



The effect on satiety of ingesting isosweet and isoenergetic sucrose- and isomaltulose-sweetened beverages: a randomised crossover trial

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Abstract

Generating feelings of satiety may be important in maintaining weight control. It has been hypothesised that the circulating concentration of glucose is a major determinant of satiety, yet the relationship between postprandial glycaemia and satiety is inconclusive. Our aim was to assess satiety following ingestion of beverages differing in glycaemic index (GI) containing either 50 g of sucrose (GI 65) or isomaltulose (Palatinose™) (GI 32). The beverages were matched for sweetness using a triangle sensory test. Seventy-seven participants were randomised to the order in which they received each beverage, 2 weeks apart. A standard lunch was given at 12.00 hours. Satiety was measured using 100-mm visual analogue scales (VAS) administered at 14.00 hours (baseline) and at 30, 60, 90, 120, 150 and 180 min after ingesting the beverage. Weighed diet records were kept from 17.00 to 24.00 hours. Mean differences for isomaltulose compared with sucrose AUC VAS were 'How hungry do you feel?' 109 (95 % CI –443, 661) mm × min; 'How satisfied do you feel?' 29 (95 % CI –569, 627) mm × min; 'How full do you feel?' –91 (95 % CI –725, 544) mm × min and 'How much do you think you can eat?' 300 (95 % CI –318, 919) mm × min. There was no between-treatment difference in satiety question responses or in dietary energy intake –291 (95 % CI –845, 267) kJ over the remainder of the day. In this experiment, feelings of satiety were independent of the GI of the test beverages. Any differences in satiety found between foods chosen on the basis of GI could be attributable to food properties other than the glycaemic-inducing potential of the food.

Key words: Satiety: Sweetened beverages: Sucrose: Isomaltulose: Glycaemia: Glycaemic index

Ultra-processing of carbohydrate-containing foods has been temporally associated with rising rates of obesity, type 2 diabetes mellitus and CHD⁽¹⁾. The ability of carbohydrates to influence metabolic disease risk via an effect on postprandial glycaemia has been debated through the glycaemic index (GI) literature since 1981⁽¹⁾. Although evidence is conflicting, the Glycaemic Index Foundation claims that low GI not only results in less glycaemic response but also can keep you feeling fuller for longer⁽²⁾. The suggestion that glycaemic responses elicited by carbohydrate-containing foods may be causal to the rising rates of metabolic diseases⁽¹⁾ demands attention be paid to the impact of postprandial glycaemia on satiety.

The glucostatic theory of food intake regulation has been a long-standing proposition⁽³⁾. The suggestion is that increased blood glucose concentrations promote satiety, whilst low blood glucose concentrations lead to increased feelings of hunger⁽⁴⁾. Following a review of the literature, it has been proposed that foods inducing a rapid rise and fall in glycaemia are satiating within an hour of eating and that foods producing a lower, but more prolonged, glycaemic response are satiating over a longer time course⁽⁵⁾. However, evidence of a low glycaemic

response correlating with higher satiation is conflicting⁽⁶⁾, and there are multifactorial determinants of appetite and satiety⁽⁷⁾. The inconsistencies among postprandial glycaemic studies may be explained by factors other than the glycaemic effect such as cooking and processing methods, the presence of fibre, the presence of other macronutrients, food form, palatability and energy density⁽⁸⁾. The differences could also be attributed to variable study designs and methods used to measure satiety⁽⁹⁾.

To examine whether GI has an effect on satiety, it is important to isolate the glycaemic response from other confounding factors. One such strategy is to use sucrose- and isomaltulose-sweetened beverages, both disaccharides comprising fructose and glucose moieties. Although a fully digestible carbohydrate, isomaltulose is digested at a slower rate than sucrose due to its more stable α -1,6 glycosidic bond connecting the fructose and glucose moieties, compared with the sucrose α -1,2 linkage⁽¹⁰⁾. The objective of the study is to assess the effect of a difference in glycaemia *per se* on primary outcomes of satiety by controlling for bias by double-blinding and controlling for confounding factors. The primary outcomes will be satiety subjectively assessed using visual analogue scales (VAS) and

Abbreviations: GI, glycaemic index; VAS, visual analogue scale.

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subsequent energy intake objectively assessed using weighed diet record data.

Methods

Participants

This study was a double-blinded randomised crossover trial, occurring during March 2018 at the University of Otago, Dunedin, New Zealand. Participants (*n* 77) were students of Human Nutrition Department from the University of Otago aged between 18 and 60 years old. Participants were not eligible if they had diabetes or an intolerance to the sweeteners being used. Randomisation of the order in which participants received the test beverages was computer-generated. Fig. 1 shows the flow of participants through the study. Ethical approval was

granted by the Human Ethics Committee of the University of Otago in October 2017 (ethics committee number 17/011). The trial was registered with the Australian New Zealand Clinical Trial Registry (ACTRN12618000901202). All subjects gave written informed consent before entering the study.

Study design

A total of seventy-seven participants were asked to attend two test sessions 2 weeks apart. As this was a crossover design, participants were asked to keep their eating and activity patterns consistent on the mornings of the two test days and to report to the testing premises at 24.00 hours. On arrival, participants were provided with a standard lunch consisting of eight pieces of sushi (1290 kJ) and a cup of water. The purpose of providing lunch

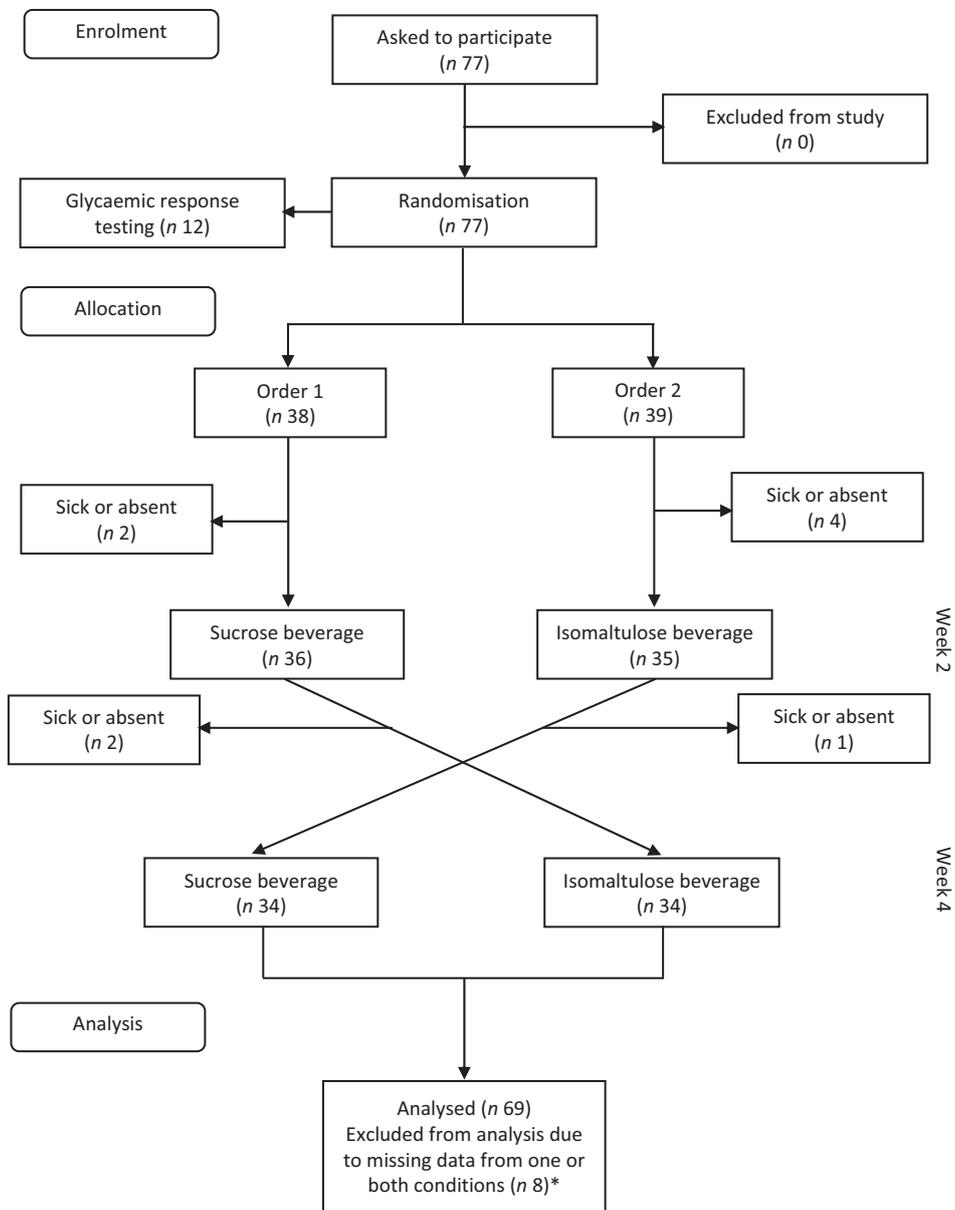


Fig. 1. Study design and flow of participants through the study. * One individual was missing from both sessions.

was to standardise appetite across the two test days. All participants consumed all of the sushi. After eating, participants were free to leave the premises with instructions not to eat or drink (except for water) or to undertake strenuous exercise and to return at 13.45 hours. Anthropometric measurements and a demographic questionnaire were completed on arrival at the first session. After removing shoes and jackets, participants were weighed using calibrated electronic scales (model 770; Seca GmbH & Co.). Height was measured using a free-standing stadiometer (Holtain Limited). The measurements were used to calculate BMI by dividing weight in kg by height in m². After a baseline measure of satiety, participants were given 10 min to drink the entire test beverage followed by assessments of satiety and subsequent food intake. The order in which participants received the test beverages was randomised using random length blocks in Stata 15.1 (StataCorp). A university staff member otherwise uninvolved in the study coded the beverages such that the principal investigators, participants and the statistician were blinded to treatment with the code revealed after statistical analysis of the data.

Test beverages

Quantities of 50 g of sucrose (caster sugar; Smart Choice) or isomaltulose (unflavoured Palatinose[®]; Myprotein) were measured on calibrated electronic scales (model 1702; Sartorius) and added to 500 ml bottles of Pure New Zealand sparkling water. The sweetness of the two beverages was matched by adding 0.035 g of sucralose (98% sucralose powder, J66736, lot: T21D050; Alfa Aesar) to the isomaltulose beverage. To ensure double-blinding, the drinks had the same volume and appearance and 0.05 ml of lemon flavouring (Lemon 59223, lot: 1002802470; Invita NZ Ltd). The beverages were matched for sweetness and immediate taste using a triangle sensory testing protocol prior to the laboratories, involving six people independent of the present study. Glycaemic and insulinaemic responses to the beverages were tested in twelve people to confirm between-drink differences in these factors; the results of these tests have been reported⁽¹¹⁾. The mean published GI value of sucrose is 65 (SEM 4)⁽¹²⁾ and of isomaltulose 32⁽¹³⁾.

Satiety and subsequent food intake

Satiety was assessed according to a published methodology⁽¹⁴⁾ using 100 mm VAS administered on paper at baseline (14.00 hours) and at 30, 60, 90, 120, 150 and 180 min following baseline. The questions were 'How hungry do you feel?' (not at all/never been more hungry); 'How satisfied do you feel?' (completely empty/cannot eat another bite); 'How full do you feel?' (not at all/totally full) and 'How much do you think you can eat?' (nothing at all/a lot). To assess subsequent energy intake over the remainder of the day, participants were asked to keep a weighed diet record of all food and beverages ingested from 17.00 hours to midnight using electronic scales reading to 0.1 g (Salter). Participants were trained in dietary recording and in the use of the scales and given a diet record sheet to fill in and return. The investigators used proprietary University of Otago software (Kaculator) to input and process the dietary data using

the New Zealand Food Composition Database as the source of nutrient information⁽¹⁵⁾.

Statistical analysis

The sample size required to provide 80% power to the $\alpha = 0.05$ level to detect a 5 mm difference in VAS scores was 70; and to detect a 400 kJ difference in subsequent energy intake, the sample size required was 60. Mean differences, 95% CI and *P* values of outcomes between treatments were calculated using mixed-effects regression analysis, with the participant as a random effect and adjusting for randomised order and baseline measures. Only participants with complete data were included in the analysis. The statistical analysis was undertaken using Stata/1C version 13.1 (StataCorp. 2013).

Results

The flow of participants is given in Fig. 1. Data from sixty-nine participants who drank both beverages were included in the analysis. Participant demographics are given in Table 1. The median (10th and 90th percentiles) age was 20.9 (95% CI 19.9, 24.8) years and BMI ranged from 17.4 to 34.1 kg/m².

Plasma glucose and insulin concentrations following ingestion of the test beverages are plotted in Fig. 2.

Results from VAS questionnaires assessing hunger, satisfaction, fullness and prospective food intake are presented as mean values and standard deviations AUC in Table 2 with no between-beverage differences for any of the four questions.

A visual illustration of appetite over time as measured by VAS is given in Fig. 3. The mean response scores after each beverage were close at all time points resulting in virtually superimposed plots for all four questions.

Table 1. Participant characteristics (*n* 69)
(Mean values and standard deviations; numbers and percentages)

Characteristics	Outcome	
	Mean	SD
Age (years)	22.0	0.7
Female		
<i>n</i>		56
%		81
BMI (kg/m ²)	23.3	2.7
Ethnicity		
New Zealand European		
<i>n</i>		42
%		61
Maori		
<i>n</i>		4
%		6
Asian		
<i>n</i>		12
%		17
Other		
<i>n</i>		11
%		16
Pre-test glucose (mmol/l)	7.0	1.29
Pre-test insulin (μ U/l)	38.2	24.5



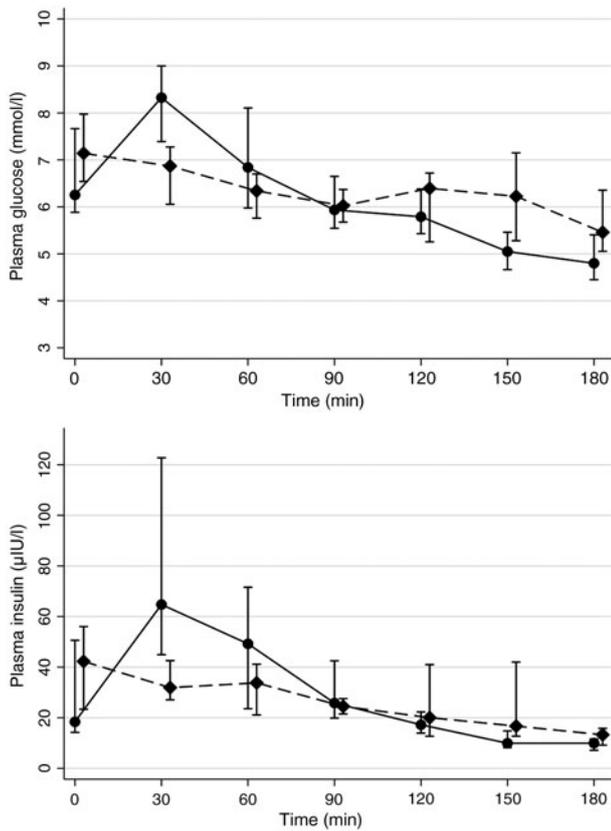


Fig. 2. Plasma glucose and insulin responses to the ingestion of sucrose and isomaltulose + sucralose beverages. Values are medians, and vertical bars represent the range of the 25th to 75th percentiles. —●—, Sucrose; - -○- -, isomaltulose.

Eight people did not complete diet records following both the sucrose- and isomaltulose-testing days, and hence, sixty-one paired records were available for analysis. The mean energy and macronutrient intake of the weighed diet records representing food intake from 17.00 to 24.00 hours are presented in Table 3. There was no between-treatment difference in macronutrient or dietary energy intake -291 (95% CI $-845, 267$) kJ over the remainder of the day. A sensitivity analysis that included the amount of energy participants consumed before or during the test had no appreciable impact on the effect sizes and significance of these results.

Discussion

There were no significant differences following ingestion of a sucrose- and an isomaltulose-sweetened beverage in either subjective satiety assessed using VAS or by an objective measure of subsequent food intake. A direct comparison between sucrose and isomaltulose on satiety has not previously been reported in humans. However, our findings are contrary to those of an animal study in which rats provided with these sugars consumed less food during a period of isomaltulose administration compared with sucrose⁽¹⁶⁾. It is unclear why this occurred but one possibility is that the sucrose solution was more palatable to the rats.

Over the years, comparable studies to ours have been carried out in humans using glucose- and fructose-sweetened beverages with variable findings. When a total sample of twenty-four normal and overweight people ingested 50 g glucose- or fructose-sweetened beverages, less energy was consumed at a subsequent buffet lunch following the fructose preload compared with the glucose preload⁽¹⁷⁾. In contrast, when four women ingested 10% solution of glucose- or fructose-sweetened preloads, there was no difference in satiety VAS ratings or subsequent energy intake of a lunch meal⁽¹⁸⁾. Similarly, giving 75 g solution of glucose or fructose to eight men resulted in no difference in satiety VAS ratings or in subsequent energy intake at a buffet lunch⁽¹⁹⁾. After ten people with type 2 diabetes and ten people with normal glucose tolerance ingested beverages sweetened with 75 g fructose or glucose, satiety assessed with VAS and subsequent energy intake of a buffet meal were favourable compared with a control beverage (flavoured water), but there were no differences in these outcomes between sugary beverages⁽²⁰⁾. When twenty-eight obese men ingested beverages sweetened with 50 g glucose or fructose, there were no between-treatment differences found for VAS responses or subsequent energy intake at a buffet lunch⁽²¹⁾. The lack of effect on satiety in these studies despite measured differences in postprandial glycaemia is not in accord with the glucostatic mechanism of food intake proposed by Mayer⁽⁹⁾. The glucostatic theory states that temporary increases in blood glucose concentration correspond to a decrease in food intake and vice versa⁽⁹⁾. When comparing short-term (1-h) satiety after consumption of high- and low-GI isoenergetic beverages, it was found that the high-GI beverage kept

Table 2. AUC visual analogue scale (VAS) questions between the sucrose- and isomaltulose-sweetened beverages (n 69) (Mean values and standard deviations; mean differences and 95% confidence intervals)

VAS (mm × min)	Sucrose		Isomaltulose		Mean difference*	95% CI	P
	Mean	SD	Mean	SD			
Hunger†	6146	3153	6167	3341	109	-443, 661	0.699
Satisfaction	8395	3112	8538	3360	29	-569, 627	0.924
Fullness	8422	3348	8311	3437	-91	-725, 544	0.780
Food intake	7143	3569	7197	3745	300	-318, 919	0.341

* Mixed-effects regression with participant's ID as a random effect and adjusting for randomised order and baseline.

† Hunger – 'How hungry do you feel?'; Satisfaction – 'How satisfied do you feel?'; Fullness – 'How full do you feel?'; Food intake – 'How much do you think you can eat?' For 'Hunger' and 'Prospective food intake', a larger AUC corresponds to greater hunger and a desire for more food. For 'Satisfaction' and 'Fullness', a larger AUC corresponds to greater satisfaction and fullness.

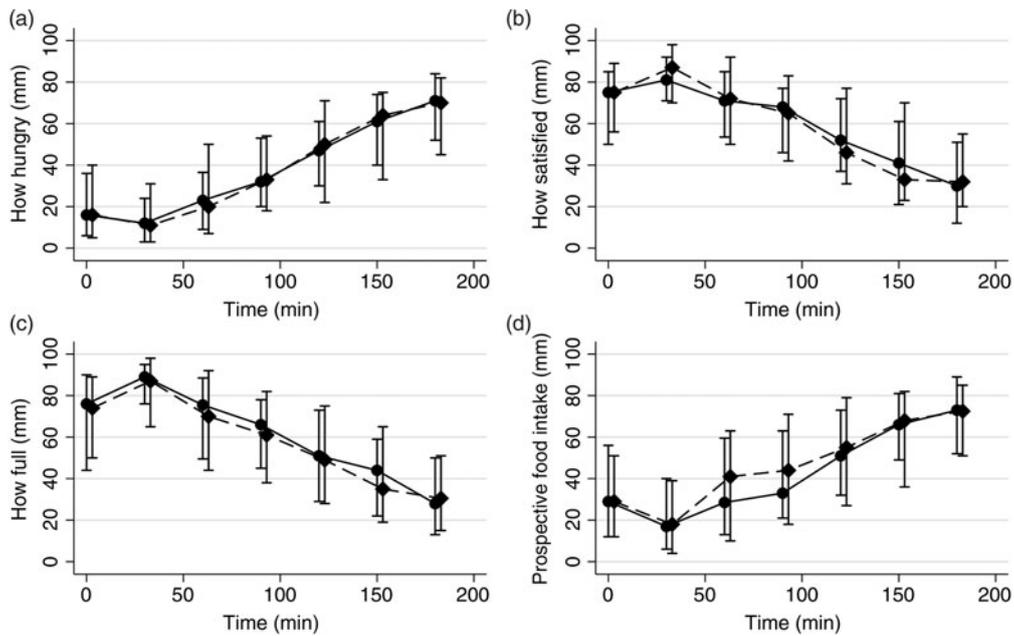


Fig. 3. Satiety scores over time to the questions (a) 'How hungry do you feel?' (b) 'How satisfied do you feel?' (c) 'How full do you feel?' (d) 'How much do you think you can eat?' (*n* 69). Values are medians, and vertical bars represent the range of the 25th to 75th percentiles. ●—, Sucrose; - - -◆, isomaltulose.

Table 3. Energy and macronutrient intake from weighed diet records (*n* 61) (Mean values and standard deviations; mean differences and 95% confidence intervals)

Factors	Sucrose		Isomaltulose		Mean difference*	95% CI	<i>P</i>
	Mean	SD	Mean	SD			
Energy (kJ)	4059	2396	3768	2330	-291	-845, 267	0.306
Fat (g)	41	26	34	27	-6.6	-13.3, 0.2	0.056
Fat (% of energy)	39.7	14.9	34.2	13.4	-5.5	-9.5, -1.5	0.007
Protein (g)	41	26	39	24	-2.3	-8.8, 4.3	0.498
Protein (% of energy)	19.3	8.6	18.2	6.1	-1.1	-3.4, 1.2	0.360
Carbohydrate (g)	100	88	102	72	1.6	-17.2, 20.5	0.864
Carbohydrate (% of energy)	39.5	15.7	45.9	14.3	6.4	2.6, 10.3	0.001

* Mixed-effects regression with participant's ID as a random effect and adjusting for randomised order.

participants feeling more full at 60 min, in accordance with the glucostatic theory⁽²²⁾. It was thus proposed that high GI keeps you fuller short-term and that low GI may sustain satiety long-term⁽²²⁾.

The proposition that GI affects satiety is not specific regarding the timing of ingestion, although most studies are undertaken after an overnight fast. In our study, participants abstained from food and beverage for 2-h following a mid-day meal and the glycaemic and insulinaemic responses in response to isomaltulose ingestion remained below the pre-ingestion values. This pattern of response differs to that found after an overnight fast in which rises in blood glucose and insulin concentrations to an isomaltulose beverage have been found^(23,24). A possible explanation is that our participants were still in a postprandial state at the time of test beverage ingestion as suggested by the mean pre-ingestion glucose concentration of 7.0 mmol/l. This is relatively high for a young group of people given the overnight fasting blood glucose concentration in a Caucasian group with

a mean age of 27.5 years was 4.8 mmol/l⁽²³⁾. Indeed, blood glucose concentrations are affected by the duration of fast, continuing to decline in young people past a 2-h postprandial period⁽²⁵⁾. Nevertheless, in our study, there was a glycaemic and insulinaemic differential at 30 min between the two test beverages with the magnitude of separation comparable with that found when these sugars are tested following an overnight fast^(10,24). Although our data do not support an effect on satiety of differing glycaemic responses induced by these beverages, our subjective findings are limited to a non-overnight fasting condition monitored over 3 h.

However, over time, a relationship between the glycaemic response and satiety to solid food has been found. Twelve obese teenage boys ate 81% more energy over 5-h following consumption of high-GI meals compared with low-GI meals⁽²⁶⁾. This finding is quite different to that of the sweetened beverage trials, in which generally no differences in subsequent energy intake were found. The explanation may lie with the



composition of the meals. The low-GI meal comprised fruit (grapefruit and apple) and a vegetable omelette with an initial weight of solid food of 670 g. In comparison, the high-GI meal consisted of 61 g instant oatmeal and 19 g dextrose, with the remaining ingredients being liquid (160 ml milk, 15 ml cream and 397 ml water). There is substantial evidence that solid foods are more satiating than liquids^(27–29) with mechanisms being discussed in a review paper⁽³⁰⁾. One such mechanism is the action of chewing which would have differed between the low-GI omelette and fruit meal, and the high-GI meal of instant oatmeal, with chewing eliciting a higher degree of satiety due to alterations in gut hormone responses⁽³¹⁾. Controlling for food texture and macronutrient content, mean hunger and perceived fullness in fifty participants were favourable after eating a low-GI carob cookie compared with a high-GI chocolate cookie 15 min after eating with no between-treatment difference thereafter; and subsequent energy intake at lunch following the preload was some 7% higher for the high-GI chocolate cookie⁽³²⁾. This might suggest a role for GI in satiety, although the carob cookie contained considerably more fibre than the chocolate cookie, and the palatability of the cookies was not reported, factors that have been variably associated with satiety^(33,34). In a trial involving twenty-eight men consuming fourteen different breakfast meals having a range of GI, subjective feelings of satiety were unrelated to glycaemic response, whilst energy intake at a subsequent lunch was positively associated with the glycaemic response⁽³⁵⁾. Again this might suggest that the glycaemic response and satiety are related, but the breakfast meals were not matched on energy content such that the total energy intake of the breakfast and subsequent lunch was lower for the highest-GI breakfast (reference bread) and highest for the lowest-GI breakfasts (reference bread with butter and cheese; Finnish bread with butter and cheese and German bread with butter and cheese)⁽³⁵⁾. In a study in which the energy content of foods was standardised, the volume of ingested food was found to be the main determinant of satiety independent of the glycaemic response⁽³⁶⁾.

From such work, it may be concluded that there is no clear relationship between the glycaemic impact of food and satiety. Discrepancies in findings may be due to study designs in which properties of the foods other than the glycaemic characteristics have not been controlled. Confounding factors are particularly prominent in long-term studies regarding associations between postprandial glycaemia and satiety. There appears to be little relationship between the GI of foods and weight gain over periods of months and years^(37–39). This is probably attributable to the GI of foods being unrelated to the energy density of foods, for example, cake and apples have comparable GI but very different energy densities⁽³⁶⁾. Whilst controlling for energy density, our findings support a role for ingested volume as a causal factor in feelings of satiety as the beverages were isovolumetric. By using a beverage, we were able to standardise energy density whilst controlling for macronutrient content and palatability. The major strength of this study was the control for confounding and bias that allowed for glycaemic differences, whilst participants and investigators were blinded to treatment. A potential limitation is that we did not assess mood. Mood has been found to affect food intake⁽⁴⁰⁾ and if people had different moods

on the two test days, this could have confounded feelings of satiety. In some studies, subsequent energy intake from a provided meal has been assessed by observing and measuring food intake under investigator-controlled conditions^(41,42). In contrast, our participants were asked to record food and beverage intake under free-living conditions, a technique that has been found to result in under-reporting⁽⁴³⁾. This is likely a limitation to our estimate of absolute subsequent energy intake although being a crossover study, energy intake estimates on each testing day have been controlled for potential under-reporting by making within-person comparisons. Another limitation is that subsequent energy intake was assessed over a time frame of 7 h (17.00 hours to midnight). Although subsequent energy intakes have been assessed over shorter periods of 1–3 h following interventions designed to elicit differences in postprandial glycaemia, these study designs do not account for possible longer term carryover effects⁽⁴⁴⁾. The findings may be limited to a young, primarily female, university-educated demographic with normal glucose tolerance, and as such it would be of interest to test these beverages in males, other age and socio-demographic groups, and in people of different metabolic states to assess whether glycaemic response, *per se*, affects feelings of satiety.

In conclusion, the present study is the first to assess the satiating properties of isomaltulose compared with sucrose beverages in humans. In a healthy, young cohort of participants, feelings of satiety and subsequent energy intake were unaffected. For the magnitude of glycaemic differences attained in this study, our data do not support a relationship between postprandial blood glucose concentration and feelings of satiety.

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B. J. V. conceived the study. All authors designed the study. B. M. M., C. T. K. and B. J. V. undertook the practical work. B. J. V. supervised the study. J. J. H. analysed the data. B. M. M. drafted the manuscript. All authors edited the manuscript.

None of the authors has any conflicts of interest to declare.

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