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Compression characteristics of granulated materials:

VI. Pore size distributions, assessed by mercury penetration, of compacts of two lactose granulations with different fragmentation propensities

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Summary

Tablets were compacted at a pressure of 50 MPa from two granulations which had identical composition (95% lactose and 5% PVP) but different physical properties, i.e., porosity, compressive strength and fragmentation propensity during compaction. The pore system of the tablets was assessed by mercury penetration measurements. A bimodal distribution in pore size was observed for compacts made from the granulation with the lower fragmentation propensity, while a unimodal and comparatively narrower pore size distribution was found for compacts made from the granulation with the higher fragmentation propensity. Thus, it was concluded that a tablet compacted from granules has a pore structure consisting of inter- and intragranular pores and that the degree of fragmentation of the granules during the compression phase especially affects the size of the intergranular pores. The results support the validity of using the air permeability technique for the characterisation of granule fragmentation.

Introduction

It is well known from the literature that granulations of one specific formulation, i.e., a certain combination of binder and substrate, might show different compactibility when the granulations have been differently processed. To gain an understanding of the mechanisms behind this observation, the physical properties of a series of granulations, prepared under a variety of processing conditions during the agglomeration phase, have been studied (Alderborn et al., 1987; Wikberg and Alderborn, 1990a,b, 1991, 1992). The results show that the variation in processing conditions provides granules of varying porosity and compressive strength. Furthermore, compaction of these granulations produces tablets with different physical properties, i.e., air permeability and me-

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chanical strength. It has been found that the porosity and the compressive strength of the granules correlate with the air permeability of the tablets, i.e., the pore structure of the formed tablet.

In the discussion of these results, a model was used in which the tablet was described as a large aggregate consisting of a number of smaller cohered aggregates. It is thereby assumed that the granules will maintain their integrity to some extent during the compression phase. Consequently, as granules are porous particles, the pore system of the resultant tablet will be composed of both inter- and intragranular pores. This physical description of a tablet is in accordance with earlier reports (Selkirk and Ganderton, 1970) on the pore size distribution of tablets compacted from granules. When a certain mass of granules is compressed in-die, the granules will be forced into closer proximity but their physical structure will also change, i.e., the granules will fragment into smaller aggregates, be deformed and their porosity will be reduced (Alderborn et al., 1987; Wikberg and Alderborn, 1990a,b, 1991, 1992). Thus, the actual pore size distribution in the tablet is probably affected by the porosity of the tablet, the size and the shape of the granules before compaction and, finally, the volume reduction properties of the granulations.

Our results show that granules of a higher porosity and a lower compressive strength produce tablets with a lower air permeability, i.e., a smaller mean pore diameter. It was suggested that this is the result of more marked fragmentation during compression than seen with granules of a lower porosity and higher compressive strength. Thus, fragmentation would lead to the formation of smaller intergranular pores and thereby reduced intergranular separation distances.

The air permeability technique used in the studies is a simple and fast method of characterizing the pore structure within the tablet. However, a more detailed description of the pore structure can be obtained by estimating the pore size distribution with a mercury penetration technique. The intention behind this study was, therefore, to provide evidence to support the theory of the duality of the pore system of compacts of granulated materials and to support the effect of the degree of granule fragmentation on the pore size distribution.

Materials and Methods

Granulation method and primary characterisation of the granulations

A series of granulations consisting of 95% by weight lactose (α-monohydrate, 200 mesh, DMV, The Netherlands) and 5% by weight of polyvinylpyrrolidone (Plasdone, K 26/28, GAF, U.S.A.) was prepared by wet granulation in a high-shear mixer (Fielder PMAT 25, Fielder, U.K.). After drying in a fluid-bed dryer (Glatt, model TR 5, Germany) the size fraction 500–710 μm was separated by dry sieving (Retsch, Germany) and used in all experiments. Details concerning the processing conditions as well as evaluation of some physical and compaction characteristics have been presented earlier (Wikberg and Alderborn, 1991, 1992). Two granulations, selected on the basis of their porosity, were chosen for further investigation. These granulations are hereafter denoted as LP (low porosity) and HP (high porosity), respectively. Data concerning the porosity and the compressive strength of these granulations are presented in Table 1.

Compaction and characterization of tablets

Air permeability For each granulation, six tablets were compacted by hand at a series of compaction pressures, i.e., 20–70 MPa, and the air permeability of these was measured with a Blaine apparatus. The procedure and the equation used for calculating the tablet surface area have been described earlier (Alderborn et al., 1985). In this paper, a mean pore radius, calculated according to Eqn 1, is given as a measure of the pore system of each tablet:

$$r = \frac{2\epsilon \times 10^4}{S_v(1-\epsilon)} \quad (1)$$

where r is the mean pore radius in the tablet (μm), ϵ the total tablet porosity, and S_v the volume specific surface area of the tablet (cm^2/cm^3).

Mercury penetration Two tablets of each granulation were compacted at a maximum upper punch pressure of 50 MPa in an instrumented single punch press (Korsch EK 0, Germany) as earlier described (Wikberg and Alderborn, 1990b). Using a mercury penetration porosimeter (Micromeritics Pore Sizer 9310, U.S.A.), the relationship between the penetrated volume of mercury and the penetration pressure was measured for the tablets. Penetration pressures between 0.03 and 206 MPa were used. The limiting pore size for mercury penetration was calculated from the penetration pressure assuming circular pore openings, a surface tension for mercury of 480 mN/m and a contact angle between mercury and the material of 130° (Orr, 1969/70).

Tensile strength Three tablets of each granulation were compacted at maximum upper punch pressures of 50, 100 and 188 MPa. The diametral compression strength of the tablets was measured and the radial tensile strength calculated as earlier described (Wikberg and Alderborn, 1990b). Tablets made from granulation HP were of considerably higher mechanical strength (Table 1).

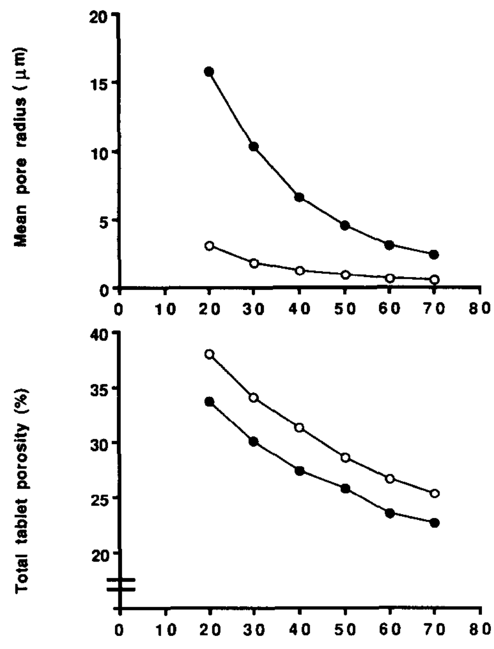

Fig. 1. Mean pore radius (upper panel), calculated from the air permeability measurements, and the total tablet porosity (lower panel) as a function of the compaction pressure. (○) Granulation HP; (●) granulation LP.

Results and Discussion

In the upper panel of Fig. 1, the mean pore radius (calculated according to Eqn 1) is presented as a function of the compaction pressure. For both granulations, the mean pore radius of the tablet decreases with the compaction pressure. It can also be seen that the calculated pore radius for tablets of granulation HP generally is lower than for tablets of granulation LP. This cannot be explained by differences in the total tablet porosity, i.e., the degree of densification of the mass (Fig. 1, lower panel). The total tablet porosity decreased for both materials in a similar fashion with the compaction pressure but there

TABLE 1

Denomination of granulation, granule porosity, granule compressive strength and tensile strength of tablets compacted at maximum upper punch pressures of 50, 100 and 188 MPa

Denomination of granulation	Granule porosity [a] (%)	Granule compressive strength [b] (N)	Tensile strength of tablet (MN/m^2) [c]		
			50 MPa	100 MPa	188 MPa
LP	12.3 ± 0.3	3.1 (0.5)	0.42 ± 0.05	1.03 ± 0.09	2.17 ± 0.22
HP	31.3 ± 0.6	0.7 (0.3)	0.72 ± 0.05	1.67 ± 0.06	3.38 ± 0.07

[a,c] Arithmetic mean ± S.D., $n = 3$.
[b] Median, interquartile range given within parentheses, $n = 100$.

was a tendency for tablets of granulation HP to be of a higher porosity. The differences in air permeability are believed to be caused by variations in the degree of granule fragmentation during compression. Granules of granulation HP are, due to their higher porosity, of a lower compressive strength and are therefore expected to fragment into smaller aggregates to a greater extent during compression (Table 1). Consequently, the granules of granulation LP, which are of higher compressive strength, are expected to maintain their integrity to a greater extent during compression. This suggests that the distribution of pore sizes within the tablets could also differ between the two granulations.

To produce tablets for the mercury penetration analysis, a compaction pressure of 50 MPa was chosen. This pressure was chosen to ascertain the formation of tablets of sufficient mechanical strength to withstand the stresses during the analysis. To allow for comparison, the compaction pressure was also to be within the same range of pressures used for the air permeability measurements, i.e., 20–70 MPa.

The total volume of mercury which penetrated the compacts during the measurement was 0.20 cm^3/g for granulation LP and 0.22 cm^3/g for granulation HP. The total pore volumes calculated from the weight and the dimensions of the compact and the apparent density of the granulations, as estimated by an air comparison pycnometer (Beckman model 903, U.S.A.), were 0.24 and 0.27 cm^3/g, respectively. The discrepancy between these calculated values and those obtained from the penetrated volumes might be due to closed pores within the compact and the existence of very small pores, e.g., within the lactose particles, which are not accessible for the mercury.

The results from the mercury penetration measurements are presented in Fig. 2. In the upper panel of Fig. 2, the cumulative penetration volume is presented as a function of the penetration pressure. Tablets of granulation HP gave cumulative penetration curves which were narrower and more S-shaped than those from tablets of granulation LP. For tablets of granulation HP, most of the mercury appeared to penetrate the

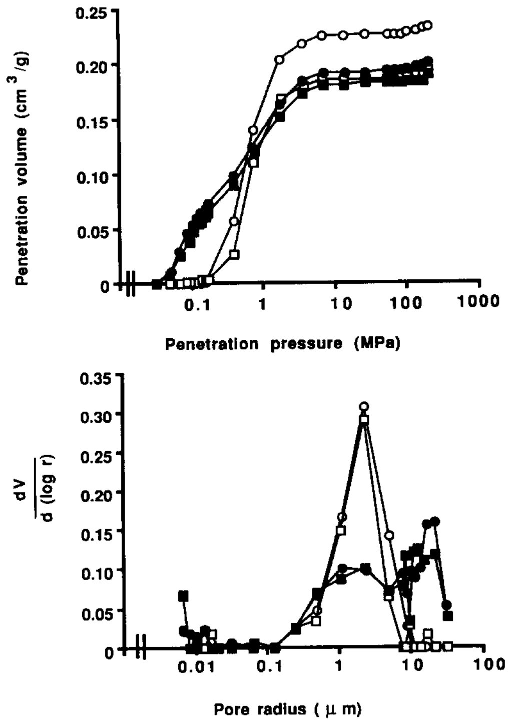

Fig. 2. Cumulative penetration volume as a function of the penetration pressure (upper panel) and the pore size distribution (lower panel), calculated from the mercury penetration measurements. (○, □) granulation HP; (●, ■) granulation LP.

tablets at pressures between 0.3 and 7 MPa. For tablets of granulation LP, mercury penetrated at lower pressures, i.e., above 0.05 MPa, but the upper limit appears to be the same as for granulation HP, i.e., 7 MPa.

In the lower panel of Fig. 2, the calculated pore size distributions (Orr, 1969/70) are presented. The tablets of granulation HP appear to have a unimodel pore size distribution with a peak pore radius around 2 μm. The distribution of pore sizes is narrower than for tablets of granulation LP. The tablets of granulation LP have a much wider distribution of pore sizes and what appears to be a bimodal pore size distribution, with peaks corresponding to pore radii of 2 and 16 μm.

It should be pointed out that the absolute values of the pore radius have to be considered with some caution, due to simplifications and inaccuracy in both methods, and this will make a detailed comparison between Figs 1 and 2 difficult. For the mercury penetration analysis, the assumption of circular pore openings, the value of the contact angle between mercury and the material (e.g., Good and Mikhail, 1981) and eventual 'ink-bottle' effects (Dees and Polderman, 1981) are possible errors. The calculated pore radius from the permeability measurements will also be affected by difficulties, for example, of defining the actual intergranular pore space in the tablet (Wikberg and Alderborn, 1990b). However, if Figs 1 and 2 are compared, the results confirm that a change in the pore size characteristic is reflected as a change in the air permeability of the compact. The permeability of the compact might be related to either the size of the largest pores (Garcia-Bengochea et al., 1979) or to the total pore size distribution (Selkirk and Ganderton, 1970) within the compact.

The results in this study support the hypothesis that the pore system of compacts of granulated materials consists of intra- and intergranular pores. For a granulation with a low fragmentation propensity, the granules retain the original structure to a comparatively larger extent during compaction and the compacts will display comparatively larger intergranular pores. Thus, a distinction between intra- and intergranular pores will be obtained, i.e., a bimodal pore size distribution. With an increased degree of fragmentation during compaction, the size of the intergranular pores will be reduced due to fracturing of the granules. When the size of the intergranular pores is reduced, a change to a unimodal pore size distribution will be observed, i.e., a distinction between intra- and intergranular pores cannot be made.

Although the pore size distribution will probably be affected by the compaction pressure, it is difficult to state how. Nevertheless, the difference in the mechanical strength of tablets made from the two granulations is not eliminated by an increase in the compaction pressure (Table 1).

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