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COMMUNICATIONS

The effect of blending time on particle adhesion in a model interactive system

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The adhesive tendency of drug particles in a model drug carrier interactive system increased with blending time. The degree of interaction was measured using a centrifuge technique; the resultant adhesion profile of per cent retained on the carrier versus the square of the speed of rotation was a logarithmic normal function that allowed the determination of the S50 to characterize the adhesion tendency. The relative degree of adhesion of the drug particles in the interactive mixtures and the rate to attain adhesion saturation in the interactive system during the mixing process was markedly different for the three mixtures studied. The increased adhesive tendencies during blending were probably associated with triboelectrification of the drug and carrier particles.

Static electrification of two dissimilar materials occurs by the making and breaking of contacts between surfaces (Harper 1967). The degree of electrostatic charge accumulation will increase with increasing number of contacts and collisions between surfaces. During powder processing, the number of contacts and collisions can be increased by increasing the speed of particle motion (i.e. the degree of agitation in the mixer) and the time of processing (Peterson 1954; Kittaka & Murata 1976; Kittaka et al 1979; Lee & Weser 1979; Staniforth & Rees 1982). For example, during the preparation of an interactive mixture, the exchange of adherent drug particles between the carriers occurs as the particles are displaced from one carrier and randomly readhere to another (Travers & White 1971; Travers 1975; Barbosa Canovas & Peleg 1985). If particles can interact triboelectrically, this exchange process will allow the particle to experience contact events with other carriers thereby forming a large number of point charges on their surfaces (Donald 1972). Therefore, longer blending times should increase the spot charge distribution over the particle surfaces producing stronger electrostatic interaction between the drug and carrier. The relationships between blending time and the adhesive tendency of an interactive mixture therefore was investigated using a model interactive system and the centrifuge technique described by Kulvanich & Stewart (1987a, b).

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Materials and methods

The carrier consisted of glass beads (500 μm; Selby Scientific, Australia) coated with hydroxypropyl methylcellulose phthalate (HP-55, Shin-Etsu Chemical Co., Japan) using an air suspension technique (Uni-Glatt laboratory unit, Glatt GmbH, FRG). The adherent drugs were sulphapyridine (Sigma Chemical Co., USA: d_v = 27·2 μm), sulphamerazine (Sigma Chemical Co., USA; d_v = 17·7 μm) and succinylsulphathiazole (Sigma Chemical Co., USA; d_v = 23·4 μm). All materials were equilibrated in an environment chamber (Thermoline Scientific Equipment Pty Ltd, Australia) at a controlled relative humidity of 26·0 + 1·0% and temperature of 25·0 + 0·5 °C for 24 h. The interactive systems were prepared in an environmental chamber at relative humidity and temperature of 26% and 25 °C, respectively, using a system previously described (Kulvanich & Stewart 1987a, b). The blending time varied between 3 and 25 min and four or five replicate mixes were prepared for adhesion observations at each blending time. The degree of adhesion of the drug particles in the interactive system was measured using a centrifuge method (Kulvanich & Stewart 1987a, b). The adhesion measurements on the mix were carried out immediately after preparation.

Results and discussion

The centrifuge method allowed the determination of the adhesion profile which was a logarithmic normal function when the per cent of drug remaining on the carrier was regressed against the square of the speed of rotation (Kulvanich & Stewart 1987a, b). The profile could be characterized by the S50, i.e. the speed required to dislodge 50% of adherent particles, and the geometric standard deviation of the adhesive distribution. In these experiments the degree of adhesion of the particles during blending was measured by the S50 parameter.

The S50 values corresponding with the blending times of the three interactive systems are presented in Fig. 1. In the interpretation of the mixing profiles of S50 versus time, each point on the profile represents the adhesive tendency of a different mix, e.g. the mixing profile of the sulphapyridine interactive mix was determined using 25 mixing procedures. This experimental design was necessary to enable the adhesion measurements to be made immediately after mixture preparation to eliminate the charge decay effects. The technique would be expected to inflate the variance of the system and contribute to the scatter of data seen in the profiles.

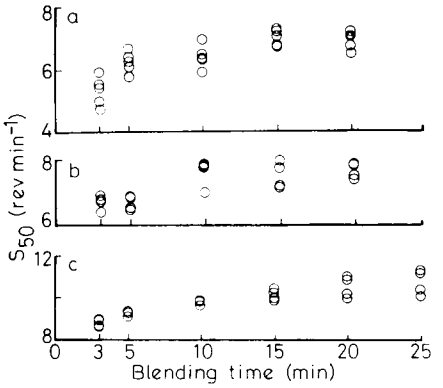

FIG. 1. The dependence of the adhesive tendency measured by the S50 on the blending time for (a) a sulphapyridine interactive mixture, (b) a sulphamerazine interactive mixture and (c) a succinylsulphathiazone interactive mixture.

All the drug interactive systems showed an increased adhesive tendency with time of blending. The succinylsulphathiazole interactive mixture reached an equilibrium level after about 10 min of mixing while the sulphamerazine mixture was still slowly increasing at 25 min. The adhesive tendency of each system was different with the saturation S50 values ranging from 6956 ± 272 rev min^{-1} for sulphapyridine mixture to 10 868 ± 620 rev min^{-1} for the sulphamerazine mixture.

Total adhesion in interactive systems will be comprised of several components including electrical, capillary and molecular forces (Zimon 1982). The increase in the adhesive tendency probably is caused by changes in the electrical force component due to triboelectrical charging. Different drug materials will possess different tendencies to be triboelectrically charged with the result that rates of adhesion saturation with blending time will differ (Kittaka & Murata 1976). Verification of electrostatic charge accumulation in the system is not possible in freshly prepared mixtures because of the limitations of the air stream Faraday cage for determining the charge measurement at the interactive unit interface due to incomplete drug particle removal from the carrier and interaction with the cage (Kulvanich & Stewart 1987c). However, the electrostatic interaction might not be the sole factor affecting the degree of adhesion of the drug powders. Other factors which could cause the change in adhesion tendency with time of blending include (i) the existence of powder aggregates causing low S50 values at shorter blending times, (ii) greater intermolecular interaction as the degree of impact and surface deformation increases with time, and (iii) the fracture of some large particles on prolonged blending which results in an increase in adhesion tendency because of the new surfaces available for interaction.

The significance of this study is that an optimum blending time exists in relation to the adhesion saturation of the interactive system. Interactive mixtures prepared under conditions of optimum particle carrier adhesion will be most stable to segregating conditions encountered in further processing. The blending time during interactive mixture preparation should be optimized not only with regard to the degree of homogeneity but also with consideration of adhesion saturation.

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