International Journal of Pharmaceutics, 28 (1986) 229–238
Elsevier

IJP 00956

Studies on tableting properties of lactose. IV. Dissolution and disintegration properties of different types of crystalline lactose

H.V. van Kamp [1], G.K. Bolhuis [1], K.D. Kussendrager [2] and C.F. Lerk [1]

[1] *Laboratory for Pharmaceutical Technology and Dispensing, University of Groningen, 9713 AW Groningen and* [2] *DMV, P.O. Box 13, 5460 BA Veghel (The Netherlands)*

(Received August 26th, 1985)
(Accepted October 8th, 1985)

Key words: tablets – α-lactose monohydrate – anhydrous α-lactose – β-lactose – dissolution – disintegration

Summary

In this study the relationship between the dissolution properties of different types of crystalline lactose and the disintegration of tablets, containing these lactoses, was investigated. Tablets, compressed from either α-lactose monohydrate or crystallized β-lactose disintegrated very quickly in water, as a result of rapid liquid uptake and fast dissolution of the bonds. Tablets compressed from anhydrous α-lactose did not disintegrate at all when brought into contact with water, but dissolved during the disintegration procedure. This effect, which was shown to be caused by poor water penetration into the tablets, is attributed to a combination of both small pore diameters and precipitation in the pores of dissolved anhydrous α-lactose as α-lactose monohydrate, in the course of the penetration process. This precipitation is an effect of the smaller initial solubility of α-lactose monohydrate compared with that of anhydrous α-lactose. The same phenomenon could be seen for tablets containing roller-dried β-lactose when they were compressed at high forces. In this case the poor disintegration of the tablets is attributed to the combination of the presence of about 20% anhydrous α-lactose in roller-dried β-lactose and the small pore diameters in the tablets.

Introduction

From a pharmaceutical point of view, lactose is probably the most widely used diluent in tablet formulations. Lactose is a disaccharide, produced by isolation from cow's milk, in which the concentration is about 4.6%. The most common, commercially available form is α-lactose monohydrate. It is generally used in powdered form as a filler for tablets, prepared by means of wet granulation techniques. Sieved crystalline fractions of α-lactose monohydrate, like the 100 mesh quality, have excellent flow properties and for that reason α-lactose monohydrate is used in direct compression systems (Gillard et al., 1972; Bolhuis and Lerk, 1973). However, the moderate binding properties need the incorporation of a good dry binder (Delattre and Jaminet, 1974; Lerk et al., 1974). The binding properties of hydrous lactose could be improved by spray-drying (Gunsel and Lachman, 1963) or by conversion into a granulated form (Tablettose) (Shangraw et al., 1981).

Another form of lactose, which has been especially designed for direct compression, is anhydrous lactose (Batuyios, 1966). The commonly used type is anhydrous lactose with a high β-content. The

Correspondence: G.K. Bolhuis, Laboratory for Pharmaceutical Technology and Dispensing, University of Groningen, Ant. Deusinglaan 2, 9713 AW Groningen, The Netherlands.

commercial products consist of a granulation of extremely fine crystals, produced by roller-drying, subsequent breaking up and sieving (Shangraw et al., 1981). The resultant particle structure presents a large surface for binding, resulting in good compressibility. The flow properties of the rather irregular particles were found to be less than optimum, however (Bolhuis and Lerk, 1973). A product that has been marketed recently is anhydrous lactose with a high α-content. It is prepared by dehydration of α-lactose monohydrate (Lerk et al., 1983). In comparison with anhydrous lactose having a high β-content, the anhydrous product having a high α-content has about the same binding properties. Due to its more regular form and smaller particle size distribution, however, it has better flow properties (Bolhuis et al., 1985).

Although the binding and flow properties of the different types of lactose have been studied extensively, little attention has been paid to the effect of the presence of lactose on the disintegration time of tablets. As there are great differences between the initial solubilities of different kinds of lactose (Van Kreveld, 1969) and since it is known that excipients with a high water solubility are able to increase the disintegration time of tablets (Lerk et al., 1979; Graf et al., 1982), it could be expected that the choice of the lactose would have a marked effect on tablet disintegration.

The first three studies in this series were dealing with the consolidation and binding properties of different types of crystalline lactose (Vromans et al., 1985a and b; De Boer et al., submitted for publication).

The aim of this work was to study the relation between the dissolution properties of different types of crystalline lactose and the disintegration of the tablets made.

Materials and Methods

Materials

The lactoses used were: (i) α-lactose monohydrate 100 mesh (α/β ratio 96.5 : 3.5); (ii) anhydrous α-lactose (DCLactose 30) (α/β ratio 82.5 : 17.5); (iii) crystallized (anhydrous) β-lactose (α/β ratio 3 : 97); and (iv) roller-dried (anhydrous) β-lactose (DCLactose 21) (α/β ratio 19 : 81).

The crystallized β-lactose was prepared by crystallization from a saturated lactose solution by evaporation at boiling temperature. After addition of hot glycerol and filtration of the crystals at about 100°C, the crystals were washed subsequently with ethanol and acetone and dried. The other types of lactose were commercial products, supplied by DMV, Veghel, The Netherlands. Alcohol Eur.Ph. and methylcellulose 400 mPa's Eur.Ph. were obtained from Lamers and Indemans, 's-Hertogenbosch, The Netherlands. Dried dimethylsulfoxide pro analysis quality was supplied by E. Merck, Darmstadt, F.R.G.

Methods

α/β ratio. The α/β ratio of the lactose was determined according to the GLC method of Buma and Van der Veen (1974).

Initial solubility. The initial solubility of the different types of lactose was determined by pouring 150 g of α-lactose or 225 of β-lactose by means of a vibrating feeder in a 600 ml beaker containing 300 g of water of 37 $\pm$ 0.5°C, which was stirred with a high speed mixer at 600 rpm. The dissolved fraction was determined refractometrically.

Preparation of tablets. Tablets were prepared by manually introducing 500 mg of the lactose into a 13 mm die of a punch and die assembly, mounted between the plates of a hydraulic press (Hydro Mooi, Appingedam, The Netherlands). The tablets were compressed at a specific load with both a compression and a decompression rate of 2 kN/s. The die was prelubricated by compression of a magnesium stearate tablet.

Tablet porosity and pore volume. Tablet porosity and pore volume were calculated from the tablet weight and volume and the density of the material, as measured with an air comparison pycnometer (model 930, Beckman Instruments, Fullerton, CA).

Crushing strength and disintegration time. The crushing strength of the tablets was measured, using a motorized instrument (model E-2, Dr. K. Schleuninger, Zürich, Switzerland). The data given are the mean of at least 5 tablets. The disintegration time was measured, using the Eur.Ph. proce-

dure without disks. If not otherwise stated, water was used as a test fluid. Other disintegration media used were: dried dimethylsulfoxide, alcohol and a 1% methylcellulose solution in water, having a viscosity of 51 ± 1 mPa's. The data given are the mean of the disintegration time of 5 individual tablets.

Penetration of liquid into the tablets. Alcohol penetration into the tablets was performed at 0°C as described earlier (Lerk et al., 1979). The penetration data given are the mean of at least 5 measurements. Water penetration measurements were performed, using a recently developed computerized method, described in an earlier paper (Van Kamp et al., 1986). The tests were performed at 20 ± 0.5°C. The data are given with a relative standard deviation and are the mean of at least 3 determinations.

Results

Fig. 1 shows initial solubility profiles for different types of lactose powders. The figure shows a higher dissolution rate and initial solubility for the products consisting mainly of β-lactose when compared to the products with a high α-content. The initial solubility of anhydrous α-lactose is higher than that of α-lactose monohydrate but decreases after reaching a maximum. Of the β-lactoses, the highest initial solubility was found for roller-dried β-lactose. It should be noticed, however, that the solubilities shown here are initial solubilities. Due to mutarotation of lactose in aqueous solution, the final solubility of all lactose types (in the mutarotated form) will be the same.

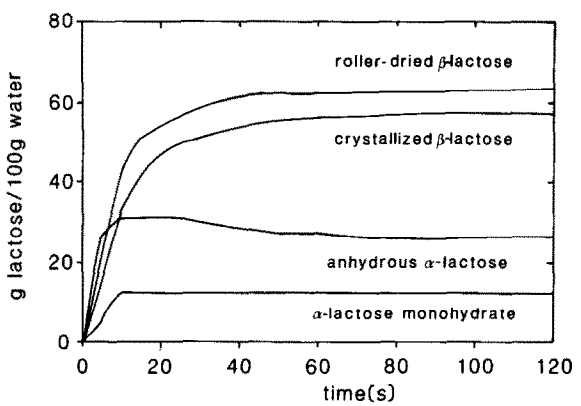

Fig. 1. Initial solubility profiles of different types of crystalline lactose powder in water of 37 ± 0.5°C.

Table 1 gives the crushing strength and disintegration time of tablets from four types of lactose, compressed at four force levels. Both anhydrous α-lactose and roller-dried β-lactose can be compressed into harder tablets at a specific load than tablets compressed from α-lactose monohydrate or crystallized β-lactose. Likewise, Table 1 shows a great difference between the disintegration properties of tablets compressed from the different products. A fast disintegration time of less than 1 min can be seen in the case of tablets containing α-lactose monohydrate or crystallized β-lactose, even when compressed at the highest force level. Tablets from roller-dried β-lactose showed only a fast disintegration when compressed at low forces. Tablets from anhydrous α-lactose exhibited much longer disintegration times, even when their higher

TABLE 1

CRUSHING STRENGTH AND DISINTEGRATION TIME IN WATER OF TABLETS COMPRESSED FROM DIFFERENT TYPES OF CRYSTALLINE LACTOSE AT 4 COMPRESSION FORCE LEVELS

	Compression force (kN)	Crushing strength (kg)	Disintegration time (s)
α-Lactose monohydrate	5	<1.0	7
	10	2.2	8
	20	5.6	14
	40	9.4	28
Anhydrous α-lactose	5	4.3	600
	10	7.9	610
	20	15.0	690
	40	> 20.0	690
Crystallized β-lactose	5	0.8	4
	10	1.0	5
	20	4.3	13
	40	7.8	42
Roller-dried β-lactose	5	3.0	21
	10	6.1	43
	20	10.9	205
	40	>18.9	350

TABLE 2

POROSITY, CALCULATED PORE VOLUME, VOLUMETRIC ALCOHOL UPTAKE AT 0°C AND VOLUMETRIC WATER UPTAKE AT 20°C OF TABLETS, COMPRESSED FROM DIFFERENT TYPES OF CRYSTALLINE LACTOSE AT 4 COMPRESSION LEVELS

Type of lactose and density (g/cm^3)	Compression force (kN)	Porosity (%)	Calculated pore volume (cm^3)	Volumetric alcohol uptake (cm^3)	Volumetric water uptake (cm^3)
α-Lactose monohydrate ($\rho = 1.545$)	5	24.5	0.104	0.092	0.180
	10	18.7	0.074	0.068	0.182
	20	13.6	0.051	0.049	0.181
	40	9.2	0.033	0.043	0.159
Anhydrous α-lactose ($\rho = 1.565$)	5	26.1	0.113	0.095	0.135
	10	19.6	0.078	0.078	0.116
	20	13.1	0.048	0.058	0.025
	40	7.5	0.026	0.044	0.019
Crystallized β-lactose ($\rho = 1.59$)	5	21.7	0.087	0.081	0.110
	10	16.3	0.062	0.057	0.107
	20	11.1	0.040	0.040	0.104
	40	7.3	0.025	0.026	0.097
Roller-dried β-lactose ($\rho = 1.59$)	5	28.5	0.127	0.102	0.260
	10	22.4	0.091	0.073	0.251
	20	15.7	0.059	0.055	0.077
	40	9.6	0.034	0.045	0.018

crushing strength levels are taken into account. Moreover, the disintegration time of these tablets was hardly if at all dependent on the compression force used. There is also a difference in disintegration behaviour: tablets compressed from anhydrous α-lactose showed, in contrast to tablets compressed from the other lactoses, a dissolution rather than a real disintegration. For tablets containing roller-dried β-lactose, the disintegration behaviour was dependent on the compression force used. Tablets compressed at 5 or 10 kN showed a rather rapid disintegration, tablets compressed at 20 kN disintegrated when dissolution was almost completed and only a small core was left, and tablets compressed at 40 kN did not disintegrate at all but dissolved completely.

Table 2 gives porosity data, calculated pore volume and volumetric alcohol and water uptake of the tablets mentioned in Table 1. The porosities of tablets compressed at a specific load do not differ very much in the case of α-lactose. As to the β-lactoses a higher porosity was found in the case of the roller-dried product in comparison with the crystallized form. The rather good similarity between the calculated pore volumes and the volumetric alcohol uptake indicates that in all the tablets a large majority of the pores could be reached by the penetrating liquid. Figs. 2 and 3

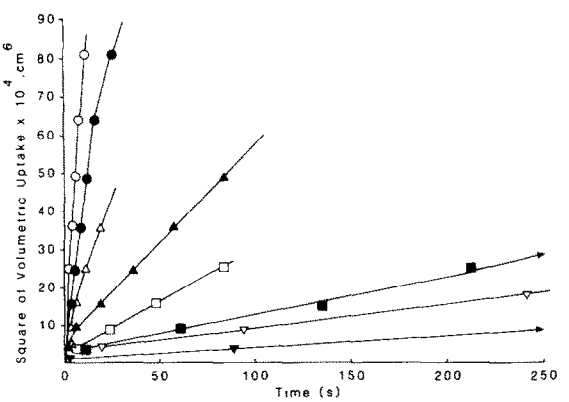

Fig. 2. Alcohol penetration into tablets compressed from α-lactose monohydrate (open symbols) and anhydrous α-lactose (closed symbols), respectively. Compression force: 5 kN (○, ●); 10 kN (△, ▲); 20 kN (□, ■); 40 kN (▽, ▼).

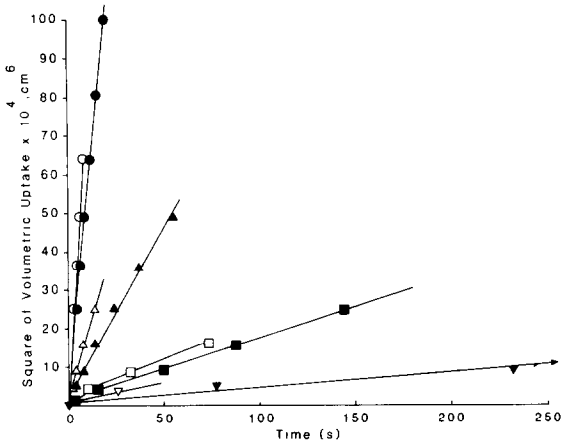

Fig. 3. Alcohol penetration into tablets compressed from crystallized β-lactose (open symbols) and roller-dried β-lactose (closed symbols), respectively. Compression force: 5 kN (○, ●); 10 kN (△, ▲); 20 kN (□, ■); 40 kN (▽, ▼).

show rates of alcohol penetration into the tablets. A linear relation was found between the square of the volumetric liquid uptake and the time for all the tablets investigated.

In contrast with alcohol, great differences between calculated pore volume and volumetric uptake were found when water was used as penetrating liquid (see Table 2). For tablets consisting of α-lactose monohydrate or crystallized β-lactose, the water uptake was found to be much larger than the calculated pore volumes. For tablets compressed from anhydrous α-lactose, the penetrated water volume was only higher than the calculated pore volume in the case of tablets compressed at low forces. The water uptake decreased, however, at increasing compression forces down to values below the calculated pore volume. For roller-dried β-lactose the volumetric water uptake was much higher than the calculated pore volume when the tablets were made at low compression forces. At the highest compression force, the measured water uptake was, however, lower than the calculated pore volume.

Fig. 4 shows water penetration profiles of the tablets. In the case of α-lactose monohydrate (Fig. 4a) or crystallized β-lactose (Fig. 4c) it can be seen that an increase in compression force causes an initial retardation of the penetration rate into the tablets. This effect can also be seen for roller-dried β-lactose at the lowest compression forces. For tablets from anhydrous α-lactose or roller-dried β-lactose, water uptake was poor and incomplete when high compression forces were used (Fig. 4b and d).

In Table 3 the disintegration times in different media of tablets compressed from α-lactose monohydrate and anhydrous α-lactose, respectively, are mentioned. The disintegration time of tablets from α-lactose monohydrate in dried dimethylsulfoxide was much longer than that in water. The disintegration behaviour of tablets containing anhydrous α-lactose in dimethylsulfoxide was similar to that of tablets compressed from the hydrous form and was strongly dependent on the compression

TABLE 3

DISINTEGRATION TIME OF TABLETS COMPRESSED FROM α-LACTOSE MONOHYDRATE AND ANHYDROUS α-LACTOSE, RESPECTIVELY, IN DIFFERENT MEDIA

	Compression force (kN)	Disintegration time (s) in:			
		Water	Dimethyl-sulfoxide	Alcohol	1% Methyl-cellulose solution
α-Lactose monohydrate	5	7	70	> 1800	80
	10	8	175	> 1800	95
	20	14	625	> 1800	100
Anhydrous α-lactose	5	600	105	> 1800	800
	10	610	410	> 1800	890
	20	690	1050	> 1800	870

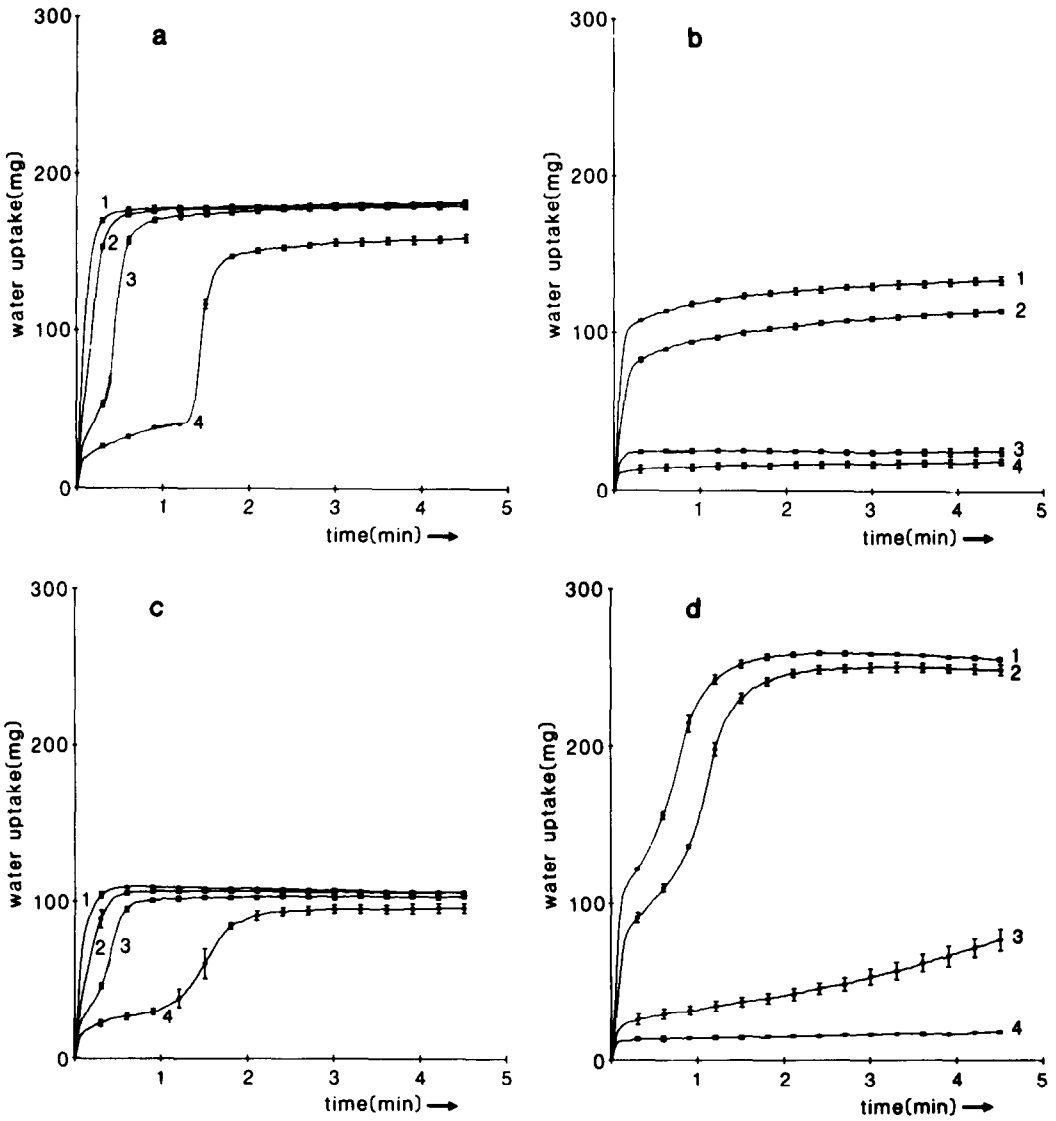

Fig. 4. Water penetration into tablets compressed from different types of crystalline lactose. (a) α-Lactose monohydrate; (b) anhydrous α-lactose; (c) crystallized β-lactose; (d) roller-dried β-lactose. Compression force: (1) 5 kN; (2) 10 kN; (3) 20 kN; (4) 40 kN.

force used. This in contrast to the disintegration time in water, which was dependent on the compression force. Using alcohol as a disintegration medium, none of the tablets investigated showed disintegration. In a viscous medium, 1% methylcellulose in water with a viscosity of 51 mPa's, all the disintegration times showed an increase when compared with those in water.

Discussion

The far longer disintegration times in water of tablets from anhydrous α-lactose and from roller-dried β-lactose compressed at high forces, when compared to those of tablets from α-lactose monohydrate or crystallized β-lactose (Table 1) correspond qualitatively with the differences in water

penetration into the respective tablets (Table 2 and Fig. 4). The high water uptake, which is much larger than the calculated pore volumes of tablets from α-lactose monohydrate or crystallized β-lactose and from roller-dried β-lactose tablets made at low compression forces may be caused by dissolution of lactose at binding places and at pore walls during the penetration process. This results in wider pores or even a partial opening of the tablets. This process gives rise to an increase in pore volume during penetration, just as it was found in previous research (Lerk et al., 1979) for tablets containing the highly soluble spray-dried dextrose. The kink in the penetration curves (Fig. 4a, c and d) can be explained by the observation of a sudden widening of the tablet structure. This may be caused by the dissolution of the bonds after an initial slow penetration into the small pores. The incomplete water penetration into tablets, being composed of anhydrous α-lactose or roller-dried β-lactose compressed at high force levels, is consistent with the observation that these tablets did not disintegrate into smaller particles as in the case of other lactoses but dissolved during disintegration. The high water uptake of these tablets, compressed at low compression forces can most probably be attributed to an increase in diameter of the pores that are situated at the outside of the tablets. This is caused by the dissolution of the highly soluble lactoses. The shorter disintegration time of tablets from roller-dried β-lactose compressed at 40 kN, in comparison with tablets containing anhydrous α-lactose (Table 1) is a consequence of the higher initial solubility of roller-dried β-lactose.

The differences in water penetration and the consequent differences in disintegration behaviour among the tablets compressed from different types of lactose should be explained by differences in the properties of these lactoses. These properties include the amount and the strength of the interparticulate bonds, the compression behaviour, in particular the resultant porosity and pore size distribution as well as the initial solubility and the resulting increase in viscosity of the solution.

Differences in amount and strength of interparticulate bonds may be derived from the crushing strength data in Table 1. It can be seen that the disintegration time of tablets from anhydrous α-lactose with a low crushing strength was much longer than that of tablets from other lactoses with a comparable hardness. It was shown in previous work (Vromans et al., 1985b) that the crushing strength of different types of crystalline lactose was only related to the pore surface area, created during compression, and hence on the extent of fragmentation. For this reason it may be assumed that the nature of the bonds of all the lactoses investigated is the same. Although this nature of the bonds is not exactly known, it may be assumed that they are lactose bonds which easily dissolve when they come into contact with water. It can be seen from Table 1 that tablets from α-lactose monohydrate, which has the lowest initial solubility of the lactoses tested, disintegrated in a short time, even when compressed at a high force. Hence it can be seen that the binding properties of the different lactoses are not important factors contributing to the differences in the disintegration behaviour found.

An increase in viscosity of the penetrating liquid, caused by the dissolution of tablet material during penetration can retard water uptake. This was also shown in previous work (Lerk et al., 1979) in the case of tablets containing spray-dried dextrose. The solubility of the lactoses is lower, however, than that of dextrose and the viscosity of saturated and even that of super-saturated lactose solutions are relatively low (Buma, 1980). Moreover, of tablets containing crystallized β-lactose a higher viscosity may be expected than of tablets containing anhydrous α-lactose. The reason is that crystallized β-lactose has a higher initial solubility (Fig. 1). It was shown, however, that water penetration into the tablets from crystallized β-lactose proceeded faster and in a more complete way (Fig. 4b and c). The effect of a viscous fluid on tablet disintegration was demonstrated by performing the disintegration test in a 1% methylcellulose solution in water, having a viscosity of 51 ± 1 mPa's. The data in Table 3 show that an increase in viscosity of the disintegration medium delays tablet disintegration of all tablets tested. It can be seen, however, that the effect of the viscosity of the penetrating liquid is too small to be responsible for the great differences in disintegration times

of tablets compressed from the different types of lactose (Table 1).

Differences in the mean pore size of the lactose tablets investigated will affect the rate of liquid penetration. The linear relation found between the square of volumetric alcohol uptake and time (Figs. 2 and 3) are in accordance with Washburn's equation (Washburn, 1921). This was to be expected because the lactoses are insoluble in alcohol so that the bonds are not loosened during the penetration process and the pore structures remain constant (Lerk et al., 1979). The slower rate of penetration into tablets containing anhydrous α-lactose in comparison with the hydrous product (Fig. 2) indicates that anhydrous α-lactose tablets have smaller pores. These differences in pore size distribution correspond with the results obtained by mercury porosimetry in previous research (Lerk et al., 1983; Vromans et al., 1985b). The differences referred to were attributed to a strongly increased fragmentation of anhydrous α-lactose during compression. Fig. 3 indicates that there are only small differences in the mean pore size of tablets compressed from the β-lactoses. The existence of different pore sizes cannot be responsible, however, for the incomplete water penetration into tablets from anhydrous α-lactose or roller-dried β-lactose, compressed at high forces. This is obvious when the alcohol uptake of tablets from α-lactose monohydrate, compressed at 20 kN, is compared with that of tablets from anhydrous α-lactose, compressed at 10 kN (Fig. 2). In spite of a faster alcohol penetration into the anhydrous α-lactose tablets, the water penetration was much slower and less complete than that of tablets compressed from α-lactose monohydrate (Fig. 4a and b). Likewise, in the case of β-lactose, the differences in water penetration into the tablets (Fig. 4c and d) cannot be explained by differences in pore sizes (Fig. 3).

In conclusion, the viscosity of the penetrating liquid and the differences in pore size of tablets of the lactoses investigated do not fully explain the incomplete and slow water uptake and the lack of disintegration of tablets containing anhydrous α-lactose and tablets containing roller-dried β-lactose compressed at high forces. Hence there must be another factor which has a deleterious effect on water penetration into these tablets. It may be assumed that this factor is the difference in initial solubility of the different types of lactose in water, which can be seen from Fig. 1. The deviating dissolution behaviour of anhydrous α-lactose is caused by the fact that the anhydrous product will be immediately converted into the hydrate form when it is in solution (Van Kreveld, 1969). For this reason the solubility of anhydrous α-lactose shows a maximum and will decrease very soon as a result of the lower solubility of α-lactose monohydrate. During water penetration into tablets or into a powder bed only a limited amount of water comes into contact with the solid. When this solid is anhydrous α-lactose, after a rapid initial dissolution, α-lactose monohydrate will precipitate in consequence of its lower initial solubility. This phenomenon can be easily seen by the solidification of a given quantity of anhydrous α-lactose powder, when it is moistened with water. The effect can be demonstrated quantitatively by pouring 20 g of water on 10 g of lactose on a 34 mm G3 glass filter and varying the time between water addition and suction. For the experiment the liquid was sucked immediately and after 2 min, respectively, dried by evaporation and weighed quantitatively. Table 4 shows the resultant weight of the dissolved and precipitated lactose. In the case of α-lactose monohydrate, the dissolved quantity of lactose increased, as was to be expected, when filtration was carried out after a waiting time of 2 min. In the case of anhydrous α-lactose, however, there was an opposite effect: if the solution was sucked directly, the lactose content in the filtrate was higher than when the solution was sucked after 2 min. This indicates that a part of the

TABLE 4

QUANTITY OF DISSOLVED LACTOSE, MEASURED IMMEDIATELY OR WITH 2 MIN DELAY AFTER ADDITION OF WATER. DESCRIPTION IN THE TEXT

	Quantity of dissolved lactose (g)	
	Suction immediately	Suction after 2 min
α-Lactose monohydrate	1.5	1.8
Anhydrous α-lactose	4.5	3.5

dissolved anhydrous α-lactose has precipitated in the powder bed as α-lactose monohydrate. It may be assumed that the same phenomenon also occurs in tablets containing anhydrous α-lactose: during water penetration, the anhydrous product exhibits a fast dissolution and will be converted into α-lactose monohydrate, which partially precipitates. This precipitation can have a marked effect on water penetration into small pores where the penetration rate is low, so there is more time to dissolve lactose. Moreover, small pores will first be stopped up by the precipitation of α-lactose monohydrate, resulting in incomplete penetration of water into the tablet and in incomplete tablet disintegration. In dimethylsulfoxide both α-lactose monohydrate and anhydrous α-lactose are soluble. The solubilities at 37°C are 6.0% and 0.6%, respectively. In contrast to what happens in water, a conversion of anhydrous α-lactose into the hydrous form is not possible in dried dimethylsulfoxide. For this reason a precipitation of α-lactose monohydrate during the penetration of dimethylsulfoxide will not occur. This establishment corresponds with the disintegration times in dimethylsulfoxide (Table 3), where a similar and compression pressure-dependent disintegration behaviour was found for both types of α-lactose. The longer disintegration times for tablets from anhydrous α-lactose in comparison with tablets of the hydrous form can be explained by their higher crushing strengths (Table 1), smaller mean pore sizes (Fig. 2) and lower solubility in dimethylsulfoxide.

The poor water uptake and rather long disintegration time of tablets from roller-dried β-lactose compressed at high forces, may be caused by both the presence of small pores in the tablets and the presence of about 20% anhydrous α-lactose in the substance, which can precipitate in the hydrous form during water penetration.

In conclusion, it was shown that unlubricated tablets, compressed from either α-lactose monohydrate or crystallized β-lactose, disintegrate very quickly in water as a result of rapid liquid uptake and fast dissolution of the bonds. Tablets from anhydrous α-lactose do not disintegrate at all when brought into contact with water. They dissolve during the disintegration process. This effect which is caused by bad water penetration into the tablets, is attributed to a combination of small pore diameters and precipitation of dissolved anhydrous α-lactose as α-lactose monohydrate in the course of the penetration process. The same phenomenon can be seen for tablets containing roller-dried β-lactose when they are compressed at high forces.

The results of an investigation on the effect of both lubricants and disintegrants on the disintegration and drug dissolution of tablets containing different types of lactose will be presented in a future publication.

Acknowledgement

The authors are indebted to Drs. H. Vromans for the valuable discussions about this work.

References

Batuyios, N.H., Anhydrous lactose in direct tablet compression. J. Pharm. Sci., 55 (1966) 727–730.

Bolhuis, G.K. and Lerk, C.F., Comparative evaluation of excipients for direct compression. I. Pharm. Weekbl., 108 (1973) 469–481.

Bolhuis, G.K., Reichman, G., Lerk, C.F., Van Kamp, H.V. and Zuurman, K., Evaluation of anhydrous α-lactose, a new excipient in direct compression. Drug. Dev. Ind. Pharm., 11 (1985) 1657–1681.

Buma, T.J., Viscosity and density of concentrated lactose solutions and of concentrated cheese whey. Neth. Milk Dairy J., 34 (1980) 65–68.

Buma, T.J. and Van der Veen, H.K.C., Accurate specific optical rotations of lactose, and their dependence on temperature. Neth. Milk Dairy J., 28 (1974) 175–185.

De Boer, A.H., Vromans, H., Lerk, C.F., Bolhuis, G.K., Kussendrager, K.D. and Bosch, H., Studies on tableting properties of lactose. Part 3. The consolidation behaviour of sieve fractions of crystalline α-lactose monohydrate. Submitted for publication.

Delattre, L. and Jaminet, F., Étude de quelques facteurs influençant le pouvoir liant d'excipients pour compression directe. Pharm. Acta Helv., 49 (1974) 108–116.

Gillard, J., Delattre, L., Jaminet, F. and Roland, M., Étude des paramètres influençant l'écoulement des agents diluants utilisés en compression directe. J. Pharm. Belg., 27 (1972) 713–742.

Graf, E., Ghanem, A.H. and Mahmoud, H., Studies on the Direct Compression of Pharmaceuticals. Part 8: Role of liquid penetration and humidity on tablet formulations. Pharm. Ind., 44 (1982) 200–203.

Gunsel, W.C. and Lachman, L., Comparative evaluation of tablet formulations prepared from conventionally-processed and spray-dried lactose. J. Pharm. Sci., 52 (1963) 178–182.

Lerk, C.F., Andreae, A.C., De Boer, A.H., Bolhuis, G.K., Zuurman, K., De Hoog, P., Kussendrager, K.D. and Van Leverink, J., Increased binding capacity and flowability of α-lactose monohydrate after dehydration. J. Pharm. Pharmacol., 35 (1983) 747–748.

Lerk, C.F., Bolhuis, G.K. and De Boer, A.H., Comparative evaluation of excipients for direct compression, II. Pharm. Weekbl., 109 (1974) 945–955.

Lerk, C.F., Bolhuis, G.K. and De Boer, A.H., Effect of microcrystalline cellulose on liquid penetration in and disintegration of directly compressed tablets. J. Pharm. Sci., 68 (1979) 205–211.

Shangraw, R.F., Wallace, J.W. and Bowers, F.M., Morphology and functionality in tablet excipients for direct compression. Pharm. Technol., 5 (1981) 68–86.

Van Kamp, H.V., Bolhuis, G.K., De Boer, A.H., Lerk, C.F. and Lie-A-Huen, L., The role of water uptake on tablet disintegration. Design of an improved method for penetration measurements. Pharm. Acta. Helv., 61 (1986) in press.

Van Kreveld, A., Growth rates of lactose crystals in solutions of stable anhydrous α-lactose. Neth. Milk Dairy J., 23 (1969) 258–275.

Vromans, H., Bolhuis, G.K., De Boer, A.H., Lerk, C.F. and Kussendrager, K.D., Studies on tableting properties of lactose. Part 1. The effect of initial particle size on binding properties and dehydration characteristics of lactose. Acta Pharm. Suec., 22 (1985a) 163–172.

Vromans, H., De Boer, A.H., Bolhuis, G.K., Lerk, C.F., Kussendrager, K.D. and Bosch, H., Studies on tableting properties of lactose. Part 2. Consolidation and compaction of different types of crystalline lactose. Pharm. Weekbl., 7 (1985b) 186–193.

Washburn, E.W., The dynamics of capillary flow. Phys. Rev., 17 (1921) 273–283.