Food and Chemical Toxicology 46 (2008) S61–S69

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

The use of a sweetener substitution method to predict dietary exposures for the intense sweetener rebaudioside A

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ARTICLE INFO

Article history:
Received 4 October 2007
Accepted 7 May 2008

Keywords:
Rebaudioside A
Dietary exposure
Intake assessment
Intense sweetener
Diabetics
Children

ABSTRACT

There are more published dietary exposure data for intense sweeteners than for any other group of food additives. Data are available for countries with different patterns of sweetener approvals and also for population groups with high potential intakes, such as children and diabetic subjects. These data provide a secure basis for predicting the potential intakes of a novel intense sweetener by adjustment of the reported intakes of different sweeteners in mg/kg body weight by their relative sweetness intensities. This approach allows the possibility that a novel sweetener attains the same pattern and extent of use as the existing sweeteners. The intakes by high consumers of other sweeteners allows for possible brand loyalty to the novel sweetener. Using this method, the estimated dietary exposures for rebaudioside A in average and high consumers are predicted to be 1.3 and 3.4 mg/kg body weight per day for the general population, 2.1 and 5.0 mg/kg body weight per day for children and 3.4 and 4.5 mg/kg body weight per day for children with diabetes. The temporary ADI defined by the JECFA for steviol glycosides [JECFA, 2005. Steviol glycosides. In: 63rd Meeting of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization (WHO), Geneva, Switzerland, WHO Technical Report Series 928, pp. 34–39] was set at 0–2 mg/kg body weight (expressed as steviol equivalents); after correction for the difference in molecular weights, these estimated intakes of rebaudioside A are equivalent to daily steviol intakes of less than 2 mg/kg. In consequence, this analysis shows that the intakes of rebaudioside A would not exceed the JECFA temporary ADI set for steviol glycosides.

1. Introduction

The leaves of the plant *Stevia rebaudiana* are sweet tasting and contain a number of active components, the most important of which are stevioside and rebaudioside A. Both compounds are glycosides of steviol and are hydrolysed in the intestinal tract to steviol, which is lipid soluble and absorbed. Stevioside was evaluated by the JECFA (Joint FAO/WHO Expert Committee on Food Additives) in 2005 and a temporary ADI of 0–2 mg/kg body weight was established based on toxicology data on steviol and stevioside (JECFA, 2005). The ADI was expressed as steviol equivalents because the potential for toxicity resides in the steviol moiety, and because many stevioside preparations contain other glycosides in addition to stevioside. The future use of pure rebaudioside A as an intense sweetener requires an assessment of potential intake for comparison with the temporary ADI established by the JECFA (2005).

Various methods have been used to estimate the dietary exposures to food additives, which range in sophistication from simple screening methods to complex and expensive dietary records (Kroes et al., 2002).

Screening methods are normally used prior to the approval of a novel additive and are highly conservative in order to determine if there is any potential for the human dietary exposure to exceed the acceptable daily intake (ADI). A commonly used initial approach is the so-called Danish budget method (Hansen, 1979), which in the worst-case assumes that the compound is present at the maximum permitted concentration and is consumed daily in all foods (100 kcal per kg body weight) and liquids (100 ml per kg body weight). A modified budget method assumes that the compound is present in all food groups for which it is approved and uses high consumption data for the relevant food groups. Such methods overestimate real exposures, but a more sophisticated approach is not necessary if the dietary exposures are below the ADI. An alternative screening method, the sucrose replacement method, has been used in the past for intense sweeteners. As the name implies, this method assumes that the intense sweetener replaces all dietary sucrose. This approach is highly conservative because it ignores the many non-sweetener functions of sucrose.

Abbreviations: ADI, acceptable daily intake; EU, European Union; FDA, Food and Drug Administration; JECFA, Joint FAO/WHO Expert Committee on Food Additives; kg, kilogram; kcal, kilocalorie; mg, milligram; NHANES, National Health and Nutrition Examination Survey; UK, United Kingdom; USA, United States of America.

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doi:10.1016/j.fct.2008.05.009

Table 1
Average intakes by consumers of different intense sweeteners (means or medians if means were not given in the publication)

Date	Country	Number	Average daily intake by consumers in mg/kg body weight/day						References
			Acesulfame	Alitame	Aspartame	Cyclamate	Saccharin	Sucralose	
1977	USA	1135	–	–	–	–	2.0*	–	Morgan et al. (1982)
1980	*Finland*	*National data*	–	–	–	*0.2*	*0.1*	–	Pentilla et al. (1988)
1987	Canada	10416	–	–	1.3	–	–	–	Heybach and Ross (1989)
1987	UK	681	0.7*	–	1.0*	–	0.9*	–	MAFF (1987)
1988	UK	647	0.6	–	0.4	–	0.4	–	Hinson and Nicol (1992)
1988	Germany	2291	–	–	1.2	3.0	0.3	–	Bär and Biermann (1992)
1990–1991	Brazil	673	–	–	1.2	1.7	0.8	–	Toledo and Ioshi (1995)
1991	Denmark (all ages plus diabetics)	1233	0.5	–	0.7	2.0	0.3	–	Renwick (1999)
1992	Netherlands	6218	0.2	–	1.5	1.1	0.2	–	Hulshof et al. (1995)
1992	Spain	2450	–	–	–	2.4	–	–	Serra-Majem et al. (1996)
1993	*Norway*	*National data for children*	*1.7**	–	*3.4**	*4.3**	*0.4**	–	Bergsten (1996)
1994	Australia	128	0.2	–	2.8	2.5	0.5	–	NFA (1995)
1994–1996	Spain – men	784	–	–	–	0.6	–	–	Serra-Majem et al. (2003)
1995	Denmark	3098	0.1		0.8	0.1	0.01		Leth et al. (2007)
1996	Italy – teenagers	212	0.02	–	0.03	0.24	0.21	–	Leclercq et al. (1999)
1997	France – diabetics aged 2–20 years	227	1.1	–	2.4	–	0.4	–	Garnier-Sagne et al. (2001)
1997–1998	Netherlands	National Food Survey	0.0	–	0.1	0.1	0.02	–	van Rooij-van den Bos et al. (2004)
Not stated	UK – various ages	188	0.7	–	–	–	0.5	–	Wilson et al. (1999)
1998	Korea	11525	–	–	0.14	–	0.03	–	Chung et al. (2005)
1999	*Sweden – worst-case in diabetics*	*243 children, +547 adults*	*4*	–	*8*	*5*	*1*	–	Ilback et al. (2003)
2000–2001	Italy – teenagers including high consumers	362	0.02	–	0.05	0.25	0.03	–	Arcella et al. (2004)
2001	UK – children aged 1.5–4.5 years	1110	0.9	–	3.4	4.5	1.2	–	Food Standards Agency UK (2001)
2001–2002	USA – NHANES database	9701	–	–	4.9	–	–	–	Magnuson et al. (2007)
Not stated	Canada – diabetic children	56	0.6	–	4.1	0.0	–	0.2	Devitt et al. (2004)
2002–2003	Australia and New Zealand – consumers	400 high consumers	0.51	–	2.42	2.93	0.46	0.52	Food Standards Australia New Zealand (2004)

Data shown in italics are theoretical worst-case analyses based on national food intake data and maximum permitted use levels; data from these studies are excluded from further analyses.
* The study subdivided the data into various groups; the value given is the highest reported value.

Usually a tiered approach is used and more sophisticated and complex methods are employed when screening methods indicate the need for a more refined dietary exposure assessment (Gibney and Lambe, 1996). More sophisticated methods use food diaries combined with either permitted use levels or measured concentrations in different foods and beverages. The long-term average dietary exposures of consumers are most relevant for risk assessment purposes, but in reality, food diaries become increasingly unreliable with increase in duration, so that detailed food diaries are usually less than two-weeks duration.

A large number of intake surveys have been undertaken on intense sweeteners since 1977 (reviewed in Renwick, 1999, 2006), and there is a more extensive database available for intense sweeteners than for any other type of food additive. In this paper published data on dietary exposures to approved intense sweeteners have been used to predict the maximum likely intake of rebaudioside A. The method is equally applicable to other novel or recently approved intense sweeteners for which specific intake data are lacking.

2. Method[1]

The method is based on published intake data for approved intense sweeteners. The amount of sucrose replaced by an intense sweetener equals the dietary exposure for that sweetener multiplied by its relative sweetness intensity compared with sucrose. The intake of a novel intense sweetener is then calculated by dividing the estimated sucrose equivalent intakes by the relative sweetness of the novel sweetener.

There have been many published studies performed in a number of different countries with different patterns of sweetener approval. Approval scenarios range from the USA in the late 1970s and Canada in the 1990s, when saccharin or aspartame, respectively were the only sweeteners used in foods and beverages, to recent data for Australia and New Zealand, where six intense sweeteners are permitted. The various studies represent a massive database covering many thousands of individuals in different countries.

Many papers reported the average intakes for the whole population and also for consumers only; inclusion of data for non-consumers lowers the intake estimates and is not useful for risk assessment purposes; the intake data used in this paper are for "consumers only".

The "ideal" dietary exposure assessment would use a two-weeks prospective brand-specific questionnaire with accurate measurement of the amount of each food/beverage consumed on each eating occasion. Such a study would be complex and costly and few such data exist for any additive. In practice, most intake surveys on intense sweeteners have included conservative assumptions to some degree (see Renwick, 2006). Realistic estimation of dietary exposure requires exclusion of data from studies where the intake estimates were based on modified budget methods, or the dietary records did not differentiate between low-calorie and regular products. The data used in the present analysis were mostly from studies that used specifically-designed food diaries combined with actual use levels or approved levels in different foods and beverages. Some studies were based on the intakes of categories of foods, rather than diary records of specific products; the extent to which such studies would overestimate exposure would depend on how broad the categories were, and whether they grouped together products sweetened with sucrose or with an intense sweetener.

A number of studies given in Table 1 were excluded from further analysis. The studies of Pentilla et al. (1988), Bergsten (1996) and Ilback et al. (2003) were theoretical screening analyses using national food intake data combined with maximum permitted use levels. The study of Chung et al. (2005) analyzed the concentrations of aspartame, saccharin and stevioside in different food products in Korea and

[1] The FDA has used a similar method to predict the intakes in the USA of acesulfame-K (http://frwebgate.access.gpo.gov/cgi-bin/getpage.cgi?dbname=1998_register&position=all&page=36345) and sucralose (http://frwebgate.access.gpo.gov/cgi-bin/getpage.cgi?dbname=1998_register&position=all&page=16418) (M.J. Dinovi – personal communication).