

## Evaluation of compressibility of tableting mixtures using the compaction equation

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### Introduction

Tablets as a pharmaceutical dosage form are most commonly made by compaction of the same volumes of powders or granulates. It is necessary to evaluate the properties of the mentioned materials used for the preparation of tablets. These properties include e.g. the moisture content, flow properties, the particle size distribution, compressibility, and compactibility.

The main aim of this work was to evaluate the usability of the compaction equation [1] in the description of the effect of two selected lubricants on the compressibility of tableting mixtures of -lactose monohydrate. The study of the relations between the parameters of the compaction equation and the results of mass flow rate, Hausner ratio, and the tablet tensile strength were the further aim.

### Experimental methods

#### Materials and methods

Sieved -lactose monohydrate Lactochem Fine Crystals (Lactochem) was used as the filler. Hydrophobic sodium stearyl fumarate PRUV (PRUV) and/or hydrophilic modified colloidal silicon dioxide Syloid FP 244 EU (Syloid), respectively, in the concentration of 0.5% were used as lubricants.

Particle size distribution was determined using a Malvern Mastersizer. A Quantachrome Instruments Nova Station A was used for the measurement of the specific surface area and a scanning electron microscope MIRAVESCAN (TESCAN) was used for the observation of the particle shape and the surface. Moisture content was measured using a moisture analyser Kern MLB 50-3.

The tableting mixtures were prepared using a cube blender Erweka (AR401 + KB15S). The flow properties of the filler and the mixtures were evaluated using an Erweka GTB instrument (200 ml stainless steel conical hopper with a 10 mm outlet nozzle) and a tapped density tester Erweka SVM 102. The average of ten measurements is shown in Table 1 including the standard deviation s.

#### Compaction equation

A material testing machine Zwick/Roell T1 FRO 50

was used for the compaction of tablets with the mass of 500 mg and 13 mm in diameter, and for the measurement of their strength according to Fell and Newton<sup>1)</sup>. Compaction was carried out at the compaction force of 40 kN.

To evaluate the compaction process and to compare the tableting mixtures, the compaction equation [1] was used<sup>2)</sup>:

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

where  $V$  is the volume ( $\text{mm}^3$ ) of the compacted material at the current compaction pressure  $p$  (MPa).  $V_0$  is the volume of the compacted material ( $\text{mm}^3$ ) at zero pressure (MPa). The equation (1) has parameters which can be estimated from the relationship between the volume reduction of a tableting material and the compaction pressure. 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  $1/t_i$  (a slope) describes the speed of the volume reduction at a particular phase ( $\text{MPa}^{-1}$ ), and the parameter  $y_0$  (d.u.) describes the maximal theoretical volume reduction at the infinite compaction pressure. In order to study the influence of the excipients on the compaction process, the parameters  $a_i$  and  $1/t_i$  are useful.

The parameters of the compaction equation can be used for the calculation of the energy  $E_i$  (J) used during a compaction process in a particular phase. These energetic parameters can be calculated according to equation [2], where all symbols have the same meaning as those mentioned above:

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

Analysis of variance (ANOVA) was used to test the significance of the lubricants effect on the parameters of the compaction equation.

### Results and discussion

#### Flow properties

Figure 1 illustrates the regularly shaped, smooth crystals of  $\alpha$ -lactose monohydrate.

The results of the flow properties measurements are summarized in Table 1. An increase in the mass flow rate and a decrease in Hausner ratio after an addition of hydrophobic PRUV and/or hydrophilic Syloid, respectively, is seen. The lubricants improve the flow properties of the particulate material by forming a film on the surface of filler particles<sup>3)</sup>. All samples had good flow properties.

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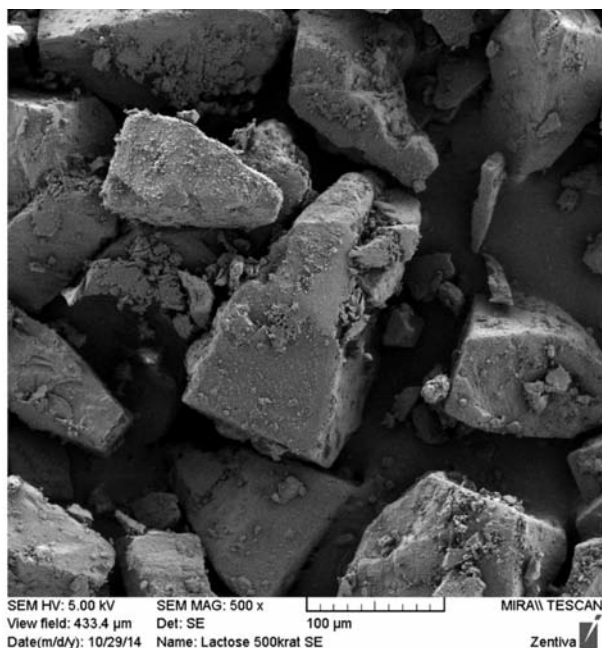


Fig. 1. SEM image of  $\alpha$ -lactose monohydrate Lactochem Fine Crystals

### Compaction equation

The three-exponential equation [1] similar to Cooper-Easton's equation<sup>4)</sup> was developed for the evaluation of the pharmaceutical materials<sup>2,5)</sup>. This equation divides the

compaction process into three simultaneously running 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 particular process 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] are summarized in Tables 2, 3 and 4.

The results show that an addition of both lubricants decreases the volume reduction in the precompression phase ( $a_1$ ), speeds it up ( $1/t_1$ ) and decreases the energy consumption ( $E_1$ ). These parameters are affected by the volume of material before compaction, which depends on its flow and compressibility properties.

Lubricants generally facilitate the particle rearrangement of a powder material and decrease the difference between the bulk and the tapped volume. The lower is the volume of material before compaction, the faster is the volume reduction and less energy is consumed for the precompression phase.

The phase of elastic deformation is affected mainly by the filler type. The brittle Lactochem with very low elasticity fragments easily when compressed and forms weak van der Waals bonds. The noted effect of lubricants on the parameters of the phase of elastic deformations ( $a_2$ ,  $1/t_2$ ,  $E_2$ ) was insignificant ( $p = 0.05$ ).

The phase of plastic deformation is the most important part of the compaction process. Being a brittle material,

Table 1. Mass flow rate ( $\dot{m}$ ), Hausner ratio (HR) and tablet tensile strength ( $\sigma$ )

Material	$\dot{m}$ (g/s)		HR (d.u.)		$\sigma$ (MPa)	
	x	s	x	s	x	s
Lactochem	10.14	2.41	1.17	0.01	0.39	0.04
Lactochem + PRUV	11.40	1.96	1.16	0.01	0.37	0.04
Lactochem + Syloid 1	11.11	1.89	1.12	0.01	0.35	0.06

Table 2. The  $a_i$  parameters of tableting materials

Material	$a_1$ (d.u.)		$a_2$ (d.u.)		$a_3$ (d.u.)	
	x	s	x	s	x	s
Lactochem	0.107	0.015	0.242	0.008	0.651	0.019
Lactochem + PRUV	0.104	0.011	0.254	0.003	0.642	0.012
Lactochem + Syloid	0.102	0.012	0.249	0.007	0.631	0.012

Table 3. The  $1/t_i$  parameters of tableting materials

Material	$1/t_1$ (MPa <sup>-1</sup> )		$1/t_2$ (MPa <sup>-1</sup> )		$1/t_3$ (MPa <sup>-1</sup> )	
	x	s	x	s	x	s
Lactochem	1.43	0.48	0.082	0.006	0.0034	0.0002
Lactochem + PRUV	1.72	0.37	0.059	0.004	0.0037	0.0001
Lactochem + Syloid	2.10	0.22	0.093	0.003	0.0038	0.0002

Table 4. The energetic parameters of tableting materials

Material	$E_1$ (J)		$E_2$ (J)		$E_3$ (J)	
	x	s	x	s	x	s
Lactochem	0.052	0.011	1.90	0.10	122.47	8.97
Lactochem + PRUV	0.040	0.006	1.92	0.06	110.95	3.89
Lactochem + Syloid	0.038	0.003	1.78	0.11	111.64	4.62

Lactochem tends to fragment repeatedly during the compaction. This fragmentation is connected with the creation of new bonds and surfaces<sup>6)</sup>. In comparison with Lactochem itself, the values of the volume reduction  $a_3$  and the consumed energy for compaction  $E_3$  were lower, and the process was faster in the presence of lubricants.

The film of lubricants on the particle surface, generally, can affect the properties of tablets, particularly their tensile strength. The tablets prepared from the mixtures had a lower  $\sigma$  (MPa) than the tablets made from Lactochem itself as is shown in Table 1.

Although the energy consumed in the third phase  $E_3$  was almost the same for both lubricants used, a difference in the tensile strength was observed. This may be caused by the difference in the specific surface area and the particle size of the lubricants. The measured specific surface area was 1.62 m<sup>2</sup>/g for PRUV and 274.48 m<sup>2</sup>/g for Syloid, respectively. This corresponds to smaller particle size diameters of Syloid  $D_{v,10} = 1.87 \mu\text{m}$ ,  $D_{v,50} = 3.52 \mu\text{m}$ , and  $D_{v,90} = 7.43 \mu\text{m}$  when compared with those found for PRUV  $D_{v,10} = 5.39 \mu\text{m}$ ,  $D_{v,50} = 17.16 \mu\text{m}$ , and  $D_{v,90} = 39.52 \mu\text{m}$ . These two factors can greatly affect the lubricant activity<sup>7)</sup>.

## Conclusions

Based on the results, the used compaction equation is suitable for the evaluation of compressibility behaviour of  $\alpha$ -lactose monohydrate and its mixtures with the lubricants during the direct compression process. Correlations were found between the parameters of flow

properties ( $m$  and HR) and the parameters  $a_1$ ,  $l/t_1$  and  $E_1$  of the compaction equation which describes the first phase of the compaction process, i.e. the precompression phase. However, more experiments are necessary to make general conclusions. The relations between the energetic parameter  $E_3$  and the tensile strength  $\sigma$  of tablets will be further investigated.

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## References

1. **Fell J. T., Newton J. M.** Determination of tablet strength by the diametral-compression test. *J. Pharm. Sci.* 1970; 59, 688–691.
2. **Řehula M., Rysl T.** Characterization of microcrystalline celluloses by means of the parameters of a three-exponential compression equation. *Ces. slov. Farm.* 2008; 57, 165–169.
3. **Li J., Wu Y.** Lubricants in pharmaceutical solid dosage forms. *Lubricants* 2014; 2, 21–43.
4. **Cooper A. R., Eaton L. E.** Compaction behavior of several ceramic powders. *J. Am. Ceram. Soc.* 1962; 45, 97–101.
5. **Ondřejček P., Řehula M., Svačinová P., Stoniš J., Rabišková M.** The effect of a new glidant Syloid on pressing of drug tablets. *Chem Listy* 2014; 108, 687–693.
6. **Eriksson M., Alderborn G.** The effect of particle fragmentation and deformation on the interparticulate bond formation process during powder compaction. *Pharm. Res.* 1995; 12, 1031–1039.
7. **Wang J., Wen H., Desai D.** Lubrication in tablet formulations. *Eur. J. Pharm. Biopharm.* 2010; 75, 1–15.