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Material properties

Influence of process parameters on microstructure and mechanical properties of starch-cellulose acetate/silver sulfadiazine matrices prepared by melt extrusion

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ABSTRACT

Starch-cellulose acetate matrices containing silver sulfadiazine were produced using melt extrusion for application in drug delivery devices (DDDs). The influence of the extrusion parameters (screw speed and temperature) on the morphological and mechanical properties of the matrices was evaluated at three different levels. The microstructural characterization of all matrices showed that an increase in the screw speed enhances the porosity and drug dispersion, while an increase in the extrusion temperature decreases the pore diameter of the matrices. Mechanical results did not show significant differences between the elastic modulus values for the matrices; however, a faster screw speed led to higher ultimate strength and strain at failure values. Results obtained in the dynamic mechanical analysis showed that the glass transition and loss tangent (tan δ) peak values became higher with increasing screw speed and temperature.

1. Introduction

Melt extrusion (ME) is a well-known technique in the field of polymer science and is used to produce tubes, pipes and films [1]. In comparison with other techniques, ME offers several advantages, for instance, the different steps (mixing, melting, homogenizing and shaping) are carried out on a single machine [2], it has a lower environmental impact (absence of solvents) and it is associated with reduced costs (fewer processing steps and continuous operation) [3]. In addition, variables such as the processing temperature and screw speed can potentially be used to control the rheological, mechanical and morphological properties of the matrices produced by ME [4].

These attributes have attracted considerable interest in relation to the search for efficient production processes for pharmaceutical drug delivery systems. Regarding this technique, the preparation of different dosage forms, such as implants, tablets, pellets and films, as well as transdermal delivery systems, has been investigated [3,5,6]. Liu et al. (2010) investigated the effects of the extrusion process parameters (set mixer temperature, screw speed and residence time) on Eudragit®E PO polymeric matrices containing indomethacin. The results showed that increases in the mixer temperature or screw speed led to a decrease in the polymer torque and viscosity, which in turn could increase the dissolution of drug particles held within extruded polymeric matrices [7]. Likewise, previous studies have revealed that the residence time, screw speed and heating temperature are significant factors in terms of the crystallinity and solubility of drugs in extruded matrices [8]. In addition, the presence of a drug in an extruded polymeric

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matrix can affect the morphology and porosity, resulting in changes in the mechanical properties of the matrix [5].

However, the selection of the material is as important as the choice of the technique and parameters used for the production of drug delivery devices, and in this regard the use of polymers, especially biopolymers, has increased in recent years. This is partly due to the properties of biopolymers, such as biodegradability and biocompatibility, making then applicable in pharmaceutical development and biomedical devices. For example, cellulose and its derivatives have been used in the development of films containing drugs [9], sustained-release mini-matrices [2] and tablets [1].

Starch is another example of a biopolymer. It has been applied in the development of transdermal films [10] and matrices for controlled drug delivery [11]. Nevertheless, the applicability of natural polymers like starch and cellulose is sometimes restricted due to their mechanical and swelling properties. In order to overcome these limitations, cellulose and starch blends have been investigated. Previous studies have shown that cellulose and starch blends are biocompatible [12], the blend leading to an increase in the thermomechanical stability, while the water sensitivity decreases with an increase in the cellulose content [13,14].

A study previously carried out by our group [15] demonstrated that starch and cellulose blends are potential candidates for the manufacturing of drug delivery systems. In this context, the purpose of this study was to investigate the microstructure and mechanical properties of matrices containing starch, cellulose acetate and the antibiotic silver sulfadiazine, produced by ME, applying different process parameters (temperature and screw speed) for the future development of polymeric films for burn treatments.

2. Experimental

2.1. Materials

Starch-cellulose acetate (SCA) (trade name Mater-Bi® Y101U) was received from Novamont, (Novara, Italy) in the form of granules. This material has a glass transition temperature (Tg) of around 105 °C and can be processed at temperatures ranging from 150 to 200 °C [16]. Silver sulfadiazine (SSDAg) was obtained from Henrifarma (São Paulo, Brazil) with a particle size range of 975 nm to 3.5 μm.

2.2. Melt extrusion

The SSDAg particles were dispersed in SCA granules by mechanical mixing using a cylindrical blender, for 30 min at 100 rpm, with a SSDAg:SCA ratio of 1:9 (w/w). The extrusion was performed using a laboratory-scale single-screw extruder with a length to diameter ratio (L/D) of 20:1. Matrices were produced by ME using 3^2 full factorial designs with the variables investigated being screw speed and barrel zone temperature. The extrusion conditions used are outlined in Table 1.

2.3. Scanning electron microscopy

The extruded matrices were examined using a Jeol JSM-6390LV scanning electronic microscope (SEM) equipped with an energy dispersive spectrometer (EDS) in order to investigate their SSDAg dispersion, fracture surface and microstructure. Matrices were coated with gold using a sputter coater (D2 Diode Sputtering System).

Table 1
Variables and levels studied in 3^2 full factorial designs.

Variables	Levels		
	−1	0	1
Temperature zone (°C)	160	175	190
Screw speed (rpm)	40	60	80

2.4. Mechanical analysis

Dynamical mechanical analysis (DMA) was performed using a TA Instruments (model Q800) analyzer in single cantilever mode. Quasi-static tests were conducted and stress-strain curves were obtained with the loading rate increasing at 2 N/min up to 18 N at 30 °C. Dynamic tests were conducted at a frequency of 1 Hz within the temperature range of 50–170 °C using a heating rate of 3 °C/min. Dynamic tests provided the values for the storage modulus (E′), the loss factor (E″) and tan δ (E″/E′).

3. Results and discussion

Fig. 1 shows the micrographs of fractured surfaces of the matrices containing SCA/SSDAg extruded under different process conditions.

The fractured surfaces of the matrices demonstrated that, regardless of the extrusion temperature employed, an increase in the screw speed enhances the matrix porosity. This is because increasing the screw speed leads to a higher shear rate, which results in a greater degree of starch expansion and, consequently, extruded matrices with increased porosity and pore diameter [11]. This enhanced porosity with faster screw speeds may also occur due to the evaporation of water molecules and additives during the extrusion process [17].

An increase in the matrix temperature during the ME process caused a reduction in the pore size, as can be seen on comparing the matrices extruded at 160 °C, which had larger pores, with those extruded at 175 °C and 190 °C. The presence of larger pore diameters (approximately 50 μm) can be attributed to the low plastification of SCA when extruded at 160 °C. Furthermore, for all extrusion conditions, the dispersion of silver sulfadiazine occurred in a homogeneous way, considering the absence of clusters in the micrographs of the extruded matrices. This factor, as in the case of porosity and drug dispersion, could modify the mechanical properties of the matrix.

Table 2 shows the average values for the elastic modulus, ultimate strength and strain at failure for SCA/SSDAg matrices extruded under different temperature and screw speed conditions.

The average values for the elastic modulus of the extruded SCA/SSDAg matrices did not show a significant difference ($p = 0.001$) with an increase in screw speed. However, an increase in the extrusion temperature significantly changed the elastic modulus values, matrices