Evaluation of some tablet disintegrants and the effect of disintegrant type on the dissolution efficiency/compressional force relation

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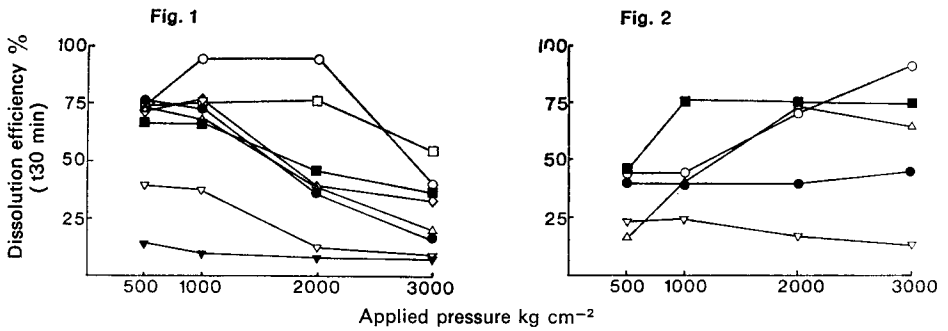
Several workers have studied the effect of compressional force upon *in vitro* dissolution. The relation, however, remains obscure and is often described as complex because it does not lend itself to simple interpretation. Most research workers have explained the dissolution data in terms of changes in particle size, or specific surface area, during compression (e.g. Smith, Baker & Wood, 1971). Although most of the systems investigated contained starch as a disintegrant, no reference was made to its possible influence. Khan & Rhodes (1972, 1974) have proposed that disintegrant type may have an effect upon this relation. However, because of the scarcity of data to support their hypothesis it has not received general recognition.

In this report we present results of the disintegration properties of four tablet disintegrants which have previously been subjected to only partial evaluation. The disintegrants include a relatively insoluble sodium carboxymethyl cellulose (Nymcel ZSD16), casein formaldehyde (Dr. Mann's), calcium carboxymethyl cellulose (E.C.G. 505) and a cross linked polyvinylpyrrolidone (Polyclar AT). Three widely used disintegrants; sodium carboxymethyl cellulose (Courlose P20), sodium starch glycolate (Primojel) and a cation exchange resin (Amberlite IRP 88) were used for comparison.

The disintegrants were incorporated internally in a lactose system and their properties examined. The effect of extragranular disintegrant concentration ranging from 2·5 to 10% w/w was determined upon tablets prepared both from a wet granulation system containing lactose and an insoluble, direct compression system (dicalcium phosphate dihydrate). For dissolution studies, 1% w/w amaranth was used as a tracer (Khan & Rhodes, 1972). The tablets, containing disintegrant and 1% w/w magnesium stearate, were made on an instrumented single punch machine. The dissolution rates were measures using a stirred flask method and are expressed as dissolution efficiencies, (Khan & Rhodes, 1972). Disintegration times were measured using the B.P method and hardness was determined on an Erweka hardness tester. Some of the results are shown in Figs 1 and 2.



FIGS 1 and 2. Compressional force/dissolution efficiency relations for a lactose system (Fig. 1) and a dicalcium phosphate dihydrate system (Fig. 2). Disintegrants (5% w/w): cross linked polyvinylpyrrolidone ○; cation exchange resin □; sodium carboxymethyl cellulose (Nymcel) ■; sodium starch glycollate ◇; calcium carboxymethyl cellulose △; casein formaldehyde ●; sodium carboxymethyl cellulose (Courlose) ▽; no disintegrant ▼.

From the above figures it is apparent that disintegrant type can have a significant effect upon the compressional force/dissolution efficiency relationship. This study also shows the relative effectiveness of these disintegrants, both in a soluble and an insoluble system. These results, together with those of the effect of disintegrant concentration upon disintegration time, are interpreted in terms of the properties of these substances as disintegrants and the differing mechanism by which they act.

In conclusion, it is suggested that because of the changes of disintegrant effect over the pressure range, full compressional studies are necessary for disintegrant evaluation.

The authors thank Mr. E. Salole for his assistance.

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The effects of binding agents on granule strength and tablet strength

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The binding agent employed in the wet granulation of tablets imparts strength to the granules and to the subsequent tablets. This report presents results showing a correspondence between granule strength and tablet strength.

The ratio of radial or die-wall pressure to the axial pressure applied during the tableting of sulphadiazine granules, made with various binding agents, was found to be related to the strength of the individual granules.

Granules prepared from sulphadiazine and alginic acid (8%, as disintegrating agent), containing one of four binding agents, namely, PVP, acacia, starch and methylcellulose, at a concentration of 4% were tested individually for their resistance to deformation as a result of the application of a range of small loads up to 330 mg in a Micro-tensile testing machine (Marsh, 1961), modified to test the granules in compression. Despite the wide scatter of results straight line relation between strain and load applied to the granule were obtained and a ranking order of the binding agents could be drawn up on this basis. The cross-sectional area and therefore the stress could not be measured. Granules made with methylcellulose showed a greater resistance to deformation than PVP granules.

The forces involved in tableting on a single punch tablet machine were measured with strain gauge instrumented top and bottom punches and the pressure exerted on the die-wall was measured with a piezo-electric transducer. The ratio of radial pressure to axial pressure for granules prepared with methylcellulose as binding agent was less than that for granules made with PVP. This difference was manifested by lower values of tablet crushing strength for methylcellulose than for PVP-containing tablets. A low ratio of radial to axial pressure implies a low shearing action which would tend to give weaker tablets. The methylcellulose granules also gave tablets of higher porosity than the PVP granules and with an increased tendency to cap.

A simple method for measuring granule friability was employed (Baba & Sugimoto, 1965) which gave a similar ranking order for the binding agents as the measurement of individual granule strength. Thus, granules made with methylcellulose proved to be more resistant to the abrasive forces involved in the friability test than granules made with PVP. For the range of binding agents studied, this test could be used in a limited way as a screening method for the granules before compression to give some indication of the likely behaviour of the granules under compression.

The viscosity of aqueous solutions of the various binding agents appeared to be an important factor in the strength of the individual granules, the more viscous solutions giving stronger granules.

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