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Research paper

Effect of the manufacturing conditions on the structure and permeability of polymer films intended for coating undergoing phase separation

Mariagrazia Marucci *, Johan Arnehed, Annica Jarke, Hanna Matic, Mark Nicholas, Catherine Boissier, Christian von Corswant

AstraZeneca R&D Mölndal, Mölndal, Sweden

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ABSTRACT

The major aim of this work was to study the effect of two process parameters, temperature and coating flow, on permeability to water and structure of free films sprayed from mixtures of ethyl cellulose (EC), hydroxypropyl cellulose (HPC), and ethanol. The films were sprayed in a new spraying setup that was developed to mimic the film coating process in a fluid bed and to provide well controlled conditions. EC and HPC phase separated during the film drying process, and EC- and HPC-rich domains were formed. The process parameters had a great impact on the structure and the permeability to water of the films. The longer the time before the film structure was locked by a high film viscosity, that is, the lower the temperature and the higher the coating flow, the larger the domains and the lower the film permeability. The effective diffusion coefficient of water in the films varied by about six times within the range of the process parameters studied. Structures of sprayed films and water effective diffusion coefficients in sprayed films were compared to those of cast films. For the cast films, the domains were bigger, and the permeability to water was significantly lower compared to those of the sprayed films. The results indicate that the process parameters can be used as a mean to regulate structure and permeability of coating films undergoing phase separation.

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1. Introduction

Polymer film coating is often used in oral modified release systems. Several parameters can be varied to obtain a specific release profile, for example, the type of polymer, coating thickness, type and amount of plasticizer [1,2], and type and concentration of the pore-forming agent [3]. Moreover, by blending two or more polymers that exhibit different physicochemical properties, a very broad range of release patterns can be achieved [4,5]. Importantly however, polymers with different physicochemical properties are often not completely miscible and will consequently phase separate during the film formation process.

The use of isolated free films is a convenient way to screen the properties of films intended for coating. Free films have been used to study how the mechanical properties [9] and the permeability [5] of the film change from the dry to the wet state, and to better understand the release mechanisms from coated formulations [5,10]. Free films are usually prepared by cast or spraying, and, for each of the two mentioned methods, there is a large variety of process conditions, which can be used. The kinetic of solvent evaporation is much slower for cast films than for sprayed films. When films are prepared from a mixture of non-miscible polymers initially dissolved in a common solvent, solvent evaporation induces phase separation and an increase in viscosity of the polymeric mixture in the course of film drying. The film phase separated structure is frozen by a high film viscosity at a certain solvent concentration. For cast films, it has been shown that the process conditions may be critical parameters for the structure of films undergoing phase separation as they affect the extent of the phase separation [11–14]. The slower the solvent evaporation rate, the slower the increase in viscosity of the polymeric mixture and the larger the extent of the phase separation [14].

When pellets are spray coated, the process conditions are usually preferably adjusted to obtain a quick coating process with a high coating yield and a high coating quality. The effect of the process parameters on the film thickness homogeneity of the coating [6] and on the roughness of the film surface [7,8] has been recently presented. However, to the best of our knowledge, the effect of the process parameters on the structure and permeability of films sprayed from solutions of non-miscible polymers initially dissolved in a common solvent and undergoing phase separation during film formation has not been investigated yet. This is surprising given the wide use of film coats made from blends of non-miscible polymers to modify the drug release rate from oral formulations. Moreover, despite the use of sprayed and cast free films to predict

* Corresponding author. AstraZeneca R&D Mölndal, SE-431 83 Mölndal, Sweden. Tel.: +46 31 7064532; fax: +46 31 7763729.
E-mail addresses: mariagrazia.marucci@astrazeneca.com, mariagrazia.marucci@gmail.com (M. Marucci).

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the properties of films sprayed onto pellets or tablets, the differences between the structure and permeability of cast and sprayed films have not been investigated in detail.

The principal aim of this work was to study the effect of two process parameters, temperature and coating flow, on the extent of the phase separation and on the structure and water permeability of free films sprayed from mixtures of ethyl cellulose (EC), hydroxypropyl cellulose (HPC), and ethanol. A novel spraying technique was developed to mimic the film coating process in a fluid bed, and to spray the films at well controlled conditions. Cast films were also characterized in order to better understand how the structure and permeability of the films is affected when the polymers have very long time to phase separate, and the results were compared to those of the sprayed films.

Films made of the water-insoluble polymer EC and the water-soluble polymer HPC with a weight ratio of 70:30 were used in this work as it has been shown that the two polymers are not miscible and phase separate [15–17]. Moreover, they were chosen because EC/HPC films are easily processed, have low toxicity and offer the possibility of obtaining various release profiles by changing the EC/HPC ratio [5,18,19]. The film structure was investigated using the noninvasive confocal laser scanning microscopy (CLSM) technique.

2. Materials and methods

2.1. Materials

EC (EC N10CR) was supplied by Dow Chemical Co., USA. HPC grade LF was supplied by Aqualon, USA. Part of the HPC was labeled by CarboMer Inc., USA. Fluorescein was used for labeling at a concentration of 0.005 mol per mol of glucose. Tritium-labeled water (Amersham, UK) was used in the measurements of the effective diffusion coefficient of water in the films.

2.2. Preparation of polymer films

The films were prepared from mixtures containing 94% w/w hydrous ethanol (95%) and 6% w/w polymers, as it has been shown that at this low polymer concentration EC and HPC do not phase separate [20]. The dry films consisted of 70% EC and 30% HPC. Six percent of the HPC used was fluorescein-labeled. Labeled HPC was used in order to increase the fluorescence contrast between EC and HPC in the confocal laser scanning microscopy analysis of the films phase separated structure.

2.2.1. Sprayed films

EC/HPC films were prepared by spraying the coating mixture onto a rotating drum. The width of the drum was 9.8 cm, while its diameter was 5 cm. The drum was inserted into a modified fluid bed chamber. The diameter of the air distributor plate of the fluid bed was 9.7 cm. A horizontal-moving spraying nozzle positioned below the drum was used to spray the polymeric mixture. A schematic representation of the experimental setup is shown in Fig. 1. Fluidizing air flow, temperature of inlet fluidizing air, atomizer air pressure, atomizer air flow, rotation rate of the drum, velocity of the spray raster, and coating flow (polymer and ethanol) were accurately controlled. The process conditions of the sprayed films were chosen in order to allow for a good film formation, that is, (a) to let the coating drops coalesce into each other, thus avoiding granules on the films and (b) to have a film which adhered to the drum. Fluidizing air flow, atomizer air pressure, atomizer air flow, rotation rate of the drum, and velocity of the spray raster were kept constant for all the sprayed films and had values of 40 Nm^3/h, 2 bar, 1.6 Nm^3/h, 80 rpm and 1.3 cm/s, respectively. The temperature of the inlet fluidizing air and the coating flow were varied. The values of the coating flows investigated were 13, 16, and 18 g/min. The temperature of the inlet fluidizing air, T_{in}, was regulated to achieve the desired value for the temperature of the exhaust air, T_{out}. The values of the T_{out} achieved were 42, 49, and 57 °C. The values of the process parameters used are reported in Table 1. Hydrous ethanol 95% alone was sprayed onto the drum before the spraying of the polymer mixture. The value of its flow was equal to the value of the ethanol flow sprayed during film preparation. T_{out} was monitored and the spraying of the coating mixture started when its value became constant. In this way, it was possible to spray the films at a pretty constant temperature. Heating of the incoming air was stopped when spraying was ended. Despite stopping the heating, T_{out} increased by ca. 7–8 °C during the first minute after the completion of spraying. This was caused by the lower energy demand to dry the film when no fresh ethanol was supplied. After spraying, the films were kept in the fluid bed for about 20 min to completely dry and then were peeled off the drum

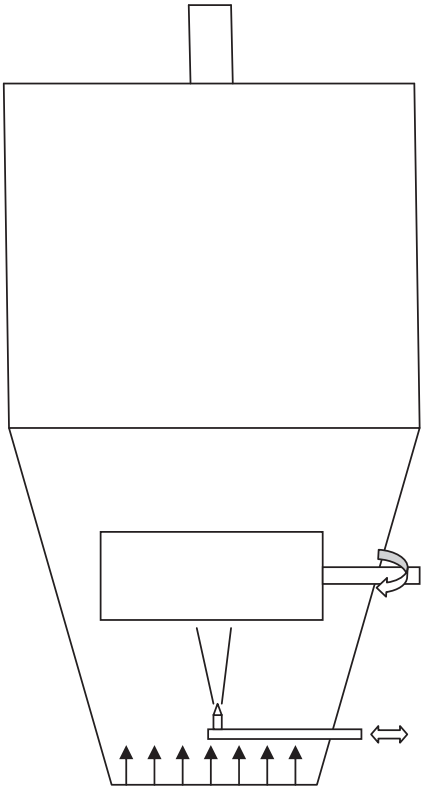

Fig. 1. Schematic representation of the setup used for the preparation of sprayed films. The chamber is a modified fluid bed and a horizontal-moving spraying nozzle was used to spray the coating mixture into the rotating drum. Fluidizing air flow, temperature of the inlet fluidizing air, atomizer air pressure, atomizer air flow, rotation rate of the drum, velocity of the spray raster and coating flow could be accurately controlled. The temperature of the exhaust air leaving the modified fluid bed, T_{out}, was monitored.

Table 1
Process parameters used for the manufacturing of the sprayed films.

Film number	1	2	3	4
T_{out} (°C)	42	42	57	49
Coating flow (g/min)	18	13	16	13
T_{in} (°C)	68	65	90	72
Fluidizing air flow (Nm^3/h)	40	40	40	40
Atomizer air pressure (bar)	2	2	2	2
Atomizer air flow (Nm^3/h)	1.6	1.6	1.6	1.6
Spray raster velocity (cm/s)	1.3	1.3	1.3	1.3
Drum rotation rate (rpm)	80	80	80	80

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