

## Calorie Control Council Response to Stanhope/Havel, et.al. “Consumption of Fructose-, but not Glucose-Sweetened Beverages Produces an Atherogenic Lipid profile in Overweight/Obese Men and Women”

Stanhope KL, Griffen S, Keim NL, Ai M, Otokozawa S, Nakajima K, Schaefer EJ and Havel PJ. Consumption of fructose-, but not glucose-sweetened beverages produces an atherogenic lipid profile in overweight/obese men and women. 67th Annual Scientific Session of the American Diabetes Association. Chicago, IL, 2007:Abstract 0062-OR

### **Background**

Peter Havel is on the faculty of the University of California at Davis. He is a frequent contributor to the literature on metabolic influences of fructose. This paper was an oral presentation at the June 2007 Scientific Session of the American Diabetes Association in Chicago. It is similar in subject matter and conclusions to other papers presented earlier in the year by Havel, et.al. at Experimental Biology(1) and NAASO (2). In this paper the authors investigated the effects of 10 weeks of fructose vs. glucose consumption on lipid metabolic markers in 23 overweight/obese adults.

### **Hypothesis**

Increased consumption of beverages with fructose-containing sweeteners between 1977 and 2001 (+135%) may be a contributing factor to increased incidence of metabolic syndrome<sup>1</sup>.

The authors cite as risk factors for atherosclerotic cardiovascular disease increased postprandial triglycerides, LDL-C, apoB, small dense (sd) LDL-C, remnant lipoproteins (RLP), oxidized LDL and intracellular adhesion molecules (ICAM). These factors are measured in the current study.

### **Experimental Design**

2-week clinical residence: energy-balanced, moderate fat (30%), high complex carbohydrate (55%) diet

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<sup>1</sup> Metabolic syndrome increases risk of coronary heart disease and other diseases related to plaque buildup in arterial walls (e.g., stroke and peripheral vascular disease) and type 2 diabetes. Metabolic syndrome has become increasingly common in the United States; perhaps as many as 50 million Americans have it. The American Heart Association and the National Heart, Lung, and Blood Institute recommend that three or more of the following criteria be present before a correct diagnosis of metabolic syndrome is appropriate (3):

- Elevated waist circumference: □ men  $\geq$  40 inches (102 cm); women  $\geq$  35 inches (88 cm)
- Elevated triglycerides  $\geq$  150 mg/dL
- Reduced HDL (“good”) cholesterol: □ men  $<$  40 mg/dL; women  $<$  50 mg/dL
- Elevated blood pressure  $\geq$  130/85 mm Hg
- Elevated fasting glucose  $\geq$  100 mg/dL

8-week outpatient: fructose- or glucose-sweetened beverages at 25% of calories + *ad libitum* self-selected diet

2-week clinical residence: beverages sweetened as above + energy-balanced diet (above)

24-hour blood collections at weeks 1, 2, 8 and 10

## Results

- Increased in fructose subjects: 24-hour postprandial triglycerides (+212%); fasting plasma LDL-C (+17%), apoB (+28%) and sd-LDL-C (+27%); RLP-triglycerides (+77%) and RLP-cholesterol (+53%); plasma oxidized LDL-C (+15%); ICAM (+8%).
- Decreased in glucose subjects: 24-hour postprandial triglycerides (-30%); remaining metabolic parameters unchanged.

## Author Conclusions

1. Consumption of fructose at 25% of energy promotes an atherogenic lipid profile within 2 weeks; glucose does not.
2. Those at risk for metabolic syndrome and cardiovascular disease should avoid over-consumption of fructose-containing beverages.

## Critique

- Though consumption of total added sugars is higher today than in 1977, the focus on increased consumption of fructose-sweetened beverages as justification for the current study presents an exaggerated view of nutrient intake history. The authors are to be faulted for suggesting that added sugars alone has significantly changed. In fact, added sugars consumption has increased at a slightly slower pace than total calories (+24%) over this time, while calories from fats and cereals have increased at a slightly faster pace (4). The balance of calories from added sugars clearly has not changed significantly since 1977.
- Havel and others commonly test pure fructose vs. pure glucose at elevated intake levels in order to exaggerate metabolic effects. This approach is inappropriate for modeling the human diet:
  - sweeteners in the human diet are not restricted to either pure fructose or pure glucose — the two are consumed together;
  - the fructose-to-glucose ratio in the human diet is approximately 0.7, a ratio that has remained unchanged for more than 30 years (5); and
  - experiments using fructose-to-glucose ratios commonly encountered in added sweeteners have consistently revealed no significant difference in metabolic markers for obesity — including triglycerides — between sucrose and high fructose corn syrup (6-10).
- The level of fructose tested by the authors likely exceeds 25% of calories, at least in the 8-week outpatient phase of the study, since subjects were allowed to supplement fructose-sweetened beverages with any foods and amounts they desired. This value represents an approximate 3-fold excess of fructose in the diet over that calculated by Park & Yetley in a comprehensive estimate of caloric sweetener intakes (11).
- Havel's report of elevated fructose-induced triglycerides at Experimental Biology was pointedly criticized by James Rippe, a co-speaker on the same program (1). Rippe countered with data of his own showing that Havel's purported elevated levels were

within the range considered normal by cardiologists. The authors' switch from reporting numerical data to percentage change in this presentation makes it more difficult for Rippe and others to critique the range of reported data. This deficiency will presumably be rectified when the data are published, where numerical data will be required.

In summary, the metabolic syndrome and closely associated diseases obesity and diabetes are complex medical problems with a host of causative factors. This paper offers no proof that dietary fructose in the ratio and amount consumed in the human diet is uniquely responsible.

Since an LTE is not appropriate for this oral presentation, it is recommended that this critique be posted to the Calorie Control Council's [www.fructose.org](http://www.fructose.org) website.

## References

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## Consumption of Fructose-, but not Glucose-Sweetened Beverages Produces an Atherogenic Lipid Profile in Overweight/Obese Men and Women

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**Results:** Consumption of sugar-sweetened beverages containing fructose has increased by 135% from 1977 to 2001 and may be a contributing factor to an increased incidence of metabolic syndrome. Direct experimental evidence that fructose consumption promotes the metabolic syndrome in humans is lacking. We investigated the effects of 10 weeks of fructose compared with glucose consumption on lipid parameters in overweight/obese (BMI: 25-35 kg/m<sup>2</sup>) adults. Subjects resided in the Clinical and Translational Science Research Center (CCRC) for 2 weeks. Baseline procedures, including a 24-hr blood collection, were conducted while subjects consumed an energy-balanced, moderate fat (30%), high complex carbohydrate (55%) diet. Subjects then began an 8-week outpatient intervention and consumed either fructose- (n=13) or glucose- sweetened (n=10) beverages at 25% of energy requirements with a self-selected *ad libitum* diet. At 2, 8, & 10 weeks of intervention, additional 24-hr blood collections were performed. At intervention week 9, subjects returned to the CCRC for 2 weeks while consuming the beverages with the energy balanced diet. 24 hr postprandial triglyceride (TG) profiles were increased by 212±59% after 2 weeks of fructose consumption (p<0.0001), but tended to decrease (-30±23%) in subjects consuming glucose. Fasting plasma concentrations of LDL-C (+17±4%), apoB (+28±7%), small dense (sd)LDL-C (+27±11%), & postprandial concentrations of remnant lipoprotein (RLP)-TG (+77±19%) and of RLP-cholesterol (+53±12%) were increased (p<0.01) in subjects consuming fructose-sweetened beverages, but were unchanged in those consuming glucose beverages. These changes were maintained after 8 & 10 weeks of fructose consumption. In addition, plasma concentrations of oxidized LDL-C were increased by 15±2% (p<0.0001) and intracellular adhesion molecule (ICAM) increased by 8±3% (p< 0.05) in subjects consuming fructose, but not in those consuming glucose. Increased postprandial TGs, LDL-C, apoB, sdLDL-C, RLPs, oxidized LDL, and sICAM are considered risk factors for atherosclerotic cardiovascular disease. Thus, consumption of 25% of energy requirements from fructose promotes an atherogenic lipid profile within 2 weeks, whereas consuming 25% of energy from glucose does not. Persons at risk for developing metabolic syndrome and cardiovascular disease should avoid over-consumption of fructose-containing beverages.

**Category:** Nutrition – Clinical

**Meeting:** Am Diabetes Assoc Annual Scientific Session, June 22-26, Chicago

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