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Lactose Chemistry

Thomas A. Nickerson*

The importance of lactose in the overall problem of whey utilization and disposal has led to greater interest in all aspects of lactose chemistry. Three general areas of research are discussed—complexing with metal ions, adsorption of volatile compounds, and development of efficient crystallization processes. Anhydrous forms of lactose have been shown to adsorb a large variety of volatile compounds. Within a homologous series, the amount adsorbed increased with increase in chain length. Heats of adsorption and structure of volatile compounds were used to explain mode of adsorption by different forms of lactose. CaO can be used to precipitate sucrose from molasses (Steffen process) and has been shown to remove lactose from whey, lactose being more readily complexed than sucrose under similar conditions. By proper control of the reaction, over 90% of the lactose can be recovered as an insoluble calcium–lactose complex. Lactose was shown to combine with many cations in a one-to-one ratio, but no complexing could be demonstrated with K^+ and NH_4^+. With the commercialization of reverse osmosis and ultrafiltration processes, the feasibility of using the permeate for crystallization of lactose is being investigated, but calcium phosphate is a problem. Attempts are being made to improve the lactose recovery process.

Lactose, the carbohydrate of milk, is except for milkfat produced by a few breeds, the major constituent in milk. It normally forms over 50% of the solids in the skimmilk portion and an even greater portion of the solids in whey. Thus, in whey utilization and disposal we are concerned largely with lactose utilization and disposal, which accounts for much of the increased interest in lactose in recent years. The other major reason for increased interest in lactose is the problem of lactose intolerance (Rosensweig, 1975).

The importance of lactose in the overall problem of whey utilization and disposal has led to greater interest in all aspects of lactose chemistry. Developments in three general areas of research are reviewed in this paper: adsorption of volatiles on lactose, complexing of metal ions with lactose, and crystallization processes for recovery of lactose.

ADSORPTION OF FLAVORS

Lactose has served as an extender for spices and volatile aromas (Reger, 1958). At one time it was used in the manufacture of instant coffee to adsorb volatiles during roasting and drying. When this lactose was incorporated into the coffee powder the flavor was improved. Some other food uses of lactose are based on its ability to accentuate flavors in conjunction with its low sweetness level. However, there has been a lack of experimental evidence to illustrate this point.

In an attempt to measure flavor adsorption quantitatively, Nickerson and Dolby (1971) measured adsorption

of diacetyl by lactose and other selected sugars. They found that the form (type) of lactose had a marked influence on its adsorption capacity. Regular α-hydrate powder, for example, adsorbed much less diacetyl than did the anhydrous forms. Converting the hydrate to the anhydrous forms of α- or to β-lactose increased the quantity of diacetyl adsorbed under a standard set of conditions.

Lee et al. (1975) investigated adsorption by stable anhydrous α-lactose of three homologous series of normal aliphatic alcohols, methyl esters, and methyl ketones. The amount adsorbed varied greatly, but was related linearly with the increase in chain length within a homologous series. Adsorbed in greatest quantity were the alcohols, followed by the methyl esters and, then the methyl ketones (Figure 1). Adsorption was from a flowing gas stream at 25 °C with nitrogen as the carrier gas. As the boiling point within a homologous series increased, the amount adsorbed also increased (Figure 2).

McMullin et al. (1975) expanded the number of organic compounds to include aldehydes and hydrocarbons as well as alcohols, esters, and ketones, and measured the heats of adsorption when these compounds were adsorbed by stable anhydrous α-lactose. The heats of adsorption were calculated from the retention times measured at five different temperatures. A plot of $\ln t_{corr}$ against reciprocal absolute temperature yields a straight line, and the heat of adsorption can be calculated from the slope of the line (Gale and Beebe, 1964). Heats of adsorption on lactose ranged from about 6 to 18 kcal/mol for the compounds studied (Figure 3). The functional group of a molecule was important in determining the heat of adsorption, with alcohols having considerably higher heats than the other

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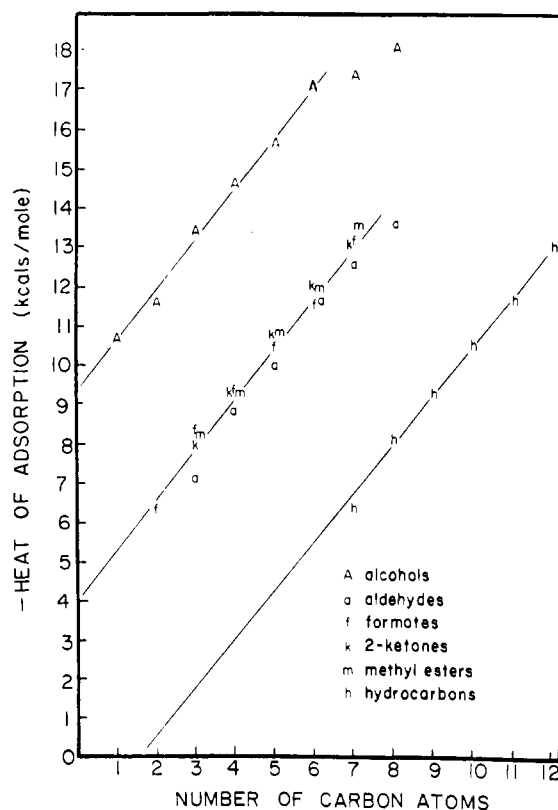*J. Agric. Food Chem.*, Vol. 27, No. 4, 1979 **673**
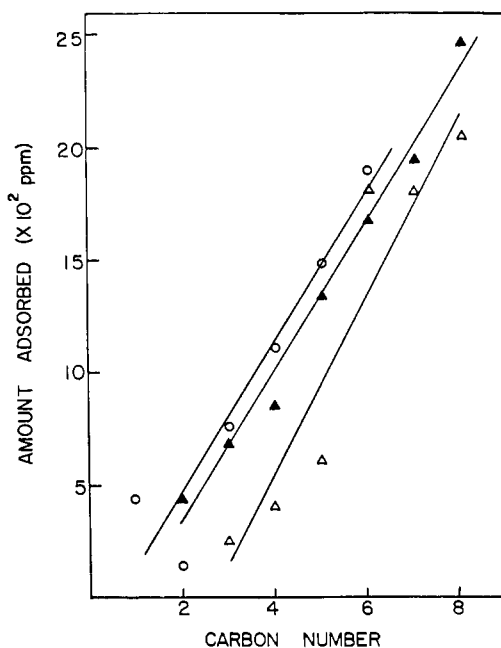
Figure 1. Relationship of chain length of a homologous series to the adsorption of volatile compounds by stable anhydrous lactose (▲) methyl esters, (△) methyl ketones, (○) alcohols.
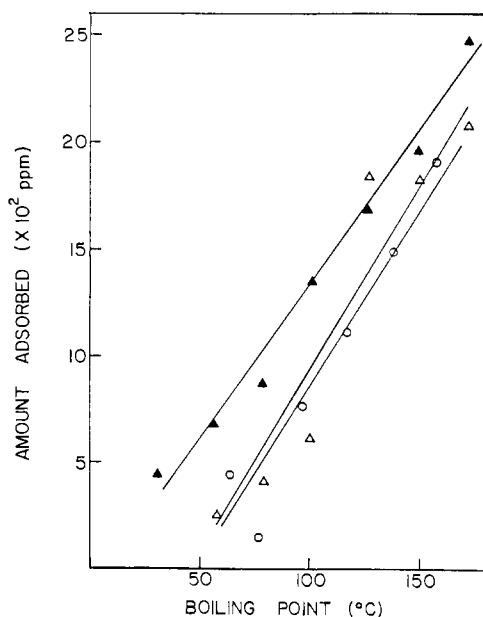
Figure 2. Relationship of the boiling point of a homologous series to the adsorption of volatile compounds by stable anhydrous α-lactose: (▲) methyl esters, (△) methyl ketones, (○) alcohols.

Figure 3. Heats of adsorption on stable anhydrous α-lactose vs. number of carbon atoms in the molecule.

Table I. Interactions between Lactose and Adsorbates

adsorbate	type of interaction
hydrocarbons	nonspecific interaction, van der Waals type
esters, aldehydes, and ketones	van der Waals attraction, as with hydrocarbons; plus alignment of dipoles, possible small specific interaction; plus hydrogen bond between oxygen on adsorbate and lactose hydroxyl group proton
alcohols	van der Waals attraction; plus alignment of dipoles, as above; plus hydrogen bond, as above; plus second hydrogen bond, involving alcoholic proton and oxygen on lactose; minus possible decrease in stability due to strained ring from simultaneous formation of two hydrogen bonds

compounds and hydrocarbons considerably lower heats.

The strength of adsorption is determined by the sum of the interactions between the adsorbent and the adsorbate and hence is reflected in the heat of adsorption. On the basis of these values and the structure of the compounds involved, McMullin et al. (1975) suggest that the saturated hydrocarbons adsorb on lactose by van der Waals attraction only, giving a minimum heat of adsorption for a given number of carbon atoms. Aldehydes, ketones, and esters have heats of adsorption about 6 kcal/mol higher than the heats for hydrocarbons of an equal number of carbon atoms. Those workers reason that a hydrogen bond likely forms between the lactose and these types of compounds [group B by Kiselev and Yashin's (1969) classification]. Since the alcohols have heats of adsorption on lactose which are an additional 5

kcal/mol above those of the B group, alcohols must undergo yet another specific intersection with lactose, supposedly another hydrogen bond. Thus, the interactions between lactose and the adsorbates can be summarized as shown in Table I.

Using similar procedures, Fritts (1974) determined heats of adsorption on β-lactose. All the compounds studied except the hydrocarbons showed higher heats of adsorption on β-lactose than had been found on stable anhydrous α-lactose (Figure 4). That could not be explained on the basis of particle size or surface area. The greater heats of adsorption found on β-lactose may be accounted for, at least partly, by the β configuration of the anomeric carbon atom. The equatorial hydroxyl group in the β configuration (Fries et al., 1971) is suggested as allowing an additional possibility for hydrogen bonding. All of the compounds that had higher heats of adsorption on β-lactose are postulated to adsorb to the lactose surface via hydrogen bonding. The hydrocarbons did not show higher heats of adsorption on β-lactose, and van der Waals forces
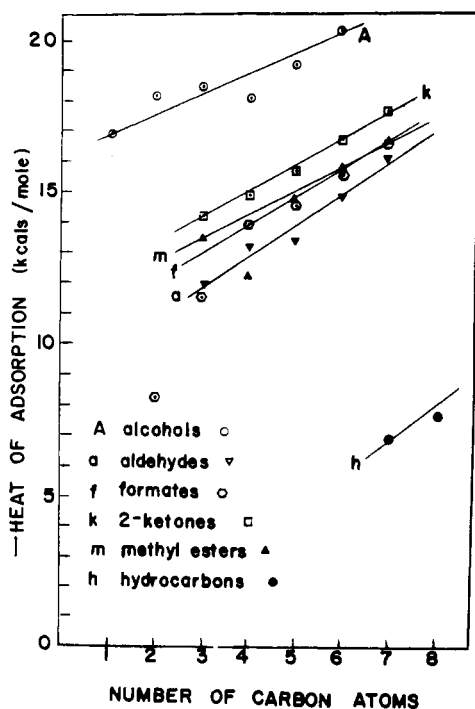
Figure 4. Heats of adsorption on β-lactose vs. number of carbon atoms in the molecule.

Table II.   Equations for Predicting Heat of Adsorption on Lactose[a]

adsorbed compound	stable, anhyd. α-lactose, kcal/mol	β-lactose, kcal/mol
alcohols	$-\Delta H = 1.32n + 9.21$	$-\Delta H = 0.65n + 16.3$
esters, aldehydes, ketones	$-\Delta H = 1.31n + 3.84$	$-\Delta H = 0.95n + 10.2$
hydrocarbons	$-\Delta H = 1.30n - 2.54$	$-\Delta H = 1.12n - 1.0$

[a] $-\Delta H$ = heat of adsorption, n = number of carbon atoms.

alone are suggested as the adsorption mechanism in this case.

Equations for predicting the heat of adsorption on stable anhydrous α- and on β-lactose were derived from carbon number and reactive group, as shown in Table II.

Adsorption of compounds under static conditions has also been studied. Lee et al. (1975) found much higher adsorption values under static than under dynamic or flowing conditions, but longer times were required to reach equilibrium at these higher levels. Wright (1974) used this method to measure adsorption of compounds in mixtures and to study stability during storage.

Simple mixtures of organic molecules involving two, four, or eight components exhibited various amounts of adsorption, depending upon the number and types of other compounds. Further, rates of desorption were discontinuous during a 10-month storage period (Figure 5). As the number of compounds in the adsorbing mixture is increased, the amount adsorbed of each individual component decreased, indicating a finite number of adsorption sites on the lactose surface. More research is needed in this area and on adsorption of specific odors and flavors.

COMPLEXING OF LACTOSE WITH METAL IONS

Various carbohydrates have been known to complex with alkaline-earth metal hydroxides. This reaction is the basis for the Steffen process for recovery of sucrose from beet
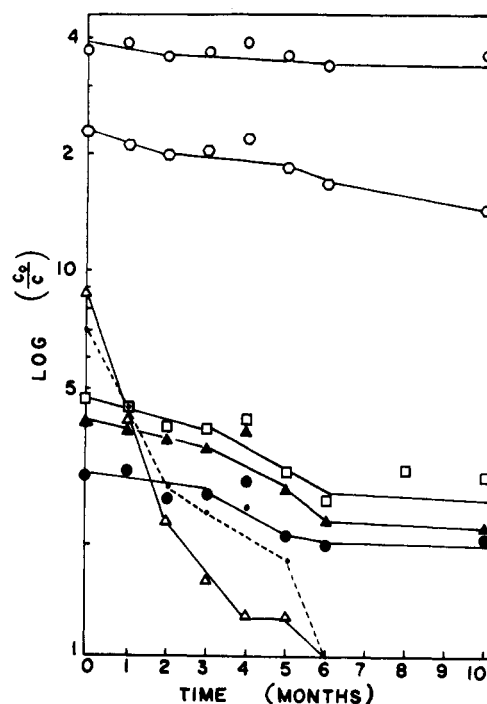

Figure 5. Log (C_0/C) vs. storage time for seven compounds of an eight-component mixture. (O) 1-Hexanol, ($\circ$) cyclohexanol, ($\triangle$) 1-butanol, ($\square$) ethyl hexanoate, (▲) hexyl acetate, (●) heptyl acetate, (·) 2-heptanone (propylbenzene did not adsorb).
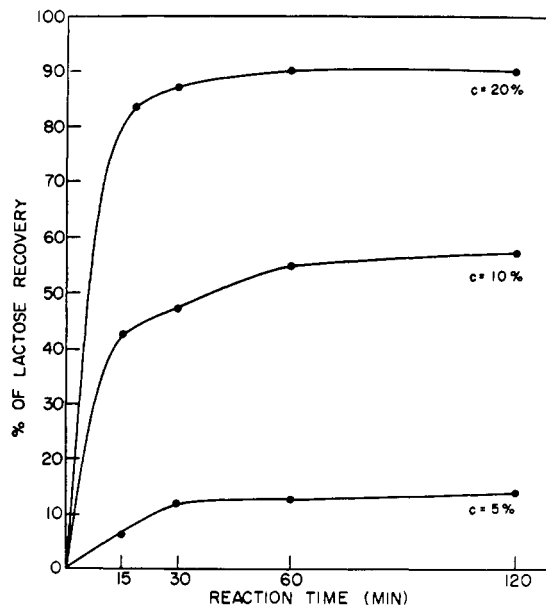
Figure 6. Recovery of lactose with $Ca(OH)_2$ powder; g of $Ca(OH)_2$/g of lactose = 0.60.

sugar molasses. Using CaO, Cerbulis (1973) applied the Steffen process successfully to the recovery of lactose from whey. This reaction suggests possibilities for improving lactose recovery processes, and further study is warranted by the importance of improved whey utilization.

Calcium oxide has been used traditionally in the Steffen process since the saccharate is postulated as being adsorbed on the surface of colloidal unhydrated lime. Olano et al. (1977a), however, showed that powdered slaked lime, $Ca(OH)_2$, is satisfactory in recovering lactose and is more convenient, economical, and less hazardous than CaO.

Figure 6 shows that the percentage recovery of lactose in the calcium precipitate depends directly on the initial concentration of lactose in the solution. When the Ca-

Table III. Addition of NaOH[a] to the
Ca(OH)$_2$-NH$_4$Cl-Lactose Solution[b]

NH$_4$Cl[c]	distribution of lactose, %	
	precipitate	solution
0.5	37.5	62.4
1.0	74.3	25.6
2.0	88.5	11.4
3.0	90.6	9.3

[a] 40 mmol/100 mL of solution. [b] Initial lactose concentration was 5% (w/v). [c] Grams of NH$_4$Cl/100 mL of solution.

Table IV. Addition of NaOH[a] to
Ca(OH)$_2$-NH$_4$Cl-Lactose Solution[b]

NH$_4$Cl[c]	distribution of lactose, %	
	precipitate	solution
0.0	65.2	34.3
0.5	75.2	24.7
1.0	84.3	15.6
2.0	91.2	8.7
3.0	93.3	6.6
4.0	92.5	7.4
5.0	91.9	8.0
6.0	83.3	16.6

[a] 40 mmol/100 mL of solution. [b] Initial lactose concentration was 10% (w/v). [c] Grams of NH$_4$Cl/100 mL of solution.

(OH)$_2$/lactose ratio was as high as 1.2 (w/w), the mixture became very viscous and a considerable volume of liquid was retained by the filter cake. When the Ca(OH)$_2$/lactose ratio was 0.6 (w/w), however, the system was easy to handle and assured adequate calcium in the system. Although the reaction between Ca(OH)$_2$ and lactose was nearly complete within the first 30 min, it continued slowly for several hours. The reaction temperature was kept below 10 °C because higher temperatures destroyed lactose under the high pH of the system (Corbett and Kenner, 1953). Cerbulis (1973), for example, recovered 30% less lactose at 25 °C than at 3–5 °C.

Adding NH$_4$Cl increased the solubility of Ca(OH)$_2$ but did not decrease the quantity of lactose–calcium hydroxide complex recovered in the precipitate. Tables III and IV show that over 90% of the lactose can be recovered by optimizing the quantities of alkali and NH$_4$Cl in the system.

The complex can be produced also by adding NaOH to solutions containing CaCl$_2$ and lactose. Since the solubility of the complex increased as the concentration of CaCl$_2$ increased, it was necessary to increase the NaOH to recover the lactose in the precipitate (Tables V and VI). The ratio of lactose/Ca(OH)$_2$ in the precipitate depends strictly on the initial lactose/NaOH ratio in the solution when the CaCl$_2$ is held constant. The optimum lactose CaCl$_2$ ratio under our conditions was 1.25 (5% lactose, 4% CaCl$_2$).

When the initial concentration of lactose in solution was increased, the solubility of the complex increased, requiring a greater amount of alkali before precipitation occurred. Therefore, more alkali was needed to obtain the same percentage of lactose recovery. On the other hand, higher initial concentrations of lactose resulted in greater lactose recovery under optimum conditions (Table VI).

Since the solubility of the lactose–Ca(OH)$_2$ complex is decreased by adding organic solvents to the system, they permit greater recovery of the lactose (Olano et al., 1977b). Addition of 10% solvent in the total volume gave a considerable increase in recovered lactose. Acetone was more effective than alcohol (ethanol or methanol) (Figure 7). When the solvent was increased to 20% of the final

Table V. Effect of CaCl$_2$ Concentration on the Recovery of Lactose from Solution

initial concn,[a] g/100 mL		lactose recov. in the precip., %	mol Ca(OH)$_2$/ mol lactose in the precip.
NaOH	CaCl$_2$		
1.1	2	21.5	1.3
	3	21.5	1.3
	4	21.3	1.4
	6	5.2	1.2
	8	0.0	
1.6	4	69.1	1.5
	6	58.7	1.6
	8	41.7	1.7
2.1	4	85.2	1.8
	6	77.7	1.8
	8	67.5	1.9
2.4	4	90.0	2.0
	6	86.9	2.0
	8	83.0	2.1

[a] Initial lactose concentration was 5% (w/v) for all the experiments.

Table VI. Influence of Lactose Concentration on the Recovery of Lactose from Solution[a]

initial concn, g/100 mL		lactose recov. in the precip., g	mol Ca(OH)$_2$/ mol lactose in the precip.
NaOH	lactose		
1.2	5.0	0.52	1.2
	7.5	0.0	
	10.0	0.0	
2.1	5.0	3.37	1.9
	7.5	3.88	1.4
	10.0	0.52	1.2
2.4	5.0	4.15	2.1
	7.5	5.38	1.5
	10.0	4.26	1.2
3.2	7.5	6.81	1.9
	10.0	8.03	1.5

[a] Initial concentration of CaCl$_2$ was 8% (w/v) for all experiments.
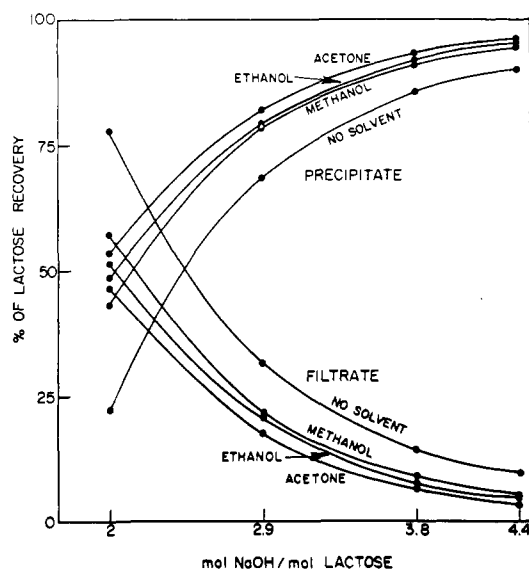

Figure 7. Effect of the presence of 10% organic solvent on the recovery from 5% lactose solution.

volume, recovery of the lactose was almost complete, with all three solvents being equally effective (Figure 8).
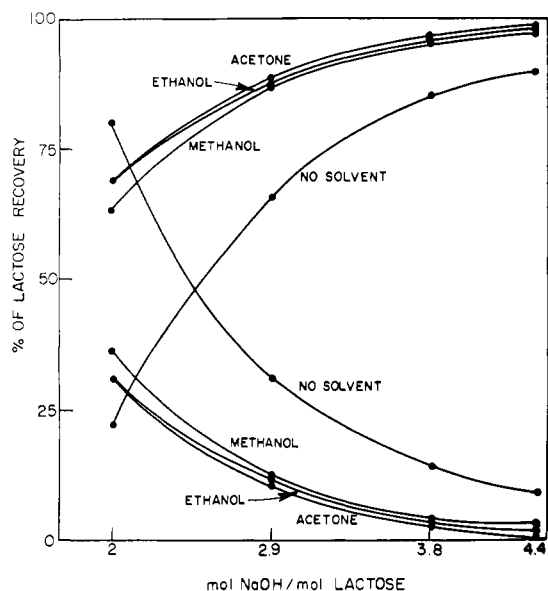
Figure 8. Effect of the presence of 20% organic solvent on the recovery of lactose from 5% lactose solution.

Since barium hydroxide has been used to recover sucrose from molasses, some experiments were repeated with $BaCl_2$ used in place of $CaCl_2$. No precipitate formed on addition of alkali, however, showing that the Ba complex is much more soluble than the Ca complex. Even adding as much acetone as 20% of the final volume gave much lower recovery of lactose than $CaCl_2$ gave under similar conditions. In other experiments with alkali-earth metals, results with lactose are often very much different from these with sucrose, as seen here with barium.

Binding between lactose and metal salts was investigated by Swartz et al. (1978) by measuring the change in specific rotation. The specific rotation of complexes was determined by saturating a lactose solution with salts until 100% of complex was formed, then the amount of complex in various mixtures was calculated from the observed rotation. Equilibrium constants were found to be 0.205 M^{-1} for lactose with Ca^{2+}, 0.379 M^{-1} for lactose with Li^+, and 0.527 M^{-1} for lactose with Na^+. Except for K^+ and NH_4^+, lactose combined with metal salts in a ratio of 1:1 for all cations studies (Ca^{2+}, Ba^{2+}, Sr^{2+}, Fe^{2+}, Mg^{2+}, Zn^{2+}, Na^+, and Li^+) as shown in Figure 9.

DEVELOPMENTS IN LACTOSE RECOVERY

With the commercialization of reverse osmosis and ultrafiltration processes, whey protein concentrates are being produced, but so are large volumes of permeate. The permeate still represents 90–95% of the original whey volume. Since the protein has been removed, potential uses in foods and feeds have also been greatly reduced, so that disposal of permeate is looked upon as a greater problem than disposal of whey.

Availability of permeate, however, has stimulated interest in lactose production since lactose is the major solid remaining in the permeate and also the major constituent causing disposal problems, because of its high biological oxygen demand. With removal of the whey proteins, a more suitable medium is produced for manufacture of lactose because the protein normally interferes with the crystallization and recovery steps. The permeate is similar to the whey originally used in Europe for lactose production, where the proteins were removed by heat coagulation before condensing to cause lactose crystals to develop. The permeate would therefore appear to be a logical medium for lactose production. However, there is

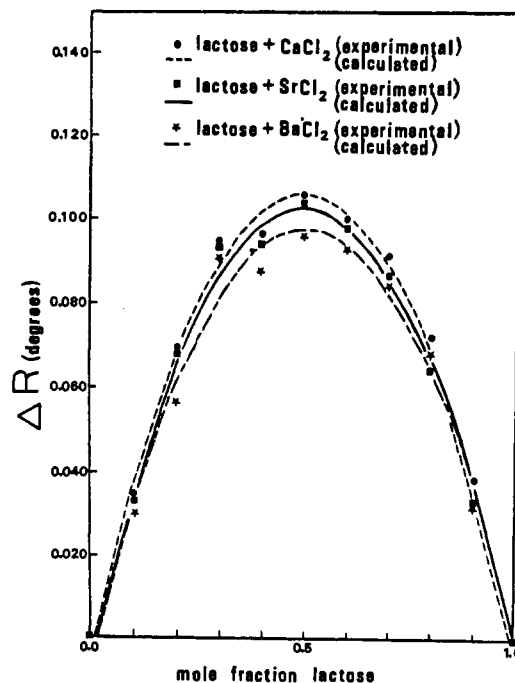**Figure 9.** Change in optical rotation vs. mole fraction lactose for $CaCl_2$, $SrCl_2$, and $BaCl_2$.
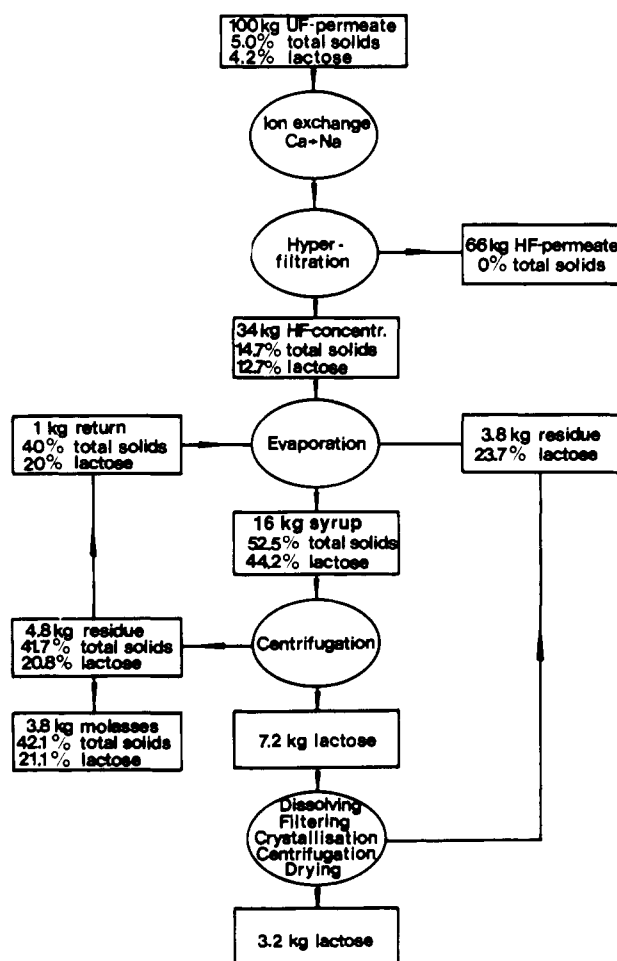

Figure 10. DDS flow sheet for production of lactose. The Danish Sugar Corporation Ltd. (DDS) process.

one major problem—calcium phosphate.

Milk contains about 30 mM of calcium/L, of which 10 mM is soluble (diffusible) but only 2–3 mM is ionized (Parry, 1974). Thus, whey is essentially saturated with

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.

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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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