The effect of polymer molecular weight on the incidence of film cracking and splitting on film coated tablets

R. C. ROWE*, S. F. FORSE, *ICI Pharmaceuticals Division, Alderley Park, Cheshire SK10 2TG, U.K.*

Over the past decade there has been a considerable increase in the polymer film coating of tablets. However, the application of a polymer film to a tablet surface is associated with a number of problems, one of which is film cracking or splitting. This defect can occur either over the crown of the tablet (Fig. 1) or more commonly at the edges, where it is known as edge splitting and peeling (Fig. 2). It has been suggested that this defect occurs when the stresses inherent in the film and caused by the film shrinking during the evaporation of the solvent exceed the tensile stress required to rupture the film. (Technical bulletin on hydroxypropyl methylcellulose phthalate—Shinetsu Chemical Co. Ltd., Japan). If this is the mechanism then the incidence of the defect will be dependent on the molecular weight of the polymer used, since it has already been shown for tablets coated with hydroxypropyl methylcellulose (Rowe 1976) that as the molecular weight of the polymer is increased the films become harder, less elastic and more resistant to abrasion. This effect has been studied in our laboratories and the results are summarized in this report.

The tablet substrate used was one that had been found to be prone to edge splitting and peeling when aqueous coated with hydroxypropyl methylcellulose. It consisted of magnesium carbonate and maize starch granulated with gelatin solution and lubricated with magnesium stearate. The tablets were coated with hydroxypropyl methylcellulose using either the commercially available grades (Methocel E5, E8, E10 and E15–Dow Chemical Co., U.S.A.) or mixtures composed of Methocel E5 and E50 blended to give the same nominal viscosity as the equivalent commercially available grade. The peak molecular weights of all the grades of polymer used were calculated using the equation derived by Rowe (1980). The polymers were applied as 6% aqueous solutions containing glycerol as plasticizer (20% w/w based on polymer) and titanium dioxide as pigment (30% w/w based on polymer). Film coating was carried out in a 24 inch Accelacota (Manesty Machines Limited) using an airborne spray system at an application rate of 50 ml min^{-1} and inlet air temperature of 60 °C. In order to assess the degree of edge splitting, 1000 tablets were withdrawn at the end of the run, visually inspected and the number with any signs of the defect counted and expressed as a percentage. No further splitting was seen on storage.

The incidence of the defect on tablets coated with both the commercially available grades and for the mixtures of equivalent peak molecular weights is shown in Fig. 3. It can be seen that, in both cases, there is a marked decrease in the incidence of edge splitting as the molecular weight is increased from $4{\cdot}8 \times 10^4$ to $5{\cdot}8 \times 10^4$ (equivalent to a change from Methocel E5 to Methocel E8) with much less of a decrease as the molecular weight is increased further to $7{\cdot}8 \times 10^4$ (equivalent to Methocel E15). A comparison of these results with those showing the relationship between the tensile strength of a free film and the polymer molecular weight (Rowe 1980), reveals that at low molecular weights there

* Correspondence.

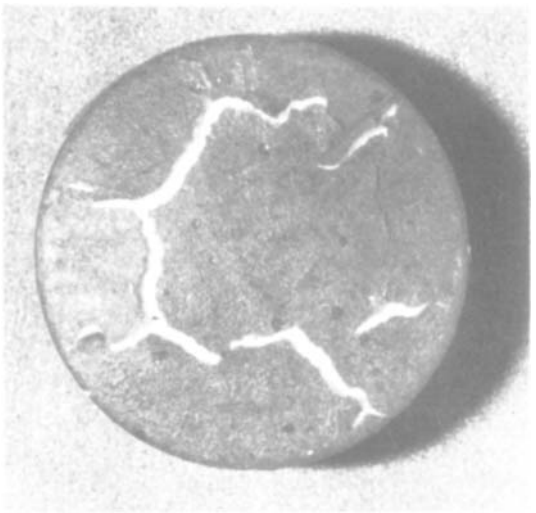

FIG. 1. A cracked film on a film coated tablet.

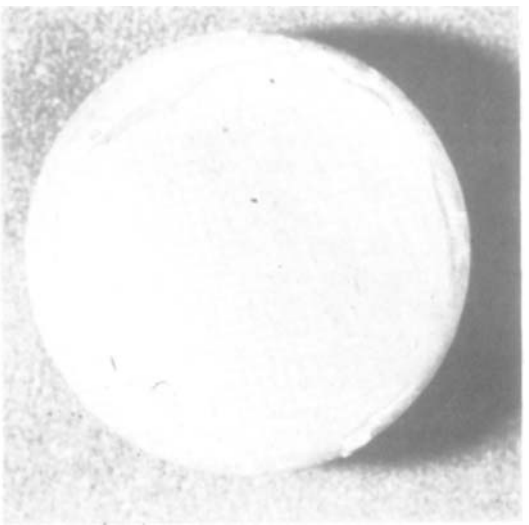

FIG. 2. Splitting and peeling at the edges of a film coated tablet.

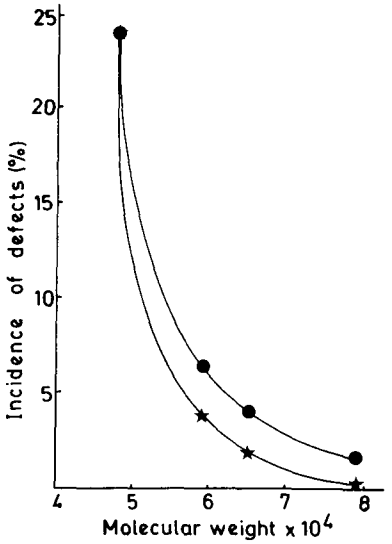

FIG. 3. The effect of molecular weight of hydroxypropyl methylcellulose on the incidence of edge splitting on tablets coated with ● commercially available grades and ★ blends prepared from a low and high molecular weight grade.

is an inverse relationship between the incidence of edge splitting and polymer tensile strength, and that the molecular weight at which the incidence of the defect becomes negligible is the same as that at which there is no further increase in tensile strength. This implies that this defect is related to the tensile strength of the polymer used to prepare the film and confirms the mechanism postulated.

From the results (Fig. 3) it would appear that polymer blends had a greater influence on the reduction of the incidence of edge splitting than commercially available grades of the same molecular weight. Although small, this effect is significant and is attributable to the presence in the blends of an increased proportion of a very high molecular weight ($>5 \times 10^5$) component obtained from the Methocel E50 portion (Rowe 1980) compared with the commercially available grade. These high molecular weight components are thought to increase the effective tensile strength of the polymer and hence lower the incidence of edge splitting.

The trends reported here for hydroxypropyl methylcellulose are likely to be the same for all polymers and hence this study illustrates the usefulness to the formulator of such data as tensile strength, molecular weight and molecular weight distribution in optimizing film formulations.

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Action of sodium aurothiopropanol, chloroquine, D-penicillamine and levamisole on picryl chloride-delayed hypersensitivity in mice

J. P. TARAYRE*, H. LAURESSERGUES, *Department of Pharmacology, P. Fabre Research Centre, 17, avenue J. Moulin, 81100 Castres, France*

Little is known of the mechanisms of action of gold salts, chloroquine, D-penicillamine and levamisole in rheumatoid arthritis. Delayed hypersensitivity processes play a major part in the pathology of the disease (Dumonde 1971; Sheldon et al 1974; Stastny et al 1975; Loewi et al 1975; Van Boxel & Paget 1975). In animal pharmacology, the most used delayed hypersensitivity test in investigations for antirheumatic or anti-inflammatory activities is Freund's adjuvant polyarthritis in rats. Gold salts reduce this condition (review by Walz et al 1974), but the effects of chloroquine (Newbould 1963; Graeme et al 1966; Ward & Cloud 1966; Winter & Nuss 1966; Perrine & Takesue 1968), D-penicillamine (Liyanage & Currey 1972; Arrigoni-Martelli & Bramm 1975; Watnick 1975) and levamisole (Dieppe et al 1976; Trabert et al 1976) are null or controversial. We have studied the action of sodium aurothiopropanol sulphonate (Sarbach), chloroquine diphosphate (Rhône-Poulenc), D-penicillamine (Fluka) and levamisole (Specia) on contact delayed hypersensitivity to picryl chloride in mice (Asherson & Ptak 1968) which gives reproducible results and is easy to perform.

Swiss male mice, 25 g at the beginning of the experiment, were used. The laboratory and the animal house were lit by daylight supplemented by electric lighting from 8 a.m. to 6 p.m. Tests were performed in Summer and Autumn. 0·1 ml of a 3% picryl chloride (BDH) solution in acetone was applied to the shaved abdomen of the animals. 7 days later, early in afternoon, 0·025 ml of an antigen solution prepared in the same conditions was applied on both sides of the right ear. 24 h later, the animals were killed and both ears weighed. The delayed hypersensitivity reaction was measured by the increase in weight of the right compared with the left ear. In non-sensitized animals the increase in weight at

* Correspondence.