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An investigation of the pore structure of tablets of sucrose and lactose by mercury porosimetry

ALASTAIR B. SELKIRK* AND DAVID GANDERTON†

*Department of Pharmaceutical Technology, School of Pharmacy, University of Strathclyde, Glasgow, C.*1, *U.K.*

The pore structure of tablets has been investigated by mercury porosimetry. Tablets, when prepared from ungranulated powder, showed a narrow pore size distribution, the mode of which decreased from 9 to 1 μm over the pressure range studied. Granulation caused the size distribution of tablet pores to widen. Large robust granules, compressed at low pressures, gave tablets with a bimodal pore size distribution. Decrease in granule size and strength, promoted a more uniform tablet structure and fine, friable, granules, compressed at high pressures, gave tablets with almost the same structure as those prepared from ungranulated powder.

Some investigations of the pore structure of tablets of sucrose and lactose using permeability and liquid penetration tests were recently reported (Ganderton & Selkirk, 1970). The inferences drawn from experiments in which the properties of the granules and the degree of compression were varied were of a wide and possibly discontinuous distribution in the size of the pores. The measurement of such a distribution can be made by the intrusion of a non-wetting liquid. In the work reported below this technique is described and its application to the estimation of tablet structure assessed.

THEORETICAL CONSIDERATIONS

An external force must be applied to any non-wetting liquid, such as mercury, for its penetration into a pore. The surface tension, γ, opposing entry acts along the perimeter. If the capillary is circular in cross section, the force opposing entry normal to the plane of contact is given by

$$F_o = -2\pi r\gamma \cos\theta$$

where r is the radius of the pore and θ the contact angle the liquid makes with the pore surface.

The external force, which must be applied for penetration to occur, acts over the area of the circle of contact and is given by the equation

$$F_a = \pi r^2 p$$

where p is the applied external pressure.

At equilibrium

$$\pi r^2 p = -2\pi r\gamma \cos\theta$$

$$\therefore pr = -2\gamma \cos\theta \quad .. \quad .. \quad .. \quad .. \quad (1)$$

No pores will be penetrated by a non-wetting liquid under zero external pressure but as the pressure is increased the amount of liquid forced into the pores will increase

Present address: *School of Pharmacy, Sunderland Polytechnic, Sunderland;
†ICI Pharmaceuticals Division, Alderley Park, Cheshire.

and will be proportional to the differential pore volume, the size of which is related to the changing pressure by equation (1).

This derivation assumes the pore is circular in cross section, the assumption appearing as the ratio of perimeter to area, 2/r. While the pore network within a tablet is invariably complex and seldom are the pores circular in shape, the variation of this ratio for non-circular cross sections will not be great. The shape of the distribution curve will not be appreciably altered and the calculated radius will be changed by a consistent factor.

Pore size distribution function

If, within a tablet, the volume of the pore having a radius between r and r + dr is dV, then,

$$dV = D(r)dr \quad .. \quad .. \quad .. \quad .. \quad (2)$$

where D(r) is the pore size distribution function of that tablet, i.e. the fraction of the pore volume with a radius between r and r + dr.

If a constant surface tension and contact angle are assumed, differentiation of equation (1) with respect to r and p gives

$$pdr + rdp = 0 \quad .. \quad .. \quad .. \quad .. \quad (3)$$

Combining equations (2) and (3)

$$dV = -D(r)\, r/p \cdot dp$$

$$\text{or } D(r) = -p/r \cdot \frac{dV}{dp} \quad .. \quad .. \quad .. \quad .. \quad (4)$$

For a tablet with a given pore size distribution, an increase in pressure on the non-wetting liquid gives a unique pressure uptake volume curve; conversely a given pressure–volume curve affords a determination of the pore size distribution.

For a number of values of p the experimental pressure volume curve may be differentiated to obtain dV/dp while r may be calculated from equation (1). A plot of D(r) against r gives the pore size distribution.

EXPERIMENTAL

Granulation. The finely powdered lactose and sucrose were massed in a Z blade mixer with water for 5 min. The resultant wet mass was passed through an oscillating granulator fitted with a coarse screen. The granules were dried to a constant weight at 70° and rescreened.

Two sucrose batches were made with a massing water content of 5% in one case and 9% in the other. With lactose, the massing water content was varied in four equal steps from 13 to 25%. The granules were finely sieved and the sieve fractions −8 + 16 and −60 + 85 were collected for study.

Compression. Granules (0·5 g) were compressed in a punch and die set of diameter 12·7 mm by means of a hydraulic press. Using a predetermined pressure and thickness, tablets were prepared with a porosity of 29, 26·5, 22 or 15%.

Mercury intrusion. The relation between the mercury penetration volume and intrusion pressure was measured with a mercury penetration porosimeter (Model 905–1, Coulter Electronics Ltd., Dunstable). Five tablets were used in each deter-

mination; they were placed in the sample cell and this in turn was placed in the bomb of the porosimeter.

The cell was evacuated and mercury was allowed to enter; when full, the pressure was allowed to rise to 3·5 kNm^{-2}. This, the initial penetration pressure, is the lowest pressure readily usable since the dimensions of the sample holder are such that the hydrostatic pressure of the mercury above the tablets is of a similar magnitude. The pressure was incrementally increased to atmospheric and the volume of mercury penetrating the tablet at each pressure was measured by the apparent volume of the mercury in the sample holder. Pressure above atmospheric was applied with compressed air after filling the bomb with oil. The maximum pressure used was 350 MNm^{-2}.

In deriving the pore size distribution, the surface tension of the mercury was assumed to be 0·474 Nm^{-1} and its contact angle with lactose and sucrose 130°. From equation (1) this allows a corresponding pore radius to be calculated for any given pressure. As the volume of the void space in each tablet was known, the saturation of the tablet by mercury at each pressure level was calculated and expressed as a percentage.

RESULTS AND DISCUSSION

Sucrose. Fig. 1 shows typical porosimetric results for tablets made from ungranulated sucrose powder. These results are presented both as the percentage of voids filled for a given penetration pressure (Fig. 1a) and as the corresponding pore size distribution (Fig. 1b). The sigmoid shape of the curve shown in Fig. 1 is characteristic of this determination. Absence of intrusion at low pressure followed

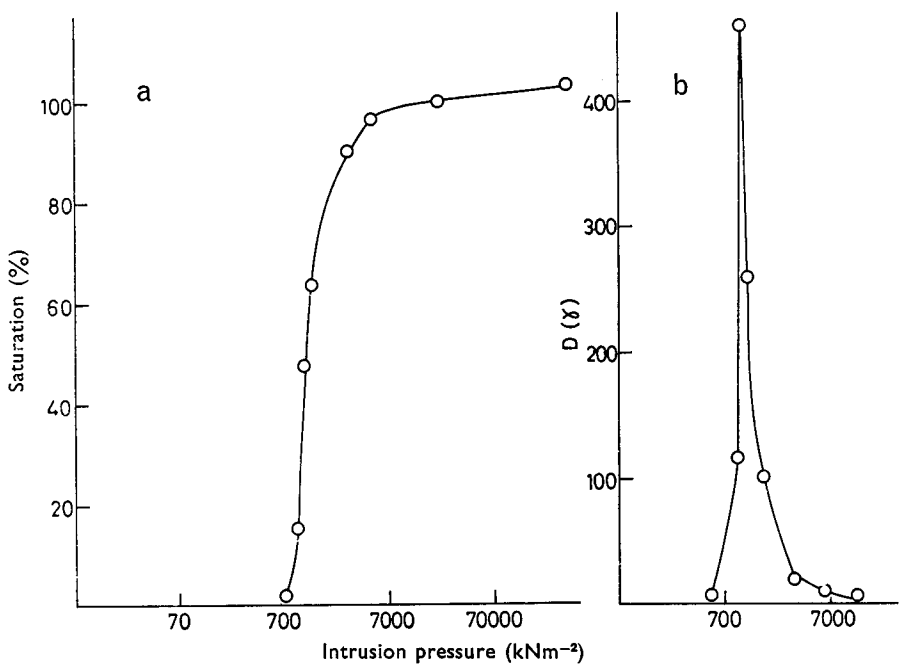

FIG. 1. Cumulative pore size distribution curve (a) and pore size distribution (b) of tablets of sucrose powder at 22% porosity.

by rapid saturation over a relatively small pressure range is indicative of a system of a narrow pore size distribution containing few coarse pores. However, as shown in Fig. 1b some tailing off at lower pore sizes does occur.

The susceptibility of the pore structure of these tablets to compression pressure is illustrated in Fig. 2. As the porosity is decreased the position of the curves moves steadily towards the lower pore sizes. This shift is relatively small, the pore radius at 50% saturation decreasing from 1·6 to 0·6 μm for a reduction of 14% in porosity. Microscopic examination of the uncompressed sucrose powder showed a narrow size distribution, 80% of the particles lying between 8 and 25 μm. Compression of this material will form a tablet of small pores and such a system will be characterized

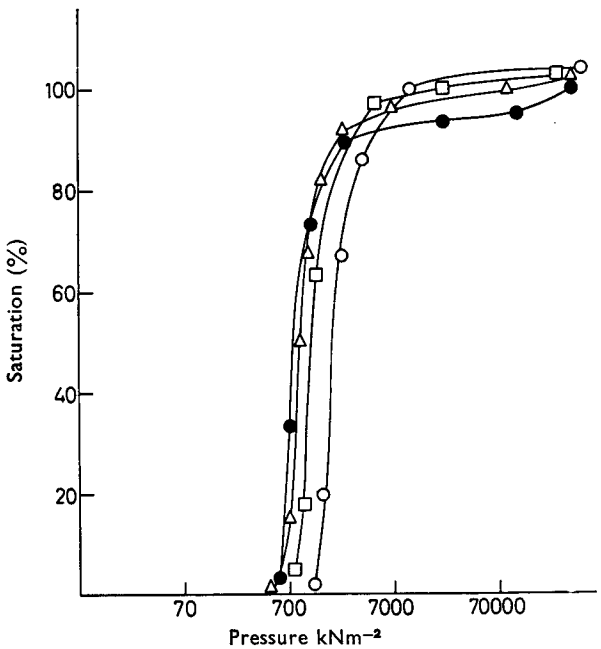

FIG. 2. The effect of compression on the pore structure of tablets of sucrose powder. ● 29% porosity. △ 26·5% porosity. □ 22% porosity. ○ 15% porosity.

by low permeability. Marshall (1958) has derived a relation between permeability and size distribution of pore in an isotropic medium. If the mean radius of the pores in each of n equal fractions of the total pore space is represented in decreasing order of size r_1, $r_2 \ldots r_n$ cm, then the permeability B_o is given by

$$B_o = \frac{\epsilon^2 n^{-2} (r_1^2 + 3r_2^2 + 5r_3^2 + \ldots + (2n-1)r_n^2)}{8} \quad \ldots \quad (5)$$

where ϵ = porosity.

This equation enables a calculation of the permeability of a tablet from a knowledge of its pore size distribution, and its application to a tablet prepared at 29% porosity from sucrose powder gave a permeability value of $8{\cdot}5.10^{-14}$ m^2. This is in close agreement with the experimental value of $7{\cdot}0.10^{-14}$ m^2 (Ganderton & Selkirk, 1970).

The structure of such a system containing only small powder particles will not

be readily susceptible to breakdown with increase in compression pressure. This is manifest in the small shift in pore distribution as the porosity is reduced.

The effect of granulation on the pore structure of sucrose tablets is shown in Fig. 3. This process leads to a very marked increase in the proportion of coarse pores present and to a considerable widening of the pore size distribution. Such marked opening of the pore structure is maintained even at relatively low porosities. Opening of pore structure will result in a more permeable tablet. Calculation of the permeability from a knowledge of the pore size distribution (eqn 5) again gave values much higher than those from tablets of the ungranulated powder. These values were in close agreement with the values found experimentally.

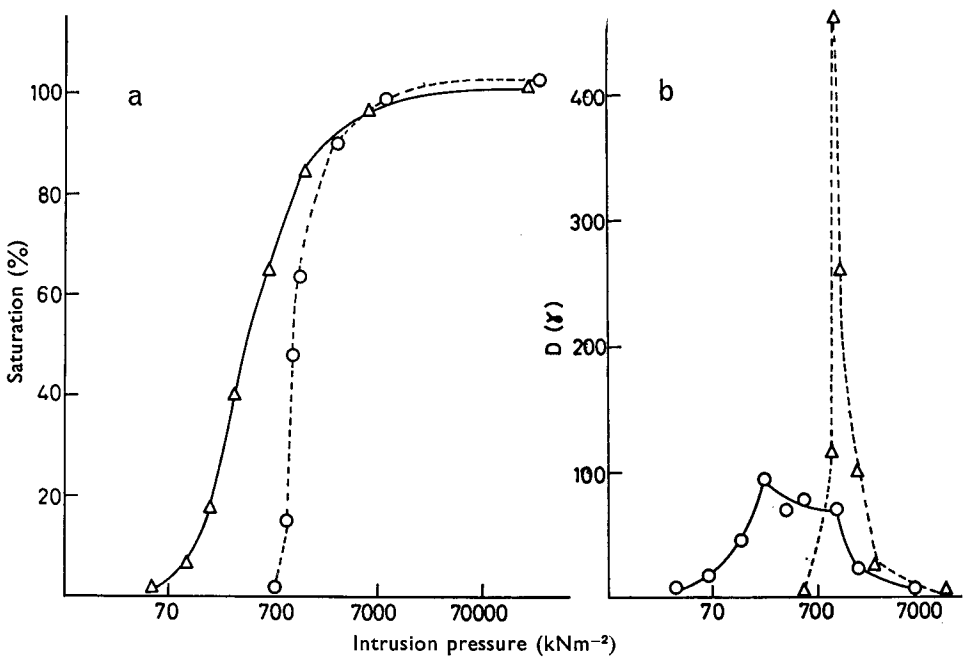

FIG. 3. (a) The effect of granulation on the cumulative pore size distribution of sucrose tablets of 22% porosity. △ Tablets prepared from −16 + 22 mesh granules massed with 5% water. ○ Tablets prepared from ungranulated powder.
(b) The effect of granulation on the pore size distribution of sucrose tablets of 22% porosity. ○ Tablets prepared from −16 + 22 mesh granules massed with 5% water. △ Tablets prepared from ungranulated powder.

Within a tablet compressed from granular material there are two types of pores. The first, intragranular pores, are formed within the granules themselves during the aggregation of the powder. The second type, intergranular pores, are formed between the granules during tabletting. While the former are invariably small the latter, especially in an uncompressed bed or a tablet of high porosity may be relatively large. Thus tablets made from these materials have a wide and perhaps discontinuous pore size distribution. On compression, however, fragmentation of the granules leads to a breakdown of the coarse intergranular pore network resulting in a tablet of more even pore size distribution. This process is described in Fig. 4. On compression, a large change in the pore structure occurs with the pore radius at 50% saturation decreasing from 9·0 to 1·0 μm for a 14% reduction in porosity.

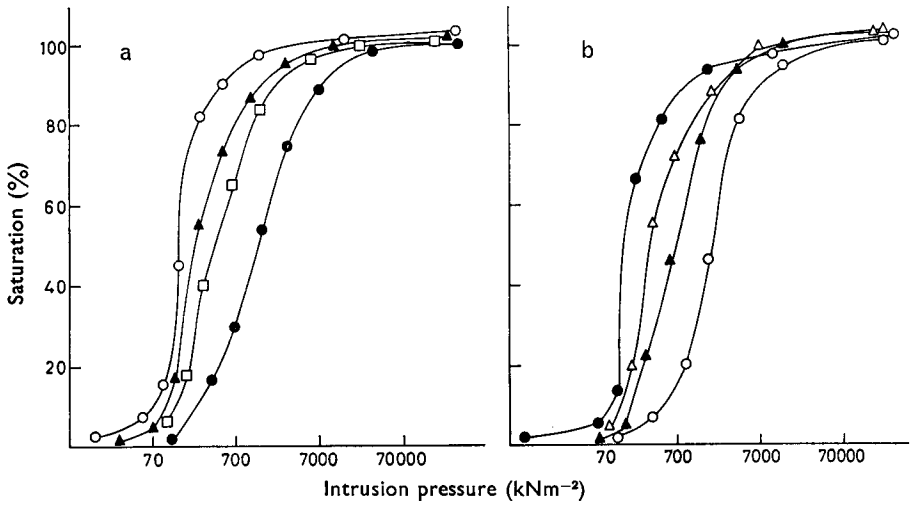

FIG. 4. The effect of compression on the pore structure of tablets prepared from —16+22 mesh sucrose (a) and —8+16 mesh lactose (b) granules. ○ 29% porosity. ▲ 26·5% porosity. □ 22% porosity. ● 15% porosity.

The photographs in Fig. 5 show that for a tablet made from granular material the coarse intergranular pores are not randomly distributed within the tablet but are closely related to the original granule configuration. As expected, tablets prepared from the ungranulated powder gave no visual evidence of any intergranular pore network.

Granule size and massing water concentration during granulation also affect the pore size distribution of the resultant tablets and a summary of such effects is given in Table 1.

An increase in granule size and massing water concentration simultaneously operates to open the pore structure of the tablet. Granule size initially defines the size of the intergranular pores with the coarser granules promoting a more open pore structure. In the early stages of compression while fragmentation is still small this

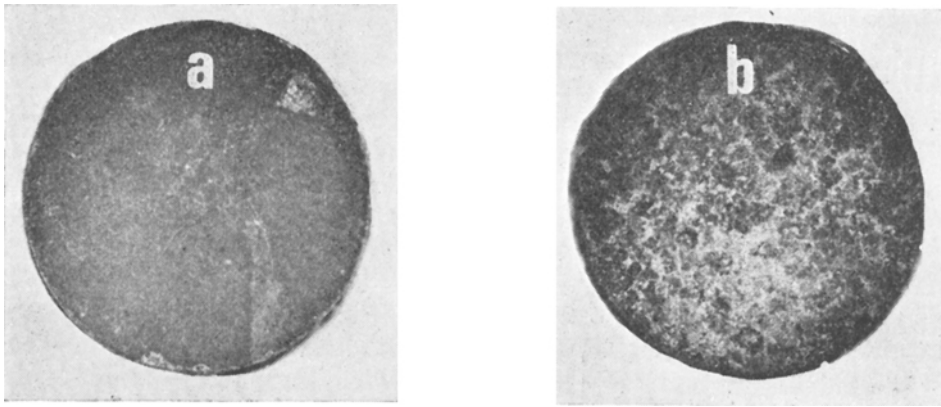

FIG. 5. Photographs of sucrose tablets on completion of a mercury intrusion determination. a. Tablets prepared from the ungranulated powder. b. Tablets prepared from —16+22 mesh granules.

Table 1. *Granule size and massing water concentration during granulation of sucrose and lactose*

Granule size	29% Porosity % Voids ⩾ 12 μm	29% Porosity % Voids ⩽ 1·2 μm	15% Porosity % Voids ⩾ 12 μm	15% Porosity % Voids ⩽ 1·2 μm	29% Porosity % Voids ⩾ 12 μm	29% Porosity % Voids ⩽ 1·2 μm	15% Porosity % Voids ⩾ 12 μm	15% Porosity % Voids ⩽ 1·2 μm
Sucrose	5% Massing water concentration				9% Massing water concentration			
—16 + 22	25·0	5·0	0	52·0	49·0	9·5	0	51·0
—60 + 55	15·0	7·0	0	49·5	16·5	4·0	0	49·0
Lactose	13% Massing water concentration				25% Massing water concentration			
—16 + 22	7·0	12·5	0	30·0	14·5	15·0	0	33·0
—60 + 85	6·5	13·0	0	31·0	8·0	14·0	0	30·0

influence is sustained. As compression is increased and as fragmentation becomes marked, these effects disappear.

Massing water concentration affects both intragranular porosity and the resistance of the granules to deformation. Since intragranular porosity is decreased by higher massing water concentrations (Ganderton & Selkirk, 1970), compaction to a given overall porosity requires less deformation. This, together with their increased robustness, results in tablets of a more open pore structure. Thus at 29% porosity, tablets prepared from coarse granules massed with 9% water had 49% of the void space as pores greater than 12 μm. The corresponding material massed with 5% water had 25% greater than 12 μm. Again this effect was eroded by an increase in compression pressure.

Lactose. The change in the pore size distribution with a decrease in porosity is similar to the changes observed with sucrose tablets with the pore radius corresponding to 50% saturation decreasing from 8 to 0·8 μm. The effect of granule size and massing water concentration is shown in Table 1 which indicates that the contribution of the coarse pores to the overall porosity is less than with the sucrose. For example, lactose massed with 13% water, compressed to 29% porosity gave a tablet with 7·0% of the voids present as pores greater than 12 μm.

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REFERENCES

GANDERTON, D. & SELKIRK, A. B. (1970). *J. Pharm. Pharmac.*, **22**, 345–353.
MARSHALL, T. J. (1958). *J. Soil Sci.*, **9**, 1–8.