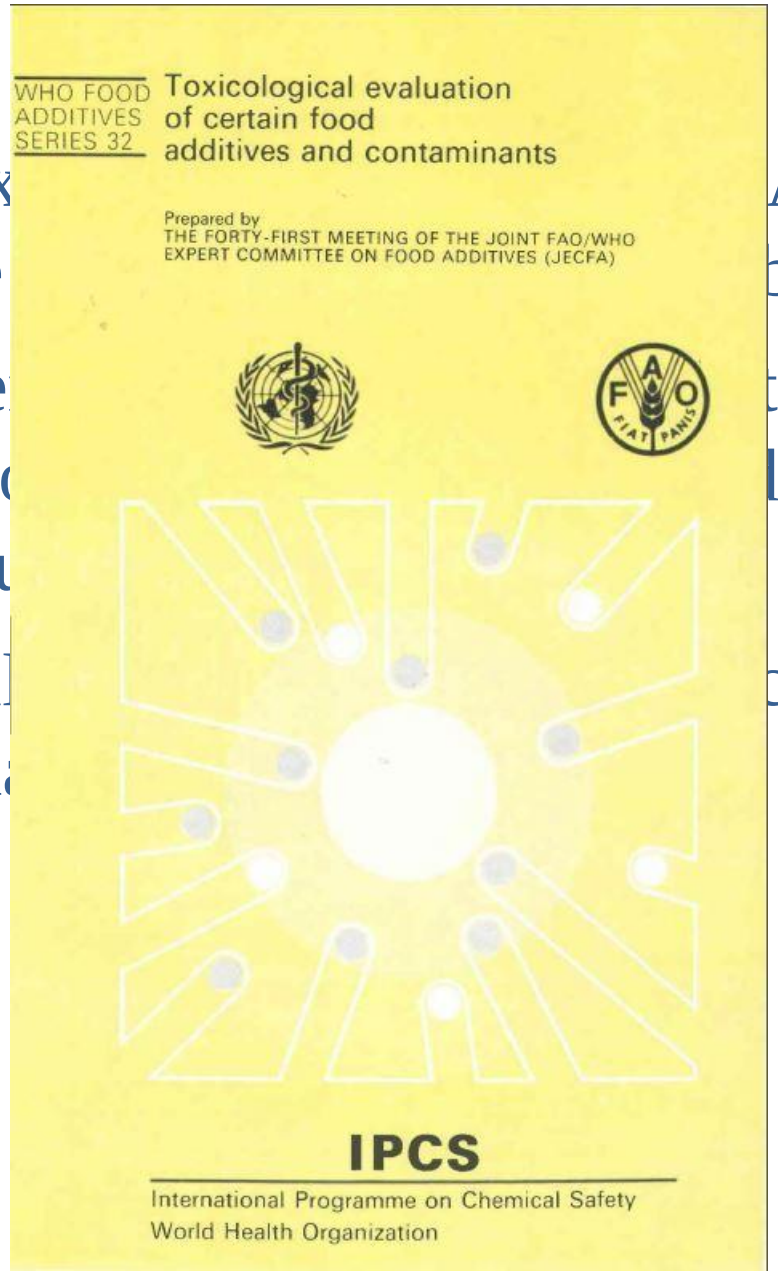


ADI for saccharin

• The Joint FAO/WHO Ex Additives (JECFA) established an Acceptable body weight/day.

• It was based on a 2 gene ts, where they were fed the equivalent of 500 mg ly weight per day, and the application of a 100-fold u

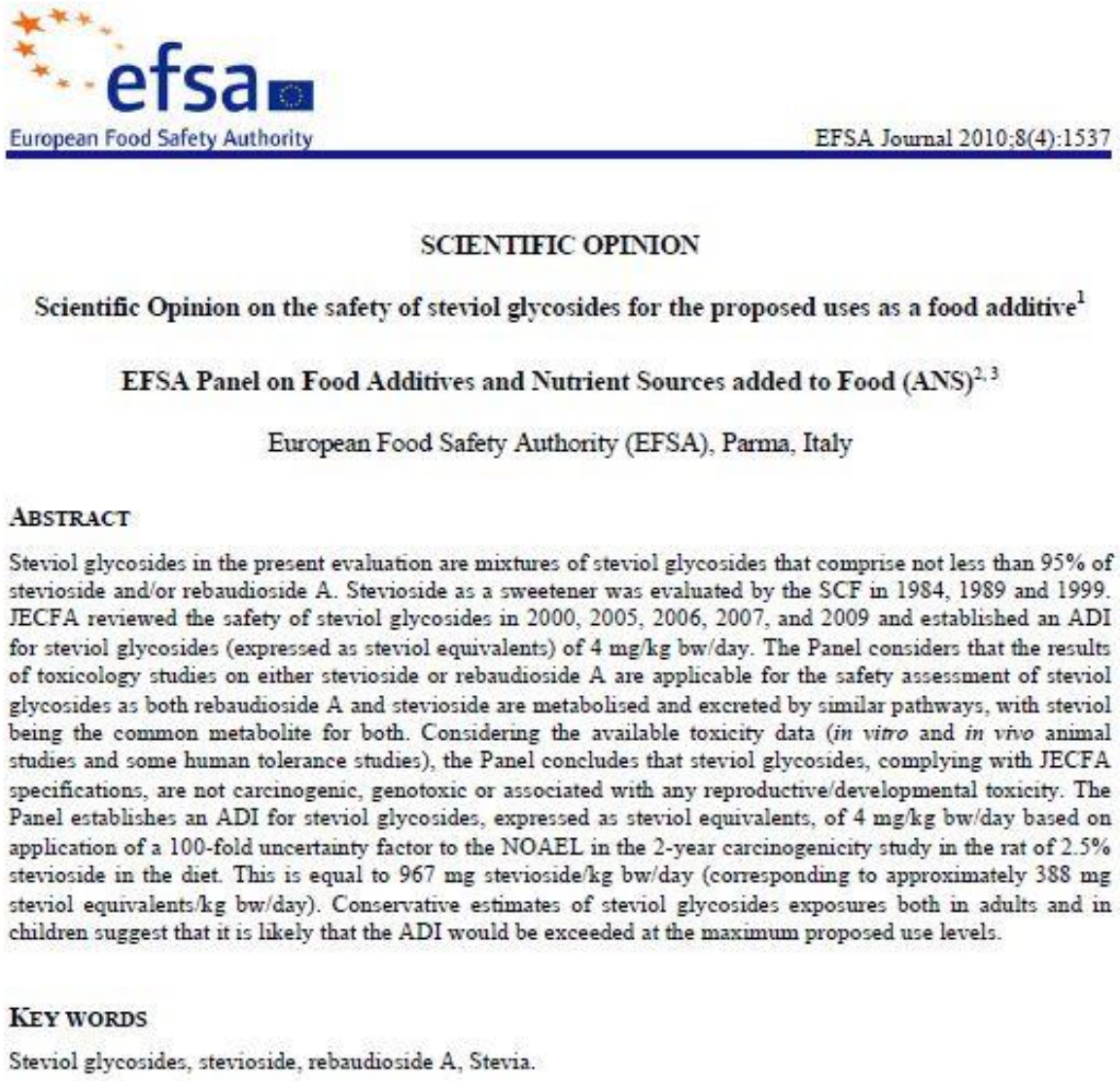
• A 60 kg Australian woul chets of a typical saccharin sweetener per da



JECFA, Series 32, WHO, 1993.

ADI for steviol glycosides

- EFSA considered [illegible] ducts, metabolism and toxicology for [illegible] ceptable Daily Intake, expressed a[illegible] eight/day.
- It was based on a[illegible] r to the NOEL for stevioside of 967 m[illegible] o approximately 388 mg steviol equ[illegible] ogenicity study in rats.
- A 60 kg Australi[illegible] typical stevia sweetener per day [illegible]



European Food Safety Authority EFSA Journal 2010;8(4):1537

SCIENTIFIC OPINION

Scientific Opinion on the safety of steviol glycosides for the proposed uses as a food additive[1]

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Steviol glycosides in the present evaluation are mixtures of steviol glycosides that comprise not less than 95% of stevioside and/or rebaudioside A. Stevioside as a sweetener was evaluated by the SCF in 1984, 1989 and 1999. JECFA reviewed the safety of steviol glycosides in 2000, 2005, 2006, 2007, and 2009 and established an ADI for steviol glycosides (expressed as steviol equivalents) of 4 mg/kg bw/day. The Panel considers that the results of toxicology studies on either stevioside or rebaudioside A are applicable for the safety assessment of steviol glycosides as both rebaudioside A and stevioside are metabolised and excreted by similar pathways, with steviol being the common metabolite for both. Considering the available toxicity data (*in vitro* and *in vivo* animal studies and some human tolerance studies), the Panel concludes that steviol glycosides, complying with JECFA specifications, are not carcinogenic, genotoxic or associated with any reproductive/developmental toxicity. The Panel establishes an ADI for steviol glycosides, expressed as steviol equivalents, of 4 mg/kg bw/day based on application of a 100-fold uncertainty factor to the NOAEL in the 2-year carcinogenicity study in the rat of 2.5% stevioside in the diet. This is equal to 967 mg stevioside/kg bw/day (corresponding to approximately 388 mg steviol equivalents/kg bw/day). Conservative estimates of steviol glycosides exposures both in adults and in children suggest that it is likely that the ADI would be exceeded at the maximum proposed use levels.

KEY WORDS

Steviol glycosides, stevioside, rebaudioside A, Stevia.

EFSA Journal 2010;8(4):1537

ADI for sucralose

- EFSA established an A ng/kg body weight/day.
- US FDA 5 mg / kg bv
- EFSA was based on t day from a long-term study in rats, which hac d a safety factor of 100.
- A 60 kg Australian w ts of sucralose per day to exceed this.

EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions
C3 - Management of scientific committees II; scientific co-operation and networks

SCIENTIFIC COMMITTEE ON FOOD

SCF/CS/ADDS/EDUL/190 Final
12/9/2000

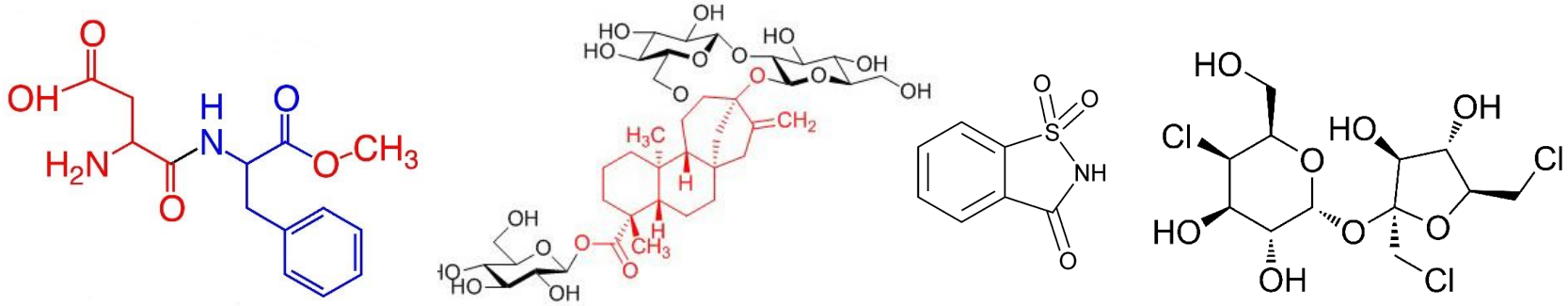
Opinion of the Scientific Committee on Food on sucralose

(Adopted by the SCF on 7 September 2000)

Rue de la Loi 200, B-1049 Brussels.
Telephone: direct line 295 81 10, 296 59 48, 296 48 70 - standard: 299 11 11, fax: 299.48 91
Telex COMEU B 21877, Telegraphic address COMEUR Brussels
P:\food2\hojovi\scf\op_final\Sucralose2000.doc

EC.SCF, 2000

How much are we consuming?



Intense sweetener consumption in Australia

FSANZ non-nutritive sweetener surveys: 1994 and 2003

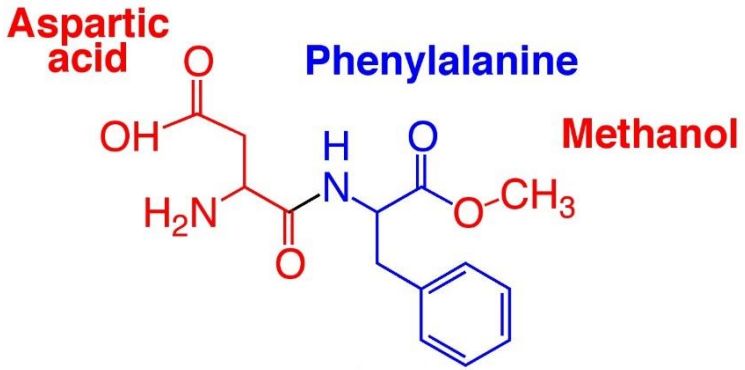
- 1994: 51%
- 2003: 66%

Food/Drink		1994	2003
Soft drinks (mL)	Diet	58	81
	Regular	257	249
Cordials (mL)	Diet	12	31
	Regular	162	151
Flavoured milks (mL)	Diet	4	10
	Regular	13	19
TT sweetener (g)	Diet	0.3	1
	Regular	9	13
Yoghurt/mousse (g)	Diet	4	10
	Regular	13	19
Jellies/puddings (g)	Diet	0.4	1
	Regular	4	2
Jams (g)	Diet	0.1	0.3
	Regular	3	2

Food Standards Australia New Zealand, 2004.

Aspartame consumption in Australia

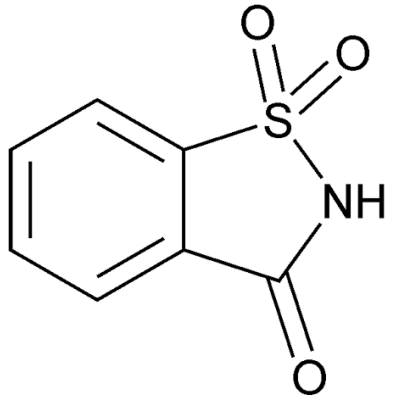
- **1994:** 182 mg / day, or **2.4 mg / kg body weight / day**.
- **2003:** 187 mg / day, or **2.6 mg / kg body weight / day**, which was 7% of the ADI.
- The **95th Centile** of intake in 2003 was 628 mg / day, or **7.5 mg / kg body weight / day**, which was **~20% of the ADI**.
- In 2003, 96% of **people with diabetes** consumed aspartame, with mean intake for consumers 2.31 mg / kg body weight / day and the **95th Centile 7.47 mg / kg body weight / day**.



Food Standards Australia New Zealand, 2004.

Saccharin consumption in Australia

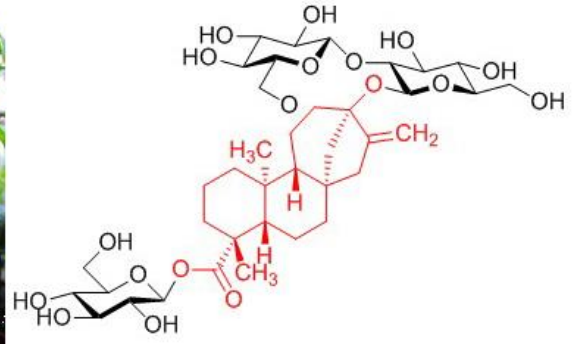
- In **1994**, people aged 12-39 years consumed **31 mg saccharin / day**
- In **2003**, they consumed **25 mg / day**.
- Average intake of consumers in 2003 was 33 mg / day, or **0.53 mg / kg body weight / day**, which was **~11% of the ADI**.
- The **95th Centile of intake** in 2003 was 168 mg / day, or 2.54 mg / kg body weight / day, which was **~50% of the ADI**.



Food Standards Australia New Zealand, 2004.

Steviol consumption estimates

- Steviol glycosides (95%+ Stevioside and Reb A) approved by FSANZ for use in foods and beverages in 2008.
- No data on actual consumption of “stevia” currently available.
- FSANZ conducted extensive modelling using DIAMOND for 2 scenarios prior to its approval:
  - 100% replacement of added sugars, and
  - 30% replacement of added sugars.



Food Standards Australia New Zealand, Application A540, 2008.

Australia and NZ steviol consumption estimates

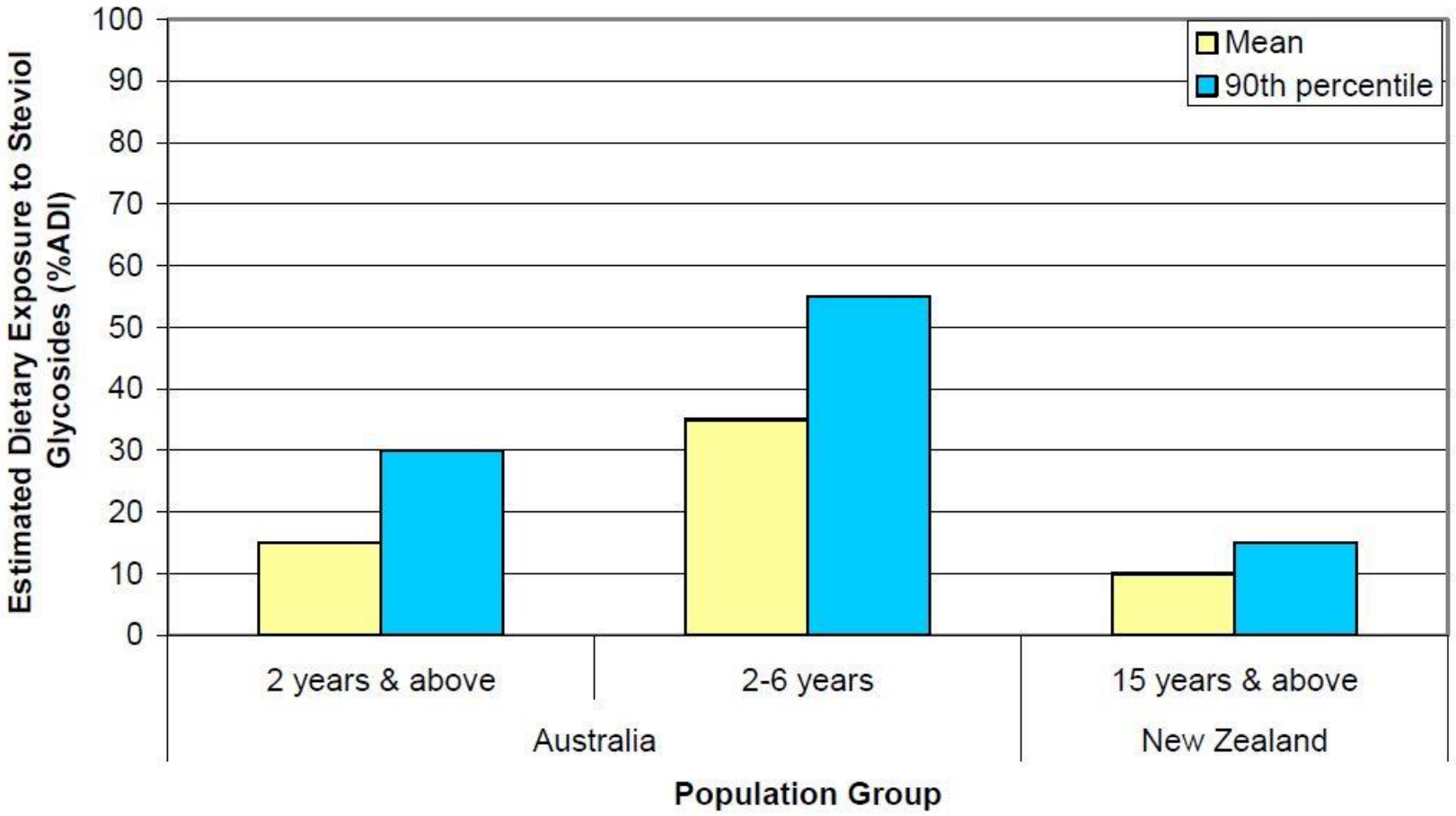
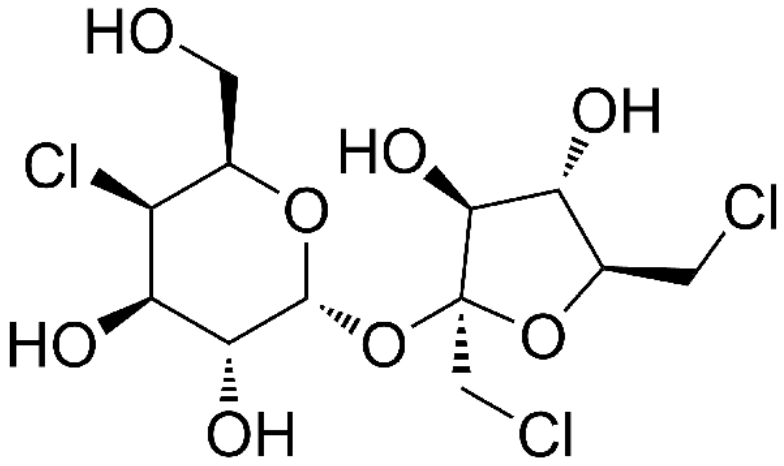


Figure 7: Estimated dietary exposures to steviol glycosides for the 30% market share scenario, as a percentage of the ADI

Food Standards Australia New Zealand, Application A540, 2008.

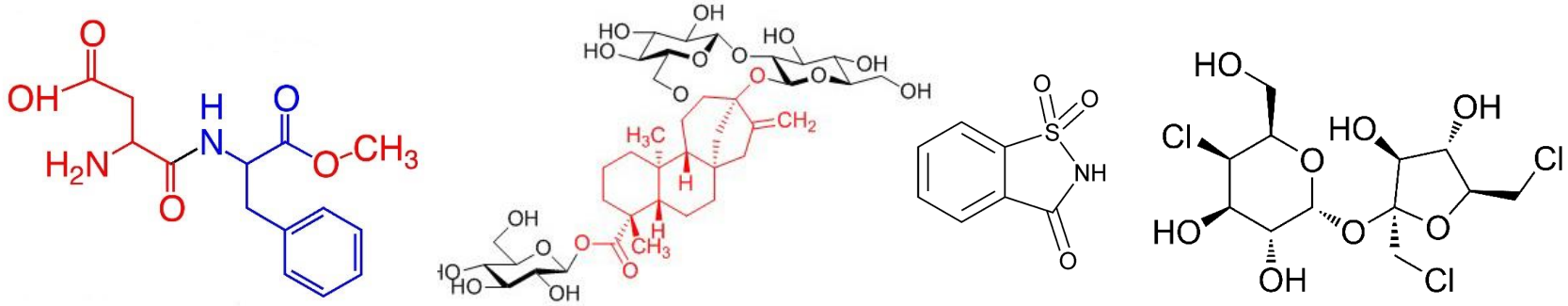
Sucralose consumption in Australia

- No data are available for 1994
- In **2003**, Australians consumed an average of **11 mg / day**.
- Average intake of consumers in 2003 was 29 mg / day, or **0.45 mg / kg body weight / day**, which was **3% of the ADI**.
- The **95th Centile** of intake of consumers was 188 mg / day, or **2.44 mg / kg body weight / day**, which was **16% of the ADI**.

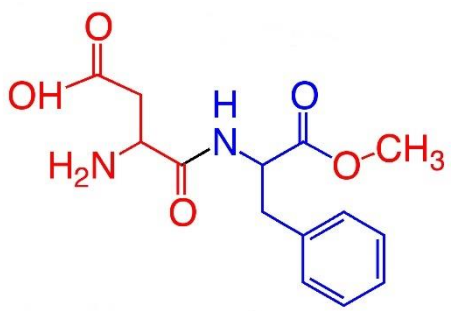


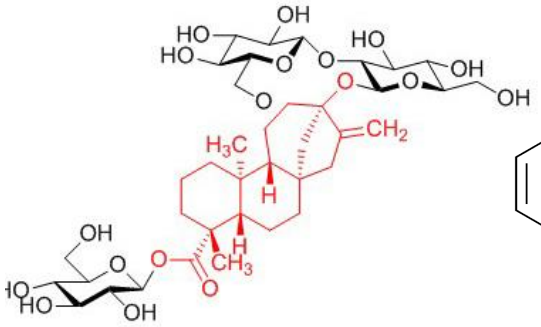
Food Standards Australia New Zealand, 2004.

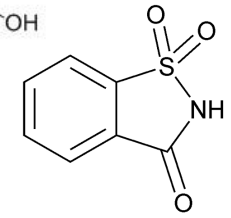
Intense sweeteners and health

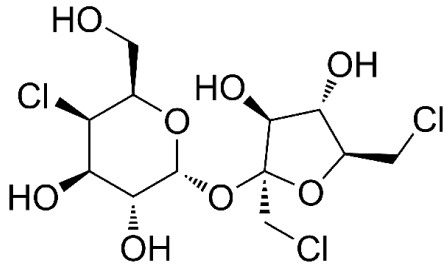


Intense sweeteners and weight









“Artificial sweeteners are just as bad as sugar”

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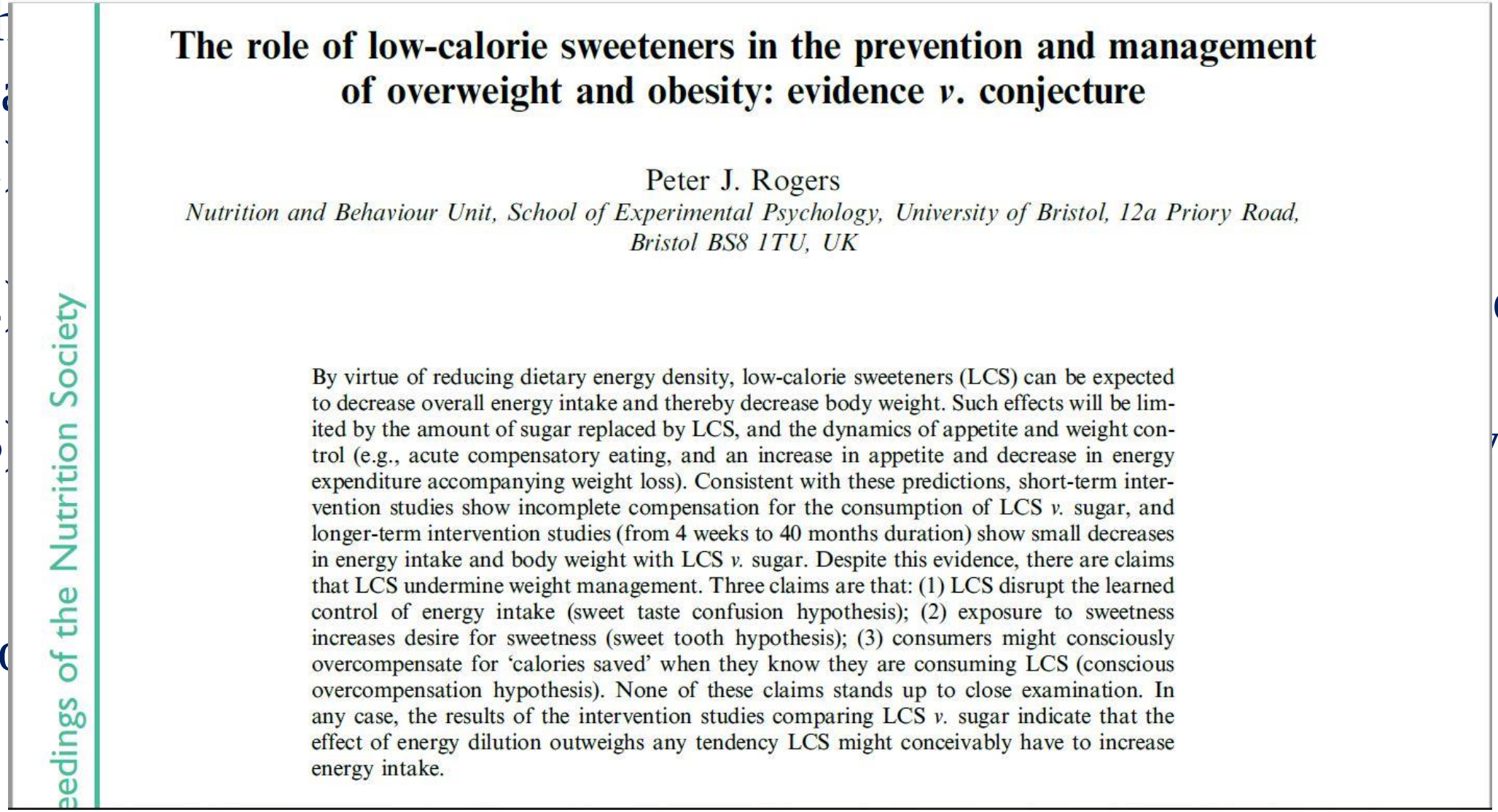


The role of low-calorie sweeteners in the prevention and management of overweight and obesity: evidence *v.* conjecture

Peter J. Rogers
Nutrition and Behaviour Unit, School of Experimental Psychology, University of Bristol, 12a Priory Road, Bristol BS8 1TU, UK

By virtue of reducing dietary energy density, low-calorie sweeteners (LCS) can be expected to decrease overall energy intake and thereby decrease body weight. Such effects will be limited by the amount of sugar replaced by LCS, and the dynamics of appetite and weight control (e.g., acute compensatory eating, and an increase in appetite and decrease in energy expenditure accompanying weight loss). Consistent with these predictions, short-term intervention studies show incomplete compensation for the consumption of LCS *v.* sugar, and longer-term intervention studies (from 4 weeks to 40 months duration) show small decreases in energy intake and body weight with LCS *v.* sugar. Despite this evidence, there are claims that LCS undermine weight management. Three claims are that: (1) LCS disrupt the learned control of energy intake (sweet taste confusion hypothesis); (2) exposure to sweetness increases desire for sweetness (sweet tooth hypothesis); (3) consumers might consciously overcompensate for ‘calories saved’ when they know they are consuming LCS (conscious overcompensation hypothesis). None of these claims stands up to close examination. In any case, the results of the intervention studies comparing LCS *v.* sugar indicate that the effect of energy dilution outweighs any tendency LCS might conceivably have to increase energy intake.

eedings of the Nutrition Society

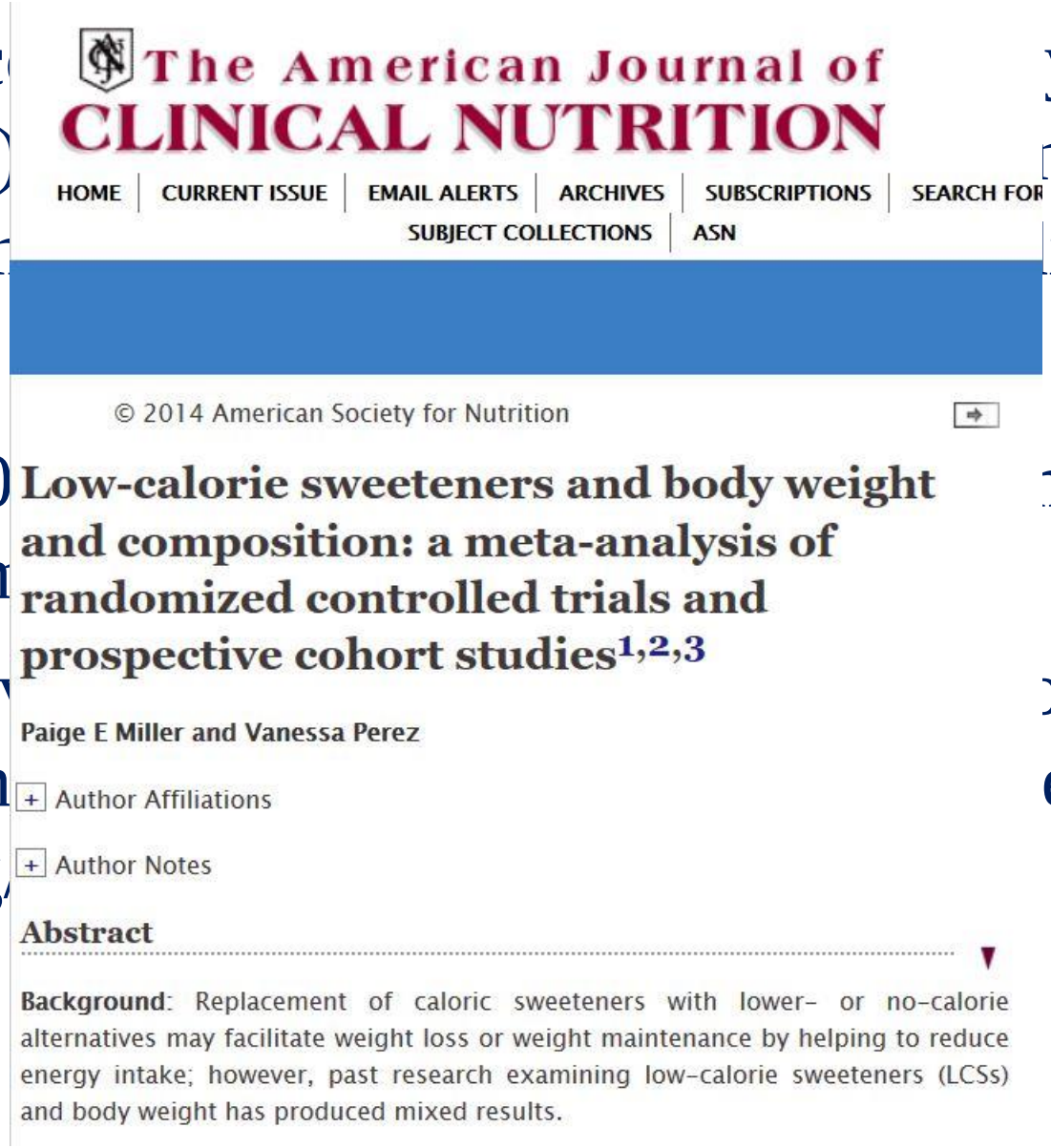
Rogers. Proc Nutr Soc. 2017; Mattes and Popkin. AJCN. 2009

IS and overweight/obesity

• In 15 randomised c y/o) where aspartame (9 studies) ned foods and beverages are consur ies of 3 – 78 weeks duration.

• Body weight (-0.80 m^2), fat mass (-1.10 kg), and waist circun

• Among 9 prospecti ot associated with body weight or fat m ed with slightly higher BMI (0.03 kg/



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Low-calorie sweeteners and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohort studies[1,2,3]

Paige E Miller and Vanessa Perez

+ Author Affiliations

+ Author Notes

Abstract

Background: Replacement of caloric sweeteners with lower- or no-calorie alternatives may facilitate weight loss or weight maintenance by helping to reduce energy intake; however, past research examining low-calorie sweeteners (LCSs) and body weight has produced mixed results.

Miller and Perez. AJCN, 2014

IS and overweight/obesity

• An SLR and M… …uming IS with *ad libitum* access to …

• Twelve prospec… …o association between IS use a… …ear, 95%CI −0.009 to 0.005).

International Journal of Obesity

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Review

International Journal of Obesity (2016) **40,** 381–394; doi:10.1038/ijo.2015.177; published online 10 November 2015

Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies

OPEN

P J Rogers[1], P S Hogenkamp[2], C de Graaf[3], S Higgs[4], A Lluch[5], A R Ness[6], C Penfold[6], R Perry[6], P Putz[7], M R Yeomans[8] and D J Mela[9]

[1]School of Experimental Psychology, University of Bristol, Bristol, UK
[2]Department of Neuroscience, Uppsala University, Uppsala, Sweden
[3]Division of Human Nutrition, Wageningen University, Wageningen, the Netherlands
[4]The School of Psychology, University of Birmingham, Birmingham, UK
[5]Danone Research, Centre Daniel Carasso, RD, Palaiseau Cedex, France
[6]National Institute for Health Research Biomedical Research Unit in Nutrition, Diet and Lifestyle at the University Hospitals Bristol NHS Foundation Trust and the University of Bristol and School of Oral and Dental Sciences, University of Bristol, Level 3, University Hospitals Bristol Education Centre, Bristol, UK
[7]European Branch, ILSI Europe a.i.s.b.l., Brussels, Belgium
[8]School of Psychology, University of Sussex, Brighton, UK
[9]Unilever R&D Vlaardingen, Vlaardingen, the Netherlands

Correspondence: Dr P Putz, European Branch, ILSI Europe a.i.s.b.l., Avenue E. Mounier 83, Box 6, Brussels B-1200, Belgium. E-mail: publications@ilsieurope.be

Received 13 November 2014; Revised 28 August 2015; Accepted 28 August 2015
Accepted article preview online 14 September 2015; Advance online publication 10 November 2015

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Papers by Rogers

Abstract

By reducing energy density, low-energy sweeteners (LES) might be expected to reduce energy intake (EI) and body weight (BW). To assess the totality of the evidence testing the null hypothesis that LES exposure (versus sugars or unsweetened alternatives) has no effect on EI or BW, we conducted a systematic review of relevant studies in animals and humans consuming LES with *ad libitum* access to food energy. In 62 of 90 animal studies exposure to LES did not affect or decreased BW. Of 28 reporting increased BW, 19 compared LES with glucose exposure using a specific 'learning' paradigm.

Rogers et al. IJO, 2016.

IS and overweight/obesity

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RESEARCH

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Association between intake of non-sugar sweeteners and health outcomes: systematic review and meta-analyses of randomised and non-randomised controlled trials and observational studies

Ingrid Toews,[1] Szimonetta Lohner,[2] Daniela Küllenberg de Gaudry,[1] Harriet Sommer,[1,3] Joerg J Meerpohl[1,4]

[1]Institute for Evidence in Medicine (for Cochrane Germany Foundation), Medical Centre of the University of Freiburg, Faculty of Medicine, University of Freiburg, Breisacher Straße 153, 79110 Freiburg, Germany
[2]Cochrane Hungary, Clinical Centre of the University of Pécs, Medical School, University of Pécs, Pécs, Hungary
[3]Institute for Medical Biometry and Statistics, Medical Centre of the University of Freiburg,

ABSTRACT

OBJECTIVE

To assess the association between intake of non-sugar sweeteners (NSS) and important health outcomes in generally healthy or overweight/obese adults and children.

DESIGN

Systematic review following standard Cochrane review methodology.

DATA SOURCES

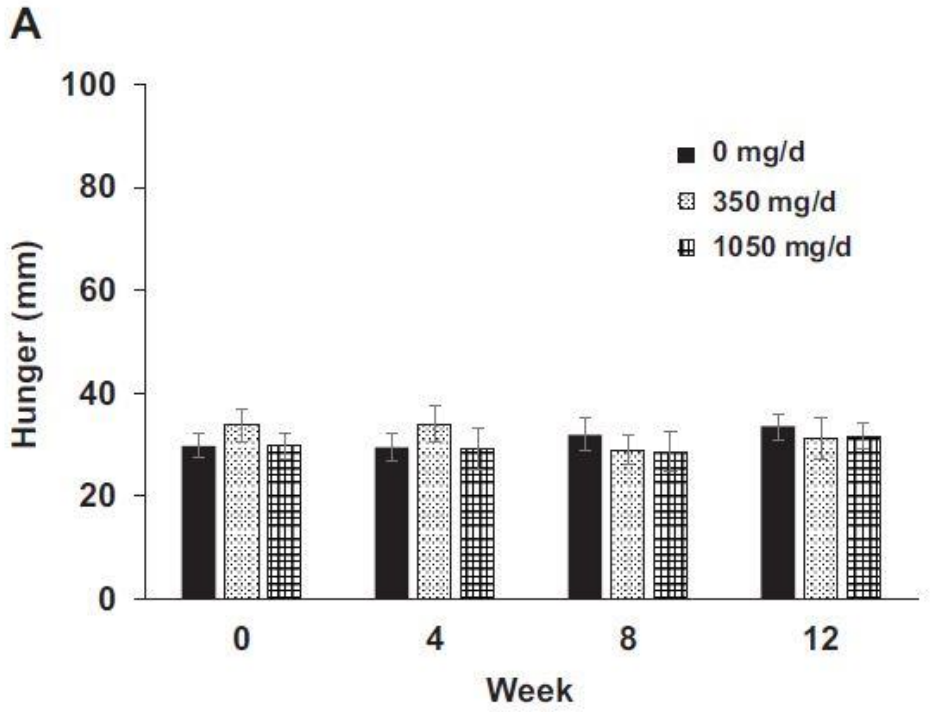
Medline (Ovid), Embase, Cochrane CENTRAL, WHO International Clinical Trials Registry Platform,

35 were observational studies. In adults, evidence of very low and low certainty from a limited number of small studies indicated a small beneficial effect of NSSs on body mass index (mean difference −0.6, 95% confidence interval −1.19 to −0.01; two studies, n=174) and fasting blood glucose (−0.16 mmol/L, −0.26 to −0.06; two, n=52). Lower doses of NSSs were associated with lower weight gain (−0.09 kg, −0.13 to −0.05; one, n=17 934) compared with higher doses of NSSs (very low certainty of evidence). For all other outcomes, no differences were detected between the use and non-use of NSSs, or between

Toews et al. BMJ, 2019.

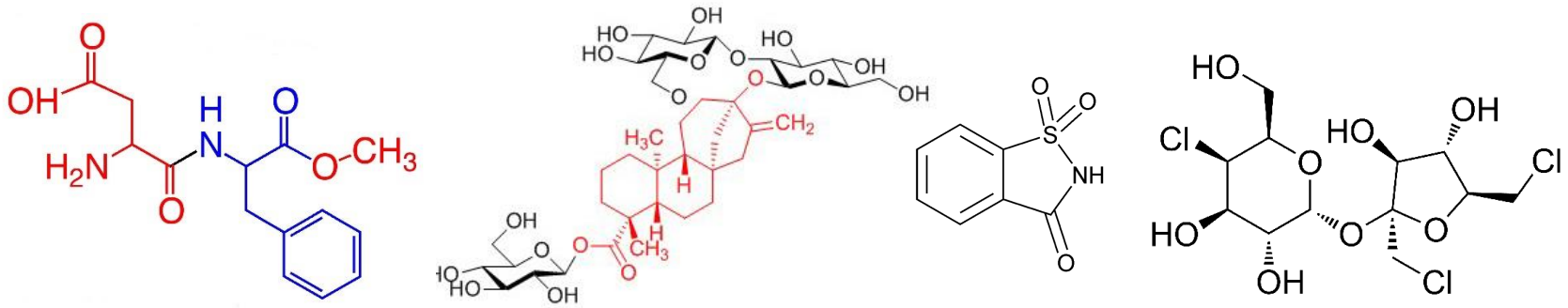
Aspartame and weight gain

- RCT in adults (18 – 60 years) consuming 0, 350 (1 can diet soft drink), or 1050 mg (95th Centile in USA) aspartame/day in a beverage for 12 weeks.
- Compliance with the beverage intervention was ~95%.
- There were **no effects** of aspartame ingestion on **appetite** (hunger, fullness, desire to eat/drink), body **weight**, or body **composition** (fat mass or fat-free mass).



Higgins et al. Journal of Nutrition, 2018.

Intense sweeteners and diabetes



Intense sweeteners and blood glucose levels

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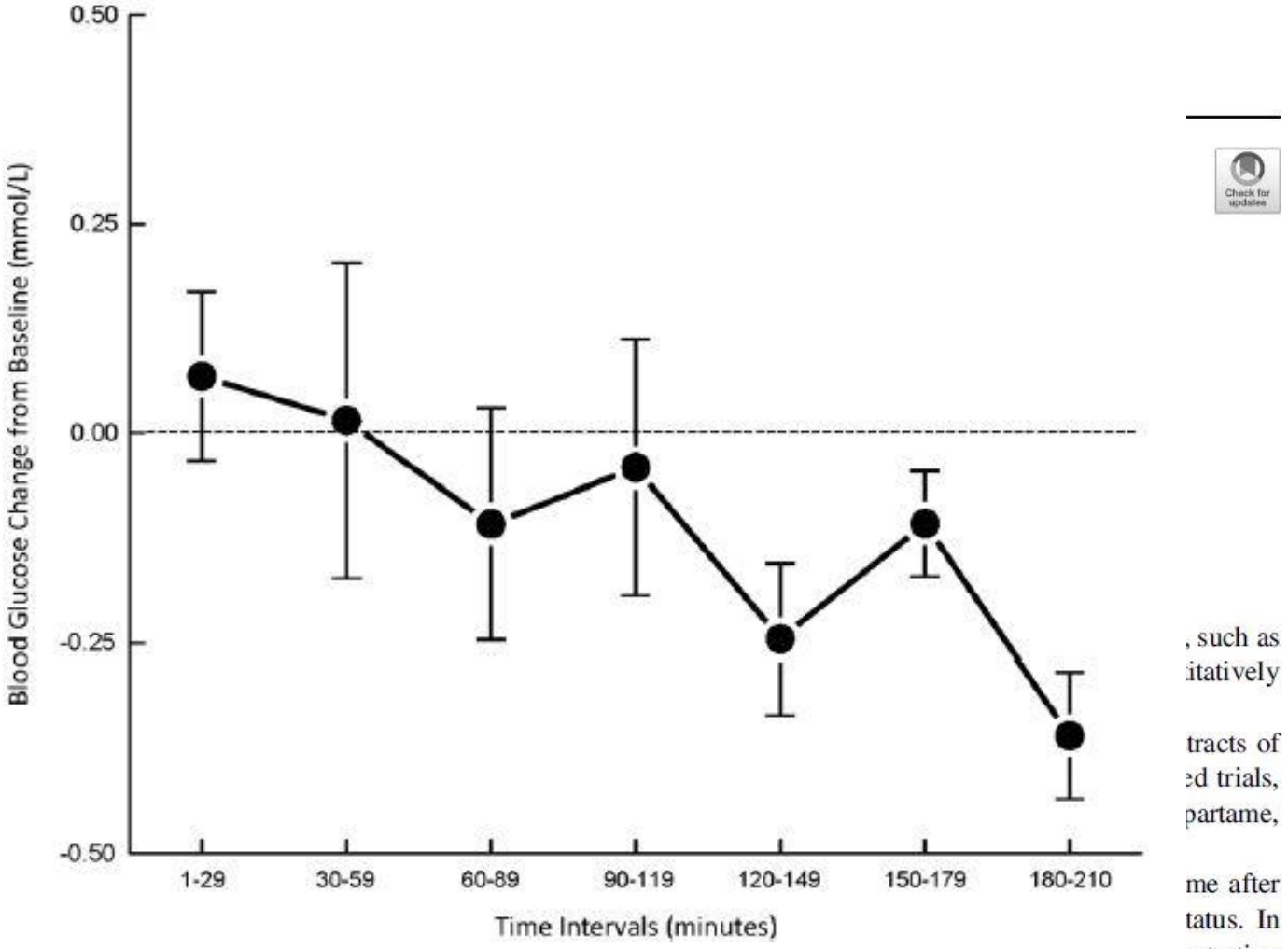

Fig. 2 Estimated trajectory for glycemic impact of NNS consumption estimated in the meta-analysis. Error bars indicate 95% confidence intervals

Nichol et al. EJCN, 2018.

Soft drinks and risk of type 2 diabetes

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British Journal of Nutrition, page 1 of 10
© The Authors 2014
doi:10.1017/S0007114514001329

Association between sugar-sweetened and artificially sweetened soft drinks and type 2 diabetes: systematic review and dose–response meta-analysis of prospective studies

D. C. Greenwood[1]*, D. E. Threapleton[2], C. E. L. Evans[2], C. L. Cleghorn[2], C. Nykjaer[2], C. Woodhead[2] and V. J. Burley[2]

[1]*Division of Epidemiology and Biostatistics, Level 8, Worsley Building, University of Leeds, Leeds LS2 9JT, UK*
[2]*Nutritional Epidemiology Group, School of Food Science and Nutrition, University of Leeds, Leeds LS2 9JT, UK*

(Submitted 18 November 2013 – Final revision received 23 April 2014 – Accepted 8 May 2014)

Abstract

The intake of sugar-sweetened soft drinks has been reported to be associated with an increased risk of type 2 diabetes, but it is unclear whether this is because of the sugar content or related lifestyle factors, whether similar associations hold for artificially sweetened soft drinks, and how these associations are related to BMI. We aimed to conduct a systematic literature review and dose–response meta-analysis of evidence from prospective cohorts to explore these issues. We searched multiple sources for prospective studies on sugar-sweetened and artificially sweetened soft drinks in relation to the risk of type 2 diabetes. Data were extracted from eleven publications on nine cohorts. Consumption values were converted to ml/d, permitting the exploration of linear and non-linear dose–response trends. Summary relative risks (RR) were estimated using a random-effects meta-analysis. The summary RR for sugar-sweetened and artificially sweetened soft drinks were 1·20/330 ml per d (95 % CI 1·12, 1·29, $P<0·001$) and 1·13/330 ml per d (95 % CI 1·02, 1·25, $P=0·02$), respectively. The association with sugar-sweetened soft drinks was slightly lower in studies adjusting for BMI, consistent with BMI being involved in the causal pathway. There was no evidence of effect modification, though both these comparisons lacked power. Overall between-study heterogeneity was high. The included studies were observational, so their results should be interpreted cautiously, but findings indicate a positive association

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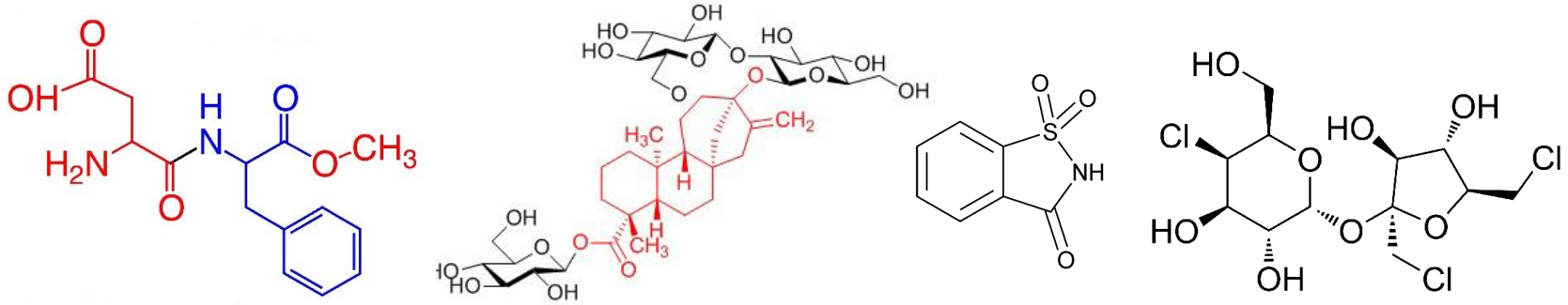
Greenwood et al. BJN, 2014; Lean and Te Morenga. Br Med Bull, 2016.


Diet

Intense sweeteners and dental health

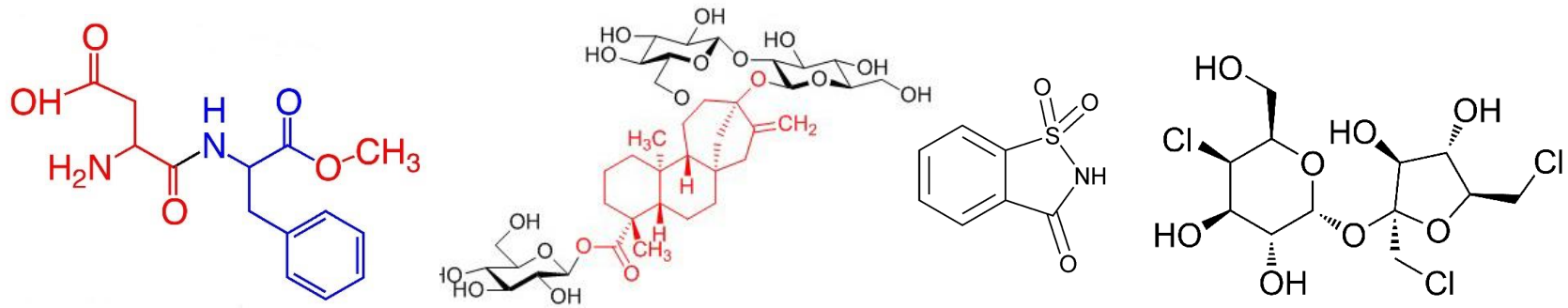


Intense sweeteners and dental health

• In their pure form, intense sweeteners do not provide available carbohydrate for bacterial fermentation.

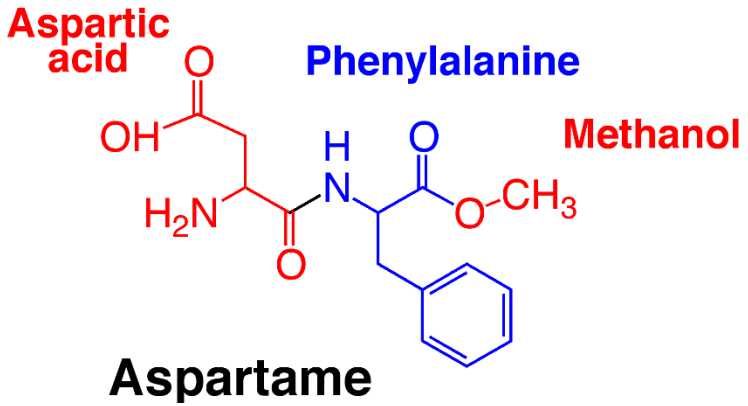
• When not combined with cariogenic fillers (i.e., maltodextrins or lactose), intense sweeteners do not adversely affect oral pH, and they reduce the number of cariogenic bacteria in the mouth.

Intense sweeteners and the microbiome



Aspartame and the microbiome

• Aspartame is completely and rapidly digested to aspartic acid, phenylalanine and methanol in the duodenum, and absorbed into the blood, it is not likely that it will adversely affect the microbiome.



• Limited studies in humans (cross-sectional analysis of 31 adult aspartame consumers) support this.

Frankenfeld et al. Ann Epi, 2015

Saccharin, microbiome and glucose tolerance

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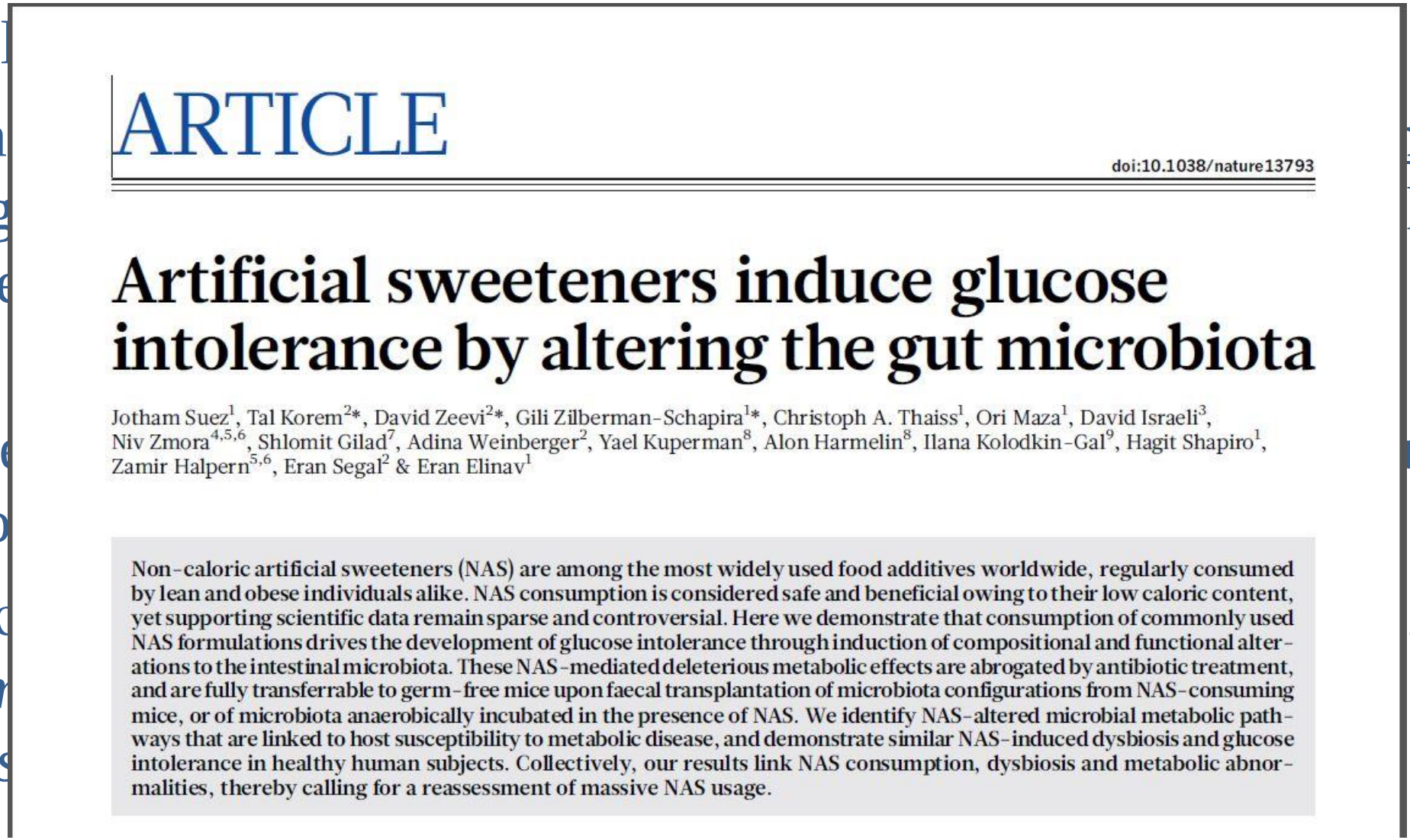


ARTICLE

doi:10.1038/nature13793

Artificial sweeteners induce glucose intolerance by altering the gut microbiota

Jotham Suez[1], Tal Korem[2]*, David Zeevi[2]*, Gili Zilberman-Schapira[1]*, Christoph A. Thaiss[1], Ori Maza[1], David Israeli[3], Niv Zmora[4,5,6], Shlomit Gilad[7], Adina Weinberger[2], Yael Kuperman[8], Alon Harmelin[8], Ilana Kolodkin-Gal[9], Hagit Shapiro[1], Zamir Halpern[5,6], Eran Segal[2] & Eran Elinav[1]

Non-caloric artificial sweeteners (NAS) are among the most widely used food additives worldwide, regularly consumed by lean and obese individuals alike. NAS consumption is considered safe and beneficial owing to their low caloric content, yet supporting scientific data remain sparse and controversial. Here we demonstrate that consumption of commonly used NAS formulations drives the development of glucose intolerance through induction of compositional and functional alterations to the intestinal microbiota. These NAS-mediated deleterious metabolic effects are abrogated by antibiotic treatment, and are fully transferrable to germ-free mice upon faecal transplantation of microbiota configurations from NAS-consuming mice, or of microbiota anaerobically incubated in the presence of NAS. We identify NAS-altered microbial metabolic pathways that are linked to host susceptibility to metabolic disease, and demonstrate similar NAS-induced dysbiosis and glucose intolerance in healthy human subjects. Collectively, our results link NAS consumption, dysbiosis and metabolic abnormalities, thereby calling for a reassessment of massive NAS usage.

Suez et al. Nature, 2014

Saccharin, microbiome and glucose tolerance

- A “long term” observational study of 381 people and a small (n=7) feeding trial (saccharin at ADI) of 1 week duration.
- In the observational study, NNS consumers increased weight and waist-to-hip ratio; had higher fasting blood glucose, HbA1C and glucose tolerance test results and elevated serum ALT.
- In the trial, 4 out of 7 developed poorer glycemic response and had evidence of dysbiosis.
- Both human studies small for their type, validity of FFQ unknown for the observational study and the trial was uncontrolled and not blinded.
- More research required.

Suez et al. Nature, 2014

Sucralose and the microbiome

- Splenda® was administered by oral gavage to male rats at 100, 300, 500, or 1000 mg/kg for 12-weeks.

- Equivalent to a dose of sucralose between 1.1 and 11 mg / kg /day.

- Faecal samples were collected weekly for bacterial analysis.

- Half the were allowed to recover for an additional 12-wk, and further assessments of faecal microflora.

Abou-Donia et al. , J Toxicol Environ Health A, 2008

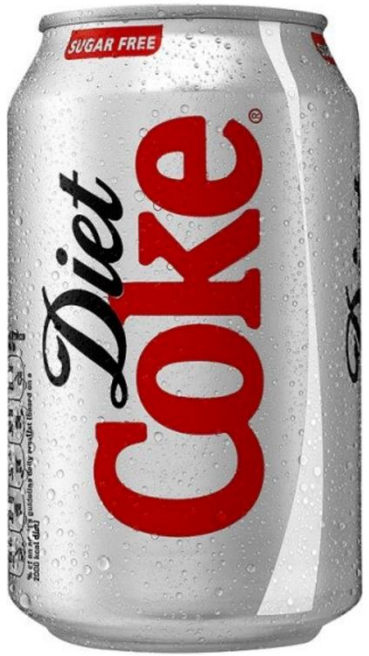
Sucralose and the microbiome

- Numbers of total anaerobes, bifidobacteria, lactobacilli, Bacteroides, clostridia, and total aerobic bacteria were significantly decreased.
- There was no significant treatment effect on enterobacteria, however.
- Following the 12-wk recovery period, only the total anaerobes and bifidobacteria remained significantly depressed, whereas pH values remained elevated.
- Methodological weaknesses include lack of a control group and use of wet faecal samples, and its important to note that a dose response was not observed.

Abou-Donia et al. , J Toxicol Environ Health A, 2008

Substitute free sugars with intense sweeteners in order to meet WHO guidelines

Substitute intense sweeteners for free sugars to meet WHO guidelines



Energy = 675 kJ
Free sugars = 40 g

Energy = 6 kJ
Free sugars = 0 g

Substitute intense sweeteners for free sugars to meet WHO guidelines

Energy = 144 kJ
Free sugars = 9 g

Energy = 15 kJ
Free sugars = 0.1 g

Substitute intense sweeteners for free sugars to meet WHO guidelines

Energy = 3360 kJ
Free sugars = 210 g

Energy = 422 kJ
Free sugars = 0.7 g

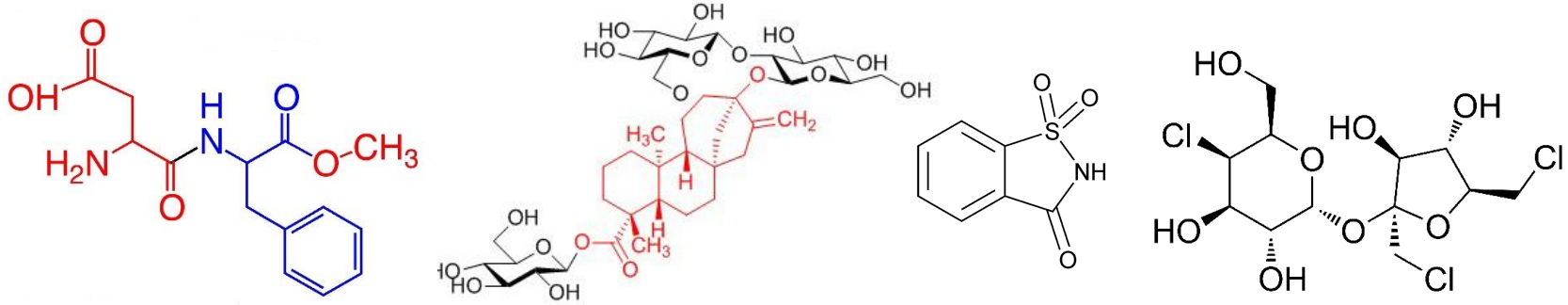
Average diet with 17 percent of energy from free sugars		
Breakfast 2/3 cup rolled oats 1 cup reduced-fat (1–2%) milk 1 tablespoon (3 teaspoons) wildflower honey ½ grapefruit 1 Cup tea / coffee with reduced fat milk and 2 teaspoons sugar	*Lunch* 2 slices of hearty whole grain bread 2 teaspoons olive oil margarine 3½ ounces (100 g) canned red salmon ½ cup mixed salad (lettuce, cucumber, and tomato) 200 g container low-fat vanilla yogurt ½ banana Can regular soft drink	*Dinner* 2 ounces (60 g) beef strips 1½ cups Asian-style stir-fry noodles 2 cups Asian-style stir-fry vegetables 1 tablespoon sesame oil ¼ cup Asian stir-fry sauce ½ cup reduced-fat vanilla ice cream ½ cup strawberries 1 piece (8 g) milk chocolate 1 Cup tea / coffee with reduced fat milk and 2 teaspoons sugar
9550 kJ; 108 g protein; 64 g fat; 16 g saturated fat; 306 g total carbohydrate; 160 g total sugars; 102 g free sugars; 25 g fibre; 1824 mg sodium		

Barclay, Sandall and Slavin. The Ultimate Guide to Sugars and Sweeteners. The Experiment, 2014.

Average diet with 10 percent of energy from free sugars		
Breakfast 2/3 cup rolled oats 1 cup reduced-fat (1–2%) milk 1 tablespoon (3 teaspoons) wildflower honey ½ grapefruit 1 Cup tea / coffee with reduced fat milk and intense sweetener	*Lunch* 2 slices of hearty whole grain bread 2 teaspoons olive oil margarine 3½ ounces (100 g) canned red salmon ½ cup mixed salad (lettuce, cucumber, and tomato) 200 g container low-fat vanilla yogurt ½ banana Can "diet" soft drink	*Dinner* 2 ounces (60 g) beef strips 1½ cups Asian-style stir-fry noodles 2 cups Asian-style stir-fry vegetables 1 tablespoon sesame oil ¼ cup Asian stir-fry sauce ½ cup reduced-fat vanilla ice cream ½ cup strawberries 1 piece (8 g) milk chocolate 1 Cup tea / coffee with reduced fat milk and intense sweetener
8730 kJ; 108 g protein; 64 g fat; 16 g saturated fat; 255 g total carbohydrate; 107 g total sugars; 50 g free sugars; 25 g fibre; 1822 mg sodium		

Barclay, Sandall and Slavin. The Ultimate Guide to Sugars and Sweeteners. The Experiment, 2014.

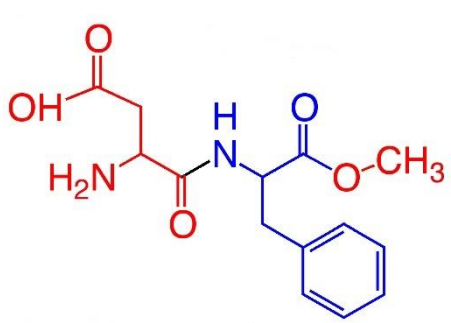
Intense sweeteners summary

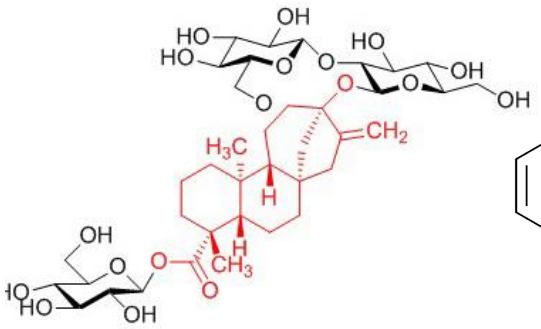


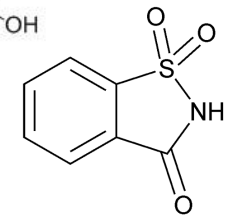
- To consume 5-10% of energy from free sugars, Australians can swap intensely sweetened foods and beverages for their regular nutritively-sweetened counterparts, minimising dietary disruption and aiding long-term dietary adherence.
- A variety of intense sweeteners have been evaluated and approved for use in Australian foods and beverages, with aspartame, saccharin, steviols and sucralose being the most popular variants at present.
- Independent Food Regulatory Agencies around the globe have reviewed these intense sweeteners and have determined them to be safe provided they are consumed in amounts less than their respective ADIs.

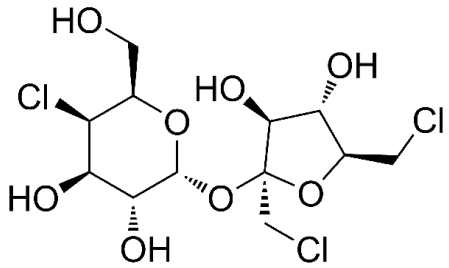
- Dietary surveys indicate that average consumption of these IS in Australia is ≤ 11% of the ADI.
- When substituted for nutritively sweetened counter-parts, there is level 1 evidence that IS help people lose weight in the medium-term, but there are no long-term RCTs.
- SLRs and MAs of long-term observational studies demonstrate no association between IS use and weight.
- There is no evidence when consumed in amounts < ADI that ISs adversely affect glucose homeostasis in the short-medium term.
- There is emerging evidence that saccharin and sucralose may adversely affect the microbiome, but more research is needed.

Intense sweeteners conclusions









- The common belief among both consumers and health professionals that “artificial” sweeteners are no better than the sugars that they are replacing is not based on high-level evidence from randomised controlled trials in humans.
- Intense sweeteners - particularly aspartame and “stevia” – are both safe and effective substitutes for added sugars in foods and beverages.
- Individuals can use intensely sweetened tabletop sweeteners instead of table sugars, syrups, honey, etc...
- Most (not all) can also be used in recipes.

Further Information

Alan Barclay, PhD

02 9785 1037

0416 111 046

alan@dralanbarclay.com
www.dralanbarclay.com
@DrAlanWBarclay