# The Age-Dependent Response of Serum Triglycerides to Dietary Fructose[1] (36113)

M. CHEVALIER, J. H. WILEY, AND G. A. LEVEILLE[2]

*Laboratory of Nutritional Biochemistry, Department of Animal Science, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801*

Although numerous studies have indicated that substitution of sucrose or fructose for glucose in the diet produces an elevation in circulating triglycerides in the rat (1–9), the effect has not been consistently observed. Recently Hill (1) reported that age may be a determining factor in the ability of dietary fructose to elevate circulating triglycerides relative to dietary glucose. By administering fructose in the drinking water of young and mature rats, he found that fructuse did not affect serum triglyceride levels in young rats but caused a significant increase on serum triglycerides in mature rats.

The present report considers further the effects of age and diet on circulating triglyceride levels in the rat. Since fructose is generally consumed as sucrose, purified diets containing sucrose as well as fructose and glucose were fed to the rats. The sugars were fed as major components of purified diets rather than in the drinking water for maximum control of dietary carbohydrate intake. Both weanling and mature rats were studied.

*Materials and Methods.* Male rats of the Sprague–Dawley strain were used in all experiments. The animals were housed individually in metal cages having raised wire floors and kept in a temperature-regulated room (22°). Water was available at all times, and body weight and food consumption were determined weekly. The diets were fed *ad libitum* and contained, as a percentage by weight: 18% casein, 0.3% L-cystine, 2.0% solka-floc, 4.0% mineral salt,[3] 0.4% vitamin mix,[4] 0.2% choline chloride, 5.0% corn oil, and 70.1% carbohydrate. The carbohydrate varied as noted in Tables I and II. The length of feeding and the final weight of the animals is also given in the tables. Serum triglycerides were assayed by the method of Leveille *et al.* (10).

*Results.* In Expt. 1, glucose and sucrose were fed to young weanling rats for 3 weeks. As indicated in Table I, sucrose feeding did not elevate serum triglyceride levels. To insure that the glucose present in the sucrose diet was not modifying the effect of the fructose on circulating triglyceride levels, a group fed a purified fructose diet was included in Expt. 2. A diet in which half of the carbohydrate was present as glucose and half as fructose was also included. The diets were fed to weanling rats for 2 weeks. The results of this experiment are given in Table I. Again no significant differences in serum triglyceride levels were found among the different dietary treatments.

Older rats were tested in Expts. 3 and 4. Experiment 3 involved feeding starch, glucose, sucrose, or fructose diets to rats weighing about 500 g for 3 weeks. As shown in Table II, dietary fructose or sucrose significantly raised the serum triglyceride levels compared to dietary glucose or starch. Experiment 4 was conducted to determine how rapidly the increase in serum triglyceride level could be seen. In this experiment, mature rats were fasted for 2 days and then refed the glucose or fructose diet for 2 days. As the data in Table II indicate, elevated triglyceride levels could be induced within 2

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[2] Present address: 204 Food Science Building, Department of Food Science and Human Nutrition, Michigan State University, East Lansing, Michigan 48823.

[3] Mineral mix, see Leveille and O'Hea (11).

[4] Vitamin mix, see Leveille (12).

TABLE I. The Effect of Dietary Carbohydrate on Serum Triglyceride Levels in Weanling Rats.

| Dietary carbohydrate | Expt. 1[a] Final wt (g) | Expt. 1[a] Serum triglycerides (μmoles/100 ml) | Expt. 2[b] Final wt (g) | Expt. 2[b] Serum triglycerides (μmoles/100 ml) |
|---|---|---|---|---|
| Glucose | 161 ± 3[c] | 108.5 ± 13.7 (8)[d] | 133 ± 2 | 110.2 ± 10.0 (6) |
| Sucrose | 160 ± 4 | 115.5 ± 6.9 (7) | 135 ± 2 | 93.4 ± 5.5 (5) |
| Fructose | — | — | 130 ± 2 | 111.6 ± 9.8 (5) |
| Glucose + fructose[e] | — | — | 136 ± 2 | 99.8 ± 9.8 (5) |

[a] Diets were fed for 3 weeks.
[b] Diets were fed for 2 weeks.
[c] Values are mean ± SEM.
[d] Number of animals tested is given in parentheses.
[e] Dietary carbohydrate was half glucose and half fructose.

days of fructose feeding.

*Discussion.* The results of these experiments demonstrate that the effect of dietary fructose on circulating triglycerides is age dependent. Dietary fructose or sucrose as opposed to glucose caused an increase in serum triglyceride levels in mature rats but not in young rats. These results may help to explain the conflicting reports in the literature on the effects of dietary fructose on serum triglycerides.

Webb *et al.* (2) found no effect on serum triglyceride levels when glucose or fructose was administered to rats in the drinking water for 6–7 weeks. The final weight of the rats was about 310 g. Zakim *et al.* (4) used rats weighing 225–350 g. By fasting for 48 hr, then refeeding a diet containing 70% glucose or fructose for 48 hr, they were able to show a significant increase in serum triglyceride levels in the fructose-fed animals. Cohen and Teitelbaum (5) used rats whose initial weights were 90–100 g and fed them a diet containing 72% starch, glucose, or fructose for 65 days. They found lower serum triglyceride levels in the glucose-fed animals and elevated levels in the fructose-fed animals. Intermediate levels were found in the starch-fed animals. By feeding a 68% starch, sucrose, fructose, glucose, or maltose containing diet for 7 weeks, Naismith and Khan (6, 7) showed that the starch-fed rats had lower serum triglyceride levels than the other four groups which had similar levels. However, when these workers administered Triton, an agent which abolishes the activity of lipopro-

TABLE II. The Effect of Dietary Carbohydrate on Serum Triglyceride Levels in Mature Rats.

| Dietary carbohydrate | Expt. 3[a] Final wt (g) | Expt. 3[a] Serum triglyceride (μmoles/100 ml) | Expt. 4[b] Final wt (g) | Expt. 4[b] Serum triglyceride (μmoles/100 ml) |
|---|---|---|---|---|
| Starch | 494 ± 12[c] | 176 ± 11[d,f] (4)[e] | — | — |
| Glucose | 502 ± 10 | 173 ± 34[f] (4) | 467 ± 9 | 123 ± 12[f] (9) |
| Sucrose | 530 ± 12 | 341 ± 62[g] (5) | — | — |
| Fructose | 524 ± 13 | 259 ± 32[g] (6) | 456 ± 9 | 214 ± 11[g] (10) |

[a] Diets were fed for 3 weeks.
[b] Animals were fasted for 48 hr, then refed glucose or fructose diets for 48 hr.
[c] Values are mean ± SEM.
[d] Values followed by the same superscript letter ($f$ or $g$) in a column are not significantly different ($p > .05$).
[e] Number of animals tested is given in parentheses.

tein lipase, they observed significantly higher serum triglyceride levels in the fructose-fed animals.

Bar-on and Stein (9) have postulated that the increase in serum triglyceride levels found in fructose-fed animals is partially due to a decreased tissue uptake of triglycerides from the serum. These workers found the activity of lipoprotein lipase to be much higher in rats given 10% glucose in their drinking water than in those given fructose. The age of the animals used in the experiments was not specified. Further investigation is needed to determine if this mechanism is age dependent.

*Summary.* Diets containing 70.1% glucose, starch, sucrose, or fructose were fed to weanling and mature rats. Dietary fructose or sucrose increased serum triglyceride levels in the mature but not in the weanling rats. The results help to explain some of the conflicting reports found in the literature.

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1. Hill, P., Lipids **5**, 621 (1970).

2. Webb, W., Nestel, P. J., Foxman, C., and Lynch, A., Nutr. Rep. Int. **1**, 189 (1970).

3. Kritchevsky, D., and Tepper, S. A., Med. Exp. **19**, 329 (1969).

4. Zakim, D., Pardini, R. S., Herman, R. H., and Sauberlich, H. E., Biochim. Biophys. Acta **144**, 242 (1967).

5. Cohen, A. M., and Teitelbaum, A., Life Sci. **7**, 23 (1968).

6. Naismith, D. J., and Khan, N. A., Proc. Nutr. Soc. **29**, 63A (1970).

7. Naismith, D. J., and Khan, N. A., Proc. Nutr. Soc. **29**, 64A (1970).

8. Nikkila, E. A., and Ojala, K., Life Sci. **5**, 89 (1966).

9. Bar-on, H., and Stein, Y., J. Nutr. **94**, 95 (1968).

10. Leveille, G. A., Shockley, J. W., and Sauberlich, H. E., U.S. Army Med. Res. Nutr. Lab, Rep. No. 255, 1961.

11. Leveille, G. A., and O'Hea, E. K., J. Nutr. **93**, 541 (1967).

12. Leveille, G. A., J. Nutr. **91**, 267 (1967).

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