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The effect of anionic surfactants on the release of chlorpheniramine from a polymer matrix tablet

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Matrix tablets have long been used to obtain sustained drug delivery and it was Higuchi (1963) who first presented a detailed mathematical analysis of such release. Bamba et al. (1979) further developed the mechanisms of release from matrix systems that swell at the tablet periphery to form a gel which acts as a barrier to drug diffusion.

It is becoming increasingly apparent that the viscosity characteristics of the polymers, that go to make the matrix tablet, are of great importance in determining the final release properties of the dosage form. Huber and Christensen (1968), when investigating the release of a tracer (tartrazine) from two hydroxypropyl methylcellulose (HPMC) matrix tablets, found that the higher viscosity grade HPMC released the tracer at a significantly slower rate than the lower grade. More recently Nakano et al. (1983) studied the release of theophylline from hydroxypropyl cellulose tablets; here again the rate of release was slower for the higher viscosity grades. The sustained drug release from these two systems is achieved by the polymer swelling to a gel-like consistency at the tablet periphery and forming a barrier to drug diffusion. Harwood and Schwartz (1982), when investigating the release of pilocarpine from ophthalmic HPMC matrix preparations also found the release to be slower from the higher viscosity grades. The present study firstly concerns the release of chlorpheniramine from tablets made from 4 different viscosity grades of HPMC and secondly the effect of an anionic surfactant, sodium lauryl sulphate (SLS), on drug release from HPMC tablets.

Tablets of nominal weight, 300 mg containing 45 mg chlorpheniramine maleate, were prepared using an instrumented Manesty F3 machine, fitted with 10 mm diameter flat-faced punches and die, at an upper punch compaction pressure of 175

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$MN \cdot m^{-2}$. Tablets outside the weight range 290–310 mg were rejected. The dissolution of the drug from the tablets was monitored using either a manual sampling or continuous flow technique. In the case of the manual method 1000 ml of 0.1 N hydrochloric acid was introduced into 6 vessels of an Erweka DT-D6 USP method 1 dissolution apparatus with a rotation speed of 100 rpm. Samples were periodically withdrawn for spectrophotometric assay at 265 nm (Cecil Instruments, Model CE292) and then returned to the dissolution vessel. The continuous flow technique used the same dissolution apparatus but the dissolution medium was pumped through a spectrophotometer (Kontron, Model Uvikon 810) fitted with an automatic 6 cell changer. A microprocessor (Commodore Business Machines, Model 8032) interfaced to the spectrophotometer gave digital absorbance values for each cell. The two sampling techniques have been shown to give equivalent results. The dissolution data were plotted as the percent remaining in the tablets against time.

Viscosity determinations on 2% solutions of four HPMC grades were carried out at 37°C using a U-tube viscometer (Grade D) (British Pharmacopoeia 1980, method 1).

The dissolution profiles of chlorpheniramine tablets made from the different viscosity grades of HPMC are shown in Fig. 1. From the time for 50% release ($T_{50\%}$) values shown in Table 1 it can be seen clearly that the drug dissolution from the tablets is significantly slower for the higher viscosity grade HPMCs. This fits with the findings of Huber and Christensen (1968) and Nakano et al. (1983) as described earlier.

A substance that could affect the viscosity of an HPMC may be of use in changing the release of drug from tablets made from this material. It has been reported extensively in the literature (for example, Saito 1960) that the viscosity of

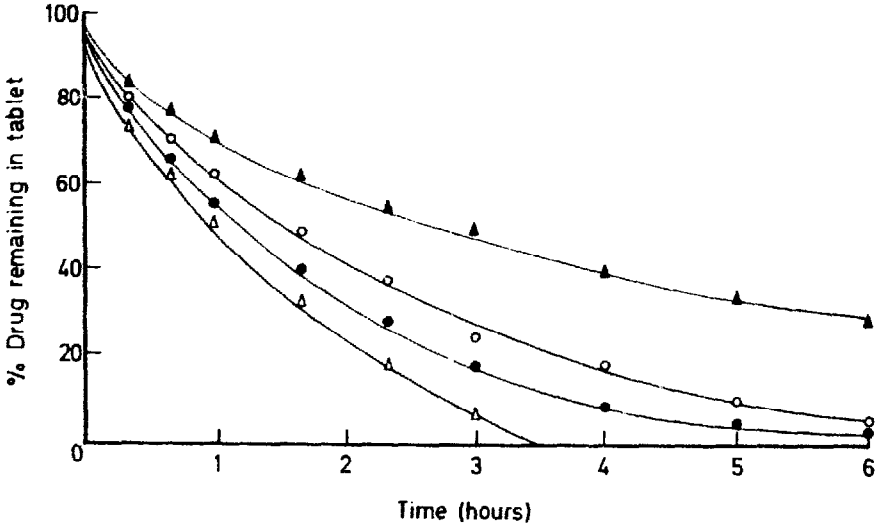

Fig. 1. The release of chlorpheniramine from different viscosity grade HPMCs. Key: Methocel E5, △; Methocel E15, ●; Methocel E50, ○; Methocel E4M, ▲.

non-ionic polymers can be increased by the addition of anionic surfactants. A similar type of effect has been reported more recently by Walker and Wells (1982) who found that a combination of the anionic sodium carboxymethyl-cellulose with cellulose produced a synergistic increase in viscosity. Thus the effect of the anionic surfactant sodium lauryl sulphate (SLS), on a modified HPMC (Synchron), used commercially to manufacture sustained release tablets, was studied to determine whether a more sustained action could be obtained through the incorporation of a surfactant.

Firstly, the effect of SLS on the viscosity of a 2% Synchron solution at 37°C was studied. Table 1 shows that the viscosity is enhanced by the addition of SLS. Table 1 also shows, for comparative purposes, the viscosity data obtained under the same conditions, for the four HPMCs used above.

To study the effect of SLS on the release of drug from HPMC tablets three different batches of Synchron were manufactured to contain 5, 10 and 15% surfactant. Fig. 2 shows that tablets containing 15% SLS give a zero-order in vitro release profile with a considerable retardation of release rate. From Fig. 2 it is evident that the retardation is dependent upon the amount of surfactant incorporated in the formulation.

It is possible that this retardation is not due to the increased gel viscosity at the tablet periphery, but due to complex formation between the cationic chlorpheniramine and the anionic surfactant. However, this is unlikely to be the principal mechanism by which a more sustained action is achieved since similar release effects were obtained with anionic drugs. Changes in tablet porosity in the presence of

TABLE 1

A COMPARISON BETWEEN THE RELEASE OF CHLORPHENIRAMINE AND THE VISCOSITY GRADE

HPMC	Viscosity [a] (centistokes)	Time for 50% release ($T_{50\%}$) (h)
Methocel E5 [b]	3.5	1.1
Methocel E15	9.9	1.3
Methocel E50	25.2	1.7
Methocel E4M	2662.0	2.9
Synchron [c]	21.5	1.7
Synchron 2% + 0.25% sodium lauryl sulphate	45.7	–
Synchron 2% + 0.5% sodium lauryl sulphate	70.0	–

[a] Viscosity of a 2% solution (except where indicated) determined at 37°C.

[b] Methocel supplied by Colorcon Ltd., Kent.

[c] Synchron supplied by Pharmax Ltd., Kent.

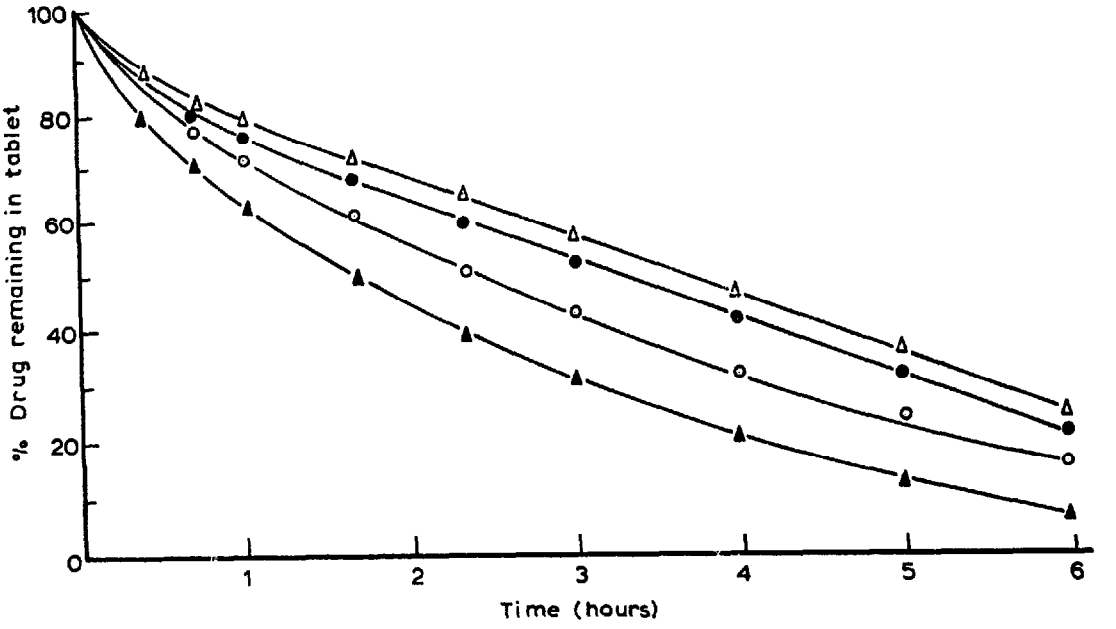

Fig. 2. The effect of sodium lauryl sulphate (SLS) on the release of chlorpheniramine from Synchron. Key: no SLS, ▲; 5% SLS, ○; 10% SLS, ●; 15% SLS, △.

surfactant are also unlikely to account for the change in release rates because compaction pressures in the range 50–200 $MN \cdot m^{-2}$ do not significantly alter the release rates from HPMC tablets (Daly, 1984). A series of non-ionic surfactants, Brij 35, Myrj 59, Pluronic F88 and the cationic surfactant cetrimide, were also investigated. No change in the release rate of chlorpheniramine was noted, indicating that the observed behaviour is restricted to anionic surfactants.

It can be concluded that the anionic surfactant, SLS, is able to modify the release profiles of drugs from HPMC tablets giving an increased duration of release. It is considered that the mechanism involved is related to the ability of anionic surfactants to bind to non-ionic polymers acting to increase the viscosity.

It is appreciated that SLS at high concentrations is not suitable for oral administration but another anionic surfactant, dioctyl sodium sulphosuccinate, has been incorporated into HPMC tablets. The dissolution of this formulation has been assessed in human subjects using gamma scintigraphy. Again the surfactant gave a more sustained action, the results from this study have been reported elsewhere (Davis et al., 1983).

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