

## Can artificial sweeteners help control body weight and prevent obesity?

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The possible role played by artificial sweeteners in the long-term maintenance of body weight is considered. Although artificial sweeteners can play a role in a short-term energy-controlled diet, the evidence that they are helpful over a longer period is limited. In those in the recommended weight range there is evidence of compensation; that is, the consumption of low-energy foods is followed by an increased energy intake to make up the lost energy. Energy compensation is more likely in those not displaying dietary restraint. The desire to remove sugar from the diet reflects an assumption that its intake is associated with obesity. However, the consumption of energy-dense food, that almost entirely reflects a high fat and low water content, is the best predictor of obesity. Diets offering a high proportion of energy in the form of carbohydrate tend to contain low levels of fat. There are several reports that the use of artificial sweeteners leads to an increased consumption of fat. The weak ability of fat to satisfy hunger makes it easy to overeat fatty foods; in contrast, carbohydrates promote a feeling of 'fullness'. Various short-term studies have found that carbohydrate consumed as a liquid, rather than a solid, is more likely to result in weight gain.

**Artificial sweeteners: Obesity prevention: Body-weight maintenance: Energy density:  
Eating behaviour: Sugar**

### Introduction

The view of the American Dietetic Association (2004) was that: 'consumers who want the taste of sweetness without added energy may select non-nutritive sweeteners to assist in the management of weight . . .'. Unless the context of such a statement is clear there is a risk that it will mislead. As two-thirds of Americans use sugar-free products when not on a diet (O'Brien Nabors, 1999), there is a need to distinguish a role of sweeteners while dieting, from a role as part of a daily weight-maintenance programme. Is there evidence that artificial sweeteners are useful both while dieting and at a later stage to prevent regaining weight? The influence of artificial sweeteners on aspects of physiology and eating-related behaviour is therefore reviewed.

There are two generations of artificial sweeteners. The first included aspartame, saccharin and cyclamate. Aspartame is 200 times sweeter than sucrose and has been approved for use in more than 100 countries. As heating decreases the perception of sweetness it is used in cold foods and drinks. Saccharin is the oldest high-intensity sweetener and has been used since the turn of the last century. It is 300 times as sweet as sucrose but has a metallic aftertaste. Cyclamate, that is thirty times as sweet as sucrose, is heat-stable and often used together with other sweeteners, particularly saccharin.

The second generation of products included acesulfame-K, alitame, neotame and sucralose. Acesulfame-K is about

300 times sweeter than sucrose and, although it can have a bitter aftertaste, is often combined with other low-energy sweeteners to produce a more sugar-like taste. Acesulfame-K has a delayed bitter aftertaste that is longer and more artificial than aspartame, alitame or sucrose (Ott *et al.* 1991). Alitame is 2000 times sweeter than sucrose and is approved for use in Australia, China and Europe. Neotame is a recently developed product, a derivative of aspartame with a clean sweet taste. Sucralose is chemically modified from sugar and is about 600 times sweeter. It maintains its sweetness during cooking.

It is inevitable that body weight will increase if the intake of energy is greater than energy expenditure. The general public, hoping to decrease energy intake and hence control weight, often use artificial sweeteners in the place of sugar. The logic is superficially simple. If a product with zero energy replaces energy-containing food items then there will be less energy to be deposited as adipose tissue. However, the argument may well be too simple. Potentially there are a number of ways the body can adjust to the decreased intake of energy associated with the use of artificial sweetener. Do any of the following apply?

Do artificial sweeteners induce satiety to the same extent as sugar; that is, do you eat more when consuming artificial sweeteners? Having eaten a low-energy-density meal how long are you satiated; are you more likely to snack between meals having avoided energy? When the next mealtime arises do you compensate for the previous low energy intake

**Abbreviations:** GI, glycaemic index; HFCS, high-fructose corn syrup; 5-HT, 5-hydroxytryptamine (serotonin).

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by eating more? If energy compensation occurs, what form does the increased macronutrient intake take? If you ate more fat you might put on weight. Even if sweeteners can help in the short term while dieting, what impact do they have when included as part of the long-term diet when the vigilance of the period of dieting is passed? Is there evidence that the use of artificial sweeteners is associated with a prolonged decline in energy intake?

The impact of artificial sweeteners on appetite and obesity is contrasted with that of natural sweeteners. Medline (National Library of Medicine, Bethesda, MD, USA) was used to find relevant literature together with studies referred to in these papers. The first question addressed was the relative importance of carbohydrate and fat in the development of obesity. The routine use of artificial sweeteners to prevent weight gain implicitly assumes that carbohydrate intake plays an important role in fat deposition; can such a view be supported?

### Macronutrients and obesity

Although at one stage there was a tendency to see carbohydrate consumption as conducive to obesity, by the 1990s fat became the nutritional villain.

Hill & Prentice (1995) commented: 'Metabolic studies show that diets high in fat are more likely to result in body fat accumulation than are diets high in carbohydrate. There is no indication that simple sugars differ from complex sugars in this regard. Epidemiologic data show a clear inverse relation between intake of sugar and fat. Further, although high intake of dietary fat is positively associated with indexes of obesity, high intake of sugar is negatively associated with indexes of obesity. There is ample reason to associate high-fat diets with obesity but, at present, no reason to associate high-sugar diets with obesity.'

The importance of fat reflects its high energy density, its palatability and that it is less satiating than other macronutrients. It is common to talk about the 'sugar-fat seesaw' – diets with a high amount of energy in the form of fat contain low amounts of sugar, whereas diets low in fat tend to be high in sugar. One study found that high sugar consumers tended to be thinner than high fat consumers (Bolton-Smith & Woodward, 1994), leading to the suggestion that sugar may even protect against obesity, if it drives fat from the diet. In a multi-centre trial, a low-fat diet for 6 months, rich in either simple or complex carbohydrate, led to a fall in body weight. There was no difference between those consuming different forms of carbohydrate (Saris *et al.* 2000). A diet high in carbohydrate is less likely to result in weight gain, as lipogenesis is a limited cause of adiposity (Poppitt & Prentice, 1996); rather, carbohydrate is preferentially disposed of by oxidation.

In summary the weight of evidence is that sugars are not the primary concern when considering the aetiology of obesity. Thus, the replacement of sugars with artificial sweeteners would not be expected to have such a dramatic effect on weight gain as decreasing fat intake. The emerging picture is that energy-dense diets, those high in fat, play a causal role in causing obesity. In contrast, carbohydrate and

sugar consumption has often been viewed as at the worst neutral in this respect (Bolton-Smith & Woodward, 1994; Astrup & Raben, 1995; Poppitt & Prentice, 1996; Mela, 1997).

### Energy density

In recent years, rather than considering the role of particular macronutrients, attention has been directed to energy density (Poppitt & Prentice, 1996; Drewnowski, 1999; Rolls *et al.* 1999); that is, the amount of available energy per weight of food (kJ/g). The major factors that determine energy density are water and fat content, to the extent that these account for 99 % of the variance, with water content having the greater influence (Drewnowski, 1998). The World Health Organization (2003) review concluded that there was 'convincing evidence' that a high intake of energy-dense foods is associated with an increased risk of obesity. As high-energy-dense foods are more palatable they are eaten in greater amounts. In reality it is rarely possible to disassociate energy density and palatability; attempts to do this have varied energy density over a very limited range.

When exposed to an *ad libitum* supply of food, under laboratory conditions, subjects consume a relatively constant weight of food, rather than a constant amount of energy (Poppitt & Prentice, 1996). In the short term the body responds to the amount of food consumed, so more energy is consumed when there is more energy for a given weight of food. Stubbs *et al.* (1993) studied food intake when the energy density of fat-containing meals was varied. The increase in energy intake, when eating a high-fat diet, almost completely disappeared when the energy density of meals was kept constant. Energy density rather than fat content was important. When the two have been separated it is energy density and not fat content that determines energy intake (van Stratum *et al.* 1978; Duncan *et al.* 1983; Drewnowski *et al.* 1994; Stubbs *et al.* 1996; Rolls *et al.* 1998).

As there is a tendency to eat a daily set amount of food, the eating of energy-dilute foods should help control weight. The problem is that a low-energy-dense diet has less sensory appeal (Drewnowski, 1999), although sweeteners can increase palatability (Pliner & Stallberg-White, 2000).

As energy density was a major concern for the World Health Organization (2003), they recommended a decrease in the intake of fat and free sugar, although they recognised that a '... population goal for free sugars of less than 10 % of total energy is controversial'. A reduction in the energy density of the diet will reduce weight but only if consumption can be maintained. In the longer term the approach will often fail as it takes a physiological rather than psychological perspective. One problem is palatability; individuals choose to eat appetising food. If you remove fat and sweetness there is little chance that a diet will be consumed for extended periods – it will taste unattractive. A second problem is that if you remove carbohydrate you will tend to eat a similar amount of the food that now lacks carbohydrate. The risk is that you will either eat more protein, that has slightly more energy than carbohydrate, or fat that for a given weight offers 140 % more energy.

### *The glycaemic index and food intake*

A decline in fat intake typically leads to an increased consumption of carbohydrate, often with a high glycaemic index (GI). Anderson *et al.* (2002) contrasted the effect of GI on satiety; less hunger and lower food intake were associated with a greater increase in blood glucose. Do artificial sweeteners, as they do not increase blood glucose, have a smaller impact on satiety? In fact the opposite argument can also be addressed, as there is a debate about the value of a low-GI diet in weight control; while some argue its value (Pawlak *et al.* 2002), others question its usefulness (Raben, 2002).

A rise in blood glucose stimulates the release of insulin that facilitates nutrient storage. Rats fed a high-glycaemic-load diet displayed metabolic changes that favoured fat deposition (Lerer-Metzger *et al.* 1996). In human subjects a low- rather than high-glycaemic-load diet produced a similar weight loss, but a greater loss of fat (Bouche *et al.* 2002). Slabber *et al.* (1994) contrasted two low-energy diets and found in obese females that weight was less after the low-insulin-release diet. Ludwig (2000) reviewed sixteen studies that had considered the short-term influence of GI on subsequent food intake. He found that all studies bar one associated low GI and increased satiety or decreased food intake. However, a review of a wider range of studies was less positive and found that a low-GI meal was beneficial in fifteen out of thirty-one studies (Raben, 2002). If meals of the same energy content were compared, twelve studies reported that a low-GI meal increased satiety whereas twelve did not. However, if GI does prove to be important, artificial sweeteners may influence food intake via their effect on blood glucose levels.

### *High-fat diets*

The conclusion that fat has an important role in weight gain may superficially conflict with the popularity of high-fat diets. The Atkins diet initially allows almost no carbohydrates and works by inducing a state of ketosis. As the body is deprived of carbohydrates it begins to burn fat. The present discussion has been of a traditional mixed diet. The biochemistry of starvation differs from the situation presently discussed. Any success associated with a high-fat diet is in no way incompatible with the conclusion that fat consumption plays a major role in the obesity epidemic amongst those consuming a normal diet.

### *Summary*

- (1) Carbohydrates promote a feeling of 'fullness' to a greater extent than fat, making it easier to overeat fatty foods.
- (2) The consumption of energy-dense foods is the best predictor of obesity. Energy density is almost entirely predicted by the fat and water content. Given the importance of fat rather than carbohydrate, the use of artificial sweeteners by themselves is unlikely to have a major impact on body weight.
- (3) Diets high in fat result in an increase in weight. Diets high in fat tend to be low in carbohydrate.

- (4) Reports that a low-GI meal enhances satiety are inconsistent.
- (5) Carbohydrate intake in general, and sugar intake in particular, are not the primary concern when considering obesity. In fact a high carbohydrate–low fat intake is associated with a lower body weight.

## **Neural control of feeding**

### *Reward mechanisms*

There has been an interest in the neurochemical modulation of macronutrients intake. A role for opioid agonists and galanin in the control of fat, and neuropeptide Y in the control of carbohydrate intake, has been discussed (Levine *et al.* 2003). More recently the importance of palatability has been established. Morphine increases the intake of a preferred diet rather than one high in fat, although preferred foods are often high in fat (Gosnell *et al.* 1990). In human subjects opioid antagonists reduce the palatability of food rather than hunger (Yeomans *et al.* 1990). Opioid mechanisms play a major role in the hedonic response to food (Kelley *et al.* 2002).

The nucleus accumbens and associated areas of the brain are important in a number of motivated behaviours such as feeding, drinking and sexual behaviour (Kelley *et al.* 2002). In industrialised societies, eating highly palatable energy-dense foods can, via these mechanisms, give a powerful message that the behaviour is beneficial. During evolution when food supply was intermittent it was adaptive to store energy for later times of starvation. However, a plentiful supply of energy brings the risk of obesity; the stimulation of the ventral striatum rewards undesirable behaviour. Both dopamine (Pal & Thombre, 1993) and opioid peptides (Kelley *et al.* 2000) modulate the ventral striatum and in this area stimulate the intake of palatable foods.

In rats, drinking a glucose solution for 30 d increased dopamine D-1 receptor binding in the accumbens core and shell, and decreased D-2 binding in the dorsal striatum. In addition  $\mu$ -1 opioid receptor binding increased significantly in the cingulate cortex, hippocampus, locus coeruleus and accumbens shell (Colantuoni *et al.* 2001). The dopamine projection to the nucleus accumbens has been implicated in rewarding the consumption of palatable foods but does it respond to energy rather than palatability? If sucrose but not artificial sweeteners influenced the neural response to palatable foods then this would have implications for the control of food intake.

The infusion of a selective  $\mu$ -opioid agonist into the nucleus accumbens of rats increased the intake of both sucrose- and saccharin-flavoured water, but not water alone (Zhang & Kelley, 1997, 2002). Zhang *et al.* (1998) found that a selective  $\mu$ -opioid agonist introduced into the nucleus accumbens increased the intake of either fat or carbohydrate, when a macronutrient was presented individually. However, the effect on fat intake was much greater than carbohydrate when both were present. They concluded that ventral striatal opioids regulate the intake of highly palatable foods.

In summary, both dopamine and opioid peptides within the ventral striatum play a key role in the affective response to highly palatable foods such as those containing fat and sugar. Artificial sweeteners act in a similar manner to sucrose in this respect.

#### Serotonin

It has been known since the 1970s that brain serotonin (5-hydroxytryptamine; 5-HT) was involved in the control of eating, playing an important role in postprandial satiety. Activation of the 5-HT<sub>1A</sub> site increases food intake but the effect is rapidly down regulated. This is a paradoxical finding as 5-HT inhibits feeding but reflects its action at autoreceptors that decrease 5-HT-mediated neuronal firing. 5-HT<sub>1B</sub> and 5-HT<sub>2C</sub> agonists decrease food intake (Vickers & Dourish, 2004). Drugs such as sibutramine that block 5-HT and noradrenaline re-uptake are used to treat the obese.

Richard and Judith Wurtman linked carbohydrate intake to the synthesis of brain 5-HT (Wurtman *et al.* 1981). Insulin release, stimulated by blood glucose, causes the uptake of most amino acids by peripheral tissues such as muscle. In contrast, insulin increases the affinity of albumin for tryptophan. Thus the ratio of tryptophan to the other amino acids in the blood increases. As tryptophan and the other large neutral amino acids compete for a transporter molecule, relatively more tryptophan is transported into the brain where Wurtman *et al.* (1981) proposed it was metabolised into 5-HT that initiates satiety. Although there are supportive rat data it has been suggested that the mechanism does not apply when humans eat any likely meal (Benton, 2002).

Benton & Donohoe (1999) summarised studies of the influence of meals that differed in the percentage of energy that came as carbohydrate. An increased availability of blood tryptophan only occurred when protein offered less than 5% of the energy. It is difficult to find meals that contain so little protein; for example, no increase in the availability of tryptophan occurs with bread, potato or pasta, so-called high-carbohydrate foods. There is no evidence in man of an increased release of 5-HT into the cerebrospinal fluid, even when there are increased blood levels of tryptophan (Teff *et al.* 1989).

It has been argued that if the Wurtman hypothesis is valid the failure of artificial sweeteners to increase blood glucose and insulin levels, and hence stimulate 5-HT synthesis, could promote carbohydrate intake. Fernstrom (1988) considered whether aspartame might disrupt the putative regulatory loop for carbohydrate intake and promote its intake. Aspartame increases phenylalanine and tyrosine levels in the blood, long-chain amino acids that compete with tryptophan for entry into the brain. The concern was that aspartame, via this mechanism, might decrease the levels of brain tryptophan and hence 5-HT synthesis, thus stimulating carbohydrate intake. Fernstrom (1988) argued that there was little cause for concern. Firstly, he believed that the feedback loop for the control of carbohydrate intake probably does not exist. Secondly, although aspartame can block the uptake of tryptophan by the brain, the dose required is so large that it is unlikely to be consumed; it is over 500 mg/kg in rats (Fernstrom *et al.* 1986).

#### Insulin

The release of insulin is a potentially important factor in the regulation of body weight. Insulin and insulin receptors are widely distributed throughout the brain; in particular they are found in areas associated with energy homeostasis. It has been suggested that insulin has both short- and long-term influences on food intake and the regulation of body weight (Gerozissis, 2004).

As in the periphery, where it stimulates anabolic activity and the synthesis of lipids, insulin has been suggested to cause weight gain. Both fasting insulin levels and its response after a meal are correlated with adiposity. Over 24 h, overall insulin secretion is proportional to the fat content of the body (Havel *et al.* 1999). Various diets have been developed based on the view that minimising insulin secretion leads to less fat deposition. In this spirit the consumption of sucrose rather than artificial sweetener, as it would stimulate greater insulin secretion, is viewed as being more likely to lead to weight gain. Havel (2001) took issue with this perspective when he asserted that it failed to distinguish chronically high levels of insulin, that occur in those with insulin resistance, from the response of a healthy individual, in whom after a single meal peripheral insulin rises and falls rapidly. In fact a larger insulin response to a single glucose load is predictive of a smaller future gain in weight, rather than a tendency to become obese (Schwartz *et al.* 1995).

In the 1970s it was proposed that insulin is a long-term regulator of food intake (Woods *et al.* 1974). Over several hours, following its release into the blood, insulin is transported into the brain by a receptor-mediated mechanism that is saturated by high concentrations. The slow nature of this mechanism is not consistent with insulin having an immediate influence on satiety but is consistent with a role in the long-term regulation of adiposity (Havel, 2001). An additional perspective is offered by the finding that brain insulin enhances the short-term satiety effect of cholecystokinin (Figlewicz *et al.* 1986). Using microdialysis, the administration of glucose to the median hypothalamus has been found to cause a large and rapid increase in extracellular insulin levels (Gerozissis *et al.* 2001); the release of brain insulin decreases food intake.

In summary, the level of insulin in the brain reflects the nature of the diet; it is higher after carbohydrate meals. The introduction of insulin to the brain inhibits feeding. The use of artificial sweeteners is certain to decrease peripheral insulin release and hence influence neurochemistry. The mechanisms controlling feeding are, however, complex and there remains much to be discovered concerning the role of insulin in the cascade of food-related neurochemical activity.

#### Summary

- (1) Dopaminergic and opioid mechanisms in the ventral striatum mediate the response to palatable food. Artificial sweeteners and natural sugars have a similar impact on this area of the brain.
- (2) The suggestion that blood glucose and insulin levels following carbohydrate consumption lead to 5-HT-induced satiety is not supported by the evidence.

- (3) Insulin plays an important role in the longer-term regulation of body weight although it is unclear if such mechanisms are influenced by the lower levels of insulin that result from artificial sweetener consumption.

### Satiety

#### *Macronutrient intake*

As macronutrients differentially influence satiety, any decision to replace sugar has potential consequences in this respect. Holt *et al.* (1995) found that the levels of protein, fibre and water in test foods were correlated positively with satiety. In contrast, the level of fat in food items was negatively associated with satiety – the more fat there was in the meal the less satisfying it proved. The level of sugar and total carbohydrate did not predict satiety. Palatability was positively correlated with both fat and sugar content, to a greater extent with fat than sugar, but negatively with the amount of protein and starch.

When all aspects of the meal were considered in regression equations the strongest association was found between satiety and the size of the meal (the energy intake was constant); the more in terms of weight that was eaten the greater was satiety. The other predictor of satiety was palatability; more palatable foods were less satiating. When asked how much they wanted to eat of the food, fat content but not sugar or total carbohydrate content predicted the answer.

#### *Artificial sweeteners*

Holt *et al.* (1995) did not consider artificial sweeteners, but their findings raise an important issue – there is a tendency to consume more of palatable foods but these are less satiating. The only reason to add artificial sweeteners is to increase palatability with the consequence that food consumption will be encouraged. If an artificial sweetener is added to a food item that does not previously contain sugar then there is the potential to increase consumption. Whether increased consumption is beneficial in terms of body weight depends on the food involved.

There is a motivation to eat sweet-tasting foods; for example saccharin intake increased the food consumption of rats (Tordoff & Friedman, 1989). As rats ate more in a sham-feeding paradigm, where an artificial sweetener enters the mouth but not the stomach, the phenomenon was pre-digestive (Tordoff, 1988).

In human subjects there are reports that the consumption of aspartame was associated with increased appetite. Blundell & Hill (1986) found that glucose decreased appetite following its consumption. In contrast, aspartame increased the motivation to eat and decreased feelings of fullness. As ratings of hunger and the amount eaten do not always correspond, it is unfortunate that no food intake data were reported. Subsequently the same group found that aspartame, saccharin and acesulfame-K all increased hunger, but they did not increase food intake after 1 h (Rogers *et al.* 1988). Using chewing gums containing different concentrations of aspartame, Tordoff & Alleva (1990) also found that aspartame increased hunger.

Epidemiological evidence at about the same time found that the use of artificial sweeteners was associated with obesity, adding to the credibility of the initial observations (Stellman & Garfinkel, 1986).

The majority of studies on the topic have given a drink that contained either sugar or an artificial sweetener and then monitored the food eaten at a meal. Aspartame has been reported to increase satiety in some (Birch *et al.* 1989; Rogers *et al.* 1990, 1995; Hall *et al.* 2003) but not all such studies (Anderson *et al.* 1989; Leon *et al.* 1989; Rodin, 1990). A key difference may be that when aspartame has been found to induce satiety it has been administered in a capsule, removing the sensation of sweetness.

Renwick (1993) summarised this topic under various headings. The first was whether artificial sweeteners increase perceived hunger. Subsequent studies failed to confirm the initial findings of Blundell & Hill (1986). The adding of the sweetener to water without any other flavour may have produced an unnatural stimulus and atypical result. The second question was whether artificial sweeteners resulted in an increased intake of food at the next meal. Renwick (1993) considered fifteen studies of that question and found only one that reported an increased intake of food. He concluded that there was no evidence that artificial sweeteners increased energy intake. If artificial sweeteners stimulated the release of insulin, the level of blood glucose would fall and hunger might be stimulated. Renwick (1993) considered ten studies and found only one that had reported an influence on insulin release.

#### *Summary*

- (1) The level of protein, fibre and water in foods predicts satiety. Fat levels are negatively associated with satiety whereas the levels of sugar and total carbohydrate do not predict satiety.
- (2) Energy-dense foods are not very satiating but are highly palatable.
- (3) The fat content of a food, but not the sugar or total carbohydrate content, predicts how much you want to eat.
- (4) Artificial sweeteners do not increase energy intake or ratings of hunger.

### The regulation of food intake

The influence of artificial sweeteners on food intake has been considered both at the next meal and over the longer term. In a series of short-term studies, it was reported that the use of artificial sweeteners results in a later increase in energy intake to compensate for the energy lost. Birch *et al.* (1989) found that children under 5 years compensated completely for the energy removed from soft drinks by the use of artificial sweeteners. Lavin *et al.* (1997) found that on days when sugar rather than artificially sweetened lemonade was drunk by young women there was no difference in total energy intake, although the sugar-containing drink was associated with a lower daily intake of fat and protein. Other studies have reported only partial energy compensation (Anderson *et al.* 1989; Rolls *et al.* 1990; Drewnowski *et al.* 1994).

The extent of energy compensation may reflect the subjects. Rolls *et al.* (1994) reported less-perfect energy compensation in young women who reported dietary restraint, while near-perfect compensation in young men who were prepared to eat freely. Energy compensation is better in children than adults.

#### Intervention studies

The more important question is the impact of the long-term use of artificial sweeteners. Tables 1 and 2 summarise studies that have examined the use of artificial sweeteners for more than 1 d.

Early studies measured food intake by presenting it as a liquid pumped on demand into the mouth. Campbell *et al.* (1971) reported that lean subjects adjusted the volume consumed when nutritive density was manipulated, to maintain a near-constant energy intake. In contrast, obese subjects failed to adapt to changes in energy density. Wooley (1971) gave liquid diets to both lean and obese subjects and found incomplete compensation when a lower-density food was supplied. The volume drunk increased when consuming a liquid of low energy, although the total energy intake was greater with the higher-density food. Spiegel (1973) found that when a dilute source of energy was introduced, 40 % of subjects dramatically compensated by increasing their intake, although she found compensation was not usually complete and began typically 2 to 5 d after beginning the dilute diet. Porikos *et al.* (1977) criticised these early studies as they used bland-tasting liquids that obese subjects did not consume in sufficient quantities to maintain weight.

When considering the intake of solid food, two types of study need to be distinguished: firstly, those that add items to the existing diet; secondly, those that replace sugar-containing items in the existing diet with others sweetened with artificial sweeteners. Table 1 includes two studies that consider the addition of an additional source of sugar. Raben *et al.* (2002) found that body weight increased when subjects were instructed to consume traditional soda containing 152 g sugar/d rather than the low-energy equivalent. Similarly Tordoff & Alleva (1990) had found that the instruction to consume additional sugar-sweetened soda increased body weight although the use of artificial sweeteners prevented weight gain. The body finds it difficult to compensate when energy is added to the existing diet. If in this context artificial sweeteners prevent the consumption of additional energy, they can help to prevent weight gain.

The conclusion of Vermut *et al.* (2003) that: 'replacing (added) sugar by low-energy sweeteners ... might result in lower energy intake and reduced body weight' relied on only four of the studies included in Tables 1 and 2 and disproportionately selected studies that had added sugar to an existing diet. A more balanced view is obtained if you also consider studies that have replaced sugar already in the diet; Table 2 lists such studies. It has been suggested that individuals are better able to compensate for the energy dilution of a meal rather than energy supplementation (Poppitt & Prentice, 1996).

When considering Table 2 it is necessary to consider the populations studied. When samples of those in the accepted

**Table 1.** The longer-term influence of consuming foods containing sugar or artificial sweeteners on other aspects of the diet

Study	Sample	Treatment	Duration	Dietary changes	Weight
Liquid diet Wooley (1971)	Six obese and five lean males	Liquid diet, days 1–5, high energy; days 6–10, low energy	15 d	Incomplete compensation* for low energy	NS
Campbell <i>et al.</i> (1971)	Five lean males, two male and four female obese	Days 1–7, baseline; days 8–30, liquid diet	30 d	Lean, but not obese, compensated for low energy	Declined in obese with more-dilute liquids
Spiegel (1973)	Two female and thirteen lean males	Standard followed by dilute liquid diet	10–21 d	Six of fifteen subjects dramatically compensated for dilution	Failure to compensate resulted in weight loss
Porikos <i>et al.</i> (1977)	Six female and two male obese	Days 4–6 and 10–12, 25 % less energy due to AS	15 d	No compensation for lost energy	Tended to increase with sugar
Sugar added to diet Tordoff & Alleva (1990)	Twenty-one males and nine females of normal weight	1.2 litres soda/d containing sugar or AS	3 weeks	AS reduced energy intake	Sugar increased weight
Raben <i>et al.</i> (2002)	Thirty-five female and six male overweight	Instructed to drink soda with 152 g sugar/d or AS	10 weeks	Sugar drink: fall in intake of fat and protein Sweetener: fall in intake of sucrose	Sugar increased weight

AS, artificial sweetener.

\*The energy not consumed because of the use of AS was replaced with an increased intake of other nutrients.

**Table 2.** The longer-term influence of replacing sugar in the existing diet with artificial sweeteners

Study	Sample	Treatment	Duration	Dietary changes	Weight
<b>Weight in accepted range</b>					
Porikos <i>et al.</i> (1982)	Six normal-weight males	Days 1–3, high sugar; days 6–18, 25% less energy	24d	Days 1–3, none; days 4–6, 40% then 80% compensation* for lost energy	Initial gain prevented by fall in energy intake
Foltin <i>et al.</i> (1988)	Six normal-weight males	Days 6–11, 2092 kJ (500 kcal) fewer; days 12–14, original diet	14d	Days 6–11, complete compensation; days 12–14, failed to compensate	Not reported
Louis-Sylvestre <i>et al.</i> (1989)	Seventeen males	Snack: normal or low-energy (AS + fat)	6d	No initial compensation. Day 6, precise compensation	Not reported
Foltin <i>et al.</i> (1990)	Six normal-weight men	Lunch 1807 or 3531 kJ (432 or 844 kcal) with or without fat and aspartame	13d	Complete compensation for low energy intake	No change
Naismith & Rhodes (1995)	Ten free-living males	Covertly removed 2092 kJ (500 kcal)/d	10d	85% Compensation. Fall in fat intake	No change
Gatenby <i>et al.</i> (1997)	Forty-nine free-living females	Replaced normal diet with low-sugar items	10 weeks	Compensation. Falls in sugar and fat intake; energy intake remained the same	No change
Reid & Hammersley (1998)	Fourteen males and thirteen females free-living	Replaced usual soda with sugar or AS	7d	Fall in carbohydrate intake on day 1, then compensation	No change
<b>Obese subjects</b>					
Kanders <i>et al.</i> (1988)	Fifty-nine obese males and females	Diet with or without aspartame	12 weeks	Prescribed by study	Weight, appetite NS with or without aspartame
Evans (1989)	Sixteen obese women who had slimmed	Diet with or without aspartame	3 weeks	With or without aspartame NS	Not reported
Kanders <i>et al.</i> (1990)	Fifty-nine obese	Maintenance: behaviour modification and exercise with or without aspartame	1 year	Prescribed by study	Less weight regained with aspartame consumption only in males
Blackburn <i>et al.</i> (1997)	163 obese females	Diet with or without aspartame Exercise with or without aspartame	19 weeks 1–2 years	Prescribed by study Prescribed by study	With or without aspartame NS Less weight regained with aspartame

AS, artificial sweetener.

\* The energy not consumed because of the use of AS was replaced with an increased intake of other nutrients.

weight range have been studied, the energy saved by the use of artificial sweeteners has been made up subsequently by 100 % (Foltin *et al.* 1988, 1990; Louis-Sylvestre *et al.* 1989; Gatenby *et al.* 1997; Reid & Hammersley, 1998), 85 % (Porikos *et al.* 1982) and 50 % (Naismith & Rhodes, 1995). Gatenby *et al.* (1997) are unusual in that they considered over an extended period the effects of reducing sugar in the diet. The sucrose intake was found to decrease in those using artificial sweeteners, although overall intake did not differ from controls. There was, however, a slight increase in protein intake although little overall effect on total energy intake or body weight. They concluded that: 'many reduced-sugar foods in practice are simply added to a preexisting diet rather than specifically used to replace sugar-containing foods'.

A complication is that learning may occur; Bellisle & Perez (1994) suggested that those who regularly use artificial sweeteners learn to compensate for the missing energy. Louis-Sylvestre *et al.* (1989) gave low- and high-energy versions of an afternoon snack and measured the amount of food eaten during a meal 1 h later. Initially the low-energy snack was not compensated for at a later meal. However, after consuming the snack for 5 d precise energy adjustments were made. The authors questioned the value for weight control of food products with a lower than usual energy content. Similarly, Reid & Hammersley (1998) found only that on day one out of seven did the use of drinks sweetened with artificial sweeteners result in a lower carbohydrate intake.

The evidence supports the view that for those in the accepted weight range, the substituting of natural for artificial sweeteners does not result in a reduction in energy intake. There is consistent evidence of subsequent energy compensation. Although on occasions compensation occurred in the entire sample, in other studies only some subjects responded. Attention should be directed to establishing the characteristics that determine whether energy compensation does or does not take place.

When samples of the obese were considered, a different pattern emerged. Kanders *et al.* (1988) found no significant differences in weight and appetite associated with the use of aspartame-containing products. Similarly with obese subjects, Porikos *et al.* (1977) found that substituting 25 % of energy in normal food, by using aspartame, did not produce energy compensation. It may be critical that the energy-reduced diets were only consumed for 3 d, perhaps not sufficient time for energy compensation to occur.

A potentially important observation was that artificial sweeteners were helpful in a maintenance diet (Blackburn *et al.* 1997). A group of obese subjects either did or did not consume aspartame as part of their energy-restricted diet. However, energy intake and weight loss were similar when followed for another 2 years; those who used artificial sweeteners regained less weight. Such data are difficult to interpret, as over time the intake of aspartame decreased in those asked to consume high levels of the sweetener and increased in those asked not to use it. Although subjects were randomly allocated to an experimental condition, the study could not be blind and the intake of artificial sweeteners may be an indication of the motivation to lose weight by various means. It was not possible to distinguish

the impact of aspartame from a range of other interventions introduced to discourage relapse. It is possible that the request that the control group avoid artificial sweeteners may have resulted in an increased intake of sugar and hence weight gain.

A differential response to removing as opposed to increasing energy can be viewed as reflecting an evolutionary history of food shortages. If you live with a shortage of food it makes sense to try to replace lost energy. However, you would wish to store any surplus energy for later periods of starvation rather than cutting down intake in times of plenty.

Poppitt & Prentice (1996) suggested that an important variable in whether energy compensation occurred following the use of artificial sweeteners might be if the entire diet, or only some foods, were of the lower-energy variety. They found that only when some available foods were high in energy did energy compensation tend to occur. When the entire diet was low in energy, compensation tended not to occur. They explained this difference in terms of energy density. If the entire diet was of low energy density, and a constant weight of food was consumed, then there would be no opportunity to consume a food of higher energy density to make up the lost energy. Essentially this explanation suggested that a fall in total energy intake in short-term studies, when an experimental diet of uniformly low-energy-dense foods was available, was an experimental artifact. The more normal approach of adding a few low-energy-dense items to a generally high-energy-dense diet leads to later compensation; that is, over time no overall decline in energy intake occurs.

#### *Surveys of the use of artificial sweeteners*

As any single alteration of the diet results in a cascade of compensatory changes, studies of free-living individuals are of interest. Surveys of the use of artificial sweeteners offer a snapshot of their long-term impact. Anderson & Leiter (1996) related the consumption of sugar and artificial sweeteners to obesity. The increase in the consumption of artificial sweeteners in the USA has been paralleled by a rapid increase in obesity. It is probable that the increased use of artificial sweeteners was a response to obesity rather than a cause. It is, however, clear that the widespread use of artificial sweeteners has not prevented the high incidence of obesity, although it is unclear what would have happened if they had not been used.

In female college students the use of artificial sweeteners was associated with the consumption of less sugar, but in men with a greater sugar intake (Chen & Parham, 1991). Overall the use of artificial sweeteners was not associated with significant differences in the intake of carbohydrate, protein, fat or total energy. Chen & Parham (1991) concluded that the pattern of intake indicated 'that users expressed their weight concerns by choosing to use a high-intensity sweetener rather than by restricting their overall food intake'. The pattern differed from a similar earlier study where, in women, the use of artificial sweeteners had been associated with a lower intake of energy, protein, total carbohydrate and simple sugars (Parham & Parham, 1980). Gender and dietary restraint may be important factors. Chen

& Parham (1991) commented that in some individuals the 'use of high intensity sweeteners may contribute to an excessive sugar intake simply because users are more blasé about their intake of sweets'.

Bellisle *et al.* (2001) examined a cross-section of the French population and considered those consuming artificial sweeteners. Those using low-sugar products were heavier, had higher triacylglycerols and poorer glucose tolerance. This type of observation is difficult to interpret. It is unclear whether those who were heavier chose artificial sweeteners or alternatively whether their consumption led to increased weight. Bellisle *et al.* (2001) concluded, whereas the use of fat-reduced products improved the quality of the diet, the response tended to be less favourable when a low-sugar product was consumed. In men the consumption of artificial sweeteners was associated with a lower energy intake but a greater percentage of energy came as fat and protein, and less as carbohydrate. In women the pattern was similar although there was an increased intake of protein but not fat. Although there was a lower energy intake the effect was modest. The average intake in men who did not use low-sugar products was 10 293 kJ/d (2460 kcal/d) compared with 9150 kJ/d (2187 kcal/d) in high consumers. In women there was no significant difference in energy intake.

de Castro (1993) considered 7 d food diaries and commented: 'Diet soda users ingest significantly less carbohydrate and have lower intakes than non-users. These findings could be interpreted as indicating that ingesting non-caloric beverages is effective in reducing intake. However, individuals who used diet soda did not differ in their total caloric intakes on days or in meals during which they drank the non-caloric beverages in comparison to days or in meals during which they did not. Thus, noncaloric beverage users would appear to be individuals who ingest fewer calories overall regardless of whether the beverages are included in their meal or daily intake or not.' (de Castro, 1993)

This is an important observation and confirms other reports that those using diet soda are generally more concerned with their weight (Tuorila *et al.* 1990). It is unclear to what extent the decision to consume diet soda is a marker for a range of other behaviours aimed at controlling weight and hence whether any differences exclusively reflect soda intake.

#### *Macronutrient profile*

A concern is that if you replace sucrose with an artificial sweetener you will simply eat the same weight of food that now contains a higher proportion of fat. There are experimental reports that the decreased energy intake associated with artificial sweeteners was compensated for by an increased intake of fat (Naismith & Rhodes, 1995; Gatenby *et al.* 1997). A similar finding was found in survey data (Bellisle *et al.* 2001). Beaton *et al.* (1992) argued that, theoretically, an increase in fat and protein intake would be expected when carbohydrates were replaced in the diet. You eat the same weight of food that now has a higher energy density. The long-term health implications of the macronutrient profile associated with the use of artificial sweeteners have not been addressed.

#### *Summary*

- (1) Possibly because of methodological problems there is no body of evidence to support the view that the long-term use of artificial sweeteners helps to prevent weight gain.
- (2) In longer-term studies of those of normal weight the use of artificial sweeteners results in a compensatory increase in energy at a later time. Men rather than women, and children rather than adults, are more likely to demonstrate energy compensation. In women, restrained eating is associated with being less likely to display energy compensation.
- (3) It has been suggested that a failure to display energy compensation, while eating freely, may be a laboratory artifact in short-term studies. If only foods of a low energy density are on offer there will be no opportunity to increase the intake of energy-dense foods.
- (4) In surveys the use of artificial sweeteners tended to be associated with higher weight, although it is more likely that this is a response to, rather than a cause of, weight gain.

#### **Beverages**

A common approach amongst those trying to lose weight is to use soft drinks sweetened artificially (Levy & Heaton, 1993). Particularly in the USA, soft drinks are consumed in large quantities, on average two cans per d. Soft drinks are the greatest sources of added sugars in the diet, on average providing in America 36.2 g/d for adolescent girls and 57.7 g/d for boys (Guthrie & Morton, 2000). There are two main reasons why beverages have attracted adverse attention. The body finds it less easy to monitor energy intake in a liquid form. As high-fructose corn syrup (HFCS) is often used in the USA to sweeten drinks, a second concern is that its consumption may predispose towards obesity.

There is evidence that the effect of energy intake on satiation is different when consumed as a liquid rather than combined into solid food. It may be that faster transit times and smaller gastric distension are more poorly monitored. A meta-analysis (Mattes, 1996) of forty-two studies concluded that there was little compensation for energy consumed as a liquid: 'There was no mean compensatory response to energy challenges presented in fluids. Indeed there was a small counter-compensatory effect, such that, relative to a control condition, energy intake was incremented by a level equal to the challenge plus 9 %.' (Mattes, 1996)

A key difference between these studies and the report of Reid & Hammersley (1998) that energy compensation occurred is that they replaced existing soda rather than adding it to the existing diet. The second general concern is the use of HFCS. Bray *et al.* (2004) related food consumption patterns over several decades to the growth of obesity. They found that it was mirrored by the increased consumption of HFCS that has risen over 1000 %. HFCS represented over 40 % of the energy-containing sweeteners added to food and drink. In the USA it is the only sweetener in soft drinks. A concern is that the metabolism of fructose in the liver favours lipogenesis. Fructose does not stimulate the secretion of insulin and leptin,

mechanisms important in the regulation of food intake (Bray *et al.* 2004).

Much of the increased energy intake of American children has been attributed to soft drinks (Guthrie & Morton, 2000; Krebs-Smith, 2001). Krebs-Smith (2001) found that 20% of the total energy of American adolescents came in the form of added sweeteners, of which one-third was in carbonated soft drinks and another 10% in fruit drinks. Troiana *et al.* (2000) reported that soft drinks contributed a greater proportion of daily energy in overweight children. Dennison *et al.* (1997) found that in 2- and 5-year-old children, those consuming more than 355 ml (12 fluid ounces)/d of fruit juice were more likely to be greater than the 90th weight percentile. In the Bogalusa Heart Study, dietary patterns were used to predict the weight of 10-year-old children. The frequency of the consumption of sweetened beverages predicted obesity (Nicklas *et al.* 2003).

Thus the intake of soft drinks has been related to the incidence of obesity. Ludwig *et al.* (2001) studied 11-year-old school children and found that for every additional daily serving of naturally sweetened drink there was, over time, an increase in BMI and an increased frequency of obesity. However, it would be instructive to consider a sample with a full range of BMI before generalising this finding. Berkey *et al.* (2004), similarly in a prospective study of 9- to 14-year-olds, found that over 1 year the drinking of naturally sweetened beverages was associated with a greater increase in BMI. It should be recalled that in such studies causality could not be assumed, as the consumption may be a marker for other variables. One possibility would be an increased likelihood of drinking while watching television with a consequent lower level of activity. It would be instructive to look for evidence that changing the nature of drinks results in a dose-dependent fall in weight that is proportional to the habitual level of consumption.

Raben *et al.* (2002) considered the effect of artificial sweeteners in a sample of obese individuals who were feeding *ad libitum*. For 10 weeks they consumed either naturally or artificially sweetened drinks and food. The body weight increased in those consuming naturally sweetened, and decreased in those drinking artificially sweetened, drinks. A concern is the high level of sucrose that was consumed with this experimental design (28% energy) and it is important in future studies to explore the phenomenon using lower levels.

An interesting English study randomly gave school classes a 1 h session per term on the adverse effects of carbonated drinks. Over 1 year those receiving the information drank fewer carbonated drinks, whereas the controls drank a similar number. The proportion of overweight children decreased in those attending the information sessions (James *et al.* 2004). A curious aspect of this study was that the decrease in obesity was observed only when the consumption of energy-containing and artificially sweetened drinks were added together, making the role of sweetener unclear.

The conclusion of the World Health Organization (2003) was that: 'the evidence implicating a high intake of sugars-sweetened drinks in promoting weight gain was considered moderately strong'.

The intake of sweetened drinks is not, however, associated with obesity in all individuals. There is a need to understand the variables that predispose some to be less able to accommodate energy in a liquid form. As obesity is a reflection of an imbalance between the input of energy, and its use, it is important that studies monitor diet and activity in parallel. The possibility should be excluded that the consumption of soft drinks is a marker for other behaviour that influences weight gain.

#### Summary

- (1) When energy is consumed as a liquid it tends to be added to total intake as it has little influence on the size of the next meal.
- (2) Carbohydrate when consumed as a liquid is more likely to result in weight gain.

#### General observations

A problem when evaluating the everyday use of artificial sweeteners is that the decision to use them is made by those concerned about their weight. At one extreme there are individuals for whom the use of the occasional artificial sweetener is the only attempt to control weight, individuals for whom they offer a psychologically satisfying substitute to making a coordinated and adequate response to their weight problem. At the other extreme this dietary change may be only one amongst many others, such that the use of artificial sweeteners is little more than an indication of a healthy lifestyle. It is essential that future evaluations place artificial sweeteners in a general context that includes information concerning the entire diet and patterns of energy expenditure. It is unreasonable to expect a simple yes or no answer to the question of whether artificial sweeteners help to control weight. If they work it will be in prescribed circumstances in particular types of individuals.

One major consideration is likely to be the extent to which individuals are displaying dietary restraint. Logically, as part of an energy-controlled diet, if artificial sweeteners replace energy they must aid the loss of weight. However, for many, weight control is a rollercoaster of weight gain followed by a diet, followed by weight gain. The need is to establish a food environment that does not lead to the rapid or even gradual regaining of weight. It is the stage when dieting has finished, when the aim is to maintain the weight achieved, that the role played by artificial sweeteners is uncertain. If less conscious effort is directed to the control of food intake, the opportunity arises for underlying physiological and psychological mechanisms to express themselves. There is, however, evidence that those who continue to exercise dietary restraint benefit to some extent from non-nutrient sweeteners (Rolls *et al.* 1994). For those not displaying dietary restraint the resulting reduction in energy leads to compensation by consuming more energy at later meals (Porikos *et al.* 1982; Foltin *et al.* 1988, 1990; Louis-Sylvestre *et al.* 1989; Gatenby *et al.* 1997; Reid & Hammersley, 1998).

Only the powerful approach of a prospective study where the decision to use artificial sweeteners was made randomly, in a blind manner, will allow causality to be established.

Subjects must be matched initially in terms of diet and exercise. Laboratory studies should be interpreted with caution as their short-term nature, and the isolation of subjects from the multitude of other factors that influence food intake, may result in findings that do not generalise. To consider the real world, studies need to replace sugar already in the diet rather than artificially adding additional sources. Tables 1 and 2 list the studies to date, although they all have methodological problems and fail to fully meet the above specifications.

Even if convincing evidence of the beneficial use of artificial sweeteners were to result from long-term studies, the findings should be generalised with caution. It is almost inevitable that volunteers to take part in such studies will be well-educated and highly motivated. The use of artificial sweeteners in an unsystematic manner, by those not motivated to take a consistent series of approaches to the control of weight, can be expected to have a lesser, if any, impact.

In conclusion, obesity results from a multitude of factors of which diet is only one. In turn, artificial sweeteners and sugars are only two of many aspects of diet. It is unreasonable to expect that modification of a single aspect of diet will have a major impact when isolated from the rest of the diet, basic physiology, behaviour and the environment. The data are so limited that definite conclusions would be premature; there has been no satisfactory study that has considered the value of artificial sweeteners in long-term weight maintenance.

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