

Compaction equation and its use in the determination of compressibility of pharmaceutical materials

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INTRODUCTION

Tablets are dosage forms made by a compression of the same powdered mixture volumes of one or more active ingredients and excipients. This work studies the flow and compressibility properties of three pharmaceutical excipients. The compressibility of used materials is evaluated using the three exponential compaction equation.

METHODS

Flow properties measurement

Moisture analyzer (Precisa XM60) was used for the evaluation of loss on drying at 105 °C. According to the European Pharmacopoeia, the bulk density of used materials was determined using the Scott's Volumeter (Copley Scientific). Tapped density meter (Erweka SVM 102) was used for the evaluation of Hausner ratio (HR).¹ To determine the angle of repose α (°) and the mass flow rate \dot{m} (g/s) of excipients, the granulate and powder flow tester (Erweka GT) with the 200 ml stainless steel conical hopper and a 10 mm outlet nozzle was used. The average of ten measurements with the standard deviation (SD) is shown in Table 1.

Tablet preparation

Material testing instrument (Zwick/Roell T1 FRO 50; Fig 1) was used for the preparation of tablets with the mass of 500 mg and 13 mm in diameter. Tablets used for the evaluation of compaction process were made using the compaction force of 40 kN. The radial strength was evaluated in tablets compacted at the force of 10 kN.

The compaction process was evaluated using the three-exponential equation (1).^{2,3} Where V is the volume (mm^3) of the tested material at the current compaction pressure p (MPa) and V_0 is the volume of the compacted material (mm^3) at zero pressure (MPa). The parameter a_i (d.u.) describes the theoretical maximal volume reduction of a tableting material at a particular phase of the compression process, the parameter $1/t_i$ describes the speed of the volume reduction at a particular phase (MPa^{-1}), and the parameter y_0 (d.u.) describes the maximal theoretical volume reduction at the infinite compaction pressure. In order to study the behavior of the excipients during the compaction process, the parameters a_i and $1/t_i$ are useful. In contrast to the often used Cooper and Eaton equation⁴, the three parameters of the equation (1) are estimated from the relationship between the volume reduction of a compacted material and the applied compaction pressure. The equation (1) divides the compaction process into three particular phases. The first one describes the precompression that includes the particle rearrangement, the interparticulate friction and the friction between the material and the walls of the die. The second one characterizes the elastic deformation of the particles. In the third phase of the process, the plastic deformation of the compacted material is described. The parameters of the compaction equation (1) can be used for the calculation of energy E_i (J) needed for the compaction in a particular phase of the process according to equation (2). Used symbols have the same meaning as described above.

Evaluation of tablet properties

Tablet hardness was estimated using the same instrument used for the compaction of tablets (Zwick/Roell T1 FRO 50). The tablet hardness was used to express the radial strength according to Fell and Newton.⁵

MATERIALS

Microcrystalline cellulose (MCC, Comprecel 102, Mingtai Chemical) lactose monohydrate (LAC, Spherolac 100, Meggle), and calcium phosphate anhydrate (DC, DI-CAFOS A150, Budenheim) were used as fillers. The particle size of the used materials was estimated using the optical microscope (Olympus BX51) at 10x magnification. The median particle size (x_{50}) was expressed automatically.



Fig. 1 Material testing machine Zwick/Roell

$$\frac{V}{V_0} = a_1 \cdot e^{-\frac{1}{t_1}p} + a_2 \cdot e^{-\frac{1}{t_2}p} + a_3 \cdot e^{-\frac{1}{t_3}p} + y_0 \quad (1)$$

$$E_i = V_0 \cdot a_i \cdot t_i \quad (2)$$

RESULTS AND DISCUSSION

The most important parameters of the used compaction equation are the parameters a_i that describe the volume reduction and E_i expressing the amount of energy used in the particular phase of compaction process. In Table 2, the results of the theoretical volume reduction at each of three compaction phases are summarized. The values of parameter a_1 , i.e. the theoretical volume reduction caused by particle rearrangement, depend greatly on the flow properties and the bulk density of the evaluated material. The better the flowability and the lower the bulk density, the lower values of this parameter can be observed.

Material	\dot{m} (g/s)	α (°)	HR (d.u.)
MCC	9.75 (1.39)	47.33 (1.46)	1.39 (0.01)
LAC	16.22 (2.18)	44.50 (1.04)	1.16 (0.02)
DC	32.91 (0.16)	39.90 (0.30)	1.13 (0.01)

Table 1 Mass flow rate, angle of repose and Hausner ratio

Material	a_1 (d.u.)	a_2 (d.u.)	a_3 (d.u.)
MCC	0.28 (0.01)	0.35 (0.01)	0.37 (0.01)
LAC	0.19 (0.02)	0.26 (0.03)	0.55 (0.02)
DC	0.12 (0.01)	0.25 (0.01)	0.63 (0.02)

Table 2 Results of volume reductions

Material	E_1 (J)	E_2 (J)	E_3 (J)
MCC	0.12 (0.01)	2.80 (0.17)	39.8 (2.0)
LAC	0.03 (0.05)	1.93 (0.42)	119.7 (10.2)
DC	0.05 (0.01)	2.16 (0.13)	148.4 (11.1)

Table 3 Results of energetic parameters

In Table 1, the mass flow rate (\dot{m}), the angle of repose (α) and Hausner ratio (HR) are summarized. DC showed the best flow properties. The worst flow properties were measured in MCC. Differences are caused by the particle size and the surface properties (Fig. 2 to 5). Particles of MCC were acicular having the mean diameter of 77.66 μm and the lowest bulk density (0.32 g/ml). Particles of LAC and DC were equant, larger ($x_{50} = 145.54 \mu\text{m}$, and 209.12 μm , respectively) and relatively smooth. Also the bulk density of LAC and DC was higher (0.60 g/ml and 0.68 g/ml). Worse flow properties of MCC can also be caused by the highest moisture content in comparison with LAC and DC (4.49%, 0.46 %, and 1.02 %, respectively). In Table 2, parameter a_2 describes the volume reduction caused by elastic deformations. Being related to the material elasticity, the higher values are expected for the viscoelastic materials than for the brittle ones. This was observed for MCC in comparison to LAC and DC. The parameter a_3 describes the volume reduction caused by the plastic deformations. Values of this parameter depend on the material properties mentioned above, moreover, the bonding mechanism is also important.⁶

The results of energetic parameters E_i are summarized in Table 3. Parameter E_1 describes the amount of energy used during the particle rearrangement. The values are influenced by the interparticulate friction that is connected with the particle shape and the surface roughness. The rounder and the smoother the particles the lower is the energy consumption. However, such particles are usually less compressible than the irregular and rougher ones.⁷ The lowest value of the parameter E_1 was found in LAC with the regular, smooth particles. The parameter E_2 describes the amount of energy used during the elastic deformations. The viscoelastic MCC showed the highest values. Comparing the values for DC and LAC, the higher values for DC could result from removal of the air trapped inside the agglomerates of DC. The parameter E_3 describes the amount of energy used at plastic deformation; it mostly depends on the bonding mechanism. The formation of hydrogen bonds and the bridges are the main mechanisms for viscoelastic MCC while the creation of van der Waals bonds is typical for brittle materials (LAC and DC) that tend to fragment repeatedly during the compaction. The fragmentation is connected with the creation of the new bonds and surfaces which leads to higher energy consumption.⁸ This corresponds with the radial strength measurement; the highest values were detected for viscoelastic MCC (3.31 MPa) contrary to the significantly lower values for LAC and DC (0.24 MPa and 0.30 MPa, respectively).

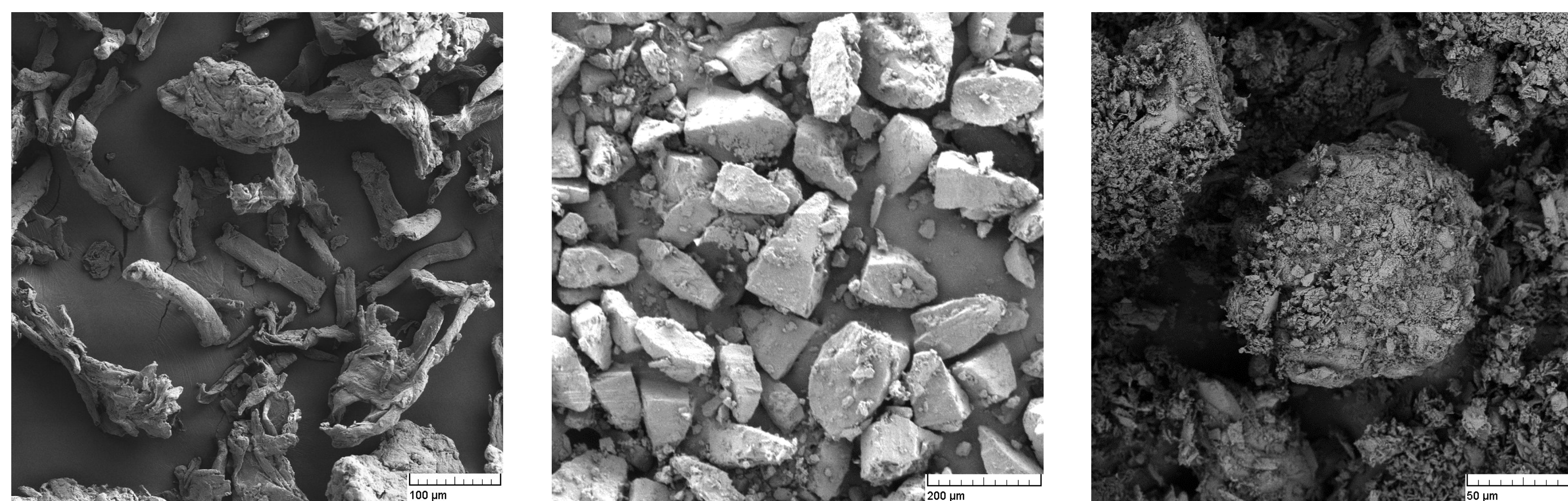


Fig. 2 to 4 SEM Images of Comprecel 102, Spherolac and DI-CAFOS A150 particles (mag. 550x, 250x and 1000x)

CONCLUSIONS

The results of this study proved that the used three exponential compaction equation is suitable for the compressibility evaluation of pharmaceutical excipients. The parameters a_i and E_i directly relate to the material flowability while the parameter E_3 reflects the bonding mechanisms. Further study of the relationship between the tablet strength and the parameters of the compaction equation for other excipients is necessary in future.

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