THE USE OF P/B RATIOS FOR SEMI-QUANTITATIVE ANALYSIS OF ORDERED UNITS IN POWDERS

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Ordered units, formed when fine particles adhere to coarser carrier particles can be characterised using SEM combined with X-ray energy dispersive analysis. (Anno et al, 1985). The technique was previously employed qualitatively using spot mapping to identify adherent particles but in the present study we have analysed binary and ternary powder mixtures semi-quantitatively. The geometry of rough macroscopic particles modifies the total X-ray spectrum comprising of characteristic and background radiation. Though these two types of emission are produced by different mechanisms, they both show similar 'geometric' effects for a given electron energy. Consequently, the background radiation provides a suitable internal standard and the ratio, p/b, of the characteristic elemental intensity (p) to the total background (b) minimises errors in the quantitative analysis of irregularly shaped particles (Goldstein et al, 1981).

Phenytoin sodium (P), <45 μm particle size was used as a model drug with Lactose samples D_1 and D_2 and Calcium sulphate dihydrate D_3 as coarse carrier diluents, 250 - 355 μm. The effect of mixing sequence was studied using magnesium stearate (L) as a ternary component. X-ray spectra of mixes containing 5% $^{w}/_{w}$ drug were recorded at random locations on the diluent surface, phenytoin Na and Mg stearate being identified by Na^+ and Mg^{2+} emissions respectively. The best Gaussian curve was fitted to each spectrum and p/b ratios computed. Twenty diluent surfaces were examined in each sample and the results assessed by analysis of variance. The p/b ratios represent the amount of drug and lubricant adhering to diluent particles.

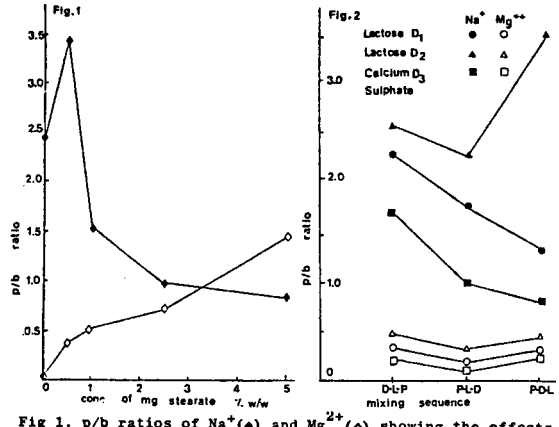

Fig 1. p/b ratios of Na^+(♦) and Mg^{2+}(◊) showing the effects of adding different concentrations of Mg. stearate to a binary mix of drug and diluent D_2 (95% $^{w}/_{w}$). Mixing sequence: P-D-L.

Fig 2. The effect of mixing sequence in a ternary mix on the p/b ratios of Na^+ and Mg^{2+}. Lubricant conc: 0.5% $^{w}/_{w}$.

In Fig 1, the values p/b for Na^+ and Mg^{2+} show the effect of adding different concentrations of lubricant to a drug-lactose D_2 mixture, the mixing sequence being P-D-L. With 0.5% $^{w}/_{w}$ lubricant, interaction is evident between lubricant and drug which increases significantly ($p=0.05$) the amount of drug adhering to the diluent. At higher lubricant concentrations the drug was progressively stripped from the diluent. Lactose D_1 and calcium sulphate D_3 showed a similar fall in p/b ratios, without an initial peak at 0.5% $^{w}/_{w}$ lubricant. Compared to lactose, calcium sulphate particles exhibited the least interaction with both drug and lubricant.

The extent of ordering depended on the sequence of mixing the three components (Fig 2). When diluent was first mixed with lubricant, in the sequence D-L-P, adhesion of drug and lubricant was more extensive than when the drug was first in contact with lubricant: sequence P-L-D. In P-D-L systems the amount of lubricant on the diluent surface was similar to D-L-P mixes but the quantity of adhering drug depended on whether the lubricant impaired (stripped) or facilitated the adhesion of drug.

Anno, E. M. & Rees, J. E. (1985) J. Pharm. Pharmacol. 37, 52P.

Goldstein, J. I. et al. (1981) Scanning Electron Microscopy and X-ray microanalysis, Plenum Press, New York.