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Research paper

Influence of hydroxyethylcellulose on the drug release properties of theophylline pellets coated with Eudragit® RS 30 D

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Abstract

The objective of this study was to investigate the influence of a hydrophilic polymer, hydroxyethylcellulose (HEC), on the release properties of theophylline from pellets coated with Eudragit® RS 30 D, and the physicochemical properties of Eudragit® RS 30 D cast films. The release rate of theophylline from Eudragit® RS 30 D coated pellets decreased during storage at 25 °C/60% RH due to the further coalescence of colloidal acrylic particles. In addition, water-vapor permeability and tensile strength of Eudragit® RS 30 D cast film decreased after 1-month storage at 25 °C/60% RH. The presence of 10% hydroxyethylcellulose in the coating formulation was shown to stabilize the drug release rate from coated pellets, the water-vapor permeability and the tensile strength of free films. Atomic force microscopy and scanning electronic microscopy were used to demonstrate that the HEC was immiscible with Eudragit® RS 30 D in the cast films. The stabilization effect of HEC was investigated and determined to be due to the formation of an incompatible phase between the latex particles which impaired further coalescence of the colloidal acrylic particles.

Keywords: Eudragit® RS 30 D; Hydroxyethylcellulose; Stabilization; Coalescence; Drug release rate

1. Introduction

Polymeric film coatings are widely used in solid oral dosage forms to mask the taste of bitter drugs, as moisture barriers and as functional coatings to target or control drug delivery in the gastrointestinal tract. Film coatings based on aqueous latex dispersions have several advantages over traditional organic solvent-based coating systems, including fewer health, safety and environmental concerns. Due to the low viscosity of latex dispersions, a higher solids content can be used, thus reducing the processing time to coat a solid substrate.

Film formation from the coalescence of latex particles during coating occurs in three stages. During the first stage, water evaporates from the colloidal latex at a constant rate, concentrating the polymeric particles at the surface of the substrate [1–3]. During the second stage, the particles come into irreversible contact with each other and water evaporates from the interstitial voids at a reduced rate resulting in deformation of the latex particles [4–6]. Formation of the film coating occurs in the third stage from the coalescence of discrete polymeric particles and the interdiffusion of polymer chains. The remaining water leaves the film through the inter-particulate channels between the latex particles and by diffusion through the fused polymeric film. During this final stage, the polymer film becomes more homogenous and gains its mechanical properties as polymer chain interdiffusion occurs and the particle interface becomes less distinct [7,8].

This final stage of film formation can proceed for days or even weeks after initial film formation, and changes in drug release rates of sustained release dosage forms coated with latex dispersions over time have been reported [9–14]. Amighi and Moës reported that the theophylline release rate from pellets coated with Eudragit® RS 30 D and with

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Eudragit® NE 30 D (acrylic copolymer aqueous dispersions) decreased continuously during storage [9,10]. Goodhart et al. demonstrated that phenylpropanolamine release rate from pellets coated with Aquacoat (aqueous ethylcellulose dispersion) decreased significantly upon storage [11].

This 'aging' phenomenon is thought to result from further coalescence/interdiffusion of latex particles, which occurs during the final stage of film formation, resulting in a decrease in permeability due to a decrease in polymer chain mobility and reduced free volume. The drug release rate of polymeric coated dosage forms will therefore decrease with increasing storage time. Furthermore, the interdiffusion of polymer particles can also cause the exudation of film additives, such as surfactants and plasticizers, resulting in changes in drug release rate due to changes in the free volume, porosity and hydrophobicity of the film. Studies have shown that interdiffusion rates increase with increasing temperature and decreasing molecule weight [7,8]. Other factors have been demonstrated to affect the rate of polymer interdiffusion during film formation, including coalescing aids [15], organic solvents [16], surfactants [17] and crosslinking of particles [18,19].

One approach that has been used to solve the aging problem is to 'cure' film coated dosage forms by post-coating storage at elevated storage conditions to complete the film formation process and to ensure a reproducible drug release profile. The curing time required to obtain a stable product has been found to be dependent on the storage temperature and humidity as well as the plasticizer level in the acrylic coating [9,13]. However, a prolonged curing process following manufacturing is not desirable since it is both time consuming and expensive.

Amighi and Moës demonstrated that a film coating can be stabilized by utilizing high plasticizer levels [9]. Plasticizers were used to decrease the glass transition temperature (T_g) and to facilitate the coalescence of latex particles during the film formation process. However, this approach to achieve an equilibrated film coating has limited applications since coating, curing and high temperature storage may result in an increase in the tackiness of the resulting film. In addition, instability may also arise due to greater chain mobility caused by a lowering of the glass transition temperature.

Maejima and McGinity reported that theophylline release from Eudragit® RS\RL 30 D coated pellets was stabilized after storage for 3 months at 40 °C/75% RH by using a coating formulation containing a high content of talc (200% based on the dry polymer weight) [12]. Polymer blends have also been utilized to stabilize the drug release from Eudragit® NE 30 D coated pellets [14].

The objective of the current study was to investigate the influence of a hydrophilic polymer, hydroxyethylcellulose, on film formation and physical aging of theophylline pellets coated with Eudragit® RS 30 D.

2. Materials and methods

2.1. Materials

Eudragit® RS 30 D was donated by Röhm GmbH & Co. KG (Darmstadt, Germany). Theophylline and lactose monohydrate were purchased from Spectrum Chemical Mfg Corp. (Gardena, CA, New Brunswick, NJ). Polyvinylpyrrolidone K-30 (Kollidon® 30) was supplied by BASF Corp. (Mount Olive, NJ). Microcrystalline cellulose (Avicel® PH-101) was donated by FMC Corp. (Newark, DE); Talc (ALTALC 500 V) was supplied by Luzenac American Inc. (Englewood, CO.). Hydroxyethylcellulose (Natrosol® 250L NF) was provided by Aqualon Company (Wilmington, DE), and triethyl citrate, NF (TEC) was donated by Morflex, Inc (Greensoro, CA).

2.2. Preparation of core pellets

Theophylline anhydrate (25%), lactose monohydrate (25%) and Avicel® PH-101 (45%) were passed through a 60-mesh sieve, mixed in a twin shell blender for 15 min and then wet granulated with Kollidon® 30 (5%) as a 20% w/w aqueous solution. The moistened mass was extruded using a LCI Benchtop Granulator (Tokyo, Japan) at a rotation speed of 50 rpm. The extrudates were spheronized using a Caleva model 120 Spheronizer (Dorset, England) for 4 min at a spheronization speed of 1000 rpm. The pellets were sieved after drying at 40 °C for 12 h, and the 16–20 mesh pellets were selected for further studies.

2.3. Preparation of coating dispersions

The hydroxyethylcellulose (10% w/w based on dry polymer weight) was dissolved in purified water before mixing with the Eudragit® RS 30 D. The polymer dispersion was plasticized with TEC (20% w/w based on the dry polymer weight) using low-shear mixing for 1 h. Talc (50% w/w based on dry polymer weight) was previously dispersed in purified water using a POLYTRON® (Brinkmann Instruments, Westbury, NY, Ont., Canada) and then stirred continuously with the desired amount of pre-plasticized polymer dispersion. The concentration of polymers and the total solids content in the final dispersion were 10 and 15% w/w, respectively.

2.4. Film coating

A 250 g batch of pellets (16–20 mesh) was transferred to a fluidized bed coater (Strea-1® Areomatic-Fielder, Columbia, MD), and the acrylic dispersions were applied until the desired polymer weight gain of 12% was achieved. The inlet and outlet temperatures were 33 ± 2 and 30 ± 2 °C, respectively. The coating dispersion was applied at a rate of 2.0–3.0 g/min, and the pneumatic spray pressure was 1.5 bar. The aqueous dispersion was stirred continuously

throughout the coating process to prevent sedimentation of the talc. Following the application of the coating dispersion, the pellets were dried for an additional 10 min at 33 ± 2 °C in the fluidized bed unit, and then removed and dried at 40 °C for 24 h.

2.5. Film casting

Polymer dispersions containing 15% solid content were cast onto a Teflon plate. The films were dried at ambient conditions followed by storage for 72 h in a desiccator containing desiccants (Drierite®) to remove residual water.

2.6. Surface morphology

The surface morphology of the cast film was observed with a Hitachi S-4500 field emission scanning electron microscope (Rolling Meadows, IL). A gold–palladium layer was applied to the pellets for 50 s under an argon atmosphere using a Pelco Model 3 cold sputter module (TED Pella Inc., Tustin, CA).

Atomic force microscopy (AFM, Thermomicroscope, Autoprobe, Park Scientific Instruments) was used to determine the surface roughness and to examine the surface morphology of the cast films. Eudragit® RS 30 D cast films, with and without 10% HEC, were cut into 10 mm × 10 mm rectangular specimens and examined using AFM with contact mode. The scan area was 2 μm × 2 μm. The surface roughness of the sample was quantified by average roughness (R_a) and root-mean-square roughness (RMS) using Eqs. (1) and (2)

$$R_a = \frac{1}{N}\sum_{i=1}^{N}|Zi - \bar{Z}| \quad (1)$$

$$\mathrm{RMS} = \left[\frac{1}{N}\sum_{i=1}^{N}(Zi - \bar{Z})^2\right]^{1/2} \quad (2)$$

where N is the number of measurements, Zi is the height and Z bar is the average height.

2.7. Water-vapor permeability of cast films

The water-vapor permeability of the cast films was determined according to ASTM guideline E 96-00 using the Desiccant Method [20]. The thickness of the film was determined by measuring 8 points along the film circumference using a micrometer and the results were averaged. The film specimen was secured to the open mouth of an aluminum permeability cup (4 cm inner diameter and 3 cm depth) containing 20 g Drierite® desiccant. The permeability cups were accurately weighed and placed into a chamber maintained at 75% RH using a saturated sodium chloride solution stored at 25 °C. The cups were weighed periodically to determine weight gain, and the water-vapor transmission rate (WVT) and permeability (P) were calculated using the following equations [20]

$$\mathrm{WVT} = (G/t)A \quad (3)$$

$$P = (\mathrm{WVT}/S) \times (R_1 - R_2) \times d \quad (4)$$

Where G is the weight change, t is the time during which G occurred, G/t is the slope of the straight line, A is the test area (cup mouth area), S is the saturation vapor pressure at test temperature, R_1 is the relative humidity in the test chamber, R_2 is the relative humidity inside the cup (0% RH for the desiccant method) and d is thickness of the film.

2.8. Polymeric film acetone treatment

Polymeric cast films were cut into 1 cm × 2 cm strips and, then suspended in acetone for 12 h. The films were vacuum dried for 72 h to remove the residual solvent. The morphology of the films was investigated using SEM.

2.9. Mechanical properties of cast films

The mechanical properties of cast films were investigated using an Instron (Model 4201) according to ASTM guideline D 883-02 [21]. The polymeric cast films were cut into 90 mm × 13 mm strips. A 1000 N capacity load cell was mounted on the instrument. The distance between the grips was 50 mm. The load range was 50 N and the cross-head speed was set at 25 mm/min. The mechanical properties including tensile strength at maximum and tensile strength at failure were calculated according to the following equations

Tensile strength at maximum

= load at maximum/minimum cross-sectional area (5)

Tensile strength at failure

= load at failure/minimum cross-sectional area (6)

2.10. Polymer interactions

To investigate possible polymer interactions, Fourier transform infra-red (FTIR) spectra were obtained using a Perkin–Elmer 2000 FTIR spectrophotometer (Beaconsfield, Buckinghamshire, England). Cast films of Eudragit® RS 30 D, HEC and Eudragit® RS 30 D containing 10% HEC were ground into fine powder using a mortar and pestle and then compressed into pellets with KBr (30 mg sample in 300 mg KBr). The scanning range was 0–7000 cm^{-1}.

2.11. Drug release properties of coated pellets

Drug release properties of coated theophylline pellets were studied using a USP 26 Apparatus 2 (Vankel VK 6010; Cary, NC) with 900 ml of pH 7.4, 50 mM phosphate

buffered solutions maintained at 37 °C and agitated at 50 rpm. Samples were withdrawn by an auto sampler (Vankel VK 8000; Cary, NC) at 0.5, 1, 2, 4, 6, 8, 10 12 h time points. The sample concentrations were determined by UV spectroscopy (DU-65, Beckman instruments; Fullerton, CA) at a wavelength of 272 nm. Dissolution tests were performed in triplicate.

3. Results and discussion

The influence of storage time on the release rate of theophylline from pellets coated with Eudragit® RS 30 D is shown in Fig. 1. An initial 2-h delay in drug release was followed by a zero order release phase. In addition, the theophylline release rate decreased continuously over a 1-week period of time when stored at 25 °C/60% RH.

Eudragit® RS 30 D is a copolymer of acrylic and methacrylic acid esters with a low content of hydrophilic quaternary ammonium groups, which causes the polymer to slowly swell in aqueous media. The mechanism of drug release from Eudragit® RS 30 D coated pellets is believed to be a diffusion-controlled process. Diffusion-controlled passage across the film can be defined in the simplest terms by Fick's law

$$Q = DS(C_1 - C_2)t/h \quad (7)$$

Where Q is the quantity of drug diffusion in time t, h is the film thickness, C_1 is the concentration in the dosage form, C_2 is the concentration of drug in the aqueous receptor, D is the diffusion coefficient of the drug and S is the area of diffusion. The diffusion coefficient, D, has been modified to account for the recognized film structure by Iyer [22]

$$D = D_w e/\tau \quad (8)$$

Where D_w represents the diffusion coefficient in the medium, e is the porosity factor and τ is the tortuosity factor. Therefore, changes in the film porosity or tortuosity during storage would alter the diffusion coefficient, resulting in a change in drug release rate. As latex particles coalesced during the final stage of film formation, the polymer chains diffused across particle boundaries, making the boundaries less distinct. At the same time, the decrease in free volume resulted in a densification of the film and further decreased film permeability. According to Eq. (8), the drug diffusion coefficient would decrease as a result of decreased porosity, which explains the observed reduction in drug release from the dosage form (Fig. 1).

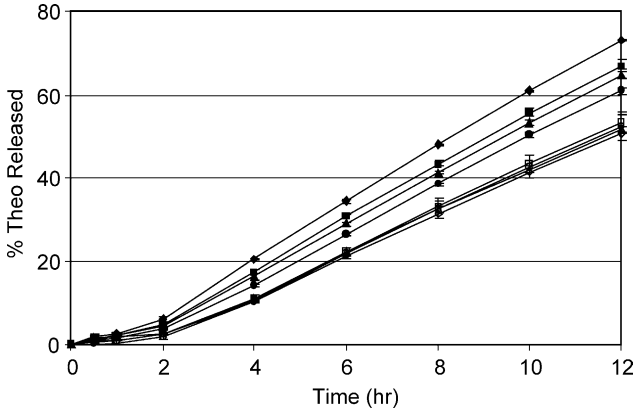

Fig. 1. Influence of storage time on the release rate of theophylline from pellets coated with Eudragit® RS 30 D stored at 25 °C/60% RH in open HDPE containers (USP 26 Apparatus 2, 900 ml, 50 mM phosphate buffer, pH 7.4, 37 °C, 50 RPM, $n=3$). Key: ♦, initial, ■, 1 week; ▲, 2 weeks; ●, 4 weeks; ◇, 4 months.

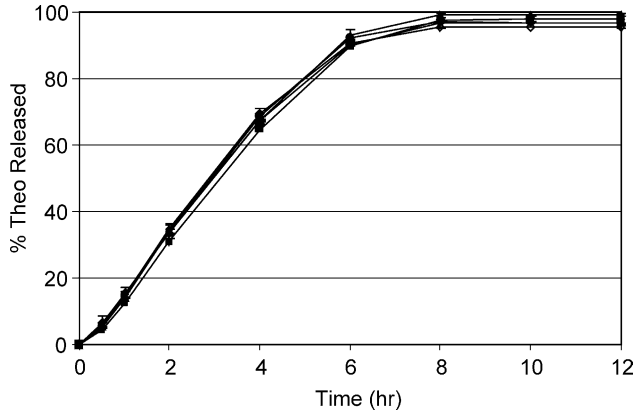

Fig. 2. Influence of storage time on the release rate of theophylline from pellets coated with Eudragit® RS 30 D containing 10% HEC stored at 25 °C/60% RH in open HDPE containers (USP 26 Apparatus 2, 900 ml, 50 mM phosphate buffer, pH 7.4, 37 °C, 50 RPM, $n=3$). Key: initial, 1 week, 2 weeks, 4 weeks, 4 months.

The influence of storage time on theophylline release from pellets coated with Eudragit® RS 30 D containing 10% HEC is illustrated in Fig. 2. The release rate of the model drug was stable over 4 months when stored at 25 °C/60% RH. The pellets coated with Eudragit® RS 30 D containing 10% HEC also demonstrated a higher drug release rate compared to pellets coated with Eudragit® RS 30 D alone due to the hydrophilic properties of hydroxyethylcellulose. Furthermore, the initial delay in drug release observed with pellets coated with Eudragit® RS 30 D was eliminated with the inclusion of 10% HEC.

The water-vapor permeability of cast films is shown in the Fig. 3. The film containing 10% HEC showed

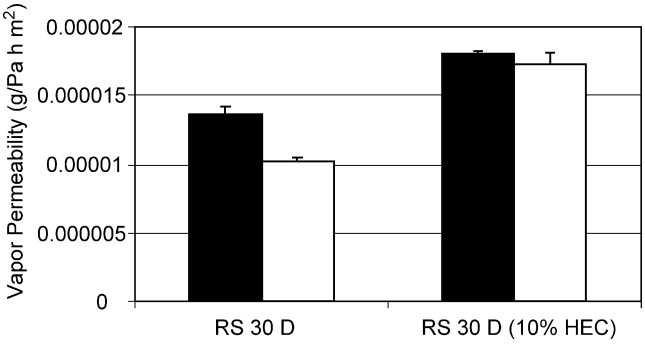

Fig. 3. Influence of hydroxyethylcellulose on the water-vapor permeability of cast films containing 20% triethyl citrate stored at 25 °C/60% RH in open containers ($n=3$). Key: ■, initial; □, 1 month.

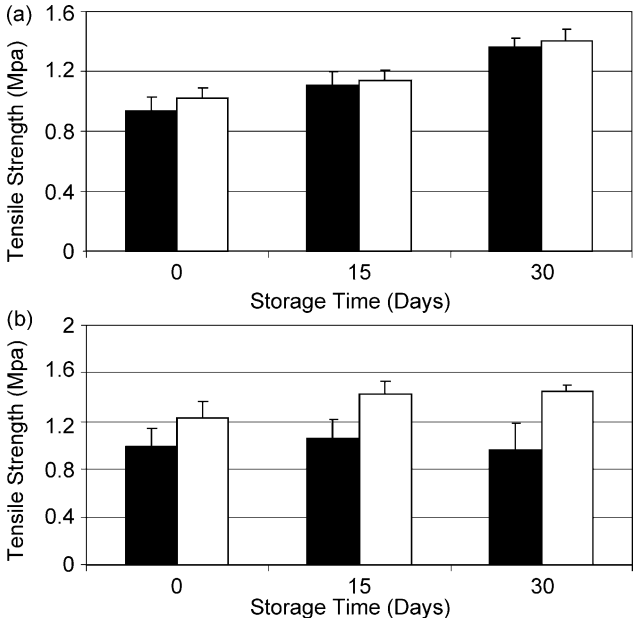

Fig. 4. Influence of storage time on the tensile strength of (a) Eudragit® RS 30 D cast films; (b) Eudragit® RS 30 D cast films containing 10% hydroxyethylcellulose stored at 25 °C/60% RH in open containers ($n=5$). Key: ■, tensile strength at failure; □, tensile strength at maximum.

higher water-vapor permeability ($1.80\times10^{-5}\pm0.02\times10^{-5}$ g/Pa h m) than that of the Eudragit® RS 30 D film ($1.36\times10^{-5}\pm0.05\times10^{-5}$ g/Pa h m), due to the hydrophilicity of HEC. In addition, the water-vapor permeability of the Eudragit® RS 30 D film showed a significant decrease in permeability ($1.02\times10^{-5}\pm0.02\times10^{-5}$ g/Pa h m) after storage at 25 °C/60% RH for one month (ANOVA, $P<0.05$). The permeability of the film containing HEC, however, remained unchanged ($1.72\times10^{-5}\pm0.09\times10^{-5}$ g/Pa h m) after storage for 1 month under the same conditions (ANOVA, $P>0.05$). The film permeability results were in agreement with the findings from the dissolution study.

The influence of storage time on the tensile strength of cast films is shown in Fig. 4. The tensile strength of the Eudragit® RS 30 D film increased during storage at 25 °C/60% RH, due to further coalescence of the polymeric latex particles (Fig. 4a). Interdiffusion of polymer chains, which occurs during the final stage of film formation provides the latex film with its mechanical strength. Zosel and Ley reported that after initial formation of a continuous film, the increase in film strength occurs in two main steps: (1) the interdiffusion of chain ends and small chains in

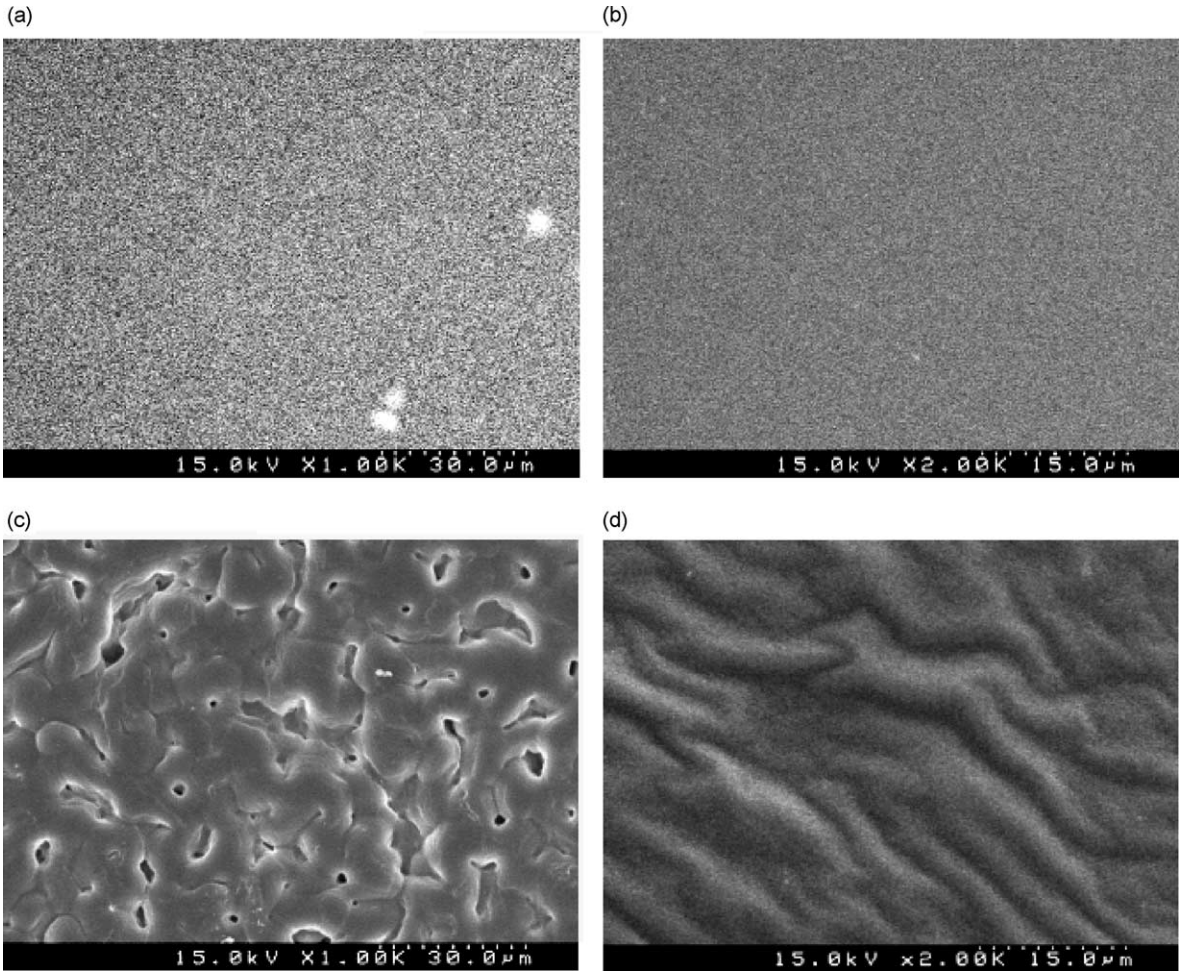

Fig. 5. Influence of hydroxyethylcellulose on the surface morphology of cast films. (a) Eudragit® RS 30 D; (b) Eudragit® RS 30 D containing 20% TEC; (c) Eudragit® RS 30 D containing 10% HEC; (d) Eudragit® RS 30 D containing 10% HEC and 20% TEC.

the particulate membranes; (2) the interdiffusion of longer chains and the formation of entanglements. The former step is apparent as a change from brittle to tough fracture behavior, while the latter step provides the film with increasing toughness [13]. In contrast, the tensile strength of cast films containing 10% HEC did not change during storage at the studied condition, indicating that no further coalescence of polymer particles occurred (Fig. 4b).

The presence of 10% HEC in the Eudragit® RS 30 D film stabilized the theophylline release rate from coated pellets, the water-vapor permeability and the tensile strength of cast films. This stabilization effect is believed to be the result of a 'coalescence blocking mechanism'. Since Eudragit® RS 30 D is a hydrophobic acrylic polymer, it is immiscible with the hydrophilic polymer, HEC. During curing, the HEC forms an incompatible phase around the Eudragit® RS 30 D particles and prevents further coalescence of acrylic polymer particles and chain interdiffusion. The film structure and porosity remain unchanged during storage, resulting in a stable drug release rate. In order to verify this hypothesis, surface and cross-section morphologies of cast films were investigated by scanning electronic microscopy (SEM). The photomicrographs shown in Fig. 5(a) and (b) demonstrate that the surface of Eudragit® RS 30 D films with or without 20% TEC as a plasticizer, are smooth and continuous. However, the surface of Eudragit® RS 30 D film without TEC, but containing 10% HEC, is rather porous and discontinuous as seen in Fig. 5(c). In Fig. 5(d), the surface became continuous with 20% TEC, however, a unique surface texture pattern was visible, indicating some extent of incompatibility. The cross-sectional SEM picture showed more clearly the morphology of the cast polymeric films. In Fig. 6(a) the cross-sectional area of the Eudragit® RS 30 D film with 20% TEC illustrates that the film was continuous and dense. However, the SEM of the cross-sectional film containing 10% HEC in Fig. 6(b) showed a more porous and discontinuous morphology. These structural differences can explain the observed water-vapor permeability and dissolution data. According to the Iyer equation (Eq. (8)), a higher porosity leads to an increase in the diffusion coefficient, which results in a higher water permeability and a faster release rate.

To further investigate the distribution of the hydrophilic polymer in the Eudragit® RS 30 D film, cast films were subjected to acetone treatment. Acetone was selected because it will dissolve the acrylic polymer without affecting HEC. Water was not employed because although HEC dissolves in water, Eudragit® RS is swellable in water and therefore the original film structure would not be retained. The SEM micrographs showed two distinct phases following acetone treatment, indicating that the polymers are immiscible (Fig. 7). In addition, when the ratio of Eudragit® RS 30 D and HEC was 90:10, the acrylic polymer was the continuous phase, and HEC formed clusters dispersed around the RS 30 D phase (Fig. 7a). However, when HEC percentage was increased to 25 or 50%, HEC became the continuous phase and Eudragit® RS 30 D formed spherical domains dispersed in the film (Fig. 7 (b) and (c)).

Surface properties of cast films were also investigated using atomic force microscopy (AFM), which scans the film surface at a fixed distance with a sharp triangular tip mounted on a cantilever. The deflections of the cantilever in the height co-ordinate, z, are measured with a focused laser beam which is reflected to a two-element photodiode detector, while a piezoelectric scanner provides information about the stage movements in x and y co-ordinate planes. AMF images of the structure of the cast films are shown in Fig. 8. The AFM pictures were taken after the polymeric cast films had been stored for 14 days at 25 °C/60% RH. The surface scan of the Eudragit® RS 30 D film showed a smooth and continuous pattern, and all latex particles boundaries had disappeared as supported by surface roughness measurements. The R_a and RMS measurements of the Eudragit® RS 30 D film were 3.417 and 4.608 nm, respectively. However, the acrylic film containing 10% HEC showed a much rougher surface, and the boundaries of the individual latex particles remained distinct. The surface

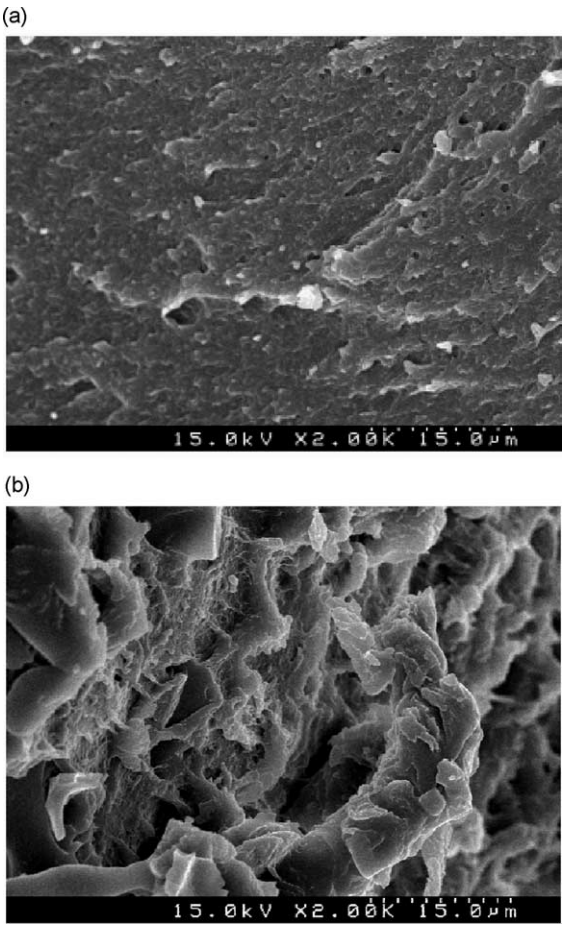

Fig. 6. Influence of hydroxyethylcellulose on the cross-sectional morphology of cast films containing 20% TEC. (a) Eudragit® RS 30 D; (b) Eudragit® RS 30 D containing 10% HEC.

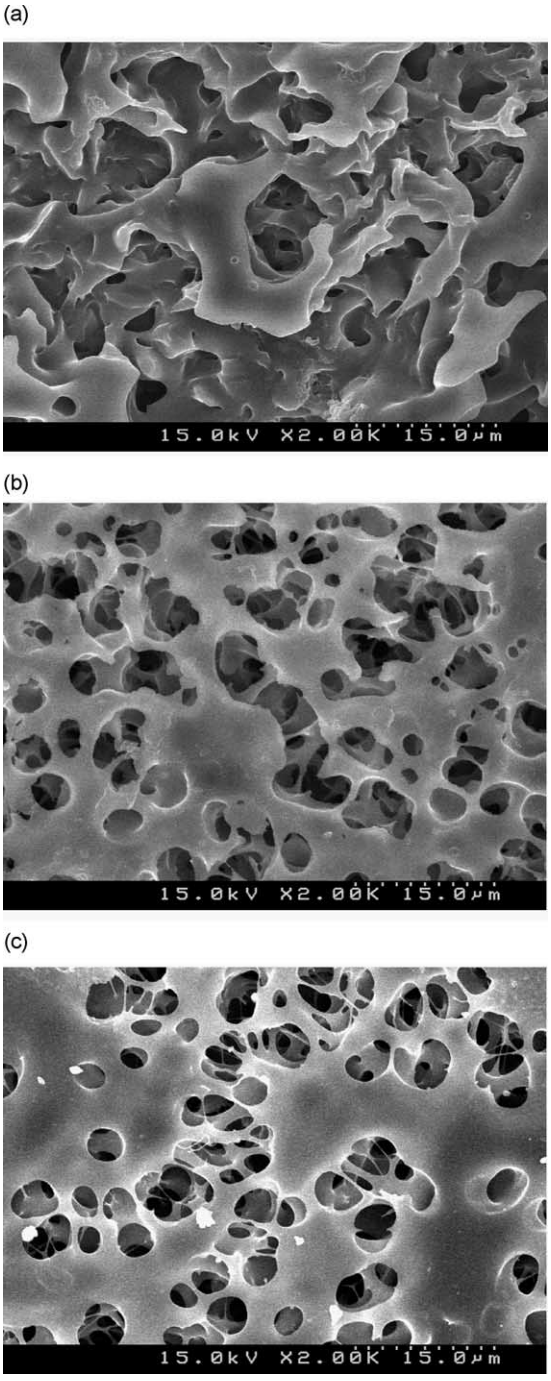

Fig. 7. SEM micrographs of Eudragit® RS 30 D/HEC films containing 20% TEC following acetone treatment. (a) RS 30 D: HEC = 90:10; (b) RS 30 D: HEC = 75:25; (c) RS 30 D: HEC = 50: 50.

roughness measurement of the Eudragit® RS 30 D film containing 10% HEC showed significantly higher R_a and RMS readings of 28.58 and 43.70 nm respectively. From the SEM and AMF images, the hydrophilic polymer, HEC, clearly acted as an incompatible phase surrounding the hydrophobic Eudragit® RS 30 D latex particles to prevent further coalescence and densification of the film. The HEC retained the film structure during storage, and stabilized the permeability and mechanical properties of the film.

Diffusion and transport of molecules in polymers depend upon the nature of fillers, the degree of adhesion and the compatibility of the fillers with the polymer matrix. If compatible with the polymer, the filler will occupy the free volume within the polymer matrix and create a tortuous path for the permeating molecules [23]. The degree of tortuosity is dependent on the volume fraction of the filler and the shape and orientation of the filler particles. When the filler is incompatible with the polymer, voids tend to occur at the polymer–filler interface, which would increase the permeability of the film. For our system, HEC is immiscible with Eudragit® RS 30 D, so the film demonstrated a more porous structure, which explains the high water-vapor permeability of the cast film and the faster drug release rates from the coated pellets.

The presence of a chemical interaction between the hydrophilic polymer HEC and the hydrophobic acrylic polymer Eudragit® RS 30 D was investigated using FTIR, and the spectra are presented in Fig. 9. The spectrum of

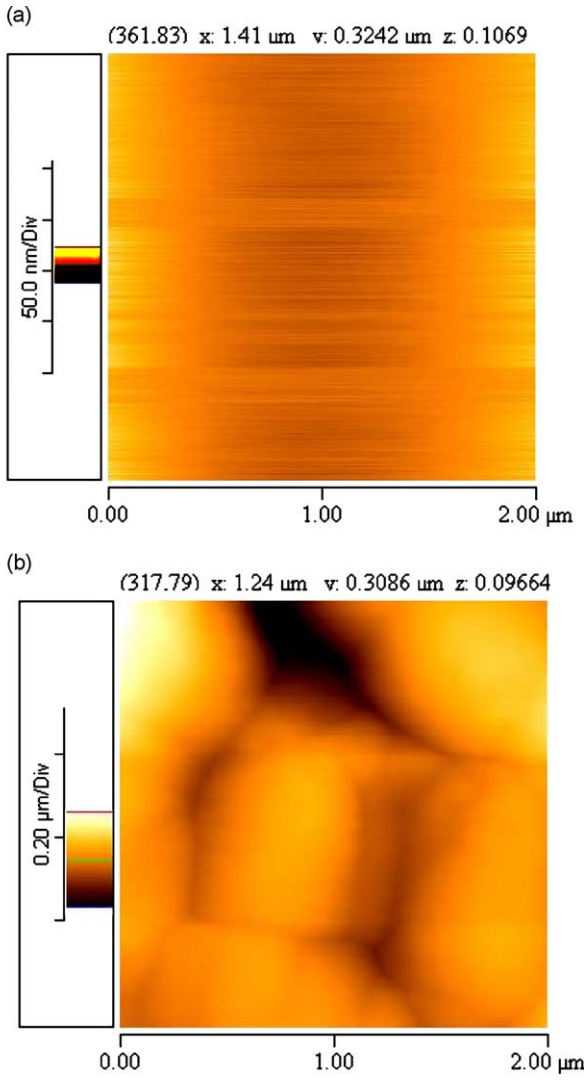

Fig. 8. AFM image of cast polymeric films. (a) Eudragit® RS 30 D; (b) Eudragit® RS 30 D containing 10% HEC.

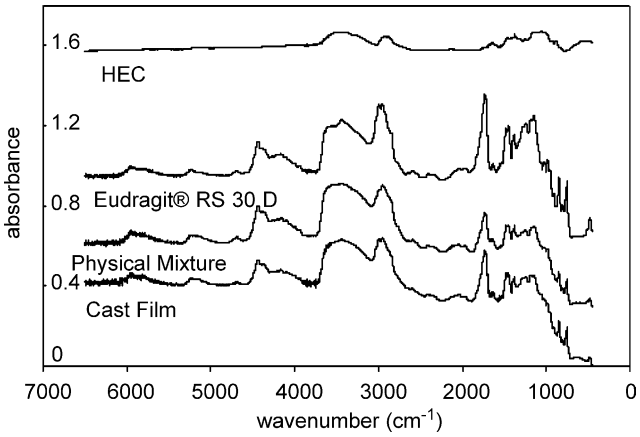

Fig. 9. FTIR spectrum of Eudragit® RS 30 D and hydroxyethylcellulose.

the Eudragit® RS 30 D cast film showed the characteristic bands of the ester groups at 1150–1190 and 1240–1270 cm^{-1}, as well as the C=O ester vibration at 1730 cm^{-1}. In addition, CH_x vibrations can be identified at 1400, 1450, 1500 and 2950–3000 cm^{-1}. The physical mixture of Eudragit® RS 30 D and HEC in a 9:1 ratio, and the cast film of Eudragit® RS 30 D containing 10% HEC showed identical IR spectra, indicating no significant interactions between the hydrophobic and hydrophilic polymers.

4. Conclusions

The drug release rate of theophylline from pellets coated with Eudragit® RS 30 D decreased continuously during the first week of storage due to the further coalescence of the latex particles. This coalescence of latex particles also resulted in changes in the water-vapor permeability and the mechanical properties of cast polymer films during storage. The presence of HEC in the acrylic dispersion was shown to stabilize the dissolution rate permeability and mechanical properties of the Eudragit polymer. 'Coalescence blocking' of the latex particles was the proposed mechanism of stabilization to prevent physical aging of the film coated pellets. Hydroxyethylcellulose, being hydrophilic, was immiscible with the hydrophobic Eudragit® RS 30 D, resulting in the formation of an incompatible phase around the Eudragit® RS 30 D latex particles to prevent complete coalescence and interdiffusion of polymer chains. The presence of HEC in the Eudragit® RS 30 D produced a more porous film, which resulted in a higher water-vapor permeability of cast films and a faster dissolution rate of theophylline from coated pellets. The FTIR spectra showed no significant interactions between Eudragit® RS 30 D and hydroxyethylcellulose.

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