Citation:

Soenen S, Westerterp-Plantenga MS. No differences in satiety or energy intake after high-fructose corn syrup, sucrose, or milk preloads. *Am J Clin Nutr.* 2007;86(6):1586-94.

PubMed ID: 18065574

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the satiating effects of HFCS and sucrose in comparison with milk and a diet drink.

Inclusion Criteria:

- Normotensive
- Nonsmokers
- Nonrestrained eaters
- Regular breakfast consumers
- At most moderate alcohol users
- Had a stable body weight (a change of <2 kg over at least the past 2 mo)
- Did not use prescription medication
- Subjects who were willing to participate in the study
- Good health

Exclusion Criteria:

Athletes, defined as those who trained >10 h/week.

Description of Study Protocol:

Recruitment

- Thirty subjects (equal numbers of men and women) participated in the first study, 40 in the second study. Subjects were recruited by means of an advertisement in local newspapers and on notice boards at Maastricht University.

Design: Randomized crossover trial; A within-subjects design was used, with each subject returning for 4 separate test days ≥ 1 wk apart. The preloads were offered blindly and in randomized order to avoid the order-of-treatment effect.

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Blinding used (if applicable): single blind

Intervention (if applicable)

- The effects of four 800-mL drinks [corrected] containing no energy or 1.5 MJ from sucrose, HFCS, or milk on satiety were assessed, first in 15 men and 15 women with a mean (+/-SD) body mass index (BMI; in kg/m^2) of 22.1 +/- 1.9 according to visual analogue scales (VAS) and blood variables and second in 20 men and 20 women (BMI: 22.4 +/- 2.1) according to ingestion of a standardized ad libitum meal (granola cereal + yogurt, 10.1 kJ/g).
- The appetite profile,VAS ratings and blood samples for the measurement of GLP-1, ghrelin, insulin, and glucose concentrations were determined before and after preload consumption in the first study. The last moment in time at which relevant differences in satiety were present was determined to decide on the timing of the test meal in the second study.
- The 4 beverages were as follows: a beverage containing sucrose, one containing HFCS, one containing milk, and a diet drink. All 4 drinks were isovolumetric and had a volume of 800 mL. The energy drinks were isoenergetic and provided 1.5 MJ.
- The diet drink had an energy content of 0.2 MJ. The drinks containing sucrose or HFCS and the diet drink were orange-flavored custom-made beverages and were equally sweet. The sucrose-containing preload had the same consistency as a commercially available sucrose-sweetened drink containing 450 g sucrose and 236 g glucose syrup (91% glucose and 9% fructose).
- The HFCS-containing preload had the consistency of a commercially available HFCS-sweetened drink containing 55% fructose and 45% glucose syrup (91% glucose and 9% fructose). The diet preload consisted of the sweeteners aspartame, acesulfame-K, and sodium cyclamate.
- Additionally, all 3 preloads contained water, citric acid, orange flavoring, coloring E160, preservative E202, and antioxidant E300. Drinks were prepared by diluting 133 mL syrup with 667 mL water. All 4 beverages were served chilled at 8°C.
- The test meal that was served in the second study consisted of a granola cereal with yogurt. An ad libitum meal (granola cereal and yogurt) was served 50 min after participants completed the preload; all foods were preweighed at the time of serving, and plate waste was collected and weighed.
- The subjects' attitude toward eating was determined during screening with the use of a validated Dutch translation of the Three-Factor Eating Questionnaire (TFEQ).
- The subjects' feelings of hunger, satiety, fullness, prospective food and drink consumption, and desire to eat and drink were scored on anchored 100-mm VAS at 6 different 0.5-h time points in study 1 and at 7 time points in study 2. The scale ranged from "not at all" on the left to "extremely" on the right.
- Subjects were instructed to mark, with a single vertical line, a point where the length of the line matched their subjective sensation. All VASs were provided on a separate form at each time point and were collected immediately after they had been completed.
- Subjects rated their taste perception and hedonics for the 4 test drinks on anchored 100-mm VAS during screening and at the first and last sip of the beverage consumed during each test day. Blood samples were determined for the concentrations of plasma GLP-1, ghrelin, insulin, and glucose.

Statistical Analysis

- Data are presented as means ± SDs or SEs. VAS ratings were measured in millimeters from the left end of the scale.
- The changes in concentrations of the hormones from baseline and changes from baseline in VAS ratings of the appetite profile were compared by analysis of variance (ANOVA), repeated-measures ANOVA (analysis of change score), and analysis of covariance (ANCOVA) with the baseline values as covariates.
- An ANCOVA may give bias because of the "weight" of the baseline values.
- Post hoc analysis was carried out with a Fisher's protected least-significant difference test, Sheffe's *F* test, or a Tukey's test.
- Taste perception and energy intake after the preloads were compared by ANOVA. Differences in responses between the drinks containing sucrose and HFCS were compared with a 2-tailed paired Student's *t* test.Sex differences were assessed by using ANOVA.
- Time-by-sex interactions were assessed by using repeated-measures ANOVA, and time-by-treatment-by sex interactions were assessed by using multivariate ANOVA with preload condition and sex as fixed factors. Changes in the desire to eat from baseline were analyzed as a function of changes in concentrations of hormones and glucose from baseline by regression analysis.
- Compensation was calculated as the difference between energy intake after the diet preload and energy intake after any of the energy preloads as a percentage of the energy content of these preloads. Overconsumption was calculated as a difference between total energy intake after any of the energy preloads and total energy intake after the diet preload as a percentage of energy intake after the diet preload.
- All analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 11.0.3 for Macintosh OS X (SPSS Inc, Chicago, IL). Differences were regarded as significant if $P < 0.05$.

Data Collection Summary:

Timing of Measurements

- A within-subjects design was used, with each subject returning for 4 separate test days
- VAS at 6 different 0.5-h time points in study 1 and at 7 time points in study 2.
- Venous blood samples were taken at 5 time points: one fasting sample at baseline before and 4 samples 15, 30, 60, and 120 min after preload consumption and the appetite profile 20, 50, 80, 110, and 140 (last time point only in study 2) min after preload consumption.
- An ad libitum meal (granola cereal and yogurt) was served 50 min after participants completed the preload; all foods were preweighed at the time of serving, and plate waste was collected and weighed.

Dependent Variables

- Test meal energy intake and total meal energy intake (preload+meal)
- Change (Δ) in VAS rating
- Change (Δ) in hunger
- Changes in concentrations of hormones and glucose
- Insulin (ΔAUC) and glucose (ΔAUC)

Independent Variables

- Drink preload: a beverage containing sucrose, one containing HFCS, one containing milk, and a diet drink

Control Variables

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Description of Actual Data Sample:

Initial N:

- 30 subjects participated in the first study (15 women/15 men)
- 40 subjects participated in the second study (20 women/20 men).
- (13 participants participants participated in both studies)

Attrition (final N): Same as above

Age:

Characteristic	Study 1		Study 2		P (ANOVA) Diff between sexes
	Women (*n* = 15)	Men (*n* = 15)	Women (*n* = 20)	Men (*n* = 20)	
Age (y)	21.1 ± 1.5	21.5 ± 1.8	21.2 ± 2.2	22.3 ± 4.5	
Weight (kg)	63.7 ± 7.3	75.8 ± 9.5	65.0 ± 7.7	76.2 ± 6.0	P < 0.001
Height (cm)	171.4 ± 5.6	183.3 ± 8.0	171.6 ± 4.6	183.0 ± 7.2	P < 0.001
BMI (kg/m^2)	21.6 ± 1.9	22.5 ± 1.8	22.0 ± 2.1	22.8 ± 2.0	

Ethnicity: not reported

Other relevant demographics: None

Anthropometrics: See table above

Location: Maastricht University, Netherlands

Summary of Results:

Key Findings

- Fifty minutes after consumption of the 1.5-MJ preload drinks containing sucrose, HFCS, or milk, 170%-mm VAS changes in satiety were observed.
- Glucagon-like peptide 1 (GLP-1) (P < 0.001) and ghrelin (P < 0.05) concentrations changed accordingly. Compensatory energy intake did not differ significantly between the 3 preloads and ranged from 30% to 45%. Energy intake compensations were related to satiety (r = 0.35, P < 0.05).
- No differences were observed between the effects of the sucrose- and HFCS-containing drinks on changes in VAS and on insulin, glucose, GLP-1, and ghrelin concentrations.
- Changes in appetite VAS ratings were a function of changes in GLP-1, ghrelin, insulin, and glucose concentrations.
- Drinks containing sucrose or HFCS (800 mL, 1.5 MJ) did not differ in taste perception or palatability. The milk preload (800 mL,1.5 MJ) was perceived as less sweet, sour, refreshing, and pleasant ($P < 0.01$) and more rich and creamy than the preloads containing sucrose or HFCS ($P < 0.005$).
- The diet preload (800 mL, 2kJ) was perceived as less pleasant and less sweet than preloads containing sucrose or HFCS ($P < 0.001$).
- Taste perception did not differ between sexes. Perceptions of thirst after the preloads did not differ between the preloads.
- Thirst was significantly more reduced in women than in men [change in area under the curve (AUC) from baseline: –18 ± 9 compared with–31 ± 16 mm VAS/min respectively; $P < 0.05$].
- The reduction in hunger relative to baseline after a preload differed significantly between men and women ($P < 0.05$).

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- Men had a significantly greater reduction in hunger after the preload containing HFCS than after the preload containing sucrose at the 50-min timepoint (–8 ± 14 compared with –17 ±15 mm VAS, respectively; $P < 0.05$), whereas women showed the opposite.
- Women had a significantly greater reduction in hunger ratings at the 50-, 80-, and 110-min time points, with the maximal difference occurring 50 min (–24 ±18 compared with –7 ± 19 mm VAS; $P < 0.05$) after consumption of the preload containing sucrose compared withthe preload containing HFCS. The adequate moment in time to serve the test meal in study 2 was 50 min, as underscored by the significant treatment-by-sex interaction at 50 min ($P< 0.05$). Differences in VAS ratings between treatments differed by sex.
- Stepwise multiple linear regression analysis of VAS appetite ratings showed that change in GLP-1 ($r = –0.242$, $P = 0.014$) and insulin ($r = –0.239$, $P = 0.029$) independently predicted changes in satiety. Moreover, glucose and insulin concentrations were related after preload consumption, as expected, and GLP-1 and ghrelin concentrations were related to insulin concentrations.
- Test meal energy intake was significantly lower after consumption of preloads containing sucrose or HFCS or the milk preload (with no differences between the energy-containing preloads) than after the diet preload ($P < 0.05$). Total energy intake (preload + meal) with the energy-containing preloads was significantly higher than total energy intake with the diet preload ($P < 0.01$). Therefore, during the meal, energy intake was only partly compensated for. Compensation for energy intake from the preloads containing sucrose, HFCS, or milk did not differ significantly and ranged from 30% to 45%.
- Compensation after the energy-containing preloads was a function of the magnitude of change in satiety scores from baseline ($r= 0.350$, $P = 0.023$). In the men, overconsumption after the preload containing sucrose ($r = –0.934$, $P = 0.020$) or milk ($r= –0.999$, $P < 0.001$) was a function of the magnitude of change in satiety scores from baseline; after the preload containing HFCS, this relation was not observed.
- Hunger ratings were significantly more suppressed at each time point after the milk preload than after the diet preload ($P < 0.05$).The change from baseline in GLP-1 concentrations was significantly larger ($P < 0.05$) 30 min after the milk preload (3.6 ±3.4 pmol/L) than after the preloads containing sucrose (2.1± 2.3 pmol/L) or HFCS (2.1 ± 3.3 pmol/L). In men, this difference was observed at each time point ($P < 0.05$).
- Plasma glucose concentrations were significantly higher over time after the drinks containing sucrose or HFCS than after the milk or diet preloads ($P <0.001$). Moreover, plasma glucose concentrations were linearly related to the content of glucose of the preloads ($r = 0.581$,$P < 0.001$).

Author Conclusion:

- Energy balance consequences of HFCS-sweetened soft drinks are not different from those of other isoenergetic drinks, eg, a sucrose-drink or milk.
- A 1.5-MJ preload containing sucrose or HFCS or a milk preload did not affect energy intake differently 50 min later. Differences in satiety were absent despite different mechanisms underlying satiety due to sucrose- or HFCS-containing drinks or milk.
- Sucrose and HFCS triggered GLP-1 release, which triggered insulin release and a related increase in satiety. The different responses in GLP-1, glucose, and thirst when preloads of the same sizes were offered could explain the sex effect that was observed in VAS ratings, energy intake, and energy compensation and overconsumption. Obviously, the preloads that were consumed represented a smaller part of the energy requirement in men than in women.
- Despite differences in the biochemical properties of preloads containing sucrose, HFCS, or milk and differences in the mechanisms underlying satiety in relation to GLP-1 release and ghrelin release, no differences in satiety, compensation, or overconsumption were observed.

Reviewer Comments:

Relatively small sample size and short study duration. Differences between subjects in study 1 and 2 at baseline.

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Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes

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3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	???
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

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6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	???
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes

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8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	???
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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