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 measurements

Moisture analysis (Precisa 350MD) 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 (Enweka SVM 102) was used for the evaluation of Hausner ratio (HR). 1 To determine the angle of repose (α) and the mass flow rate (m, g/s) of the excipients, the granulate and powder flow tester (Enweka 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.

Table 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). 1,3,7 Where V is the volume (mm³) of the tested material at the current compaction pressure p (MPa) and V₀ is the volume of the compacted material (mm³) at zero pressure (MPa). The parameters a (d,u) describes the theoretical maximal volume reduction of a tabletting material at a particular phase of the compresion process, the parameter p₀ describes the speed of the volume reduction at a particular phase (MPa⁻¹), and the parameter q (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 a₂ and a₃/2, u₁ are useful. In contrast to the often used Cooper and Eaton equation 9, 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 interparticle 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 and 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

RESULTS AND DISCUSSION

The most important parameters of the used compaction equation are the parameters a that describe the volume reduction and E, expressing the amount of energy used in the particular phase of compaction process. In Table 1, the results of the theoretical volume reduction at each of three compaction phases are summarized. The values of parameter a, 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.

In Table 1, the mass flow rate (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). Particles of MCC are angular having the mean diameter of 77.76 μm and the lowest bulk density (0.32 g/ml). Particles of LAC and DC were equal, larger α = 145.54 μm, and 209.12 μm, respectively and relatively smooth. The bulk density of LAC and DC was higher [0.60 g/ml and 0.68 g/ml] compared to MCC. Also the Hausner ratio of LAC and DC was higher [30.9 ± 2.3 and 30.9 ± 2.2], respectively. In contrast to MCC, the lower values were observed for the MCC (12.01 ± 2.01 and 12.01 ± 2.01, respectively) than for the brittle ones. This was observed for MCC in comparison to LAC and DC. The parameter α 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 are summarized in Table 3. Parameter E₁ describes the amount of energy used during the particle rearrangement. The value is connected with the interparticle friction and the volume surface contact. The rougher and the smoother the particles the lower is the energy consumption. However, such particles are usually less compressible than the irregular and rougher one. 7 The lowest value of the parameter E₁ was found in LAC as the regular, smooth particles. The parameter E₂ describes the amount of energy used in the plastic deformations; 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. 7 This corresponds with the radial strength measurement; the highest values were detected for viscoelastic MCC (33.51 MPa) contrary to the significantly lower values for LAC and DC (0.24 MPa and 0.30 MPa, respectively).

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 and E, directly relate to the material flowability while the parameter E₁ 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.

REFERENCES

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