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COMMUNICATIONS

Polysorbate 20 as a drug release regulator in ethyl cellulose film coatings

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Tablet coatings of hydrophobic ethyl cellulose have been made more hydrophilic by the addition of a non-ionic surfactant, polysorbate (Tween) 20, to the film. As its content increased, so did the release of sodium salicylate from the coated tablets. With a certain content of surfactant and specific thickness of the tablet coat, zero order release kinetics were observed. Leaching of the polysorbate 20 occurred from all formulations. Scanning and transmission electron micrographs showed that the structure of the coats consisted of several layers parallel to the tablet surface. Polysorbate 20 was seen as small drops in some coats.

In the coating process, surfactants have been shown to facilitate spreading of the coating mixture on tablets (Banker 1966; Pickard & Rees 1974). Small amounts of non-ionic surfactant have been used to wet and homogenize the coating mixtures (Lehman & Dreher 1972; Pickard & Rees 1972; Takamura et al 1973; Parker et al 1974; Patt 1975; Tomassini et al 1975; Lehman 1975, 1982). Surfactants can also change the permeability of the coats (List & Kassis 1982). We have previously shown that the release rate of salicylic acid from coated tablets depended on the surfactant added (polysorbate (Tween) 20, 81 or Span 20) to the ethyl cellulose coating (Lindholm & Juslin 1982).

In the present study we have used tablets with ethyl cellulose film coats that contained 10–60% w/w polysorbate 20. The aims of this study were firstly to determine the effect of surfactant content and coat thickness on the release of sodium salicylate, secondly to obtain information about the structure of the coats, and thirdly to investigate the relationship between coat composition and release kinetics.

Materials and methods

The tablet composition was: sodium salicylate (Ph. Eur., particle size 300 μm) 33·1% w/w, microcystalline cellulose (Avicel PH 101, FMC Corp.) 66·4% w/w, and magnesium stearate (Ph. Eur.) 0·5% w/w as lubricant. Tableting, coating and measurement of the release of sodium salicylate from tablets were as described previously (Lindholm & Juslin 1982; Lindholm et al 1985).

The release data were fitted to the cube root, first order, zero order and Higuchi's diffusion equation as in Lindholm et al (1985).

The amount of polysorbate 20 dissolved from the free coats (detached carefully from the cores) was determined gravimetrically. The pieces of the coats were weighed before and after they had been soaked in water at 37 °C and dried. In addition, the undetached coats containing 50% polysorbate 20 were studied. The tablets were weighed, kept in the rotating basket apparatus for different time intervals, dried and then weighed again. The amount of dissolved sodium salicylate (determined spectrophotometrically) was subtracted from the difference between the two weights.

The structure of the coats was studied using scanning and transmission electron microscopy. In the former the samples were either cut with a microtome or fractured under liquid nitrogen before being coated with gold. In the latter the samples were embedded in Ladd's epon (Griffin 1972) and then cut with an ultramicrotone.

Results and discussion

Much of polysorbate 20 leached away (Table 1). Leaching was fast in the beginning and increased slightly with time. In the micrographs that were taken from the coats containing 50% polysorbate 20 and 50% ethyl cellulose, the surfactant can be seen as small drops in ethyl cellulose (Fig. 1A). These micrographs also show the leaching of surfactant; no dark points are left in the 5 h samples, where only small, empty regularly ordered holes are left (Fig. 1B). The coats containing 10 or 30% surfactant were homogenous (Fig. 1C).

However, some of the polysorbate 20 could have dissolved during work, when the thin sections were collected on the surface of the water bath after having been cut with a diamond knife. In that instance the number of points or pores may not be considered an exact measure of the amount of the surfactant in any

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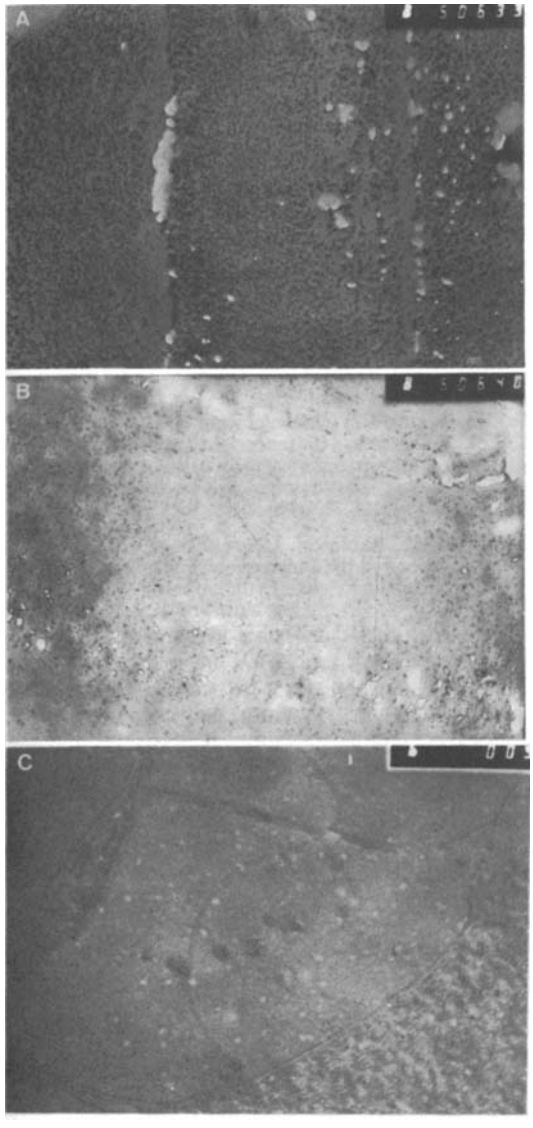

FIG. 1. Transmission electron micrographs from cross section of the ethyl cellulose coats containing polysorbate 20. The coat with 50% polysorbate 20 from the tablet (A) before and (B) after being 5 h in the dissolution test, (C) the coat containing 30% polysorbate 20 after the tablet had been 3 h in the dissolution test (4500x).

sample. Minor dissolution of it into Ladd's epon can not be excluded, but no evidence of this could be detected from the micrographs.

In this work, the coating formulation was sprayed onto the tablet mass, and the tablets were allowed to dry several times during the coating process to prevent them from sticking to each other (Lindholm & Juslin 1982). The effect of such a coating process can be seen from the scanning electron micrographs, where there are many layers parallel to the tablet surface (Fig. 2).

Sodium salicylate can move in the water-filled holes

Table 1. Amount of polysorbate 20 dissolved in water at 37 °C from coats containing ethyl cellulose and polysorbate 20. Except for one case, the coats were detached from cores. Results were determined gravimetrically. E = ethyl cellulose, Tw = polysorbate 20.

Composition of the coat	Thickness of the coat (μm)	Tw dissolved (% of the amount of Tw in the coat) 1 h	3 h	6 h
E 90%, Tw 10%[a]	74 ± 1	47·4 ± 3·1	55·6 ± 3·0	66·4 ± 5·7
E 70%, Tw 30%[a]	74 ± 2	65·3 ± 1·0	74·1 ± 0·5	78·4 ± 1·4
E 50%, Tw 50%[a]	148 ± 3	82·9 ± 0·8	84·3 ± 0·2	87·1 ± 1·8
E 50%, Tw 50%[b]	148 ± 3	27·5 ± 2·2	42·8 ± 2·1	49·3 ± 3·3

[a] Coats detached from the cores.
[b] Coats not detached from the cores.

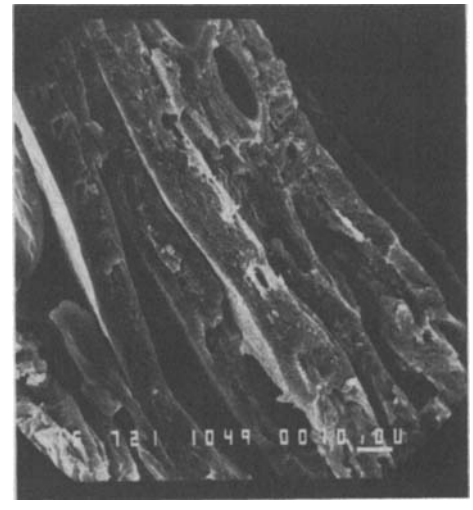

FIG. 2. A scanning electron micrograph from a cross section of an ethyl cellulose coat containing 50% polysorbate 20. The section was broken after a piece of the coat had been immersed in liquid nitrogen. The section was from a tablet that had been in the dissolution test for 1 h (500x).

and cavities between the layers of the coat (Fig. 2), and because of the amount of sodium salicylate released from the tablets (Fig. 3), it can also move between the layers. On the scanning micrographs, irregularly formed, connecting pores or cavities can be seen (Fig. 2).

Release curves for coated tablets with cores of different breaking strengths (9, 11, 13 kg) did not differ significantly from each other. When the amount of polysorbate 20 in the coat increased, release of sodium salicylate from the coated tablets was accelerated and the lag times were shortened (Fig. 3). Similar results have been obtained with another hydrophilic additive, hydroxypropyl methylcellulose, in ethyl cellulose (Kannikoski 1984; Kannikoski et al 1984). In most cases the release kinetics of sodium salicylate was of the first order or according to the cube root equation. With quite thick coats, when the amount of polysorbate 20 was 50% w/w of the dry coat, linearity of the release profile

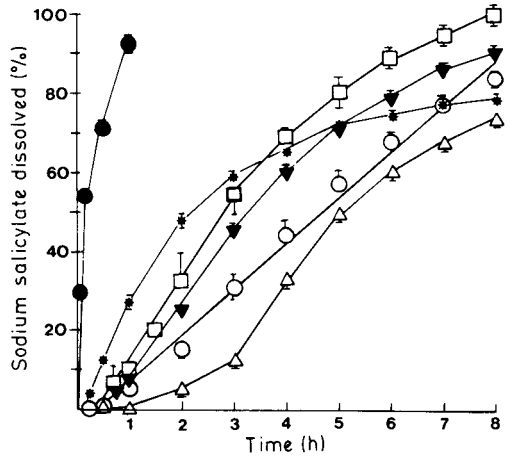

FIG. 3. Release profiles of sodium salicylate from uncoated (●) and coated tablets as a mean of six samples ± s.e.m. Composition of the coats: △ 90% ethyl cellulose and 10% polysorbate 20 (thickness 101 ± 1 μm), ▼ 70% ethyl cellulose and 30% polysorbate 20 (thickness 74 ± 2 μm), ○ and □ 50% ethyl cellulose and 50% polysorbate 20 (thickness 148 ± 3 μm and 80 ± 1 μm), ★ 40% ethyl cellulose and 60% polysorbate 20 (thickness 155 ± 2 μm). Masses and breaking strengths of the cores were: ● and △ 200 mg, 8 kg, □, ○ and ★ 300 mg, 8 kg, ▼ 400 mg, 9 kg, 12 kg and 13 kg. Statistically significant ($P < 0{\cdot}05$) linearity was obtained for the release profile when the content of polysorbate 20 was 50% and thickness was 148 ± 3 μm.

was observed. With some thick coats, however, the release became too slow, and linearity was not achieved. When the surfactant content was 60%, the coat was so hydrophilic that release was rapid (Fig. 3).

First order kinetics, the theoretical equation dealing with the release mechanism of film-coated tablets and free films, do not apply when the film changes with time (Goldman 1970; Shah & Sheth 1972; Lee & Robinson 1978; Friedman et al 1979; Lippold & Förster 1981; Donbrow & Benita 1982) and, in some cases, zero order release kinetics can be obtained with appropriate changes in the coat. Leaching of polysorbate 20 changed the coat during the dissolution test, which may be a reason for zero order kinetics. In addition, it was necessary to use the appropriate content of surfactant and suitable coat thickness.

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