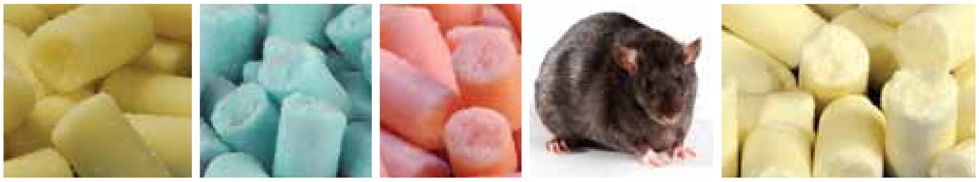


OpenSource DIETS®

Diabetes/ Insulin Resistance

Report ▸ Repeat ▸ Revise

Effect of High Fructose/Sucrose Diets on Plasma Lipid Levels and Insulin Resistance in Rodents

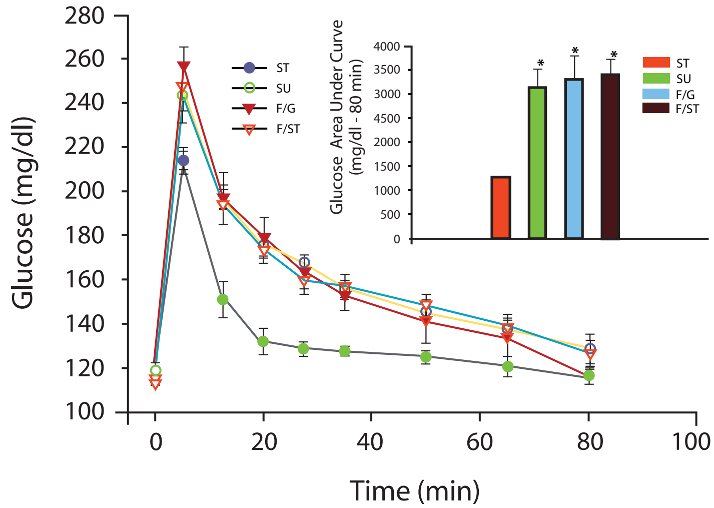
by Matthew R. Ricci, Ph.D. VP, Science Director, Research Diets, Inc. and Michael A. Pellizzon, Ph. D., Senior Scientist, Research Diets, Inc.

High Fructose Diets

Refined carbohydrate sources such as high fructose corn syrup (HFCS) are used in many processed foods and surveys in the U.S. have suggested that the intake of this sweetener has increased dramatically since the 1970s (3). As we have learned over the past few decades, an excess intake of refined carbohydrates is associated with increased weight gain, hypertriglyceridemia (hyper-TG), and insulin resistance (IR) in humans and animal models (5, 1). In order to understand more about the impact of refined carbohydrates on health and therapies to reduce these metabolic syndrome (MS) phenotypes, certain rodent models have been useful. Purified diets containing around 60% - 70% (by energy) fructose or sucrose (which is a 50:50 molar mixture of fructose and glucose) are capable of elevating TG and glucose production in the liver, ultimately leading to IR and hyper-TG relative to diets containing mainly glucose carbohydrate sources (i.e. dextrose, corn starch) (5, 1). Typically, rodent chow diets contain only 4% sucrose and < 0.5% free fructose with most carbohydrate as both digestible starch and non-digestible fiber from grain sources (i.e. wheat, corn, soy). In contrast, low-fat purified diets can contain higher levels of sucrose and this will depend heavily on the formula being used. If desired, it is easy to modify purified diets by manipulating the carbohydrate sources to promote MS while maintaining essential nutrients at recommended levels. However, each rodent model responds differently to high levels of sucrose and fructose.

Rat Models

Sprague-Dawley and Wistar rats are both established models of sucrose-induced IR and hyper-TG (12,10). Both of these phenotypes can develop as quickly as 2 weeks when these animals are fed a diet containing 68% sucrose (by energy) relative to one with the same level of carbohydrate as corn starch (12). It appears that the fructose component of sucrose is largely responsible for the hyper-TG and IR produced by high sucrose diets (13, 17, 16). While a very high concentration of sucrose or fructose induces this phenotype quickly in male rats, a lower level of sucrose (17% of energy) can also allow for IR when fed to rats for 30 weeks relative to a diet containing mainly corn starch (11). Furthermore, gender is important in the development of sucrose induced IR and hyper-TG in rats as females (unlike males) are typically not responsive to elevations in dietary sucrose (6). Other than IR and hyper-TG, high sucrose or fructose diets can promote marginal weight gain in rats, but this typically requires a prolonged period of time and a significantly greater energy intake (4).



Plot of plasma glucose (mg/dl) across time for starch (St)-sucrose (SU)-, fructose/glucose (F/G)-, and F/ST-fed rats in response to a glucose bolus of 0.4 g/kg body wt injected intravenously. Values are means + SE for 10 rats/group. *Inset:* glucose incremental area under the curve. Values are means + SE for 10 rats/group. *Significantly different from ST-fed animals (P< 0.05).
Graphic respresention - for detail see reference (17).

Hamster Models

Similar to rats, hamsters fed high fructose diets (~60% of energy) may develop IR and elevations in circulating TG levels after only 2 weeks compared to those fed low fructose (7, 15). However, unlike rats, hamsters fed high-sucrose diets (60% by energy) may not elevate TG and develop only mild IR (7). Since sucrose is one-half fructose, it appears that the level of dietary fructose is quite important in the rapid development of IR and hyper-TG in hamsters. Other factors, including the addition of cholesterol (0.25%) may also allow the researcher to induce a combination of hypercholesterolemia, greater IR, and hyper-TG in this model compared to fructose alone (2) further improving the fructose-fed hamster's use as a model of dyslipidemia.

Mouse Models

In contrast to rats and hamsters, the mouse is used less frequently as a model for sucrose/fructose-induced IR and hyper-TG as the commonly used C57BL/6 mouse either does not develop IR or develops the phenotype more slowly (9, 14). Despite not developing IR, glucose tolerance can be induced in C57BL/6 mice fed a high sucrose diet (50% sucrose) relative to those fed a similar diet high in corn starch from 10 – 55 weeks, which has been attributed to a reduced pancreatic insulin secretion (14). However, the mouse genome is much easier to manipulate than that of the rat allowing for several knockout models, including the LDLr KO mouse, to show responses (i.e. hyper-TG) to high dietary fructose (8).

Contact our Resource Center for valuable insight from more than 25 years of product experience in the field of diabetes and insulin resistance. Let us formulate the diets to meet your specific study needs.

Custom OpenSource Diets

Research Diets, Inc has pioneered the formulation and production of diets which promote hypertriglyceridemia and insulin resistance in rodents. Our scientists specialize in providing custom purified OpenSource diets. By carefully designing the diet formula to fit your protocol, you have complete control over small or large changes in diet composition. Plus you are able to report what your animals were fed, repeat the formula and revise diet composition as necessary.

Incorporate Test Compounds

Research Diets, Inc. will incorporate your test compound into pelleted diets for simple, safe dosing. Feeding test compounds eliminates dosing related stress to the animal, eliminates vehicle effects, and saves time and labor. Consult with one of our scientists on the formula, determine the dosage required and the diet will be produced and shipped in 5 to 7 business days.

Value Added Resource

The value of our products is in the scientific support we provide. Our Resource Center is staffed with Masters and Ph.D. level scientists with access to over 14,000 original formulas and a database of more than 3,800 journal articles. We welcome the opportunity to talk science with researchers throughout the world as we maintain our leadership role as the knowledge base for OpenSource Diet formulation.

BioDAQ Episodic Intake Monitor

BioDAQ E2 Episodic monitoring system measures the ad libitum food and water intake behavior of singly housed lab rats and mice at very high resolution in their home cage. Computer controlled electronics record food and water intake episodically by measuring the moment-to-moment, undisturbed intake behavior of the animals being studied. BioDAQ E3 features a programmable automated gate to restrict access to food or liquid by time or amount consumed.

www.ResearchDiets.com

Where NutriPhenomics Begins

References

1. Basciano, H., Federico, L. & Adeli, Khosrow, 2005. Fructose, insulin resistance, and metabolic dyslipidemia. Nutrition & Metabolism, 2(1), p.5.
2. Basciano, H. et al., 2009. Metabolic effects of dietary cholesterol in an animal model of insulin resistance and hepatic steatosis. American Journal of Physiology. Endocrinology and Metabolism, 297(2), pp.E462-73.
3. Bray, G.A., Nielsen, S.J. & Popkin, B.M., 2004. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. The American Journal of Clinical Nutrition, 79(4), pp.537-43.
4. Chicco, A. et al., 2003. Muscle lipid metabolism and insulin secretion are altered in insulin-resistant rats fed a high sucrose diet. The Journal of Nutrition, 133(1), pp.127-33.
5. Daly, M.E. et al., 1997. Dietary carbohydrates and insulin sensitivity: a review of the evidence and Clinical implications. The American Journal of Clinical Nutrition, 66(5), pp.1072-85.
6. Horton, T.J. et al., 1997. Female rats do not develop sucrose-induced insulin resistance. The American Journal of Physiology, 272(5 Pt 2), pp.R1571-6.
7. Kasim-Karakas, S.E. et al., 1996. Effects of dietary carbohydrates on glucose and lipid metabolism in golden Syrian hamsters. The Journal of Laboratory and Clinical Medicine, 128(2), pp.208-13.
8. Merat, S. et al., 1999. Western-type diets induce insulin resistance and hyperinsu linemia in LDL receptor-deficient mice but do not increase aortic atherosclerosis compared with normoinsulinemic mice in which similar plasma cholesterol levels are achieved by a fructose-rich diet. Arteriosclerosis, Thrombosis, and Vascular Biology, 9(5), pp.1223-30.
9. Nagata, R. et al., 2004. Single nucleotide polymorphism (-468 Gly to A) at the promoter region of SREBP-1c associates with genetic defect of fructose-induced hepatic lipogenesis [corrected]. The Journal of Biological Chemistry, 279(28), pp.29031-42.
10. Pagliassotti, M.J. et al., 2000. Developmental stage modifies diet-induced peripheral insulin resistance in rats. American Journal of Physiology. Regulatory, Integrative and comparative Physiology, 278(1), pp.R66-73.
11. Pagliassotti, M.J. & Prach, P.A., 1995. Quantity of sucrose alters the tissue pattern and time course of insulin resistance in young rats. The American Journal of Physiology, 269(3 Pt 2), pp.R641-6.
12. Pagliassotti, M.J. et al., 1996. Changes in insulin action, triglycerides, and lipid composition during sucrose feeding in rats. The American Journal of Physiology, 271(5 Pt 2), pp.R1319-26.
13. Sleder, J. et al., 1980. Hyperinsulinemia in fructose-induced hypertriglyceridemia in the rat. Metabolism: Clinical and Experimental, 29(4), pp.303-5.
14. Sumiyoshi, M., Sakanaka, M. & Kimura, Y., 2006. Chronic intake of high-fat and high-sucrose diets differentially affects glucose intolerance in mice. The Journal of Nutrition, 136(3), pp.582-7.
15. Taghibiglou, C. et al., 2000. Mechanisms of hepatic very low density lipoprotein overproduction in insulin resistance. Evidence for enhanced lipoprotein assembly, reduced intracellular ApoB degradation, and increased microsomal triglyceride transfer protein in a fructose-fed hamster m. The Journal of Biological Chemistry, 275(12), pp.8416-25.
16. Thorburn, A.W. et al., 1989. Fructose-induced in vivo insulin resistance and elevated plasma triglyceride levels in rats. The American Journal of Clinical Nutrition, 49(6), pp.1155-63.
17. Thresher, J.S. et al., 2000. Comparison of the effects of sucrose and fructose on insulin action and glucose tolerance. American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 279(4), pp.R1334-40.

Research Diets, Inc.
20 Jules Lane
New Brunswick, NJ 08901 USA
Tel: 732.247.2390
Fax: 732.247.2340
info@researchdiets.com