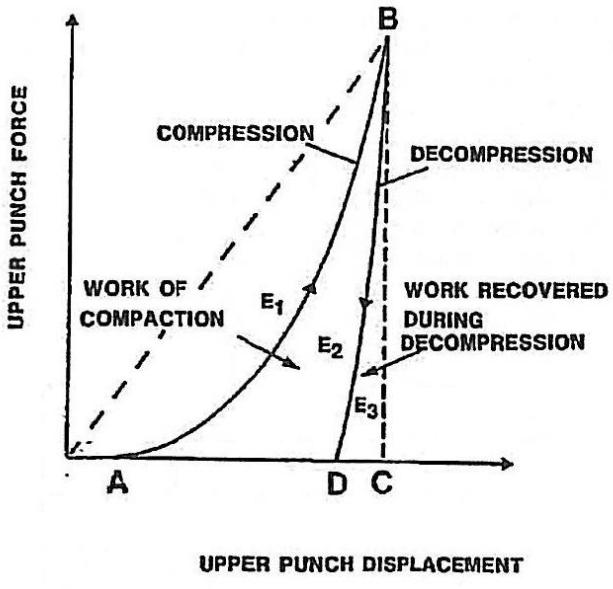
Evaluation of tablet compressibility and effect of lubricants in tableting materials.

Theory I: Energy profile of the compression process

Sufficient energy is required for the formulation of solid compacts, the parameters of which can be evaluated by means of a force-displacement“. This is a graphical record of the force and displacement of the upper punch of the tablet press acting on the tableting material in the die.

The compression cycle can be divided into three phases. The following graph shows a schematic representation of the force of the upper punch versus its displacement during compression and decompression:



Total compression energy (Emax) includes the following individual energy types:

- E1 - precompression energy, used mainly for friction between particles and between particles and matrix surface
- E2 - plastic deformation energy - remains in the tablet, it is important for the formation of bonds
- E3 - energy of elastic deformation, it is the energy of decompression released from the tablet after compression

The E1 value should be as small as possible and the (E2 + E3) / E1 and E2 / E3 ratios as large as possible.

E2 + E3 = E com - compression energy

E1 + E2 + E3 = Emax - total energy of the compression process

From the given energies, the plasticity value can be calculated as the ratio of plastic deformation energy to compression energy: P1 = 100. E2 / (E2 + E3); ↑ Pl → ↑ tablet strength

Theory 2: Lubricants and lubricant sensitivity of dry binders in tableting material

Lubricants reduce a friction during compression, prevent adhesion of the tablet to the compression punches and die walls, improve the ejection of the tablet from the die after compression. Lubricants may also the function as a glidant, which improves the flowability of the tableting material. Lubricants are added at a concentration of 0.25 % - 5.0 %.

Lubricants can be divided into hydrophobic and hydrophilic. The most commonly used hydrophobic stearates are magnesium, calcium, zinc and aluminum stearate, stearic acid and sodium stearyl fumarate. Hydrophilic lubricants include sodium lauryl sulfate, magnesium lauryl sulfate, polyethylene glycols (PEG 4000, 6000).

The effect of lubricants can be evaluated by the *ejection force*, which is the force required to eject the tablet from the die.

The addition of a lubricant to the directly compressible tableting material can greatly affect the properties of the tablets, such as their strength and disintegration time. Hydrophobic lubricant extends tablet disintegration time. The addition of a powdered lubricant to the tabletting mixture during the mixing process results to the formation of a lubricant film on the particles of the other ingredients of the tableting material. As a result, the formation of this film causes a decrease of tablet strength. The basic excipient in the directly compressible tableting material is a dry binder, and the action of the lubricant in the bond strength is strongly dependent on the compression mechanism.

The lubricant senstitivity can be expressed by lubricant sensitivity ratio (LSR), which can be calculated according to the formula:

LSR = (CSu-CSl) / CSu

where CSu is the strength of the tablet without lubricant and CS1is the strength of the tablet with lubricant. The closer the LSR is to 1, the greater the lubricant sensitivity is

Equipments:

Special die for compression:

Material testing equipment Zwick

Schleuniger apparatus

Mixing cube

Task 1:

Influence of microcrystalline cellulose type on the energy profile of the compression process, tablet strength and lubricant sensitivity.

The essence of the task:

The essence of the task is to determine the differences of three types of microcrystalline cellulose in the compressibility, tablet strength and lubricant sensitivity.

Needs:

Raw materials: MCC 102, MCC 200, Prosolv SMCC 90, magnesium stearate

Aids: weighing spoon, cards

Equipments: digital scales, material testing equipment T1-FRO 50 TH.A1K Zwick / Roell with special die of 13 mm diameter, Schleuniger apparatus, mixing cube Erweka

Procedure:

1. Weigh fiveteen times 0,5 ± 0,0010 g on cards of : Avicel PH 102, Avicel PH 200 and Prosolv SMCC 90.
2. Set compression process parameters to obtain the compression energy profile: compression speed 40 mm / min, preload 2 N, preload speed 2 mm / s. The compression forces for A 102 are 3, 3.5 and 4 kN; for A 200 and P 90 3 kN
3. Spread the dry binder into the die and compress 5 tablets from each compression force. During pressing, the force-dispplacement record is recorded and the energy profile of the compression process is quantified. Between pressing the individual tablets, the die is cleaned with dry gauze. After compression of all tablets at a given compression force, a compression report is printed.
4. Measure the tablet dimensions and destruction force on a Schleuniger apparatus, and calculate the tensile strength of the tablets according to formula 1. Evaluate it statistically

   $$P = 2F / \pi.dh \qquad (1)$$

   F - destruction force / N /, d - tablet diameter / mm /, h - tablet height / mm /
5. Prepare 20 g mixtures of all dry binders with 1 % magnesium stearate in a mixing cube. Rotation speed of cube is 112, mixing time 2.5 min.

6. Compress from these mixtures 5 tablets at a compression force of 3 kN. Again, the energy profile of the pressing process is simultaneously evaluated and therefore printed

7. Using a Schleuniger apparatus, measure the dimensions of the tablets and the destruction force, and calculate the tensile strength of the tablets, and evaluate is statistically.

8. Calculate the lubricant sensitivity of dry binders according to formula 2 from the obtained average tensile strength values:

LSR = (CSu - CS1) / CSu (2)

CSu - tablet strength without lubricant / MPa / and CSl - tablet strength with lubricant / MPa /

9. The average values of all parameters (Emax, E1, E2, E3, Elis, P1, P) and LSR values for the dry binders enter into the computer tables and evaluate.

Suggestion for discussion:

Influence of properties of tested microcrystalline celluloses on evaluated parameters.

Conclusion:

From the obtained results, compare the tested microcrystalline celluloses in terms of their compressibility and sensitivity to the addition of magnesium stearate lubricant.

Example of protocol – energy profile of compression process:

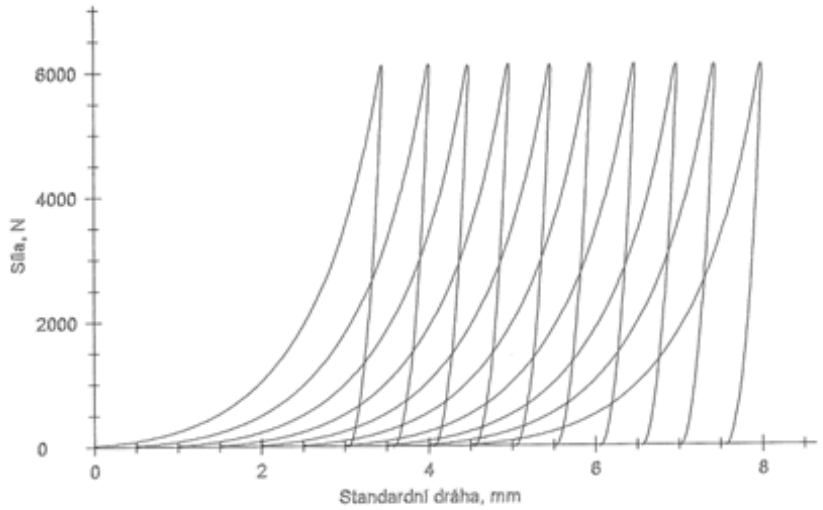
Zwick/Roell Protokol 27.02.2013

Materiál : fl. 100+met. 100 000 1:1 + 1%st 6kN
Zkušební systém: Řízení Výrobní číslo: 156573
Příčník Výrobní číslo: 156573
Síla Výrobní číslo: 156574 50 kN

Výsledky:

Nr	Fmax. N	E1 Nm	E2 Nm	E3 Nm	Emax Nm	Elis Nm	EP %	PI %
1	6108,74	5,589	4,120	0,845	10,55	4,97	52,96	82,99
2	6122,39	5,753	4,158	0,849	10,76	5,01	53,47	83,04
3	6106,83	5,681	4,105	0,849	10,64	4,95	53,42	82,85
4	6125,89	5,672	4,132	0,842	10,65	4,97	53,27	83,07
5	6114,30	5,601	4,151	0,851	10,60	5,00	52,82	82,98
6	6119,52	5,559	4,145	0,852	10,56	5,00	52,66	82,95
7	6123,66	5,665	4,140	0,855	10,66	5,00	53,14	82,87
8	6111,29	5,652	4,120	0,851	10,62	4,97	53,21	82,88
9	6114,14	5,558	4,095	0,848	10,50	4,94	52,93	82,84
10	6115,54	5,708	4,125	0,855	10,69	4,98	53,41	82,84

Grafické záznamy zkoušek:



Statistika:

Série n = 10	Fmax. N	E1 Nm	E2 Nm	E3 Nm	Emax Nm	Elis Nm	EP %	PI %
x̄	6116,23	5,644	4,129	0,850	10,62	4,98	53,13	82,93
s	6,45	0,065	0,020	0,004	0,07	0,02	0,28	0,08
v	0,11	1,15	0,48	0,47	0,70	0,43	0,52	0,10

Task 2:

Influence of lubricant concentration and compression force on the energy profile of the compression process, ejection force and strength of spray-dried lactose tablets.

The essence of the task:

The essence of the task is to find out the difference between two concentrations of magnesium stearate on compressibility, ejection force and strength of spray-dried lactose tablets at two compression forces

Needs:

Raw materials: Flowlac 90, sodium stearyl fumarate

Aids: weighing spoon, cards

Equipments: digital scales, material testing equipment T1-FRO 50 TH.A1K Zwick / Roell with special die of 13 mm diameter, Schleuniger apparatus, mixing cube Erweka

Procedure:

1. Prepare mixtures of Flowlac 90 with 0.5 and 1 % sodium stearyl fumarate weighing 20 g in a mixing cube. Rotation speed of cube 112, mixing time 2.5 min.
2. Compress 3 tablets from both mixtures at the 10 and 13 kN . At the same time, the energy profile of the compression process is evaluated and the reports are printed. After each compression, the ejection force evaluation program is switched and the locking member and the lower punch are removed from the die. Subsequently, the die is reinserted between the jaws of the press, the movement of the upper part is started and the ejection force is evaluated.
3. Using a Schleuniger apparatus, measure the dimensions of the tablets and the destruction force, and calculate the tensile strength of the tablets. It is statistically evaluated.
4. The average values of the test parameters together with their standard deviations are entered into tables in a computer and plots of the test parameters versus the compression force are plotted.

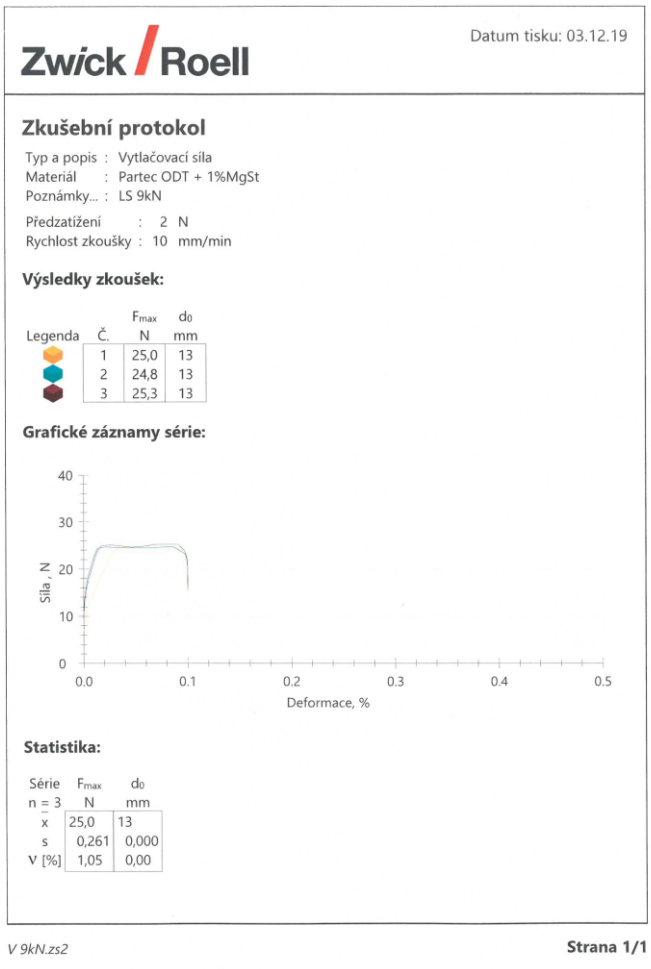
Suggestion for discussion

The function of lubricants in the tableting material, their mechanism of action, evaluation of their effectiveness.

Conclusion

Based on the obtained results, evaluate the effect of sodium stearyl fumarate concentration on the compressibility, the ejection force and the tensile strength of spray-dried lactose tablets at two compression forces.

Example of protocol – the measuring of ejection force:



Zwick / Roell

Datum tisku: 03.12.19

Zkušební protokol

Typ a popis : Vytlačovací síla
Materiál : Partec ODT + 1%MgSt
Poznámky... : LS 9kN

Předzatížení : 2 N
Rychlost zkoušky : 10 mm/min

Výsledky zkoušek:

Legenda	Č.	F_{max} N	d_0 mm
	1	25,0	13
	2	24,8	13
	3	25,3	13

Grafické záznamy série:

Statistika:

Série n = 3	F_{max} N	d_0 mm
x̄	25,0	13
s	0,261	0,000
v [%]	1,05	0,00

V 9kN.zs2

Strana 1/1