Journal of Thermal Analysis and Calorimetry, Vol. 89 (2007) 3, 757–760

STRUCTURAL STUDY OF α-LACTOSE MONOHYDRATE SUBJECTED TO MICROWAVE IRRADIATION

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The aim of this work was to investigate the influence of different levels of microwave irradiation on the structure and particle size characteristics of α-lactose monohydrate. The structural study of the samples was carried out by XRD, the presence of lactose polymorphs in the test samples was determined by DSC and the particle size distribution was measured by laser diffraction.

The samples subjected to microwave irradiation retained their original X-ray patterns. No significant differences in thermal transition characteristics and particle size were observed. Hence, neither the occurrence of crystalline–amorphous transition resulted by microwave irradiation nor the presence of lactose polymorphs in the test samples can be assumed. The unmodified properties can be attributed to the fact that the water of crystallization is very difficult to remove from the crystal structure and is not free to move during microwave treatment, which results in stability to microwaves.

Our results allow the conclusion that microwave processing of α-lactose monohydrate has no influence on further pharmaceutical technological properties, which are related to the structure and the particle size distribution of this substance.

Keywords: *DSC, lactose, microwave, particle size, X-ray powder diffraction*

Introduction

Applications of microwave energy have been developed primarily for communications and some areas of processing such as cooking food, tempering and thawing, and curing of wood and rubber products. The primary benefits of microwave applications are reduction in manufacturing costs due to energy savings and shorter processing times, better production quality, synthesis of new materials and products as well as reduced hazards to the environment [1]. These advantages have led to attempts to use this energy in many industrial applications including heating, drying, sintering, sterilization, tempering, microwave activated chemical reactions, etc. [2–6].

Microwave energy is delivered directly to materials through molecular interactions with electromagnetic field via conversations of electromagnetic energy into thermal energy [7].

Due to the volumetric heating effect, microwave drying offers a fast alternative of moisture removal from several substances [8, 9]. The effects of dielectric heating are related to molecular motion by migration of ions and rotation of dipoles. The energy of microwave photons is very low relative to the typical energies of chemical bonds. Thus, microwaves do not directly affect molecular structure [10, 11]. However, as observed in a previous study [12], moisture content has a major influence on the crystalline structure of starches and the water removal from these polymers is accompanied by irreversible structural changes which result in modified physico-chemical properties.

The excipients starch and α-lactose monohydrate are known to behave completely differently on dielectric heating [13]. As discussed by Vromans, crystalline materials will behave like lactose, while non-crystalline, amorphous substances will behave like starch.

Since the influence of microwave irradiation on the structure and physico-chemical properties of starches has been clarified previously, the aim of this work was to investigate the influence of different levels of dielectric heating on the properties of α-lactose monohydrate. Crystallinity, size, shape and surface characteristics of the particles play an essential role during manufacturing and formulation of lactose [14–17]. Hence, this study focused on the investigation of the crystalline structure, the thermal transition characteristics and on the determination of particle size distribution of α-lactose monohydrate subjected to microwave processing.

Experimental

Materials and microwave processing

20 g of α-lactose monohydrate (Pharmatose® DCL 11, DMW, Veghel, the Netherlands) was subjected to dif-

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1388–6150/$20.00
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Table 1 Process parameters, particle size distributions and transition energies of the samples

Sample	Duration of microwave processing/min	T_{end}*/°C	Particle size/μm			ΔH**/J g^{-1}	
			$d_{0.1}$	$d_{0.5}$	$d_{0.9}$	peak 1 145°C	peak 2 175°C
Reference	–	–	58.21±0.54	123.26±1.21	226.84±1.71	164.79	6.95
100 W	20	60	57.24±0.38	120.52±1.30	222.13±2.41	158.55	5.54
500 W	8	125	59.85±1.13	124.80±1.34	229.02±1.96	154.32	4.12
900 W	3.5	131	58.66±0.44	122.35±0.49	223.75±1.59	154.06	3.15

*T_{end} – temperature measured at the end of microwave processing, **ΔH – enthalpy of transition

ferent levels of microwave irradiation using a Milestone MicroSYNTH labstation (Milestone, Sorisole, Italy). The samples were treated in Milestone reference vessels made from Weflon® under constant stirring. The microwave power was kept constant during the processing periode (100 W for 20 min, 500 W for 8 min, 900 W for 3.5 min). The temperature of the samples was measured by a high-sensitivity IR sensor. The process parameters were controlled by the EasyWAVE Process Control Software (Table 1). The temperature of the samples was constantly increasing during the processing. The highest temperature values detected at the end of the thermal treatment are given as T_{end} in Table 1.

Methods

Thermoanalytical study

The thermoanalytical study was carried out by a Mettler-Toledo DSC 821^e differential scanning calorimeter (Mettler-Toledo GmbH, Greifensee, Switzerland) operating under an argon atmosphere. About 5 mg sample was sealed into an aluminium pan. The temperature was raised from 20 to 240°C at a scanning rate of 5°C min^{-1}.

Particle size distributions

Particle size distributions were measured by laser diffraction (Malvern Mastersizer 2000, Malvern Ltd., Worcestershire, UK). For the measurements, the samples were dispersed in air.

X-ray diffraction

X-ray diffraction was performed using a D4 Endeavour Diffractometer (Bruker AXS GmbH, Karlsruhe, Germany). The measurement conditions were as follows: radiation source: CuK_α, angle of diffraction scanned: from 1 to 40°, step size: 0.01°, step time: 10 s.

All measurements and investigations were carried out in triplicate.

Results and discussion

Pharmatose® DCL 11 by DMW is a free flowing, spray-dried, hydrous lactose, which is composed of spherical particles. DSC curve of the reference shows three characteristic peaks (Fig. 1). From the literature it is known that the endothermic peak at 145°C corresponds to the temperature at which α-lactose monohydrate loses its crystal water (peak 1), while the amorphous form of lactose is identified by the presence of an exothermic peak at 175°C (peak 2). The multiple peak above 200°C is related to the melting of the sample (peak 3) [18, 19].

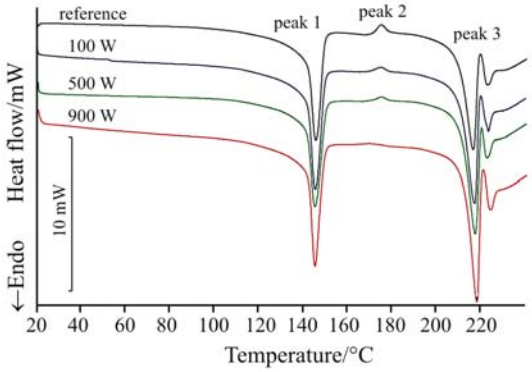

Fig. 1 DSC curves of the samples; peak 1 – presenting the loss of crystal water, peak 2 – the amorphous form of lactose, peak 3 – melting peak of the sample

All of the test samples exhibited the characteristic dehydration peak of α-lactose monohydrate (peak 1), while the exothermic peak representing the amorphous form became significantly smaller after microwave treatment (peak 2) which is attributed to the transformation of amorphous to crystalline form. The transition energy values of the peaks are included in Table 1. Gombás *et al*. observed a close correlation between the transition energy of the exothermic peak and the crystallinity of lactose. With the increase of the crystalline fraction, the height of the exothermic peak (typical for amorphous form) and its energy value decreased [18].

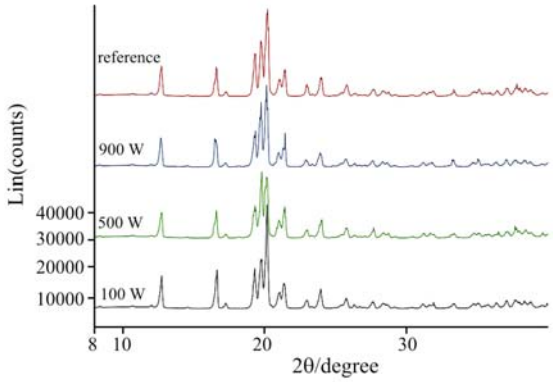

Fig. 2 X-ray patterns of α-lactose monohydrate subjected to different levels of microwave irradiation

Samples were investigated by XRD in order to compare their crystallinity. As shown in Fig. 2, the X-ray profiles did not show remarkable differences between the crystallinity of the test samples and the reference.

On the basis of the results obtained by DSC and XRD, the polymorphic transition of α-lactose monohydrate induced by microwave irradiation and the presence of lactose polymorphs in the test samples, such as anhydrous α- and β-lactose, can not be assumed.

Microwave processing of Pharmatose® DCL 11 did not result in significant changes in particle size distribution (Table 1).

α-lactose monohydrate is the common form of crystalline lactose. It can be observed in a variety of shapes (prism, diamond, pyramid, tomahawk) depending on the conditions of crystallization but the crystal lattice is always the same [20–22]. The water of crystallization is tightly bond and is difficult to remove. Since the water of crystallization is not free to move like liquid water, α-lactose monohydrate exhibits a low dielectric constant and a low loss factor [13].

The stability of lactose to microwave irradiation can be explained by the above-mentioned structural and dielectric properties. However, the changes in transition energies might be related to the effect of dielectric heating. The decreased energy values of dehydration allow the conclusion that the temperature during microwave processing did not reach the critical temperature which is needed for the loss of crystalline water but microwave treatment might facilitate the dehydration of α-lactose monohydrate during a following heating procedure. The decrease in the exothermic transition energy clearly indicates the occuring of crystallization induced by dielectric heating. However, it must be noted, that an increase in crystallinity could not be detected by XRD. By the amount of change in transition energy, the quantity of amorphous content is small and the resolution of the applied equipment may not be sufficient to detect such a small difference.

Conclusions

As known, several physical properties of powders, such as adhesion, cohesion, flowability, compactibility and wettability, are significantly influenced by their crystalline structures and particle size characteristics [15, 23]. On the basis of our measurements, it is reasonable to assume that microwave processing of α-lactose monohydrate does not result in remarkable changes in pharmaceutical technological parameters, which are related to the structure and the particle size of this substance.

Acknowledgements

The authors gratefully acknowledge for the support provided by the German Academic Exchange Service and by the Hungarian National Research Foundation (OTKA T-047166).

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Received: November 17, 2006
Accepted: January 16, 2007
OnlineFirst: April 29, 2007

DOI: 10.1007/s10973-006-8258-y