FLOW PROPERTIES AND TABLET WEIGHT UNIFORMITY: EFFECTS OF GRANULE SIZE AND MACHINE SPEED

S.B. Tan, R.C. Moreton, D. Smith, Pharmaceutical Research and Development Department, Pfizer Central Research, Sandwich, Kent.

It is generally assumed that a good, uniform granule flow rate is a pre-requisite for good tablet weight uniformity. To date, a clear correlation between the flow properties of granulations and uniformity of tablet weights has not been established (Gunsel and Lachman 1963; Gold et al. 1968; Kristensen and Jensen 1969). Cole et al. (1974) observed little correlation between powder flow rate and uniformity of flow.

Our investigations have shown that there is a correlation between orifice flow rate, uniformity of flow and inter-tablet weight variation. Granules prepared from calcium carbonate, lactose and maize starch were sieved into various size fractions between 90 to 1000 μm. Using a flowmeter similar to that described by Cole et al. (1974), flow studies were performed on each size fraction of the unlubricated granules. Both mean flow rate and the coefficient of variation (c.v.) of flow rate were determined. Similar studies were carried out on five of the sieve fractions, lubricated with magnesium stearate. The amount of lubricant was adjusted to compensate for the different surface area for each size fraction. Using a Betapress 16 rotary machine with standard feed frame, the lubricated granules were compressed at 4 different indicated speeds (650,900, 1050 and 1200 tablets per minute). Tablet weight uniformity was determined.

The results from the powder flowmeter investigations clearly show that flow of both lubricated and unlubricated granules was markedly affected by granule size. Granules which have a good flow rate also exhibited uniformity of flow. Whilst lubrication with magnesium stearate increased the flow rate, the flow became more erratic (as measured by the c.v.). Optimal flow properties were achieved when granules of average sizes 200 to 400 μm were used. Results from the compression studies using the Betapress show that inter-tablet weight variation is dependent on granule size and machine speed. At each machine speed, there was an optimal granule size range (200-350 μm) which produced tablets with the least weight variations. Comparison of the results from both flow and compression studies indicates that granules which exhibit good uniform flow should produce tablets with the least weight variations.

Strong interparticle attractive forces and mechanical interlocking of angular granules are plausible explanations for the poorer flow of very small and large granules respectively. Uneven die filling of such granules may account for the higher weight variation. The larger inter-tablet weight variation observed at the highest machine speed for all size fractions is attributed to the very short filling time such that fluidity of the granules becomes limiting.

By careful manipulation of the processing conditions, e.g. milling or granulation, for formulations which are slugged or wet granulated, it may be possible to optimise granule size range. The powder flowmeter may be a useful tool in predicting the flow properties of such granulations on a rotary tableting machine.

Cole,E.T., Elworthy,P.H., Sucker,H. (1974) J.Pharm.Pharmac. 26: Suppl. 57P
Gold, G., Duvall, et al. (1968) J.Pharm.Sci. 57: 2153-2157
Gunsel, W.C. Lachman, L. (1963) Ibid. 52: 178-182
Kristensen, H.G., Jensen, V.G. (1969) Danst.Tidsskr.Farm. 43: 205-212