Antiketogenic Action of Fructose, Glyceraldehyde, and Sorbitol in the Rat in Vivo

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SUMMARY

The purpose of this study was to compare the metabolism and antiketogenic properties of fructose, glyceraldehyde, and sorbitol.

Fructose, glyceraldehyde, and sorbitol were readily metabolized and exhibited an antiketogenic effect in both blood and liver when injected intramuscularly to starved (forty-eight hours) rats.

Sorbitol had the most pronounced antiketogenic effect and produced an 80 to 90 per cent decrease in the blood ketone bodies sixty minutes after administration. Fructose and glyceraldehyde were equally effective and produced about a 60 to 70 per cent decrease in ketone bodies. Fructose, glyceraldehyde, and sorbitol caused a significant decrease in the concentration of hepatic ketone bodies. In liver, sorbitol was found to be most effective in its antiketogenic action. The concentration of plasma free fatty acids remained unchanged after injection of all three antiketogenic substrates.

Fructose, glyceraldehyde, or sorbitol caused increased blood lactate and pyruvate concentrations, and fructose was the most effective of the three substrates.

Fructose administration resulted in a significant decrease in hepatic lactate/pyruvate and β-OH-butyrate/acetoacetate concentration ratios, whereas sorbitol caused an increase in the concentration ratio of these two substrat pairs.

Decreases in blood and liver ketone body levels were associated with lowering of liver acetyl-CoA concentration. However, the decrease in hepatic acetyl-CoA produced upon the administration of antiketogenic substrates was not pronounced.

Sorbitol administration resulted in the most pronounced increase in hepatic α-glycerophosphate concentration. Fructose or glyceraldehyde also caused an increase in α-glycerophosphate content. Administration of each of the three antiketogenic substrates produced an increase in hepatic dihydroxyacetone phosphate concentration.

All three antiketogenic compounds increased liver glycogen and blood glucose concentrations. No significant changes were observed in hepatic ATP, ADP, or AMP concentrations sixty minutes after the injections of any of the antiketogenic substrates.

Although decreased liver acetyl-CoA levels were associated with the antiketogenic effects of the compounds tested, the increased liver α-glycerophosphate content best explains the differences between fructose or glyceraldehyde and sorbitol. DIABETES *24*:926-32, October, 1975.

It is well known that under conditions of starvation and diabetes, the concentration of ketone bodies in liver and blood increases dramatically.[1-3] The regulation of ketogenesis has been the topic of many reviews, including those of Wieland[4] and McGarry and Foster.[5] Although increased delivery of free fatty acids from adipose tissue is necessary for increased ketogenesis, ketone body production can be decreased in spite of an unchanged high level of free fatty acid.[3,6] It seems that the metabolic state of the liver plays a very important role in whether ketone bodies are produced, since the same level of free fatty acid produces distinct differences in the rate of ketogenesis in isolated perfused liver, depending on whether the liver is taken from a fasted or fed animal.[7-9] Then the central question is the fate of the fatty acid: complete oxidation, ketone body production, or triglyceride synthesis. In starvation, esterification of free fatty acids is depressed[10] and the acetyl-CoA resulting from β-oxidation cannot be utilized for fatty acid synthesis.[8] With an unaltered or slightly depressed Krebs cycle, the increased supply of acetyl-CoA units has only one fate, ketone bodies. Several other theories of ketogenesis have been postulated, including an absolute overproduction of acetyl-CoA,[11] a depression of the Krebs cycle, or an inhibition of the citrate synthase by long-chain acetyl-CoA[12] or by ATP.[13]

The antiketogenic nature of glycerol,[14] lactate,[9,15]

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fructose,[8,16] and certain polyhydric alcohols[16-19] has been known for a long time. One characteristic common to all of these is that they increase triglyceride formation[9,14,19] thereby diverting fatty acids from β-oxidation. Although the concentration of α-glycerophosphate seems important for triglyceride synthesis, it is hard to explain the fact that lactate is a potent antiketogenic agent that does not change the α-glycerophosphate concentration.[9]

In the present investigation, experiments were designed to obtain further information on the factors that may contribute to the antiketogenic effect of fructose, glyceraldehyde, and sorbitol. The relative importance of factors controlling ketogenesis in the rat in vivo has been obtained by measuring the concentration of various metabolites following intramuscular injection of fructose, glyceraldehyde, or sorbitol.

MATERIALS AND METHODS

Rats. Male rats of the Wistar strain were obtained from Carworth Farms, New York. The animals were fed Purina rat chow. Rats weighing 200 to 250 gm. were used in the present investigation. Unless otherwise stated, all rats were starved for forty-eight hours before use.

Chemicals. Fructose, D-sorbitol, and glucose were obtained from Fisher Scientific Company, Fairlawn, New Jersey. D-Glyceraldehyde was obtained from Calbiochem, Los Angeles. The enzymes and cofactors used in the present study were obtained from C. F. Boehringer Corp., New York.

Blood. Blood was collected in heparinized tubes after decapitation of the rats. A sample (0.5 ml.) was immediately deproteinized with 3 ml. of ice-cold 3 per cent (w/v) $HClO_4$. The precipitated protein was removed by centrifugation. The supernatant fluid was neutralized with $KHCO_3$. After the mixture had been left in the cold for thirty minutes, the precipitate of $KClO_4$ was removed by centrifugation. The supernatant fluid was used for the determination of metabolites. For the determination of blood glucose, a blood sample (0.1 ml.) was diluted to 1.5 ml. with water and proteins precipitated with $ZnSO_4$ and $Ba(OH)_2$. Another sample of blood (1.0 ml.) was taken for the determination of free fatty acids.

Treatment of liver. After the rats were killed by decapitation a portion of liver was rapidly frozen between the aluminum blocks precooled in liquid N_2. The frozen liver was then treated as previously described.[20]

Determination of metabolites. The following metabolites were determined enzymatically as described previously by Rawat:[21] lactate, pyruvate, α-glycerophosphate, dihydroxyacetone phosphate, malate, β-OH butyrate, acetoacetate, glutamate, α-ketoglutarate, citrate, acetyl-CoA, and ATP. The hepatic concentrations of AMP were determined as described elsewhere,[22] and ADP was determined according to Adam.[23] Hepatic glycogen was determined according to Walaas and Walaas.[24] Blood glucose was determined enzymatically[25] and plasma free fatty acids titrimetrically as described previously.[26]

Administration of antiketogenic agents. The rats were given an intramuscular injection of fructose, glyceraldehyde, sorbitol, or glucose sixty minutes before the commencement of the experiment. The control animals were treated similarly with 1.0 ml. of 0.9 per cent NaCl. The fed animals were given no treatment.

RESULTS

Effect of fructose, glyceraldehyde, and sorbitol administration on concentration of metabolites in the blood of starved rats. Administration of fructose, glyceraldehyde, sorbitol, or glucose intramuscularly to starved rats resulted in a marked decrease in the concentration of ketone bodies in the blood (table 1). Sorbitol was found to be the most effective of the antiketogenic substrates tested. At sixty minutes after the injection of antiketogenic substrates, the decrease in blood ketone bodies was 86 per cent for sorbitol, 69 per cent for fructose or glyceraldehyde, and 60 per cent for glucose. Treatment with glucose, fructose, glyceraldehyde, or sorbitol increased blood glucose concentration (table 1).

Fructose or glyceraldehyde injections resulted in pronounced increases in lactate and pyruvate concentrations, and the lactate/pyruvate concentration ratio was decreased to about one-third that of the fasted control (table 1). Sorbitol administration increased lactate and pyruvate concentrations. However, the increase with sorbitol was not as pronounced as with fructose or glyceraldehyde (table 1). The lactate/pyruvate concentration ratio remained elevated sixty minutes after sorbitol injection. Glucose administration, however, did not result in a change in the lactate/pyruvate ratio. Starvation for forty-eight hours resulted in a threefold increase in plasma free fatty acid levels (table 1). However, treatment with glucose, fructose, glyceraldehyde, or sorbitol resulted in only a small decrease in plasma free fatty acid levels.

Effect of fructose, glyceraldehyde, and sorbitol on the

TABLE 1

Effects of administration of fructose, glyceraldehyde, or sorbitol on the metabolites in blood and plasma of starved rats

Nutritional state	Injections	β-Hydroxybutyrate	Acetoacetate	Total ketone body	Lactate	Pyruvate	Glucose	Plasma free fatty acids
			(μmoles/ml.)					(μ Eq./L.)
Fed	None (10)	0.08±0.006	0.066±0.004	0.146	1.50±0.05	0.140±0.01	5.8±0.6	230±23
Starved (48 hr.)	NaCl (6)	1.17±0.050	0.50 ±0.040	2.21	0.58±0.02	0.025±0.02	4.0±0.3	750±40
	Glucose (6)	0.63±0.03	0.21 ±0.030	0.84	0.79±0.06	0.035±0.05	8.2±0.6	690±32
	Fructose (6)	0.48±0.010	0.21 ±0.021	0.69	2.35±0.15	0.330±0.07	7.5±0.5	675±33
	Glyceraldehyde (6)	0.48±0.009	0.21 ±0.020	0.69	2.10±0.10	0.280±0.05	6.3±0.7	700±30
	Sorbitol (6)	0.24±0.005	0.08 ±0.017	0.32	0.98±0.10	0.034±0.01	6.5±0.6	680±35

Intramuscular injection of (a) 1.0 ml. 0.9 per cent NaCl, (b) 1 ml. 30 per cent glucose, (c) 1 ml. 30 per cent fructose, (d) 1 ml. 30 per cent sorbitol, or (e) 1 ml. 30 per cent D-glyceraldehyde was given to forty-eight-hour-starved rats. The rats were killed by decapitation sixty minutes after injection, and blood was collected in heparinized tubes. The details of experimental procedure are given in the section on Materials and Methods. Results are expressed as average ± S.E.M., with the number of animals used in parentheses.

concentration of hepatic metabolites in starved rats. Ketone bodies. Fructose, glyceraldehyde, or sorbitol administration to starved (forty-eight hours) rats resulted in a marked fall in liver ketone body concentration (table 2). The fall in liver ketone bodies was associated with a fall in blood levels, and sorbitol was found to be the most effective. Fructose and glyceraldehyde were equally effective in their antiketogenic action.

Substrate pairs of the lactate dehydrogenase and glutamate dehydrogenase systems. Marked increases in hepatic pyruvate and lactate concentrations were observed after the intramuscular injection of fructose and glyceraldehyde and were similar with both substances. However, sorbitol resulted in only a small increase in pyruvate levels (table 2). A twofold increase in hepatic α-ketoglutarate concentrations was observed after administration of fructose, glyceraldehyde, or sorbitol. However, hepatic glutamate concentrations showed only a small increase upon administration of these antiketogenic substrates (table 2).

Extra- and intramitochondrial NADH/NAD ratio. Hepatic lactate/pyruvate concentration ratio reflects the NADH/NAD ratio in the cytoplasmic compartment of the liver.[27] This ratio was found to decrease to about one-third the original value sixty minutes after fructose or glyceraldehyde injection, which was about that of the fed animal (table 2). The β-OH-butyrate/acetoacetate concentration ratio reflects the NADH/NAD ratio of mitochondrial cristae.[27] A small decrease in this ratio was observed upon fructose or glyceraldehyde administration and a small increase sixty minutes after sorbitol injection (table 2). Hepatic concentration of α-glycerophosphate increased about twofold upon administration of fructose and glyceraldehyde (table 3). However, sorbitol injection resulted in the largest increase in α-glycerophosphate concentration in liver (threefold).

As in changes in liver α-glycerophosphate levels, hepatic dihydroxyacetone phosphate concentrations

TABLE 2

Effect of fructose, D-glyceraldehyde, or sorbitol on the concentration of the substrate pairs of NAD-linked dehydrogenase systems in livers of starved rats

Nutritional state	Injections	Lactate	Pyruvate	Lactate/ pyruvate	β-Hydroxy-butyrate	Aceto-acetate	β-Hydroxy-butyrate/ acetoacetate	Glutamate	α-Ketogluta-rate
		μmoles/gm.			μmoles/gm.			μmoles/gm.	
Fed	None (10)	1.50±0.057	0.138±0.012	10.8	0.103±0.010	0.076±0.002	1.3	1.9±0.10	0.10±0.0
Starved (48 hr.)	NaCl (6)	0.60±0.032	0.023±0.005	26.0	2.00 ±0.06	0.70 ±0.03	2.8	2.6±0.16	0.10±0.0
	Fructose (6)	2.30±0.100	0.265±0.026	8.6	0.48 ±0.01	0.21 ±0.05	2.2	3.0±0.18	0.22±0.0
	Glyceralde-hyde (6)	2.00±0.090	0.270±0.025	7.4	0.48 ±0.01	0.21 ±0.04	2.2	2.9±0.17	0.23±0.0
	Sorbitol (6)	0.98±0.075	0.032±0.007	30.6	0.25 ±0.01	0.08 ±0.002	3.1	3.2±0.18	0.24±0.0

Intramuscular injection of (a) 1.0 ml. of 0.9 per cent NaCl, (b) 1 ml. 30 per cent glucose, (c) 1 ml. 30 per cent fructose, (d) 1 ml. 30 per cent glyceraldehyde, or (e) 1 ml. 30 per cent sorbitol was given to forty-eight-hour-starved rats. The rats were killed by decapitation sixty minutes after injection and livers rapidly frozen by aluminum clamps, precooled in liquid nitrogen. Concentration of various hepatic metabolites was determined enzymatically; for details of experimental procedure see Rawat.[21] The results are expressed as average ± S.E.M., with the number of animals used in parentheses.

TABLE 3

Hepatic concentration of α-glycerophosphate, dihydroxyacetone phosphate, and acetyl-CoA of starved rats injected with either fructose, D-glyceraldehyde, or sorbitol

Nutritional state	Injection	α-Glycerophosphate	DHAP	α-Glycerophosphate/ DHAP	Acetyl-CoA
				μmoles/gm. fresh liver	
Starved (48 hr.)	NaCl (6)	0.172±0.010	0.020±0.002	8.6	0.085±0.003
	Fructose (6)	0.300±0.015	0.055±0.003	5.4	0.077±0.002
	Glyceraldehyde (6)	0.300±0.012	0.055±0.002	5.3	0.074±0.001
	Sorbitol (6)	0.500±0.011	0.070±0.002	7.1	0.069±0.002

Rats starved (forty-eight hours) were given intramuscular injection of (a) 1.0 ml. 0.9 per cent NaCl, (b) 1.0 ml. 30 per cent fructose, (c) 1.0 ml. 30 per cent D-glyceraldehyde, or (d) 1.0 ml. 30 per cent sorbitol. Hepatic concentrations of various metabolites were determined sixty minutes after injections in the freeze-clamped sample of liver. The details of the technic are given in the section on Materials and Methods. Results are expressed as average ± S.E.M. with the number of animals used in parentheses.

increased after administration of antiketogenic substances. Intramuscular injection of fructose, glyceraldehyde, or sorbitol resulted in about a threefold increase in hepatic dihydroxyacetone phosphate concentration. Sorbitol was the most effective of the three antiketogenic substrates (table 3). Fructose or glyceraldehyde resulted in a decrease in the α-glycerophosphate/dihydroxyacetone phosphate ratio; however, sorbitol injection did not change this ratio.

Acetyl-CoA correlated. Administration of fructose, glyceraldehyde, or sorbitol resulted in a fall in hepatic acetyl-CoA levels (table 3). However, the change in these levels was not very pronounced.

Adenine nucleotides. The concentration of hepatic adenine nucleotides was measured after injection of all three antiketogenic substrates for consideration of the possibility that phosphorylation of fructose, glycerol, or glyceraldehyde might cause a decrease in liver ATP concentrations. However, sixty minutes after the intramuscular injection of antiketogenic substrates, no significant change in hepatic adenine nucleotides was observed (table 4).

Malate and citrate. Because of technical reasons, it was not possible to measure liver oxaloacetate levels precisely, but hepatic malate concentrations were measured. Intramuscular injection of fructose or glyceraldehyde to forty-eight-hour-starved rats did not result in a marked change in hepatic malate concentrations. Sorbitol administration, however, resulted in an elevation in malate content. The concentration of hepatic citrate was doubled after fructose and glyceraldehyde injection and showed a threefold increase after sorbitol injection (table 5).

Glucose and glycogen. Hepatic glucose and glycogen content increased significantly after injection of fructose, glyceraldehyde, or sorbitol. Fructose resulted in the most pronounced increase in both glucose and glycogen contents of liver (table 6).

DISCUSSION

Metabolism of sorbitol, fructose, and glyceraldehyde. The first step in the metabolism of sorbitol is the oxidation to fructose.[17] It is generally accepted that fructose is phosphorylated in the liver by fructokinase (figure 1) to fructose-1-phosphate,[28] which is split by aldolase into dihydroxyacetone phosphate and glyceraldehyde. Glyceraldehyde so produced has several possibilities of further metabolism. It can be phosphorylated to glyceraldehyde-3-phosphate by the triokinase described by Hers.[29] Other possibilities are oxidation to D-glycerate by aldehyde dehydrogenase[30] or reduction to glycerol by alcohol dehydrogenase.

TABLE 4

Effect of fructose, D-glyceraldehyde, or sorbitol administration on the concentration of hepatic adenine nucleotides in starved rats

Nutritional state	Injection	ATP	ADP	AMP	Total adenine nucleotides	Total ketone bodies
			μmoles/gm. fresh liver			
Starved (48 hr.)	NaCl (4)	2.17±0.15	1.60±0.10	0.38±0.06	4.15	2.7
	Fructose (4)	2.20±0.20	1.58±0.13	0.34±0.05	4.18	0.69
	Glyceraldehyde (4)	2.32±0.19	1.55±0.14	0.34±0.05	4.21	0.65
	Sorbitol (4)	2.22±0.23	1.56±0.12	0.36±0.04	4.14	0.45

Rats starved (forty-eight hours) were given intramuscular injection of (a) 1.0 ml. 0.9 per cent NaCl, (b) 1.0 ml. 30 per cent fructose, (c) 1.0 ml. 30 per cent glyceraldehyde, or (d) 1.0 ml. 30 per cent sorbitol. Hepatic concentrations ATP, ADP, and AMP were determined in freeze-clamped liver samples sixty minutes after the injection. The details of the technic are given in the section on Materials and Methods. Results are expressed as average ± S.E.M., with the number of animals used in parentheses.

TABLE 5

Effect of administration of fructose, glyceraldehyde, or sorbitol on the concentration of malate and citrate in the livers of starved rats

Nutritional state	Injections	Malate	Citrate
		μmoles/gm. liver	
Starved (48 hr.)	NaCl (10)	0.41±0.02	0.43±0.02
	Fructose (6)	0.52±0.03	1.00±0.06
	Glyceraldehyde (6)	0.50±0.03	1.10±0.05
	Sorbitol (6)	0.58±0.02	1.30±0.04

The administration of fructose, glyceraldehyde, and sorbitol has been described in table 1. The hepatic concentration of malate and citrate were determined on freeze-clamped liver samples. Results are expressed as ± S.E.M., with numbers of animals used in parentheses.

TABLE 6

Effects of administration of fructose, glyceraldehyde, or sorbitol on the concentration of glucose and glycogen in the livers of starved rats

Nutritional state	Injections	Glucose	Glycogen
		μmoles/gm. liver	
Starved (48 hr.)	NaCl	4.6±0.53	7.8±0.65
	Fructose	10.5±0.69	18.9±0.80
	Glyceraldehyde	8.7±0.75	15.6±0.50
	Sorbitol	9.5±0.60	16.8±0.63

The administration of fructose, glyceraldehyde, and sorbitol has been described in table 1. The values for glucose and glycogen (expressed as glucose) are mean values of at least four experiments. The results are expressed as μmoles per gram fresh weight of liver.

Based on the formation of (1,6-^{14}C) glycogen from (6-^{14}C) fructose, Hue and Hers (1972) discarded the notion of participation of the glycerol pathway in the metabolism of glyceraldehyde, since this pathway would have resulted in the formation of (3,4-^{14}C) glycogen. Hue and Hers,[31] utilizing (4-^{3}H) fructose and (4-^{3}H) glucose as substrates, came to the conclusion that the glyceraldehyde formed in the metabolism of fructose is metabolized by phosphorylation to glyceraldehyde-3-phosphate by the triokinase and precluded any importance of the glycerate pathway. Sillero, Sillero, and Sols[32] also concluded that the main pathway for D-glyceraldehyde metabolism in the liver is phosphorylation by triokinase.

On the basis of the metabolic pathway just described (figure 1), fructose and glyceraldehyde should have similar effects on liver metabolism. It might be suggested that sorbitol may differ in its metabolism from fructose and glyceraldehyde, since an additional, initial dehydrogenation is required for its metabolism.

Adenine nucleotides and ketogenesis. It was suggested by Shepherd and Garland[13] that ATP levels affect citrate synthesis by an inhibition of citrate synthase. In the present investigation, although differences in the antiketogenic effect of sorbitol, fructose, and glyceraldehyde were observed, there was no effect of these substances on either the liver ATP levels or the total adenine nucleotides in livers. Although intravenous fructose[33,34] or sorbitol[33] results in depressions of liver ATP levels, our results indicate that the intramuscular route of administration does not have this effect.

Liver acetyl-CoA levels and ketogenesis. Increases in liver acetyl-CoA are associated with increasing ketone body formation in the transition from the fed to fasted state,[3] suggesting that the concentration of acetyl-CoA is directly related to ketosis. Although in the present study there was a correlation between the ketone body level either in the blood or in the liver and the liver acetyl-CoA, the changes were of a small magnitude, with a maximum depression with sorbitol from 85 nmoles per gm. wet weight in the control to 65 nmoles in the treated. Similar small and nonsignificant changes in liver acetyl-CoA level were observed in the studies of Williamson et al.[3] following administration of glycerol or dihydroxyacetone to fasted rats. Menahan, Ross, and Wieland[15,35] observed that, in the perfused liver, large increases or decreases in the rate of ketogenesis could be accomplished without a significant change in liver acetyl-CoA level. Thus, the large decreases in ketone body levels in the present study following the administration of either sorbitol, fructose, or glyceraldehyde cannot be explained solely on changes in liver acetyl-CoA levels.

Plasma free fatty acid and ketogenesis. In the present study, no significant depression in plasma free fatty acid occurred following the administration of all three

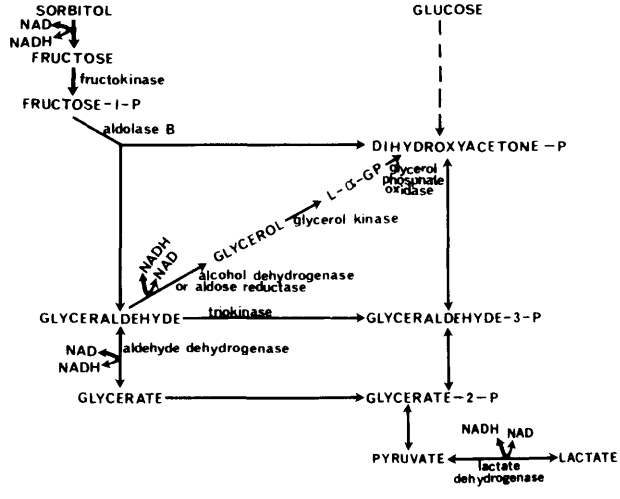

FIG. 1. Pathway of sorbitol, fructose, and glyceraldehyde metabolism.

of the antiketogenic compounds (table 1). Also, in the studies of Williamson et al.,[3] intramuscular injection of dihydroxyacetone or glycerol resulted in little or no change of the plasma free fatty acid level. Thus, antiketogenic compounds, at least in intramuscular administration, do not exert their effect by decreasing the delivery of substrate in the form of fatty acids for ketogenesis.

Liver α-glycerophosphate concentration and ketogenesis. As outlined in the previous sections of the Discussion, changes and/or their lack in adenine nucleotides, redox state, acetyl-CoA level, or free fatty acid supply do not seem to explain the antiketogenicity of glyceraldehyde, fructose, or sorbitol. However, in our study there was a definite relationship between the hepatic α-glycerophosphate level and the antiketogenicity of sorbitol, fructose, or glyceraldehyde (figure 2). Older evidence for participation of α-glycerophosphate in the antiketogenic effect of glycerol has been summarized by Fritz.[14] Williamson and coworkers[3] concluded that they could dissociate the antiketogenicity of glycerol from an increase in liver α-glycerophosphate levels in triiodothyronine (T_3)-treated rats. However, if one closely analyzes their data, one finds an increase in liver α-glycerophosphate content with glycerol-injected and T_3-treated rats that is comparable to dihydroxyacetone-injected normal rats. The antiketogenicity of the two substances was quite comparable.

Redox state in relation to ketone body formation. It has been proposed that alteration in the intramitochondrial NADH/NAD ratio would result in either decreases or increases in the concentration of oxaloacetate,[4] thus controlling the rate of oxidation of acetyl-CoA in the Krebs cycle. Although sorbitol was markedly antiketogenic in the present study, it actually increased the NADH/NAD ratio in both the cytosol and the mitochondria. On the other hand, fructose or glyceraldehyde resulted in a decrease in NADH/NAD ratios. Thus, there seems to be no correlation between the antiketogenicity of a compound and its effect on the redox couples.

The work of McGarry and Foster[9] would indicate that antiketogenic agents such as fructose, glycerol, and lactate may exert their effect by accelerated triglyceride synthesis. However, they concluded that rates of triglyceride formation were not a simple function of α-glycerophosphate concentration because perfusion with lactate caused only a 50 per cent increase in α-glycerophosphate concentration while resulting in ketone body production depression similar to that caused by perfusion with glycerol or frustose.

Furthermore, McGarry and Foster[36] have shown (+)-deconoylcarnitine, an inhibitor of long-chain acylcarnitinetranseferase, results in the diversion of fatty acids from β-oxidation and subsequently to ketone body formation by esterification. It is not likely that this agent results in an increase in hepatic α-glycerophosphate content. Based on experiments with (+) and (-) octanoylcarnitine, McGarry and Foster[37] have concluded that carnitine acyltransferase may be a primary site for the regulation of ketogenesis.

Of particular interest in the present study was the finding that sorbitol is more antiketogenic than fructose. This confirms earlier work with sorbitol.[17-19] However, no explanation for antiketogenic potency of sorbitol was given. The present investigation indicates that the concentration of α-glycerophosphate was raised with sorbitol when compared with either fructose or glyceraldehyde, and this resulted in the diversion of fatty acids from β-oxidation to triglycerides by esterification.

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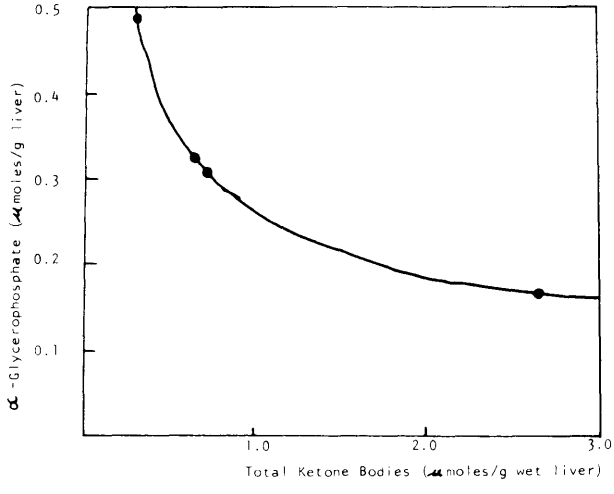

FIG. 2. Changes in total ketone body concentration in relation to the α-glycerophosphate concentration in liver. The details of experimental procedure are given in the section on Materials and Methods. Each point represents values from at least six animals.

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