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

2016 - Brief Scientific Literature Review
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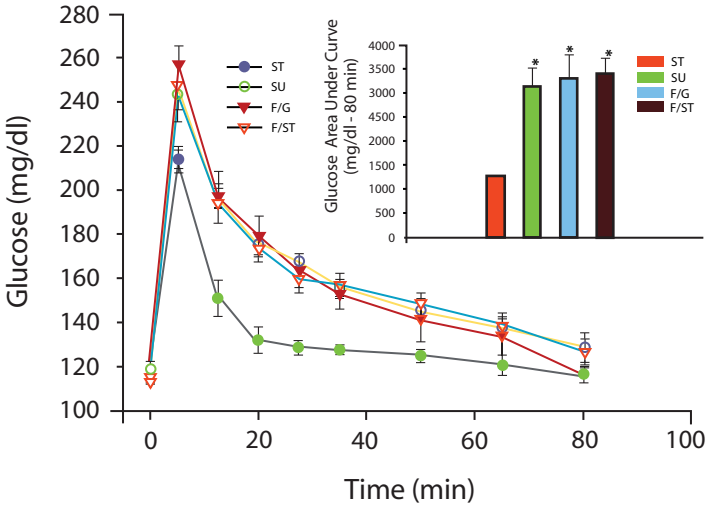
High Fructose Diets

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 grain-based (GB) 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.



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).

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 induce 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).

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 intolerance 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).

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.

References - Diabetes/Insulin Resistance

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