Cooling as a possible method for increasing the flowability of certain pharmaceutical and other powders

A. O. ONYEKWELI AND N. PILPEL*

Department of Pharmacy, Chelsea College, University of London, Manresa Road, London SW3 6LX, U.K.

Measurements have been made of the rates of flow under gravity of powdered sugars and of fatty acids through circular orifices at temperatures between -25 and $110\ °C$. The flow rates decrease considerably as the powders are heated; conversely they increase as the powders are cooled from a high ambient temperature of 40 to $-25\ °C$. The results are ascribed to changes in the cohesiveness of the powders caused by softening and plastic deformation of particles at elevated temperatures. Lactose, paracetamol and griseofulvin granule formulations have been reported to show similar effects and the possibility is discussed of using cooling to increase the flowability of particular powders in pharmaceutical production. The rates of flow of the powders are given by the expression

$$Do = A \left(\frac{4W}{60\pi\rho\sqrt{g}} \right)^{\frac{1}{n}}$$

where W is the flow rate in g min^{-1}, Do is the orifice diameter in cm, ρ is the particle density in g cm^{-3}, g is the gravitational constant, and A and n are numerical terms which depend on temperature and particle size.

A survey of the literature on the flow of pharmaceutical and other powders through circular orifices reveals that although a large amount of work has been done at room temperature and numerous equations proposed for relating flow rate to variables of the apparatus and of the powders (for reviews see Brown & Richards 1959; Beverloo et al 1961; Harmens 1963; Neumann 1967) comparatively little has been done at temperatures above or below ambient (Pilpel & Britten 1979).

Powdered drugs, fillers, excipients, lubricants, plastics and other materials employed in pharmaceutical solid dose formulations melt or soften as their temperature is raised. The particles form into aggregates or lumps, their flow becomes irregular and eventually ceases as the orifice blocks.

The flow rates of powders depend on many variables which include the shape and size of the orifice, the ratio of the orifice diameter, Do, to that of the containing vessel, the shape, size, density, roughness, moisture content of the particles. (Ahmad & Pilpel 1969).

In all cases it is found that dry powders flow faster than damp ones and that the flow rate first increases with increase in particle size, Dp, up to a maximum between 100 and 400 μm (depending on the nature of the powder) and then decreases as the ratio Dp/Do increases towards a value of 0·2.

* Correspondence.

It is difficult to measure the flow rates of powders accurately when they are beginning to exhibit cohesive properties (Neumann 1967) either as a result of their small particle size, or because they are damp or because they have been heated to near their softening/melting point. Nevertheless the subject is of interest in pharmacy since it is relevant to the large scale handling of powders during mixing, formulation, tablet making and the filling of capsules.

By choosing materials which are available in a range of particle sizes and which have relatively low melting/softening points so that their flow can be measured over a reasonably easily attainable range of temperature ($-25°$ to $+110\ °C$), it was hoped in the present work to establish

(a) whether there is any quantitative relationship between the flow rate of a powder and its temperature and

(b) whether a typical flow equation which has been shown to apply satisfactorily to a large number of different powders at room temperature, is also applicable at other temperatures.

MATERIALS AND METHODS

Materials
The materials investigated were palmitic acid 99% pure and stearic acid 95% pure from BDH and two varieties of cane sugar—Demarara brown sugar and granulated white sugar—from the British Sugar Corporation. The sugars were milled in a Moulinex

mill and all the materials were then classified into close size fractions using a mechanical siever and B.S. sieves. They were dried in the oven for up to 12 h at appropriate temperatures (about 40 °C for the fatty acids and about 60 °C for the sugars) and were stored over silica gel in airtight containers. Their relevant physical properties are listed in Table 1, with those of lactose and a paracetamol tablet formulation consisting of % w/w paracetamol 90, maize starch 10, plus 5% polyvinyl pyrrolidone, for comparison.

Table 1. Physical properties of materials.

Material	m.p. °C	m.p. °K	Particle density × 10^{-3} kg m^{-3}	Moisture content* % (w/w)	Size range available μm
Palmitic acid	61	334	0·85	<0·1	215–605
Stearic acid	64	337	0·90	<0·1	152–605
Brown sugar	177	450	1·61	<1	76–600
White sugar	182	455	1·64	<1	76–600
Lactose	204	477	1·54	<1	160
Paracetamol granules	150 (Decomp)	423	1·29	<1	350

* measured with a vacuum moisture tester (Townson & Mercer).

Flow measurements

The flow rates of the different size fractions of the materials were measured through circular orifices, with diameters of 0·75, 1·10 and 1·45 cm, at temperatures between −25 and +110 °C in the apparatus shown in Fig. 1. It was located in a room maintained at a relative humidity of 40 ± 5% with a Drymatic dehumidifier and consisted of an insulated metal tube, 7·7 cm in diameter tapering at one end into a cone with a vertical angle of 25°, into which the required orifice could be inserted. The orifice was opened or closed by means of a hinged flap fitted with a spring. A gauze metal cup containing silica gel desiccant was fitted into the upper end of the flow tube as an added precaution against moisture.

The sample of powder was either placed in an oven or (within its airtight container) in solid carbon dioxide and heated or cooled for 15 min to approximately the temperature required for carrying out the flow measurement. It was then rapidly transferred to the flow tube and gently fluidized in a stream of carefully dried nitrogen gas which had been pre-heated or pre-cooled to the required temperature by passing through a heat exchanger. Fluidization ensured maximum control over the moisture content
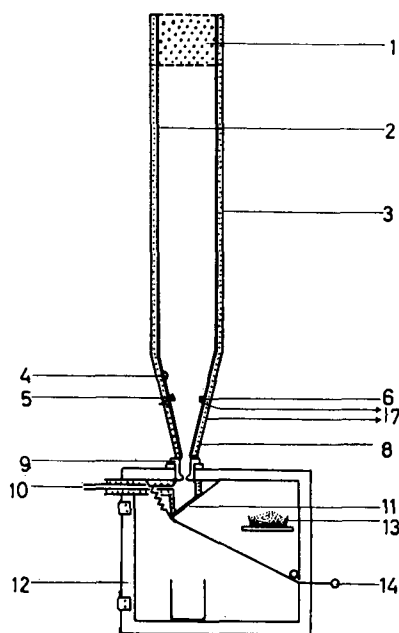

FIG. 1. Flow tube apparatus. 1 Desiccant. 2 Extension tube (65 cm long, 7·7 cm diam). 3 Polystyrene insulation. 4 Earth connection. 5 Thermistor (−25 to +50 °C). 6 Thermistor (50 to 150 °C). 7 Leads to galvanometer/recorder. 8 Conical hopper (cone angle 25°). 9 Outlet with variable orifice. 10 Gas inlet. 11 Flap arrangement. 12 Cabinet. 13 Desiccant. 14 Flap control.

and temperature of the powder and also served to break up any aggregates.* The gas was turned off, the orifice flap opened and the rate of flow was measured in triplicate by weighing the amount of powder collected in the beaker in a known time after about 2 seconds when 'flooding' has ceased and the flow rate had become constant.* The moisture contents of the samples were rechecked periodically.

RESULTS

Fig. 2 shows how the rates of flow of the four materials through the 1·45 cm orifice varied with particle size at room temperature, 20 °C. Fig. 3 is representative of how the rates of flow of palmitic acid and white sugar through the same orifice varied with temperature. In both cases the statistical variation was ±5%. The flow of each material

* Preliminary experiments showed that prolonged fluidization tended to generate 'fines' and appreciable electrostatic charge on the particles both of which caused the flow rates to vary beyond the limit of reproducibility of ±5% which was accepted for determinations carried out in triplicate. For this reason the period of fluidization was kept as short as possible (1 min) consistent with the attainment of temperature.
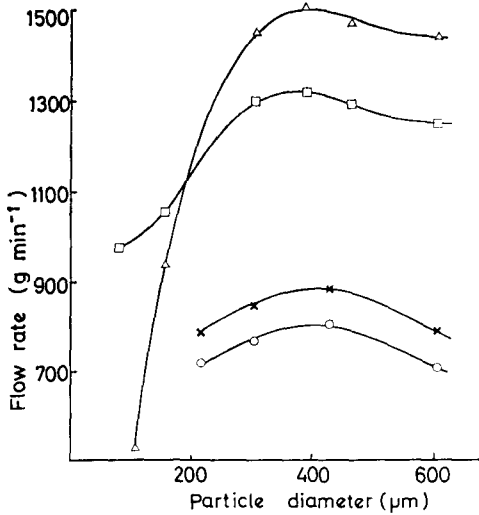
FIG. 2. Flow rates at 20 °C versus particle diameter through 1·45 cm orifice. △ = white sugar. □ = brown sugar. × = palmitic acid. ○ = stearic acid.

increased with increase in orifice diameter reaching a maximum at a particle diameter of about 400 μm. It was highest at the lowest temperature and decreased as the temperature was increased becoming zero near the melting point.

This is illustrated in Fig. 4 for particles with a diameter of 302 μm flowing through the 1·10 cm diameter orifice; some literature results (Pilpel & Britten 1979) for the 350 μm paracetamol granules and for the 160 μm lactose through a 0·75 cm diameter orifice are included for comparison.
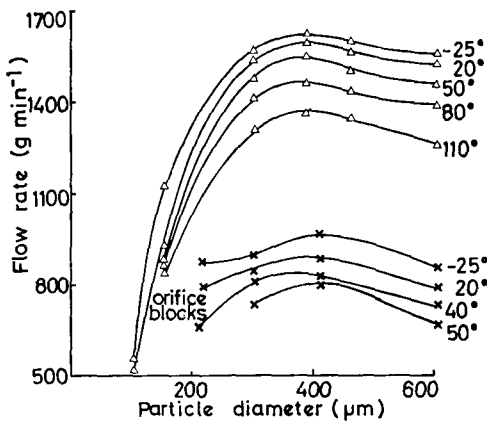

FIG. 3. Flow rates at different temperatures versus particle diameter through 1·45 cm orifice. △ = white sugar. × = palmitic acid.
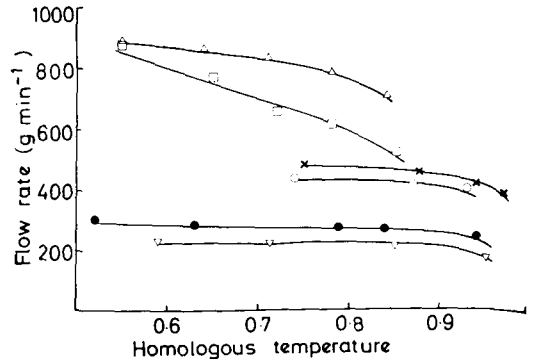

FIG. 4. Flow rates of 302 μm particles versus homologous temperature through 1·10 cm orifice. △ = white sugar. □ = brown sugar. ○ = stearic acid. × = palmitic acid. ▽ = paracetamol formulation (350 μm through 0·75 cm orifice, Pilpel & Britten 1979). ● = lactose (160 μm through 0·75 cm orifice, Pilpel & Britten 1979).

In Fig. 4 and elsewhere the homologous temperature is defined as the ratio of the temperature of measurement to the melting point of the material in °K and at the melting point the homologous temperature is 1·0. The reason why the orifice diameters in Fig. 4 were selected differently to those in Figs 2 and 3 was so that the resulting graphs should be conveniently spaced and not cross, which would have been confusing. It was not found possible to extend the measurements further towards the limiting homologous temperature of 1·0 because in this region the flow becomes erratic and cannot be measured accurately.

Analysis of the results for all the materials at all the temperatures investigated showed that they could be fitted to the general equation (Jones & Pilpel 1966; Ahmad & Pilpel, 1969).

$$Do = A\left(\frac{4W}{60\pi\rho\sqrt{g}}\right)^{\frac{1}{n}} \quad .. \quad .. \quad .. \quad (1)*$$

with an average accuracy of ±5%. This is illustrated in Table 2 and is as expected since the estimated errors in the determination of A and n, from which W_{cal} was derived, were also about ±5%.

* Do orifice diameter cm; Dp particle diameter μm; W flow rate (gm min⁻¹) subscripts obs and cal indicate observed and calculated values respectively; ρ particle density gm cm⁻³ (measured by liquid immersion); ρ_F packing fraction = $\left(\frac{\text{bulk density}}{\text{particle density}}\right)$; g gravitational constant 981 cm s⁻²; A and n are numerical terms in equation 1.

Table 2. Comparison of measured flow rates with those calculated from Equation 1.

Material	Dp (μm)	Do (cm)	Temp. (°C)	Temp. (°K)	Wobs (g min⁻¹)	Wcal (g min⁻¹)	n	A	Difference between obs. and cal. flow rate (%)
Stearic acid	302	1·45	50	323	—	—	—	—	—
			40	313	738–758	773	2·38	1·82	−3·2
			20	293	788–806	795	2·37	1·80	0·3
			−25	248	796–878	865	2·51	1·72	−3·3
Palmitic acid	302	1·45	50	323	735–760	748	2·27	1·82	−0·1
			40	313	817–840	820	2·33	1·74	1·0
			20	293	848–860	840	2·27	1·73	1·7
			−25	248	967–1028	970	2·32	1·62	2·8
Brown sugar	462	1·45	110	383	913–1007	991	2·12	2·19	3·1
			80	353	1062–1082	1160	2·10	2·04	−7·7
			50	323	1240–1310	1248	2·10	1·97	2·2
			20	293	1371–1388	1314	2·07	1·93	5·0
			−25	248	1370–1452	1449	2·08	1·84	−2·6
White sugar	462	1·45	110	383	1269–1306	1273	1·95	1·65	1·1
			80	353	1386–1485	1365	1·98	1·59	5·2
			50	323	1441–1546	1403	1·95	1·57	6·5
			20	293	1480–1560	1514	1·94	1·51	0·4
			−25	248	1509–1560	1534	1·94	1·50	0·0

The values of A and n were derived from the intercepts and slopes respectively of the straight lines obtained by plotting log Do versus log $\left(\dfrac{4W}{60\pi\rho\sqrt{g}}\right)$.

(No attempt was made to fit these lines by regression analysis since only three orifices had been employed.)

Representative plots of A versus particle diameter are shown in Fig. 5 for the white and brown sugar and for stearic acid (the values of A for palmitic acid were approximately 0·9 lower than those for stearic acid).
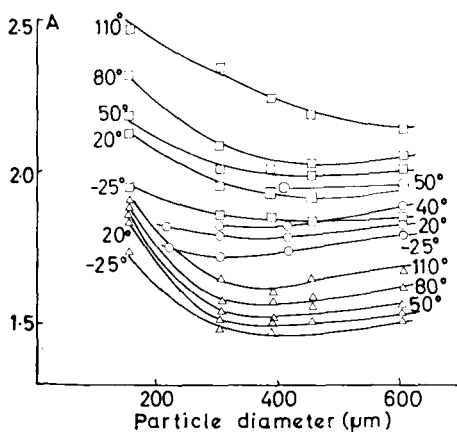
For all the materials investigated, A tended to decrease with increase in particle diameter between 100 and 400 μm, then, if considered in conjunction with other published results (Ahmad & Pilpel 1969), tended to increase. Values of n plotted against particle diameter—more conveniently against log Dp—showed a similar pattern which is illustrated schematically in Fig. 6. For each size fraction of each
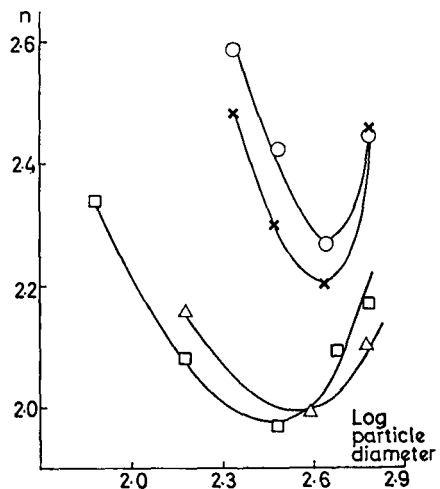

Fig. 5. Values of A at different temperatures versus particle diameter. △ = white sugar. ○ = stearic acid. ☐ = brown sugar.

Fig. 6. Values of n at 20 °C versus particle diameter. △ = white sugar. × = Palmitic acid. ☐ = brown sugar. ○ = stearic acid.

material, A increased with temperature. The values of n remained practically constant but a slight decrease became apparent in the cases of palmitic and stearic acids at homologous temperatures above 0·9. (Theoretically n should decrease to zero as the homologous temperature approaches unity and flow ceases.)

DISCUSSION

The shapes of the flow curves typified by Fig. 2 are similar to those that have been obtained by other workers (Jones & Pilpel 1966; Harwood & Pilpel 1969; Ahmad & Pilpel 1969; Danish & Parrott 1971) differing only in that with the present materials maximum flow occurs at particle diameters between 300 and 500 μm whereas with materials such as glass, magnesia, lactose the maxima occur at particle diameters between 100 and 200 μm.

These differences in the positions of the maxima can be ascribed to the fatty acids and sugars being more cohesive than the other materials mentioned—see later. As a result it is now possible to detect minima in the plots of A and n versus Dp—Figs 5 and 6—at the points corresponding to maximum flow, whereas previously these minima were not clearly observed, although their presence was suspected (Ahmad & Pilpel 1969).

Since it has been shown (Jones & Pilpel 1966) that equation 1 is algebraically identical to several earlier published flow equations (Zenz 1957; Fowler & Glastonbury 1959; Brown & Richards 1959, 1960; Harmens 1963; Neumann 1967) which, however, had only previously been tested at room temperature, it follows from the present results that when the appropriate values of A and n are inserted, equation 1 should also satisfactorily describe the flow at different temperatures of more than 50 other powders, ranging in diameter from about 100 to over 1500 μm and varying in nature from inorganic oxides with high melting points, through metals, glass, vegetable seeds, crystalline and amorphous pharmaceutical drugs and formulations to soft organic compounds with low melting points. This is providing that appropriate allowance has been made for the effects of particle shape, rugosity, presence of moisture and fines and for the effects of hopper size and design, notably the angle of the cone and the ratios of tube to orifice to particle diameter (Jones & Pilpel 1966; Ahmad & Pilpel 1969).

The point of interest about the present results is that the flow rates of particular low melting powders might be increased by cooling them in the range of homologous temperatures from 1·0 down to about 0·7. Thus Fig. 3 shows that small, 150 to 220 μm, size fractions of the present powders which do not flow at high ambient room temperatures e.g. 40 °C, because they block the orifice, become quite free flowing if cooled sufficiently. The flow rate of the 302 μm diameter brown sugar through the 1·10 cm orifice doubled when it was cooled from 100 to −25 °C. That of the 350 μm diameter paracetamol granules through the 0·75 cm orifice increased from 175 to 225 g min^{-1} after cooling from 125 to −25 °C. Similar results have been reported for lactose and griseofulvin (Pilpel & Britten 1979).

Although cooling below a high ambient temperature of 40 °C would only be expected to produce a significant (say 20%) increase in the flow rates of powders or granules whose melting/softening points were below about 100 °C (because their homologous temperature at 40 °C is then about 0·84) there are formulations which begin to soften at about 100 °C because they contain small amounts of low melting sugars, gums, waxes, fatty acids, esters, surfactants. Thus the present findings might be of interest in manufacture since they offer a possible means of overcoming problems associated with the manipulation of formulations with low softening points which may be difficult to handle at high ambient temperatures, for example in the tropics. The cooling method would require the same precautions as have been employed in the present work to prevent the powders absorbing moisture at temperatures below the dew point; otherwise they would again become cohesive and cease to flow.

The cohesion of powders as measured in Jenike or annular shear cells (Pilpel 1971; Kočova & Pilpel 1972) decreases as the temperature is reduced. For example, at 160 °C and a packing fraction of 0·52, the cohesion of 10 μm diameter lactose is 4·6 kNm^{-2} decreasing to 0·23 kNm^{-2} at 23°, at 48 °C and ρ_F 0·66, the cohesion of 23 μm diameter stearic acid is 1·46 kNm^{-2} decreasing to 0·55 kNm^{-2} at 23 °C (York & Pilpel 1972).

These results have been explained in terms of the reduction in plasticity and in the inability of asperities on the surface of neighbouring particles to form welded bonds as the temperature of the sample is reduced (York & Pilpel 1972; Pilpel & Britten 1979).

It may be concluded that the changes now observed in the values of A and n, in Equation 1, and in the flow rates of powders as they are cooled in the range of homologous temperatures from 1·0 to about 0·7, are due to them becoming intrinsically less cohesive.

REFERENCES

Ahmad, M., Pilpel, N. (1969) Rheol. Acta 8 (4): 448–456

Beverloo, W. A., Leniger, H. A., Van der Velde, J. (1961) Chem. Eng. Sci. 15: 260–269

Brown, R. L., Richards, J. C. (1959) Trans. Inst. Chem. Eng. 37: 108–119

Brown, R. L., Richards, J. C. (1960) Ibid. 38: 243–256

Danish, F. Q., Parrott, E. L. (1971) J. Pharm. Sci. 60: 548–554

Fowler, R. T., Glastonbury, J. R. (1959) Chem. Eng. Sci. 10: 150–156

Harmens, A. (1963) Ibid. 18: 297–305

Harwood, C. F., Pilpel, N. (1969) J. Pharm. Pharmacol. 21: 721–730

Jones, T. M., Pilpel, N. (1966) Ibid. 18: 81–93, 429–442

Kočova, S., Pilpel, N. (1972) Powder Technol. 5: 329–343

Neumann, B. S. (1967) in: Advances in Pharm. Sci. Vol. 2, 194–221, Academic Press, London

Pilpel, N., Britten, J. R. (1979) Powder Technol. 22: 33–44

Pilpel, N. (1971) in Adv. in Pharm. Sci. Vol. 3, 173–219 Academic Press, London

York, P., Pilpel, N. (1972) Mater. Sci. Eng. 9: 281–291

Zenz, F. A. (1957). Petroleum Refiner 36 (10): 162–170