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INFLUENCE OF DRYING TO THE STRUCTURE OF LACTITOL MONOHYDRATE

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Abstract

The purpose of this study is to find out the effect of the crystal water content on the crystal structure of lactitol monohydrate. Crystal water was removed by drying over silicagel at 40°C and by using phosphorus pentoxide as drying agent at 20°C.

The amouts of water removals were identified by thermogravimetry, the melting points and the heat of fusions were calculated from the results of differential scanning calorimetry measurements and the structure of samples were identified by X-ray powder diffraction method.

Over 23 *w/w*% of total water content could removed by gently drying until significant structural changes could be detected. The melting point of anhydrous lactitol obtained by drying lactitol monohydrate was 120°C and the melting enthalpy was 102 J g^{-1} when measured with heating rate 10°C min^{-1} by DSC.

Keywords: dehydration, drying method, DSC, lactitol, lactitol monohydrate, TG, X-ray powder diffraction

Introduction

Lactitol (4-O-β-D-galactopyranosyl-*D*-glucitol) is not found in nature but is usually obtained by hydrogenation of lactose [1]. Lactitol is entirely non-toxic with sweetness of about 35% of that of sucrose, whereas its nutritional value is much smaller than would be expected from its theoretical energy content. For this reason lactitol offers many promising applications for the food industry, in particular in the fields of dietic and low-calorie foods [1, 2]. Lactitol exists at least in four crystalline forms: anhydrous lactitol [3], lactitol monohydrate [2], lactitol dihydrate [4, 5] and lactitol trihydrate [6]. The space group of lactitol monohydrate is $P2_12_12_1$ and unit cell parameters are a =7.808(2) Å, b =12.685(2) Å, c =15.931(3) Å [2]. The crystals of lactitol monohydrate melt at 94°C (onset, isothermal melting). Lactitol monohydrate is converted to anhydrous lactitol (called A1). This phase melts about at 119°C while anhydrous lactitol (called A2) with defined crystal structure [3] melts at 148°C according to the DSC measurements. The molecular formula of lactitol is

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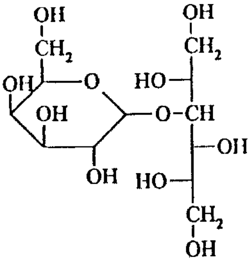

In the present study TG, DSC and X-ray powder diffraction were used to study the drying process of lactitol monohydrate.

Experimental

Pure lactitol monohydrate was obtained from Cultor Ltd. and its purity was over 98.5% (determined by HPLC by Cultor Ltd.). The melting point and the heat of fusion of lactitol monohydrate were defined by DSC.

Lactitol monohydrate was dried by using phosphorus pentoxide as drying agent. The volume of the desiccator was 2.3 dm^3 and 150 g P_2O_5 was weighed in it. The samples (2.000 g) were held in Petri dishes (Ø 5.6 cm) for varying times at 20°C. The dried samples were mixed identically to get homogenous mixture.

Drying of lactitol monohydrate was started by searching the appropriate temperature. When the drying temperature was 50°C, the air condition in the oven and the slight changes in temperature affected too much on drying. At the temperature of 49°C without air condition in oven, the sample didn't lose its crystal water in three weeks. When the temperature was raised to 60°C, crystal water was lost faster but the reaction was not so reproducible. Even the location of the sample in the oven affected the results. In order to minimize the effect of the unwanted variables to the results the samples were put in the desiccator over silicagel. The appropriate temperature was found to be 40°C. Each drying were done in the same condition: the volume of desiccator was the same size as before and there was only one sample (2.000 g) at each time in the desiccator. After drying the samples were conserved at room temperature in desiccator over silicagel where the content of the samples didn't change during long conservation. Each sample was mixed identically before measuring.

Changes in lactitol monohydrate were observed as a function of drying time. TG, DSC and X-ray diffraction measurements were carried out for each sample.

TG and DSC were used in the following hardware configurations (PE=Perkin Elmer, HP=Hewlett Packard):

TG: PE TGA7, PE TAC7/DX, Digital DECpc LPv^+ 466d2, HP Plotter 7470A, PE 7 Series/UNIX Thermal Analysis System software

DSC: PE DSC-7, PE TAC/PC, Digital DECpc LPv^+ 466d2, HP Plotter 7470A, PE 7 Series/UNIX Thermal Analysis System software

The TG-measurements were run for each sample before and after X-ray powder measurement with sample weights of 4–7 mg in Pt-pans in dynamic nitrogen atmosphere with a flow rate of 50–60 cm^3 min^{-1}. The heating rate was 2°C min^{-1} and the temperature range 25–200°C.

The DSC measurements were carried out in 50 μl aluminium pans with holes with sample weights of 4–5 mg, the heating rates were 2 and 10°C min^{-1} and the temperature range was 25–200°C.

The X-ray powder diffraction patterns were measured with ENRAF NONIUS PDS 120 diffractometer equipped with an INEL CPS 120 curved-position-sensitive detector, which allows simultaneous data recording of a diffraction pattern over a range of 120° of 2-theta. The radiation used was monochromatic CuK_α-radiation ($\lambda = 1.54056$ Å). X-rays were produced using 45 kV and 25 mA. Silicon and Mica-mixture (70 wt%/30 wt%) was used as internal standard. The amount of internal standard in the flat spinning horizontal powder sample was 5 wt%. ENRAF-GUFI [7] software was used for analysis of diffraction patterns.

The program PIRUM, which is an interactive calculation method, were used to analyze the X-ray powder diffraction measurements [8].

Results and discussion

The water losses of the samples and their deviation from the average which were dried by using P_2O_5 as drying agent calculated as percentage of the total water content of lactitol monohydrate are in Table 1. The amount of water has decreased when the drying time was 4 h. In three weeks there is only about 1 wt% of water in the structure. There are deviations in the results of thermogravimetric curves because it is very difficult to arrange the experimental conditions identical for each sample.

Table 1 Water losses of the samples dried by P_2O_5 calculated from the total water content of the lactitol monohydrate

Sample	Drying time	Water loss/wt%	Heat of fusion of M1/	Heat of fusion of A1/
			$J g^{-1}$	
1	–	–	158	–
2	4 h	1.7±1.0	155	0
3	16 h	6.7±1.2	152	0
4	48 h	22.9±0.9	138	22
5	60 h	28.1±0.1	126	28
6	3 days	34.3±1.6	106	45
7	4 days	59.9±1.4	61	73
8	5 days	72.9±1.6	42	86
9	7 days 22 h	91.4±0.7	7	96
10	2 days	97.0±0.2	2	98
11	21 days	98.9±0.4	1	103

When measured at heating rate of 2°C min^{-1} lactitol monohydrate can recrystallize to anhydrous form, so the last peak of curve consists the heat of fusions of the recrystallized lactitol monohydrate and the anhydrous lactitol. With lower heating rates monohydrate may dehydrate during measurement. The optimum heating rate was 10°C min^{-1}.

The heat of fusions of monohydrate and anhydrous lactitol of partly dried samples measured with 10°C min^{-1} are also in Table 1.The melting peak of lactitol monohydrate in DSC curve when measured 10°C min^{-1} is about at 97°C and the melting peak of anhydrous lactitol form Al is about at 120°C and the heat of fusion is 102 J g^{-1}. In Fig. . there are DSC curves of samples which were dried for varying times over P_2O_5. In the first curve there is only the melting peak of monohydrate consisting partly water removal and when the drying time increase the melting peak of anhydrous lactitol became larger. After drying for 21 days there is only a minor melting peak of lactitol monohydrate.

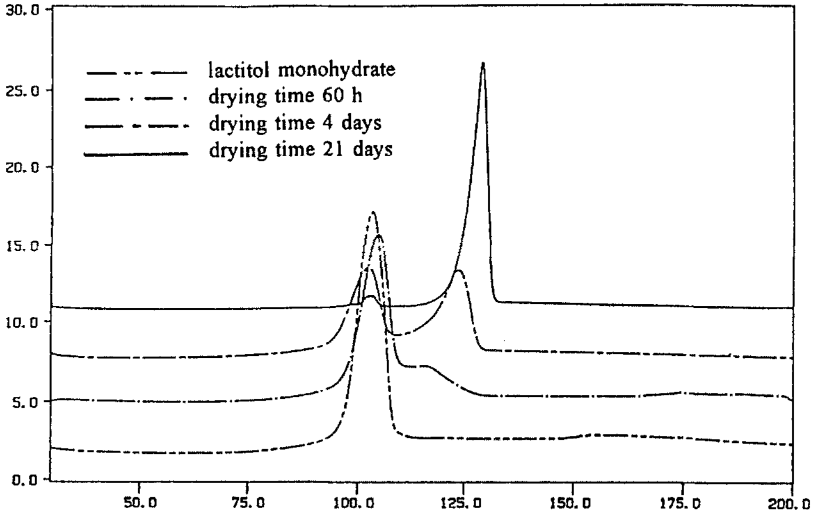

Fig. 1 DSC curves of samples which were dried for varying times over P_2O_5

The samples 8–11 (Table 1) have also a small peak about at 103°C, which may be due to a conformational change in the acyclic part of lactitol. The entalpies of these peaks were 1–4 J g^{-1}. In other samples this peak was not resolved well enough from the melting peaks, and its enthalpy in these curves is a part of melting enthalpy. In samples 2 and 3 the melting of A1 could not confidently be detected, which is in line with powder diffraction results. In sample 4 the melting peak of A1 can be clearly detected. Because no peaks originating from A1 could be detected with X-ray powder diffraction, it is possible that when heated with DSC the partly dried monohydrate has separated into two phases. No separate peak could be detected with DSC to this reaction, and so it is hidden in the melting peak of monohydrate. The same conclusions can be made by the fact that the measured enthalpies is larger than the enthalpy calculated from the water content. The measured enthalpy of melting for sample 5 was also larger than the expected one, because the partly dried monohydrate has not fully separated into two crystalline phases. The same behaviour could be detected for lactitol monohydrate dried at 40°C over silicagel. The difference between the melting enthalpies of lactitol monohydrate and anhydrous lactitol is due to dehydratation and structural changes. With high heating rates the enthalpy value of A1 is more confident than that of M1 because the melting peak of M1 includes slightly dehydration and a possible phase transformation whose enthalpy values are not known. The separation of these phases caused by elevated temperature can be noticed from the DSC measurements: the sum of the experimental melting enthalpies obtained from the DSC measurements are in several samples higher than the sum of the melting enthalpies calculated from the pure phases.

The crystal system and unit cell dimensions are needed as initial values for PIRUM calculations. The powder diffraction study of lactitol monohydrate has been carried out by our investigation group [9]. The crystal system must be correct for calculation (orthorhombic for lactitol monohydrate) but the unit cell initial values need not to be accurate. One criteria for the survey of the reliability of the results is to use M_{20} [10] and F_{20} [11] values of figures of merit. If M_{20} is larger than 6, the study is done by correct way. Large F_{20} value is better than small when goodness of results are considered [10, 11].

The M_{20} and F_{20} values and the number of unindexed lines and total number of lines are given in Table 2. Peaks with intensity below 2% were ignored. A closer study of F_{20} values and its minimum value for sample 4 indicate that crystal defects increase when proceeding from sample 1 to sample 4 without any change in the number of phases. The strong increase in the F_{20} figures to next measuring point can be explained so that the dried product was separated into a crystalline phase of

Table 2 M_{20} and F_{20} values and number of unindexed lines (*n*) and total lines (*N*) from powder diffraction data when dried by P_2O_5

Sample	M_{20}	F_{20}	*n*	N
1	9	16	–	40
2	8	14	–	39
3	8	14	–	40
4	9	16	3	39
5	8	20	10	47
6	8	22	9	42
7	10	28	17	48
8	9	27	14	48
9	8	22	18	48
10	13	36	25	47
11	6	19	19	43

its own and the unit cell is now determined from lactitol monohydrate of better crystal quality. The best indication of a structural change is given by the increase in the number of unindexed peaks in PIRUM when proceeding from sample 4 to sample 5. Samples 1–3 do not have unindexed peaks and the three unindexed peaks of sample 4 were very small (intensity <3%). The powder diffraction patterns of lactitol monohydrate and samples dried for 60 h and 12 days are in Fig. 2.

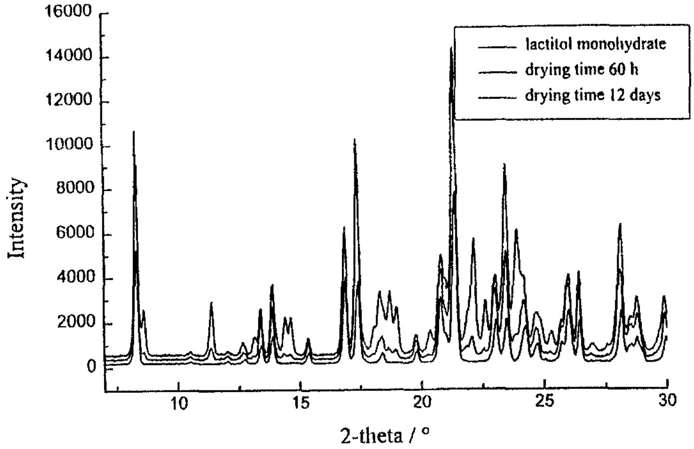

Fig. 2 The powder diffraction patterns of lactitol monohydrate and samples dried for 60 h and 12 days

Consequently, according to the M_{20} and F_{20} values and the number of unindexed lines a significant structural change could be detected when over 23% *w/w* of the total water was removed. It is also remarkable that the unit cell of lactitol monohydrate can be recovered with powder diffraction from a sample from which up to 98.9% *w/w* of water has been removed but in this case about half of all peaks remains unindexed. No sample has so-called amorphous sphere in their powder diffraction pattern, thus the samples have been very crystalline. The DSC curves end up with the same conclusion. No significant rehydration is observed during the X-ray powder diffraction measurements.

The water losses of samples (and their deviations from the average) which were dried at 40°C over silicagel for different times calculated from total water content of lactitol monohydrate (4.97%) are given in Table 3. The water content has decreased about 23% when the sample is conserved 16 h at 40°C and the sample has lost almost all of its crystal water in 14 days. This phenomenon will also been seen from DSC measurements where the heat of fusion of the melting peak of lactitol monohydrate decreased and finally there is only the melting peak of anhydrous lactitol form A1 at 120°C. DSC curves were same kind than when dried by P_2O_5.

The M_{20} and F_{20} values and number of unindexed lines and the total number of lines of the samples dried by heat measured by powder diffractometer are in Table 4.

When dried by heat over silicagel the lactitol monohydrate samples dried remarkably faster but the results of powder diffraction patterns of partly dried samples were same kind when dried by P_2O_5.

Table 3 Water losses of the samples dried at 40°C calculated from the total water content of lactitol monohydrate

Sample	Drying time	Water loss/ wt%	Heat of fusion of M1/ J g^{-1}	Heat of fusion of A1/ J g^{-1}
1	–	–	158	–
2	16 h	23.1±3.8	140	16
3	18 h	25.2±2.1	126	30
4	19 h	26.9±1.6	130	25
5	20 h	33.1±1.4	111	40
6	22 h	34.8±5.2	117	37
7	24 h	48.8±3.9	93	56
8	48 h	89.6±1.2	16	93
9	2 weeks	98.3±0.5	1	101

Table 4 M_{20} and F_{20} values and number of unindexed lines (*n*) and total lines (*N*) from powder diffraction data of the samples dried at 40°C

Sample	M_{20}	F_{20}	*n*	N
1	9	16	–	40
2	6	8	1	22
3	8	18	5	36
4	7	14	4	32
5	10	25	9	41
6	7	14	4	28
7	9	23	17	47
8	7	19	18	51
9	8	20	23	47

Conclusion

Over 23 *w/w%* of total water content could removed by gently drying until significant structural changes could be detected from X-ray powder diffraction measurements.

The amount of crystal water can reliably be determined with TG. Measured with DSC the monohydrate can dehydrate or recrystallize to anhydrous form. In determing the phases in a sample the values of the melting enthalpies are affected by the slight dehydration during the measurement and the phase transformation caused by elevated temperature. Neither the energy of the phase transformation nor the energy of dehydration are known, so the shares of phases cannot be calculated from melting enthalpies accurately. In order to determine confidently the structural changes of lactitol monohydrate both DSC and X-ray powder diffraction measurements are needed.

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