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Brief/Technical Note

Note on the Measurement of Bulk Density and Tapped Density of Powders According to the European Pharmacopeia

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Abstract. The apparent volume and compressibility index of commonly used excipients were evaluated according to European Pharmacopeia monograph (seventh edition) in order to study the influence of the procedure conditions. The results suggested that the leveling of the powder inside the cylinder ought to be avoided.

KEY WORDS: bulk density; compressibility index; excipients; tapped density.

INTRODUCTION

Flowability of powders is an important aspect in the manufacturing of solid dosage forms (1). In recent years the compressibility index (CI) first described by Carr (2) or closely related Hausner's ratio (3) have become the simple, fast, and popular methods of predicting powder flow characteristics. To calculate these parameters, which are not intrinsic properties and can be influenced by size and shape, surface area, moisture content, and cohesiveness of the material, it is necessary to determine the unsettled apparent volume and final tapped volume or the corresponding bulk and tapped density. The European Pharmacopeia (Ph. Eur.) has issued a new monograph (2.9.34 of seventh edition). The standardization of these tests is a key issue in order to get reproducible and meaningful results, and although there has been an effort made by Pharmacopoeial Discussion Group, from which resulted the mentioned monograph, some particular aspects should be discussed in more detail. One of these aspects is the way to read the volume of powder which does not normally form a horizontal surface in the graduated cylinder (4).

The influence of the procedure conditions in the measurement of apparent volume according to the Ph. Eur. was studied using nine commercially available and commonly used excipients. Intentionally, some of the excipients chosen have very different flow properties and some although chemically similar have different physical properties (particle size or moisture content).

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MATERIALS AND METHODS

Materials

The excipients used were as follows: Avicel® PH-200 and Avicel® PH-101 (FMC); Emcompress®, Emcompress® Anydrous, Emdex®, and Sugar Spheres—20–25 mesh (JRS PHARMA); Pharmatose 200M® (DMV-FONTERRA EXCIPIENTS); Starch 1500® (COLORCON); and Tablettose 80® (MEGGLE PHARMA).

Apparent Volume

The determination of the unsettled apparent volume, V_0, and the final tapped volume, V_f, was done according to the method 1 of the monograph 2.9.34 Bulk density and tapped density of powders of the Ph. Eur. The powder was introduced in a graduated 250 mL cylinder using a powder funnel. To read the unsettled apparent volume, two methods were used: (a) mean plane (semi-sum of the values corresponding to the highest and lowest points of powder surface—Fig. 1) and (b) leveling (the powder was carefully leveled with a spatula before reading—Fig. 1). Ten runs were conducted for each sample using ten equivalent graduated cylinders in method A. To evaluate the influence of using different (not the same) graduated cylinders, method A_1 was executed using the same graduated cylinder ($n=12$) as a prerequisite to perform the procedure described above, in order to verify if it is correct to reutilize the same cylinder to perform the replicate determinations. Method B was conducted using the same graduated cylinder (as in method A_1). In order to fulfill the volume condition of Ph. Eur. (between 150 and 250 mL), a variable mass was used (75, 100, 125, or 150 g). The final tapped volume was evaluated using the tap density tester EDT-1020 Electrolab.

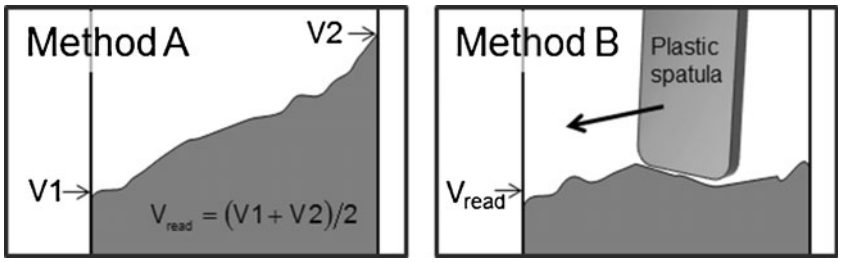

Fig. 1. Methods used to read the apparent volume (method A—mean plane, method B—leveling)

Table I. Evaluation of Unsettled Apparent Volume (in Milliliter) Using: Method A (Mean Plane), Method A_1 (Same Cylinder), and Method B (Leveling)

Substance	Method A	Method A_1	Method B
Avicel® PH101	228 (1.1)	228 (1.4)	228 (0.9)
Avicel® PH200	198 (1.9)	198 (2.1)	196 (2.6)
Emcompress® A.	205 (0.5)	206 (0.8)	203 (0.7)
Emcompress®	177 (1.3)	178 (1.3)	178 (1.2)
Tablettose® 80	178 (1.8)	178 (1.7)	174 (1.0)
Pharmatose® 200 M	186 (3.8)	181 (5.5)	179 (2.4)
Emdex®	229 (1.0)	230 (0.8)	226 (0.9)
Starch 1500®	237 (0.8)	236 (0.9)	239 (1.3)
Sugar Spheres	181 (1.3)	182 (1.1)	182 (1.5)

Results are expressed as mean (coefficient of variation, in percent)

To complete this study, CI was also calculated according to following equation:

$$100(V_0 - V_f)\Big/V_0$$

Statistical Analysis

In the first part of the study, the apparent volumes obtained were analyzed using the Student's *t*-test. In the second part, one-way ANOVA followed by Tukey HSD was utilized to analyze CI results. The CI results were also analyzed by linear regression. All analyses were performed using PASW Statistic 18.0 or Microsoft Excel 2010. Differences were accepted as statistically significant at $\alpha = 0.05$.

RESULTS AND DISCUSSION

Ambient relative humidity is a parameter that may influence the determination of apparent volume. For this reason, relative humidity was evaluated during this study (it oscillated between 56 and 72% at room temperature).

From Table I, it is evident that the mean values of V_0 obtained using method A or A_1 are similar for all the excipients tested and can be considered equivalent ($p > 0.05$). The results obtained by leveling the surface of the powder (method B) are statistically different ($p < 0.05$) from those obtained by method A_1 for Emcompress® Anydrous, Tablettose® 80, and Emdex®. These differences are not technologically relevant to the determination of bulk density since differences in the bulk density of these powders are ≤ 0.02 g/cm^3.

According to Table II, the mean values of V_f obtained using either method A or A_1 can be considered equivalent ($p > 0.05$). The same result can be observed when method A_1 is compared with method B with a unique exception for Emdex®. Again, these differences in tapped density are not technologically relevant.

Table III shows the mean values of CI. The results obtained using either method A, A_1, or B can be considered equivalent ($p > 0.05$) with the exception of Emdex® and Tablettose 80® for method B.

Applying a linear regression model to the mean results of methods A, A_1, and B, higher residuals square sums were obtained

Table II. Evaluation of Final Tapped Volume (in Milliliter) Using: Method A (Mean Plane), Method A_1 (Same Cylinder), and Method B (Leveling)

Substance	Method A	Method A_1	Method B
Avicel® PH101	171 (1.2)	172 (1.1)	172 (1.9)
Avicel® PH200	161 (1.8)	161 (0.8)	160 (1.2)
Emcompress® A.	170 (1.2)	170 (1.1)	169 (0.8)
Emcompress®	150 (1.4)	151 (1.2)	150 (1.3)
Tablettose® 80	137 (0.8)	138 (0.7)	138 (0.8)
Pharmatose® 200 M	118 (1.6)	116 (1.4)	116 (1.2)
Emdex®	214 (1.4)	215 (1.3)	209 (0.5)
Starch 1500®	186 (0.5)	186 (0.6)	186 (0.5)
Sugar Spheres	169 (1.0)	170 (0.8)	171 (0.6)

Results are expressed as mean (coefficient of variation, in percent)

Table III. Results of Compressibility Index (in Percent) Using: Method A (Mean Plane), Method A_1 (Same Cylinder), and Method B (Leveling)

Substance	Method A	Method A_1	Method B
Avicel® PH101	25.1 (1.4)	24.8 (1.4)	24.6 (0.9)
Avicel® PH200	18.7 (1.5)	18.4 (1.9)	17.9 (2.5)
Emcompress® A.	17.1 (1.2)	17.5 (1.5)	16.4 (0.8)
Emcompress®	15.0 (1.7)	15.5 (1.3)	15.6 (1.2)
Tablettose® 80	22.9 (1.6)	22.9 (1.7)	20.7 (1.1)
Pharmatose® 200 M	36.8 (1.9)	36.0 (2.9)	35.2 (1.3)
Emdex®	6.6 (1.0)	6.7 (0.7)	7.6 (0.6)
Starch 1500®	21.7 (0.6)	21.2 (0.9)	22.1 (1.2)
Sugar Spheres	6.8 (1.6)	6.5 (0.7)	6.0 (1.4)

Results are expressed as mean (standard deviation)

for A and B (15.3) or A_1 and B (15.5) than for the A and A_1 methods (3.5). It is possible that the leveling (method B) may affect the reproducibility of the determinations because sometimes a slight compaction may occur. We think that this may happens mainly in free flowing powders where particle interactions are less strong.

The results suggested that the apparent volume of some excipients is affected by the way of measuring the volume, in particular V_0, yet it appears that the influence on bulk and tapped density is technologically irrelevant. Nevertheless considering also the results of CI leveling of the powder inside the cylinder with a spatula (method B), suggested by Ph. Eur., ought to be avoided.

CONCLUSION

The apparent volume of nine commonly used excipients was measured according to the current Ph. Eur. monograph in order to study the influence of the procedure conditions. Compressibility index was also determined. The results suggested that the leveling of the powder inside the cylinder, allowed by European Pharmacopeia, ought to be avoided.

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