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COMMUNICATIONS

Ordered mixing with lubricant and glidant in tableting mixtures

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Ordered powder mixtures are formed when a fine component has sufficient intrinsic cohesiveness to adhere to the surface of a more coarse component (Hersey 1975). Mixing of tablet lubricants such as magnesium stearate with tablet ingredients causes a lubricant film around the ingredient particles. This film formation is dependent on mixing intensity and mixing time and can be considered as an ordered mixing procedure. The lubricant film is a result of the adhesion to the substrate surface of magnesium stearate molecular layers, which are sheared off from the magnesium stearate crystals during the mixing process (Bolhuis et al 1975).

Although ordered mixing may be advantageous with respect to drug content uniformity in tableting mixtures, it is an undesirable effect in lubricant mixing. During the mixing process more and more lubricant will adhere to ingredient particles and the degree of ordering will increase. Increasing ordering of ingredient/lubricant blends decreases the binding properties of tableting mixtures (Bolhuis et al 1975) and will have a deleterious effect on the wettability, tablet disintegration and drug release (Lerk & Bolhuis 1977; Lerk 1981).

When mixing with lubricant is carried out, ordering should be limited, this can be attained by keeping the blending time as short as possible. Ragnarsson et al (1979) found that a short mixing time for magnesium stearate/excipient blends, resulting in a poor distribution of the lubricant, did not impair the lubricating efficiency in tablet compression.

In a recent letter, Lai & Hersey (1979) considered the effect of addition of a third component in ordered drug/carrier mixtures. Two possibilities were mentioned: a) the third component adheres preferentially to the carrier particles, displacing the original drug particles from their adhesion sites; b) the third component strips drug particles effectively from carrier particles, but is not bound itself to the carrier particles. The authors found the latter phenomenon to be true for ordered sucrose/salicylic acid mixtures, when they were admixed with magnesium stearate.

Similar effects may be observed when there is an interaction between lubricant particles and glidant particles. In previous work, we found that an ordered system of magnesium stearate on sodium chloride particles can be stripped from the substitute by colloidal silica under the formation of colloidal silica/magnesium stearate spheres. The original binding properties of the sodium chloride particles were restored when the ratio between the concentration of colloidal silica and magnesium stearate was 4:1 (Lerk & Bolhuis 1977). In other work, it was shown that a low colloidal silica concentration (0·2%) can suppress the deleterious effect of 0·5% magnesium stearate on tablet binding when a directly compressible blend was first mixed with the glidant and subsequently for a short time with the lubricant (Lerk et al 1977). The latter effect may be elucidated by competitive inhibition of magnesium stearate molecular layers at the adhesion sites which are occupated by colloidal silica particles.

In conclusion, ordered mixing of lubricants with tablet ingredients should be limited. This can be attained when the mixing procedure and the mixing sequence are carefully considered. Tablet ingredients including glidant but without lubricant should be intimately blended. After the addition of lubricant, the mixing procedure should be continued for as short a time as possible for limited ordered lubricant mixing. When an active ingredient has to be brought onto carrier particles by ordered mixing, special attention must be paid to possible interactions of glidants and/or lubricants with the ordered mix.

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