# Effects of Consuming Dietary Fructose versus Glucose on de novo Lipogenesis in Overweight and Obese Human Subjects

**Patrick H. Lam[1,5], Kelley Ng[1,5], Kimber L. Stanhope[3,4], Jean Marc Schwarz[5,6] Nancy L. Keim[7], Steven C. Griffen[8], Andrew A. Bremer[9], James L. Graham[3,4], Bonnie Hatcher[4], Chad L. Cox[4], Artem Dyachenko[5], Wei Zhang[8], John P. McGahan[10], Anthony Seibert[10], Ronald M. Krauss[11], Sally Chiu[11], Ernst J. Schaefer[12], Masumi Ai[12], Seiko Otokozawa[12], Katsuyuki Nakajima[12,13], Takamitsu Nakano[13], Carine Beysen[14], Marc K. Hellerstein[14,15], Lars Berglund[8,16], and Peter J. Havel[3,4], J.M. Schwarz[1] and A. Dyachenko[1]**

[1]*Department of Molecular Environmental Biology, College of Natural Resources, UCB, Berkeley, USA.*
[2]*Department of Integrative Biology, College of Letters and Science, UCB, Berkeley, USA.*
[3]*Department of Molecular Biosciences, School of Veterinary Medicine, Davis, California, USA*
[4]*Department of Nutrition, UCD, Davis, California, USA.*
[5]*College of Osteopathic Medicine, Touro University, Vallejo, California, USA.*
[6]*UCSF, San Francisco, California, USA.*
[7]*United States Department of Agriculture, Western Human Nutrition Research Center, Davis, California, USA.*
[8]*Department of Internal Medicine, School of Medicine, UCD, Sacramento, California, USA*
[9]*Department of Pediatrics, School of Medicine, UCD, Sacramento, California, USA.*
[10]*Department of Radiology, UCD Medical Center, Sacramento, California, USA.*
[11]*Children's Hospital Oakland Research Institute, Oakland, California, USA.*
[12]*Lipid Metabolism Laboratory, Jean Mayer United States Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, and Tufts University School of Medicine, Boston, Massachusetts, USA.*
[13]*Diagnostic Division, Otsuka Pharmaceutical Co., Tokyo, Japan.*
[14]*KineMed, Emeryville, California, USA.*
[15]*Nutritional Sciences and Toxicology, University of California, Berkeley, California, USA.*
[16]*Veterans Affairs Northern California Health Care System, Sacramento, California, USA.*

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## ABSTRACT

**The effects of consuming a diet high in fructose, compared to a diet high in glucose, on the rate of hepatic de novo lipogenesis (DNL) in overweight and obese individuals were studied. These subjects were given a diet in which either glucose or fructose was substituted for 25% of their energy requirements for 10 weeks. During the fasted state, subjects' DNL for those on a glucose and fructose diet were similar. However, in the fed state, DNL was increased significantly in subjects given a fructose diet. This suggests that consuming a diet from fructose-sweetened beverages increases DNL.**

## INTRODUCTION

Not many studies have been conducted on humans to prove the consumption of fructose increases de novo lipogenesis (DNL). Glucose and fructose are the two most popular simple sugars in one's diet today; their effects on hepatitis DNL were compared. Most, if not all, of the fructose from one's diet is metabolized in the liver (90-100%); on the other hand, glucose is mostly metabolized in extra-hepatic tissues (80%) (Figure 1). Also, fructose is metabolized faster than glucose because it bypasses the early steps of glycolysis.

[1]*Corresponding author: for questions, contact Patrick H. Lam.*
*Phone number: (408) 887-7898*
*E-mail: patricklam@berkeley.edu*

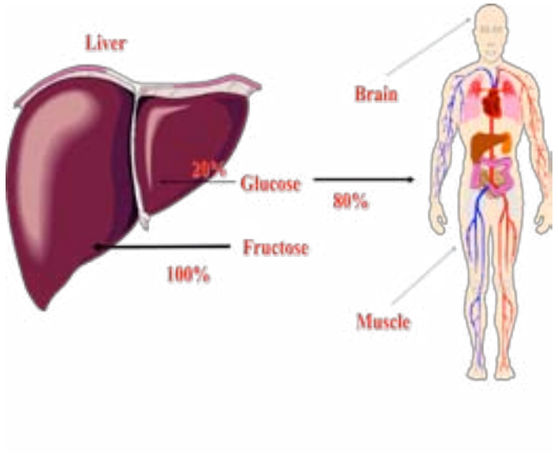


**Figure 1.** Fructose vs. glucose metabolism in the body.

Any excess dietary carbohydrate (CHO) that is not metabolized or stored is converted to fat by the process of (DNL) in the liver (Figure 2). Preliminary studies have shown that fructose consumption leads to higher levels of triglycerides in the blood (Bizeau and Pagliassotti, 2005). The effects of a fructose versus glucose diet on fractional hepatic DNL in overweight and obese human subjects were examined.

## MATERIALS AND METHODS

Subjects were admitted to the UC Davis School of Medicine/Sacramento Veterans Affairs Medical Center General Clinical Research Center (GCRC) for a double-blinded diet intervention study to evaluate lipid metabolism. The study was divided into three phases – inpatient baseline (2 weeks), outpatient intervention (8 weeks), and inpatient intervention (2 weeks). For the 2-week inpatient baseline phase, subjects were fed an energy-balanced, high-complex carbohydrate (CHO) diet (55% energy from CHO, 30% fat, 15% protein) for the first two weeks. During the 8-week outpatient intervention, subjects consumed either glucose- (n=3) or fructose-sweetened (n = 7) beverages providing 25% of daily energy requirements in addition to their ad libitum diet. After 2 outpatient weeks, the subjects returned to the clinic for an inpatient study and blood draw and then finished the remaining 6 weeks outside. In the final 2 weeks of inpatient intervention, subjects consumed an energy-

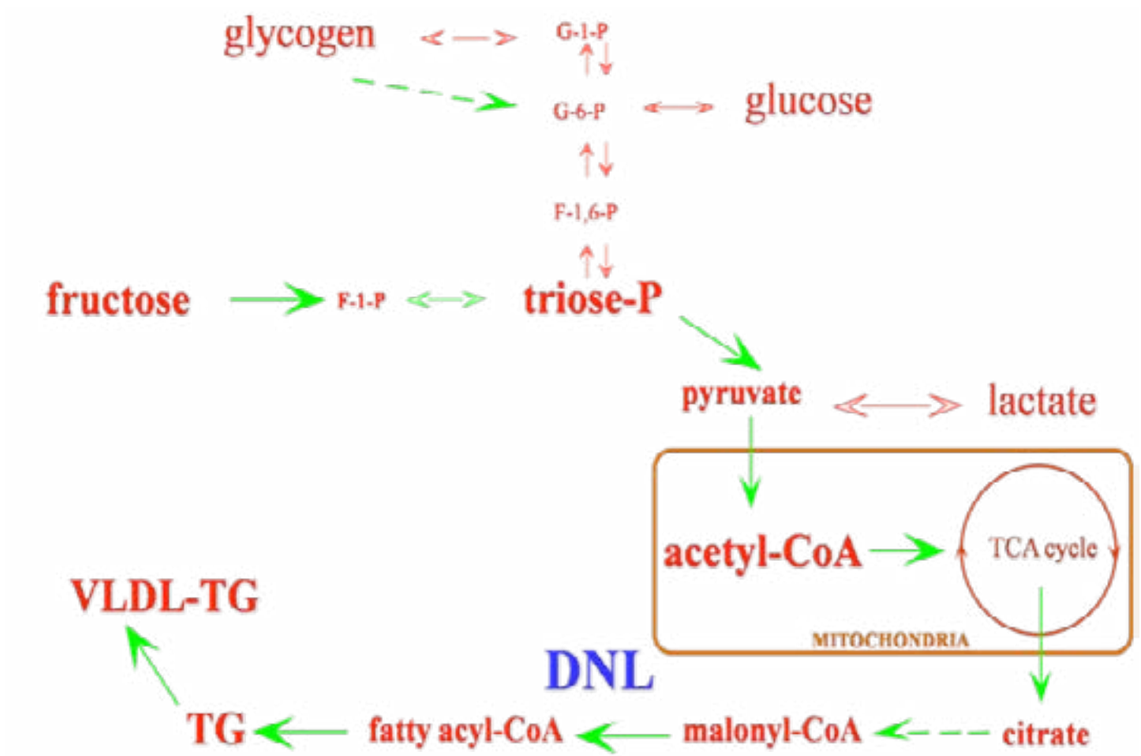


**Figure 2.** Metabolic pathways of fructose vs. glucose, leading up to de novo lipogenesis (DNL)

| Study Period | Study Week | Mon | Tues | Wed | Thur | Fri | Sat | Sun |
|---|---|---|---|---|---|---|---|---|
| Inpatient - Baseline | Wk 1 | | | DXA Postprandial postheparin blood draw | | Oral glucose tolerance & disposal test | | |
| | Wk 2 | Gluteal adipose biopsy | 26-h stable isotope infusion | CT Scan | | 24-h blood collection | Fasting postheparin blood draw | Check-out |
| Diet | Energy balance: 55% of energy requirement Complex CHO; 30% Fat; 15% Protein | | | | | | | |
| Outpatient-Intervention | Wk 1 | | | | | | | |
| | Wk 2 | | | | | | | |
| | Wk 3 | | *Ad lib* buffet | 24-h blood collection | | | | |
| | Wk 4 | | | | | | | |
| | Wk 5 | | | | | | | |
| | Wk 6 | | | | | | | |
| | Wk 7 | | | | | | | |
| | Wk 8 | | | | | | | |
| Diet | *Ad libitum* self-selected +25% of energy requirement as sugar-sweetened beverage | | | | | | | |
| Inpatient - Intervention | Wk 9 | *Ad lib* buffet | 24-h blood collection | DXA Postprandial postheparin blood draw | | Oral glucose tolerance & disposal test | | |
| | Wk 10 | Gluteal adipose biopsy | 26-h stable isotope infusion | CT Scan | | 24-h blood collection | Fasting postheparin blood draw | Check-out |
| Diet | Energy balance: 25% sugar beverage; 30% Complex CHO; 30% Fat; 15% Protein | | | | | | | |

**Figure 3.** 12-week experimental design.

balanced diet where 25% of daily energy requirements came from glucose- or fructose-sweetened beverages. During all inpatient stays, blood was collected. Other procedures during the inpatient stays included a postprandial postheparin blood sampling, oral glucose tolerance test (OGTT), gluteal adipose biopsy, stable isotope tracer infusion to determine fractional DNL (the percent of newly synthesized fat from the liver in the fasted and fed states), and CT scan of the abdomen. The experimental design is outlined in Figure 3. Triglycerides were isolated from very low density lipoproteins (VLDL) and subsequently derivatized to methyl palmitate esters for gas chromatography/mass spectrometry (GC/MS) analysis. The data were then used to calculate fractional DNL by applying mass isotopomer distribution analysis (MIDA).

## RESULTS

The baseline parameters and characteristics of the 10 subjects were similar (Figure 4). Fasting fractional hepatic DNL from the baseline to intervention phases for both glucose and fructose diets showed a similar negative trend and decreased about 2.5%. A negative trend also appeared for postprandial DNL during glucose consumption, decreasing 5.8%. However, postprandial DNL during fructose consumption showed a positive trend, increasing about 6% (Figure 5).

| | Parameter | | | | | | |
|---|---|---|---|---|---|---|---|
| | n | Male : Female | Avg. Age (yr.) | Avg. BMI | Avg. Fasting Insulin (uU/ml) | Avg. Fasting Triglyceride (mg/dl) | Avg. HDL (mg/dl) |
| **Fructose** | 7 | 4 : 3 | 48.9 ± 2.7 | 29.4 ± 1.0 | 14.4 ± 2.4 | 153.3 ± 22.0 | 34.3 ± 1.4 |
| **Glucose** | 3 | 1 : 2 | 54.7 ± 3.5 | 28.4 ± 0.7 | 16.7 ± 5.6 | 203.3 ± 63.0 | 35.3 ± 0.3 |

**Figure 4.** Clinical and metabolic parameters of patients

| Outcome | Complex CHO (baseline) | Glucose (intervention) | % change |
|---|---|---|---|
| **Fasting fractional DNL (%)** | 14.2 ± 2.3 | 11.3 ± 2.6 | ~ - 2.9 |
| **ostprandial fractional DNL (%)** | 22.4 ± 1.0 | 16.6 ± 3.6 | ~ - 5.8 |

| Outcome | Complex CHO (baseline) | Fructose (intervention) | % change |
|---|---|---|---|
| **Fasting fractional DNL (%)** | 11.2 ± 1.6 | 9.3 ± 0.6 | ~ - 1.9 |
| **stprandial fractional DNL (%)** | 12.4 ± 1.6 | 18.1 ± 1.6 | ~ 5.7 |

**Figure 5.** Average baseline and intervention levels of fractional hepatic DNL after consumption of glucose (n = 3) or fructose-sweetened beverages (n = 7).

## DISCUSSION AND CONCLUSIONS

Two diets with the same macronutrient composition but different types of carbohydrate (fructose vs. glucose) affect hepatic DNL differently. Fructose consumption but not glucose consumption increases fractional hepatic DNL, elevating triglyceride levels in blood. It makes sense because fructose metabolism is independent of phosphofructose kinase regulation, unlike glucose metabolism (Mayes, 1993). It has been also shown that fructose may activate a sterol receptor binding protein which activates genes in DNL (Matsuzaka, 2004). In addition, hepatic lipids may increase because increased DNL supplies more endogenous fatty acids and hepatic DNL limits fatty acid oxidation in the liver via production of malonyl-CoA, which reduces the entry of fatty acids into the mitochondria (McGarry, 1995). Nonetheless, additional studies on dose-responses are necessary to evaluate the different amounts of fructose in one's diet and their effect on hepatitis DNL and lipids. Also, a follow-up study may be needed because the 25% of daily energy being provided by the sweetened beverages may be too high compared to the average intake of added sugars by Americans (Guthrie and Morton, 2000).

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