Fatty Acid Synthetase Activity in the Liver and Adipose Tissue of Rats Fed with Various Carbohydrates

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1. The inclusion of sucrose in the diet of rats led to an increase in hepatic fatty acid synthetase activity compared with that of rats fed with starch as the sole carbohydrate. The higher activity occurred within 18 h of the introduction of sucrose and persisted with fluctuations for the 30 days of the experiment. Reversal of the diets in some rats after 21 days led to changes in the enzyme activity to values appropriate to the second diet. The plasma triglyceride concentration followed a similar pattern. 2. A comparison of the effects of diets with starch, glucose, maltose, sucrose or fructose showed that fructose gave the highest values of triglyceride content and of fatty acid synthetase activity in liver, but the lowest values of the synthetase activity in adipose tissue and the lowest values of plasma insulin concentration. These effects may perhaps be attributed to the low insulin response to fructose and to the high affinity of the liver for this sugar. 3. When the diet contained fructose or sucrose there was a correlation between hepatic synthetase activity and plasma triglyceride concentration. Neither of these, however, was related to plasma insulin concentration. On the other hand, there was a correlation between plasma insulin concentration and fatty acid synthetase activity in adipose tissue. 4. When rats were starved and then re-fed the differences in enzyme activities induced by fructose or glucose were minimized. This, together with the varying degree of difference during the course of the experiments, may explain why other workers, using the starvation-re-feeding technique and making measurements on one day only, have failed to observe differences in the activities of lipogenic enzymes in animals fed with either fructose or glucose.

The substitution of sucrose for all or part of the starch in the diets of rats or human subjects leads to an increase in the plasma triglyceride concentration (Macdonald & Braithwaite, 1964; Akinyanju & Yudkin, 1967; Szanto & Yudkin, 1969). A similar effect is seen in rats fed with fructose instead of glucose (Nikkilä & Ojala, 1965).

Since the major source of plasma triglyceride is the liver, several workers have studied the effect of dietary sucrose or fructose on hepatic enzymes concerned with lipogenesis. An increased activity has been found in several hepatic enzymes, including malate dehydrogenase (decarboxylating) (NADP) (EC 1.1.1.40) (Fitch & Chaikoff, 1960), ATP citrate lyase (EC 4.1.3.8) (Kornacker & Lowenstein, 1965) and pyruvate kinase (EC 2.7.1.40) (Yudkin & Krauss, 1967). On the other hand, the activity of acetyl-CoA carboxylase (EC 6.4.1.2) was no different in rats fed with fructose from that in rats fed with glucose (Zakim *et al.*, 1967). As far as we know, no studies have been made of the effect of different dietary carbohydrates on the multienzyme complex fatty acid synthetase.

The activity of this enzyme complex is known to be depressed by starvation (Butterworth *et al.*, 1966). In

the liver the activities of fatty acid synthetase and of acetyl-CoA carboxylase are of the same order (Chang *et al.*, 1967; Chakrabarty & Leveille, 1969).

We have studied, with rats, the effects of diets containing different carbohydrates on the activities of fatty acid synthetase in the liver and in adipose tissue; a preliminary account of some of the results has been given (Bruckdorfer *et al.*, 1971a).

Materials and Methods

Animals

The rats were of the Sprague-Dawley strain ASH/CSE from Scientific Products Farm (Ash, Canterbury, Kent, U.K.) and weighed about 200 g at the beginning of the experiments. Male animals were divided into groups at random and placed on the experimental diets, made up with 68% carbohydrate, 23% casein and 1.6% corn oil, with appropriate vitamins and mineral salts (Bruckdorfer *et al.*, 1971b). Control animals were given a diet of Oxoid cubes (Lillico and Son Ltd., Betchworth, U.K.), containing 49% starch. The rats were given food and water *ad libitum*.

Preparation of liver homogenates

The rats were killed by a blow on the head between 10.00 and 11.00 h; this time was adhered to in order to avoid errors caused by possible circadian variation. The liver and sometimes also the epididymal fat-pads were rapidly excised and placed in ice-cooled 0.9% NaCl. About 0.8 g of tissue was homogenized at 4°C in 0.1 M-potassium phosphate buffer, pH 8.0, in a Potter-Elvehjem homogenizer with a Teflon pestle. The amount of buffer was 8 vol. with the liver and 5 vol. with the fat-pads. The homogenates were centrifuged for 30 min at 30000g at 4°C (MSE High Speed 18 centrifuge, angle rotor no. 69181). The clear supernatant was carefully removed with a syringe to avoid disturbance of either the floating lipid or the deposit.

It is more usual to use supernatants obtained by centrifugation at 100000g for 1 h, but to do this would have seriously decreased the number of homogenates that we could assay. We found that our centrifugation procedure gave enzyme values only 5% greater than those given by centrifugation at higher speed.

Enzyme assay

The method used was adapted from the spectrophotometric method of Gibson & Hubbard (1960). The assay mixture (final volume 1.0 ml) contained 100 µmol of potassium phosphate buffer, pH 6.5, 1 µmol of EDTA, 10 µmol of cysteine, 0.3 mg of bovine serum albumin [Sigma (London) Chemical Co., London S.W.6, U.K.], 0.04 µmol of acetyl-CoA (trilithium salt) (P-L Biochemicals, Milwaukee, Wis., U.S.A.), 0.075 µmol of NADPH (Sigma Chemical Co., St. Louis, Mo., U.S.A.) and 0.01–0.2 ml of liver or adipose-tissue preparation, depending on the activity. The reaction mixture was placed in a quartz cuvette of a Unicam SP.500 spectrophotometer and readings made on a Unicam SP.22 recorder. A blank run was made to measure background activity, then the reaction was begun by the addition of 0.075 µmol of malonyl-CoA (trilithium salt) (P-L Biochemicals) and the change in extinction at 340 nm noted at intervals. The initial rates of activity are expressed as the rate of utilization of NADPH in µmol/min per g wet wt. of liver at 37°C.

Liver composition

The weighed livers were assayed for water (constant weight at 102°C), total N (Markham, 1942) and total lipid (Folch *et al.*, 1957). Protein content was calculated by multiplying the N values by 6.25. Major lipid fractions were assayed by the following methods: cholesterol by that of Zlatkis *et al.* (1953), phospholipid by that of Fiske & SubbaRow (1925) and triglyceride by that of Van Handel & Zilversmit (1957).

Plasma triglycerides

Blood taken from the beating heart immediately after the rats were killed was centrifuged at 2000g for 15 min. Triglyceride was assayed in the plasma by the fluorimetric semi-automated method of Kessler & Lederer (1965). From time to time the results were checked by the manual procedure of Van Handel & Zilversmit (1957).

Plasma insulin

This was measured with the radioimmunoassay kit supplied by The Radiochemical Centre (Amersham, Bucks., U.K.) by the method of Hales & Randle (1963). Rat insulin standards were kindly provided by Novo Industries (Copenhagen, Denmark).

Statistical analysis

This was done by Student's *t* test. Correlation coefficients, *r*, expressed relationships between measured parameters.

Results

Experiment 1

A total of 108 rats was divided into groups of four. One group was killed immediately for assay of triglycerides and hepatic fatty acid synthetase activity. Of the remainder, some groups were fed on the diet with starch and some on the diet with sucrose; two groups were kept on the stock laboratory diet.

One group on each diet was killed for assay at intervals over a period of 30 days. After 21 days the diets of some of the groups on starch or sucrose were reversed.

After 18 h on the experimental diets there was already a considerable difference in enzyme activity (Fig. 1). Maximum values were reached after 2–3 days, after which they decreased somewhat, giving a minimal difference at 7 days and reaching more-or-less steady values at about 14 days. Thereafter the activity in the sucrose-fed rats was about three times that in those fed with starch. Rats fed on the control diets had a lower activity than did those fed on the experimental diets.

After the change-over of the diets at 21 days, enzyme activity decreased in the rats changed from the sucrose diet to the starch diet, taking about 42 h to reach the value in those fed with starch from the beginning of the experiment. In rats changed from the starch diet to the sucrose diet there was an increase in activity to the value of those fed with sucrose from the outset; this took place within 18 h.

Plasma triglyceride concentrations followed a rather similar pattern (Fig. 2). They were substantially

Fig. 1. Liver fatty acid synthetase activity of rats fed on diets with sucrose or starch

Male rats were fed either on stock cube diet (□) or on purified diet with either 68 % sucrose (○) or 68 % corn starch (●) for 30 days. Groups of four rats were killed at intervals for determination of fatty acid synthetase activity in 30000g supernatants prepared from liver homogenates. After 21 days some groups were transferred from one purified diet to the other (—, original diet; ----, reversed diet). Points represent the means of four values.

higher in rats fed with sucrose than in those fed with starch and lowest in the rats fed on the stock diet, and the change from one experimental diet to the other brought about a rapid change in triglyceride concentration.

Experiment 2

Five groups each of eight rats were fed on diets with starch, sucrose, glucose, fructose or maltose.

The livers from rats fed with sucrose or fructose were larger than those fed with the other carbohydrates. Since sucrose and fructose did not produce any increase in the proportions of water, fat or protein, which together accounted for over 90 % of the liver weight, the effect of these sugars must have been to produce a general increase in weight and not in the relative accumulation of one or other of these constituents.

There appeared to be some differences in the triglyceride concentration of the livers in some groups, but because of the wide variation in values none of the differences in any of the lipid fractions was of statistical significance (Table 1).

The values for phospholipid and triglyceride contents in the livers of individual animals were inversely

related; taking all the animals together, the correlation coefficient $r = -0.83$, $P < 0.00001$. This relationship was also significant in the individual groups of animals, except in those receiving sucrose. It appeared, then, that there is a reasonable constancy among the animals of the sum of the values for phospholipid and triglyceride concentrations in the liver. There was no correlation between this sum and the type of carbohydrate fed to the animals.

The concentration of plasma triglyceride was higher in rats given fructose or sucrose than in those given other carbohydrates.

The values of plasma insulin concentration were highest in rats fed with glucose or maltose and lowest in those fed with sucrose or fructose.

The activity of fatty acid synthetase was measured both in liver and in adipose tissue (epididymal fat-pad). In the liver the enzyme activity was highest in rats fed with sucrose or fructose and lowest in those fed with glucose or starch; feeding with maltose gave intermediate results (Table 2). In adipose tissue on the other hand dietary sucrose and fructose led to the lowest values and maltose to the highest.

When the results from the rats in all the groups of Expt. 2 were taken together there was a significant correlation between hepatic fatty acid synthetase

Fig. 2. Plasma triglyceride concentrations of rats fed on diets with sucrose or starch

Male rats were fed either on stock cube diet (□) or on purified diet with either 68 % sucrose (○) or 68 % corn starch (●) for 30 days. Groups of four rats were killed at intervals for determination of plasma triglyceride. After 21 days some groups were transferred from one purified diet to the other (—, original diet; ----, reversed diet). Points represent the means of four values.

activity and plasma triglyceride concentration (Table 3). This correlation also existed for the rats in the sucrose and fructose groups taken together, but not for those in the remaining groups.

With the values for the rats in all the groups the activity of adipose-tissue fatty acid synthetase was found to be inversely correlated with plasma triglyceride concentration. On the other hand, there was here no correlation between the values within each of the groups or any combination of groups.

With all groups together there was a significant correlation between plasma insulin concentration and fatty acid synthetase activity in the adipose tissue. There was, however, no correlation between plasma insulin concentration and fatty acid synthetase activity in the liver, nor between plasma insulin concentration and plasma triglyceride concentration.

Experiment 3

The experiments of Zakim *et al.* (1967), who found that glucose or fructose in the diets of rats made no difference to the activity of acetyl-CoA carboxylase,

were carried out rather differently from the way in which we carried out the experiments described above. These authors starved their rats for 48 h and then re-fed them for 48 h with diets containing glucose or fructose. We have repeated their procedure and measured fatty acid synthetase activity in liver and adipose tissue.

Two groups, each of six rats, were fed on the laboratory cube diet for a few days, then starved for 48 h and finally re-fed for 48 h with purified diets containing either glucose or fructose.

In the liver the fatty acid synthetase activity was greater in rats fed with fructose than in those fed with glucose (Table 4). The difference was less than in the previous experiment in which the animals had not been starved, chiefly because there was now a higher enzyme activity in rats fed with glucose. In adipose tissue there was, as before, a higher fatty acid synthetase activity in rats fed with glucose, although both with glucose and fructose the values were higher than in the earlier experiment without starvation. Fructose again increased liver weight and plasma triglyceride concentration.

Table 1. *Composition of liver in rats fed on diets with 68% carbohydrate for 30 days*

The results are given as means $\pm$ S.D. for eight rats. There were no significant differences in the contents of protein, phospholipid and cholesterol. For total lipid content the only significant difference was between glucose and fructose ($P < 0.05$). For triglyceride content the only significant difference was between maltose and fructose ($P < 0.05$). The results of tests for significance for liver weight and water content are given at the foot of the table (N.S., not significant, i.e. $P > 0.05$).

Dietary carbohydrate	Wt. of liver (g/100g body wt.)	Water content (mg/g)	Protein content (mg/g)	Lipid content (mg/g)	Triglyceride content (mg/g)	Phospholipid content (mg/g)	Cholesterol content (mg/g)
Starch	3.19 $\pm$ 0.41	713 $\pm$ 13	204 $\pm$ 9	40 $\pm$ 3	7.7 $\pm$ 5.1	28.3 $\pm$ 5.1	3.0 $\pm$ 0.4
Maltose	3.36 $\pm$ 0.13	726 $\pm$ 10	195 $\pm$ 5	38 $\pm$ 3	7.8 $\pm$ 3.4	27.6 $\pm$ 4.6	3.0 $\pm$ 0.4
Glucose	3.32 $\pm$ 0.11	713 $\pm$ 7	202 $\pm$ 9	39 $\pm$ 2	10.7 $\pm$ 7.3	25.5 $\pm$ 5.8	3.0 $\pm$ 0.4
Sucrose	3.68 $\pm$ 0.24	710 $\pm$ 10	195 $\pm$ 9	39 $\pm$ 5	9.3 $\pm$ 6.2	24.4 $\pm$ 4.7	3.0 $\pm$ 0.5
Fructose	4.42 $\pm$ 0.19	707 $\pm$ 15	183 $\pm$ 16	42 $\pm$ 5	16.0 $\pm$ 8.6	23.4 $\pm$ 4.3	3.0 $\pm$ 0.3

Comparison	<i>P</i> values	
	Wt. of liver	Water content
Starch versus maltose	N.S.	<0.05
Starch versus glucose	N.S.	N.S.
Starch versus sucrose	<0.01	N.S.
Starch versus fructose	<0.01	N.S.
Maltose versus glucose	N.S.	N.S.
Maltose versus sucrose	<0.01	<0.05
Maltose versus fructose	<0.001	<0.05
Glucose versus sucrose	<0.01	N.S.
Glucose versus fructose	<0.001	N.S.

Discussion

We have demonstrated that the activity of fatty acid synthetase in both liver and adipose tissue depends on the nature of the dietary carbohydrate. In particular, fructose or sucrose, compared with starch or glucose, induces a higher activity of the enzyme in the liver and a lower activity in the adipose tissue. In the liver the increase produced when sucrose is given occurs within 18 h, and the decrease when this is changed to starch occurs within 42 h. The difference in the rates may be caused by the low rate of enzyme decay compared with the rate of enzyme synthesis. By incorporation of labelled leucine Tweto *et al.* (1971) have shown that the half-life of synthetase is 71 h. The more rapid decrease in enzyme activity that we have found may be caused by the more rapid turnover of the acyl-carrier protein than of the remainder of the enzyme complex, as demonstrated by Tweto *et al.* (1971).

There have been several reports of the effects of dietary fructose and glucose on enzymes involved in lipogenesis. The results we report in the present paper show that fructose produces a much greater activity of hepatic fatty acid synthetase than does glucose, but much of the published work contains conflicting reports about other enzymes. Glucose 6-phosphate dehydrogenase was said to be unaffected by fructose

as compared with glucose (Fitch & Chaikoff, 1960), whereas Naismith (1971) found that fructose produced a significantly higher value. Again, the activity of ATP citrate lyase was claimed by Kornacker & Lowenstein (1965) to be increased by fructose, but Zakim *et al.* (1967) could not confirm this.

Our results offer two possible reasons why the choice of experimental conditions may minimize differences in enzyme activity induced by different dietary carbohydrates. First, we found that the minimum difference of some 50% in hepatic fatty acid synthetase activity was seen some 7 days after the animals were put on the diets with starch or with sucrose; both before and after this time differences of as much as 300% were seen. Kornacker & Lowenstein (1965) also found the smallest differences in hepatic ATP citrate lyase activity after 7 days of feeding with fructose or glucose. Thus measurements of enzyme activity made on one occasion only may give a misleading impression of the magnitude of differences induced by different carbohydrates.

Secondly, it seems that, compared with continual feeding, the technique of starvation and re-feeding results both in a decrease in the difference induced by fructose or glucose in the activity of the hepatic fatty

Table 2. *Fatty acid synthetase activities in liver and adipose tissue, plasma triglyceride concentration and plasma insulin concentration in rats fed on diets with 68% carbohydrate for 30 days*

The results are given as means $\pm$ S.D. for eight rats. Fatty acid synthetase activities are expressed in units of μ mol of NADPH utilized/min per g of tissue at 37°C. There was no significant difference in body weight. The results of tests for significance for liver enzyme activity, adipose-tissue enzyme activity, plasma triglyceride concentration and plasma insulin concentration are given at the foot of the table (N.S., not significant, i.e. $P > 0.05$).

Dietary carbohydrate	Body wt. (g)	Fatty acid synthetase activity		Concn. of plasma triglyceride (mg/100 ml)	Concn. of plasma insulin (μ units/ml)
		Liver	Adipose tissue		
Starch	336 $\pm$ 8	1.8 $\pm$ 0.4	0.24 $\pm$ 0.04	54 $\pm$ 18	45 $\pm$ 16
Maltose	358 $\pm$ 24	2.7 $\pm$ 0.8	0.40 $\pm$ 0.06	49 $\pm$ 10	55 $\pm$ 19
Glucose	346 $\pm$ 20	1.8 $\pm$ 0.2	0.28 $\pm$ 0.04	57 $\pm$ 12	56 $\pm$ 20
Sucrose	354 $\pm$ 27	4.2 $\pm$ 0.4	0.12 $\pm$ 0.04	79 $\pm$ 13	34 $\pm$ 16
Fructose	346 $\pm$ 18	5.6 $\pm$ 0.6	0.06 $\pm$ 0.02	99 $\pm$ 18	33 $\pm$ 8

<i>P</i> values				
Comparison	Liver enzyme activity	Adipose-tissue enzyme activity	Concn. of plasma triglyceride	Concn. of plasma insulin
Starch versus maltose	<0.05	<0.01	N.S.	N.S.
Starch versus glucose	N.S.	N.S.	N.S.	N.S.
Starch versus sucrose	<0.001	<0.001	<0.001	N.S.
Starch versus fructose	<0.001	<0.001	<0.001	N.S.
Maltose versus glucose	N.S.	N.S.	N.S.	N.S.
Maltose versus sucrose	<0.001	<0.001	<0.001	<0.05
Maltose versus fructose	<0.001	<0.001	<0.001	<0.05
Glucose versus sucrose	<0.001	<0.001	<0.001	<0.05
Glucose versus fructose	<0.001	<0.001	<0.001	<0.05
Sucrose versus fructose	<0.001	<0.01	<0.01	N.S.

Table 3. *Correlation coefficients, *r*, between measurements on rats fed on diets with 68% carbohydrate for 30 days*

The correlation coefficients, *r*, and *P* values (N.S., not significant, i.e. $P > 0.05$) are for the results given in Table 2.

Liver fatty acid synthetase and plasma triglyceride

All groups	$r = 0.834$	$P < 0.00001$
Sucrose + fructose groups	$r = 0.760$	$P < 0.001$
Starch + maltose + glucose groups	$r = -0.109$	N.S.

Adipose-tissue fatty acid synthetase and plasma triglyceride

All groups	$r = -0.658$	$P < 0.0001$
Sucrose + fructose groups	$r = -0.400$	N.S.
Starch + maltose + glucose groups	$r = 0.273$	N.S.

Liver fatty acid synthetase and plasma insulin

All groups	$r = -0.252$	N.S.
Sucrose + fructose groups	$r = 0.202$	N.S.
Starch + maltose + glucose groups	$r = 0.300$	N.S.

Adipose-tissue fatty acid synthetase and plasma insulin

All groups	$r = 0.428$	$P < 0.025$
Sucrose + fructose groups	$r = 0.134$	N.S.
Starch + maltose + glucose groups	$r = 0.170$	N.S.

Plasma triglyceride and plasma insulin

All groups	$r = -0.257$	N.S.
Sucrose + fructose groups	$r = 0.136$	N.S.
Starch + maltose + glucose groups	$r = -0.030$	N.S.

Table 4. *Fatty acid synthetase activities in liver and adipose tissue and plasma triglyceride concentration in rats starved for 48h and re-fed on diets with 68% glucose or fructose for 48h*

The results are given as means $\pm$ s.d. for six rats. Fatty acid synthetase activities are expressed in units of μ mol of NADPH utilized/min per g of tissue at 37°C. The results of tests for significance are given in the bottom row (N.S., not significant, i.e. $P > 0.05$).

Dietary carbohydrate	Body wt. (g)	Fatty acid synthetase activity		Liver wt. (g/100g body wt.)	Concn. of plasma triglyceride (mg/100ml)
		Liver	Adipose tissue		
Glucose	252 $\pm$ 9	3.4 $\pm$ 0.9	0.41 $\pm$ 0.07	4.2 $\pm$ 0.1	74 $\pm$ 15
Fructose	253 $\pm$ 10	5.1 $\pm$ 1.1	0.12 $\pm$ 0.01	5.0 $\pm$ 0.4	128 $\pm$ 32
<i>P</i> values	N.S.	<0.05	<0.001	<0.05	<0.001

acid synthetase and in a higher enzyme activity induced by both sugars. It is likely that these findings with fatty acid synthetase would occur also with acetyl-CoA carboxylase, since it has been shown that the activities of these two enzymes run parallel (Chang *et al.*, 1967; Chakrabarty & Leveille, 1969; Saggerson & Greenbaum, 1970). Thus the starvation-re-feeding technique might well be a factor in the failure of Zakim *et al.* (1967) to find any significant difference in the activity of acetyl-CoA carboxylase in rats fed with fructose or glucose.

The production of hypertriglyceridaemia by dietary fructose could be caused either by an increased synthesis of triglyceride or by a diminished plasma clearance. The relative importance of these two mechanisms appears to be different in the two situations of starvation-re-feeding and of continual feeding.

As we observed, in starvation-re-feeding, the difference in activity of lipogenic enzymes induced by fructose or glucose is diminished or abolished. Nevertheless there seemed to be little or no diminution in plasma triglyceride concentration induced by fructose. This is, then, likely to have been caused chiefly by a diminished plasma clearance. The observations made by Bar-On & Stein (1968) support this, in that they have shown that the feeding of glucose to starved rats, but not the feeding of fructose, induces after a few hours an increased activity of lipoprotein lipase in adipose tissue.

In rats fed continually, on the other hand, fructose induces considerably higher activity than does glucose in fatty acid synthetase and in other lipogenic enzymes. Although we have no information about the effect of dietary fructose on lipoprotein lipase in the adipose tissue of rats fed continually, we have shown that dietary sucrose only slightly decreases the activity of this enzyme (Bruckdorfer *et al.*, 1972). In this situation it therefore seems that the hypertriglyceridaemia produced by sucrose and fructose is largely due to increased hepatic synthesis and not so much to diminished clearance. It will be recalled that we found a relationship between hepatic fatty acid synthetase

activity and the plasma triglyceride concentration in the presence of dietary sucrose or fructose. On the other hand there was no relationship between the plasma insulin and plasma triglyceride concentrations, although administration of insulin is known to lower triglyceride concentrations, presumably by stimulating the activity of lipoprotein lipase (Nikkilä, 1969).

It remains to explain why dietary fructose and sucrose lead to a high fatty acid synthetase activity in the liver and a low activity in adipose tissue. Fructose is rapidly removed from the portal vein by the liver, possibly because of its high fructokinase activity. Moreover, it is rapidly converted into acetyl-CoA because it is phosphorylated to fructose 1-phosphate rather than to fructose 6-phosphate, and so avoids rate-limiting enzymes such as phosphofructokinase in the glycolytic pathway. Since fructolysis leads to an increase in α -glycerophosphate, this may increase the formation of triglyceride from fatty acyl-CoA and this in turn would stimulate fatty acid synthesis from the increased supply of acetyl-CoA. An adaptive increase in synthetase activity might follow.

We found that a low fatty acid synthetase activity in adipose tissue was associated with the low plasma insulin concentration when sucrose or fructose was fed to the animals. It may be that insulin is involved in regulating the fatty acid synthetase activity in adipose tissue. This is supported by the work of Schotz *et al.* (1971), who showed that the incubation of isolated adipocytes with insulin and glucose resulted in an increase in fatty acid synthetase activity. Moreover, adipose tissue from rats fed with sucrose has been shown to be less sensitive to insulin than is adipose tissue from rats fed with starch (Vrana *et al.*, 1971).

The variation in hepatic fatty acid synthetase activity found in rats fed with the non-fructose carbohydrates (starch, glucose or maltose) seems to be random, and unrelated to the concentration of plasma triglycerides. When, however, sucrose or fructose is fed to the animals there was an increase in both of these parameters, and the particular values they reached were now closely related. This is consistent

with the view that, in the absence of dietary sucrose or fructose, the rate of hepatic lipogenesis is not the major determinant of plasma triglyceride concentration. With these sugars in the diet, however, it appears that the rate of lipogenesis in the liver is a more important factor determining plasma triglyceride concentration.

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