

THE SEGREGATION OF PERFECT POWDER MIXES

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Mechanisms of segregation which apply to a random mix (Williams, 1968) are unlikely to separate a perfect ordered mix, such as that described by Yip and Hersey (1977). Elcema G250 (E) and DiPac sugar (DP), two direct compression excipients which may produce segregation in random mixes because of their particle size and flow properties, were mixed separately with 0.5% of a fine-particle, model drug, potassium sorbate (PS) using a Y-cone blender. The mixed powders were filled into a brass cylinder and samples ranging from 250 to 1000 mg were analysed; the homogeneity was independent of sample size, confirming that a perfect mix had been formed. The cylinder was subjected to low frequency vibration in a jolting volumeter. This produced a non-dilating bed with interparticulate voids smaller than the excipient particles but large enough to allow movement of any dislodged PS particles. After vibration, 5 samples were removed from each of 4 levels in the cylinder, zone I being at the top, zone IV at the bottom. The coefficients of variation (CV%) were compared with the theoretical CV% of a random mix (Johnson, 1975) as shown in Fig. 1. DP shows a tendency for PS to segregate throughout the bed although CV% diminishes towards the cylinder base because, due to consolidation, the voids become smaller, restricting free movement of drug. Microscopic surface examination of DP and E particles showed that E was far more pitted than DP, and mercury porosimetry showed that the surface area of pores accessible to particles greater than 2 μm was 1,365 cm^2/g for DP and 5,400 cm^2/g for E. Of the total number of small particles, diameter d , in a mix, the theoretical fraction f , which will adhere to carrier particles, diameter D , is given by the relationship $f = nd^2/4D^2$, where n is the number of small particles adhering to each large particle (Hersey, 1975). Using our experimental values for surface areas accessible to PS particles, f is greater than unity showing that there are many more sites of adhesion than adhering particles. Thus, stereometrically, both DP and E are capable of carrying the fine particles but PS appears to form stronger bonds with E than with DP. We conclude that particles enclosed in cavities on the surface of E will experience greater surface interaction including electrostatic attraction, so that the force of adhesion is greater than the vibrational force of segregation. The different segregation behaviour of PS when mixed with DP and E indicates that the theoretical parameter, f , varies depending on the surface and electrical properties of carrier particles.

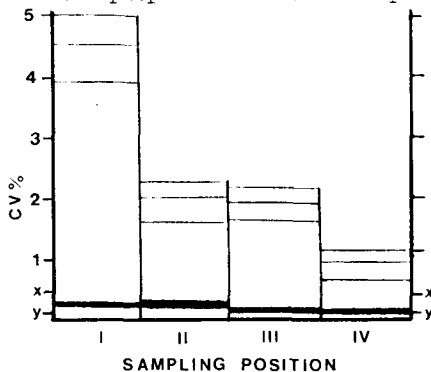


Fig. 1 Mean CV% at different sampling positions, with 95% confidence limits for DiPac sugar \square and Elcema G250 \blacksquare ; x and y are theoretical upper and lower 99% confidence limits for a random mix.

Williams, J. C. (1968/69). *Powder Technol.*, 2, 13-20.

Yip, C. W. and Hersey, J. A. (1977). *Powder Technol.*, 16, 189-192.

Johnson, M. C. R. (1975). *Pharm. Acta Helv.*, 50, 60-63.

Hersey, J. A. (1975). *Powder Technol.*, 11, 41-44.