Diabetes/ Insulin Resistance

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

Refrained 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 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 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).

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).
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**References**

8. Merat, S. et al., 1999. Western-type diets induce insulin resistance and hyperinsulinemia 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.