J. Pharm. Pharmacol. 1981, 33: 174–175
Communicated October 15, 1980

0022–3573/81/030174–02 $02.50/0

The effect of plasticizer type and concentration on the incidence of bridging of intagliations on film-coated tablets

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In a recent communication (Rowe & Forse 1980b), results were presented to show that bridging of the intagliations or monograms on a film coated tablet was a manifestation of the stress distribution within the film and occurred when the stresses inherent in the film due to shrinkage on the evaporation of solvent were very high. It was also shown that the incidence of this defect could be minimized by decreasing the thickness of the film. This study reports data on the effects of plasticizer and plasticizer concentration on the incidence of this same defect.

The tablet substrate was the same as that used previously (Rowe & Forse 1980b). The tablets were coated with a film formulation consisting of a 5% w/v aqueous solution of hydroxypropyl methylcellulose (Pharmacoat 606–Shinetsu Chemical Co., Japan) to which was added either glycerol, propylene glycol or polyethylene glycol 200 at varying concentrations (10, 20 and 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. The same volume of coating solution was applied in each case to give a film thickness of 20–22 μm. In order to assess the incidence of bridging, 1000 tablets were withdrawn at the end of the run, visually inspected and the number with any signs of defect counted and expressed as a percentage.

The effect of plasticizer and plasticizer concentration on the incidence of bridging is shown in Fig. 1. It can be seen that at the 10 and 20% w/w level the rank order of plasticizer efficiency as measured by the lowering of the incidence of the defect is polyethylene glycol 200> propylene glycol > glycerol. At the 30% level the results for the polyethylene glycol 200 and propylene glycol are not significantly different.

The concept of stresses being developed in a film coating by its shrinking over a tablet substrate on evaporation of the solvent was first proposed by Rowe (1978) to explain apparently anomalous film/tablet adhesion results. It has now been expanded to explain the causes of such film defects as cracking, edge splitting and bridging (Porter 1980; Rowe & Forse 1980a,b). Before a discussion of how these stresses will be modified in the presence of plasticizers, it is pertinent to discuss how the stresses are developed during the formation of a polymer film from a solution of that polymer. Firstly, the solvent evaporates until, at a certain polymer concentration, a gel consisting of a solvent dispersed on an open polymer network is formed. This gel structure then contracts as further solvent is lost until a viscoelastic film is formed. It is the dimensional constraint of a film contracting on a relatively immobile substrate that invariably causes stresses to develop. During this process, polymer chain mobility is an important factor in influencing the magnitude of the stresses developed. When the polymer chains are mobile, as in the case of the polymer solution and to a certain extent the gel, they will orientate themselves in such a way as to dissipate any stresses formed. However, as solvent, and hence the free volume, is lost from the gel structure chain mobility becomes progressively restricted and any developed stresses become 'frozen' in. Plasticizers act by interposing themselves between the polymer chains and interacting with the forces holding the chains together, thereby extending and softening the matrix. By increasing the free volume, chain mobility is enhanced and the stresses can be dissipated, thus decreasing the incidence of bridging.

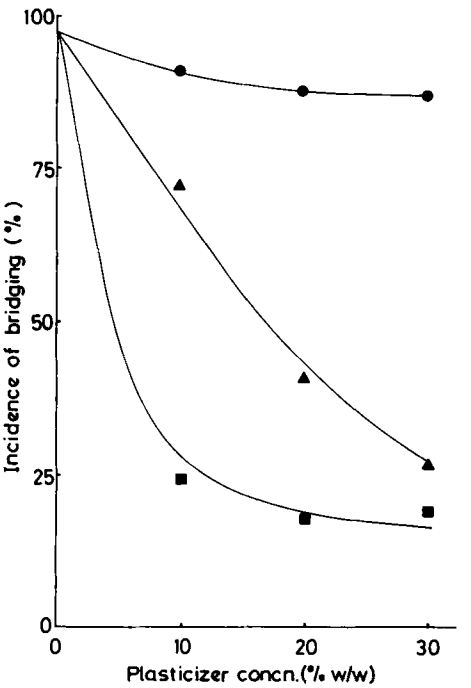

FIG. 1. The effect of plasticizer and plasticizer concentration on the incidence of bridging on film coated tablets. ● Glycerol, ▲ Propylene glycol, ■ Polyethylene glycol 200.

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Since the glass transition temperature of a particular polymer/plasticizer combination is a function of the polymer chain mobility, then the effect of plasticizers on this temperature will be a direct measure of plasticizer efficiency. In this respect, the curves in Fig. 1 are similar in shape to those reported for the same system showing the effect of plasticizer concentration on the glass transition temperature (Entwistle & Rowe 1979). There are, however, two anomalies: firstly, the rank order of plasticizer efficiency predicted by Entwistle & Rowe (1979) on the basis of decrease in glass transition temperature was propylene glycol > polyethylene glycol 200 > glycerol, and secondly, the difference in efficiency between glycerol and the other two plasticizers used in this study is greater than would be anticipated on the basis of this glass transition curve for the glycerol. The first of these discrepancies is probably due to the fact that the glass transition curves were calculated from a knowledge of the physical properties of the materials and the data used for polyethylene glycol 200 were averaged figures from manufacturer's literature. The second could well be due to plasticizer loss during the coating process. Since loss is dependent on the volatility of the plasticizer, its interaction with the polymer and its diffusivity through the polymer matrix, it would be expected that glycerol, with its low molecular weight and poor interaction with hydroxypropyl methylcellulose (as determined from intrinsic viscosity measurements—Entwistle & Rowe 1979), would be lost more readily than the other two plasticizers. This would have a detrimental effect on the incidence of bridging as shown for glycerol in Fig. 1. These results lend further support both to the concept of residual stresses in the film being the cause of bridging of the intagliations and to the adoption of a fundamental thermodynamic approach to the choice of plasticizers as advocated by Entwistle & Rowe (1979).

The authors would like to thank Mr L. Jessop for assistance in this work.

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J. Pharm. Pharmacol. 1981, 33: 175–176
Communicated November 13, 1980

0022–3573/81030175–02 $02.50/0

Relation between mixing time and segregation of ordered mixes

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A fundamental principle of ordered mixing is that fine particles of one powder adhere to other, usually coarse particles of another powder to form a near-uniform coating (Hersey 1975). The period which elapses before uniform adhesion occurs, along with any rearrangement of ordered units to produce the required homogeneity, can be defined as the ordered mixing time.

Ordered mixing times vary according to the powder system studied. Stephenson & Thiel (1980) and Travers & White (1971) found that ordered mixing was virtually complete between 4 and 10 min. Yip & Hersey (1977), studying the mixing of fine salicylic acid with coarser sucrose powder, found that after 10 min in a revolvocube blender the powders were within the required homogeneity. Bryan et al (1979) found that the ordered mixing time for microfine salicylic acid and starch/lactose granules was approximately 15 min. Similarly, Johnson (1975) reported periods of approximately 20 min for fine cyclopenthiazide mixed with various tableting excipients. In each of the cases described above, the maximum quantity of fine particles adhering to coarse particles was 1% but an increase in the percentage of fine component can significantly prolong the ordered mixing time. In the system studied by Bryan et al (1979) an increase in the fine powder component to 5 and 10% increased the ordered mixing time and even after 100 min mixing the coefficient of variation of the systems had not fallen below 10% despite an initial rapid decrease.

We have studied a system consisting of fine potassium chloride powder which formed ordered mixes with three coarse direct compression tableting excipients: a direct tableting sugar, Dipac (Amstar Corp., New York, U.S.A.); a spray crystallized maltose-dextrose, Emdex (Edward Mendell, U.S.A.) and a recrystallized lactose excipient made according to Staniforth (1980). When the potassium chloride was blended with each of the three excipients, by rotation in a Y-cone blender, the resulting ordered mixes showed different degrees of segregation tendency, or stability. Furthermore, the three excipients required different times to form ordered mixes and this also varied according to the percentage of potassium chloride in the system. In general, the more prolonged the ordered mixing time, the less stable the ordered mix that was produced. Table 1 shows the ordered

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