

Characterisation of Ethylcellulose Films containing Natural Polysaccharides by Thermal Analysis and FTIR Spectroscopy

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SUMMARY. Ethylcellulose (EC) has been widely used as a coating material for controlled release systems. Some oligo-polysaccharides such as inulin (IN), guar gum (GG) and their derivatives have been proposed as biodegradable materials for site-specific releases. The objective of this study was to characterise free films composed of EC associated to IN or GG or levan (LEV) using thermal analysis and FTIR spectroscopy. Polymer dispersions of EC/IN, EC/GG or EC/LEV, containing up to 30% of the oligo-polysaccharide, were used for film casting on a Teflon[®] plate. The FTIR spectra obtained suggest hydrogen bond interactions of EC/IN and EC/LEV polymeric chains. The thermal analysis (TGA and DSC) of the blends showed temperature dislocations of some parameters. It was observed that T_{max1} (temperature at which a thermal degradation rate goes up to a maximum) and (OH (wavenumber at which the OH absorption band are centralised) show similar trends in the composition range of the studied blends.

RESUMEN. "Caracterización de películas de etilcelulosa conteniendo polisacáridos naturales por análisis térmico y espectroscopía FTIR". La etilcelulosa (EC) ha sido ampliamente usada como material adecuado en el desarrollo de nuevos sistemas para liberación modificada de fármacos. Algunos oligo-polisacáridos como inulina (IN), goma guar (GG) y sus derivados han sido propuestos como materiales biodegradables para liberación específica de sitio. El objetivo de este estudio fue caracterizar películas aisladas de EC asociada a alguno de los siguientes oligo-polisacáridos: IN, GG y levana (LEV). Las técnicas usadas fueron: análisis térmico (TG y DSC) y espectroscopía de infrarrojo con transformada de Fourier (FTIR). Para obtener las películas, un volumen determinado de cada dispersión acuosa (EC/IN, EC/GG, EC/LEV) fue colocado en placa de teflon y luego evaporado el solvente. Los espectros FTIR sugieren la existencia de interacciones de cadenas poliméricas en los sistemas EC/IN y EC/LEV por desplazamientos de la banda debida a la vibración de O-H. En las curvas de TG y DSC también fueron observadas algunas variaciones. La temperatura en la cual la velocidad de la primera etapa de degradación térmica pasa por un máximo (T_{max1}) y la frecuencia en la cual la banda de O-H está centrada ((OH) presentaron un comportamiento semejante en los sistemas estudiados.

INTRODUCTION

The development of pharmaceutical coating technologies is useful for the preparation of controlled release formulations. The film-forming materials employed are natural or synthetic polymers. There are several patents on the use of various polymeric coatings for selective drug delivery. Polymer blends having colon specific properties and film-forming properties have also been suggested, especially those which contain cellulose derivatives¹⁻³.

Much of the technologies in the coating of per oral dosage forms include polymers that are

vulnerable under specific conditions (pH-dependent solubility; time-controlled release and enzyme-controlled release). Nondigestible oligomers of fructose and other saccharides also show great promise in pharmaceutical applications. Natural polysaccharides are extensively used in the development of coated solid dosage forms for specific drug delivery^{4,5}. In the development of new materials based on aqueous polymeric products, it has been a challenge to eliminate any traces of organic solvents in pharmaceutical coatings. Ethylcellulose (EC) is the most widely used water-insoluble polymer for

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coating pharmaceutical dosage forms. Aqueous ethylcellulose pseudolatex is commercially available as Surelease[®] (25% solids content), manufactured by Colorcon, contains ammonium oleate as a stabiliser and dibutyl sebacate as plasticizer. Inulin (IN) is a natural occurring oligosaccharide found in different plants such as onion, garlic, chicory and Jerusalem artichoke. Chemically, inulin belongs to the group of the gluco-fructans and consists of a mixture of oligomers and polymers containing from 2 up to 60 or more D-fructose molecules. Its main applications are found in several sectors: in food products as thickener, sweetener, and fat substitute; in clinical essays as a diagnostic agent for the measurement of glomerular filtration rates. Due to its resistance to gastric enzymes and its increased sensitivity to the medium of the colon, where it is affected by microflora fermentation, especially by *Bifidobacteria*, this oligosaccharide has been considered promising for colon-specific delivery dosage forms ⁶.

Many other enzymatically-synthesised polysaccharides present biological activities and have great benefits for nutritional and biological applications. It has been reported that the fructooligosaccharides produced by living organisms improve the intestinal microflora. Levan is poly-D-fructan, extracellularly produced by different bacteria and is biosynthesis by *Zymomonas mobilis*. There is consensus on the possibility of the polysaccharide levan (LEV) being a substrate for potentially beneficial bacteria (e.g., *Bifidobacteria* and *Lactobacilli*) and the importance of the molecular weight on LEV produced by strains of *Zymomonas mobilis* on antitumour activity (against sarcoma 180) ^{7,8}. It is viscous, biologically active, non-toxic and can be used as thickener or stabiliser in the food, pharmaceutical and cosmetic industries and is an adequate raw material for fructose production ⁹. Guar gum (GG) derived from the seeds of *Cyamopsis tetragonolobus* is a naturally occurring galactomannan polysaccharide, and could be potentially used as a biodegradable material for the preparation of coated dosage forms for site-specific release. This carbohydrate is susceptible to microbial degradation in a specific region of the gastrointestinal tract. GG consists on a long linear $\beta(1-4)$ mannose backbone (1000-1500 units) to which $\alpha(1-6)$ galactopyranoside subunits are attached as single unit side chains ¹⁰.

IR spectroscopy and X-ray diffraction are considered basic methods to study interactions between drugs and excipients. Thermogravimetry (TG) and differential scanning calorimetry

(DSC) are the most common methods of thermal analysis and can rapidly provide significant data on polymorphism, crystallinity, stability, interactions / compatibility and glass transition. Understanding these properties is very important for a proper development of solid drug products ¹¹.

The purpose of the present work was to characterise EC films containing polysaccharides (IN, GG or LEV). It was possible to obtain films with up to 30% of polysaccharide. The interactions of the polymeric chains in the blends were analysed using the FTIR, DSC and TGA techniques.

EXPERIMENTAL

Materials

Aqueous ethylcellulose pseudolatex Surelease[®] (25% solids content), manufactured by Colorcon (Colorcon - USA) kindly donated by Colorcon Brazil; Chicory inulin (Raftiline HP[®]; average degree of polymerisation between 22 and 25), Orafiti - Tienen - Belgium; Guar Gum (Aldrich[®], Milwaukee, WI); Levans ZAG-12, molecular weight 720.200, kindly donated by Department of Antibiotics Collection - Universidade Federal de Pernambuco (UFPE) - Brazil; Nylon[®] plate covered with Teflon[®]. Other reagents used were of analytical grade.

Film preparation

The dispersions were used in EC and EC/Polysaccharide films preparation. Isolated films were prepared by casting process. Dispersions (4% m/v) of inulin or guar gum or levan were mixed individually with Surelease[®] and stirred for 5 h. After complete homogenisation the dispersions were transferred to a filtering flask for air bubble removal using a vacuum pump. Samples of 10 ml were cast on Teflon[®]-coated nylon plates within a delimited area. Cast dispersions were dried in an oven at 60 °C for 10 h. The formed films were carefully removed from their moulds and stored in a desiccator until use.

Spectrum evaluation (FTIR spectra)

IR spectra of the films were recorded with a FTIR-BOMEN-MB-100-Michelson Spectrometer, using the photoacoustic technique. KBr pellets containing 1% of the samples were used only to obtain the pure polysaccharide spectra.

Thermal analysis

Differential scanning calorimetry (DSC) was performed on 6 mg samples with a Shimadzu

DSC-50 Calorimeter, in a nitrogen atmosphere flowing at 20 mL/min. Temperature ranged from room temperature until 500 °C at a rate of 10 °C/min. The instrument was calibrated with an indium and zinc standard.

Thermal stability of pure polymers and blends was evaluated through thermogravimetry. A Shimadzu TGA-50 instrument was used and the sample weight was 10 mg. Nitrogen flux and heating rate were 10 mL/min and 10 °C/min, respectively.

RESULTS AND DISCUSSION

FTIR spectra

EC/IN, EC/GG and EC/LEV films were prepared in three compositions: 90/10, 80/20 and 70/30. FTIR spectra of these samples and of the pure polymers were drawn and the maximum of the absorption band due to hydroxyls groups (3360-3480 cm⁻¹) were measured. The results (Fig. 1) show a similar behaviour for the EC/LEV and EC/IN systems. A pronounced shift to lower wavenumber occurs with the EC/IN 80/20 and 70/30 blends and with the EC/LEV 70/30 blend. Dislocation to lower wavenumber is characteristic of the weakening of the involved linkage and is observed with the hydroxyl band when hydrogen bonding takes place. In EC/GG, this parameter tends to attain higher values than in pure EC. This result is expected when the occurrence of hydrogen bonding is higher in the pure polymer than in the blend. This behaviour can be understood in view of the more branched structure of GG, as compared with IN and LEV, providing steric hindrance for the intermolecular hydrogen bond formation.

Thermal analysis

TG and DTG curves obtained with samples of EC, IN, GG and LEV are shown in Figs. 2 and 3, respectively. A slight mass loss in the three polysaccharides occurs near 100 °C due to moisture. EC has a more hydrophobic nature and does not retain adsorbed water. EC undergoes the greatest weight loss (92%) between 145 °C and 390 °C. The DTG curve shows a shoulder in the 180 °C to 300 °C region and an intense peak centred at 370 °C, revealing two stages of the thermal degradation reaction. At higher temperatures degradation occurs slowly, and at 1000 °C only 2% remains as residual mass. In IN, the onset temperature for weight loss is 215 °C. Two partially superposed peaks lying at 250 °C and at 289 °C are observed in the DTG curve. 45% of the mass is lost in this temperature range; and at 1000 °C, 25% of the initial mass

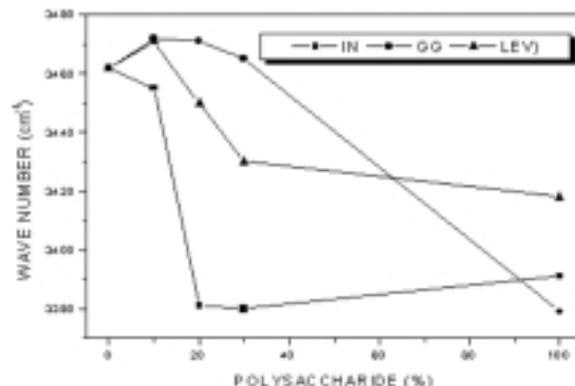


Figure 1. Wave number at the maximum of the OH absorption band in EC, IN, GG, LEV and blends, as indicated in the Figure.

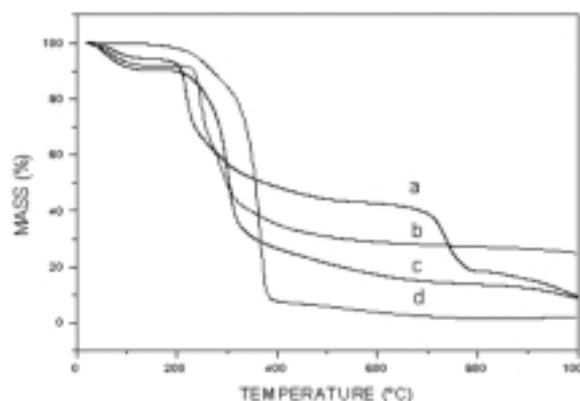


Figure 2. TG curves of LEV (a), IN (b), GG (c) and EC (d).

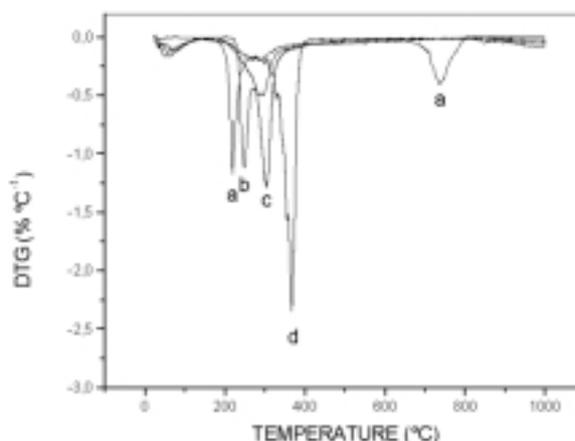


Figure 3. DTG curves of LEV (a), IN (b), GG (c) and EC (d).

remain as a residue of carbon. TG curve of GG shows that the weight loss due to pyrolysis begins at 182 °C and the greatest weight loss takes place between 182 °C and 350 °C. Residual mass at 1000 °C is of 8,9%. Thermal decomposition of LEV starts at 170 °C. The DTG curve

shows a peak at 217 °C followed by a large shoulder until 350 °C and another broad, less intense peak at 735 °C, remaining 9,5% of the initial mass at 1000 °C.

TG and DTG curves of EC/IN, EC/GG and EC/LEV with 90/10, 80/20 and 70/30 compositions were also obtained. The events observed in these curves are essentially those that present in the curves of the corresponding pure polymers, but discrete dislocations are observed in

some cases. These effects were better detected in the DTG curves, where the two peaks of higher intensity account for the two principal stages of thermal degradation. The one at lower temperature is due to polysaccharide decomposition and the other to EC decomposition. As an example, Fig. 4 shows the DTG curves of EC, IN and EC/IN blends. The temperature at the minimum of both peaks were measured for each blend and reported as T_{max1} and T_{max2} in Table 1.

Composition	T_{max1} (°C)			T_{max2} (°C)		
	90:10	80:20	70:30	90:10	80:20	70:30
EC:IN	260	249	247	369	369	369
EC:GG	shoulder	301	304	357	359	359
EC:LEV	218	217	212	341	335	335

Table 1. Temperatures at which the reaction rate is maximum, in two stages of the pyrolysis, obtained from DTG curves of EC/IN, EC/GG and EC/LEV blends.

The results of the T_{max1} show behaviour similar to the O-H wavenumber in cm^{-1} (ν_{OH}) data shown in Fig. 1. For EC/GG blends, T_{max1} and ν_{OH} show little variation due to the blend composition (10-30% GG) as can be seen in Fig.1 and Table 1. On the other hand, T_{max1} and ν_{OH} for EC/IN 80/20 and 70/30 and for EC/LEV 70/30 give the lower values. These three systems have greater hydrogen bond formation between the polymer chains, suggesting, therefore, that such an interaction can lead to a slight loss of thermal stability. The T_{max2} data do not show any relationship with other parameters, for EC/IN it remains unaltered and in EC/GG and

EC/IN it shifts to lower temperature, when compared with the corresponding peak of pure EC.

Thermal properties of EC, polysaccharides and blends were also analysed through DSC. EC, GG and LEV decomposes directly through pyrolysis in an inert gas atmosphere. Only IN melts (near 168 °C) and the transition was detected in two of the EC/IN blends, as can be seen in Fig. 5. Data of the temperature at the minimum of the mentioned peak are in Table 2. This temperature is higher in EC/IN 80/20 blend than in IN, showing that the presence of EC (which initiate its thermal degradation at 145 °C) can act in such a manner that a higher tempera-

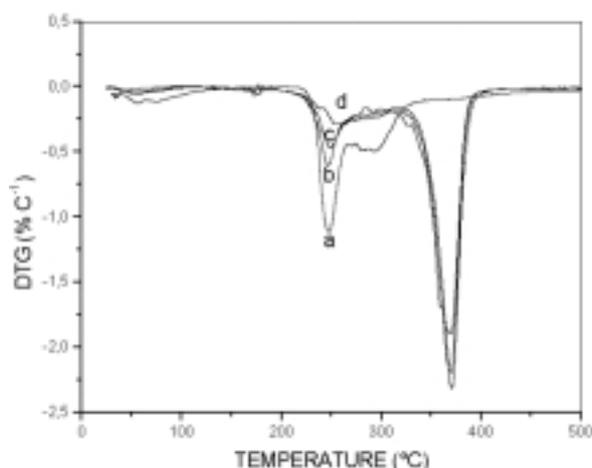


Figure 4. DTG curves of EC (a), IN (e) and EC/IN blends: (b) 90/10, (c) 80/20 and (d) 70/30.

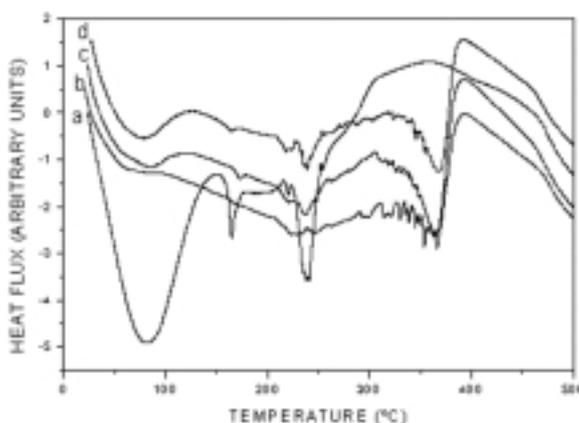


Figure 5. DSC curves of IN (a) and EC/IN blends. (b) 90/10, (c) 80/20 and (d) 70/30.

Composition EC/IN	T _m (°C)
90:10	-
80:20	173
70:30	165
0:100	165

Table 2. IN melting temperature in EC/IN blends, obtained from DSC curves.

ture is needed for the IN melting process to take place. However, his effect is not observed in the 70/30 blends. The events observed at temperatures higher than 200 °C is mainly exothermic reactions of thermal degradation and the noise in the 320 to 380 °C ranges occurs sometimes with films, which undergo creeping.

CONCLUSIONS

FTIR spectra of EC/IN and EC/LEV films suggest that hydrogen bonding occurs in both systems. This bonding occurs with polysaccharide concentration of 20% and 30% in the first case and with 30% in the other one. On the other hand, the FTIR results obtained with EC/GG indicate a great occurrence of hydrogen bonds in the pure EC than in the blends. A relationship of these results with T_{max1} (temperature at which the reaction rate in the main stage of the polysaccharide pyrolysis goes up to a maximum) was observed.

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