Serum biochemical changes in rabbits on a regular diet with and without flax lignan complex following a high-cholesterol diet

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BACKGROUND: Flax lignan complex (FLC) isolated from flaxseed suppresses development of hypercholesterolemic atherosclerosis. It does not produce regression of atherosclerosis, but prevents its regular diet-induced acceleration following a high-cholesterol diet. It is not known if replacement of a high-cholesterol diet with a regular diet has deleterious effects on body organs.

OBJECTIVES: To determine if short-term use of a high-cholesterol diet, and a regular diet with or without FLC following the high-cholesterol diet, have any adverse effects on serum electrolytes, glucose and enzymes related to the liver, kidneys, skeletal muscle and intestines.

METHODS: Blood samples were collected from the rabbits before and at various intervals during the high-cholesterol diet, and while on the regular diet with or without FLC, following the high-cholesterol diet. Measurements of serum total cholesterol, glucose, aspartate aminotransferase (AST), alkaline phosphatase (ALP), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), albumin, creatinine,

electrolytes (sodium [Na], potassium [K], chloride [Cl]) and carbon dioxide (CO₂) were taken.

RESULTS: The high-cholesterol diet produced hypercholesterolemia, which was associated with reductions in serum glucose and no significant changes in serum Na, K, Cl, CO₂, ALT, ALP, AST, GGT, albumin or creatinine. Regular diet with or without FLC, following the high-cholesterol diet, reduced serum total cholesterol and glucose, increased serum Na, Cl and creatinine, but produced no significant alterations in serum K, CO₂, ALT, AST, GGT or albumin. FLC reduced serum ALP, but regular diet produced no significant change.

CONCLUSION: Short-term use of a high-cholesterol diet, or a regular diet with or without FLC following the high-cholesterol diet, does not produce deleterious effects in the liver, kidneys, skeletal muscle, intestine or bone, as shown by changes in serum electrolytes, glucose and enzymes.

Key Words: Alanine aminotransferase; Albumin; Alkaline phosphatase; Aspartate aminotransferase; Cholesterol; Creatinine; Flax lignan complex; Gamma-glutamyltransferase; Glucose; Serum electrolytes

Flax lignan complex (FLC) isolated from flaxseed contains 34% to 38% secoisolariciresinol diglucoside, 15% to 20% cinnamic acid glucoside, and 9.6% to 11.0% hydroxymethylglutaric acid (1). Secoisolariciresinol diglucoside (2,3) and cinnamic acid (4) are antioxidants, and hydroxymethylglutaric acid is a hypolipidemic agent (5). FLC suppresses the development of hypercholesterolemic atherosclerosis; this effect is associated with decreases in oxidative stress and serum lipids (6). FLC does not produce regression of atherosclerosis, but it prevents its acceleration, induced by removal of a high-cholesterol diet (7). Because following a regular diet after a high-cholesterol diet accelerated the process of atherosclerosis, and FLC prevents this acceleration, it is possible that the former intervention has deleterious effects in the body, but the latter has beneficial effects. However, it is not known if these interventions have any adverse effects on the organs and cell systems of the body. The main objective of the present study was to investigate if short-term use of a high-cholesterol diet, and regular diet with or without FLC following a high-cholesterol diet, have any adverse effects or otherwise on serum sodium (Na), potassium (K), chloride (Cl), carbon dioxide (CO₂), glucose and serum biochemical changes related to hepatic and renal function (aspartate aminotransferase [AST], alkaline phosphatase [ALP], alanine aminotransferase [ALT], gamma-glutamyltransferase [GGT], albumin and creatinine) in rabbits.

METHODS

Protocol

The studies were carried out on New Zealand White female rabbits aged six to eight weeks old and weighing between 1.2 kg and 1.5 kg. The rabbits were assigned to four groups after one week of acclimatization. The rabbits in group I (n=5) were fed regular rabbit chow for two months, while those in group II (n=5) were fed a 0.25% cholesterol diet for two months. The rabbits in group III (n=11) received a 0.25% cholesterol diet for two months, followed by a regular diet for an additional four months. The rabbits in group IV (n=12) received a 0.25% cholesterol diet for two months, followed by a regular diet with FLC (0.08%) for an additional four months. The 0.25% cholesterol diet was prepared by the Department of Agricultural and Bioresource Engineering, University of Saskatchewan, Saskatoon, Saskatchewan, using regular rabbit chow purchased from Nestlé Purina PetCare Company, USA. The FLC diet, containing 0.08% FLC mixed in the regular diet, was prepared by the above department. This amount is equivalent to 40 mg/kg of FLC orally per day. Food and water were supplied ad libitum. The rabbits were housed in individual cages at a temperature of 20°C under a 12 h light/12 h dark cycle. The studies were approved by the Ethics Committee of the University of Saskatchewan, and the animal care followed the approved standards of Laboratory Animal Care. Blood samples after 18 h

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TABLE 1
Changes in the levels of serum total cholesterol and glucose in the four experimental groups

	Time (months)						
	0	1	2	3	4	5	6
Groups							
Total cholesterol (mmol/L)							
I	2.04±0.23	1.27±0.16*	1.29±0.07*				
II	1.70±0.15	24.00±0.44* **	33.90±3.70*†**				
III	1.42±0.13	23.11±2.44* **	23.51±3.69* **	8.04±1.86*†‡	3.56±0.97*†‡§	2.12±0.54†‡§	1.12±0.15†‡§¶
IV	1.41±0.08**	20.24±1.56* **	15.48±2.04* **††	4.64±1.34*†† ‡	2.01±0.49†‡	1.36±0.12†‡§	1.24±0.10†‡§
Glucose (mmol/L)							
I	6.1±0.1	5.5±0.2	5.8±0.3				
II	6.6±0.3	5.1±0.4*	5.4±0.2*				
III	6.7±0.3	6.2±0.1**††	5.9±0.2††	5.1±0.2*†‡	5.3±0.3*†‡	5.1±0.2*†‡	5.5±0.2*†‡
IV	6.5±0.1	5.7±0.1*†‡	5.6±0.1*	5.4±0.1*	5.0±0.5*	5.6±0.2*	5.2±0.1*†‡

Results are expressed as mean ± SEM. Group I Control; Group II 0.25% cholesterol diet for two months; Group III 0.25% cholesterol diet for two months, followed by a regular diet for four months; Group IV 0.25% cholesterol diet for two months, followed by a regular diet and flax lignan complex, 40 mg/kg per day, for four months. *P<0.05, month 0 versus other months in the respective groups; †P<0.05, month 1 versus other months; ‡P<0.05, month 2 versus other months; §P<0.05, month 3 versus other months; ¶P<0.05, month 4 versus other months; **P<0.05, group I versus other groups; ††P<0.05, group II versus other groups; ‡‡P<0.05, group III versus group IV

of fasting were collected from the ear marginal artery before the study, and at monthly intervals thereafter, for measurements of serum total cholesterol (TC), Na, K, Cl, CO₂, AST, ALP, ALT, GGT, albumin, creatinine and glucose.

Biochemical measurements

Serum TC, Na, K, Cl, CO₂, AST, ALP, ALT, GGT, albumin, creatinine and glucose were measured on an automated Beckman Synchron LX20 clinical system analyzer (Beckman Coulter Inc, USA).

Statistical analysis

Results are expressed as mean ± SEM. Repeated measures of ANOVA were used to analyze the data. The Mann-Whitney U test was used to determine the significance of differences between any two groups. A value of P<0.05 was considered significant.

RESULTS

Serum cholesterol and glucose

The changes in the values for serum TC and glucose of the four groups are summarized in Table 1. The basal levels of serum TC of all the groups were not significantly different from each other, except in group IV where levels were lower than in group I. The levels decreased in group I, but increased in all other groups at months 1 and 2, compared with month 0. The serum levels of TC at month 2 were significantly lower in group IV compared with group II. Regular diet, with or without FLC, following the high-cholesterol diet significantly reduced the levels of TC compared with month 2, and the reductions were not significantly different from each other at month 6. The levels of serum TC in groups III and IV at month 6 were not significantly different from their respective values at month 0. The initial levels of serum glucose were similar in all groups. The levels remained unchanged in group I, but decreased in all other groups at month 2, compared with the levels at month 0. The values at month 6 in groups III and IV were similar, but lower compared with the values at months 0 and 2, suggesting that a regular diet, with or without FLC following a high-cholesterol diet, lowers levels of serum glucose.

Serum electrolytes

Changes in serum levels of Na, K, Cl and CO₂ of the four groups are summarized in Table 2. Initial values of serum Na of the four groups were similar. The values at month 2 in groups III and IV were similar to their respective initial values. However, the values at month 2 were lower in group II and were higher in group I, compared with their respective initial values. Also, the values in group I were higher than those in groups II, III and IV. The levels of Na at month 6 in groups III and IV were similar, but higher compared with their respective values at month 2. The values in group III at month 6 were higher than the initial values. The initial values of serum K were similar in all groups and remained unaltered throughout the study period. The initial levels of serum Cl were similar in all the groups, except in group II, where they were lower than in group I. The values at month 2 in groups I, II and IV were similar to their initial values, but the values in group III were higher than the initial values. The values in groups III and IV at month 6 were similar, but were higher than those at month 2. The initial values for serum CO₂ in the four groups were similar and remained unchanged at month 2 in all the groups, except group II, where they decreased significantly compared with the initial values. The levels of CO₂ at month 6 in groups III and IV were similar to the values at month 2. However, the values at month 6 in group IV were higher than those in group III. These results suggested that hypercholesterolemia had practically no effect on serum electrolytes. A regular diet, with or without FLC, following a high-cholesterol diet increased serum Na and Cl to a similar extent, but did not affect serum K or CO₂.

Serum ALT and AST

Changes in the levels of serum ALT and AST of the four groups are summarized in Table 3. The initial values of serum ALT were similar in all groups, except in group IV, where they were higher than in groups I and II. The values remained unchanged in all the groups at months 1 and 2, except in group IV, where they were higher compared with their respective values at month 0. A regular diet, without (group III) or with (group IV) FLC, following a high-cholesterol diet did not affect the serum levels of ALT. Although the values for group IV were higher than those

TABLE 2
Changes in the levels of serum sodium (Na), potassium (K), chloride (Cl) and carbon dioxide (CO₂) in the four experimental groups

	Time (months)						
	0	1	2	3	4	5	6
Groups							
Na (mmol/L)							
I	136.3±4.1	139.8±0.8	141.8±0.9*				
II	136.2±1.2	136.7±0.8 ^{††}	130.5±1.1* ^{†††}				
III	137.3±0.9	134.6±0.6* ^{††}	136.8±0.6 ^{††††}	139.0±0.9 [†]	139.4±0.5 ^{††}	139.3±0.4 ^{††}	140.7±0.7* ^{††}
IV	138.8±1.2	137.7±0.6 ^{††§§}	138.0±0.7 ^{††††}	138.0±0.7	138.9±0.5	139.8±0.5 ^{††§}	141.3±0.5 ^{††§††}
K (mmol/L)							
I	3.7±0.1	3.8±0.2	3.6±0.1				
II	4.1±0.1	3.9±0.1	3.9±0.2				
III	4.0±0.1	3.9±0.1	4.1±0.2	3.8±0.1	4.0±0.1	3.8±0.1	3.8±0.1
IV	4.3±0.2	4.0±0.1	4.0±0.1	3.9±0.1	3.9±0.1	3.9±0.1	3.9±0.1
Cl (mmol/L)							
I	101.8±1.2	104.2±0.5	104.8±1.1				
II	96.3±1.3 ^{††}	98.7±1.4 ^{††}	96.2±0.9 ^{††}				
III	98.6±0.9	100.3±0.9 ^{††}	102.3±1.0* ^{††}	103.8±0.8* [†]	102.4±0.9*	103.5±0.6* [†]	104.9±0.5* ^{†††}
IV	99.2±1.3	100.9±0.6 ^{††}	101.3±0.9 ^{††††}	102.8±0.6* [†]	102.9±0.7* [†]	105.3±0.7* ^{††§†§§}	104.0±0.5* ^{††}
CO₂ (mmol/L)							
I	20.3±1.0	17.2±1.2	17.3±2.2				
II	21.8±1.4	19.7±1.7	17.5±1.0*				
III	18.1±1.3	19.5±0.6	18.2±1.2	19.3±0.8	18.5±0.6	18.8±0.8	16.3±1.0 ^{†§**}
IV	18.4±1.1	20.6±0.8 ^{††}	19.3±0.7	19.3±0.7	19.5±0.7	19.0±0.7	19.3±0.5 ^{§§}

Results are expressed as mean ± SEM. Group I Control; Group II 0.25% cholesterol diet for two months; Group III 0.25% cholesterol diet for two months, followed by a regular diet for four months; Group IV 0.25% cholesterol diet for two months, followed by a regular diet and flax lignan complex, 40 mg/kg per day, for four months. **P*<0.05, month 0 versus other months in the respective groups; [†]*P*<0.05, month 1 versus other months; ^{††}*P*<0.05, month 2 versus other months; [§]*P*<0.05, month 3 versus other months; ^{††}*P*<0.05, month 4 versus other months; ^{**}*P*<0.05, month 5 versus month 6; ^{†††}*P*<0.05, group I versus other groups; ^{††††}*P*<0.05, group II versus other groups; ^{§§}*P*<0.05, group III versus group IV

in group III at month 6, the percentage increases compared with month 2 were 2.40% versus 19.76%, respectively. The percentage increases in the values for groups III and IV at month 6 compared with their respective values at month 0 were similar (24.5% versus 27.3%). The results suggested that serum ALT was not affected by these interventions. The basal values of serum AST were similar in all groups, except in group III, where they were higher than in groups I and II, and in group IV where they were higher than in group II. The values increased in groups II and IV, but remained unchanged in the other groups at month 2. A regular diet, with or without FLC, following a high-cholesterol diet did not affect the serum levels of AST.

Serum ALP and GGT

The changes in the levels of serum ALP and GGT of the four groups are summarized in Table 4. The initial levels of ALP were not significantly different from each other, except in group IV, where the levels were lower than in group III. The values remained unchanged in all the groups at month 2, compared with their respective basal values. Regular diet (group III) following the high-cholesterol diet did not affect the serum levels of ALP until month 6, when the levels decreased significantly. However, regular diet with FLC (group IV) following the high-cholesterol diet progressively reduced the levels significantly, the maximum reduction being at month 6. These results suggest that a high-cholesterol diet does not affect serum levels of ALP, but a regular diet, with or without FLC, following a high-cholesterol diet reduces the levels. The basal levels of serum GGT were similar in all the groups. The levels

decreased in groups I and II, but remained unchanged in groups III and IV at month 2, compared with month 0. A regular diet, with or without FLC, following a high-cholesterol diet did not affect the serum GGT levels. These results suggested that, in general, a high-cholesterol diet, or a regular diet with or without FLC following a high-cholesterol diet, does not affect the serum levels of GGT.

Serum albumin and creatinine

The changes in the levels of serum albumin and creatinine of the four groups are summarized in Table 5. The basal levels of serum albumin were similar in all the groups, except in group II, where they were higher than in group I. The values increased in groups I, III and IV at month 2 compared with month 0, but remained unaltered in group II. A regular diet, with or without FLC, following a high-cholesterol diet did not alter the serum levels of albumin. These results suggested that a high-cholesterol diet, or a regular diet with or without FLC following a high-cholesterol diet, does not alter the serum levels of albumin. The initial values of serum creatinine were similar in all the groups, except in group III, where they were higher than in groups I and II, and in group IV, where they were higher than in group I. The levels increased in all the groups at month 2, compared with month 0. A regular diet, with or without FLC, following a high-cholesterol diet was accompanied by similar increases in serum creatinine from month 2 to month 6 (31.5% versus 25.5%, respectively). These results suggest that serum levels of creatinine increase regardless of diet type.

TABLE 3
Changes in the levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the four experimental groups

	Time (months)						
	0	1	2	3	4	5	6
Groups							
ALT (U/L)							
I	31.2±4.3	47.3±8.3	45.3±5.8				
II	33.0±1.5	46.3±6.1	41.5±4.0				
III	33.1±2.8	29.8±2.2 ^{‡§}	34.4±3.0	37.1±3.3	35.2±2.9	36.3±2.0 [†]	41.2±3.2 [†]
IV	40.3±2.2 ^{‡§}	41.6±2.5 [¶]	50.1±3.9 ^{*¶}	46.3±3.4	49.3±6.4	50.9±3.0 ^{*¶¶}	51.3±3.8 ^{*¶¶}
AST (U/L)							
I	23.0±1.0	27.3±1.4 [*]	27.0±2.2				
II	20.3±2.0	40.8±5.2 ^{*‡}	34.2±2.1 ^{*‡}				
III	28.7±1.2 ^{‡§}	22.1±1.5 ^{*‡§}	33.3±2.9 [†]	36.2±2.5 ^{*†}	30.4±1.5 [†]	32.1±1.7 [†]	34.1±3.0 [†]
IV	25.9±1.2 ^{‡§}	26.2±1.1 ^{§¶}	30.6±1.2 ^{*†}	27.5±1.7 [¶]	27.7±1.9	27.8±1.8	32.3±2.2 ^{*†}

Results are expressed as mean ± SEM. Group I Control; Group II 0.25% cholesterol diet for two months; Group III 0.25% cholesterol diet for two months, followed by a regular diet for four months; Group IV 0.25% cholesterol diet for two months, followed by a regular diet and flax lignan complex, 40 mg/kg per day, for four months. ^{*}P<0.05, month 0 versus other months in the respective groups; [†]P<0.05, month 1 versus other months; [‡]P<0.05, group I versus other groups; [§]P<0.05, group II versus other groups; [¶]P<0.05, group III versus group IV

TABLE 4
Changes in the levels of serum alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT) in the four experimental groups

	Time (months)						
	0	1	2	3	4	5	6
Groups							
ALP (U/L)							
I	173.0±29.5	202.3±15.7	173.8±18.2				
II	118.0±12.6	164.3±16.7 [*]	118.0±12.7 [†]				
III	211.3±31.3	193.3±22.7	193.1±33.5	170.5±46.9	135.9±56.7	110.3±47.4	92.7±43.6 ^{*†}
IV	136.9±8.2 ^{‡‡}	148.0±10.9 ^{††}	128.8±15.0	88.4±8.1 ^{*†‡}	56.8±6.0 ^{*†‡§}	43.1±4.5 ^{*†‡§}	35.0±4.5 ^{*†‡§¶}
GGT (U/L)							
I	11.7±0.5	10.3±1.1	9.2±0.3 [*]				
II	10.0±0.4	12.3±0.8 [*]	6.3±0.7 ^{*†}				
III	11.3±1.1	10.0±0.6	10.2±0.7	9.5±0.8	9.5±0.8	8.9±0.8	11.3±1.1
IV	12.1±0.8	9.5±0.4 [*]	10.5±0.7	10.8±0.8	11.1±0.9	10.1±0.7	12.6±1.0 ^{*†**}

Results are expressed as mean ± SEM. Group I Control; Group II 0.25% cholesterol diet for two months; Group III 0.25% cholesterol diet for two months, followed by a regular diet for four months; Group IV 0.25% cholesterol diet for two months, followed by a regular diet and flax lignan complex, 40 mg/kg per day, for four months. ^{*}P<0.05, month 0 versus other months in the respective groups; [†]P<0.05, month 1 versus other months; [‡]P<0.05, month 2 versus other months; [§]P<0.05, month 3 versus other months; [¶]P<0.05, month 4 versus other months; ^{**}P<0.05, month 5 versus month 6; ^{††}P<0.05, group I versus other groups; ^{‡‡}P<0.05, group III versus group IV

DISCUSSION

The results of this study indicated that a high-cholesterol diet (0.25% cholesterol) elevated the levels of serum cholesterol, which is consistent with previous findings (7-9). The results showed that hypercholesterolemia reduced serum glucose levels, and that short-term use of a regular diet, with or without FLC, further reduced the levels of serum glucose. The exact reason for the hypercholesterolemia-induced reduction in serum glucose is not known. It is possible that cholesterol increases the levels of glucagon-like peptide-1, which enhances insulin secretion from the pancreatic cells (10), leading to hypoglycemia. Glucagon-like peptide-1 secretion is closely associated with concentrations of bile acids (11). Bile acids are water-soluble components of bile derived from cholesterol metabolism. Hypercholesterolemia may increase the synthesis of bile acids. A further decrease in serum glucose levels on a regular diet, with or without FLC, following a high-cholesterol diet cannot be explained.

Hypercholesterolemia did not affect serum electrolytes. A regular diet, with or without FLC, following the high-cholesterol diet increased serum Na and Cl to similar extents, suggesting that FLC had no deleterious effects on serum electrolytes. Hypercholesterolemia did not affect total CO₂ content. The CO₂ content decreased in groups on the regular diet following the high-cholesterol diet, while it remained unaltered in groups on the regular diet with FLC, suggesting that FLC prevented acidemia.

The initial levels of serum ALT, AST and ALP were not similar among any of the groups. These differences cannot be explained. Serum levels of ALT, AST, ALP and GGT were practically unaltered by the high-cholesterol diet. Similar changes in serum AST, ALT and ALP (12), in AST and ALT (13,14), and in ALP (15) with hypercholesterolemia have been reported. However, increases in serum ALP (13), AST (15,16) and ALT (16) with hypercholesterolemia have been reported. These differences could be caused by differences in the levels of

TABLE 5
Changes in the levels of serum albumin and creatinine in the four experimental groups

	Time (months)						
	0	1	2	3	4	5	6
Groups							
Albumin (g/L)							
I	18.7±0.3	20.4±0.5*	20.5±0.5*				
II	19.7±0.2 [¶]	19.8±0.3	20.8±0.8				
III	19.0±0.5	18.9±0.2 ^{¶**}	21.3±0.6* [†]	21.8±0.6* [†]	22.1±0.7* [†]	22.0±0.4* [†]	22.5±0.4* [†]
IV	19.4±0.3	19.9±0.2 ^{††}	21.3±0.2* [†]	21.2±0.3* [†]	21.5±0.4* [†]	21.3±0.5* [†]	21.7±0.4* [†]
Creatinine (µmol/L)							
I	55.3±2.7	83.5±4.3*	106.7±3.2* [†]				
II	65.2±3.8	94.2±4.3*	114.3±3.0* [†]				
III	77.8±2.5 ^{¶**}	77.7±3.1**	104.8±4.5* [†]	115.3±3.8* [†]	120.5±3.4* ^{††}	122.4±4.4* ^{††}	131.6±5.9* ^{††§}
IV	74.2±3.0 [¶]	73.8±2.6**	97.6±3.3* **	108.0±3.6* ^{††}	117.8±4.2* ^{††}	117.7±4.0* ^{††}	128.4±5.4* ^{††§}

Results are expressed as mean ± SEM. Group I Control; Group II 0.25% cholesterol diet for two months; Group III 0.25% cholesterol diet for two months, followed by a regular diet for four months; Group IV 0.25% cholesterol diet for two months, followed by a regular diet and flax lignan complex, 40 mg/kg per day, for four months. **P*<0.05, month 0 versus other months in the respective groups; [†]*P*<0.05, month 1 versus other months; ^{††}*P*<0.05, month 2 versus other months; [§]*P*<0.05, month 3 versus other months; [¶]*P*<0.05, group I versus other groups; ***P*<0.05, group II versus other groups; ^{†††}*P*<0.05, group III versus group IV

serum cholesterol, and the duration of hypercholesterolemia. Increases in AST and ALT have been observed with a 0.5% cholesterol diet (14). Unaltered levels of serum GGT have been observed in hyperlipidemic patients (15). A regular diet, with or without FLC, following a high-cholesterol diet did not alter the serum levels of ALT, AST or GGT. A regular diet with FLC, following a high-cholesterol diet, markedly reduced the serum levels of ALP. Regular diet without FLC, following the high-cholesterol diet, did not reduce the levels of serum ALP.

ALP is found in many tissues, with the highest concentrations in the liver, biliary tract epithelium, bone and intestinal mucosa (17). FLC seems to protect these organs from injury. AST is found in several organs and tissues, including the liver, heart, skeletal muscles and red blood cells (17). ALT is found predominantly in the liver, with a moderate-sized component in the kidneys, and small quantities in the heart and skeletal muscles (17). In general, most of the elevation in ALT is due to liver disease, although significant damage in the other above-mentioned organs may also affect its serum levels. GGT is located mainly in liver cells, to a lesser extent in the kidneys, and to a much smaller extent in the biliary tract epithelium, intestines, brain, pancreas and spleen (17). GGT has better overall sensitivity than either ALP or AST in liver disease (17). The results of the present study suggested that short-term hypercholesterolemia, and a regular diet with or without FLC following a high-cholesterol diet, have no deleterious effects in the liver, kidneys, heart, bone or small intestines.

Diets with or without high cholesterol produced increases in serum albumin to a similar degree. A regular diet, with or without FLC, following a high-cholesterol diet did not affect the levels of serum albumin. Albumin is synthesized in the liver, so most acute or chronic destructive liver diseases result in decreased serum albumin (17). Mild hypoalbuminemia occurs in most acute and chronic diseases. The results in the present study suggested that neither hypercholesterolemia, nor a regular diet with or without FLC, have deleterious effects on the liver.

Serum creatinine levels increased to a similar extent in all the groups. A regular diet, with or without FLC, following a high-cholesterol diet increased the levels of serum creatinine to a similar extent, suggesting that FLC had no effect on the serum

levels of creatinine. Creatinine is a metabolic product of creatine phosphate dephosphorylation in muscle. It is present at a fairly stable serum level. Excretion occurs through a combination of glomerular filtration (70% to 80%) and tubular secretion (18). The increase in the levels of serum creatinine may therefore be due to a combination of these two factors. Because the increases in the levels of serum creatinine were similar in the control rabbits and the hypercholesterolemic rabbits, and in the groups on a regular diet with and without FLC, the increases in serum levels of creatinine may be due to increased production of creatinine, and not due to renal damage.

CONCLUSION

A short-term high-cholesterol diet reduced serum levels of glucose, but did not alter serum levels of electrolytes, CO₂, ALT, AST, ALP, GGT, albumin or creatinine. Short-term use of a regular diet, with or without FLC, following a high-cholesterol diet reduced the serum levels of total cholesterol and glucose, increased serum levels of Na, Cl and creatinine, and had no effect on the levels of serum K, CO₂, ALT, AST, GGT and albumin. An FLC diet, following a high-cholesterol diet, markedly reduced the serum levels of ALP, while a regular diet following a high-cholesterol diet did not alter the serum levels of ALP. Short-term use of FLC did not have deleterious effects on the liver, kidneys, skeletal muscles, intestines or bone.

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