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Microcrystalline cellulose from soybean husk: effects of solvent treatments on its properties as acetylsalicylic acid carrier

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Abstract

Microcrystalline cellulose (MCC) is a very important product in pharmaceutic, food, cosmetic and other industries. In this work, MCC was prepared from soybean husk, produced in large quantities in soybean oil processing industries. It was characterized through various techniques (scanning electron microscopy (SEM), infrared spectroscopy (FTIR), thermogravimetry analysis (TGA) and differential scanning calorimetry (DSC)) and compared with a commercial MCC. The results obtained show that the prepared sample has similar crystallinity and lower particle size than the commercial MCC. Both MCC samples were treated with organic solvents (chloroform, acetone, ethanol and ethyl ether), for structural modifications to be introduced, and used as acetylsalicylic acid (ASA) carrier. Pretreated MCC and MCC/ASA 1:1 mixtures were analyzed through FTIR and thermal analysis. The drug release was evaluated in buffer solution of pH 4.5 and in pure water, at 37°C. The MCC pretreated with different solvents show different thermal properties and ASA release rates, each MCC showing a particular behavior.

Keywords: Microcrystalline cellulose; Soybean husk; Thermal analysis; Acetylsalicylic acid

1. Introduction

Cellulose powders are widely used in the pharmaceutical industry as excipient, binder, disintegrant and antiaderent. Microcrystalline cellulose (MCC) has been indicated as interesting in producing medicines of controlled action (Struszczyk and Boldowicz, 1986; Picker, 1999). The active substance release rate depends on various factors such as the molecular interactions with the carrier, particle size and porous structure of the carrier and method of tablets or capsules preparation (Kalinkova, 1999). The adsorption of the drug on cellulose occurs through hydrogen bonding with the abundant aliphatic hydroxyles and some carboxylic groups, at the particles surface.

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Since cellulose from different sources differs in properties (crystallinity, moisture content, surface area and porous structure, molecular weight, etc.) different behaviors as drugs carrier are expected for MCC obtained in different ways. On the other hand, physical pre-treatments can also significantly modify MCC powder properties, which result in different dissolution profiles of drugs (Struszczyk and Boldowicz, 1986; Suzuki and Nakagami, 1999).

MCC is obtained in industrial scale from wood and cotton cellulose, but obtention from materials such as water hyacinth (Gaonkar and Kulkarni, 1987), coconut shells (Gaonkar and Kulkarni, 1989), sugar cane bagasse (Padmadisastra and Gonda, 1989; Shah et al., 1993) and jute (Abdullah, 1991) has been studied.

In the present work, MCC was prepared from soybean husk cellulose. It was characterized through scanning electron microscopy (SEM), infrared spectroscopy (FTIR) and thermal analysis (thermogravimetry analysis, TGA, and differential scanning calorimetry, DSC), and compared with a commercial MCC. With the objective of introducing some structural alterations, MCC was treated with organic solvents (chloroform, acetone, ethanol and ethyl ether). These MCC samples were analyzed through FTIR, TGA and DSC, and used as acetylsalicylic acid (ASA) carrier. The drug release was evaluated in buffer solution of pH 4,5 and in pure water, at 37°C.

2. Experimental

2.1. Reagents and chemicals

MCC (Lot No.82185) and ASA (Lot No. 78226) were obtained from Rhodia Farma. Cellulose was isolated from soybean husk as described below. All other reagents were PA grade and used as received.

2.2. Cellulose isolation

Soybean husk was supplied by a local industry (COCAMAR). Cellulose was isolated from this sample by conventional methods: pre-extraction with *n*-hexane ethanol and water sequentially in Soxhlet apparatus and delignification with aqueous sodium hydroxide at 121°C, in autoclave (Gómez et al., 1989).

2.3. MCC preparation

Cellulose isolated from soybean husk was hydrolyzed with hydrochloric acid for MCC preparation (Paralikar and Bhatawdekar, 1988).

2.4. MCC pretreatment and MCC-ASA tablets preparation

MCC was treated with four solvents (ethanol, acetone, chloroform and ethyl ether) prior to MCC-ASA tablet preparation. With each solvent, an MCC dispersion and an ASA solution was initially prepared, using the same solid mass and liquid volume. The MCC dispersion was allowed to stand for 36 h at room temperature, with stirring, for equilibrium swelling state to be reached. Solution and dispersion were mixed and maintained also at room temperature for further 36 h, to allow intra-particle diffusion. The solvent was then evaporated and the solid dried at 50°C. A fraction from this MCC-ASA 1:1 mixture was reserved for analysis and the remaining sample used for tablet preparation. A single punch press (Fabbe) was utilized, using 0.4 g of MCC-ASA and 7 mm of tablet diameter.

2.5. MCC-ASA tablets characterization

The physical properties of the tablets determined were: mass (0.4003 g), moisture content (0.4%), friability (0.40%), hardness (7.27 Kps), disintegration time (43 s). The reported results of mass, friability and hardness were calculated as average from twenty determinations. The moisture content was determined using an automatic Karl Fischer titrator (Metrohm AG-Herisau). Friability was measured with an Ética 300.1 friabilator. The hardness of the tablets was determined by using an Erweka TBH20 hardness tester.

2.6. MCC and MCC/ASA analyses

MCC, ASA and MCC/ASA blends were analyzed by FTIR, DSC and TGA using Bomem MB100, Shimadzu DSC50 and Shimadzu TA50 instruments, respectively.

For FTIR scans, KBr pellets containing 1% of the sample were prepared. For structural changes of MCC samples evaluation, three ratios of peak areas were analysed: the paracrystalline regularity index ($\phi = A_{1730}/A_{897}$) which can be related with degree of ordering of the largest macromolecules (Ershov and Klimentov, 1984) and the $I_1 = A_{1430}/A_{897}$ and $I_2 = A_{1370}/A_{2900}$ indices, which have been proposed as sensible to cellulose type I and type I and II crystallinity, respectively (Nelson and O'Connor, 1964).

For DSC scans, samples of about 6 mg were used. The heat evolved during the heating process (10°C/min) from 30 to 500°C was recorded as a function of temperature. Nitrogen atmosphere was used at a stream of 20 ml/min. The parameters evaluated were: (a) transition temperatures: MCC water loss (T_{wl}), MCC thermal decomposition (T_{MCC}), ASA melting/decomposition (T_{ASA}), obtained from the minimum of the DSC peaks; and (b) heats of fusion and/or thermal decomposition: MCC thermal decomposition (ΔH_{MCC}) and ASA melting/thermal decomposition (ΔH_{ASA}), were obtained from the area of the corresponding peaks. The instrument was calibrated with an indium standard.

Scans of TGA were carried out with ca. 6 mg of the samples, from 30 to 800°C, at a heating rate of 10°C/min and under nitrogen atmosphere flowing at 10 ml/min. Apparent activation energy of the thermal decomposition reaction (E_a) was determined through a differential method described in Haines (1995).

2.7. Dissolution tests

ASA release from MC-ASA tablets in buffer solution (sodium acetate/acetic acid, pH 4.5) and in pure water, at 37°C was determined. The ASA concentration present in the supernatant was obtained measuring the absorption at 265 nm (Varian UV spectrophotometer, Cary 50) at certain time intervals. The dissolution cube used was Dissolution DT6R Erweka. The experimental conditions were chosen according to the USP XXIII (The United States Pharmacopeia, 1995) specifications. All experiments were performed in duplicate.

3. Results and discussion

3.1. MCC characterization

Scanning electron micrographs, FTIR spectrum, DSC and TGA curves of MCC obtained from soybean husk and of the commercial MCC are shown in the Figs. 1–4.

From Fig. 1 it can be seen that both MCC samples show the typical elongated shape of MCC crystals and a nearly narrow particle size distribution. Although the prepared MCC show a little lower particle size.

The FTIR spectra (Fig. 2) are very similar and are characteristic of cellulose type I (Fengel and Stoll, 1989). The ϕ, I_1 and I_2 parameters obtained were 2.42, 7.56 and 0.12 for the commercial MCC, and 2.24, 7.82 and 0.11 for the prepared MCC, respectively. These results indicate similar crystallinities for both MCC samples.

One exothermic and two endothermic peaks are observed in the DSC curves (Fig. 3). At temperature below 140°C the water evolution occurs and both samples show very similar peak profiles. At higher temperature, between 300 and 480°C, the thermal decomposition takes place. The last two peaks appear at higher temperatures for the commercial MCC.

The mass loss that the MCC samples undergo from room temperature to 800°C are showed in Fig. 4. Some differences are also observed: the thermal decomposition initiate near 270°C for the commercial MCC and near 250°C for the prepared MCC; the first derivative of the curve show one peak with minimum at 348°C in the first case and at 333°C in the latter. Higher temperature of thermal decomposition setup and lower residual mass after the major weight portion (at ca. 350°C in Fig. 4) has been related to higher crystallinity of the cellulose (Nguyen et al., 1981).

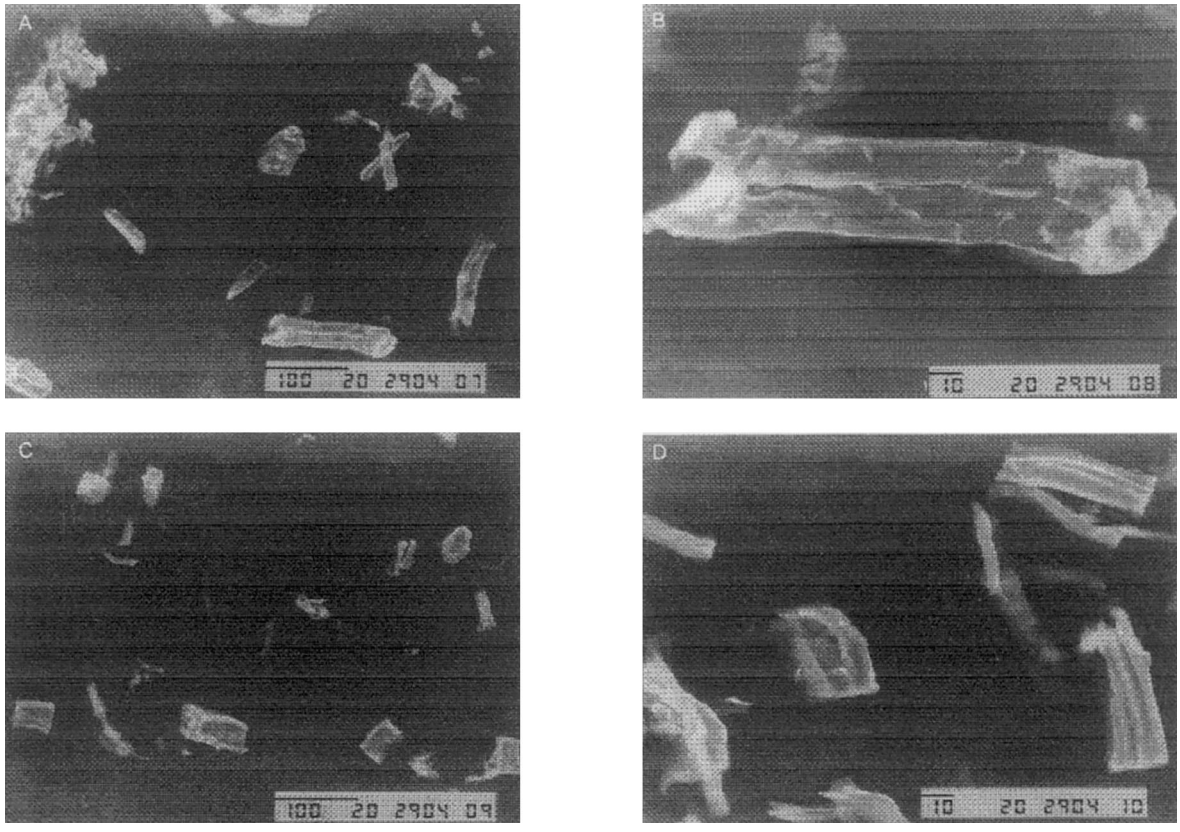

Fig. 1. Scanning electron micrographs of the commercial microcrystalline cellulose (MCC) (A and B) and of the prepared MCC (C and D).

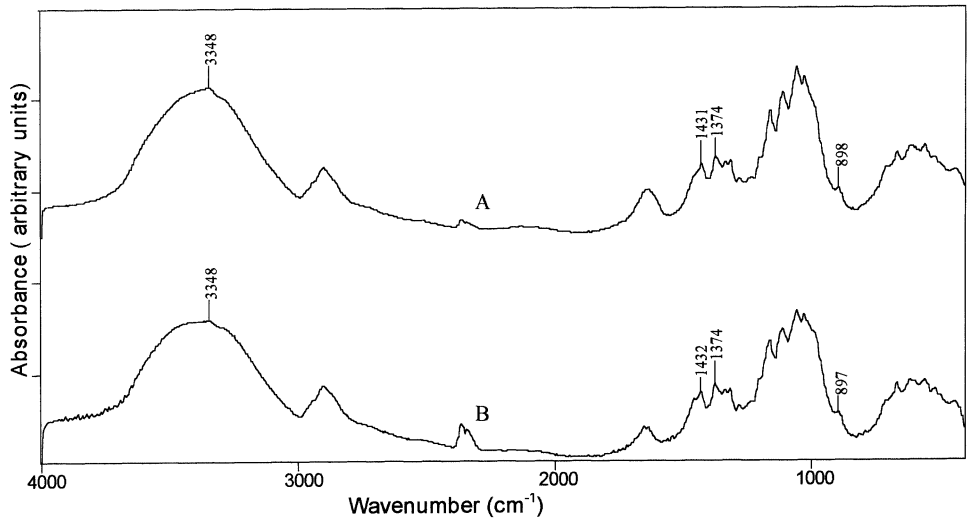

Fig. 2. Infrared spectroscopy (FTIR) spectra of the prepared microcrystalline cellulose (MCC) (A) and the commercial MCC (B).

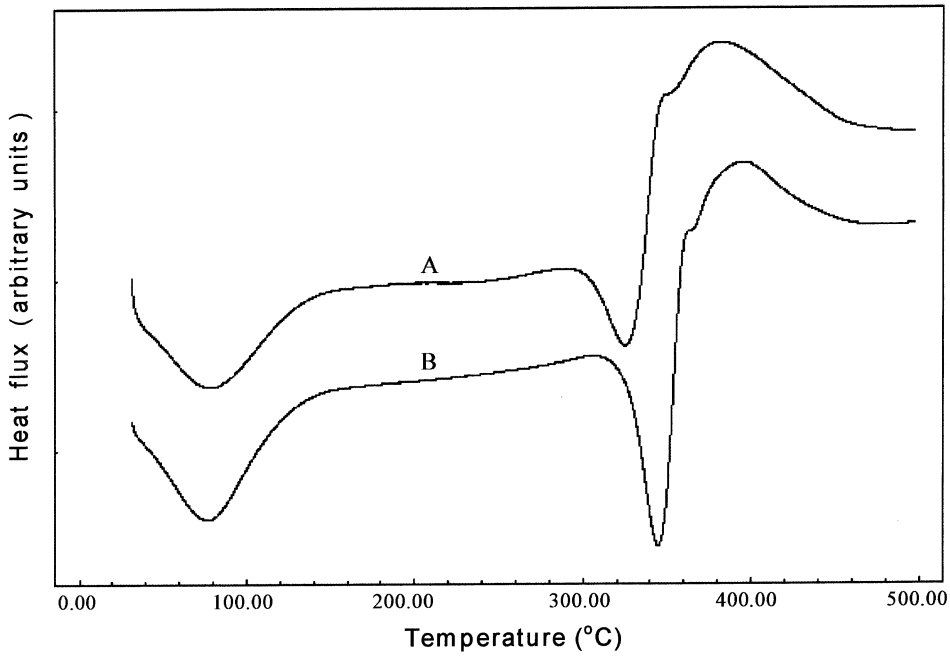

Fig. 3. Differential scanning calorimetry (DSC) curves of the prepared microcrystalline cellulose (MCC) (A) and the commercial MCC (B).

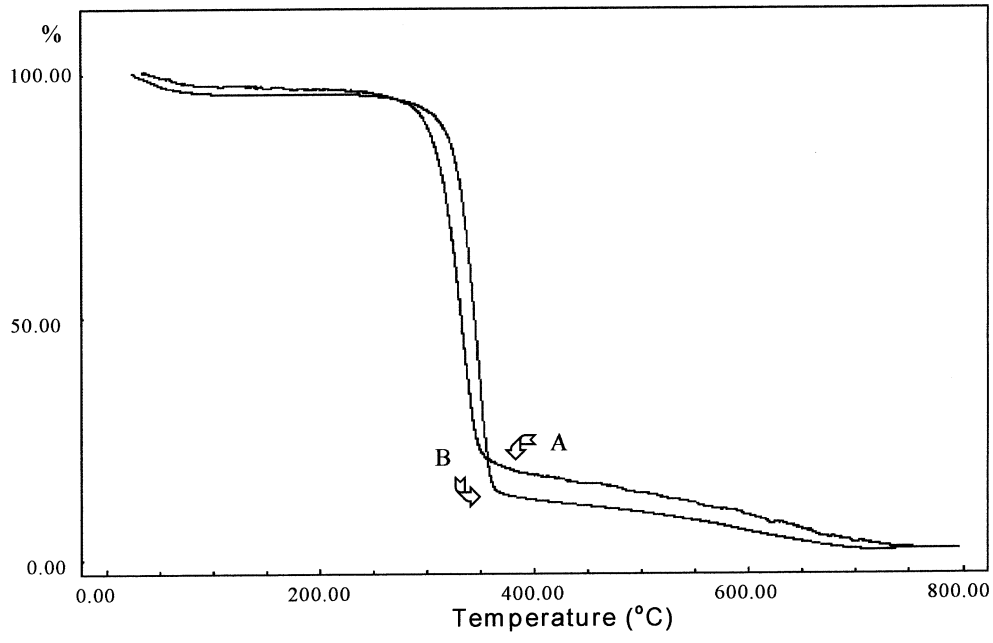

Fig. 4. Thermogravimetry analysis (TGA) curves of the prepared microcrystalline cellulose (MCC) (A) and the commercial MCC (B).

Table 1
Apparent activation energy and mechanism of the pyrolysis reaction (classified according to Dollimore (1992)) of microcrystalline cellulose (MCC) samples, pre-treated with some organic solvents, determined from thermogravimetry analysis (TGA) curves analysis

	Solvent	Mechanism	E_a (kJ/mol)
Commercial MCC	–	D2	319
	Ethyl ether	D4	388
	Ethanol	R3	244
	Acetone	D2	444
	Chloroform	D3	215
Prepared MCC	–	D3	404
	Ethyl ether	D3	445
	Ethanol	D2	372
	Acetone	D4	379
	Chloroform	D3	383

Apparent activation energy (E_a) of the pyrolysis reaction for the MCC samples were also calculated. Firstly, the mechanism which best represents the pyrolysis reaction is determined and then, through Arrhenius equation, the E_a is calculated. Comparing the result for each MCC (Table 1, without organic solvent treatment), a difference of ca. 90 kJ/mol is observed and is higher for the prepared MCC. In our previous study, E_a values showed great sensibility to differences in chemical nature such as substitution degree and molar mass (Corradini et al., 1999).

3.2. Solvent treated MCC characterization

MCC samples treated with organic solvents were also analyzed through TGA and DSC. E_a and mechanisms (Table 1) do not show similar behaviors for the MCC samples (prepared and commercial) but practically all E_a values are higher than the mentioned in the literature for crystalline cellulose, e.g. 250 kJ/mol for highly crystalline samples (Lewin et al., 1990). However, the mentioned E_a value was obtained assuming first order mechanisms (Horowitz and Metzger method; Horowitz and Metzger, 1963) and was obtained with crystalline cellulose and not with MCC. Several models have been applied to study the cellulose pyrolysis. The E_a varies greatly depending on the cellulose sample, sample mass, atmosphere, heating rate and the model used to manipulate the mass-temperature data. In these conditions, no approximation was made to treat the experimental data and all the mechanisms were applied in the differential form. For the untreated samples, diffusional mechanisms of pyrolysis adjust to experimental data: two dimensional (D2) to commercial sample and three dimensional (D3) to the prepared sample. For the treated samples, only the commercial sample treated with ethanol, do not obey diffusional mechanism and obeys the geometrical model with contracting volume (R3).

Results obtained from DSC curves are summarized in Table 2. T_{MCC} (for the thermal decompo-

Table 2
Heat of the thermal decomposition reaction (ΔH_{MCC}) and temperatures at the minimum of the water loss (T_{wl}) and thermal decomposition (T_{MCC}) differential scanning calorimetry (DSC) peaks, for untreated microcrystalline cellulose (MCC) samples and pretreated with organic solvents

	Solvent	T_{wl} (°C)	T_{MCC} (°C)	ΔH_{MCC} (J/g)
Commercial MCC	–	77	345	170
	Ethyl ether	83	344	157
	Ethanol	82	344	154
	Acetone	85	345	150
	Chloroform	78	343	148
Prepared MCC	–	78	326	130
	Ethyl ether	71	327	153
	Ethanol	78	329	118
	Acetone	81	329	110
	Chloroform	74	326	136

Table 3
Parameters obtained from infrared spectroscopy (FTIR) spectra of solvent treated and untreated microcrystalline celluloses (MCCs)[a]

	Solvent	ϕ	I_1	I_2
Commercial MCC	–	2.42	7.56	0.12
	Ethyl ether	1.83	5.23	0.12
	Ethanol	1.89	5.53	0.12
	Acetone	2.18	6.05	0.12
	Chloroform	1.77	4.96	0.12
Prepared MCC	–	2.62	7.82	0.11
	Ethyl ether	2.06	5.64	0.11
	Ethanol	2.09	5.90	0.11
	Acetone	2.11	5.63	0.11
	Chloroform	2.10	5.87	0.11

[a] $\phi = A_{1370}/A_{897}$; $I_1 = A_{1430}/A_{897}$; $I_2 = A_{1370}/A_{2900}$).

sition) is practically not altered, for the commercial sample it lies in the 343–345°C temperature range, and for the prepared sample between 326 and 329°C. T_{wl} (of water loss) and the ΔH_{MCC} show significant dislocations, being always higher values for the commercial MCC. There are no definite tendencies in these data but MCC treated with acetone gives the higher T_{wl} in both cases.

FTIR spectra from the MCC samples treated with solvents were drawn and the ϕ, I_1 and I_2 parameters were determined. These results are shown in Table 3 and show that the content of cellulose I and II is practically the same in prepared and commercial MCC and is not altered with the solvent treatments (see I_2 values in Table 3). On the other hand, the other two indexes show fluctuations indicating that internal structural rearranging occurs during the solvent treatments, which only alter the proportion of cellulose I and II. Note that the I_1 value obtained with the solvent treated samples is always lower than the corresponding MCC untreated. A linear relation was observed between ϕ and I_1 ($R = 0.962$), indicating that the ϕ parameter can also be related with crystallinity of cellulose I.

3.3. Thermal properties of MCC/ASA blends

Figs. 5 and 6 show DSC and TGA curves (from

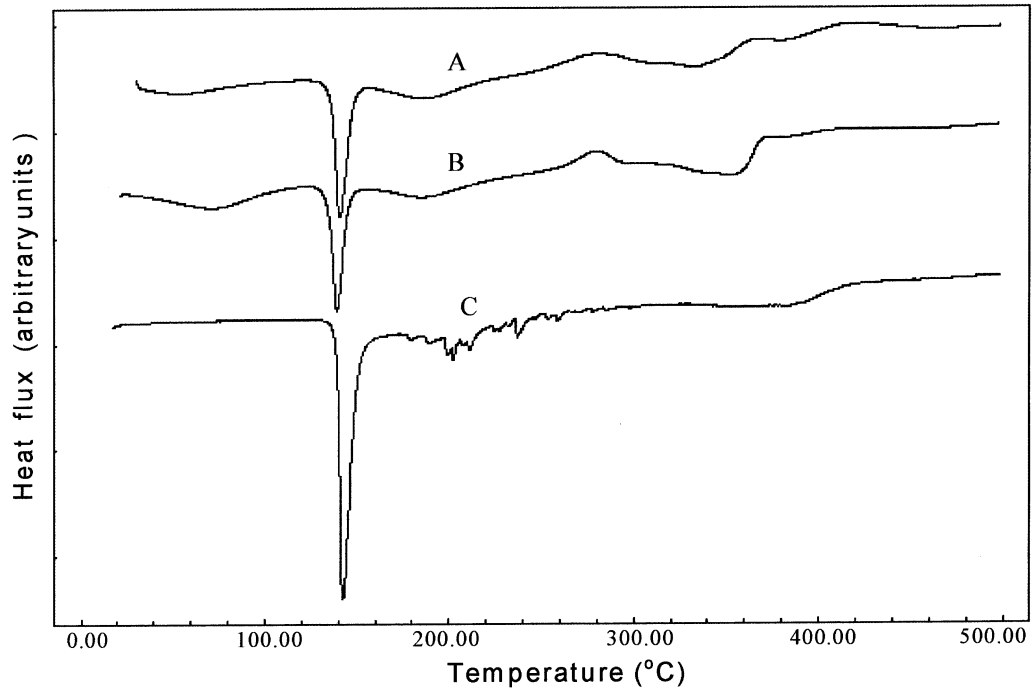

Fig. 5. Differential scanning calorimetry (DSC) curve of the prepared microcrystalline cellulose (MCC)/acetylsalicylic acid (ASA) (A); the commercial MCC/ASA (B) and ASA (C). Both MCC/ASA were pre-treated with acetone.

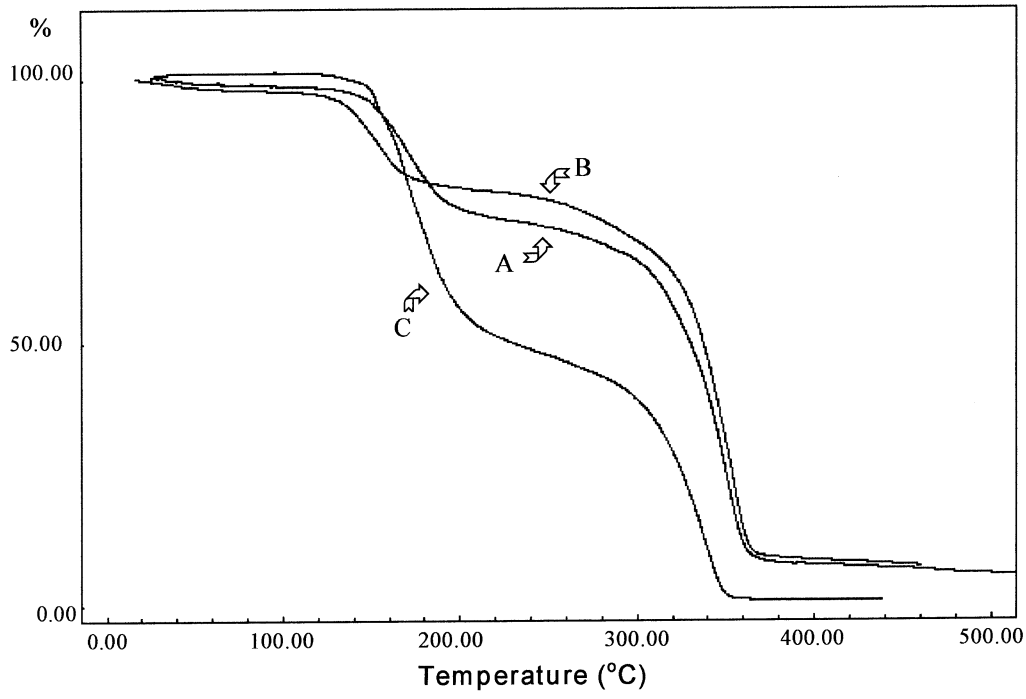

Fig. 6. Thermogravimetry analysis (TGA) curves of the prepared microcrystalline cellulose (MCC)/acetylsalicylic acid (ASA) (A); the commercial MCC/ASA (B) and ASA (C). Both MCC/ASA were pre-treated with acetone.

ASA, commercial MCC/ASA and prepared MCC/ASA blends), respectively. Only curves from MCC pre-treated with acetone are shown in these figures. ASA simultaneously undergoes melting and thermal decomposition from 140°C on. This peak shows dislocations in the blends with MCC pretreated with organic solvents. The data of the temperature at the minimum of the fusion/thermal decomposition of ASA as well as the heat of this process are shown in Table 4. A general increasing ΔH_{ASA} is observed for higher T_{ASA} and the ASA/MCC (ethanol treated) show the lower values. All the ΔH_{ASA} were lower than the corresponding value for the pure AAS, for which 183 J/g was obtained. Data of the pyrolysis kinetic from the MCC/ASA blends are summarized in Table 5. The thermal decomposition of ASA obeys always the F2 mechanism (second order of the mechanism based on 'order' of reaction) and E_a are lower for all the ASA/MCC (solvent treated) compared with the E_a for the ASA/MCC (untreated) in both cases. For the second stage of pyrolysis, where the products of the first stage of the pyrolysis of ASA and MCC decompose simultaneously, the diffusion mechanism model is observed for all samples, but the

Table 4
Heat of fusion/thermal decomposition of acetylsalicylic acid (ASA) and temperatures at the minimum of the corresponding differential scanning calorimetry (DSC) peaks, from ASA/microcrystalline cellulose (MCC) (untreated and pre-treated with organic solvents) samples

	Solvent	T_{ASA} (°C)	ΔH_{ASA} (J/g)
Commercial MCC	–	141	178
	Ethyl ether	136	122
	Ethanol	133	116
	Acetone	135	158
	Chloroform	139	180
Prepared MCC	–	142	174
	Ethyl ether	141	170
	Ethanol	115	74
	Acetone	141	112
	Chloroform	141	162

Table 5
Apparent activation energy and mechanism of the pyrolysis reaction (classified according to Dollimore (1992)) of acetylsalicylic acid (ASA) and microcrystalline cellulose (MCC) from ASA/MCC (untreated and pre-treated with organic solvents) blends

	Solvent	ASA (1st stage)		MCC and ASA (2nd stage)	
		Mechanism	E_a (kJ/mol)	Mechanism	E_a (kJ/mol)
Commercial MCC	–	F2	178	D2	248
	Ethyl ether	F2	121	D3	350
	Ethanol	F2	101	D4	337
	Acetone	F2	155	D3	434
	Chloroform	F2	155	D2	264
Prepared MCC	–	F2	155	D3	161
	Ethyl ether	F2	139	D2	293
	Ethanol	F2	135	D4	384
	Acetone	F2	147	D2	286
	Chloroform	F2	139	D3	233

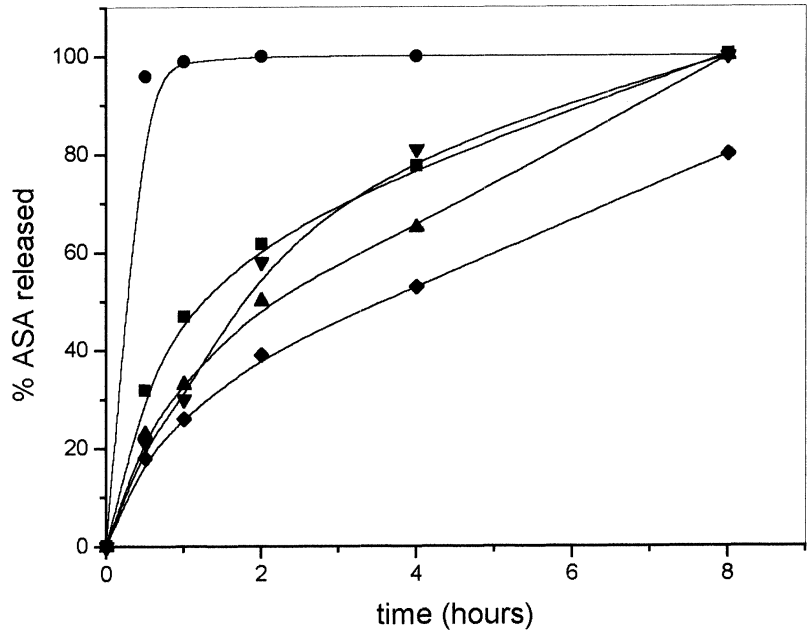

Fig. 7. Acetylsalicylic acid (ASA) released from ASA/microcrystalline cellulose (MCC) (commercial) tablets, in buffer solution (pH 4.5), at 37°C. MCC pretreated with: (◆) ether; (●) acetone; (▲) chloroform; (▼) ethanol, and (■) without solvent treatment.

specific mechanism (D2–D4) changes in practically all ASA/MCC (solvent treated) when compared with the corresponding MCC (in Table 1).

3.4. Dissolution tests of MCC/ASA tablets

The ASA percent released from ASA/MCC tablets was determined as a function of time, in buffer solution of pH 4.5 and in pure water, at 37°C. These conditions were chosen according to the USP XXIII (The United States Pharmacopeia, 1995) specifications. It states that medicaments of normal release must release 80% of the active principle in no more than 30 min, in acetate buffer solution of pH 4.5. For medicaments of controlled release the dissolution test must be

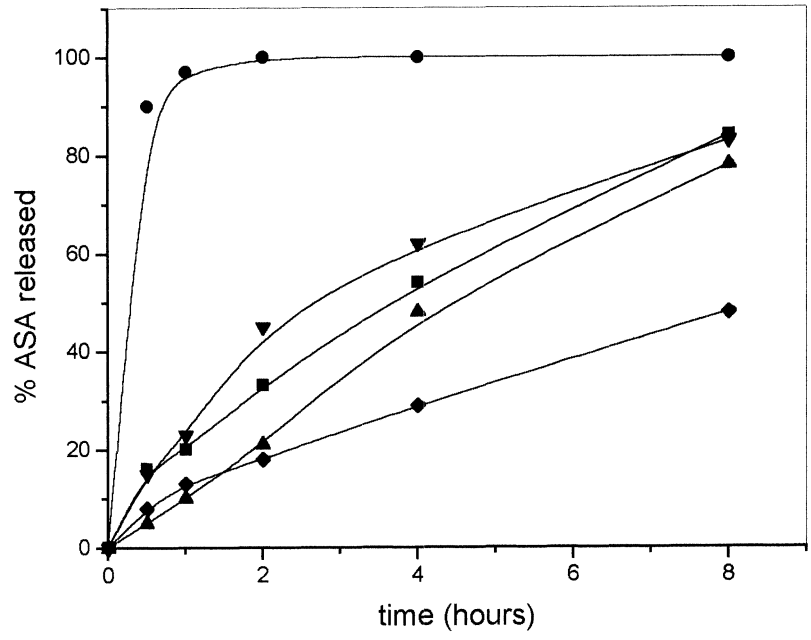

Fig. 8. Acetylsalicylic acid (ASA) release from ASA/microcrystalline cellulose (MCC) (commercial) tablets, in pure water, at 37°C. MCC pretreated with: (◆) ether; (●) acetone; (▲) chloroform; (▼) ethanol, and (■) without solvent treatment.

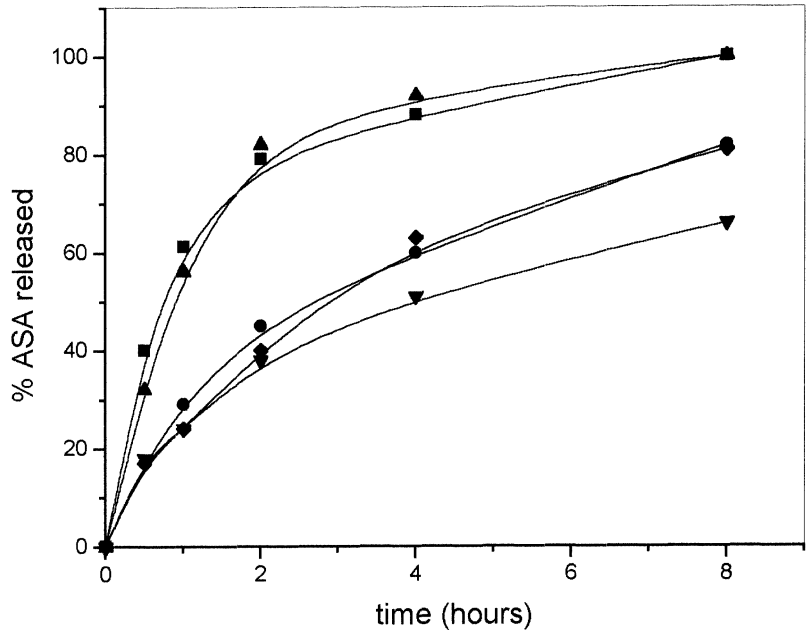

Fig. 9. Acetylsalicylic acid (ASA) release from ASA/microcrystalline cellulose (MCC) (prepared) tablets, in buffer solution (pH 4.5), at 37°C. MCC pretreated with: (◆) ether; (●) acetone; (▲) chloroform; (▼) ethanol, and (■) without solvent treatment.

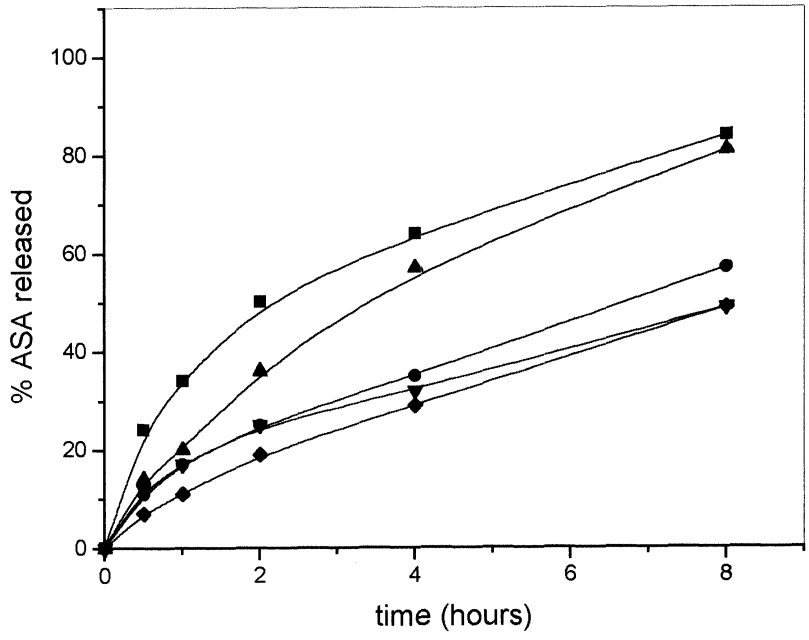

Fig. 10. Acetylsalicylic acid (ASA) release from ASA/microcrystalline cellulose (MCC) (prepared) tablets, in pure water, at 37°C. MCC pretreated with: (◆) ether; (●) acetone; (▲) chloroform; (▼) ethanol, and (■) without solvent treatment.

realized in pure aqueous medium, and followed during 8 h, time interval in which at least 70% of the active principle must be released.

The results obtained with both MCC samples are shown in Figs. 7–10. The ASA release occurs always at a higher rate in the buffer solution of pH 4.5 than in the pure water medium, because of the pH effect on hydrogen bonds. For both MCC samples the ASA release kinetic show a similar tendency for the solvent treated MCC, when the results obtained with the same MCC in the two media are compared. However, this tendency is different for each MCC. ASA release rate is very high when the commercial MCC is pretreated with acetone, and the lower rate observed with this MCC was the pretreated with ethyl ether. On the other hand, for the prepared MCC, the acetone, ethanol and ether pretreated samples show similar kinetic data, that are also comparable with the kinetic results obtained with the ether pretreated commercial MCC. In this case, the higher ASA liberation rate was observed with the chloroform pretreated and the untreated MCC. Both practically coincide (ca. 5%) when the medium is the buffer solution. In pure water, the kinetic curve of the chloroform pretreated MCC lies under the curve of the untreated MCC in ca. 10–15% in the first 4 h, and decreases thereafter. These results show that it is possible to obtain a large range of ASA release rate from MCC/ASA tablets, attaining liberation rates of controlled release and normal liberation medicaments. On the other hand, different prepared MCC seems to lead to very different behaviors.

4. Conclusions

MCC prepared in this work from cellulose extracted from soybean husk, has properties similar to that of a commercial MCC. It is possible to introduce some structural modifications in the cellulose crystals through treatment with organic solvents, which are detected by thermal analysis and FTIR. A linear relationship between two FTIR parameters (ϕ and I_1) were observed, which can be related to crystallinity of cellulose type I. The kinetic of ASA release from MCC/ASA

tablets is sensible to structural cellulose modifications. Quite different release velocities are obtained, satisfying the USP XXIII specifications for controlled release and for normal liberation medicaments. The relation between thermal properties, FTIR results and ASA liberation seems to be a complex picture, probably because various properties contribute simultaneously, each in a particular way.

Residues from annual plants such a sugar cane bagasse, cereal straws, corncobs, cereal husks, etc. are interesting alternatives as cellulose source for several applications. Such materials are renewable and vastly available in many regions of the world, and are generally burned or disposed for ambiental degradation.

Acknowledgements

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