

Interaction of dietary carbohydrate and fat in the regulation of hepatic and extrahepatic lipogenesis in the rat

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1. In order to examine the interaction of dietary fat and carbohydrate in the regulation of lipid metabolism, we have studied hepatic and extrahepatic lipogenesis, and adipose tissue lipoprotein lipase (*EC* 3.1.1.34) in rats fed on one of the following diets: a fructose-based diet containing 0 (F0) or 150 g maize oil (F15)/kg, or a glucose-based diet containing 0 (G0) or 150 g maize oil (G15)/kg.

2. The rats were meal-fed on the diets for 2 weeks after which the activities of a number of hepatic 'lipogenic' enzymes were measured and the activity of epididymal-fat-pad lipoprotein lipase. The activities of the lipogenic enzymes were: $F0 > G0 > G15 > F15$. Lipoprotein lipase activity was $F0 = G0 = F15 = G15$. The percentage of total body fatty acid synthesis which occurred in the liver was $F0 > G0 > F15 > G15$.

3. We conclude that fructose-induced hypertriglyceridaemia is primarily a result of the increased hepatic synthesis rather than decreased adipose-tissue lipoprotein lipase activity.

Studies of the effects of dietary fructose or sucrose, or both, on lipid metabolism have generally focused on the role of the liver and have used diets which contain little or no fat. It has been observed in such studies that dietary fructose or sucrose leads to hypertriglyceridaemia (Nikilla & Ojala, 1965; Bruckdorfer *et al.* 1972), enhanced enzymic capacity for hepatic fatty acid synthesis, increased synthesis of fatty acids (Cohen & Teitelbaum 1968; Sullivan *et al.* 1971; Maruhama & MacDonald, 1972; Romsos & Leveille, 1974*a*; Herzberg & Rogerson, 1982) and an increased rate of hepatic triglyceride secretion with no change in lipoprotein lipase (*EC* 3.1.1.34; LPL) activity (Kannan *et al.* 1981; Zavaroni *et al.* 1982; Bird *et al.* 1984).

Because of the well-known inhibition of hepatic lipogenesis by dietary fat (Romsos & Leveille, 1974*b*; Volpe & Vagelos, 1976; Herzberg, 1983), we felt it desirable to examine the effect of fructose on lipogenesis in animals consuming diets containing levels of dietary fat more representative of that in typical human diets. Because of our previous observation that although dietary fructose did not increase total body fat synthesis in mice, it did increase the proportion which occurred in the liver (Herzberg & Rogerson, 1982), we were also interested in the relative contributions of the liver and extrahepatic tissue to total body lipogenesis under different dietary conditions. Finally, although fructose does increase hepatic triglyceride secretion (Bird *et al.* 1984), the effect of added dietary fat on the secretory rate has not been examined in fructose-fed rats. Accordingly, we have carried out experiments which examine the interaction of the type of dietary carbohydrate and the level of fat on the activity of several hepatic lipogenic enzymes, fatty acid synthesis *in vivo*, hepatic triglyceride secretion and the activity of adipose tissue LPL.

MATERIALS AND METHODS

Male, Sprague-Dawley rats were obtained from Canadian Biobreeding Labs (Montreal). The average weight was 228 g at the start of the experiment. Animals were housed individually in plastic metabolism cages and kept in a room of 25°, having a 12 h light–12 h dark cycle (lights on 08.00–20.00 hours). The rats were given 20 g food at 08.00 hours

Table 1. *Composition (g/kg) of the experimental diets*

Maize oil . . .	0	150
Glucose or fructose	700	550
Casein	200	200
AIN mineral mix*	35	35
AIN vitamin mix†	10	10
α - Cellulose	50	50
Methionine	3	3
Choline chloride	2	2
Energy: MJ/kg	15.1	18.2
kcal/kg	3600	4350
Composition (% of energy contributed)		
Carbohydrate	77.8	50.6
Fat	—	31.0
Protein	22.2	18.4

* Obtained from ICN Nutritional Biochemicals, Cleveland, Ohio and had the following composition (g/kg): CaHPO₄ 500, NaCl 74.0, potassium citrate monohydrate 220.0, K₂SO₄ 52.0, MgO 24.0, MnCO₃ 3.5, ferric citrate 6.0, ZnCO₃ 1.6, CuCO₃ 0.3, KIO₃ 0.01, Na₂SeO₃·5H₂O 0.01, CrK(SO₄)₂·12 H₂O 0.55, sucrose 118.0.

† Obtained from ICN Nutritional Biochemicals and had the following composition (mg/kg): thiamin hydrochloride 600, riboflavin 600, pyridoxine hydrochloride 700, nicotinic acid 3, calcium-D-pantothenate 1.6, folic acid 200, D-biotin 20, cyanocobalamin 1, retinyl palmitate 800, DL- α -tocopherol acetate 20, cholecalciferol 2.5, menaquinone 5.0, sucrose 972.9 g.

which was removed at 11.00 hours. Rats were fed on the experimental diets for a total of 14 d. Water was available *ad lib.* and food consumption was measured daily. Four diets were used, with six rats per diet: fructose-based fat-free (F0), glucose-based fat-free (G0), fructose-based + 150 g maize oil/kg (F15) and glucose-based + 150 g maize oil/kg (G15)

Enzymes and lipogenesis in vivo

On the 14th day of the experiment, the animals were weighed before being fed. At 10.00 hours they were injected intraperitoneally with 1 mCi³H₂O/kg body-weight and were decapitated 60 min later. In all experiments, animals had full stomachs at the time of death. A sample of neck blood was taken for the determination of serum specific radioactivity, insulin, triglycerides, glucose and fructose. Serum specific radioactivity was determined by counting a sample of serum and assuming the concentration of water in serum is 55 M.

A portion of the liver was rapidly removed, weighed and homogenized in 3 vol. 0.15 M-potassium chloride, 1.0 mM-magnesium chloride, 0.5 M-dithiothreitol, 10 mM-N-acetyl cysteine buffer, pH 7.6. Following centrifugation at 100 000 g for 40 min, the supernatant fraction was used for quantification of enzyme activities. Fatty acid synthetase (FAS) was determined from the rate of malonyl-CoA-dependent NADPH oxidation (Gibson & Hubbard, 1960), glucose-6-phosphate dehydrogenase (*EC* 1.1.1.49; G6PD) from the rate of glucose-6-phosphate-dependent reduction of NADP under conditions which minimize the activity of phosphogluconate dehydrogenase (decarboxylating) (*EC* 1.1.1.44) (Lohr & Waller, 1974), malate dehydrogenase (oxaloacetate-decarboxylating) (NADP⁺) (*EC* 1.1.1.40; MD) from the rate of malate-dependent NADP reduction (Yeh *et al.* 1970), glucokinase (*EC* 2.7.1.2; GK) from the rate of glucose-dependent reduction of NAD in the presence of added G6PD from *Leuconostoc mesenteroides* (Newgard *et al.* 1983), ATP citrate (*pro*-3S)-lyase (*EC* 4.1.3.8; CL) by the method of Srere (1959) and fructokinase (*EC* 2.7.1.4) was measured as described by Adelman *et al.* (1966). Enzyme assays were conducted at 37°.

A second portion of the liver was used to determine fatty acid synthesis *in vivo* (Lowenstein, 1970). The tissue was weighed, deposited directly into 5 M-potassium hydroxide and heated at 70° for 4 h. After saponification, the samples were extracted with three 5 ml portions of light petroleum (b.p. 37.8–56.1°) to remove non-saponifiable material. The samples were then acidified with hydrochloric acid and the fatty acids extracted with three 5 ml portions of light petroleum. The extracts were combined in a scintillation vial and, after evaporation of the light petroleum, the radioactivity in the extracted fatty acids was determined by liquid-scintillation spectrometry using a Beckman LS7500 liquid scintillation counter. Efficiency was determined by external standard. Protein was determined by the microBiuret method of Goa (1953) using bovine serum albumin as the standard, Total liver lipid was determined gravimetrically after extraction with chloroform–methanol (2:1, v/v).

Fatty acid synthesis in the extrahepatic tissues was determined as described by Baker *et al.* (1978). Whole carcasses minus the liver were saponified in ethanolic potassium hydroxide (500 ml ethanol/1; 300 g KOH/1), 4 ml/g carcass for 4 h at 80°. Non-saponifiable lipids were removed by three extractions with light petroleum. After acidification with HCl, the fatty acids were extracted with light petroleum and after evaporation of the light petroleum the fatty acids were assayed for ³H by liquid-scintillation spectrometry in a Beckman LS 7500 liquid scintillation spectrometer.

Insulin was measured by radioimmunoassay using a commercially available kit (Amersham, Oakville, Ontario) containing ¹²⁵I-labelled anti-human insulin antibody. Radioactivity was counted using Beckman 5500 gamma counter. Glucose was measured spectrophotometrically using hexokinase (*EC* 2.7.1.1) and G6PD. Fructose was measured in the same cuvette by adding glucose-6-phosphate isomerase (*EC* 5.3.1.9) after the glucose assay had gone to completion (Bernt & Bergmeyer, 1974).

LPL

LPL was determined in a second group of animals fed identically to those previously described. LPL activity was determined in the epididymal fat pads of rats which had been fed on the day of the experiment. Acetone powders were used for LPL activity determined from the rate of release of [¹⁴C]oleate from ¹⁴C-labelled triolein emulsion according to the method of Nilsson-Ehle *et al.* (1972). Serum triglycerides were measured enzymically (Wahlfield, 1974).

Chemicals and biochemicals were obtained from Fisher Scientific Co., Sigma Chemical Co or Boehringer Mannheim. Diet components were obtained from ICN Nutritional Biochemicals (Cleveland, Ohio) except for maize oil which was obtained locally (Mazola; Canada Starch Co., Montreal). Isotopes were obtained from New England Nuclear (LaChine, Quebec).

All results were analysed by two-way analysis of variance. Effects were considered significant at $P < 0.05$.

RESULTS

Weight gain and food consumption. There was a significant effect of dietary fat on both diet consumption and weight gain (Table 2). Food intake was reduced and weight increased by the addition of maize oil to the diets. There was no difference between glucose and fructose in weight gain or food consumption.

Serum and liver metabolites. Serum glucose was not altered by dietary fructose in the absence of added fat (Table 2). In the presence of fat, serum glucose was higher in the G15 group but lower in the F15 group, resulting in an intermediate serum glucose in the F0 (fructose without fat) group. Serum fructose was higher in the fructose-fed groups. There was no effect of dietary fat on serum fructose.

Table 2. *Weight gain, food consumption, serum insulin, glucose, fructose and liver lipids in rats fed on fructose- or glucose-based diets containing 0 or 150 g maize oil/kg*

(Values are means and standard deviations for six samples)

Diet ...	Glucose				Fructose			
	Without maize oil		With maize oil		Without maize oil		With maize oil	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Food consumption (g/d) ^b	19.4	0.4	18.6	1.3	19.0	0.4	18.6	1.2
Wt gain (g) ^b	54.1	19.5	68.6	17.2	44.5	10.8	78.1	15.0
Serum glucose (mM) ^{a, c}	8.94	1.07	9.72	1.31	8.90	0.83	7.33	0.41
Serum fructose (mM) ^a	0.21	0.08	0.17	0.04	0.35	0.14	0.47	0.14
Insulin (μ U/ml) ^a	143	16	114	37	105	12	96	30
Serum triglyceride (mM) ^a	1.23	0.26	1.63	0.32	3.40	0.46	2.79	0.68
Liver lipids (mg/g liver)	67.6	16.6	76.3	8.19	99.9	39.7	78.3	4.34

^a Results with different carbohydrate sources were significantly different ($P < 0.05$).^b Results with and without added maize oil were significantly different ($P < 0.05$).^c There was a significant interaction ($P < 0.05$) between the results with different carbohydrates and those with and without added maize oil.Table 3. *Hepatic enzyme activities (nmol/mg cytosolic protein per min) in rats fed on glucose- or fructose-based diets containing 0 or 150 g maize oil/kg*

(Values are means and standard deviations for six samples)

	Glucose				Fructose			
	Without maize oil		With maize oil		Without maize oil		With maize oil	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Fatty acid synthetase ^{a, b}	26.2	7.8	19.1	5.35	62.2	12.8	35.4	8.51
ATP citrate (<i>pro</i> 3S)-lyase (<i>EC</i> 4.1.3.8) ^{a, b}	164	24	71	15	231	35	101	38
Glucokinase (<i>EC</i> 2.7.1.2) ^{a, b, c}	111	10.8	76	12.6	53	7.5	52	9.6
Glucose-6-phosphate dehydrogenase (<i>EC</i> 1.1.1.49) ^{a, b}	363	73	98	26	492	69	137	33
Malate dehydrogenase (oxaloacetate-decarboxylating) (NADP ⁺) (<i>EC</i> 1.1.1.40) ^{a, b}	249	52	85	26	466	102	127	53
Fructokinase (<i>EC</i> 2.7.1.4)	73	4.0	73	5.4	78	7.0	96	7.6

^a Results with different carbohydrate sources were significantly different ($P < 0.05$).^b Results with and without added maize oil were significantly different ($P < 0.05$).^c There was a significant interaction ($P < 0.05$) between the results with different carbohydrates and those with and without added maize oil.

Lower serum insulin was found in the F0 and F15 groups. Although there was a tendency for fat to lower insulin, the effect was not statistically significant. Rats consuming fructose had increased serum triglycerides. There was no effect of dietary fat on serum triglycerides and no effect of diet on liver lipids.

Enzyme activities. GK was highest in the G0 group and reduced by fat (Table 3). The GK

Table 4. *Lipogenesis in vivo in rats fed on fructose- or glucose-based diets containing 0 or 150 g maize oil/kg*

(Values are means and standard deviations for six samples)

Diet . . .	Glucose				Fructose			
	Without maize oil		With maize oil		Without maize oil		With maize oil	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
³ H ₂ O incorporated into fatty acid*								
/g liver ^{a, b}	73.6	33.6	30.0	11.7	126	75	41.1	18.3
/total liver ^{a, b}	1136	592	395	185	1460	166	612	274
/g carcass ^{a, b}	12.6	3.8	8.0	0.9	6.2	0.9	6.6	1.3
/carcass ^{a, c}	3173	845	2331	363	1636	293	1883	355
/whole rat ^{a, c}	4309	1662	2725	484	3096	842	2494	535
% in liver ^{a, b}	26.4	10.9	14.1	4.55	47.2	13.2	23.9	8.2

* Expressed as μmol tritium incorporated/h.^a Results with different carbohydrate sources were significantly different ($P < 0.05$).^b Results with and without added maize oil were significantly different ($P < 0.05$).^c There was a significant interaction ($P < 0.05$) between the results with different carbohydrates and those with and without added maize oil.Table 5. *Epididymal-fat-pad weights and lipoprotein lipase (EC 3.1.1.34) activity in rats fed on fructose- or glucose-based diets containing 0 or 150 g maize oil/kg*

(Values are means and standard deviations for six samples)

Diet . . .	Glucose				Fructose			
	Without maize oil		With maize oil		Without maize oil		With maize oil	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Epididymal-fat-pad wt (g) ^a	1.85	0.18	2.92	0.41	1.62	0.42	2.49	0.73
Lipoprotein lipase*:								
Units/g ^a	2.25	0.53	1.66	0.42	2.33	0.66	1.65	0.38
Total units	4.20	1.22	4.80	1.21	3.76	0.97	4.11	1.65

^a Results with and without added maize oil were significantly different ($P < 0.05$).* One unit of activity is 1 μmol product/min.

activities in the F0 and F15 groups were lower and equal to each other. The GK activities paralleled the insulin levels and were consistent with the known role of insulin in GK induction (Weinhouse, 1976). FK was unaffected by the dietary treatments.

For the lipogenic enzymes FAS, CL, G6PD and MD, activity was higher in the fructose group in the presence or absence of dietary fat (F0 > G0 > F15 > G15) which is consistent with earlier reports of the effect of dietary carbohydrate on lipogenic enzyme activity (Fitch & Chaikoff, 1960; Kornacker & Lowenstein 1965; Yudkin & Krauss, 1967; Bruckdorfer *et al.* 1972; Suzawa-Katayama & Morita, 1977; Herzberg & Rogerson, 1980; Kannan *et al.* 1981).

Lipogenesis in vivo. Hepatic lipogenesis in vivo was highest in fructose-fed rats and hepatic lipogenesis was significantly reduced by dietary fat (Table 4). Extrahepatic

lipogenesis was greater in glucose-fed rats and while it was reduced by dietary fat in glucose-fed rats, there was no effect of dietary fat in those consuming fructose. Consequently, the contribution of the liver to total lipogenesis in fructose-fed rats is nearly twice that of those consuming glucose. This is true in the presence or absence of dietary fat although with both carbohydrates, the liver's contribution was approximately halved by the inclusion of dietary fat because of a greater reduction in hepatic than extrahepatic lipogenesis.

Epididymal fat-pads. Epididymal-fat-pad weight was increased by dietary fat but unaffected by carbohydrate (Table 5). When expressed per g tissue, dietary fat reduced LPL activity but this was clearly due to the greater fat-pad weight since total fat-pad LPL was unaffected by the dietary treatment.

DISCUSSION

The 0 and 150 g maize oil/kg diets used in the present study were not isoenergetic; the fat-containing diets contained approximately 20% more energy than the fat-free diets which resulted in an energy intake about 15% greater per day in the maize-oil-fed rats (about 0.34 MJ/d compared with 0.29 MJ/d for the fat-free-fed groups). There was also less carbohydrate intake by the maize-oil-fed groups. Therefore, were the effects of added fat due to the increased energy intake, the decreased carbohydrate intake or as we believe, to the effect of the fat itself? Triscari *et al.* (1978) showed that when rats consume diets containing 200 g fat/kg, they consume sufficient carbohydrate to maintain a rate of lipogenesis identical to that in rats consuming a fat-free diet. That is, reducing the intake of a fat-free diet so that carbohydrate intake is reduced by 20% does not reduce lipogenesis. Thus it seems unlikely that the effects of dietary fat reported here are due to the decreased carbohydrate intake. Herzberg & Janmohamed (1980) gave mice diets containing 0, 50, 100, 150, 200 or 250 g maize oil or tripalmitin/kg and measured fatty acid synthesis *in vivo*. The mice were fed so that they consumed the same amount of each diet. Thus as the dietary fat increased, the energy intake increased and the carbohydrate intake decreased. At all levels of added maize oil lipogenesis was reduced, however only at 250 g tripalmitin/kg was lipogenesis reduced. Thus, increased energy intake, at least up to that in a 200 g fat/kg diet is insufficient to reduce lipogenesis. These results lead us to conclude that the effects we observed in the 150 g fat/kg diets are due to the specific effect of the added fat. Meal-feeding is known to increase hepatic lipogenesis. However, dietary fat leads to reductions in lipogenesis in *ad lib*-fed as well as meal-fed animals (Romsos & Leveille, 1974*b*; Herzberg, 1983). We chose to meal-feed the rats in the present study to improve control of the amount of food eaten and the time it was consumed.

There was a small but significant reduction in food consumption by rats receiving the fat-containing diets. However, rats eating the fat-containing diets had greater weight gains. This is probably due to the increased energy intake of the rats consuming the 150 g fat/kg diets. It was assumed that this additional weight gain is due to fat deposition in adipose tissue since the epididymal fat-pads were significantly heavier in fat-fed rats (Table 5). This is also supported by the small difference in protein intake between fat-free and fat-containing diets which is unlikely to lead to differences in lean body mass in an experiment of this duration and given the initial body-weights of the rats. There was no effect of carbohydrate on food consumption or weight gain. Although consumption of dietary fat resulted in increased weight gain and adipose tissue weight, neither fat nor fructose resulted in increased fat accumulation in the liver.

Similar to the results of most (Sullivan *et al.* 1971; Maruhama & MacDonald, 1972; Romsos & Leveille, 1974*a*; Herzberg & Rogerson, 1982) but not all (Cohen & Teitelbaum,

1968) previous studies, we observed significantly greater serum triglycerides in rats consuming fructose (Table 2). Dietary fat reduced but did not eliminate this effect. Triglycerides were nearly three times higher in F0 rats compared with G0 rats, but less than twice as high in F15 rats compared with G15 rats.

The concentration of circulating insulin has been reported by Reaven's group (Sleder *et al.* 1980) to be generally higher in fructose-fed compared with glucose or chow-fed rats, although even they do not always find it so (see Fig. 1 of Zavaroni *et al.* 1982). They have also reported insulin resistance in rats fed on fructose for 7 d (Zavaroni *et al.* 1980). Other investigators have found plasma insulin levels are unchanged following the acute administration of fructose (Njjar & Perry, 1970; Curry *et al.* 1972; Cryer *et al.* 1974; MacDonald *et al.* 1978). We found lower insulin levels in fructose-fed compared with glucose-fed rats. There was a tendency for insulin levels to be lower in fat-fed rats but this was not statistically significant. It is difficult to assess whether insulin resistance occurred, although it appears that if anything, the fructose-fed rats were more rather than less sensitive to insulin, since on the G0 and F0 diets glucose levels were identical but insulin was lower in fructose-fed rats. On the G15 and F15 diets insulin levels were similar, but glucose was lower in F15 rats. The differences between our results and those of Reaven's group (Sleder *et al.* 1980) could be due to the time at which insulin and glucose levels were measured. Sleder *et al.* (1980) usually made measurements 5–6 h after the removal of food while our measurements were made during a meal (all animals had full stomachs). Our results do not support a role for insulin resistance and hyperinsulinaemia in the production of fructose-induced hypertriglyceridaemia as suggested by Zavaroni *et al.* (1982).

The activities of the hepatic lipogenic enzymes FAS, G6PD, CL and MD reflected the changes in diet composition. Activity was increased by fructose and decreased by fat so that even in the presence of 150 g fat/kg, activity was greater in F15 than in G15 rats. This is consistent with previous reports of the effect of fructose on hepatic lipogenic enzymes (Fitch & Chaikoff, 1960; Yudkin & Krauss, 1967; Bruckdorfer *et al.* 1972; Herzberg & Rogerson, 1982).

The effect of diet on GK activity was complex. GK was lower in fructose-fed rats, consistent with the earlier report of Hill *et al.* (1954) that dietary fructose reduces hepatic glucose phosphorylation. However, in the glucose-fed animals fat reduced GK while it was unaffected by dietary fat in the fructose-fed rats. The GK results parallel the insulin levels which is consistent with the known role of insulin in the induction of GK. FK levels were unaffected by diet but it is interesting to note that the activity of FK was nearly the same as GK in the G15 group and higher than GK in the F0 and F15 groups. This finding indicates a large capacity for hepatic fructose metabolism as suggested by the much higher portal blood fructose levels compared with that in the aorta (Niewoehner *et al.* 1984).

Hepatic lipogenesis *in vivo* paralleled the activity of the lipogenic enzymes. Lipogenesis was greatest in rats consuming fructose and reduced by added dietary fat. On the other hand, extrahepatic lipogenesis was greater in glucose-fed than in fructose-fed rats. Extrahepatic lipogenesis was reduced by dietary fat in glucose-fed but not in fructose-fed rats. These results are similar to our previous results in mice (Herzberg & Rogerson, 1982). Since a significant portion of extrahepatic synthesis occurs in adipose tissue, and since adipose tissue lipogenesis is regulated by insulin, the effect of diet is probably mediated by insulin. This is supported by the similar effects of diet on circulating insulin and on extrahepatic synthesis.

As previously reported in mice (Herzberg & Rogerson, 1982), the percentage of whole-body lipogenesis which occurs in liver is greater in fructose-fed than in glucose-fed animals even in the presence of dietary fat. This is consistent with the observation of Chevalier *et al.* (1972) that a shift of lipogenesis from adipose tissue to the liver occurs in fructose-fed

animals. However, in the present study we found a reduction in the percentage of total synthesis in the liver in the presence of dietary fat. This implies a greater sensitivity of hepatic lipogenesis, compared with adipose-tissue hypogenesis, to inhibition by dietary fat, which is consistent with previous reports (for review, see Herzberg, 1983). This is in contrast to our observations in mice (Herzberg & Rogerson, 1982) where the percentage of synthesis in liver was constant over a range of dietary fat levels, although at all levels the percentage was greatest in fructose-fed rats.

There was no effect of dietary fat on serum triglycerides in the fed state. In rats fed on the fat-free diet, serum triglyceride must come from very-low-density-lipoprotein (VLDL) secretion. In the presence of dietary fat, hepatic VLDL secretion was probably reduced, otherwise we would have expected higher triglycerides in the fat-fed rats since they were still consuming a diet with a large amount of refined carbohydrate which stimulates VLDL secretion. Early reports on the mechanism of fructose-induced hypertriglyceridaemia indicated it was a result of greater removal rate of VLDL-triglyceride from the circulation of glucose-fed rats (Bar-On & Stein, 1968; Waddell & Fallon, 1973) due to increased adipose-tissue LPL. However, subsequent work (Kannan *et al.* 1981; Zavaroni *et al.* 1982) and results presented in Table 5 show no difference in LPL activity between fructose-fed or glucose-fed animals whether or not the diets contained added fat. Further, evidence in the literature shows that the removal rate of VLDL-triglyceride is the same in fructose-fed and glucose-fed rats (Kannan *et al.* 1981; Verschoor *et al.* 1985).

Our results in rats fed on fat-free diets together with results available in the literature indicate that the hypertriglyceridaemic effect of dietary fructose is due to enhanced hepatic synthetic capacity coupled to increased secretion of VLDL with no alteration in clearance rates. We have no explanation for the relative hypertriglyceridaemia in rats fed on a fructose diet containing 150 g maize oil/kg. The rate of VLDL secretion has been reported to parallel hepatic synthetic capacity (Beynen *et al.* 1981). It is also possible that LPL activity was altered in a tissue other than white adipose tissue, since white adipose tissue probably only accounts for part of the removal of circulating VLDL (Laurell, 1959). Further, we measured total tissue LPL and the portion responsible for removal of circulating triglyceride is that associated with the endothelial cells (Cryer, 1981). It is possible that this activity was altered by our dietary treatments.

We intend to pursue these questions through the use of additional techniques for measuring the triglyceride secretion rate in fed rats (i.e. injection of labelled VLDL) and by investigating heparin-extractable-LPL activity in other adipose tissues and in non-adipose tissue.

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