Compaction and Structural-Mechanical Properties of Tablets as a Function of Volume Ratios of Excipients

Valentyn Mohylyuk[1], **Artūrs Paulausks**[1], **Oskars Radzins**[2,3] and **Liga Lauberte**[1]

[1] Laboratory of Finished Dosage Forms, Faculty of Pharmacy, Rīga Stradiņš University, LV-1007 Riga, Latvia; valentyn.mohylyuk@rsu.lv

[2] Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, LV-1658 Riga, Latvia;

[3] Department of Orthodontics, Institute of Stomatology, Rīga Stradiņš University, LV-1007 Riga, Latvia

RIGA STRADIŅŠ UNIVERSITY LABORATORY OF FINISHED DOSAGE FORMS

PBP WORLD MEETING

Introduction

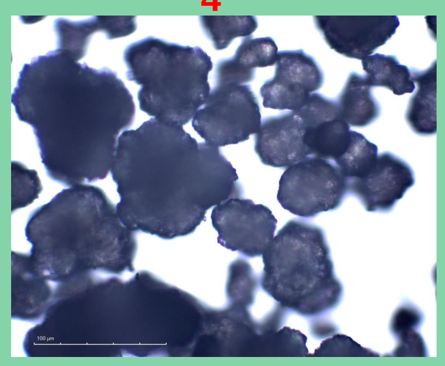
- Using in tablet formulations microcrystalline cellulose (**MCC**) with plastic behaviour and calcium phosphate anhydrous (**$CaHPO_4$**) with brittle behaviour under compaction is very popular in the pharmaceutical industry for achieving desirable structural-mechanical properties of tablets.
- **The aim of this study** was to investigate the compaction properties of mixtures of MCC and $CaHPO_4$ in different volume ratios at the range of compaction pressure to observe and explain the influence of mixture composition on the structural-mechanical properties.

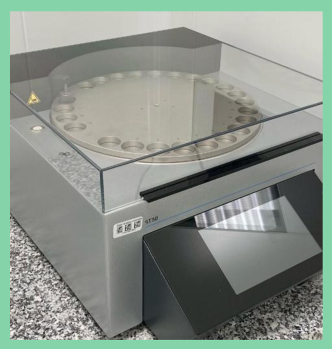
Materials

- MCC (CEOLUS UF-711; Asahi Kasei, Japan)
- CaHPO4 (DI-CAFOS A60; Budenheim KG, Germany)
- Silica (SYLOID® 244FP; Grace GmbH, Germany)
- Sodium stearyl fumarate (PRUV®; JRS Pharma, Germany)

MCC

$CaHPO_4$





Methods

- Powder mixtures (Table 1) were tableted with **11.28 mm** flat punches to obtain **500 mg** tablets using a **compaction simulator** (**STYL'One Nano,** Medelpharm, France).
- Compression cycles simulated **small rotary press** at tableting speed of **70 rpm** with pre-compaction force of **5 MPa** and compaction force of **10-50 MPa**.
- The **powder feeding** into the die was performed automatically via the feed shoe.
- The tablet height (t),diameter (d), and **hardness** (F) were measured (n=10) by a tablet tester (ST50 WTDH; SOTAX AG, Switzerland) immediately after the compaction and converted into **tensile strength** (MPa).
- The **calculated true density** of composition was obtained based on the true density (ρt) of components and their shares (x, w/w) using the **additive methodology**:

$$\rho_t = (\rho_{exc\,1} \cdot x_{exc\,1}) + (\rho_{exc\,2} \cdot x_{exc\,2}) + \cdots + (\rho_{exc\,i} \cdot x_{exc\,i})$$

- For **in-die Heckel plot**, the **relative density ln(1/ε)** was calculated with Alix software (Medelpharm).
- **X-ray Micro-Computed Tomography** (**μCT**) of samples has been done with a 3D Micro X-ray CT (CT Lab HX; Rigaku Corp., Japan) at 70 kV with a current of 50 μA, focus set on S, and with no filter.
- CT scan were exported and processed with Dragonfly soft (Object Research Systems Inc., Canada).

Table 1

Ingredients	True density	F 100-0	F 75-25	F 50-50	F 25-75	F 0-100
	mg/mm³	w/w				
CEOLUS™ UF-711	1.586	0.977	0.608	0.346	0.151	0.000
DI-CAFOS® A60	2.890	0.000	0.369	0.631	0.826	0.977
PRUV®	1.110	0.020	0.020	0.020	0.020	0.020
SYLOID® 244FP	2.200	0.003	0.003	0.003	0.003	0.003
∑	NA	1.000	1.000	1.000	1.000	1.000
Calculated true density	NA	1.578	2.060	2.401	2.655	2.852
		Volume, %				
CEOLUS™ UF-711	NA	96.9	72.3	47.9	23.8	0.0
DI-CAFOS® A60	NA	0.0	24.1	47.9	71.4	94.6
PRUV®	NA	2.8	3.4	4.0	4.5	5.0
SYLOID® 244FP	NA	0.2	0.3	0.3	0.3	0.4
∑	NA	100.0	100.0	100.0	100.0	100.0

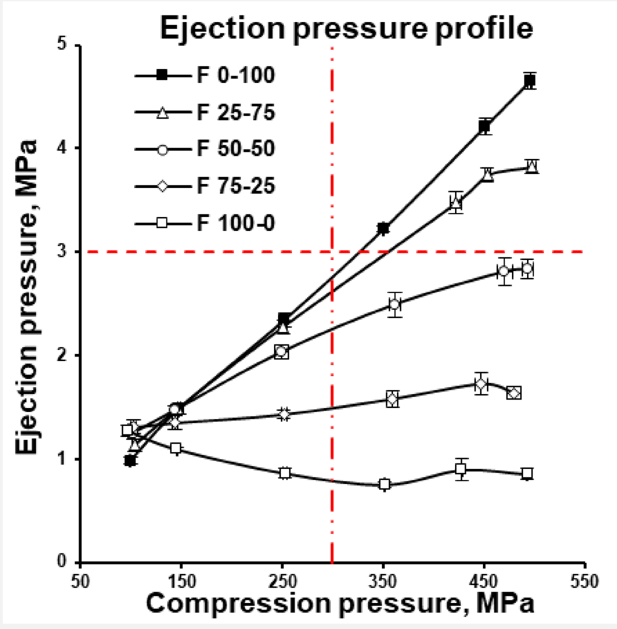


Fig. 1

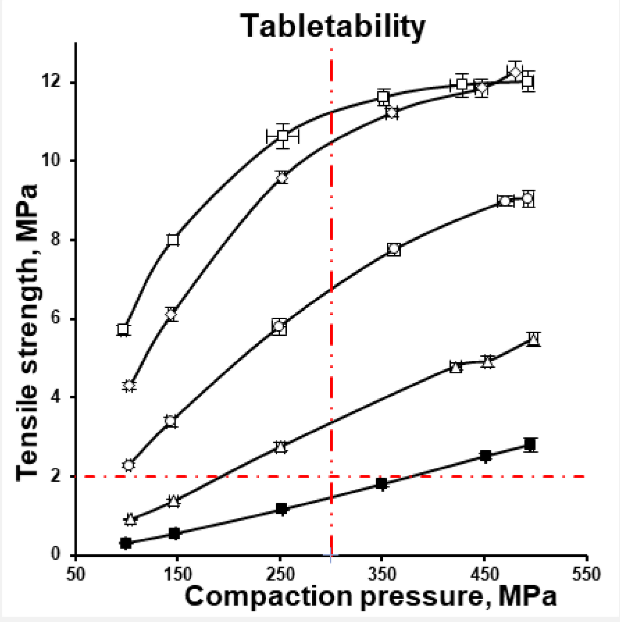


Fig. 2

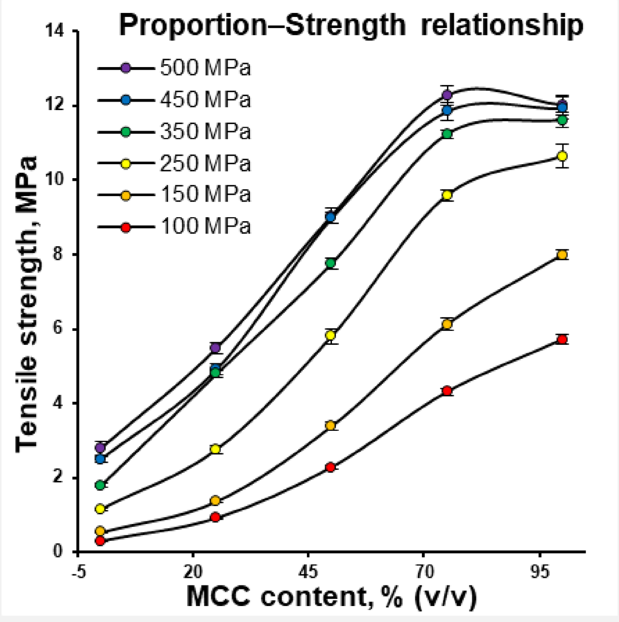


Fig. 3

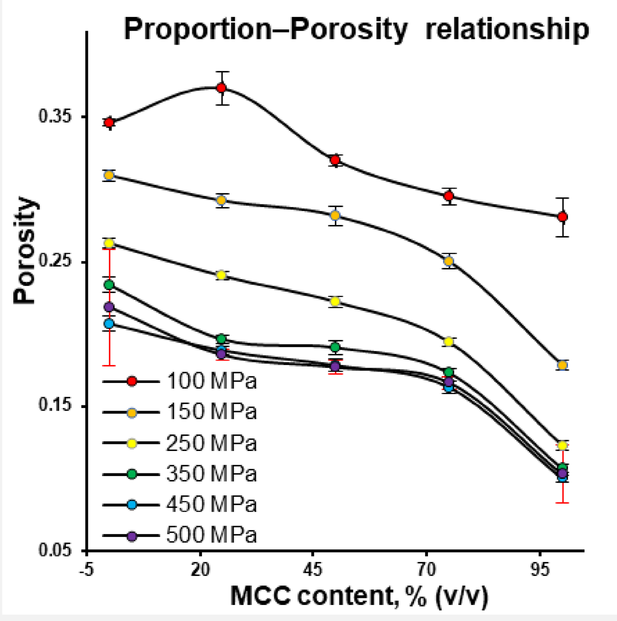


Fig. 4

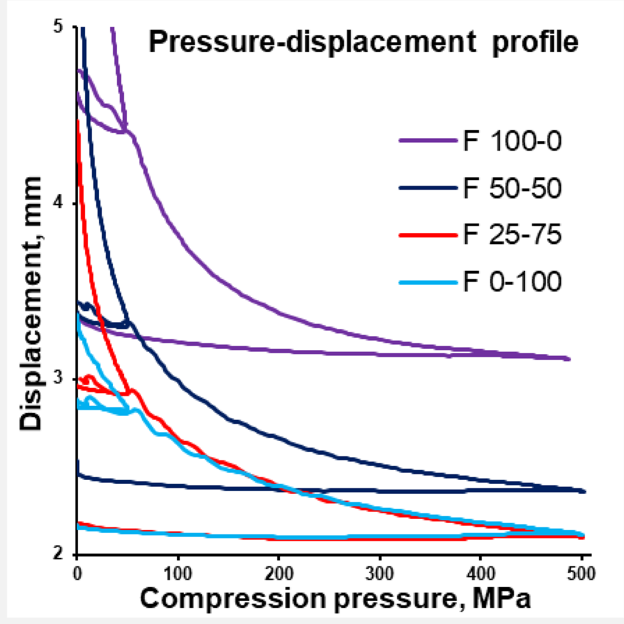


Fig. 5

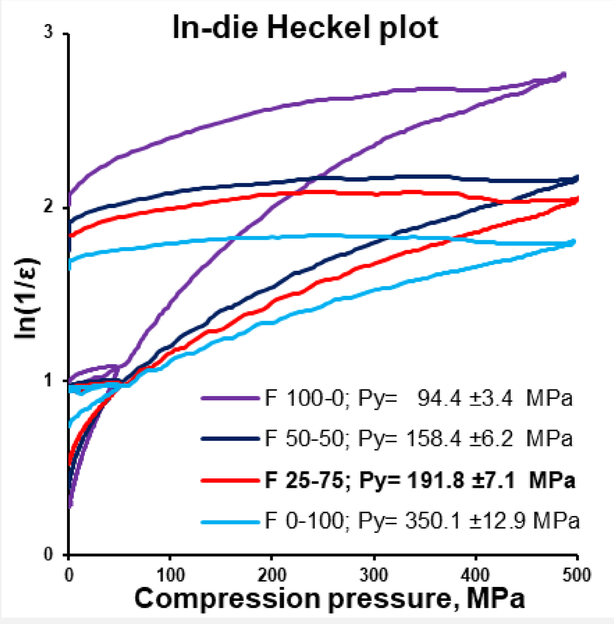


Fig. 6

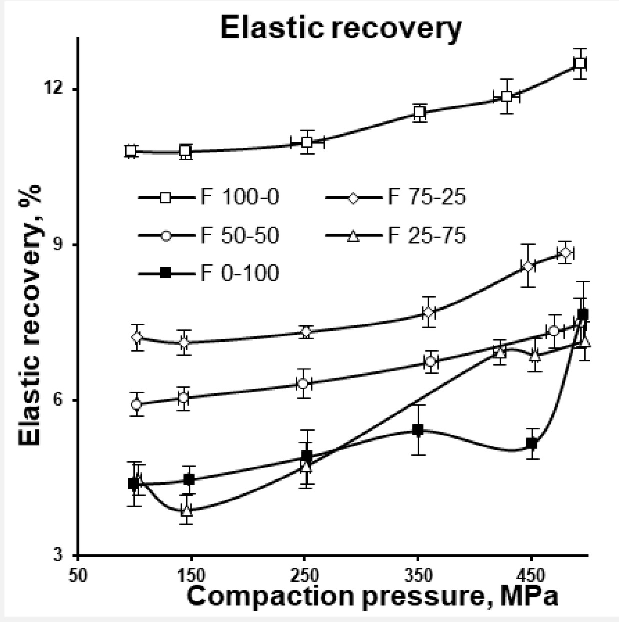


Fig. 7

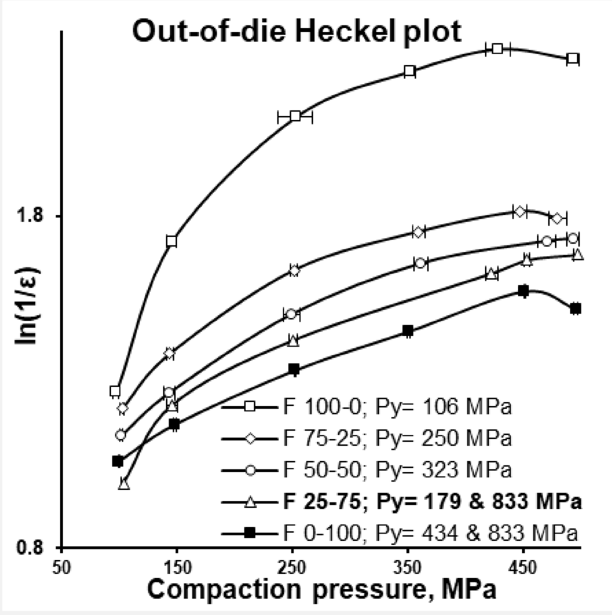


Fig. 8

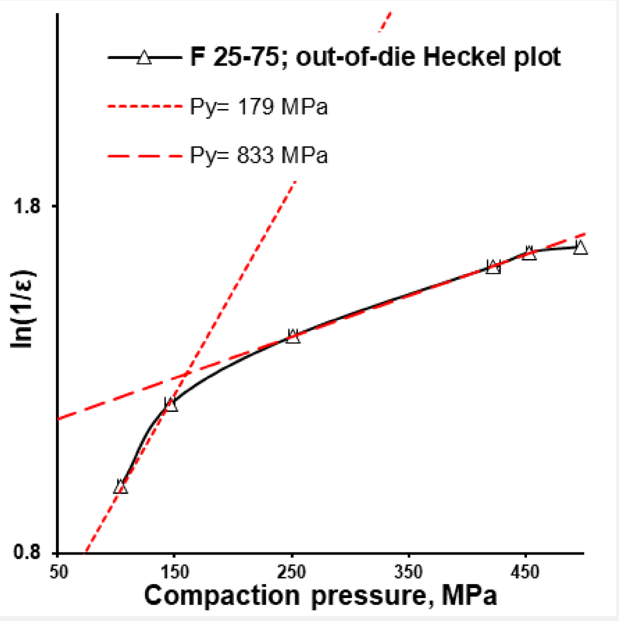


Fig. 9

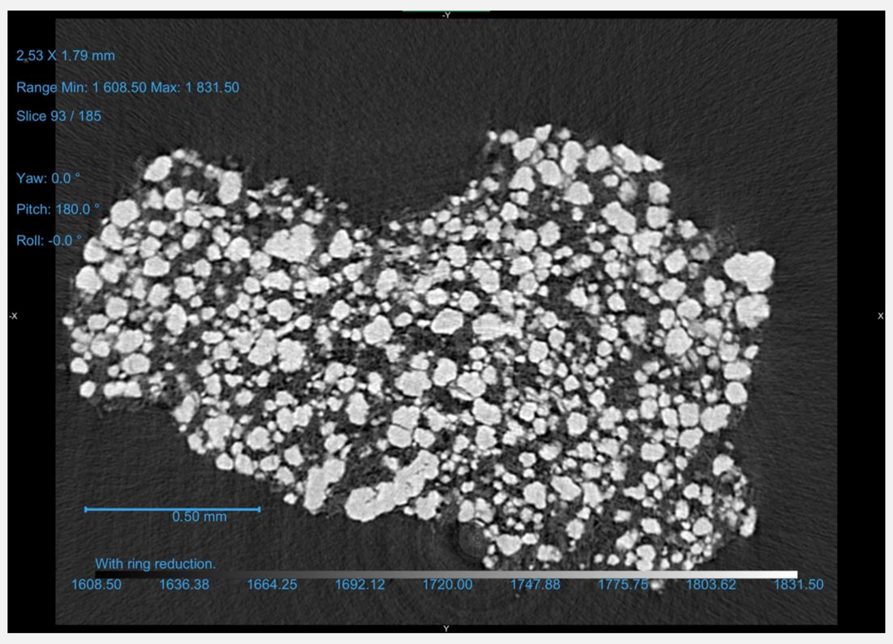


Fig. 10A: F 25-75 @ 100 MPa

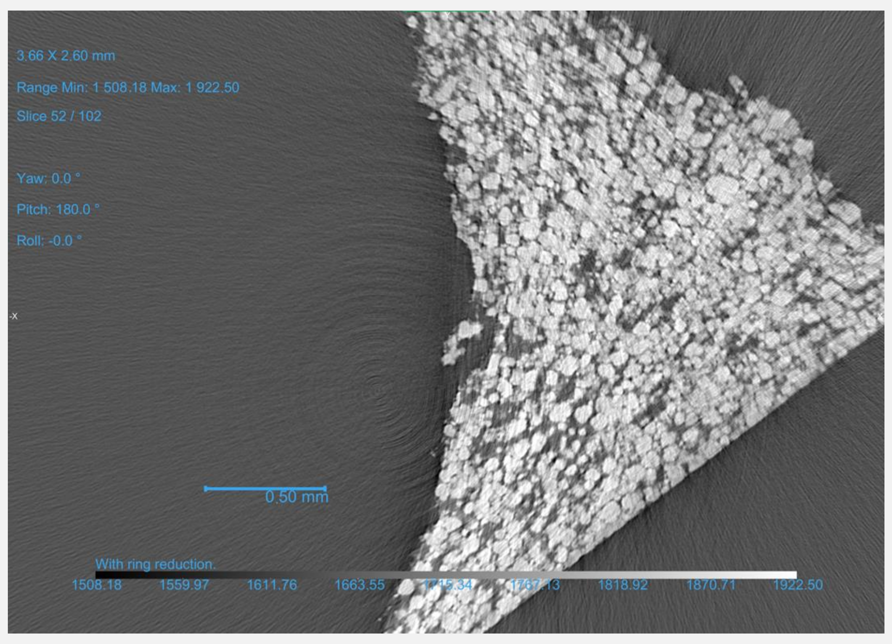


Fig. 10B: F 25-75 @ 450 MPa

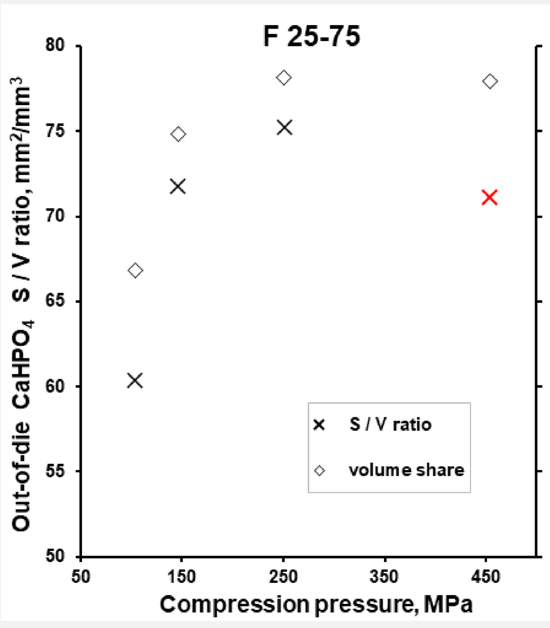


Fig. 11

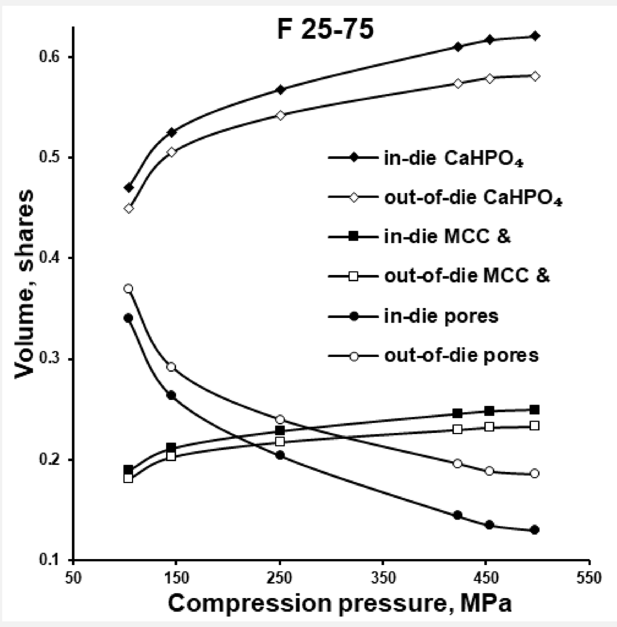


Fig. 12

Results

- Lubricant amount was justified by the tablet ejection force profile (**Fig. 1**)
- Tensile strength increased along with MCC fraction and compaction pressure (**Fig. 2**)
- Proportion–tensile strength profiles in the 25-75 vol.% MCC range is almost linear (**Fig. 3**)
- Proportion–porosity profiles in the same 25-75 %vol. MCC range is almost linear (**Fig. 4**)
- Punches' distance is smaller, tablets are thinner because of the true $CaHPO_4$ density (**Fig. 5**)
- Increasing $CaHPO_4$ portion has increased the in-die yield pressure - Py (**Fig. 6**)
- Increase in the MCC portion increased the value of elastic recovery (**Fig. 7**)
- Out-of-die was in line with in-die Heckel plot except for F25-75 (**Fig. 8**)
- Out-of-die Heckel plot of F25-75 at 100-150 and 150-500 MPa cause of MCC and $CaHPO_4$ (**Fig. 8-9**)
- μCT 100 vs 450 MPa (**Fig. 10**); Comparison of processed μCT data (**Fig. 11**) vs. calculated (**Fig. 12**)

Discussion & Conclusion

- F100-0, F75-25 and F50-50 were in the Successful Formulation Window (**Fig. 1-2**)
- Non-linear segments can be related to the percolation threshold (**Fig. 3-4**)
- The plasticity and elastic recovery increase with increasing MCC (**Fig. 6-8**)
- F25-75 has the two-stage out-of-die Heckel plot (**Fig. 8-9**)
- 1st stage controlled by MCC and 2nd - by $CaHPO_4$ (**Fig. 8-9**)
- μCT can be useful for de-formulation (**Fig. 10-12**)

Mohylyuk V, Paulausks A, Radzins O, Lauberte L. *The Effect of Microcrystalline Cellulose–CaHPO₄ Mixtures in Different Volume Ratios on the Compaction and Structural–Mechanical Properties of Tablets*. Pharmaceutics. 2024;16(3), 10.3390/pharmaceutics16030362.

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