Coca-Cola South Pacific (CCSP) Health and Wellness Advisory Council

Position Statement on the Non-nutritive Sweeteners Aspartame, Acesulphame K and Stevia

For a detailed outline of the methodology used to develop this position statement, please see appendix 1.

For information on the members of the CCSP Health and Wellness Advisory Board, see page 11.

Summary

Despite popular allegations linking the use of non-nutritive sweeteners such as aspartame, stevia and acesulphame K to adverse health effects such as cancer, neurological symptoms and effects on appetite, the scientific literature does not support these theories. Consumption of these non-nutritive sweeteners can exert a beneficial effect for certain people, in particular those with diabetes and those interested in managing their weight, due to their low kilojoule content and sweet taste. Overall, when consumed within acceptable daily intake levels as currently done in Australia and New Zealand, aspartame, stevia and acesulphame K have been shown to have no association with adverse health effects and can be a useful addition to the diets of those who are concerned with their dental health, limiting their kilojoule intake or controlling their blood glucose levels.

Purpose

The purpose of this review was to form a position statement on the non-nutritive sweeteners asparatame, acesulphame K and stevia that can be used by The Coca Cola Company as a reference for providing evidence based advice to the public (and health professionals where necessary) on the role of these sweeteners in the diet. If individuals choose to consume foods and beverages containing non-nutritive sweeteners, it is recommended they be included in moderation as part of an overall healthy diet and lifestyle that also includes regular physical activity.

Background

Low- or reduced-kilojoule sweeteners (referred to throughout this statement as non-nutritive sweeteners) are widely consumed in Australia and New Zealand. A report by Food Standards Australia New Zealand (FSANZ) has found that approximately 66% of Australians and 70% of New Zealanders consume non-nutritive sweeteners with around 51% consuming them in the form of diet sparkling beverages [1]. Consumers often select foods and beverages with these sweeteners to achieve a sweet taste without the extra kilojoules sugar provides, to reduce their chances of tooth decay, or to assist with the management of conditions such as diabetes [2]. There are a variety of non-nutritive sweeteners approved for use in beverages in Australia and New Zealand. These include saccharin, aspartame, acesulphame K, sucralose, neotame, alitame, thaumatin, cyclamate and most recently, stevia [1]. This position statement reviews the health effects and safety of aspartame, acesulphame K and stevia and provides a position on the impact of the sweeteners on weight management, disease conditions such as dental health, cancer and diabetes, pregnancy and children's health and the safety of beverages and food in which they are added.

Aspartame

Aspartame was discovered in 1965. It is one of the most widely used non-nutritive sweeteners as its taste is very similar to that of sucrose (table sugar) [2] . Aspartame has been approved for use in over 90 countries and used in over 6000 types of products and beverages worldwide [3]. The United States Food and Drug Administration (USFDA) approved aspartame for use in carbonated beverages in 1983 [4] and approved it for use as a general purpose sweetener in 1996. The National Health and Medical Research Council approved aspartame for use in Australia in 1986. According to a recent report by FSANZ, the mean daily exposure to aspartame in Australia is well below the acceptable daily intake (ADI) (table 1) [1]. The ADI for aspartame is 40mg/kg body weight per day, which was determined by the WHO/FAO Joint Expert Committee on Food Additives (JECFA) [5]. This amount was derived from the estimated level that caused no toxic effect in rats. To reach the ADI for aspartame, a person weighing 70kg would need to consume 2.8g per day. This amount is equivalent to approximately 20 cans of diet sparkling beverage or over 100 standard 1g packets of sweetener. Aspartame provides 16 kilojoules per gram – the same as protein and sugar – however it is around 180 times sweeter than sugar so only small amounts are needed to sweeten a food or beverage [2].

Many aspartame-containing products carry a label indicating that these products should not be used in baking or cooking. This is not intended as a health warning; it is because aspartame loses most of its sweetness when it is heated [2]. However aspartame can be added at the end of cooking, for example to custards and other desserts.

Metabolism of aspartame

Aspartame is a chemical compound comprised of the natural amino acids aspartic acid and phenylalanine [6]. Once consumed, aspartame is rapidly broken down into these amino acid building blocks as well as methanol [6]. These are then absorbed into the blood and used by the body for energy and building body tissues. Aspartic acid, phenylalanine and methanol are all products which are found naturally in foods e.g. fruit juices, meat and dairy products [2]. These substances are often found in larger amounts in natural foods than the amount that arises from ingestion of foods and drinks sweetened with aspartame. For example, a glass of skim milk provides about six times more phenylalanine and thirteen times more aspartic acid and a glass of tomato juice provides about six times more methanol than an equivalent volume of beverage sweetened with aspartame [6]. All components of aspartame undergo normal digestion in the body whether they come from aspartame or food [7]. For example, methanol is further broken down into water and carbon dioxide, which is excreted by the body. In general, aspartame intake does not contribute significantly to the background levels of methanol in the body [6].

Safety of aspartame

Aspartame is safe for all to consume except individuals with the rare metabolic disease phenylketonuria (PKU). People with PKU lack the enzyme necessary for converting the amino acid phenylalanine into another amino acid tyrosine. Around one in 10,000 babies born in Australia [8] and around one in 15,000 babies born in New Zealand will have PKU[9]. People with PKU must follow a low phenylalanine diet, therefore needing to minimise their intake of products containing aspartame as well as reduce their intake of foods with naturally high phenylalanine levels [10]. Because of this, all aspartame-containing products must state the product contains phenylalanine on their labels.

Aspartame is also safe for people with epilepsy or who have seizures. Studies from the early 1980s reported a possible link between aspartame intake and seizures [11], however a number of comprehensive reviews and clinical trials performed since that time have concluded that there is no proven association [6, 12, 13].

A comprehensive 2007 review on the safety of aspartame evaluated more than 500 studies, articles and reports from the last 25 years in areas such as its absorption and metabolism, current consumption levels worldwide, toxicology and recent epidemiological studies and concluded 'the weight of existing evidence is that aspartame is safe at current levels of consumption as a non-nutritive sweetener' [3].

In 2009, a report released by the European Food Safety Authority (EFSA) [14] concluded that there is no new evidence on aspartame that would require the EFSA to reassess its opinion that the sweetener is safe, although additional studies could add to knowledge of the sweetener and its metabolites. Although some studies have suggested possible adverse effects, the EFSA has scrutinised the methodology and findings of these studies and has repeatedly reaffirmed its positive safety opinion.

Despite the confidence of food authorities internationally and nationally, aspartame is still one of the most controversial sweeteners, and some people believe consuming it causes them ill effects. These claims are often based on anecdotal evidence or have arisen from unsubstantiated scientific studies and observations. Anecdotal reports claim an association between aspartame and neurological symptoms such as headaches and seizures [15, 16] and more recently, migraines [17, 18] while much of the scientific literature critical of aspartame usage focuses on its role in cancer and body weight regulation/appetite. These areas are reviewed below.

Neurological symptoms

Despite successful treatment of PKU with a low phenylalanine diet, lack of diet adherence has been linked to elevated plasma phenylalanine levels, which can lead to neurological deterioration and lower intellectual function[19, 20]. It is therefore advised that people with PKU do strictly monitor their dietary intake and adhere to a low phenylalanine diet, including the avoidance of aspartame.

In healthy people, anecdotal reports relating to aspartame use and adverse health effects claim that use of the sweetener causes a range of behavioural and neurological problems such as headaches and seizures [2]. Many of these claims are thought to be based on the mistaken belief that consuming aspartame can cause blood levels of aspartic acid and/or phenylalanine to rise to high levels that can trigger neurological symptoms [2]. In August 2008, an article was published proposing excessive aspartame ingestion might be linked to certain mental disorders and compromised learning and emotional functioning due to the formation of toxic metabolic products such as formic acid and formaldehyde [21]. Many of the claims presented in this paper were soon after refuted [22]. Despite these claims, research into aspartame and brain function has shown no consistent effects of large amounts of aspartame on brain neurotransmitter systems [23, 24]. In Australia and New Zealand, when approving the use of aspartame, FSANZ reviewed the data and found a lack of evidence that aspartame had negative health effects, and as a result permits its use in certain products within the context of the requirements of the Australia New Zealand Food Standards Code [25].

Cancer

Aspartame's role in cancer has been debated since an early study proposed a link between increasing brain cancer rates in the US and aspartame's introduction to the food supply in 1981 [26]. This study received widespread media attention despite its methodological flaws. The authors linked the then recent increase in brain tumours to the introduction of aspartame into food and beverages [26]. This observation was received with criticism from the scientific community as there was no evidence that individuals who developed brain tumours actually consumed aspartame. In addition, if aspartame were to be the causative factor for the increase in brain tumours, there would have been a latent effect [27], that is, brain tumours would not have increased for many years after the introduction of aspartame into foods and beverages.

More recent scientific reviews have failed to show an association between aspartame use and brain cancer [6, 27, 28]. A European review of case-control studies found no association between aspartame and brain tumours [28], and a case-control study in the US concluded that children with brain tumours were no more likely to have consumed aspartame than were children in the control group [29].

A 2004 review of studies on aspartame and health risks also concluded that "despite unscientific articles in the mass media and scientific press, there is no evidence that the sweetener aspartame bears a carcinogenic risk" [27].

In 2006, results from a rat study by the European Ramazzini Foundation (ERF) were released that linked aspartame consumption with an increased risk of certain cancers [30]. However, an extensive review of this study by the FDA showed that the data did not demonstrate cancer incidence was directly related to aspartame consumption [31]. A second study released in 2007 by the same research group supported their original findings [32], and once again received extensive media attention. The EFSA reviewed this study and in 2009 concluded, on the basis of all the evidence currently available, including the last published ERF study in 2007, there was no indication of any genotoxic or carcinogenic potential of aspartame and there was no reason to revise the previously established ADI for aspartame of 40 mg/kg bw/day [14].

Appetite and hunger

There have been suggestions that aspartame and other non-nutritive sweeteners may increase carbohydrate cravings following consumption, leading to possible weight gain. These assumptions stem from an early study that indicated hunger ratings increased 40-60 minutes following consumption of an aspartame-containing drink Some additional research has also found a stimulating effect of aspartame on appetite [33, 34], however a number of confounding factors have been identified such as time, sweetener concentration and gender, meaning that even if the studies showed a positive association, the results cannot be directly attributed to the intake of aspartame.

Most of the literature on aspartame and appetite consists of short-term studies of only a few hours to a few days in duration and there are currently no long-term studies that adequately assess the effects of aspartame on appetite [35]. However, the majority of recent studies which have measured food or kilojoule intake following consumption of aspartame have shown that compared to the control group, consumption of aspartame does not result in an increase in appetite ratings or subsequent food intake [36-40] Other research has suggested that aspartame neither increases nor decreases appetite, energy intake or body weight compared with consumption of sucrose [41]. A number of reviews have also failed to show a direct link between aspartame intake and appetite [42, 43].

The mechanisms behind hunger and appetite are multifactorial and the role non-nutritive sweeteners may play is yet to be confirmed. Peoples' liking of sweetness in foods and beverages and their previous exposure to the taste or flavour of sweetened foods can impact on preferences and hence behaviour in these types of studies, therefore contributing another confounding factor. It has been postulated that regular exposure to non-nutritive sweeteners may contribute to a learned liking for a highly sweetened diet, which may counter-act the objective of including non-nutritive sweeteners to reduce the energy content of the diet [35]. A review by Yang [44] provides further support for this, stating that non-nutritive sweeteners, because of their sweetness, may encourage sugar craving and sugar dependence. The author states that animals seek food to satisfy an inherent craving for sweetness, even in the absense of energy need. Lack of complete satisfaction for this craving may further fuel food seeking behaviour and may therefore contribute to weight gain. The review hypothesises that non-nutritive sweeteners

such as aspartame, provide partial, and not complete satisfaction of a sweet craving and therefore may lead to food seeking behaviour. Restricted exposure to sweet foods and beverages, including those sweetened with non-nutritive sweeteners, may be necessary to reduce this learned liking for sweet tastes [35].

The opinion of the EFSA in its 2009 report was that "there is little or no substantive data to suggest that aspartame affects appetite, hunger or food intake, but further consideration is warranted" [14].

Body weight regulation

As sugar intake has increased over the past three decades in line with an increase in overweight and obesity [45], it has been speculated that sugar may be associated with weight gain. As a result, an increasing role for non-nutritive sweeteners in weight control has emerged. However, whether non-nutritive sweetenerse such as aspartame, assist with weight management is yet to be confirmed.

For example, one recent study found an association between high baseline non-nutritive sweetened beverage intake and subsequent increase in BMI over a seven to eight year period [46]. The authors claimed that low-calorie sweeteners may be "fueling" the obesity epidemic, with their finding that people who consumed higher amounts of non-nutritive sweetened beverages at baseline, were more likely to gain more weight during the 7-8 year follow up period and have a higher BMI than non-users. However, the study is mainly speculative in nature with the authors stating that there may be no causal relationship between artificial sweetener use and weight gain.

In addition, a recent 2010 systematic review [47] examined the existing evidence supporting or refuting a link between non-nutritive sweetener use and weight change in children. The review found that overall, epidemiologic studies of non-nutritive sweetener use in children have generally shown a positive association between sweetener intake (most commonly as diet beverages) and weight gain. However, this association does not imply causality.

Randomized controlled trials in this area are very limited and do not clearly demonstrate either beneficial or adverse metabolic effects of non-nutritive sweeteners [47]. Presently, there is no strong clinical evidence for causality regarding non-nutritive sweetener use and weight gain.

In relation to weight loss, long-term intervention studies that involve energy restriction have shown the inclusion of non-nutritive sweeteners such as aspartame increases compliance to a low energy diet therefore helping maintain weight loss without reducing the palatability of the diet [48, 49].

In addition, a 2006 review reported on the effectiveness of aspartame in assisting with weight control. The findings of this review concluded that using foods and drinks sweetened with aspartame instead of those sweetened with sucrose is an effective way to maintain and lose weight without reducing the palatability of the diet [49]. Similarly, another review on aspartame and body weight has found that although there is a lack of conclusive evidence on aspartame's role in appetite, when aspartame is added to diet beverages, the energy density of the beverage is reduced, indicating that diet beverages sweetened with aspartame may be the best use of non-nutritive sweeteners in the context of a weight control strategy [50].

In relation to maintenance of weight loss, a recent study [51] compared the dietary strategies of two groups of people. One group were weight loss maintainers, that is, people who had lost weight and kept it off for at least 5 years and the other group were normal weight people, that is, those who had no history of overweight. Results found weight loss maintainers consumed three times more daily servings of non-nutritvely sweetened sparkling beverages and significantly fewer daily servings of sugar-sweetened sparkling beverages than normal

weight people. These findings suggest that weight loss maintainers use more non-nutritive sweetened drinks to help effectively maintain their weight loss.

Currently, several trials are in progress to study the effects of non-nutritive-sweetened carbonated beverages on body weight and other metabolic parameters in both children and adults [52, 53]. Studies of potential mechanisms underlying any metabolic effects of non-nutritive sweeteners are also ongoing [54]. These studies, and other similar investigations, will be critical for advancing understanding of the role of non-nutritive sweeteners in weight management.

At the current time, the role of non-nutritive sweetener use in relation to obesity management remains unclear. The American Dietetic Association's position on the intake of non-nutritive sweeteners such as aspartame in relation to weight management is that "Individuals who wish to lose weight may choose to use non-nutritive sweeteners but should do so within the context of a sensible weight management program including a balanced diet and exercise"[55].

Acesulphame potassium (K)

Acesulphame K was discovered in 1967. It is approximately 200 times sweeter than sugar and is heat stable [56], allowing it to be used in cooking and baking as well as a sweetener for foods and beverages. Unlike aspartame, acesulphame K is not metabolised by the body, hence it provides no kilojoules. It also has no influence on potassium intake even though it does contain potassium as its name suggests [55]. Acesulphame K is generally used in combination with other sweeteners as it can have a bitter aftertaste when used on its own [57]. When small amounts of acesulphame K are mixed with other non-nutritive sweeteners the resulting taste is similar to that of sucrose [58]. In Australia and New Zealand, it is commonly used in combination with aspartame to flavour diet sparkling beverages.

In regards to the effect of ace-sulphame K on appetite and hunger, a recent study showed the consumption of the non-nutritive sweeteners sucralose and ace-sulphame K incorporated into a diet beverage increased glucagon-like peptide (GLP)-1 levels [59]. GLP-1 has been shown in other studies to result in decreased post-prandial glucose and insulin levels, an effect due mainly to delayed gastric emptying [59]. Further research is required to support these findings and to determine if delayed gastric emptying may have any long term effects on appetite and hunger.

Acesulphame K underwent rigorous safety testing prior to its approval for use in foods and beverages in the US, Australia and New Zealand. The USFDA approved its use in non-alcoholic beverages in 1998 [60] and as a general purpose sweetener in 2003 [61]. In Australia and New Zealand, acesulphame K was approved for use in 1987. Acesulphame K has had no human health problems associated with its use, and has been consumed for over 20 years in many countries around the world. One breakdown product of acesulphame K, acetoacetamide, is known to be toxic if consumed in very large doses. However, the amount of this substance that could be present in an acesulphame K-sweetened product is extremely small and negligible. In approving its use, the USFDA therefore concluded no further testing of acesulphame K was necessary [2].

Over fifty scientific studies on the effect of acesulphame K in the body support its safety as a non-nutritive sweetener. Intake of acesulphame K in Australia and New Zealand is estimated to be well below the ADI of 15mg/kg body weight per day, (table 1) [1], as determined by the JECFA [62]. This amount was derived from the estimated level that caused no toxic effect in rats.

Table 1: Average Australian and New Zealand intakes of aspartame and acesulphame K [1]

Sweetener	Acceptable Daily Intake (mg/kg of body weight per day)	Current intake in Australia (mg/kg of body weight per day)	Current intake in New Zealand (mg/kg of body weight per day)
Aspartame	40	2.56 (maxm 7.46)	1.69 (maxm 5.38)
Acesulphame K	15	0.53 (maxm 1.39)	0.39 (maxm 1.59)

Stevia

Stevia is the generic term used for sweetening substances derived from the herb Stevia rebaudiana (S. rebaudiana). Steviol glycoside is a more precise term for a group of sweet compounds extracted and purified from S. rebaudiana. Of these, stevioside and rebaudioside A are the predominant steviol glycosides found in S. rebaudiana.

Stevia has zero calories [63] and is 250-300 times sweeter than sucrose. Stevia extracts are suitable for use in cooking and baking, as they are heat stable [64] .Stevia has a flavour enhancing effect when used in association with other flavours and may therefore be used in a wide range of food applications. The advantages of stevia over some other sweeteners include its stability, low kilojoule level, lack of effect on blood glucose levels, its suitability for use in people with phenylketonuria and people with diabetes [65]

Metabolism of Stevia

Both stevioside and rebaudioside A are metabolized in the same manner [66, 67]. In both rats and humans little or no stevioside or rebaudioside A is absorbed into the blood and both are completely metabolised to steviol by the microbial flora of the caecum, with excretion occurring via the faeces in animals or by the urine in humans[68].

Safety of Stevia

The safety of steviol glycosides was evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) at its 63rd, 68th and 69th meetings [69-71]. After extensive review, the JECFA determined the acceptable daily intake (ADI) for steviol glycosides as 4 mg/kg bodyweight per day, expressed as steviol.

In addition, in 2010 the EFSA Scientific Panel on additives, assessed the safety of steviol glycosides [72]. The assessment showed that the substances were not genotoxic, nor carcinogenic, or linked to any adverse effects on the reproductive human system or for the developing child. Full regulatory approval for stevia-derived sweeteners throughout Europe is expected from the European Commission in 2011.

Stevia and Appetite

To date, there has only been one published study specifically evaluating stevia and its effect on appetite and hunger [40]. In this study, nineteen lean and 12 obese subjects aged between 18 and 50 years were recruited to complete three separate food test days during which they received either a low-kilojoule pre-load sweetened with stevia or aspartame or a sucrose sweetened pre-load before lunch and dinner. Results showed food intake at lunch or dinner did not increase after consuming the low-kilojoule pre-loads compared to the sucrose sweetened pre-loads. No significant differences were reported for hunger and satiety levels. An additional effect from stevia preloads was that blood glucose levels were lower compared to the sucrose preload and insulin levels were lower compared to both the sucrose and aspartame preloads.

Stevia and blood pressure

Two long-term clinical trials [73, 74] have been conducted over 1 and 2 years respectively, in hypertensive Chinese subjects looking at the effects of stevia on blood pressure. Results of both studies showed that blood pressure

was significantly decreased in the stevia group compared to the placebo group. However, other shorter duration studies have shown no benefit of adding 15 mg/kg bodyweight/day crude stevioside preparations for 24 weeks on blood pressure in mildly hypertensive individuals [75].

Overall, the current research indicates that stevioside may exert a pharmacological effect by lowering blood pressure in those with existing hypertension, or it may have no effect on blood pressure. However, when effects have been observed they have been in studies using amounts significantly higher than the ADI level. At this stage it is reasonable to conclude that steviol glycosides, when encountered in the normal diet, are generally well tolerated and are unlikely to have adverse effects on blood pressure.

Stevia and cancer

A 1985 study [76] reported that steviol, a breakdown product from stevioside is a mutagen in the presence of a liver extract of pre-treated rats however this finding was later criticized on procedural grounds indicating that the data were mishandled so that even distilled water would appear mutagenic [77]. Despite this one report, the bulk of studies show an absence of harmful effects [65, 78]. Over the following years bioassay, cell culture, and animal studies have found stevia to be non- carcinogenic.

All of the studies conducted to date have been on rats. A study [79] in rats administered stevioside (5% in the diet) for 36 weeks and showed that stevioside did not enhance the development of bladder cancer when administered alone or when administered after a carcinogen [79]. Similarly, another study found rats given stevioside (purity of 85%) at varying amounts over a 2 year period showed no evidence of carcinogenity in any tissue[80]. A long term two year carcinogenicity study in 100 male and female rats exposed to a range of dietary amounts of up to 5% stevioside (2500 mg/kg bodyweight/day) showed no evidence of increased carcinogenity and the authors concluded that stevioside was non-carcinogenic [81].

In conclusion, the majority of evidence suggests that stevia is not carcinogenic. In the 2008 FSANZ report it was stated that 'stevioside has very low acute toxicity and there is no evidence of carcinogenicity, developmental, reproductive or genotoxicity effects [68].'

Non-nutritive sweetners during pregnancy

For ethical reasons, scientific studies on the consumption of intense sweeteners during pregnancy and lactation have only been conducted in animals. The breakdown products of aspartame are phenylalanine, aspartic acid and methanol and these substances do not cause toxic effects in the body. Phenylalanine does cross the human placenta, although maternal phenylalanine levels after consumption of aspartame have been consistently below toxic levels [82]. Toxicity from aspartic acid is non-existent as it does not cross the human placenta [83]. Methanol toxicity is also not a concern during pregnancy as methanol levels in maternal serum are only slightly elevated following consumption [83]. Although there have not been human studies on the safety of consuming aspartame or acesulphame K during pregnancy, the lack of adverse reports suggests that they are safe. Research on stevia has shown no effect on fertility in animals [23, 42, 43, 44]. Although earlier studies have suggested reduced fertility in rats, these have been widely criticised on procedural grounds. Overall, the existing body of evidence suggests stevia has no effect on fertility in animals and indicates early studies in this area suffered from methodological problems.

Research on non-nutritive sweetener consumption during pregnancy in rats has concluded that there are no data to indicate that consumption of aspartame, acesulphame K or stevia produces any adverse effects to either the

mother or foetus. The American Dietetic Association and the American Pregnancy Association also agree that consumption of aspartame and acesulphame K during pregnancy is safe. At present, the American Pregnancy Association does not recommend stevia during pregnancy indicating more research is required in this area.

Non-nutritive sweetners in diabetes

In Australia and New Zealand, non-nutritive sweetener consumption amongst people with diabetes is more common than in the general population, with aspartame being the most widely used non-nutritive sweetener [1]. In Australia, people with diabetes and impaired glucose tolerance consume more acesulphame K than their New Zealand counterparts [1]. As stevia was only permitted for use in foods and beverages by FSANZ in 2008, data on consumption of this sweetener is currently unavailable, however it is likely to be much lower than aspartame and acesulphame K.

The safety of aspartame use in people with diabetes has been widely researched and it has been consistently shown that consumption of aspartame, even at three times the acceptable daily intake, has no effect on glycaemic control [84] or insulin levels [84, 85].

The evidence to date, on the use of stevia in people with diabetes suggests effects on blood glucose levels from consumption of stevia may be different depending on the status of the subjects and that there are differences in responses between diabetic and non-diabetic animals and humans [73, 80, 86-89]. Overall the weight-of-evidence indicates that stevioside would be unlikely to produce negative effects in humans at concentrations encountered in the diet and may have a benefit in people with diabetes by increasing insulin secretion [68] however this observation needs to be confirmed with further research.

Due to their low or no kilojoule content, aspartame, acesulphame K and stevia can also be useful for people with diabetes who are trying to lose weight. Consumption of aspartame and aceulphame K is supported by the American Diabetes Association [90] as well as Diabetes Australia [91] and Diabetes New Zealand [92]. To date, the majority of evidence on stevia, has shown that the consumption of stevia, at concentrations normally encountered in the diet, is safe, however the evidence is limited.

Non-nutritive sweetners in children

Children can safely consume aspartame,acesulphame K and stevia within ADI levels. Due to their smaller size and relatively higher sparkling beverage intake compared to adults, it is likely that children will also have higher relative intakes of these non-nutritive sweeteners per kilogram of body weight per day [55]. A recent survey by FSANZ found that consumption is well below the ADI for aspartame and acesulphame K in children [1]. For stevia, children aged 2-6 could meet 100% of the ADI if stevia were added to all proposed foods at maximum concentrations, however this scenario is unlikely [68].

Data from other countries also indicates that overall consumption of these non-nutritive sweeteners by children is well below the ADI [93]. A review on aspartame intake specifically found that average consumption in children was well below the ADI in various countries around the world, including Australia [93]. There is a wide range of non-nutritive sweeteners in use in Australia and New Zealand, meaning intake of any one sweetener is likely to be less than in countries with limited sweeteners available in the food supply. Many of the approved sweeteners are blended in beverages, reducing the risk of any individual non-nutritive sweetener exceeding ADI levels in children [55].

Non-nutritive sweetners and dental health

It is well established that a person's diet can impact on their dental health. There is a large evidence base showing that frequent consumption of sugars such as sucrose can lead to an increased risk of tooth decay. Research in the area of dental health suggests that replacing sugar in foods with non-nutritive sweeteners such as aspartame and acesulphame K may lead to a reduction in the incidence of tooth decay [94]. To date no research interventions have addressed the effect of aspartame and acesulphame K on dental health in humans. One study has looked at the effect of stevia on dental caries and concluded that neither stevioside nor rebaudioside A were cariogenic [95].

Rat studies have found that compared to sucrose, intake of non-nutritive sweeteners such as aspartame results in a lower incidence of tooth decay and may even be protective [96]. Studies conducted in vitro have supported this finding [97]. However drinks containing non-nutritive sweeteners are still acidic and there is clear evidence that the acid alone can erode tooth enamel when these drinks are sipped frequently such as in sipper bottles or baby bottles [98-100]. The overall composition of a beverage should therefore be considered when assessing the impact of a product on dental health.

Evidence-based key messages:

- Aspartame, acesulphame K and stevia can safely be consumed as general purpose, non-nutritive sweeteners by the general population.
- Foods and beverages containing non-nutritive sweeteners can be consumed in moderation as part of a healthy, balanced diet and lifestyle that also includes regular physical activity.
- Those with phenylketonuria (PKU) should avoid products sweetened with aspartame. Products that are free of aspartame and are sweetened with stevia or acesulphame K are safe for consumption by people with PKU.
- Foods and beverages sweetened with aspartame and/or acesulphame K and stevia, along with other non-nutritive sweeteners, can be particularly useful in the diet of people with diabetes.
- Food and beverages sweetened with aspartame and/or acesulphame K and stevia, along with other non-nutritive sweeteners can be useful in weight loss diets as a low kilojoule substitute for sugar-sweetened foods and beverages. It is important that these non-nutritive sweeteners are used within the context of a healthy weight management program including a lower energy diet and exercise.
- Aspartame and acesulphame K are safe to use during pregnancy. More research is required on the safety of stevia during pregnancy.
- Aspartame, acesulphame K and stevia can be used to replace added sugars in the diet in an effort to reduce the risk of tooth decay, however the impact on dental health will be determined by the overall composition of the food or beverage within which the sweetener is added.

Summary

Despite popular allegations linking the use of non-nutritive sweeteners such as aspartame, stevia and acesulphame K to adverse health effects such as cancer, neurological symptoms and effects on appetite, the scientific literature does not support these theories. Consumption of these non-nutritive sweeteners can exert a beneficial effect for certain people, in particular those with diabetes and those interested in managing their weight, due to their low kilojoule content and sweet taste. Overall, when consumed within acceptable daily intake levels as currently done in Australia and New Zealand, aspartame, stevia and acesulphame K have been shown to have no association with adverse health effects and can be a useful addition to the diets of those who are concerned with their dental health, limiting their kilojoule intake or controlling their blood glucose levels.

Developed by the Coca-Cola Health and Wellness Advisory Council, in July 2007 and updated in June 2010. For review August 2012.

Advisory Council

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Appendix 1: Update of Non-Nutritive Sweetner Position Statement 2010

Methodology used to update CCSP Health & Wellness Advisory Council's position statement on the non-nutritive sweeteners aspartame, acesulphame K and stevia

Given the ongoing research conducted on non-nutritive sweeteners since 2007, the Coca Cola Health and Wellness Advisory Council recommended an update of the original position statement be undertaken in 2010. FNA conducted this update in June 2010. A review of the most recent research published since 2007 on the non-nutritive sweeteners aspartame and acesulphame K was conducted. A search for all available and relevant studies on the new sweetener stevia was also carried out. The methodology was as follows.

Searching the PubMed Database

A literature search was conducted using the PubMed database to find relevant articles. The first step of the review process was to gather studies for possible inclusion in the report using the defined search strategies established in 2007. However this time, the search also extended to the keywords: "stevia", "stevioside","steviol glycosides", "rebaudioside A" along with:

• Pregnancy	• Diabetes	• Safety	• Hunger	• Obesity
• Fertility	• Dental health/caries	• Appetite	• Weight loss/gain	• Cancer

The literature search produced 45+ new articles.

Multiple searches were run and each search was further limited by restricting retrieval to English language and to articles published after 2007 (for aspartame and acesulphame K) and containing abstracts. Search results were reviewed by FNA. Articles were considered for inclusion in the review if they met the journal selection criteria as outlined in the 2007 methodology.

Articles that appeared relevant were selected for use if they either:

1. Met the selection criteria (see 2007 journal selection criteria) or
2. Contained scientific evidence about aspartame, acesulphame K or stevia that was supported in the literature – 4 observational study and 16 experimental studies met the criteria.

Review articles were used for background information and support where relevant (14 articles were used). Documents from the EFSA, FSANZ, FAO/WHO were referred to in the document as they were determined to be relevant to the use of non-nutritive sweeteners (8 articles were used). These Organisations often conduct extensive literature reviews and critically analyse anecdotal reports when determining their position on the use of non-nutritive sweeteners. Two scientific reference books were used. Three case-studies were used which alluded to anecdotal evidence.
See appendix 2 for listings of all articles used in the position paper.

Journal selection criteria

The journal selection criteria were as per the 2007 methodology.

Appendix 2

Observational and experimental studies included in the position statement

Table 1: Observational criteria check

Study	Criteria 1	Criteria 2	Criteria 3	Criteria 4	Criteria 5
Bosetti et al; 2009	Yes	No	Yes	No	Yes
Phelan et al; 2009	Yes	Yes	Yes	Yes	Yes

Table 2: Experimental criteria check

Study	Criteria 1	Criteria 2	Criteria 3	Criteria 4	Criteria 5	Criteria 6	Criteria 7
Rowan 1995	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Monsivais, 2007	N/A	Yes	Yes	Yes	Yes	Yes	N/A
Brown, 2009	Yes	N/A	Yes	Yes	Yes	Yes	N/A
Wheeler, 2008	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Roberts, 2008*	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Anton, 2010	No	Yes	Yes	Yes	Yes	Yes	N/A
Chan, 2000	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hsieh, 2003	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ferri, 2006	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Barriocanal, 2008	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Xili, 1992*	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Toyoda, 1997*	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Jeppesen, 2003*	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Suanarunsawat, 1997*	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Gregersen, 2004	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Geuns, 2007	N/A	Yes	Yes	Yes	Yes	Yes	N/A

* Animal study

Articles that did not meet criteria but contained substantiated information

1. Pezzuto, J.M., et al., Metabolically activated steviol, the aglycone of stevioside, is mutagenic. Proceedings of the National Academy of Sciences of the United States of America, 1985. **82**(8): p. 2478-82.
2. Procinska, E., B.A. Bridges, and J.R. Hanson, *Interpretation of results with the 8-azaguanine resistance system in Salmonella typhimurium: no evidence for direct acting mutagenesis by 15-oxosteviol, a possible metabolite of steviol.* Mutagenesis, 1991. **6**(2): p. 165-7.
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4. Das, S., et al., *Evaluation of the cariogenic potential of the intense natural sweeteners stevioside and rebaudioside A.* Caries Research, 1992. **26**(5): p. 363-6.

Review articles included in position statement

1. Magnuson, B.A., et al., *Aspartame: a safety evaluation based on current use levels, regulations, and toxicological and epidemiological studies.* Critical Reviews in Toxicology, 2007. **37**(8): p. 629-727.
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Professional organisations referred to in position statement

1. European Food Safety Authority, *Opinion of the scientific panel on food additives, flavourings, processing aids and materials in contact with Food (AFC) on a request from the Commission related to a new long-term carcinogenicity study on aspartame.* The EFSA Journal, 2006. **356**: p. 1-44.
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Book used as a reference in position statement

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Case studies used in position statement

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