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High Fat Diets for Diet-Induced Obesity Models

A Brief Review of the Scientific Literature- October 2008
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Genetic and environmental factors play a role in the development of obesity, and diet is one of the main environmental factors that contributes to this disease. Human studies have shown that increased fat intake is associated with body weight gain which can lead to obesity and other related metabolic diseases. Animal rodent models are therefore useful tools for studying obesity as they will readily gain weight when fed high-fat diets (1, 2).

Matched Formulas

When planning a diet-induced obesity study, the composition of the high-fat diet deserves attention. All too often in the literature, one will find that diets used in the experiments are not well matched, thereby introducing confounding factors. For example, in many cases a chow (cereal based diet) is used as a low-fat "control" diet for a purified high-fat diet. Chows diets contain plant-derived ingredients which are subject to changes in the growing season and will vary in composition at the time of harvest. Thus, diet formulas may change based on the nutritional composition. Purified ingredients, on the other hand, are highly refined and contain just a single nutrient (ie. sucrose = carbohydrate). These ingredients have little variability and therefore provide consistency between batches. There are numerous differences between chows and purified diets, creating countless variables, thus making it difficult to interpret the results when these diets are used together in a study (3). In addition, chows contain plant-based compounds such as phytoestrogens which have been shown to reduce the degree of weight gain (4). For these reasons, a low-fat purified diet containing the same ingredients with a closely matched composition to the high-fat formula should be used as a control diet.

Cafeteria Diets

In the early days of rodent diet-induced obesity research, some scientists used what is known as the cafeteria diet. In this model, the animal self-selects from highly palatable, readily available foods including cookies, candy, cheese, and processed meats. These foods contain a substantial amount of salt, sugar, and fat and are meant to simulate the human Western diet. However, the nutritive and non nutritive components of these foods are not well defined. In addition, the animal may choose a different selection of foods each day. Therefore, these diets cannot be accurately replicated for future studies, which makes this type of diet a poor choice for scientific research (5).

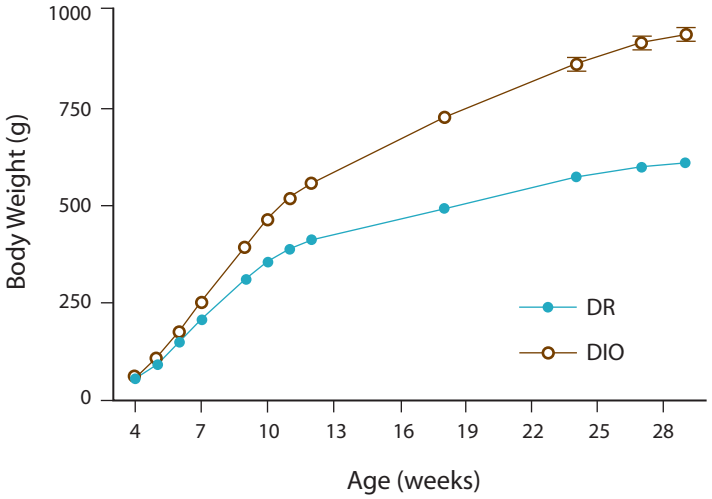

FIGURE 1. Growth rate of DIO (n = 12) and DR (n = 12) rats fed D12451 HFD (45 kcal% fat) diet used in meal analysis. Values are means ± SEM. Body weights are significantly different at all time points ($p < 0.05$). Graphic representation - for details see reference (16).

Calories from Fat

High-fat diets used in laboratory research typically contain about 32 to 60% of calories from fat. From a nutritional perspective, a human diet of 60 kcal% fat would be considered extreme. That said, diets with 60 kcal% fat are commonly used to induce obesity in rodents since animals tend to gain more weight more quickly (6, 7) thereby allowing researchers to screen their compounds after a shorter period of time. It should also be noted that when studying the effects of a drug, nutraceutical, or gene mutation on obesity, it may be more difficult to prevent or reverse the effects of a very high-fat diet, when it might be possible with a diet containing a lower percentage of fat.

Type of Fat

The type of fat should be considered when choosing a high-fat diet for an animal study. Many high-fat diets used in laboratory animal research contain more saturated fat such as lard, beef tallow, or coconut oil and these diets are quite capable of inducing obesity in susceptible strains. In contrast, omega-3 fatty acids have been studied for their health benefits. For example, it has been shown that of animals fed similar amounts of fat, those fed diets containing fish oil did not gain as much weight as those fed diets with more saturated fat (8, 9) and were more insulin sensitive (10). Since fatty acids can affect phenotype through a variety of mechanisms (gene expression, eiconsanoid production, membrane receptor function), it is important to include information about the type and level of fat used in a study in order to allow other researchers to compare data.

Animal Models

While most rodents tend to become obese on high-fat diets, there can be variable responses in weight gain, glucose tolerance, insulin resistance, triglycerides and other parameters depending on the strain. Some inbred strains are more susceptible to obesity when fed high-fat diets such as the C57Bl6 or AKR mouse (11). However, strains that exhibit similar levels of weight gain may show different responses to other parameters. For example, when fed a 58 kcal% fat diet, C57Bl6 mice and AKR mice will have similar degrees of weight gain, but C57Bl6 mice are more glucose intolerant compared to AKR mice (11). Other strains are simply more resistant to obesity, such as the SWR/J and A/J mice (12, 13). Even within the same strain, different phenotypical responses to high fat diets have been observed between animals bred in different facilities (14).

Rat models including outbred Sprague-Dawley and Wistar rats are popular strains to study obesity as they readily gain weight on high-fat diets. In particular, Sprague-Dawley rats have been studied for their ability to show a a variable response to a high-fat diet (32 or 45 kcal% fat).

Some animals rapidly gain weight while others gain only as much weight as those fed a low-fat diet (15, 16), allowing for the study of animals that are prone and resistant to obesity. These animals have been selectively bred over time to study the genetic traits of animals with the obese or lean phenotype. Another strain, the F344xBrown Norway rat, has been used as a model for age-related onset of obesity since the animals gain weight until about 30 months of age (17). When this strain was fed a diet containing 60 kcal% fat, 3 month old rats separated into resistant and obese groups. This was in contrast to 24-month-old animals which had similar levels of weight gain and did not require separation (18).

There has been a growing body of literature using rodents as models of human obesity, even though there are many confounding factors including species, strain, age of the animals, type of diet, level of fat, and type of control diet. Fortunately, there is a growing discussion about these issues which will help scientists design studies with tightly controlled conditions and therefore improve our understanding of obesity and related diseases.

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Research Diets, Inc has pioneered the formulation and production of diets leading to obesity in laboratory animals. Our DIO series diets D12450B, D12451, and D12492 are the most widely used and published high fat diets worldwide. 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.

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The "Original" High-Fat Diets

Research Diets, Inc. formulated the "original" high fat diet for diet induced obesity (DIO) studies in 1996. Today, our high fat diets are the research standard for DIO mice worldwide.

(DIO) Formulas

Product #	D12451		D12492	
	gm%	kcal%	gm%	kcal%
Protein	24	20	26	20
Carbohydrate	41	35	26	20
Fat	24	45	35	60
Total		100		100
kcal/gm	4.73		5.24	
Ingredient	**gm**	**kcal**	**gm**	**kcal**
Casein, 80 Mesh	200	800	200	800
L-Cystine	3	12	3	12
Corn Starch	72.8	291	0	0
Maltodextrin 10	100	400	125	500
Sucrose	172.8	691	68.8	275
Cellulose, BW200	50	0	50	0
Soybean Oil	25	225	25	225
Lard	177.5	1598	245	2205
Mineral Mix S10026	10	0	10	0
DiCalcium Phosphate	13	0	13	0
Calcium Carbonate	5.5	0	5.5	0
Potassium Citrate, 1 H2O	16.5	0	16.5	0
Vitamin Mix V10001	10	40	10	40
Choline Bitartrate	2	0	2	0
FD&C Red Dye #40	0.05	0		
FD&C Blue Dye #1			0.05	0
Total	**858.15**	**4057**	**773.85**	**4057**

Formulated by E. A. Ulman, Ph.D., Research Diets, Inc., 1/18/96 and 8/26/98.
Use D12450B 10% kcal fat as matched control diet.