EFFECT OF SUCROSE ON LIPID METABOLISM IN EXPERIMENTAL ANIMALS AND ITS RELATION TO THE FAT CONTENT OF THEIR DIET

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Chronic experiments on rats showed that isocaloric high-carbohydrate or balanced diets containing sucrose give rise to an increase in the total lipid concentration in the blood. A decrease in the fat content of these sucrose-containing diets causes a much greater increase in the rate of fatty acid synthesis but does not give rise to more profound changes in the integral indices of lipid metabolism. On the other hand, raising the level of saturated fats to physiologically normal values potentiates the effect of sucrose and leads to more substantial disturbances of lipid and intermediate metabolism, expressed as an increase in the blood cholesterol level and in the concentrations of total lipids, fatty acids, pyruvate, and oxaloacetate in the liver.

Increasing the proportion of carbohydrates in the diet leads to changes in the state of lipid metabolism and, in particular, to the acceleration of lipogenesis. Correlation has been established between the sucrose consumption and the total lipid level and also between the blood cholesterol and the incidence of coronary atherosclerosis [2, 5, 7, 11]. The writers have shown that replacing part of the starch by sucrose in a balanced diet leads to more severe disturbances of lipid metabolism in animals than when a diet with a high starch content and low fat content is given [1].

Since the fat content of the diet affected lipogenesis during the administration of complex carbohydrates, while oligosaccharides gave a marked effect even when included in a balanced diet, the study of the effect of sucrose on lipid metabolism in relation to the fat content of the diet was felt to be of great interest.

EXPERIMENTAL METHOD

Experiments were carried out on 120 male Wistar rats weighing initially 180-190 g and kept for 30 days on isocaloric diets (90 cal/150 g body weight) differing in their carbohydrate and fat content but with a constant protein level. The animals were given water and food ad lib. Of the total calorific value of the daily diet received by the control group of rats 18% was accounted for by protein (caseine), 26% by fat (lard), and 56% by carbohydrates (starch). In the diet of experimental group 1 the starch was replaced by sucrose (41% of the total calorific value of the diet), and carbohydrates accounted for 71% of the calorific value of the diet of group 2, 38% accounted for by sucrose and 33% by starch. All diets included the necessary amounts of salts and vitamins. After the period of feeding the animals of each group were divided into two subgroups, one of which received a subcutaneous injection of glucose-1-6-C^{14} (100 μCi/200 g body weight) 24 h before sacrifice and the other an injection of sodium acetate-2-C^{14} (150 μCi/200 g body weight) 2 h before sacrifice. The rats were killed on an empty stomach, and the content of total lipids, cholesterol, and total fatty acids and the rate of biosynthesis of cholesterol and total fatty acids from sodium acetate-2-C^{14} and metabolites of labeled glucose were determined in the liver, blood, and several other organs.

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TABLE 1. Content of Some Metabolites of Lipid and Intermediate Metabolism and Radioactivity of Cholesterol and Fatty Acids from Sodium Acetate-2-C^{14} and Glucose-1-6-C^{14} in the Blood and Liver of Rats (M ± m)

Parameters studied	Control		Experiment			
			group 1		group 2	
	blood	liver	blood	liver	blood	liver
1. Total lipids	390±27	59,2±2,2	570±35*	71±6,4*	530±28*	53±5
2. Cholesterol	56±2,2	2,8±0,3	70±6,1*	2,3±0,8	65±8,4	2,1±0,4
3. Fatty acids	321±21	27,2±2,3	485±28*	35,8±2*	450±20*	32±2,5
4. β-Lipoproteins	46,8±5,8	—	68,6±3,2*	—	57,2±6,4	—
5. Pyruvic acid	—	355±51	—	530±72*	—	300±31
6. Oxaloacetic acid	—	86±18	—	151±24*	--	114±15
7. Acetyl-CoA	—	195±35	—	175±29	—	185±36
Radioactivity from sodium acetate-2-C^{14} (in $\mu Ci \cdot 10^{-4}$/g tissue)						
Cholesterol	0,62±0,08	3,2±0,24	0,37±0,06*	2,5±0,2*	0,3±0,07	2,72±1,9
Fatty acids	1,4±0,3	10,6±2,3	1,2±0,3	23,6±2,2*	1,9±0,2	29,7±4*
Radioactivity from glucose-1-6-C^{14} (in $\mu Ci \cdot 10^{-4}$/g tissue)						
Cholesterol	0,10±0,06	0,21±0,02	0,07±0,02	0,24±0,04	0,13±0,01	0,28±0,04
Fatty acids	0,43±0,07	1,62±0,14	0,38±0,04	2,9±0,3*	0,23±0,05	2,96±0,2*

Legend: 1) Results differing statistically significantly from the control ($P < 0.05$) marked by an asterisk. 2) Content of parameters 1, 2, 3, and 4 is expressed in mg % in the blood and in mg/g tissue in the liver; content of parameters 5, 6, and 7 is expressed in μmoles · 10^{-4}/g tissue.

The content of pyruvic and oxaloacetic acids and acetyl-CoA also were determined and the presence of label was investigated in some of the animals after the injection of labeled glucose. The cholesterol concentration was estimated by the method of Sperry and Webb [9], fatty acids and total lipids after Folch et al. [3], and pyruvic and oxaloacetic acids after Käser [6]. Acetyl-CoA was estimated as acetic acid, determined by the method of formation of hydroxamates of fatty acids. The hydroxamates were determined by the method of Stadtman and Barker [10].

EXPERIMENTAL RESULTS AND DISCUSSION

The results given in Table 1 show that the total lipid content in the blood and liver of the animals of experimental group 1 was increased (by 46 and 20%, respectively), but in group 2 it was increased in the blood only (by 36% compared with the control). The fatty acid content was increased in the blood and aorta of the rats of both experimental groups, but in the liver it was increased only in animals receiving sucrose in a balanced diet. The cholesterol level also was raised only in the blood of the rats of experimental group 1.

It will be noted that when high-carbohydrate diets with a reduced fat quota were used, even though they contained sucrose, no significant changes were observed in the amounts of pyruvic and oxaloacetic acids, whereas in animals receiving a balanced diet containing sucrose all these metabolites of intermediate metabolism were increased. However, the state of some parameters was virtually identical. For instance, the acetyl-CoA content in the liver of both experimental groups was indistinguishable from the corresponding control results and the activity of glucose-6-phosphate dehydrogenase was increased in both cases.

The changes found in the concentrations of total lipids, fatty acids, and cholesterol in certain organs and tissues of animals receiving sucrose might naturally be supposed to be due primarily to changes in the intensity of their biosynthesis from the carbohydrate component of the diet. The results actually showed that the use of high-carbohydrate or balanced diets with the addition of sucrose did not lead to any increased rate of cholesterol biosynthesis but it did stimulate fatty acid formation both from metabolites of labeled glucose and from sodium acetate-2-C^{14}. The most significant changes in the rate of fatty acid biosynthesis were found in the rats receiving high-carbohydrate diets with sucrose. It is interesting to note that the percentage of incorporation of the label from metabolites of labeled glucose in the liver of the rats of experimental groups 1 and 2 was almost the same as in the control, whereas carbon from acetate was incorporated more intensively in animals receiving sucrose in a high-carbohydrate diet. In the rats of group 2 an increase in the content of newly formed labeled fatty acids was observed after administration of sodium acetate-2-C^{14} not only in the liver, but also in the kidneys, spleen, and adipose tissue. Meanwhile, no increase in the content of total lipids and fatty acids was found in these organs.

No direct correlation could thus be detected between the intensity of biosynthesis of cholesterol and fatty acids and their content in certain organs. This is evidence that the quality of the diet influences the rate and direction of subsequent chemical conversions of these substances. The two diets containing sucrose had similar effects only on the blood lipid content and the biosynthesis of fatty acids in the liver. The latter is determined by the rate of absorption of oligosaccharide and the character of metabolism of the fructose in its composition [11, 12].

However, the degree to which sucrose affects the intensity of fatty acid biosynthesis depended to some extent on the fat content of the diet. The more marked acceleration of fatty acid biosynthesis from acetate in the liver of the animals of experimental group 2 was the result of a decrease in the quota of exogenous fat and a consequent decrease in the number of long-chain acyl groups inhibiting the acetyl-CoA-carboxylase reaction [4].

Meanwhile an increase in the fat content in the isocaloric diet to physiologically normal levels led to an increase in the lipid and fatty acid concentrations in the liver and the cholesterol concentration in the serum, indicating a slowing of the liberation of lipids from the liver into the blood stream and a change in the qualitative composition of the lipoprotein complexes.

The change in the content of certain components of intermediate metabolism was evidently connected with an increase in the content of $NAD \cdot H_2$ and acetyl-CoA, products of fatty acid oxidation contributing to an increase in the content of oxaloacetate, malate, and other intermediate compounds [8].

It will be clear from these results that some disturbances of metabolism were due not so much to the action of sucrose as to the combined effect of sucrose and fat, for the fat content in the balanced diets was 2.5 times higher than in the high-carbohydrate diets. Although the two diets were identical in total caloric value, they were not of equal value physiologically; the increased fat content potentiated the action of sucrose on lipid and intermediate metabolism and led to more severe disturbances. In other words, when the effects of carbohydrates on metabolism are compared, the composition of the diet as a whole must be taken into account.

In conclusion, a decrease in the fat content in isocaloric diets, leading to greater acceleration of fatty acid biosynthesis, did not lead to more severe changes in the integral indices of lipid metabolism. Conversely, the use of diets containing physiologically normal amounts of saturated fats potentiated the effect of sucrose and led to more severe disturbances of lipid and intermediate metabolism.

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