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A NOTE ON THE COLLAPSE OF DISINTEGRATING TABLETS UNDER LAMINAR FLOW CONDITIONS

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SUMMARY

Disintegrating tablets tested in a column-type dissolution apparatus collapse off the holder, and the time for collapse appears to be related to the compaction pressure used in their preparation. However, this collapse time and the time for disintegration in the official apparatus are not directly related. Reasons for this disparity are discussed. The potential value of the laminar flow collapse time as an experimental parameter for the characterization of tablet properties is emphasized.

INTRODUCTION

It is well known that the release of medication from compressed tablets and capsules is influenced by the initial penetration of gastric or intestinal fluids into the dosage form. It is also accepted that disintegration is often the rate-limiting stage for the dissolution of the tablet ingredients. Most solid dosage forms of drugs are now required to conform to standards for disintegration and/or dissolution behaviour.

In a recent investigation of the properties of a model compressed drug formulation containing lithium carbonate, a column dissolution method was employed (Groves et al., 1975). However, it was noted that after an initial period in the apparatus the tablet collapsed off its holder and was reduced to a heap of granules. This collapse time appeared to be highly reproducible but did not correlate with results obtained in the disintegration apparatus of the British Pharmacopoeia.

The tablets, consisting of lithium carbonate with different ratios of starch and lactose and granulated with aqueous PVP, were compressed at different pressures under carefully controlled conditions. The mean hydrodynamic pore size of the compacts was determined by a low pressure gas permeability method described in detail elsewhere (Groves and Alkan, 1978). In this method the compact in its original die is mounted in the apparatus which is then evacuated and filled with nitrogen. The downstream pressure of

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the gas is maintained at 4 Pa and the decay of the upstream side monitored after admitting nitrogen at a predetermined pressure. The measured permeability rate enables a mean pore size to be calculated since, under low pressure conditions, the likely pore radius is appreciably smaller than the mean free path of the gas molecules and diffusional (Knudsen) flow may be presumed. Results from these experiments showed that there was an exponential relationship between the compaction pressure applied and the mean pore radius of the compact. However, two regions could be distinguished by differences in the rates of decrease in pore size with increase in compaction pressure. The first region is believed to be due to the collapse of inter-granular spaces whereas the second region results from collapse of the intra-granular spaces only. The point at which the cross-over between two mechanisms occurred was termed the critical pressure, although it was not considered to be a sharp change from one to another but rather a transition in which one process becomes more dominant than the other.

This effect has been found for all the formulations examined in this present investigation and could be correlated with other tablet properties, in particular tablet hardness and the collapse times in the column dissolution apparatus.

MATERIALS AND METHODS

Lithium carbonate BP (BDH Chemicals Ltd.); lactose BP crystalline (BDH Chemicals Ltd.); starch BP, maize (BDH Chemicals Ltd.); PVP, polyvinylpyrrolidone Luviscol 30, (Berk Pharmaceuticals Ltd.) used as a 5% w/v solution in water; magnesium stearate BP (BDH Chemicals Ltd.). Formulations are given in Table 1.

Tablets were prepared by a wet granulation process in which the powders were mixed in a Z-blade mixer with the PVP solution until a damp paste was obtained. This was granulated through a No. 12 B.S. sieve and dried in an air oven at 50°C for 24 h. The fraction between No. 12 and No. 16 sieves (1000–1400 μm) was collected and mixed with the magnesium stearate powder by gentle rotation in a capped jar.

Approximately 400 mg of the granules was weighed and compressed in a hydraulic press (Hydraulic Scientific Model RIK M15) at pressures ranging from 40 to 315 MPa using a 12.7 mm flat-faced punch and die set. The pressure was applied by the upper punch only and the compacts were kept under pressure for at least 30 s to reduce separation of the particles due to elastic behaviour.

TABLE 1

FORMULATIONS INVESTIGATED

Component	Per cent by weight		
	A	B	C
Lithium carbonate	68.2	68.2	68.2
Lactose	25.0	18.2	11.4
Starch	6.8	13.6	20.4
PVP solution (5%)	2% of the final dry weight		
Magnesium stearate	1	1	1

Mean pore sizes were determined by the low pressure gas permeability method described by Groves and Alkan (1978).

The dissolution apparatus employed was substantially that described by Groves et al. (1975). It consisted of a vertical column in which the tablet was suspended vertically and immersed concentrically in a stream of flowing liquid. The liquid flow rate was kept constant by a light-activated servo controlled valve system and rates of $8-17 \times 10^{-3}$ dm^3 min^{-1} (Re 10-21) were employed with water at 37°C. The tablet support described earlier was modified to a simple stirrup design so that the tablet under test was at rest on a support without being clamped.

The disintegration times were determined using the method described in the British Pharmacopoeia (1973) in water at 37°C ± 1. Tablets were tested individually without using the guided disc and results shown are the mean of five determinations.

Tablet tensile strengths were measured using an Erweka Hardness Tester, Model TBT, as modified by Summers (1972). This modification consisted of replacing the original platen with a smooth flat-faced top platen of the same size as the lower platen. A thin strip of hard polystyrene, 2 mm wide, was pasted across the surface of both platens longitudinally to ensure that the tablet fractured diametrically. The crushing load was noted from the direct reading scale and the tensile strength calculated from the Frocht equation (Frocht, 1948), with the porosity correction as suggested by Rowe et al. (1973):

$$\sigma = 2p/\pi D L (1 - e)$$

where σ = tensile strength (Nm^{-2}); p = crushing load (N); D = diameter of the tablet (m); L = thickness of the tablet (m); and e = porosity of the tablet.

RESULTS AND DISCUSSION

Although not presented here, the dissolution results showed that release of the drug was affected by the flow rate, an increase in Reynolds Number increasing the release rate until the onset of turbulent or transitional flow regimes resulted in a levelling out of the process (Alkan, 1978).

There was a linear relationship between the tablet tensile strength and the compaction force, in agreement with the data of Fell and Newton (1968). This is probably due to the fact that tensile strength is proportional to the product of the interparticulate contact area and the bond strength, and both of these parameters are influenced during the compaction process. Hardness or tensile strength cannot therefore clearly indicate changes in compaction mechanisms since it is dependent upon two independent variables. The linearity of the tensile strength and compaction force measurements are shown in Fig. 1 and indicate that the strength of the compacts increases as the amount of incorporated starch is increased.

Collapse times measured in the column apparatus were highly reproducible and decreased dramatically as the tablet strength increased, passed through a minimum and gradually increased again (Fig. 2). However, the minimum collapse time in all cases coincided with tablets prepared at around the critical compaction pressure. Interestingly those tablets with the largest pores remained suspended in the holder appreciably longer

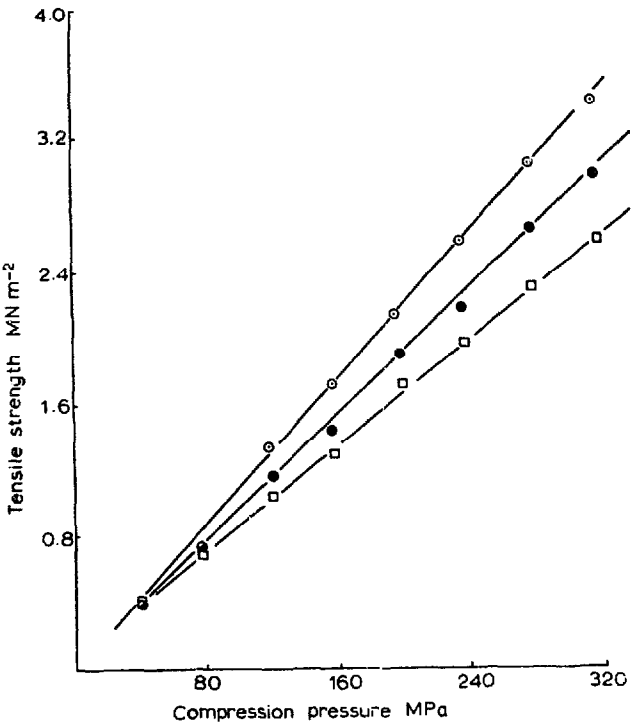

Fig. 1. The tensile strengths of tablets made at different compaction pressures. ○, formulation A; ●, formulation B; □, formulation C.

than tablets which were more strongly compressed. This would indicate that the collapse of the tablets under these conditions of closely controlled laminar flow was dependent on factors other than pore size.

On the other hand, the disintegration times using the B.P. method simply showed a general increase with increasing tabletting pressure. Although slight inflections could be observed around the critical compaction pressures for individual formulations, the general tendency was for the disruption time to increase with compaction strength (Fig. 3).

The contrasting behaviour for the two methods of disintegration measurement on tablets prepared below the critical compaction pressure requires some explanation. In the B.P. apparatus the tablets are subjected to mechanical abrasion by being passed through the liquid/air interface and by collision with the retaining sieve and tube walls. Ultimately the measurement will be affected by the bond strength of the granules as well as the liquid penetration rate. Thus, the weaker the bond strength which results when there is less compaction pressure, the faster will be the disintegration process. On the other hand, there is no mechanical abrasion in the column method and the bond strength is only affected when water penetrates in between adjacent surfaces. When the granules are not fractured, i.e. below the critical compaction pressure, the water is less effective since the inter-granular spaces will be rapidly filled and intra-granular particles will not be wetted. As the compaction pressure is increased and the granules are fractured, water can more

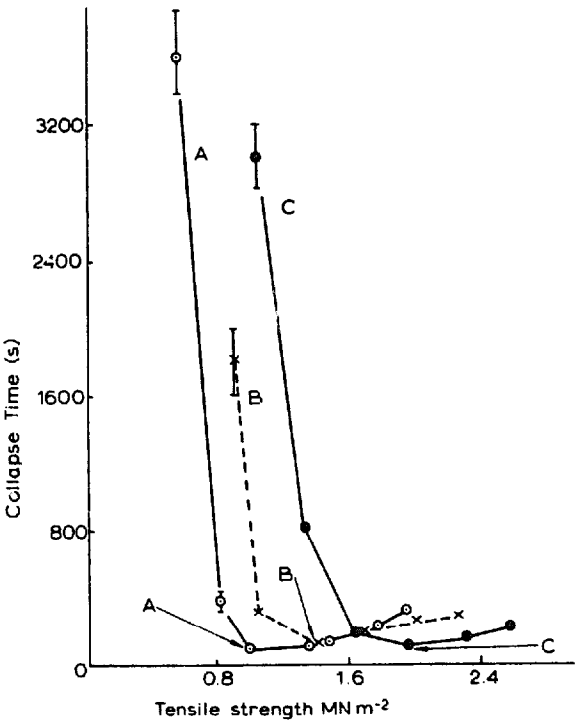

Fig. 2. The collapse times of tablets prepared at different compaction pressures in the column dissolution apparatus when tested in water at a Reynolds Number of 21 and at 37°C, as a function of tablet tensile stength. Formulations A, B and C (Table 1). The bar lines indicate scatter (maximum and minimum values) for 5 replicates at a point, where it can be shown at this scale. The arrows indicate the tablets made at the appropriate critical compaction pressure (Groves and Alkan, 1978).

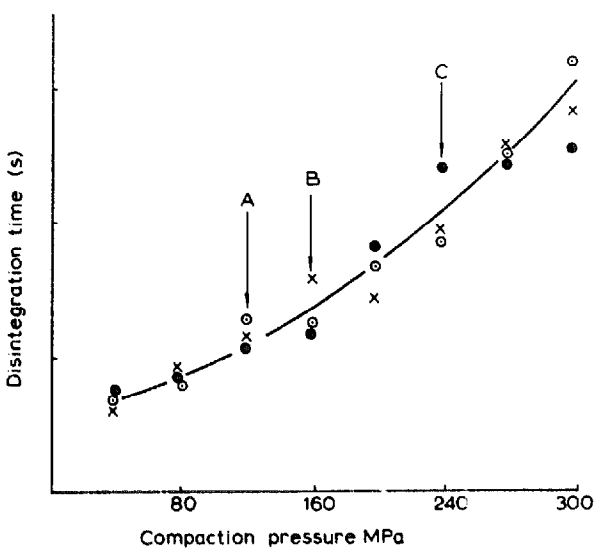

Fig. 3. The effect of compaction pressure on the B.P. disintegration test times (water at 37°C) for 3 lithium carbonate formulations (Table 1). Arrows refer to the respective critical compaction pressures (Groves and Alkan, 1978). ⊙, formulation A; X, formulation B; •, formulation C.

readily affect the interparticulate forces and produce a collapse in the structure. Finally, as the compression increases the interparticulate forces are increased and the time for the collapse again becomes more protracted.

The two methods are therefore different since the disintegration time is influenced by mechanical abrasion and is mainly related to the strength of the intergranular bonds. In the case of the streamline liquid flow around a tablet in the column dissolution apparatus, surface contact area and, most important of all, intragranular bond strength, will be involved.

The sensitivity of the results suggests that the collapse of tablets under the controlled laminar flow conditions readily produced in a column flow dissolution apparatus might prove to be a valuable investigational parameter.

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