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Penetrometry and estimation of the flow rate of powder excipients

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In this work, penetrometry with a sphere was employed to study the flow properties of non-consolidated pharmaceutical powder excipients: sodium chloride, sodium citrate, boric acid, and sorbitol. In order to estimate flow rate, the pressure of penetration in Pascals was used. Penetrometry measurement with a sphere requires modification of the measurement container, in particular by decreasing the diameter of the container, to prevent undesirable movement of material in a direction opposite to that in which the sphere penetrates. Thus penetrometry by a sphere seems to be similar to indentation by the Brinell hardness tester. The pressure of penetration was determined from the depth of penetration by analogy with the Brinell hardness number and an equation for the inter conversion of the two variables is presented. The penetration pressure allowed direct estimation of the flow rate only for those powder excipients with a size fraction in the range of 0.250–0.630 mm. Using the ratio of penetration pressure to bulk density, a polynomial quadratic equation was generated from which the flow rates for the group of all tested powders could be estimated. Finally, if the inverse ratio of bulk density and penetration pressure was used as an independent variable, the flow rate could be estimated by linear regression with the coefficient of determination $r^2 = 0.9941$. In conclusion, using sphere penetrometry, the flow properties of non-consolidated powder samples could be investigated by indentation. As a result, a linear regression in which the flow rate was directly proportional to the powder bulk density and inversely proportional to the penetration pressure could be best recommended for the estimation of the flow rate of powder excipients.

1. Introduction

Penetrometry by a cone or a needle is a standard method for measurement of the consistency of semisolids. The use of penetrometry for the evaluation of powders in pharmaceutical technology was published in Die Pharmazie many years ago (Bogs 1978). Under conditions similar to the present conditions for the measurement of consistency given in pharmacopoeias, the depth of penetration of a cone into samples of microcrystalline cellulose, lactose, talc, starches, and zinc oxide consolidated by tapping 20 times was measured. The depth of penetration expressed in tenths of a millimetre was proposed to evaluate the flow properties of powder excipients in relation to their bulk and/or tapped density.

Flowability is the result of the combination of material physical properties that affect material flow and the equipment used for storage, transporting and handling of the material. Many methods and test devices exist to measure the flowability of bulk solids (Schwedes 2003). Knight and Johnson (1988) developed a penetration test which uses a metallic cone having a half-angle of 5°. The force of penetration into consolidated powder samples was measured. The penetration force increased with the square of the penetration depth. Comparing the results with those with a shear tester, the authors concluded that penetrometry could be used to supplement shear cell measurements in the study of solids.

Penetrometry with a cone is obviously used for testing consolidated powders. The basic disadvantage is that the area of contact between the penetrating cone and the sample does not remain constant throughout the test, and that displaced sample moves in a direction opposite to that in which the cone moves. Therefore, the method is associated with high variability of results. In the case of non-consolidated powders, another problem could arise: a risk that the cone might descend through the entire sample being tested. On the other hand, penetrometry with a sphere on to the plane surface of a non-consolidated powder results in indentation of the powder layer to a limited depth. Providing that undesirable movement of material along the penetrating sphere is avoided, penetrometry with a sphere produces results with better reproducibility in comparison to penetrometry with a cone. For this reason, it may be recommended for evaluation of non-consolidated powder excipients with similar bulk densities (Zatloukal 2003).

Many physical responses of powdered pharmaceutical material such as flow rate and tensile strength are determined by the relative densities of the materials. In order to evalu-

ate the flow rate of a layer of material flowing uniformly from the outlet of cylindrical hopper, the relationship to the bulk density of the powder is more useful (Prescott and Barnum 2000) rather than the tapped density which represents the properties of the stagnant layer of non-flowing material at the periphery of the hopper (Hancock et al. 2003).

In this paper, penetrometry with a sphere was employed to study the flow properties of four powder pharmaceutical excipients. Using some similarities between the penetration of a sphere into powder and the indentation of a sphere into metal, the pressure of penetration could be expressed. In the second part of the study, the relationship between the flow rate and the pressure of penetration as well as the bulk density was investigated in detail.

2. Investigations, results and discussion

2.1. Penetrometry by a cone versus indentation by a sphere

Penetrometry by a cone is obviously used for testing consolidated powders. For non-consolidated powders, penetrometry by a sphere seems to be more useful (Zatloukal 2003). Using this, the powder sample is impacted by a sphere without the disadvantage of the displaced powder moving in an opposite direction to that in which the cone moves. From this point of view, penetrometry measurement of powders by a sphere seems to be similar to measurement using the Brinell hardness tester when the metal sample is subjected to a hardened metal sphere of 5 or 10 millimetres diameter. From the diameter of indentation obtained, the Brinell hardness number (BHN) can be calculated with the equation:

$$\mathrm{BHN} = \frac{\mathrm{L}}{\frac{\pi \cdot \mathrm{D}}{2} \cdot \left(\mathrm{D} - \sqrt{(\mathrm{D}^2 - \mathrm{d}_\mathrm{i}^2)}\right)} \qquad (1)$$

where L = load in kilograms, D = diameter of sphere in millimetres and d_i = diameter of indentation in millimetres (Anonymous 1989).

The Brinell hardness tester is primarily suitable for investigation of hard samples, such as metals, when the diameter of indentation could be measured easily. It cannot be employed directly for powders, since the diameter of indentation is difficult to estimate. Using a penetrometer, on the other hand, the depth of penetration P (in tenths of a millimetre) can be measured. In order to express the BHN in penetrometry, the depth of penetration P (in mm) could be converted to the diameter of the indentation d_i (in mm) using the equation:

$$\mathrm{d_i} = 2\sqrt{\mathrm{P}(\mathrm{D} - \mathrm{P})} \qquad (2)$$

In our work, for a sphere with diameter D = 16 mm and the actual values of load weight (L = 0.041 kg), the diameters of indentation (Eq. 2) were estimated as well as the BHN (Eq. 1). The resulting values for 16 samples of four different non-consolidated powder excipients (given in Table 1) are shown in Table 2.

As the BHN has no exact physical units, it is difficult to use it to evaluate the flowability of a powder. To study the relationship between the depth of penetration and the flow rate, the pressure of penetration expressed in Pascals is more useful.

The pressure of penetration p (in Pa) can be defined as a force of penetration F (in N) acting on the surface S (in m^2) of the part of the sphere with a radius R (in m) which is in contact with the powder sample, i.e. the force acting on the surface corresponding to the surface of the spherical cap. In so far as the force of penetration can be defined as multiple of the weight L (in kg) of the penetrating object and the acceleration due to gravity g (in $\mathrm{m \cdot s^{-2}}$), the Eq. (3) was obtained from which the pressure of penetration for a depth of penetration P (in m) could be calculated:

$$\mathrm{p} = \frac{\mathrm{F}}{\mathrm{S}} = \frac{\mathrm{L} \cdot \mathrm{g}}{2\pi \cdot \mathrm{R} \cdot \mathrm{P}} \qquad (3)$$

Equation (3) is applicable only when the depth of penetration is smaller than the radius of the sphere, i.e. $\mathrm{P} \leq \mathrm{R}$.

Using actual experimental data (L = 0.041 kg, $\mathrm{g} = 9.80665\ \mathrm{m \cdot s^{-2}}$, and R = 0.008 m) and the measured depth of penetration (in m), Eq. (3) could be simplified as follows:

$$\mathrm{p} = \frac{8.00}{\mathrm{P}} \qquad (4)$$

For all powder samples tested, the corresponding pressures of penetration were calculated from the measured values of the depth of penetration P using Eq. 4. In practice the multiple of the basic unit (kPa) is used. The results are summarized in Table 3.

Eq. (5) allows to compare the relationship between BHN discussed above and the pressure of penetration proposed

Table 1: Flow properties of tested powder excipients

Excipient	Sample	Size fraction (mm)	Q ($\mathrm{g \cdot s^{-1}}$)	d_b ($\mathrm{g \cdot cm^{-3}}$)	P (0.1 mm)
Sodium chloride	1	0.250–0.315	21.0	1.18	62.1 (1.5%)
	2	0.315–0.400	20.3	1.19	58.6 (1.7%)
	3	0.400–0.500	19.5	1.18	57.9 (1.4%)
	4	0.500–0.630	18.5	1.17	55.7 (1.9%)
Sodium citrate dihydrate	5	0.250–0.315	16.5	0.90	65.1 (1.7%)
	6	0.315–0.400	15.5	0.90	61.7 (1.7%)
	7	0.400–0.500	14.9	0.90	60.2 (2.0%)
	8	0.500–0.630	13.8	0.89	59.6 (2.4%)
Boric acid	9	0.250–0.315	11.8	0.72	62.5 (1.3%)
	10	0.315–0.400	11.5	0.71	60.9 (1.4%)
	11	0.400–0.500	10.9	0.70	58.3 (1.7%)
	12	0.500–0.630	10.2	0.68	57.4 (1.8%)
Sorbitol	13	0.250–0.315	9.7	0.63	56.8 (2.1%)
	14	0.315–0.400	9.6	0.64	55.6 (2.3%)
	15	0.400–0.500	9.2	0.65	54.1 (1.7%)
	16	0.500–0.630	8.6	0.66	52.9 (1.5%)

Table 2: Brinell hardness numbers (BHN)

Sample	d_i (mm)	BHN ($\times 10^{-4}$)
1	15.594	1.314
2	15.417	1.392
3	15.377	1.409
4	15.244	1.464
5	15.720	1.253
6	15.576	1.322
7	15.502	1.355
8	15.471	1.369
9	15.612	1.305
10	15.537	1.339
11	15.400	1.399
12	15.348	1.421
13	15.312	1.436
14	15.238	1.467
15	15.138	1.508
16	15.054	1.542

Table 3: Pressure of penetration (p)

Sample	P (0.1 mm)	p (kPa)
1	62.1	1.288
2	58.6	1.365
3	57.9	1.382
4	55.7	1.436
5	65.1	1.229
6	61.7	1.297
7	60.2	1.329
8	59.6	1.342
9	62.5	1.280
10	60.9	1.314
11	58.3	1.372
12	57.4	1.394
13	56.8	1.408
14	55.6	1.439
15	54.1	1.479
16	52.9	1.512

in our work to evaluate powder flow rate as will be discussed below:

$$p = BHN \cdot 1000 \cdot g \quad (5)$$

2.2. Estimation of flow rate

The majority of pharmaceutical solids are initially presented in powder form. Many of their physical properties such as flow rate are determined by the relative densities of these powder materials. To study the flow properties of powder excipients, the relationship between flow rate, estimated pressure of penetration and bulk density was investigated in our work.

For all the powder size fractions tested, the experimentally measured flow rates Q ($g \cdot s^{-1}$) are directly plotted against the calculated pressures of penetration (Eq. (4)) in Fig. 1. A good correlation was observed within groups of powder samples between the two variables showing that while the flow rate decreased with an increase in particle size, the penetration pressure increased. For example, for sodium chloride, $Q = 21.0\ g \cdot s^{-1}$ and $p = 1.288$ kPa were measured for the size fraction 0.250–0.315 mm (sample 1) while $Q = 18.5\ g \cdot s^{-1}$ and $p = 1.436$ kPa were found for the size fraction 0.500–0.630 mm (sample 4). Unfortunately, except for the boric acid and sorbitol samples, there was no correlation between flow rate and pressure of penetration if all four powder excipients tested were reviewed

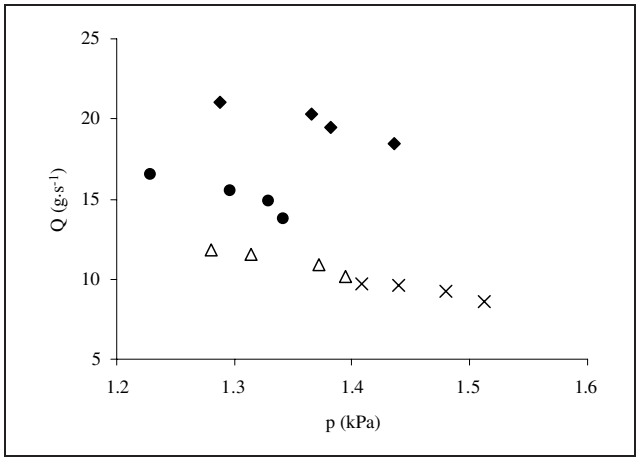

Fig. 1: Relationship between flow rate Q and penetration pressure p (◆ sodium chloride, ● sodium citrate, Δ boric acid, × sorbitol)

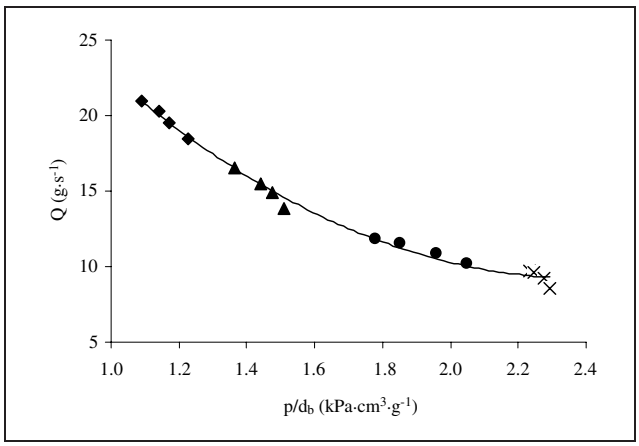

Fig. 2: Relationship of flow rate Q on the ratio of pressure of penetration and bulk density p/d_b (◆ sodium chloride, ● sodium citrate, Δ boric acid, × sorbitol)

together. Thus, the relationship between measured flow rates and calculated pressures of penetration was found to be non-significant, characterized by a coefficient of determination $r^2 = 0.2105$. The different positions of the powders in Fig. 1 may be explained by differences in their true densities. While sodium chloride and sodium citrate with higher true densities ($2.17\ g \cdot cm^{-3}$ and $1.82\ g \cdot cm^{-3}$, respectively) showed the highest flow rates and are positioned in the upper part of Fig. 1, the adjacent positions of boric acid and sorbitol correspond to their similar true densities of $1.48\ g \cdot cm^{-3}$ and $1.49\ g \cdot cm^{-3}$, respectively.

From the results presented above, a more appropriate relationship should be investigated to estimate the flow rates of all measured powder size fractions as discussed below in this work.

Powder flowability is the result of a combination of physical properties. As reported previously, there is a significant relationship between flow rate and powder bulk density. Unfortunately, by using the bulk flow rate ($cm^3 \cdot s^{-1}$), i.e. the ratio of mass flow rate to bulk density, instead of mass flow rate ($g \cdot s^{-1}$), the problem of estimating flow rate could not be solved sufficiently satisfactorily (Zatloukal 2003). A better correlation between the flow rate and the pressure of penetration, and, possibly, the volume of powder indented by a sphere was investigated as well. To estimate the flow rate, the transformation of the depth of penetration to the weight of powder indented by the pene-

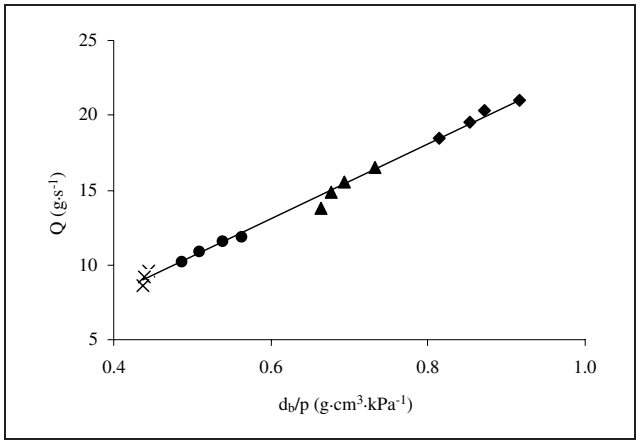

Fig. 3: Relationship of flow rate Q on ratio of bulk density and pressure of penetration d_b/p (◆sodium chloride, ● sodium citrate, Δ boric acid, × sorbitol)

trating sphere permitted an exponential equation to be obtained explaining 97.4% of the total sum of squares (Zatloukal 2005).

In this paper, a correlation between the flow rate and the ratio of the pressure of penetration to bulk density (p/d_b) as an independent variable was investigated in the second step. Plotting the powder sample flow rates against the ratio of p/d_b, a non-linear curve was obtained as shown in Fig. 2. From the polynomial equation (6) characterized by coefficient of determination $r^2 = 0.9937$, the flow rate $\hat{Q}$ could be estimated:

$$\hat{Q} = 6.988\left(\frac{p}{d_b}\right)^2 - 33.328\left(\frac{p}{d_b}\right) + 48.975 \qquad (6)$$

Although a high value of the correlation coefficient was thus obtained, the results could not be easily explained.

To rationalize the estimation of the flow rate using the penetration pressure and the bulk density, another relationship was studied in the third step of this paper. In Fig. 3, the linear relationship between the flow rate and the inverse ratio of the bulk density and the penetration pressure d_b/p is shown. A regression Eq. (7) was obtained which enabled 99.41% of the total sum of squares to be explained:

$$\hat{Q} = 25.104\left(\frac{d_b}{p}\right) - 1.9907 \qquad (7)$$

Table 4: Accuracy of estimation of the flow rate Q ($g \cdot s^{-1}$)

Sample	Measured	Estimated*)	Difference
1	21.0	21.01	0.05
2	20.3	19.90	1.97
3	19.5	19.45	0.26
4	18.5	18.47	0.16
5	16.5	16.39	0.67
6	15.5	15.43	0.45
7	14.9	15.01	0.74
8	13.8	14.65	6.16
9	11.8	12.14	2.88
10	11.5	11.57	0.61
11	10.9	10.81	0.83
12	10.2	10.26	0.59
13	9.7	9.23	4.85
14	9.6	9.18	4.38
15	9.2	9.03	1.85
16	8.6	8.98	4.42

*) calculated using Eq. (7)

From Eq. (7), the flow rate studied is directly proportional to the powder bulk density and inversely proportional to the penetration pressure. This way, the results could be easily interpreted and understood.

In Table 4, the measured and the estimated flow rates together with their percentage differences are summarized for all samples of powder excipients tested. The results presented here show good consistency between data. The accuracy of flow rate estimation by Eq. (7) could be characterized by an average value of the difference between measured and estimated flow rates equal to 1.93%, with the maximal individual deviation lower than 7%. This supports the usefulness of Eq. (7) in estimation of flow rate.

As the result of our study, the penetration pressure calculated from the measured values of the depth of penetration of a sphere (Eq. (3)) may be recommended for the study of the flow properties of powder excipients with similar density. To estimate the flow rate, Eq. (7) may be recommended in which the flow rate is directly proportional to the powder bulk density and inversely proportional to the penetration pressure.

3. Experimental

3.1. Materials

Four different powder excipients of pharmaceutical quality and various flow properties were used: sodium chloride, sodium citrate dihydrate, boric acid, and sorbitol. Size fractions of 0.250–0.315, 0.315–0.400, 0.400–0.500, and 0.500–0.630 mm were obtained using a vibrating screen (Pulverisette®0, Alfred Fritsch, Laborgerätebau, Idar Oberstein, Germany). All

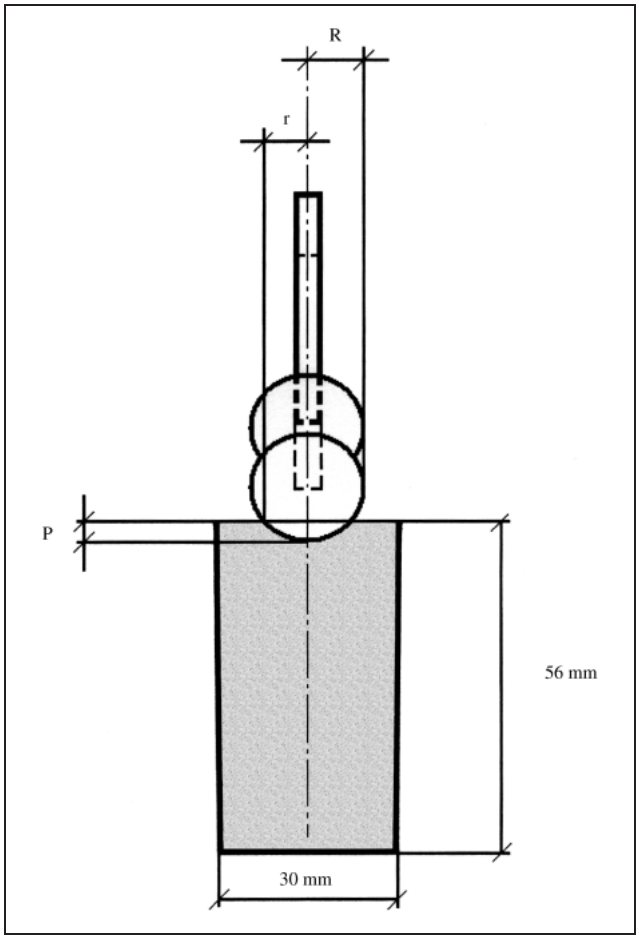

Fig. 4: Arrangement of sphere penetrometry

powder samples were characterized for bulk density and flow rate, both summarized in the first part of Table 1.

3.2. Methods

The mass flow rate Q (in grams per second) of a powder sample with a minimum mass of 100 g was estimated using a model stainless steel cylindrical hopper with a flat bottom (40 mm diameter) with a concentric orifice with a diameter of 10 mm. The mean flow rates of five measurements with a variability coefficient lower than 1% are shown in Table 1.

The bulk densities d_b (in grams per cm^3) of the non-consolidated powders were estimated in such a way that the powder size fractions were discharged free from the hopper to a cylindrical plastic container with a diameter of 30 mm and a volume of 33.0 cm^3. The heap of powder was carefully levelled to obtain a flat surface. The container with powder was weighted and the weight of powder sample per bulk volume, i.e. the bulk density, was expressed. The mean bulk densities obtained ($n = 12$) are shown in Table 1.

A standard automatic penetrometer (AP 4/2, Feinmess Dresden, Germany) was used to estimate the depth of penetration P (in tenths of a millimetre). The penetrometer consists of a steel shaft (weighting 33.5 g) and a smooth glass sphere of radius $R = 8$ mm fixed to a steel rod (diameter 2.6 mm), both of total weight 7.5 g. The modified glass sphere of the Höppler's rheoviscometer (Prüfgeräte-Werk, Medingen, Germany) with a shortened rod was used. A sectional drawing of the penetrometry equipment is shown in Fig. 4. The measurements of depth of penetration were done according to the method for determination of penetration given in the European Pharmacopoeia. The powder sample in the plastic container was placed on the base of the penetrometer and adjusted to be perpendicular to the vertical axis of the penetrometer. The sphere was adjusted to the position where it just touched the powder surface. After releasing it for a time interval of 5 seconds it was clamped and the depth of penetration was measured. The mean depths of penetration in tenths of a millimetre ($n = 12$) with their relative standard deviations (in brackets) are presented in the last column of Table 1.

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