NOTE

Structure and Barrier Property of Acrylatemethacrylate Film Coating in Aspirin Microcapsules

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INTRODUCTION

Acrylatemethacrylates are water-insoluble copolymers, which have been frequently exploited in sustained release applications.[1,2] Previous studies[3,4] showed that these polymers form microporous films with compact skin layers when cast from solutions by slow desolvation; the film cast in this manner displays a porous structure as well as permeability asymmetry.[3,4] The film's porous structure and permeability can be modified by variations in the cationic (quaternary ammonium) content in the polymer[5]; the higher the cationic content is, the higher the porosity and permeability.

The present study investigates the porous structure of a film coating of a certain acrylatemethacrylate, which is applied on aspirin crystals by spraying. The barrier property of the film coatings is also investigated.

EXPERIMENTAL

Aspirin crystals (BDH) were used as core material. An acrylatemethacrylate (Eudragit RS100, Rhom Pharma, Darmstadt, Germany) was the wall material in the formation of the microcapsules. Acetone and dibutylphthalate (both analytical grade, BDH) were used as solvent and plasticizer, respectively, in the formulation of the coating fluid.

The aspirin crystals were microencapsulated by spray application of the coating formulation consisting of 10% (w/w) polymer and 10% (w/w) plasticizer based on the polymer weight. Details of the procedures were described earlier.[6] The coating thicknesses were 11 ± 2 and 27 ± 4 μm as determined by scanning electron microscopy (SEM) of the microcapsule sections.[6] The coating thickness was varied by increasing the polymer concentration in the coating fluid. The selected coating thicknesses of 11 and 27 μm represented the lower and upper limits, respectively. Below 11 μm, imperfect microcapsules (i.e. incomplete coating) were formed; above 27 μm, there was no measurable flux. The surface structures of the film coatings were revealed by SEM of samples of the microcapsules previously vacuum coated with a gold shadow using a Balzier evaporator (model SCD 040). The pores seen in each field of view were counted and sized with the aid of micron markers (bars) on the micrographs. Three representative fields of view were used for each pore size determination. The mean pore size ($\bar{X}$) was obtained from the following expression:

$$\bar{X} = \frac{\sum fX}{\sum f} \quad (1)$$

where f is the frequency of each size X. The barrier property of the film coatings was determined by a leaching experiment. A sample of the aspirin crystals or microcapsules (100 mg) was placed in water (1000 mL) in a stoppered conical flask, which approximated a sink condition. The flask was mounted on a shaker bath maintained at 37°C. The shaker was oscillated at 50 cycles/min. At predetermined intervals of 3 min for the crystals and 30 min for the microcapsules, samples of the leaching fluid (2 mL) were withdrawn for analysis. The contents were analyzed for aspirin content spectrophotometrically at λ_{max} 267 nm (Hitachi U-1100, Hitachi Ltd., Tokyo). The parameters determined were the maximum release (m_∞), referred to as payload[7]; the time to attain it (t_∞); and the release rate, which is the slope of the linear portion of the m–t plot, where m is the mass transferred in time t. The reciprocal of the rate was taken as a measure of the barrier (film coat) resistance (R). At the end of the leaching experiment, photomicrographs of the depleted microcapsules were taken to determine whether the film coatings were intact throughout the leaching experiment.

RESULTS AND DISCUSSION

SEM of the film coating (Fig. 1) revealed numerous surface pores ranging in size from about 2 to 14 μm (mean = 7.1

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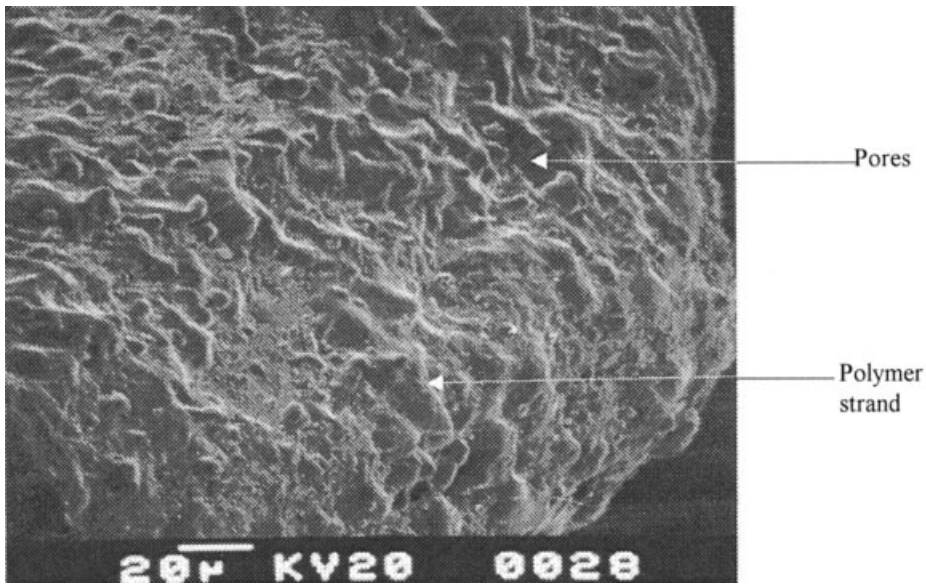

Figure 1 An SEM photograph of the microcapsule surface showing the porous and spongy structure of the acylatemethacrylate film coating.

± 4.8 μm), and a highly spongy structure. It was reported previously that this copolymer forms films with compact skin layers when cast by slow desolvation.[3,4] The highly porous but spongy film structure obtained by the present spray application technique is probably as a result of rapid desolvation. In spite of the highly porous structure of the film barrier, the solute diffusion rates were markedly retarded (Fig. 2). The m_∞ values decreased but the t_∞ values increased, both sharply after microencapsulation of the crystals (Table I), indicative of retarded flux. This observation relates to the spongy nature of the film barrier, which has the effect of increasing the tortuosity of the diffusion pathlength.

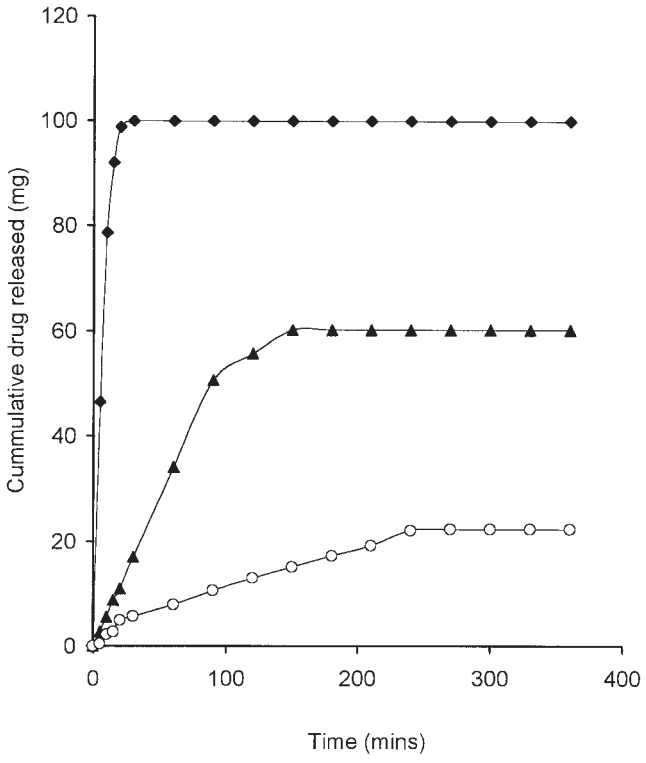

Figure 2 The solute diffusion from the microcapsules with wall thicknesses of (▲) 11 μm and (○) 27 μm and (◆) dissolution from the crystals.

The results (Table I) showed that the payload depended on the barrier thickness and hence on its resistance; a low payload was associated with a high barrier resistance. The implication is that a high proportion of the initial drug loading was retained in the microcapsules at t_∞ and in practical situations of use; this retained fraction will not be available for absorption *in vivo*. The payload is the maximum amount of solute that is transferable from the particles under sink conditions.[7] Because the initial drug loading was the same in all the systems studied, we expected that the payloads of the crystals and those of their microcapsules would be similar, although the rate of solute transfer would be slower in the microcapsules. The film coatings were intact throughout the leaching experiment (Fig. 3). It is therefore possible that the decrease in payload was the result of a fall in concentration gradient across the film barrier to a critical level as leaching progressed, such that the driving force became ineffective. The t_∞ represents the point to attain this critical concentration gradient. The thicker the film barrier is,

TABLE I
Flux Parameters for Barrier Properties of Film Coatings

Film thickness (μm)	R (min mg^{-1})	m_∞ (mg)	t_∞ (min)
0	0.16	99	20
11	1.82	58	120
27	7.78	22	280

Zero refers to the crystals. Initial drug dose = 100 mg.

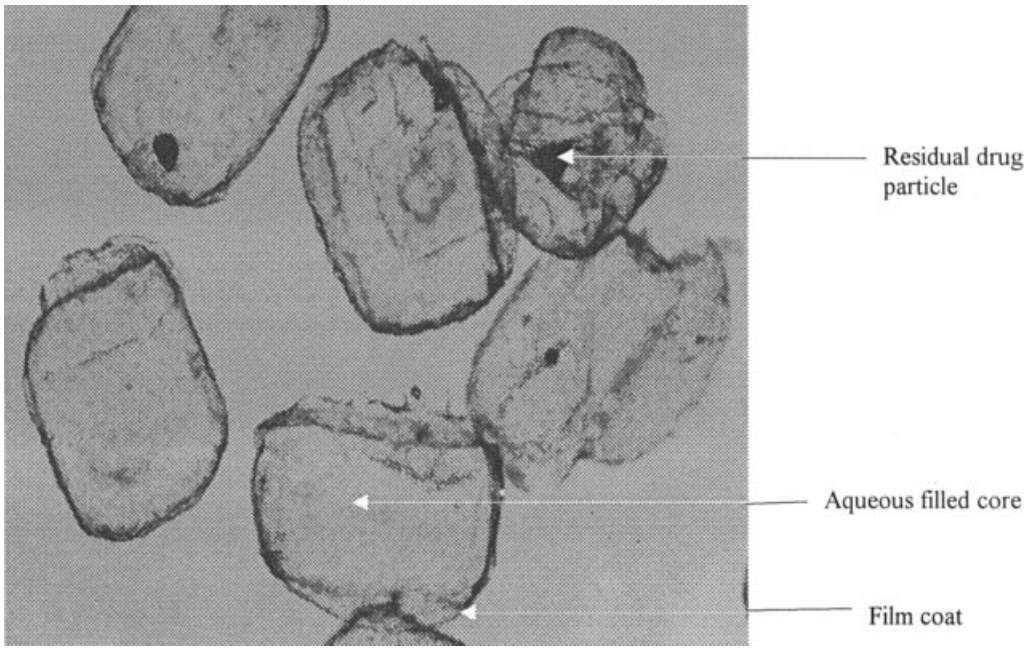

Figure 3 A photomicrograph (original magnification ×90) of the microcapsule shells taken at the end of the leaching experiment. Note the presence of residual drug in some of the shells.

the higher is its resistance, which explains the further decrease in payload with an increase in film thickness.

CONCLUSIONS

Cast films of an acrylatemethacrylate copolymer exhibit compact microporous structures.[3,4] The present study showed that the polymer can form highly porous but spongy film structures when applied on drug particles by spray coating. Nevertheless, the films form effective barriers in controlling solute diffusion rates from resulting microcapsules. The study also demonstrated that microencapsulation decreases the payload of drug particles. The extent of the decrease depends on the barrier resistance. This finding means that the film barrier affects not only the rate of solute transfer but also the payload, which is a limitation in the sustained release application of polymeric film coatings.

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