Influences of Dietary Carbohydrate-Fat Combinations on Various Functions Associated with Glycolysis and Lipogenesis in Rats

II. GLUCOSE VS. SUCROSE WITH CORN OIL AND TWO HYDROGENATED OILS[1]

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ABSTRACT Weanling rats were fed diets differing only in source of carbohydrate and fat for 2 to 4 weeks. Livers were assayed for glucose-6-phosphatase and fructose diphosphatase activities, and for content of glycogen and lipids. Effects on enzyme activities of substituting fructose for glucose were similar to those observed on substituting sucrose for rice starch (previous report). Feeding either hydrogenated coconut oil (HCO) or hydrogenated peanut oil (HPO) in place of corn oil (CO) modified the enzymatic responses to dietary fructose. Results with HPO were somewhat different than those with HCO. Labile phosphorus values were highest in groups fed sucrose or fructose with CO, and lowest in those fed rice starch or glucose with HPO. Effects of dietary carbohydrate on accumulation of lipid in liver appeared to be a function of the type of fat fed, namely, substitution of a fructose source for a direct glucose source resulted in the accumulation of less fat in livers of rats fed CO, but of more fat in livers of rats fed a hydrogenated oil. Proportions of phospholipid and cholesterol in liver lipid, and concentration of cholesterol in serum also varied with the combination of carbohydrate and fat fed.

The type of carbohydrate fed to rats influences the activity of several enzyme systems involved in carbohydrate metabolism (1–4). Freedland and Harper (1) noted that the stimulation of glucose-6-phosphatase activity resulting from the substitution of an indirect source of glucose (e.g., fructose) for a direct source (dextrin) appeared to be an adaptation of the enzyme system due to increased gluconeogenesis. Recent studies from this laboratory demonstrated that metabolic responses to the dietary source of carbohydrate are partially dependent on the type of fat in the diet (5). For example, adaptation in the activities of the glucose-6-phosphatase and fructose diphosphatase enzyme systems, and changes in glycogen content of the liver resulting from the substitution of sucrose for rice starch were modified by the type of fat fed (corn oil vs. hydrogenated coconut oil). Further evidence for an influence of the dietary source of fat on carbohydrate metabolism was the significantly greater glucose-6-phosphatase activity in livers from rats fed hydrogenated coconut oil with rice starch as compared with that in livers from rats fed corn oil with rice starch. Lipid content of the liver and cholesterol concentration of the serum also varied with the combination of carbohydrate and fat in the diet.

The experiments reported in the present paper were designed to gain more information about the above interrelationships by the following means: 1) Determining whether substitution of fructose for glucose with corn oil and with saturated fat would produce the same results as had the substitution of sucrose for rice starch; 2) comparing effects of feeding a hydrogenated fat containing long-chain fatty acids with those observed on feeding coconut oil; and 3) following the course of liver lipid variations for an additional 2 weeks.

Criteria for evaluating differences in carbohydrate and lipid metabolism were the same as used in the previous study (5) except that in the second part of the current study livers were also assayed for labile phosphorus from ADP and ATP.

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EXPERIMENTAL

Experimental animals, diets, and groups

Male, weanling rats [2] of the Sprague-Dawley strain, weighing approximately 50 g each at the beginning of the study, were fed different carbohydrate-fat combinations. Rations for all groups consisted of the following: (in per cent) protein, 20 (casein supplemented with 2% of DL-methionine); fat, 15; carbohydrate, 60.55; choline chloride, 0.2; salts (6),[3] 4; and vitamin mix,[4] 0.25. Variables were the type of carbohydrate and the type of fat.

Part 1. A total of 52 rats was divided into 8 groups (6 or 7 rats /group). Each group was fed a diet containing one of the following carbohydrate - fat combinations for 2 weeks: corn oil [5] (CO) with glucose, CO with fructose, hydrogenated coconut oil [6] (HCO) with glucose, HCO with fructose, and each of these 4 combinations with added cholesterol.[7]

Part 2. Since some differences were observed between effects of monosaccharides in part 1, and those of rice starch and sucrose in the previous study (5), part 2 was designed to investigate these differences by feeding the monosaccharides and the more complex carbohydrates simultaneously to different groups of rats. Also, hydrogenated peanut oil [8] (HPO) was used in place of HCO, to observe effects of providing more long-chain fatty acids. The approximate fatty acid content of the 2 fats, as supplied by the manufacturers, was as follows: for HPO (in per cent) palmitic, 12; stearic, 79; arachidic and longer saturated, 6; and mono-unsaturated, 3; as compared with HCO (in per cent) caprylic, 6; capric, 6; lauric, 44; myristic, 18; palmitic, 11; and stearic, 15. The iodine number of the HPO was approximately 4, and that of the HCO was 1 to 3. A total of 96 rats was divided into 8 groups of 12 rats each. Four rats from each group were fed the experimental diet for 2 weeks, four for 3 weeks, and four for 4 weeks. The 8 carbohydrate-fat combinations were: CO and HPO each with rice starch,[9] sucrose, glucose, and fructose.

PROCEDURES

After animals had been fed experimental diets for the times specified above, they were decapitated. Methods used for serum cholesterol determinations and for liver assays for activities of the glucose-6-phosphatase (G-6-Pase) and fructose diphosphatase (FDPase) enzyme systems, for glycogen, and for total lipid, phospholipid, and cholesterol are described in a previous paper (5). An additional assay carried out in part 2 was the determination of labile phosphorus from ADP + ATP. The adenosine phosphates from samples of liver homogenates were adsorbed onto charcoal, and labile phosphorus from ADP + ATP was hydrolyzed off by boiling in HCl (7). The inorganic phosphorus released was determined by the method of Fiske and Subbarow (8).

RESULTS

Growth rates and relative liver weights

The feeding of hydrogenated oil in place of corn oil resulted in a depression of the growth rate, more severe with HPO than with HCO. However, the average weekly weight gain for each group for the entire experimental period was at least 30 g, and did not fall below 26 g for any group in any single week (table 1).

Relative liver weights (liver weight/ 100 g of body weight) were significantly greater in all groups fed a source of fructose (sucrose or fructose) as compared with those of corresponding groups fed a direct source of glucose (rice starch or glucose) (table 1). Differences were significant at the 1 or 2% level [10] in all instances except one, sucrose vs. rice starch with CO at 4 weeks. This observation is consistent with previous reports from other laboratories that relative liver weight is increased by feeding fructose in place of glucose (9) or dextrin (1).

[2] Obtained from Hormone Assay Laboratories, Inc., Chicago.
[3] Salt Mixture-W, obtained from Nutritional Biochemicals Corporation, Cleveland.
[4] The vitamin mix provided the following: (in mg/ 100 g ration) thiamine·HCl, 0.08; riboflavin, 0.6; pyridoxine, 0.4; Ca pantothenate, 4.0; niacin, 5.0; inositol, 20.0; folic acid, 0.04; vitamin B_{12}, 0.004; biotin, 0.02; vitamin A powder, 10.0 (200 units); calciferol, 0.18 (150 units); DL-α-tocopherol powder, 30.0 (7.5 units); and menadione, 0.38.
[5] Mazola, Corn Products Company, Argo, Illinois.
[6] Hydrol, Durkee Famous Foods, Chicago.
[7] Cholesterol added at level of 1% of total ration at expense of dietary fat.
[8] Obtained from Procter and Gamble Company, Cincinnati.
[9] Obtained from Morningstar-Paisley, Inc., New York.
[10] Student's *t* test.

TABLE 1

Growth rates and relative liver weights of rats fed different combinations of carbohydrates and fats

Weeks fed diet	Direct glucose source with CO [1]	Fructose source with CO	Direct glucose source, saturated fat	Fructose source with saturated fat
	g	g	g	g
		Weight gain/week		
	G and CO	F and CO	G and HCO	F and HCO
1 (7) [2]	44±1 [3]	41±2	41±1	37±1
2 (7)	47±2	49±3	41±2	41±2
	G and CO+C	F and CO+C	G and HCO+C	F and HCO+C
1 (6)	44±2	45±1	41±1	41±2
2 (6)	47±3	42±3	39±3	32±3
	RS and CO	S and CO	RS and HPO	S and HPO
1 (12)	45±1	46±1	33±2	26±2
2 (12)	53±1	53±1	40±2	45±1
3 (8)	49±1	44±2	41±1	44±1
4 (4)	52±3	53±1	46±1	42±4
	G and CO	F and CO	G and HPO	F and HPO
1 (12)	43±1	40±1	33±1	27±2
2 (12)	48±1	48±1	37±1	33±1
3 (8)	46±2	43±1	34±2	30±2
4 (4)	50±4	45±6	33±2	29±2
		Relative liver weights [4]		
	G and CO	F and CO	G and HCO	F and HCO
2 (7)	4.81±0.10	6.22±0.22	5.05±0.12	6.26±0.15
	G and CO+C	F and CO+C	G and HCO+C	F and HCO+C
2 (6)	4.92±0.14	6.44±0.22	4.85±0.23	5.92±0.23
	RS and CO	S and CO	RS and HPO	S and HPO
2 (4)	4.92±0.06	5.72±0.10	4.40±0.13	5.47±0.19
3 (4)	4.77±0.10	5.43±0.13	4.54±0.12	5.28±0.07
4 (4)	4.54±0.08	4.86±0.18	4.04±0.16	5.46±0.33
	G and CO	F and CO	G and HPO	F and HPO
2 (4)	5.01±0.07	6.33±0.11	4.57±0.22	5.50±0.19
3 (4)	4.79±0.05	5.85±0.12	4.62±0.12	5.70±0.17
4 (4)	4.46±0.09	5.99±0.41	4.24±0.08	5.52±0.11

[1] Abbreviations: CO = corn oil, HCO = hydrogenated coconut oil, HPO = hydrogenated peanut oil, C = cholesterol (1% of ration), G = glucose, F = fructose, RS = rice starch, S = sucrose.
[2] Number of rats per group.
[3] SE of mean.
[4] Liver weight/100 g of body weight.

Enzyme activities and glycogen levels

The activities of the 2 enzyme systems were calculated as total activity (units/100 g of body weight) and as specific activity (units/100 mg of liver nitrogen). Qualitative relationships among groups were the same for both methods (fig. 1), although quantitative differences between the fructose-fed and glucose-fed groups were usually greater on the basis of total activity because of the larger livers in rats fed fructose. In evaluating various methods for expressing concentration of intracellular proteins, Knox (10) cites value "per 100 g of animal" as one means of relating protein content to the functional need of the whole animal, and comments that "such bases are particularly useful when great changes in size of the animal or organ have occurred during the experiment." Although activity of the enzyme system rather than concentration of the apoenzyme was measured in this experiment, the same reasoning would appear to be applicable and valid. Freedland and Harper expressed G-6-Pase and FDPase activities as total activity (1, 2), and

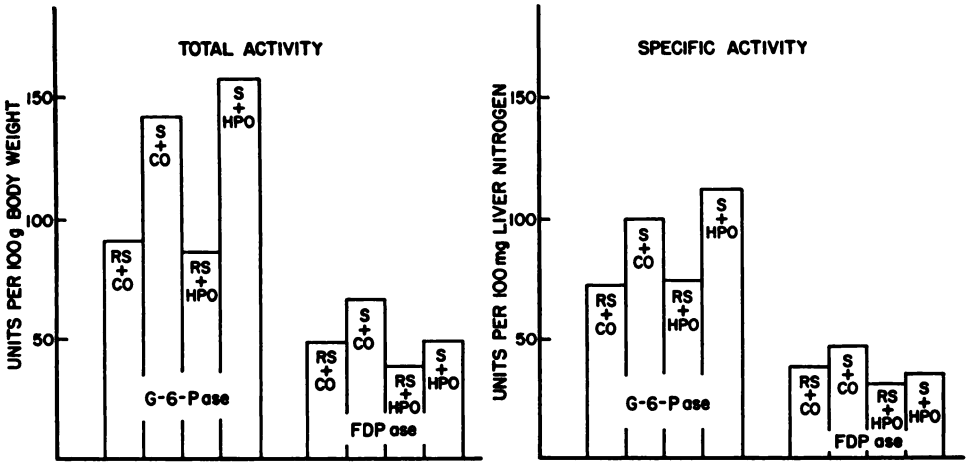

Fig. 1 Total activity and specific activity of the glucose-6-phosphatase and fructose diphosphatase enzyme systems in livers from rats fed different carbohydrate-fat combinations. Averages of values at 2, 3, and 4 weeks. RS = rice starch, S = sucrose, CO = corn oil, HPO = hydrogenated peanut oil.

pointed out that adaptation in G-6-Pase activity to fructose feeding was accomplished partly by an increase in specific activity of the enzyme and partly by an increase in total liver tissue (1). Since glucose released by the action of the G-6-Pase enzyme system of the liver is transported by the bloodstream to cells throughout the body, body weight was chosen as the more meaningful basis for evaluating functions closely associated with supply of glucose for body tissues. Therefore, as in the previous paper (5), activities of the 2 enzyme systems are expressed as total activity, and glycogen content of the liver is given in milligrams per 100 g of body weight (tables 2 and 3). Labile phosphorus was also calculated on the basis of body weight for comparative purposes (table 3).

Part 1. Substitution of glucose for fructose in CO diets resulted in a 60% increase in G-6-Pase activity ($P < 0.01$) (table 2). This degree of stimulation is almost identical with that obtained previously by the substitution of sucrose for rice starch in CO diets (5). A stimulatory effect of HCO on G-6-Pase activity was again observed, namely, activity of the enzyme system was significantly greater

TABLE 2

Enzyme activities and glycogen levels in livers from rats fed different combinations of carbohydrates and fats for 2 weeks (part 1)

Cholesterol added [1]	Glucose with CO [2]	Fructose with CO	Glucose with HCO	Fructose with HCO
	Glucose-6 phosphatase activity (units [3]/100 g of body weight)			
−	104±2 [4]	166±7	136±12	175±12
+	110±6	164±7	145±16	177±12
	Fructose diphosphatase activity (units/100 g of body weight)			
−	48±3	79±4	50±3	63±5
+	71±3	90±3	62±5	71±5
	Glycogen (mg/100 g of body weight)			
−	314±20	476±30	256±18	443±34
+	327±65	553±95	336±57	454±51

[1] Cholesterol added at level of 1% of total ration, at expense of fat.
[2] Abbreviations: CO = corn oil, HCO = hydrogenated coconut oil.
[3] One unit = activity catalyzing release of 1 μmole of inorganic phosphate/minute, at 37.5°C.
[4] SE of mean.

TABLE 3

Changes with time in enzyme activities, glycogen, and labile phosphorus (from ADP+ATP) in livers from rats fed different combinations of carbohydrates and fats (part 2)

Weeks fed diet	Direct glucose source with CO [1]	Fructose source with CO	Direct glucose source, with HPO	Fructose source with HPO
	Glucose-6 phosphatase activity (units [2]/100 g of body weight)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	92±8 [3]	158±9	84±7	168±5
3	93±6	148±10	92±6	155±7
4	89±3	120±5	83±8	148±8
	G and CO	F and CO	G and HPO	F and HPO
2	131±2	197±20	123±4	168±13
3	112±8	191±9	120±3	182±9
4	100±2	146±8	100±4	162±4
	Fructose diphosphatase activity (units/100 g of body weight)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	51±2	72±4	37±4	54±2
3	49±1	66±2	43±2	50±1
4	46±3	63±2	36±3	46±4
	G and CO	F and CO	G and HPO	F and HPO
2	52±5	89±12	45±1	62±6
3	56±4	84±6	42±2	54±3
4	51±2	63±5	38±3	51±3
	Glycogen (mg/100 g of body weight)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	199±19	325±38	152±35	266±32
3	264±45	258±29	163±7	214±20
4	225±17	268±17	150±16	245±45
	G and CO	F and CO	G and HPO	F and HPO
2	256±12	401±43	228±38	250±45
3	239±19	275±43	209±26	215±13
4	208±14	389±49	159±15	208±29
	Labile phosphorus from ADP+ATP (μg/100 g of body weight)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	463±27	590±82	327±36	433±47
3	419±45	560±67	314±25	462±66
4	384±36	492±29	269±18	480±46
	G and CO	F and CO	G and HPO	F and HPO
2	426±37	625±14	339±21	502±39
3	458±50	643±46	336±28	624±93
4	415±50	693±69	300±8	478±49

[1] Abbreviations: CO = corn oil, HPO = hydrogenated peanut oil, RS = rice starch, S = sucrose, G = glucose, F = fructose.
[2] One unit = activity catalyzing release of 1 μmole of inorganic phosphate/minute, at 37.5°C.
[3] SE of mean.

when glucose was fed with HCO than when the same carbohydrate was fed with CO ($P < 0.05$). This effect was observed both with and without incorporation of cholesterol into the diets. Highest values of G-6-Pase activity occurred when rats were fed fructose with HCO (table 2).

Using glucose and fructose as the direct and indirect sources of glucose (respectively) resulted in a pattern of FDPase responses similar to that observed with rice starch and sucrose in the previous study, namely, a substantial increase when a fructose source was substituted for a direct glucose source with CO ($P < 0.01$), no stimulation by HCO, and a small increase above the glucose-HCO group ($P < 0.05$) when fructose was fed with CO (table 2). Glycogen levels tended to parallel FDPase activity, except that the

feeding of fructose with HCO resulted in a marked increase in liver glycogen over the amount deposited with the glucose-HCO diet ($P < 0.01$).

The addition of cholesterol to the diets had no significant effect on G-6-Pase activity in any of the groups (table 2). On the other hand, FDPase activity was significantly increased by the addition of cholesterol to CO diets ($P < 0.01$ with glucose-CO diets and $P < 0.05$ with fructose-CO diets), but not by addition of cholesterol to HCO diets. No significant effect of dietary cholesterol on glycogen content of livers was evident, because of the very large variations among animals within each group.

Part 2. Absolute activities of the G-6-Pase enzyme system, and degree of stimulation of FDPase activity by a fructose source were greater in groups fed glucose or fructose than in corresponding groups fed rice starch or sucrose at 2 weeks (table 3). These differences tended to lessen with time, and had practically disappeared by the fourth week.

The effect of dietary HPO on G-6-Pase activity differed from that of HCO in part 1 (table 2) and in the previous study (5), namely, liver G-6-Pase activity in rats fed HPO with rice starch or glucose was not increased above the activity in rats fed CO with the same carbohydrate. Furthermore, the feeding of HPO with either rice starch or glucose depressed FDPase activity, glycogen levels, and labile phosphorus below corresponding values from groups fed CO (table 3). When data from determinations at 2, 3, and 4 weeks were combined, the extent of the depressing effect of HPO on FDPase activity was approximately 20% ($P < 0.01$), and on labile phosphorus about 25% ($P < 0.01$). The effect of HPO on glycogen content of livers was more variable, a 32% decrease ($P < 0.01$) with rice starch, and a barely significant decrease of 15% with glucose.

Lipid data

Part 1. The percentages of total lipid in the livers at 2 weeks varied significantly with the combination of carbohydrate and fat fed (table 4). With CO as the dietary fat, feeding fructose resulted in less total liver lipid than did feeding glucose ($P < 0.01$). But with HCO, feeding fructose resulted in more total liver lipid than did feeding glucose ($P < 0.01$). The addition of cholesterol to the diets greatly increased the deposition of fat in livers from all groups — by about 100% in CO-fed rats, and by approximately 70% in HCO-fed rats (table 4).

Percentages of phospholipid and cholesterol in liver fat of rats fed no added cholesterol showed no sharp differences among groups at 2 weeks (table 4), although percentages of both of these lipid

TABLE 4

Liver lipids and serum cholesterol in rats fed different combinations of carbohydrates and fats for 2 weeks (part 1)

Cholesterol added [1]	Glucose with CO [2]	Fructose with CO	Glucose with HCO	Fructose with HCO
	Total liver lipid (% of liver)			
−	3.35 ± 0.09 [3]	2.91 ± 0.08	3.40 ± 0.10	4.14 ± 0.16
+	6.53 ± 0.58	6.09 ± 0.46	5.64 ± 0.24	6.19 ± 0.25
	Phospholipid (% of total liver lipid)			
−	38.7 ± 1.4	42.0 ± 1.1	43.8 ± 1.4	36.7 ± 1.8
+	16.4 ± 1.2	17.3 ± 1.2	23.0 ± 2.0	21.8 ± 1.6
	Cholesterol (% of total liver lipid)			
−	13.2 ± 0.4	11.2 ± 0.6	10.0 ± 0.7	8.2 ± 0.3
+	17.9 ± 2.4	20.5 ± 2.5	24.0 ± 6.1	16.5 ± 1.6
	Serum cholesterol (mg/100 ml serum)			
−	155 ± 6	145 ± 8	123 ± 7	136 ± 5
+	108 ± 8	108 ± 11	155 ± 11	127 ± 8

[1] Cholesterol added at level of 1% of total ration, at expense of fat.
[2] Abbreviations: CO = corn oil, HCO = hydrogenated coconut oil.
[3] SE of mean.

fractions were lowest in livers containing the most fat (fructose-HCO group). The addition of cholesterol to the diets resulted in significant decreases ($P < 0.01$) in the proportion of phospholipid in total liver lipid with all carbohydrate-fat combinations (table 4). On the other hand, the proportion of cholesterol in liver lipid was significantly increased ($P < 0.01$) by addition of cholesterol to both fructose diets. Increases with glucose diets were more variable, namely, barely significant with glucose-CO and significant at the 5% level with glucose-HCO diets.

A clearer picture of overall changes in lipid content of the liver can be seen when total lipid, phospholipid, and cholesterol are expressed as milligrams per gram liver (fig. 2). Dietary cholesterol enhanced cholesterol accumulation about threefold with all carbohydrate-fat combinations. Phospholipid content of livers tended to decrease with administration of cholesterol, but the difference was significant at the 5% level only with the fructose-CO diets. When no cholesterol was fed, phospholipid content of liver was significantly greater in rats fed HCO than in those fed CO, with either glucose ($P < 0.05$) or fructose ($P < 0.01$) as the dietary carbohydrate. When cholesterol was fed, differences between effects of fat were significant ($P < 0.02$) between fructose groups only (fig. 2).

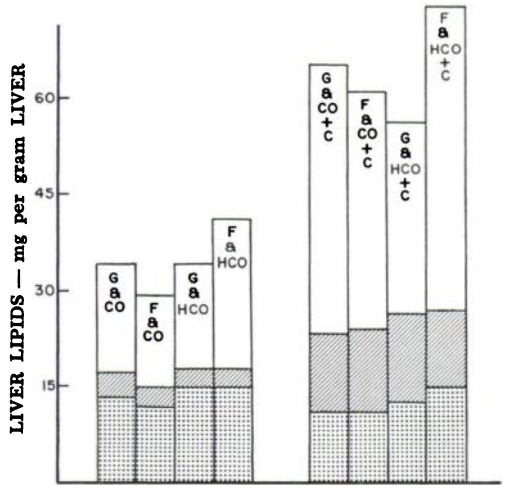

Fig. 2 Total lipid, cholesterol, and phospholipid (in mg per gram liver) in livers from rats fed different carbohydrate-fat combinations for 2 weeks (part 1). G = glucose, F = fructose, CO = corn oil, HCO = hydrogenated coconut oil, C = cholesterol. Complete bar represents total lipid, stippled portion represents phospholipid, and diagonally shaded portion represents cholesterol.

The incorporation of 1% of cholesterol in the diets did not cause accumulation of cholesterol in the serum as it did in the liver (table 4). In fact, serum cholesterol concentrations were somewhat lower ($P < 0.02$) in the CO-fed groups when cholesterol was added to the diets. Other investigators have noted the tendency of dietary cholesterol to produce sharp increases in liver cholesterol accompanied by small, variable fluctuations in serum cholesterol when the diet contains an appreciable amount of fat and linoleic acid (11, 12).

Part 2. The influence of dietary carbohydrate on accumulation of lipid in the liver varied with the type of fat in the diet. As in part 1, substitution of a fructose source for a direct glucose source resulted in the accumulation of less fat ($P < 0.01$) in livers of rats fed CO, but of more fat ($P < 0.02$) in livers of rats fed a hydrogenated oil (table 5). In most cases, differences were more pronounced at 4 than at 2 weeks.

Percentages of phospholipid in liver fat did not change progressively with time with any carbohydrate-fat combinations except rice starch or glucose with HPO, where a progressive increase was observed (table 5). It may be noteworthy that in the same rats the percentage of cholesterol in liver lipid decreased progressively with time.

When phospholipid and cholesterol content of livers were calculated on the basis of liver weight (mg./10 g of liver), no consistent pattern of changes with time was evident, and neither fraction contributed substantially to the changes in total lipid.

The concentration of cholesterol in the serum of rats fed HPO was lower than that in corresponding groups fed CO. At 4 weeks, differences were significant at the 1 or 2% level in all instances except that of HPO vs. CO with sucrose (table 5).

TABLE 5

Changes with time in liver lipids and serum cholesterol in rats fed different combinations of carbohydrates and fats (part 2)

Weeks fed diet	Direct glucose source with CO [1]	Fructose source with CO	Direct glucose source, with HPO	Fructose source with HPO
	Total liver lipid (% of liver)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	3.44 ± 0.13 [2]	3.32 ± 0.18	2.96 ± 0.29	4.08 ± 0.37
3	4.36 ± 0.46	2.92 ± 0.08	2.72 ± 0.27	3.13 ± 0.14
4	5.15 ± 0.26	3.44 ± 0.20	3.14 ± 0.14	3.96 ± 0.33
	G and CO	F and CO	G and HPO	F and HPO
2	3.74 ± 0.27	3.06 ± 0.14	3.10 ± 0.44	3.51 ± 0.11
3	3.85 ± 0.34	2.71 ± 0.18	3.04 ± 0.16	3.87 ± 0.37
4	4.42 ± 0.31	3.34 ± 0.22	3.60 ± 0.19	5.24 ± 0.52
	Liver phospholipid (% of total lipid)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	23.7 ± 3.6	29.7 ± 3.9	23.8 ± 5.2	23.3 ± 2.5
3	15.4 ± 1.1	15.2 ± 1.5	24.1 ± 4.8	23.3 ± 6.0
4	23.0 ± 2.2	30.0 ± 1.2	39.3 ± 1.5	32.1 ± 0.9
	G and CO	F and CO	G and HPO	F and HPO
2	23.9 ± 5.9	27.6 ± 5.4	27.6 ± 6.2	33.5 ± 1.8
3	24.2 ± 5.0	22.2 ± 7.6	36.5 ± 5.2	27.6 ± 4.2
4	26.0 ± 1.1	28.2 ± 0.9	41.9 ± 2.5	31.0 ± 3.4
	Liver cholesterol (% of total lipid)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	12.6 ± 1.9	9.3 ± 1.2	12.0 ± 0.9	6.9 ± 0.8
3	11.0 ± 1.2	10.0 ± 0.2	9.1 ± 0.5	8.3 ± 0.9
4	9.0 ± 0.5	7.7 ± 0.4	8.7 ± 0.9	5.8 ± 0.7
	G and CO	F and CO	G and HPO	F and HPO
2	10.4 ± 0.4	9.9 ± 1.5	9.4 ± 1.1	8.7 ± 0.2
3	9.9 ± 1.1	9.6 ± 1.0	9.1 ± 0.7	6.6 ± 0.9
4	7.9 ± 0.6	7.5 ± 0.6	7.1 ± 0.8	6.0 ± 0.7
	Serum cholesterol (mg/100 ml serum)			
	RS and CO	S and CO	RS and HPO	S and HPO
2	230 ± 45	182 ± 13	130 ± 14	141 ± 22
3	254 ± 10	248 ± 12	158 ± 6	156 ± 7
4	213 ± 32	198 ± 14	108 ± 15	144 ± 26
	G and CO	F and CO	G and HPO	F and HPO
2	187 ± 25	130 ± 10	94 ± 9	104 ± 5
3	202 ± 14	226 ± 13	128 ± 4	149 ± 6
4	192 ± 17	186 ± 18	97 ± 14	117 ± 19

[1] Abbreviations: CO = corn oil, HPO = hydrogenated peanut oil, RS = rice starch, S = sucrose, G = glucose, F = fructose.
[2] SE of mean.

DISCUSSION

The above data support the thesis that differences in G-6-Pase and FDPase activities in livers from rats fed sucrose as compared with those fed rice starch are the result of the fructose component of sucrose. Diets containing fructose as the carbohydrate would provide approximately twice as much fructose as would those containing the same weight of sucrose, since sucrose is hydrolyzed into equal parts of fructose and glucose. Therefore, the greater activity of the 2 enzyme systems after feeding fructose diets as compared with sucrose diets is probably the result of the greater amount of fructose being metabolized. The action of dietary glucose in increasing G-6-Pase activity above that attained with rice starch may be related to a more rapid absorption of the monosaccharide, releasing a greater glucose load on the liver at one time.

Differences in response of the enzyme systems to dietary HPO as compared with HCO are possibly associated with chain length of their component fatty acids, since HPO yields chiefly stearic and palmitic acids, whereas HCO yields a large proportion of shorter chain acids. Since the metabolic fate of absorbed fatty acids depends partly on their chain length (13), this could be a factor in determining influences of dietary fat on glucose metabolism.

Labile phosphorus values represent the total amount of phosphorus derived from hydrolysis of the high energy bonds of ADP and ATP. As ATP yields twice as much labile phosphorus per mole as does ADP, decreases in labile phosphorus have been assumed to indicate decreases in available ATP or ADP + ATP (7). It is conceivable that the depression in labile phosphorus values observed in groups fed HPO is related to the lack of essential fatty acids in the HPO diets, since most of the ATP of the cell is generated by oxidative phosphorylation (14), which is uncoupled in livers of rats fed diets deficient in essential fatty acids (15). No explanation can be offered at this time for the consistently higher labile phosphorus values obtained from all groups fed a source of fructose as compared with those fed a direct source of glucose (table 3).

Changes in activities of specific enzyme systems in response to changes in dietary constituents are believed by some investigators to be a reflection of alterations in throughput of the pathway(s) in which the enzymes participate (2, 4). Furthermore, Freedland and Harper (2) proposed that adaptations in the activities of the G-6-Pase and FDPase enzyme systems in response to dietary changes would provide a useful means of investigating metabolic pathways. On the basis of the above theory, the suggestion was made in a previous report from this laboratory (5) that a lack of parallelism observed in the responses of the G-6-Pase and FDPase enzyme systems to various carbohydrate-fat combinations might indicate that some fructose is converted to either glucose or glycogen, or both, by means other than the classical route via fructose diphosphate. In the current study, differences in patterns of response of the 2 enzyme systems to diets containing HPO provide further evidence for an alternate route from fructose to glucose-6-phosphate, bypassing fructose diphosphate. For example, feeding HPO with sucrose resulted in a 90% increase in G-6-Pase activity over the level in rats fed the control diet (rice starch with CO), but FDPase activity in the same rats was almost identical with the control level (table 3). Also, these same data strongly suggest that dietary HPO may influence the metabolism of fructose, because although no increase in FDPase activity occurred in rats fed HPO with fructose (above), a substantial increase did occur in rats fed CO with fructose.

The liver lipid data further illustrate the complexity of carbohydrate-fat interrelationships. Especially striking is the consistent observation that, with the type of diet used in these experiments, substitution of a fructose source for a direct glucose source results in accumulation of less fat in livers of rats fed CO, but of more fat in livers of rats fed a hydrogenated oil. Thus the type of carbohydrate in the diet can be an important factor to consider in studies concerning influences of dietary fat on lipid metabolism.

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