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Department of Laboratory Animal Science, State University, Utrecht, and Department of Human Nutrition, Agricultural University, Wageningen, The Netherlands

Increased concentrations of liver cholesterol in rats fed lactulose

(Short communication)

A. C. BEYNEN

The disaccharide lactulose (β-D-galactopyranosyl-(1-4)-D-fructofuranose) is thought to be poorly hydrolized by intestinal enzymes but is broken down by microorganisms in the colon. Thus lactulose shares with pectin similar characteristics [1]. Lactulose is used in the food industry and in the treatment of constipation. There is preliminary evidence that dietary lactulose (5%, w/w) causes increased concentrations of serum and liver cholesterol in rats when compared with pectin [2]. This paper describes dose-response relationships between dietary lactulose and cholesterol in either serum or liver.

Material and methods

Female rats of an outbred Wistar strain (Cpb/WU) were used. The animals were housed individually exactly as described [3]. At the age of 7 weeks the animals were divided into 7 dietary groups consisting of 6 rats each. The groups had similar distributions of serum cholesterol concentration and body weight; the mean values were 2.28 mmol/l and 157 g.

The basal diet consisted of (g/100 g): casein, 21; corn oil, 5; coconut fat, 15; corn starch, 24; sucrose, 25; cellulose, 2; dicalcium phosphate, 2.9; sodium chloride, 0.6; magnesium carbonate, 0.3; magnesium oxide, 0.2; potassium bicarbonate, 1.8; vitamin premix, 1.2 and mineral premix, 1.0. The composition of the vitamin and mineral premix has been described [4]. Cholesterol (1%, w/w) was added at the expense of corn starch. Lactulose (Duphalac®, Duphar BV, Amsterdam, The Netherlands) was added to diets containing cholesterol at levels of 2.5, 5, 10 or 20% (w/w) at the expense of sucrose. These concentrations refer to dry weights of lactulose; the lactulose syrup contained 66.7% (w/w) of active principle. Thus the lactulose diets contained somewhat more water than the basal diet. Pectin (10%, w/w) was also exchanged for the sucrose component of the diet. All diets were in meal form. Food and water were provided ad libitum. The experimental period lasted 28 days.

Blood samples were taken in the non-fasting state under light diethyl-ether anesthesia between 08.00 and 10.00 h. Serum total cholesterol was measured enzymatically using the kit (Monotest®) supplied by Boehringer-Mannheim GmbH, Mannheim, F.R.G. At the end of the experiment, the anesthetized rats were killed by decapitation and the livers removed. Liver cholesterol was extracted and analyzed as described [5].

Results and discussion

Lactulose at concentrations up to 10% of the diet did not affect body weight of the rats (Table 1). Feed intake was somewhat increased but this may be explained by the higher water content of the lactulose diets. However, 20% of lactulose in the diet diminished body-weight gain. This is probably associated with the slight diarrhoea and lower feed intake that were observed in the rats fed the diet containing 20% of lactulose. Lactulose tended to increase liver weight when added to the diet at levels up to 10%.

Cholesterol feeding caused a marked increase in serum cholesterol (Table 1). Lactulose at dietary levels higher than 2.5% somewhat reduced the cholesterol-induced increase in serum cholesterol but was not as effective as 10% of pectin in the diet. The addition of cholesterol to the diet resulted in a dramatic increase in liver cholesterol. As has been shown earlier [6, 7], dietary pectin partly counteracted the rise in liver chol-

Table 1
Effect of dietary lactulose on performance and serum and liver cholesterol in rats

Dietary supplements	Body weight [g]	Feed intake [g/day]	Liver weight [g]	Serum cholesterol [mmol/l]	Liver cholesterol [μmol/g]
None	209 ± 21	13.4 ± 0.8	9.1 ± 1.0	2.6 ± 0.3	4.8 ± 0.3
1% C	208 ± 23	13.4 ± 1.7	10.4 ± 1.8	4.2 ± 0.5	37.4 ± 20.0
1% C + 2.5% L	211 ± 13	13.6 ± 0.8	10.6 ± 0.9	4.4 ± 0.6	55.4 ± 13.0
1% C + 5% L	217 ± 27	14.2 ± 2.1	11.3 ± 1.6	3.8 ± 0.8	51.8 ± 19.1
1% C + 10% L	214 ± 12	14.6 ± 0.5	11.5 ± 0.7	3.9 ± 0.2	58.9 ± 12.9
1% C + 20% L	195 ± 15	12.9 ± 0.7	10.1 ± 0.6	3.9 ± 0.8	59.5 ± 10.6
1% C + 10% P	206 ± 10	13.7 ± 0.8	10.2 ± 0.4	3.5 ± 0.4	28.7 ± 15.2

Cholesterol (C) was added to the basal diet at the expense of corn starch. Lactulose (L) and pectin (P) were exchanged for the sucrose component of the diet. Results are expressed as means ± SD for 6 rats per dietary group

esterol seen after cholesterol feeding. In contrast, lactulose further increased liver cholesterol concentrations in cholesterol-fed rats. This effect of lactulose was already observed at amounts in the diet as low as 2.5%, and thus may be considered rather specific. It is clear that the fermentable carbohydrates pectin and lactulose influence cholesterol metabolism in a different manner.

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Prof. dr. A. C. Beynen, Department of Laboratory Animal Science, State University, P. O. Box. 80.166, 3508 TD Utrecht, The Netherlands

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