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Further Studies on Relation of Fat to Utilization of Lactose in Milk.*

E. J. SCHANTZ AND C. F. KREWSON. (Introduced by E. B. Hart.)

From the Department of Biochemistry, College of Agriculture, University of Wisconsin, Madison, Wis.

It was found in our laboratory¹ that rats placed on a whole milk diet mineralized with iron, copper, and manganese made very efficient use of the milk sugar but when placed on a mineralized skim milk diet 20-30% of the ingested galactose was lost in the urine. Natural fats such as lard, corn oil, coconut oil, and linseed oil could be substituted for butter fat in the milk without loss of galactose. Synthetic triglycerides such as palmitin and olein were effective while caproin was not effective in preventing the loss of galactose in the urine.

In view of these results it was thought advisable to test the effectiveness of several other triglycerides including odd chain fatty acids. It was also considered advisable to feed salts of the lower fatty acids and high levels of glucose along with skim milk.

Experimental Effect of Even Chain Triglycerides. The triglycerides of caproic, caprylic, capric, and lauric acids were synthesized from the crude acids obtained from Eastman Kodak Company. These glycerides were homogenized into fresh skim milk at a level of 4%. The metabolism experiments were performed on rats weighing between 100 and 140 g and which had been raised on mineralized whole milk. The animals were placed on a skim milk diet until they began to lose considerable galactose in the urine, which required 10-12 days. At this time 24 hour metabolism periods were run on the rats receiving the synthetic triglycerides homogenized into the skim milk. The results obtained show that caproin, caprylin, and caprin were not effective within a 10-day period in preventing any appreciable loss of galactose but laurin was quite effective. These same animals stopped losing galactose in the urine within 3 or 4 days when corn oil was substituted in the skim milk. The 18 carbon keto acid, licanic, was also fed and found to be effective.

* Published with the approval of the Director of the Wisconsin Agricultural Experiment Station. These studies were aided in part by grants from the Wisconsin Alumni Research Foundation and the Works Progress Administration.

¹ Schantz, E. J., Elvehjem, C. A., and Hart, E. B., *J. Biol. Chem.*, 1938, **122**, 381.

Effect of Feeding Odd Chain Acids. The glyceride of margaric acid, which had been isolated from natural sources¹ was fed in skim milk, and it was found to be quite effective in preventing the loss of galactose. Since Schrinier, Fulton, and Burks² have pointed out that an equimolecular mixture of palmitic and stearic may be mistaken for margaric acid and that a mixed melting point is not conclusive evidence for identification, it was considered advisable to feed a synthetic odd chain acid. Pentadecylic acid was synthesized³ and the triglyceride made and fed with skim milk. A slight response was obtained in some cases but no definite and lasting effect was noticed in preventing the loss of galactose in the urine.

Effect of Various Salts. Since some difficulty was encountered in feeding the lower triglycerides due to liberation of free acid in the milk, the sodium salts of caproic, caprylic, and capric acids were fed at levels of 4% in skim milk. These salts did not stop the loss of galactose in the urine but in some cases tended to increase the excretion of galactose. Feeding 2 per cent of NaCl or Na₂HPO₄ in the skim milk increased the excretion of galactose as much as 20%. The action of KCl was similar but not as pronounced as NaCl or Na₂HPO₄. The feeding of these salts with whole milk caused some animals to lose small amounts of sugar in the urine.

Effect of Feeding High Levels of Glucose. Previously it was reported¹ that feeding glucose along with the skim milk prevented some loss of galactose in the urine of some animals. Later it was

TABLE I.
Effect of Various Fatty Acids, Salts, and Glucose on Galactose Metabolism.

Substance	Level Fed, %	Effectiveness
Caproin	4	Very slight, if any
Caprylin	4	" " " "
Caprin	4	" " " "
Lauric acid	4	Good response
Licanic acid	4	" "
Margarin	4	" "
Pentadecylin	4	Poor response
Na salt of caproic acid	4	" "
Na " of caprylic acid	4	" "
Na " of capric acid	4	" "
NaCl	2	Increased excretion of galactose
Na ₂ HPO ₄	2	" " " "
KCl	2	" slightly in some cases
Glucose	8	Very slight
"	10	" "

† Obtained as a gift from R. W. Clark, Pharmacy Department, University of Wisconsin.

² Schrinier, R., Fulton, J., and Burks, D., Jr., *J. Am. Chem. Soc.*, 1933, **55**, 1194.

³ Krewson, C. F., Doctorate Thesis, University of Wisconsin, now being compiled.

deemed advisable to replace the calorific value of the fat with glucose, which would require feeding 8% of glucose. Glucose was fed at levels of 8 and 10% in the skim milk and the galactose excretion decreased 10 to 30%. The sugar excreted in the urine on high levels of glucose was non-fermentable.

A summary of the results obtained is shown in Table I.

It is apparent from these experiments that the fatty acids of 12 carbon atoms or more are the most effective in preventing the loss of galactose in the urine. No explanation can be offered until more is known about how the fatty acids function in galactose metabolism.

The contradiction between the results obtained with margaric acid and pentadecylic acid may be explained by the fact that the margaric acid which was isolated from natural sources may have been a eutecic mixture of even chain acids.

The fact that Na_2HPO_4 , and NaCl increased the excretion of galactose is surprising in view of the fact that McQuarrie, Tompson, and Anderson⁴ found that sodium salts caused a decrease in glycosuria in diabetic children. Crabtree and Longwell⁵ found that rats on a high salt diet containing glucose deposited almost twice as much liver glycogen as rats on a low NaCl diet. This phenomenon has not been further investigated by us, but it points again to the difference between the metabolism of galactose and glucose.

Feeding high levels of glucose in skim milk to replace the calorific value of the fat apparently does not take the place of fat. It is very likely that the small decrease in the excretion of galactose when glucose was fed was due to the retarding action of glucose upon the absorption of galactose.

Conclusions. Even chain fatty acids containing 12 carbon atoms or more when fed with skim milk to the extent of 3 to 4% were effective in preventing the loss of galactose in the urine while acids with less than 12 carbon atoms were not effective in preventing this loss. An odd chain fatty acid (pentodecylic) was not effective in preventing loss of galactose. Feeding glucose at levels of 8 and 10% in skim milk did not prevent the loss of galactose.

The excretion of galactose was increased as much as 20% by feeding 2% of NaCl or Na_2HPO_4 in the skim milk. KCl was not as effective in increasing the excretion of galactose as NaCl or Na_2HPO_4 . These salts caused some excretion of galactose on whole milk diets.

⁴ McQuarrie, I., Tompson, W. H., and Anderson, J. A., *J. Nutrition*, 1935, **11**, 77.

⁵ Crabtree, D. G., and Longwell, B. B., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 705.