respect to calcium, except for the change due to pH shift during cheesemaking. During ultrafiltration, some of the polyvalent ions are detained by the membrane, but when the permeate is concentrated to recover the lactose, calcium phosphate solubility is quickly exceeded, whereupon crystals form. These crystals obviously contaminate the lactose crystals, and since their solubility is low, they cannot be removed by simply washing.

One solution, as proposed in the Danish Sugar Corporation LTD(DDS) process (Nicolaisen, 1975), is to replace the calcium with sodium or, in special cases, with potassium, using an ion exchanger before concentration is started and thus avoid precipitation of calcium salts. Figure 10 is a flow sheet for lactose production by this sytem. Other possibilities include lowering the pH in order to increase the solubility of the calcium salts or to form soluble complexes through addition of polyphosphates. In general, calcium phosphates are more soluble in cold solutions than in hot, so it might be possible to remove the precipitated calcium salts from the hot concentrated permeate before cooling it to crystallize the lactose.

Other research on the chemistry of lactose recovery concerns crystallization kinetics. Crystallization is faster at higher levels of supersaturation, but if supersaturation becomes too high, it creates new nuclei rather than just accelerating the growth of existing crystals. Growth also is accelerated at higher temperatures, but that reduces the level of supersaturation. Current knowledge does not allow us to control these factors to optimize crystallization rate and yield. More data are needed on new approaches to make lactose recovery rapid and economically feasible. Lactose chemistry will continue to be involved also in creating new potential uses for the increased production of lactose that will surely come.

LITERATURE CITED

Cerbulis, J., *J. Agric. Food Chem.* **21**, 255 (1973).
Corbett, W. M., Kenner, J., *J. Chem. Soc.*, 2245 (1953).
Fries, D. C., Rao, S. T., Sundarelingam, M., *Acta Crystallogr., Sect. B* **27**, 994 (1971).
Fritts, K. L., M.S. Thesis, University of California, Davis, 1974.
Gale, R. L., Beebe, R. A., *J. Phys. Chem.* **68**, 555 (1964).
Kiselev, A. V., Yashin, Y. I., "Gas-Adsorption Chromatography", translated by J. E. S. Bradley, Plenum Press, New York, 1969, pp 11–141.
Lee, I., Nickerson, T. A., Bernhard, R. A., *J. Dairy Sci.* **58**, 319 (1975).
McMullin, S. L., Bernhard, R. A., Nickerson, T. A., *J. Agric. Food Chem.* **23**, 452 (1975).
Nickerson, T. A., Dolby, R. M., *J. Dairy Sci.* **54**, 1212 (1971).
Nicolaisen, B., *Nord. Mejeri-Tidsskr.* **41**(4), 125 (1975).
Olano, A., Nickerson, T. A., Bernhard, R. A., *J. Food Sci.* **42**, 1481 (1977a).
Olano, A., Nickerson, T. A., Bernhard, R. A., *J. Food Sci.* **42**, 1484 (1977b).
Parry, R. M. Jr., in "Fundamentals of Dairy Chemistry", Webb, B. H., Johnson, A. H., Alford, J. A., Ed., Avi Publishing Co., Westport, CT, 1974, p. 609.
Reger, J. V., *Cereal Sci. Today* **3**(10), 270 (1958).
Rosensweig, N. S., *Am. J. Clin. Nutr.* **28**, 648 (1975).
Swartz, M. L., Bernhard, R. A., Nickerson, T. A., *J. Food Sci.* **43**, 93 (1978).
Wright, J. A., M.S. Thesis, University of California, Davis, 1974.

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Effects of Age and Lactose Tolerance on Blood Glucose Rise with Whole Cow and Lactose-Hydrolyzed Milk

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Lactose malabsorption and associated milk rejection are reported in many populations. Prehydrolysis of the lactose may be important in making milk digestible to such groups. Forty-eight low-income black children 5–9 years of age had absorption studies to determine the change in glucose with 2 g of lactose/kg, 236 mL of unmodified unflavored whole cow milk (WCM) (<12 g of lactose), and >90% lactose-hydrolyzed milk (LHM) (≤1.0 g of lactose). Twenty subjects were absorbers and 28 were malabsorbers. No significant differences in blood glucose rise are noted in absorbers between 236 mL of WCM or LHM. The difference in the 28 malabsorbers was a blood glucose rise of 10.9 mg/100 mL with WCM and 17.8 mg/100 mL in LHM ($P < 0.005$). Differences between the two milks increase with age. Below 8 years of age there are no significant differences in the blood glucose rise with either milk in the nine malabsorbers tested. In the 13 children 8 years of age or over, the difference between a rise in glucose of 9.5 mg/100 mL and 18.1 mg/100 mL with WCM and LHM is significant ($P < 0.01$). Results indicate increased glucose absorption with LHM. The difference between WCM and LHM becomes significant with increased age.

Lactose malabsorption can be identified in major population groups throughout the world.

The prevalence of lactose malabsorption ranges from 70–90% in some adult populations studied in Africa, Asia, Latin America, and the United States. In white populations of Western Europe and the United States, the prevalence ranges from 10 to 15%. Children studied in similar populations demonstrate an increasing prevalence of malabsorption from the age of weaning.

In Third World countries such as Peru, Thailand, and Uganda, lactose malabsorption is noted in approximately 25% of the population by 2 years of age (Figure 1). By 5 years of age, almost 50% of the children studied are

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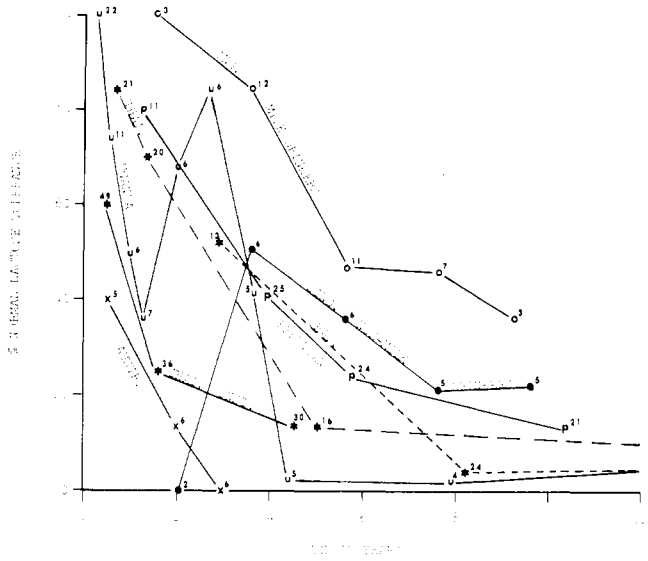

Figure 1. Normal lactose tolerance. Age-specific prevalence of lactose intolerance in developing countries. The groups reading from top to bottom are as follows: Singapore (Bolin et al., 1970), Thais (Flatz et al., 1969), Peruvian Metizos (Paige et al., 1972), Thais (Keusch et al., 1969), Ugandans (Cook, 1967), Thais (Keusch et al., 1969), Australian Aborigines (Elliott et al., 1967). Sample size is noted.

unable to adequately digest a lactose load (Paige et al., 1972; Bolin et al., 1970; Flatz et al., 1969; Keusch et al., 1969; Cook, 1967; Elliott et al., 1967).

In the United States, it was assumed that lactose malabsorption occurred at a later age. While few subjects below 5 years of age had been studied, it was presumed that improved environmental factors served to retard the onset of malabsorption in preschool children (Wotecki et al., 1976).

Recent data by our group demonstrate that 29% of United States black preschool children below 5 years of age are lactose malabsorbers (Paige et al., 1977). By 8 years of age, 59% are malabsorbing lactose and the proportion increases to 74% by 12 years of age (Paige, 1977).

The increasing prevalence of lactose malabsorption has raised questions with respect to its influence on milk drinking. Yet, controversy still surrounds this issue (Garza and Scrimshaw, 1976; Jones et al., 1976; Stephenson and Latham, 1974).

While Garza and Scrimshaw (1976) were unable to find an association between intolerance to 8 oz. of milk and intolerance noted as a result of a lactose tolerance test in 4–9-year olds, they did report symptoms in some black children with 480 mL of milk. Reddy and Pershad (1972), studying Indian children, were unable to demonstrate symptoms in subjects fed skim milk at 1 g of lactose/kg of body weight, but were able to provoke symptoms with 2 g/kg. Mitchell et al. (1975) have demonstrated symptoms with the consumption of 8 oz. of milk in 7 of 13 (54%) black adolescent malabsorbers. The symptoms were, however, less severe than those experienced with a 50-g test dose. Leichter (1973) found similar results in lactose intolerant adults following the consumption of 500 mL of skim milk.

It is becoming increasingly clear that attention must be diverted from the simplistic consideration of the presence or absence of symptoms with the consumption of a glass of milk, to objective considerations of the level of nutrient absorption. Reports on disparate populations of varying ages under different test conditions only serve to obscure the critical question; that is, whether or not there is interference with the absorption of milk.

It is the purpose of this paper to report on the level of blood glucose rise in black children consuming 236 mL of whole cow milk and lactose-hydrolyzed milk and the effect of age upon carbohydrate absorption.

PROCEDURE

Population. Forty-eight black children, ranging in age from 3 years, 8 months to 9 years, 11 months with a mean age of 7.3 years, were studied. There were 28 siblings included among the study subjects. Thirty-two children were female; 16 were male. All subjects were in good health as determined by history and a review of recent clinic visits. They were free of any overt intestinal or allergic disorders with no recent history of gastroenteritis. Formal written consent was obtained on all subjects from the parent or guardian.

All families of the study subjects were residing in census tracts in the lowest socioeconomic decile of Baltimore City. The mean annual income of black families in this area was $2688; 64.0% of the families living below the poverty level (U.S. Bureau of the Census, 1972) were medical assistance or public welfare recipients. Eighty-five percent of all persons ≥25 years of age had less than 12 years of formal education. Fifty-three percent of all women ≥14 years of age were single, separated, divorced, or widowed.

Lactose Tolerance Test. Lactose tolerance tests were performed in the morning after an overnight fast. Lactose, as a 20% suspension in water, was given orally at a rate of 2 g/kg of body weight. Microcapillary blood samples were obtained at 0, 15, 30, and 60 min. True glucose was determined by the *o*-toluidine method (Dubowski, 1962). A blood glucose rise of less than 26 mg/100 mL over fasting levels was considered a flat tolerance curve.

Clinical signs associated with the ingestion of the lactose load, such as loose stools, gas and cramping occurring during the test and for 1 h following the completion of the test, were noted and recorded by trained observers.

Following the lactose tolerance test, the subjects were studied on alternative days to determine blood glucose levels following the consumption of 236 mL of whole cow milk and lactose-hydrolyzed milk.

Lactose Hydrolysis. Hydrolysis was carried out by preheating raw milk to a temperature ranging from 70 to 100 °F, which was subsequently treated with the enzyme lactase derived from *Saccharomyces lactis*. The enzyme was dissolved in 960 mL of water and agitated by electric mixer at low speed. The resulting solute containing 125–150 ppm was added to 200 gal of raw milk and agitated for 5–10 min. The milk was then permitted to set for 36–48 h to allow for hydrolysis prior to pasteurization and homogenization.

The hydrolyzed milk had approximately 90% of the lactose converted into its component monosccharides, glucose and galactose. Experience in previous studies has demonstrated a stepwise increment in blood glucose absorption in malabsorbers when hydrolysis is increased from 50 to 90% (Paige et al., 1975).

The lactose-hydrolyzed milk was analyzed following the preparation of each solution to determine and document the level of hydrolysis. The levels were measured by oxidation using an Enzymac analyzer for determining lactose and glucose levels.

Some variation in hydrolysis does exist but is limited to narrow range from 91.0 to 96.5% (1.0 to 0.39 g of lactose/236 mL of milk).

Following an 8-h fast, the children were given the refrigerated test milks in a random manner. The technologist was not aware which milk was being tested. The

Table I. Lactose Tolerance Test (Lactose 2 g/kg)

	no.	%	age, years	Δ max. blood glucose rise, mg/100 mL
all subjects	48	100	7.28	22.8 (±14.8)
absorbers (≥26 mg/100 mL)	20	41.7	7.33	37.2 (±8.7)
malabsorbers (<26 mg/100 mL)	28	58.3	7.25	12.4 (±7.8)

milk was consumed immediately following the drawing of the fasting blood sugar. The testing procedure was similar to that previously described.

The presence or absence of symptoms associated with the lactose challenge was noted by trained and experienced observers during the test and for 1 h following its completion.

RESULTS

Lactose Tolerance Test. The blood glucose rise in the 48 subjects studied was 22.8 mg/100 mL. Of the 48 subjects, 20 (42%) were categorized as absorbers and demonstrated a mean maximum glucose rise of 37.2 mg/100 mL. Twenty-eight subjects (58%) were malabsorbers with a mean maximum glucose rise of 12.4 mg/100 mL (Table I).

Symptoms associated with the tolerance test were noted in four of the 48 (8%) children studied. One of the 20 (5.0%) absorbers evidenced symptoms with the test. Among malabsorbers, three out of 28 (10.7%) experienced symptoms. The association of symptoms with the test was infrequent and variable, with no significant differences between malabsorbers and absorbers.

The glucose rise over fasting levels following a lactose challenge of 2 g/kg is 22.8 (±14.8) mg/100 mL for all study subjects. The glucose rise following the consumption of 236 mL of unflavored whole cow milk providing 11.1 g of lactose was 11.9 (±8.5) mg/100 mL. The rise in glucose in the same children following consumption of 236 mL of lactose-hydrolyzed milk was 17.5 (±11.5) mg/100 mL. The difference is significant at the 0.01 level.

When the subjects are dichotomized by absorber and malabsorber, the mean glucose rise in the 28 malabsorbers with a lactose tolerance test is 12.4 (±7.8) mg/100 mL. In the same group, a mean rise of 10.9 (±7.2) mg/100 mL is noted with whole cow milk and a mean rise of 17.8 (±10.8) mg/100 mL with hydrolyzed milk. The difference in maximum glucose rise between whole cow milk and lactose-hydrolyzed milk is significant at the 0.005 level.

The 20 absorbers have a peak glucose rise of 37.2 (±8.7) mg/100 mL with a lactose challenge and a rise of 13.4 (±10.1) mg/100 mL with whole cow milk. The glucose rise with lactose-hydrolyzed milk is 17.1 (±12.7) mg/100 mL. There is no statistically significant difference between these two latter values (Table II).

A progressive decrement in the level of blood glucose rise following the consumption of 236 mL of whole cow milk is seen with increasing age. The level of 14.1 mg/100 mL below 8 years of age decreases to 9.5 mg/100 mL after 8 years of age. Glucose levels with consumption of the 236 mL of lactose-hydrolyzed milk do not, however, demonstrate similar decrements. The glucose level below 8 years of age is 17.0 mg/100 mL, while above 8 years of age, it is 18.1 mg/100 mL. The difference at 8 years of age and above is significant between the whole and hydrolyzed milks (Figure 2).

This increase in glucose rise with lactose-hydrolyzed milk parallels declining lactase activity with age as reflected by decreasing glucose levels following a lactose challenge. There is no significant association of increased symptoms with decreasing blood glucose levels following a lactose tolerance test and a whole cow milk challenge.

Table II. Test Results Blood Glucose (mg/100 mL)

	LTT	WCM	LHM
lactose challenge	2 g/kg	<12.0 g	≤1.0 g
all subjects (n = 48)	22.8 (±14.8)	11.9 (±8.5)	17.5 (±11.5)[a]
absorbers (≥26 mg/100 mL; n = 20)	37.2 (±8.7)	13.4 (±10.1)	17.1 (±12.7)[b]
malabsorbers (<26 mg/100 mL; n = 28)	12.4 (±7.8)	10.9 (±7.2)	17.8 (±10.8)[c]

[a] Student's t test (WCM/LHM): $P < 0.01$. [b] Student's t test: $P > 0.20$. [c] Student's t test: $P < 0.005$.

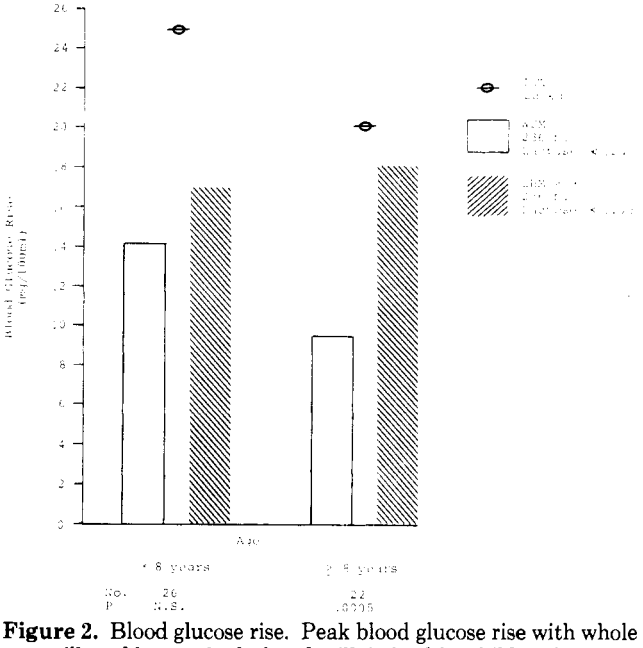

Figure 2. Blood glucose rise. Peak blood glucose rise with whole cow milk and lactose-hydrolyzed milk in healthy children less than and equal to or greater than 8 years of age. Glucose rise with a standard lactose challenge is also noted.

DISCUSSION

The high prevalence of lactose malabsorption on a worldwide basis is acknowledged. Its onset after weaning is clear. An association between lactose malabsorption and increasing milk rejection appear established. The use of symptoms associated with the consumption of a glass of milk to identify a youngster at-risk for incomplete nutrient absorption appears equivocal at best.

Data presented suggest that the steady decline in lactase activity which begins at weaning becomes clinically manifest by 8 years of age in a large segment of the United States black population. By this age, lactase levels have declined to a point whereby 59% or more of the children studied are lactose malabsorbers.

Garza and Scrimshaw also report a steady increase in the age specific prevalence of lactose intolerance. In fact, the authors reported 11% intolerance below 6 years of age while 72% of their black children were lactose intolerant at 8 years of age or above.

In association with the increasing pattern of lactose malabsorption, our study has demonstrated that glucose levels achieved with the consumption of whole cow milk and lactose-hydrolyzed milk are somewhat parallel below 8 years of age. After 8 years of age, however, the glucose levels become significantly different, demonstrating increased glucose absorption with 90% lactose-hydrolyzed

milk compared to a declining level of absorption with whole cow milk.

LITERATURE CITED

Bolin, T. D., Davis, A. E., Seal, C. S., Chua, K. L., Young, V., Kho, K., Siak, D. L., Jacob, E., *Gastroentrology* **59**, 117 (1970).
Cook, G. C., *Br. Med. J.* 1, 527 (1967).
Dubowski, K. M., *Clin. Chem.* 8, 215 (1962).
Elliott, R. B., Maxwell, G. M., Vawser, N., *Med. J. Aust.* **1**, 46 (1967).
Flatz, G., Saegudom, D., Sanguanbkokai, T., *Nature (London)* **221**, 758, (1969).
Garza, C., Scrimshaw, N. S., *Am. J. Clin. Nutr.* **29**, 192 (1976).
Jones, D. V., Latham, M. D., Kosikowski, F. V., Woodward, G., *Am. J. Clin. Nutr.* **29**, 633 (1976).
Keusch, G. T., Troncale, F. J., Miller, L. H., Promadhat, V., Anderson, P. R., *Pediatrics* **43**, 540 (1969).
Leichter, J., *Am. J. Clin. Nutr.* **26**, 393 (1973).
Mitchell, K. J., Bayless, T. M., Paige, D. M., Goodgame, R. W., Huang, S. S., *Pediatrics* **56**, 718 (1975).
Paige, D. M., Leonardo, E., Nakashima, J., Adrianzen, T. B., Graham, G. G., *Am. J. Clin. Nutr.* **25**, 467 (1972).
Paige, D. M., Bayless, T. M., Huang, S. S., Wexler, R., in "Physiological Effects of Food Carbohydrates", Allene, J., Hodge, J., Eds., American Chemical Society, Washington, DC, 1975, pp 191–206.
Paige, D. M., Bayless, T. M., Mellits, E. D., Davis, L., *Am. J. Clin. Nutr.* **30**, 1018 (1977).
Paige, D. M., "Hydrolyzed Milk: A Solution for Lactose Intolerance", presented at the 37th Annual Meeting of the Institute of Food Technologists, Philadelphia, PA, June 6, 1977.
Reddy, V., Pershad, J., *Am. J. Clin. Nutr.* **25**, 114 (1972).
Stephenson, L. S., Latham, M. C., *Am. J. Clin. Nutr.* **27**, 296 (1974).
U.S. Bureau of the Census, Department of Commerce, Washington, DC, April 1972.
Wotecki, C. E., Weser, E., Young, E. A., *Am. J. Clin. Nutr.* **29**, 19 (1976).

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Food Additives Derived from Lactose: Lactitol and Lactitol Palmitate

John A. van Velthuijsen

Lactitol is prepared by hydrogenation of a lactose solution at about 100 °C with a Raney nickel catalyst. After purification a lactitol syrup is obtained, which is crystallized. A crystalline lactitol monohydrate and a noncrystallizing lactitol syrup are the end products. The properties and applications as well as biological data and toxicity studies of lactitol are described. Lactitol palmitate is prepared by direct esterification with fatty acids of edible fats in such a way that formation of anhydropolyols is minimized. The reaction is carried out at a relatively low temperature of about 160 °C with soaps of the fatty acids as catalyst. The lactitol esters can be used as emulsifiers in foods or as detergents.

The title of this paper is, strictly speaking, somewhat optimistic; lactitol and lactitol palmitate are not yet officially approved as Food Additives by the Food and Drug Administration or the FAO/WHO.

In this study it will be shown, however, that these lactose-based derivatives have interesting potentialities as food additives. Pure lactose is abundantly available as edible or pharmaceutical grade; a considerable amount of lactose is produced in the Netherlands with an annual production of 65 000 tons in 1975. The world production of lactose is about three times as big, whereas the lactose potentially available from all the whey in the world, there is a potential availability of 3–4 million tons of lactose per annum.

LACTITOL

Preparation. The preparation of lactitol by hydrogenation of lactose with a nickel catalyst is already known for a long time (Karrer and Büchi, 1937; Wolfram et al., 1938). Lactitol can be prepared by reduction of lactose with sodium borohydride (Scholnick et al., 1975), but technically lactitol is prepared by hydrogenation of a lactose solution at about 100 °C with a Raney nickel catalyst. As lactitol is produced essentially in the same way from lactose as sorbitol is produced from glucose, only a short summary of the reaction conditions is mentioned here. The reaction is carried out in an autoclave under a pressure of 40 atm or more. Due to the lower solubility of lactose, compared to glucose, the lactose concentration at the beginning of the reaction is only 30–40 wt %. When the hydrogenation reaction is completed, the catalyst is sedimented and filtrated and the lactitol solution is purified by ion-exchange resins and activated carbon. The purified lactitol solution is then concentrated by evaporating the water, the obtained syrup is crystallized, and the crystals are separated with a centrifuge and finally dried. The lactitol mother liquor is concentrated again, giving more crops of the lactitol monohydrate. The final mother liquor can be used as a 64% solution or in mixtures with sorbitol to prepare a noncrystallizing lactitol syrup at a concentration of 70%.

Chemical and Physical Properties. Lactitol is a sugar alcohol, derived from lactose by reduction of the glucose part of this disaccharide. Synonyms for lactitol are lactit, lactosit, and lactobiosit. Lactitol ($C_{12}H_{24}O_{11}$, mol wt = 344) has the structural formula illustrated in Figure 1. The systematic name is 4-β-D-galactopyranosyl-D-sorbitol. On hydrolysis the molecule is split into D-galactose and D-sorbitol, both occurring widely in nature. Due to the absence of a carbonyl group, lactitol is chemically more stable than the related disaccharides like lactose. The stability of lactitol in the presence of alkali is markedly higher than that of lactose. Heating for 1 h at 100 °C of

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