INFLUENCE OF TERNARY COMPONENTS ON COMPRESSIBILITY OF MICRO-CRYSTALLINE CELLULOSE FOLLOWING BLENDING WITH MAGNESIUM STEARATE

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Magnesium stearate (MS) is known to form a lubricant film around carrier particles which becomes continuous following prolonged mixing (Bolhuis et al 1975). Such film formation is considered to be at least partly responsible for the reduced mechanical strength of compressed tablets and reduced homogeneity of drug-excipient mixes in the presence of MS (Lai and Hersey 1979).

In the present study, binary mixes were produced by blending approx. 300 g microcrystalline cellulose (MCC) with 0.5% w/w MS for up to 20 min in a 3 dm^3 cube mixer. Tablet normalized work of failure values were found to decrease from approx. 1700 J m^{-2} after 1 min mixing to approx 1300 J m^{-2} after 20 min. mixing, although over the same time MS homogeneity was virtually unchanged. This is considered to be due to rapid dispersion of MS agglomerates after less than 2 min mixing; further mixing simply causes agglomerate breakdown into single particles which coat MCC particle surfaces but have no effect on bulk homogeneity.

In order to restore compressibility of MCC/MS to that found after less than 2 min mixing it was considered that reversing the MS dispersion process would be beneficial. Talc (T) and colloidal silica (CS) at a concentration of 2% were mixed separately for 10 mins. with binary mixes (20 min mixing) containing MCC and 0.5% MS. Ternary mixes containing T were found to produce tablets having slightly reduced mechanical strengths, whereas tablets containing CS had increased strengths (fig. 1). The reason for the different performance of the 2 ternary components was considered to be due to T acting as a carrier for MS particles, thereby facilitating dispersion. T was found to stabilise both ternary and quaternary mixes by becoming coated with MS which would normally strip drug particles from carrier surfaces. In contrast, CS tended to coat MS due to its exceptionally high surface area thereby reducing the deleterious effect of overmixing on tablet properties. In a second set of experiments , T and CS were blended separately with MS for 10 min prior to addition of MCC. Tablets containing T showed a more marked decrease in mechanical strength whereas CS produced a more marked increase in strength, restoring compressibility to better than after only 1 min. mixing with MS. This was taken as further evidence that T became coated with MS whereas CS itself coated MS. These changes in tablet strength were not due simply to the mechanical properties of the 2 ternary components since T produced stronger tablets than CS when mixed with MCC in the absence of MS (fig. 1).

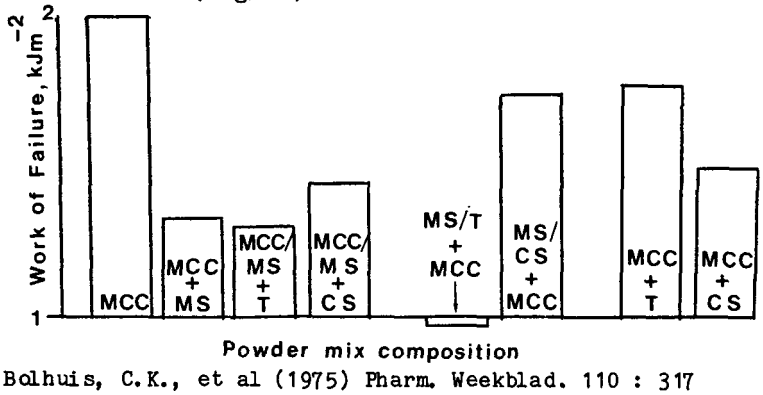

Fig. 1
Relationship between powder mixing conditions and tablet work of failure.

Bolhuis, C.K., et al (1975) Pharm. Weekblad. 110 : 317
Lai, F.K., Hersey, J.A. (1979) J. Pharm. Pharmac. 31 : 800