The packing coefficient: a suitable parameter to assess the flow properties of powders

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Abstract

A parameter, defined by Gabaude et al. in a previous work [1], was further investigated for its ability to evaluate flow properties of particulate materials. It is based on the volume reduction of the powder bed under low compaction pressure. Compaction data and the packing coefficient \( C_1 = \frac{(H_0 - H_p)}{H_0} \times 100 \) were analysed over a \([0-1]\) MPa pressure range. Comparison of the \( C_1 \) value with the flowability index (i) determined by Jenike shear cell measurements demonstrated the reliability of this packing coefficient to assess powder flow properties using small quantities of powder (<1 g). This method appeared to be helpful for an adequate determination of flowability in the early stages of drug development. Finally, because the packing assessment is performed in a compression die, improvement in the prediction of the weight variation of tablets is expected, as compared with other methods of flowability assessment.

Key words: powders, flow properties, shear cell measurements, packing coefficient

1. Introduction

There is a need in the pharmaceutical industry for easy tests to enable characterisation of the flow properties of materials to be used in tabletting or capsule filling. Indeed, poor flowability of powders or granules can result in irregular weight and low production performances. During the past 40 years, a lot of methods have been developed to assess the flow properties, including the measurement of angle of repose, mass flow rate or compressibility (reduction in volume of a powder bed due to the application of taps). Even though these methods are quite simple, they do have their limitations. The results obtained are significantly affected by experimental conditions [2], and a lack of accuracy has been reported in the case of cohesive powders [3, 4]. It is also admitted that these methods measure derived properties and are unable to represent the intrinsic flow properties of powders [5]. Finally, they also require large amounts of product (100 g at least are recommended in the European Pharmacopeia for the determination of tapped density, for example).

Against the inadequacy of the methods cited above, more sophisticated and accurate techniques such as shear cell measurements have been used for testing the flowability of powders [5, 6]. The flowability index measured by the Jenike shear cell in particular has been shown to correlate with tablet weight variations [2]. Despite the accuracy in predicting flowability during tabletting, shear measurements are seldom used in the development of a drug product because they are time- and product-consuming.

Another approach to assess flowability consists in investigating the first compression stage of a compression cycle. Actually, several stages have been identified during the compression of powders [7]: (i) filling of the die; (ii) densification by particle slippage and packing; (iii) elastic and plastic deformation of particles; (iv) cold welding, with or without fragmentation. York [7] used the Heckel equation to analyse compressional data and attributed the initial curvature of the Heckel plot to particle slippage and rearrangement. However, he did not correlate the packing fraction that quantified this part of the curve with
the flow properties of the powders, but only linked the increase of the packing fraction to the decrease of the particle size. Furthermore, in our opinion, the breakage of aggregates to primary particles is likely to be included in this parameter as the pressure range taken into account in that paper can extend to 10 MPa.

In the present study, a parameter to assess flow properties, derived from the work of York [7] and presented in a previous work [1], is further investigated. The method is based on the volume reduction of the powder bed corresponding to the first part of the force-displacement compaction curve. The purpose of this complementary work is to determine more precisely the end-compaction pressure to be considered for the calculation of the packing coefficient:

\[ C_1 = \frac{H_0 - H_P}{H_0} \times 100 \]

where \( H_P \) is the powder bed height under pressure \( P \) and \( H_0 \) the initial height.

Hence the \( C_1 \) values of a large range of products (powders, mixtures and granules of various sizes, shapes and behaviour during compaction) have been investigated using as end-compaction pressure \( P \), a pressure ranging from 0 to 1 MPa and correlated to the Jenike flowability index.

2. Materials and methods

2.1 Materials

The products used (Table I) constituted a representative selection of pharmaceutical products, with different densities, flow properties and behaviour under pressure.

Powders (drug and excipients) were used as received.

Mixture 1 (M1) is a ternary blend composed of 20% anhydrous theophylline, 60% \( \alpha \)-lactose monohydrate (Pharma 200/70) and 20% microcrystalline cellulose (Avicel PH 101). This mixture has also been processed by dry granulation (G1D) and wet granulation (G1W). Details of the manufacturing processes are given in a previous work [8].

Mixture 2 (M2) is a binary mixture with the same chemical composition as mixture 1 but, in this blend, the two excipients (lactose and cellulose) are associated in the co-processed Cellactose®.

Mixture 3 is a formulation by simple blend supplied by the Pharmaceutical Sciences Department of Sanofi-Synthelabo Recherche (patented product). Dry granules (G3D) and lubricated dry granules (G3DL) of mixture 3 were also analysed. The compaction was manufactured on an Alexanderwerk WP 150 roller compactor followed by sizing of compact on a mesh screen of 1.25 mm, and hydrogenated oil was used as lubricant mixed with G3D leading to G3DL.

Stoichiometric hydroxyapatite \( \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \) \((\text{Ca}/\text{P} = 1.667)\) was synthesized according to the process described in [9]. Granulation was performed using an oscillating granulator equipped with a 2-mm screen (Erweka AR 400, Heussenstamm, Germany) after drying of the precipitate (5% (w/w) final moisture content). Granules with a mean diameter of 200

### Table I Characteristics of the products under study

| Product                          | Supplier                  | Median diameter (µm) | Pycnometric density (g/cc) | Bulk density (g/cc) |
|----------------------------------|---------------------------|----------------------|----------------------------|---------------------|
| **Powders**                      |                           |                      |                            |                     |
| Anhydrous theophylline           | Boehringer-Ingelheim      | 17                   | 1.450                      | 0.267               |
| Pharma 200/70                    | S.A. du Sacre de Lait     | 236                  | 1.534                      | 0.844               |
| Avicel PH 101                    | FMC Corp.                 | 71                   | 1.534                      | 0.303               |
| Cellactose®                     | Meggle GmbH&CO            | 113                  | 1.529                      | 0.399               |
| **Mixtures**                     |                           |                      |                            |                     |
| Mixture 1 (M1)                   |                           | 162                  | 1.521                      | 0.483               |
| Mixture 2 (M2)                   |                           | 79                   | 1.522                      | 0.346               |
| Mixture 3 (M3)                   | Sanofi Recherche          | 60                   | 1.536                      | 0.400               |
| **Granules**                     |                           |                      |                            |                     |
| Dry granules 1 (G1D)             | Sanofi Recherche          | 250                  | 1.536                      | 0.610               |
| Wet granules 1 (G1W)             |                           | 250                  | 1.536                      | 0.490               |
| Dry granules 3 (G3D)             |                           | 500                  | 1.537                      | 0.690               |
| Lubricated dry granules 3 (G3DL) | Sanofi Recherche          | 462                  | 1.527                      | 0.720               |
| Stoichiometric hydroxyapatite    | Sanofi Recherche          | 200                  | 2.832                      | 0.640               |
| (HAP200)                         |                           |                      |                            |                     |
| Stoichiometric hydroxyapatite    |                           | 400                  | 2.786                      | 0.570               |
| (HAP400)                         |                           |                      |                            |                     |
and 400 μm (HAP400) were obtained after a calibration step using a 315-μm and a 800-μm screen, respectively.

2.2 Methods

Packing measurements

The evolution of the apparent density of a powder bed in a volumetric cylinder subjected to successive vertical vibrations was followed using the Erweka Model SVM2 unit (Erweka GmbH, Heusenstamm, Germany). The measurements were made in a 250-mL cylinder with 100 g of product, except for HAP200 and HAP400 which were only available in small quantities. For these granules, the experiments were conducted in a 125-mL cylinder with 25 g of product.

The reduction in powder volume was estimated by two parameters:
- the difference between the volumes after 10 and 500 shocks (V_{10} - V_{500}).
- the Carr index calculated as follows:
\[ L_{\text{carr}} = \frac{d_{\text{max}} - d_0}{d_{\text{max}}} \times 100 \]
where \(d_{\text{max}}\) is the maximum tapped density and \(d_0\) the bulk density after filling.

Flow rate measurements

Mass flow through a funnel was determined according to the European Pharmacopeia recommendations (3rd edition, 2.9.16 «écoulement»).

Shear cell measurements

The product flow properties were analysed using a shear cell designed by Jenike [5, 6] (Figure 1). The apparatus is composed of a base and a ring, which are filled with the tested material, and a cover on which a vertical force \(V\) is applied. Preconsolidation of the product is carried out by applying a vertical consolidation force \(V_c\) (corresponding to a consolidation stress \(\sigma_c\) varying between 3 and 10 kPa) and a number of oscillating twists. Consolidation is completed in a second stage by applying a shear force \(S\) and causing the specimen to flow under the same normal force \(V_c\) until a steady state is reached. When consolidation is completed, the vertical compacting force \(V_c\) is replaced by a smaller vertical force \(V\), and a shearing force \(S\) is applied until a failure plane has developed corresponding to the shear strength \(\tau\). The measurement of several points \((\sigma, \tau)\) allows determination of a yield locus (Figure 2). From one yield locus, two Mohr semi-circles are drawn. The first one is drawn through the origin tangentially to the yield locus. The point of intersection of this semi-circle with the \(\sigma\)-axis determines the value of the unconfined yield strength \(\tau_c\). The second Mohr semi-circle is drawn through the end-point \((\sigma, \tau)\) tangentially to the yield locus. The major consolidating stress \(\sigma_1\) is determined by the intersection of the circle with the \(\sigma\)-axis.

The determination of the flowability of the bulk solid requires the determination of \((f_c, \sigma_1)\) values for at least three consolidation stresses \(\sigma_c\). From these points, the flow-function \(FF\) \((\xi_1=f(\sigma_1))\) can be drawn. As indicated on Figure 3, the flowability of bulk solids can be classified according to the flowability index (i), which corresponds to the inverse of the slope of the flow-function. This procedure has been retained in order to ensure a more accurate determination of the values and fit in a better way the experimental points, as the flow-function is not a straight line through the origin.

Compression

Compression was performed using a Lloyd 6000R uniaxial press, Lloyd instruments Ltd., Segensworth East, England, UK. The die, 1 cm² in surface and 1 cm in depth, was lubricated with magnesium stearate before compaction. The die (1 cm³) was manually

Fig. 1 Schematic diagram of Jenike shear cell

![Schematic diagram of Jenike shear cell](image1.png)

Fig. 2 Yield loci of a powder corresponding to three consolidation stresses \((f_c, \sigma_1), (f_c', \sigma_1')\) and \((f_c'', \sigma_1'')\)
filled with an accurate mass of product, calculated from the bulk density of the material. Compression was performed by the displacement of the upper punch at a speed set at 1.14 mm/min. The pressure was measured by an accurate gauge and the upper punch displacement was measured with an external LVDT extensometer. Compression data (displacement as a function of pressure) were collected until the predefined pressure was reached. Only the beginning of the curve will be discussed here (0 to 1 MPa). In the work of Gabaude [1], a packing coefficient \( C \) was defined to quantify the first compression period that was assumed to correspond to packing and slippage of the particles. It was suggested that this packing of the powders was fully achieved when the pressure at the upper punch had reached 0.5 MPa. The packing coefficient was based on the powder bed height:

\[
C = \frac{H_0 - H_{0.5}}{H_0} \times 100
\]

where \( H_{0.5} \) is the powder bed height under pressure 0.5 MPa and \( H_0 \) is the initial height.

In the present work, the packing coefficient has been calculated not only for 0.5 MPa but in steps of 0.05 MPa for pressures ranging from 0 to 1 MPa in order to determine more precisely the pressure influence on the calculation of the \( C \) value. Three compression cycles were analysed for each sample.

### 3. Results

#### 3.1 Packing and flow rate measurements

It is generally accepted that a \( V_{10-500} \) value greater than 20 ml indicates the presence of air entrapped between the particles and consequently a high compressibility which hinders the flowability of the product [10, 11]. Concerning the flow rate, a value of at least 10 g/s is required to ensure uniform flow. On the basis of these parameters and according to Carr's classification [12], results presented in Table II point to the poor flow properties of anhydrous theophylline and Avicel PH 101, whereas Pharma 200/70 and Cellactose® have good flow properties, due to their larger particle diameter and density. The three mixtures display poor flow properties, making a granulation step necessary or the addition of a lubricant for easy handling and manufacturing of solid dosage forms. In the case of mixture 2, the presence of 80% Table II  Packing results and mass flow rates through a funnel

| Product                  | \( V_{10-500} \) (mL) | \( I_{\text{corr}} \) (%) | Flow rate (g/s) | Classification       |
|--------------------------|------------------------|--------------------------|-----------------|----------------------|
| **Powders**              |                        |                          |                 |                      |
| Anhydrous theophylline   | 44.9                   | 34.6                     | –               | very poor flow       |
| Pharma 200/70            | 3.5                    | 13.9                     | 11              | good flow            |
| Avicel PH 101            | 25.5                   | 23.5                     | 2.2             | passable flow        |
| Cellactose®              | 18.3                   | 17.5                     | 16.2            | fair flow            |
| **Mixtures**             |                        |                          |                 |                      |
| Mixture 1 (M1)           | 14.5                   | 24.6                     | –               | passable flow        |
| Mixture 2 (M2)           | 44                     | 27.2                     | –               | poor flow            |
| Mixture 3 (M3)           | 40                     | 40.0                     | –               | very poor flow       |
| **Granules**             |                        |                          |                 |                      |
| Dry granules 1 (G1D)     | 13.3                   | 21                       | 12              | passable flow        |
| Wet granules 1 (G1W)     | 11.7                   | 16                       | 10              | good flow            |
| Dry granules 3 (G3D)     | 11.1                   | 21.9                     | –               | passable flow        |
| Lubricated dry granules 3 (G3DL) | 10                  | 21.4                     | –               | passable flow        |
| Stoichiometric hydroxyapatite (HAP200) | 2.7*                | 21.6                     | 13              | passable flow        |
| Stoichiometric hydroxyapatite (HAP400) | 2.2*                | 21                       | 17              | passable flow        |

* measured with 25 g in a 125 mL cylinder
of Cellactose®, a co-processed excipient especially designed for direct compression, is not sufficient to correct the very poor flow properties of anhydrous theophylline as shown by the high Icarr value of M2 (27.2%). All granules, except the wet granules of mixture 1 (G1W), are considered to have passable flow properties based on their Icarr index being higher than 18%.

### 3.2 Shear cell measurements

The flow properties of the products that were available in large quantities were only investigated using the shear cell method (Figures 4 and 5 and Table III). From these measurements, the excipients appear to be free- (Cellactose® and Pharma 200/70) or easy-flowing powders (Avicel PH101), whereas theophylline is cohesive. The three mixtures are classified as easy-flowing according to their flowability index, but it must be said that the flow-functions of M1 and M3 are located in the cohesive area (Figure 5). As expected, granulation improved the flow properties of M1 and M3 since the flow-functions of G1D/G1W and G3D are located in the easy-flowing area. The effect of lubrication appears clearly with the improvement of the flowability index of G3DL versus G3D (from i=6.5 to 25.7).

#### Table III  Flow-function equations and related flow characteristics of the products

| Product                  | Flow-function equation | R²     | Index | Flowability  |
|--------------------------|------------------------|--------|-------|--------------|
| Powders                  |                        |        |       |              |
| Anhydrous theophylline   | \( f_i = 0.327 \sigma_1 + 2.230 \) | 0.5614 | 3.06  | cohesive     |
| Pharma 200/70            | \( f_i = 0.065 \sigma_1 + 1.173 \) | 0.4907 | 16.8  | free-flowing |
| Avicel PH101             | \( f_i = 0.210 \sigma_1 + 0.202 \) | 0.9977 | 4.76  | easy-flowing |
| Cellactose®              | \( f_i = 0.040 \sigma_1 + 0.479 \) | 0.7139 | 25.0  | free-flowing |
| Mixtures                 |                        |        |       |              |
| Mixture 1 (M1)           | \( f_i = 0.247 \sigma_1 + 0.228 \) | 0.9997 | 4.04  | easy-flowing |
| Mixture 2 (M2)           | \( f_i = 0.140 \sigma_1 + 0.150 \) | 0.9948 | 7.14  | easy-flowing |
| Mixture 3 (M3)           | \( f_i = 0.178 \sigma_1 + 1.332 \) | 0.9919 | 5.64  | easy-flowing |
| Granules                 |                        |        |       |              |
| Dry granules 1 (G1D)     | \( f_i = 0.138 \sigma_1 + 0.072 \) | 0.8901 | 7.25  | easy-flowing |
| Wet granules 1 (G1W)     | \( f_i = 0.108 \sigma_1 + 0.287 \) | 0.9337 | 9.26  | easy-flowing |
| Dry granules 3 (G3D)     | \( f_i = 0.150 \sigma_1 + 0.595 \) | 0.9182 | 8.45  | easy-flowing |
| Lubricated dry granules 3 (G3DL) | \( f_i = 0.003 \sigma_1 + 0.869 \) | 0.3863 | 25.7  | free-flowing |

### 3.3 Volume reduction on uniaxial press

The evolution of the packing coefficient as a function of the pressure is presented on Figures 6 and 7. All products display an inflection point \( P \) (mentioned in Table IV) in the curve between 0.2 and 0.5 MPa that indicates a change in the phenomena occurring in the powder bed. This point is considered as the end of the packing phenomena. The compaction pressure corresponding to this change is determined by adjusting the linearisation of the two parts of the curve to obtain optimal linear regression coefficients. The results are presented in Table IV with the \( C_1 \) values calculated for 0.5 MPa. The comparison of the packing coefficients shows that the maximum varia-
Fig. 6 Evolution of the $C_1$ value (%) as a function of the compaction pressure (MPa)

Fig. 7 Evolution of the $C_1$ value (%) as a function of the compaction pressure (MPa)

Table IV Linear regressions and $C_1$ values according to the pressure used for the packing coefficient calculation

| Product                | Linear regressions                  | P (MPa) | $C_{0.5}$ (%) | $C_{0.5} - C_1$ (%) |
|------------------------|------------------------------------|---------|---------------|--------------------|
| **Powders**            |                                    |         |               |                    |
| Anhydrous theophylline | $0.1-0.3$ MPa $C_1=53.1+26.7P$     | 0.32    | 61.6          | 62.9               | 2.1                |
|                        | $0.35-1$ MPa $C_1=59.6+6.4P$       |         |               |                    |                    |
|                        | $R^2=0.9981$ $R^2=0.9821$          |         |               |                    |                    |
| Pharma 200/70          | $0.1-0.25$ MPa $C_1=11.5+13.7P$    | 0.30    | 15.6          | 16.6               | 6.0                |
|                        | $0.35-1$ MPa $C_1=14.2+4.7P$       |         |               |                    |                    |
|                        | $R^2=0.9898$ $R^2=0.9756$          |         |               |                    |                    |
| Avicel FH 101          | $0.1-0.3$ MPa $C_1=18.5+28.2P$     | 0.34    | 28.1          | 30.2               | 6.9                |
|                        | $0.35-1$ MPa $C_1=23.8+12.8P$      |         |               |                    |                    |
|                        | $R^2=0.9970$ $R^2=0.9889$          |         |               |                    |                    |
| Cellactose®            | $0.1-0.35$ MPa $C_1=14+26.9P$      | 0.42    | 25.2          | 26.25              | 4.0                |
|                        | $0.35-1$ MPa $C_1=18.9+15P$        |         |               |                    |                    |
|                        | $R^2=0.9968$ $R^2=0.9868$          |         |               |                    |                    |
| **Mixtures**           |                                    |         |               |                    |
| Mixture 1 (M1)         | $0.1-0.3$ MPa $C_1=29.5+24.1P$     | 0.34    | 37.7          | 38.8               | 2.8                |
|                        | $0.35-1$ MPa $C_1=35.5+6.5P$       |         |               |                    |                    |
|                        | $R^2=0.9968$ $R^2=0.9781$          |         |               |                    |                    |
| Mixture 2 (M2)         | $0.1-0.35$ MPa $C_1=29.5+20.7P$    | 0.38    | 37.3          | 38.5               | 3.1                |
|                        | $0.4-1$ MPa $C_1=33.3+10.1P$       |         |               |                    |                    |
|                        | $R^2=0.9941$ $R^2=0.9919$          |         |               |                    |                    |
| Mixture 3 (M3)         | $0.1-0.25$ MPa $C_1=33.7+60P$      | 0.27    | 49.8          | 51.8               | 3.9                |
|                        | $0.3-1$ MPa $C_1=47.8+7.3P$        |         |               |                    |                    |
|                        | $R^2=0.9791$ $R^2=0.9485$          |         |               |                    |                    |
| **Granules**           |                                    |         |               |                    |
| Dry granules 1         | $0.1-0.3$ MPa $C_1=12.6+25.4P$     | 0.35    | 21.5          | 21.6               | 0.5                |
| (G1D)                  | $0.35-1$ MPa $C_1=18+9.9P$         |         |               |                    |                    |
|                        | $R^2=0.9942$ $R^2=0.9769$          |         |               |                    |                    |
| Wet granules 1         | $0.1-0.3$ MPa $C_1=9.6+32.7P$      | 0.37    | 21.7          | 23.1               | 6.1                |
| (G1W)                  | $0.4-1$ MPa $C_1=17.2+12.1P$       |         |               |                    |                    |
|                        | $R^2=0.9866$ $R^2=0.9837$          |         |               |                    |                    |
| Dry granules 3         | $0.1-0.35$ MPa $C_1=10.3+29.4P$    | 0.35    | 20.6          | 21.9               | 5.9                |
| (G3D)                  | $0.4-1$ MPa $C_1=17.7+8.4P$        |         |               |                    |                    |
|                        | $R^2=0.9516$ $R^2=0.9868$          |         |               |                    |                    |
| Lubricated dry granules| $0.1-0.3$ MPa $C_1=8.9+25.3P$     | 0.33    | 17.2          | 18.6               | 7.5                |
| 3 (G3DL)               | $0.35-1$ MPa $C_1=14.6+7.8P$       |         |               |                    |                    |
|                        | $R^2=0.9890$ $R^2=0.9854$          |         |               |                    |                    |
| HAP200                 | $0.1-0.45$ MPa $C_1=23.4+16.6P$    | 0.45    | 30.9          | 31.05              | 0.5                |
|                        | $0.45-1$ MPa $C_1=27.3+8.1P$       |         |               |                    |                    |
|                        | $R^2=0.9720$ $R^2=0.9845$          |         |               |                    |                    |
| HAP400                 | $0.1-0.4$ MPa $C_1=7.1+23.5P$      | 0.35    | 15.3          | 16.6               | 7.8                |
|                        | $0.45-1$ MPa $C_1=12+9.4P$         |         |               |                    |                    |
|                        | $R^2=0.9790$ $R^2=0.9894$          |         |               |                    |                    |

$P$ is the pressure at the intersection  
$C_{0.5}$ is the $C_1$ value at the intersection
flow between $C_{0.5}$ and the $C_1$ corresponding to the slope change is about 8%, but this leads only to a very small modification in the ranking of the products as shown in Table V (the classification of G1D and G3D only are modified). Furthermore, this variation has no consequence on the classification of the products: all powders (except Pharma 200/70), the three mixtures, and HAP200 have a packing coefficient above 25%, whereas granules are classified as products having good flow properties, whatever the calculation method used.

For the purpose of defining a standardised parameter to compare the packing of different products, it seems that the choice of 0.5 MPa is appropriate. For most of the products, the packing stage can be considered as completed without any fragmentation or deformation of the particles as the applied pressure is very low.

Table V Ranking of the products according to their packing coefficient

| Product                  | Classification | $C_{1p}$ | $C_{0.5}$ |
|--------------------------|----------------|---------|---------|
| Powders                  |                |         |         |
| Anhydrous theophylline   | 13             | 13      |
| Pharma 200/70            | 8              | 8       |
| Avicel PH 101            | 7              | 7       |
| Cellactose®              |                |         |         |
| Mixture 1 (M1)           | 11             | 11      |
| Mixture 2 (M2)           | 10             | 10      |
| Mixture 3 (M3)           | 12             | 12      |
| Granules                 |                |         |         |
| Dry granules 1 (G1D)     | 4              | 4       |
| Wet granules 1 (G1W)     | 6              | 6       |
| Dry granules 3 (G3D)     | 4              | 5       |
| Lubricated dry granules 3 (G3DL) | 3 | 5 |
| HAP200                   | 9              | 9       |
| HAP400                   | 4              | 1       |

$C_1$ value lower than 25%

4. Discussion

The comparison of the packing coefficient $C_1$ with the flowability index $i$ (Figure 8) confirms the possibility of evaluating the flowability by calculation of the packing coefficient, despite the difference in the stress region applied. Globally, materials with a low $C_1$ have easy- or free-flowing properties according to the Jenike classification, whereas products with a high packing coefficient have a low flowability index, which is characteristic of poor flow properties. Thus a rapid assessment of the flow properties of a product can be obtained from the analysis of the first part of its compression curve.

It should be noted that some products classified as easy-flowing (Avicel and the three mixtures) or free-flowing (Cellactose®) according to Jenike are considered to have inadequate flow properties according to their packing coefficient. This observation indicates that this new parameter seems to be more “reliable” than the flowability index determined by Jenike shear cell measurements. One hypothesis that could explain this discrepancy is the fact that considering only the flowability index reduces the information given by the flow-functions. In particular, the flow-functions of mixtures M1 and M3 (Figure 5), which are classified as easy-flowing products based on their flowability index, are situated in the cohesive area which is in accordance with their high $C_1$ value. Likewise the flowability index of Cellactose® is one of the best of the products under consideration, whereas the $C_1$ value is not as favourable (higher than 25%). In fact, mass flow through a funnel and tapped density measurements confirm this result; in spite of a high flow rate (16.2 g/sec), the flow properties of Cellactose® are not as good, as shown by the $I_{car}r$ value (17.5%), which indicates relatively high compressibility of the product. This tabletting limiting characteristic is indicated by the packing coefficient of Cellactose® around the limit value of 25%. Thus, this method permits better discrimination of the products with poor flow properties, as for example M3 and G3D, than the...
flowability index measured by Jenike shear cell, and fits rather well with our objective which is to characterise and classify products available in small quantities in the early stages of drug development.

Particulate materials with a C1 value below 25% can be considered to have adequate flow properties for industrial use, while a higher packing coefficient indicates too much compressibility that has to be corrected by the formulation and/or the manufacturing process.

5. Conclusion

This work has confirmed the possibility of investigating the flow properties of particulate materials by means of the packing coefficient calculated at 0.5 MPa. This new method has the advantage of being very easy, rapid and above all of requiring very small amounts of product. It has been shown to be in good correlation with flow-functions results and furthermore to better discriminate cohesive materials. In a recent paper, J.K. Prescott and R.A Barnum [13] specified that flowability is not an inherent material property, but is rather a result of the combination of material physical properties and the equipment used. As the packing assessment is performed in experimental conditions close to the industrial ones, i.e. in a compression die, improved prediction of the weight variation of tablets as compared to other methods may be expected, although parameters such as speed or punch shapes have not been taken into account. In addition, the flow properties assessed by the packing coefficient are less favourable as compared to the results from other methods, more efficiently preventing flow problems that can occur in a given application.

6. References

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