Mechanical properties of tablets: direct compression vs. twin-screw melt granulation with PEG 8000

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Introduction

- Replacing batch wet granulation with twin-screw melt extruder as a continuous solventless process is gaining popularity. **PEG 8000** being one of the most popular excipients used for melt granulation lacks thorough investigation regarding its effect on the mechanical properties of tablets. Along with PEG 8000, a mixture of microcrystalline cellulose (**MCC**) and calcium phosphate anhydrous (**$CaHPO_4$**) was chosen for granulation due to its unsatisfactory flowability.

- **This study aimed to** investigate the effect of PEG 8000 particle size and twin-screw melt granulation temperature on the properties of resultant MCC-$CaHPO_4$ granules and their tablets
- and to compare tablet mechanical properties of ungranulated (**DC**) and melt-granulated MCC-$CaHPO_4$

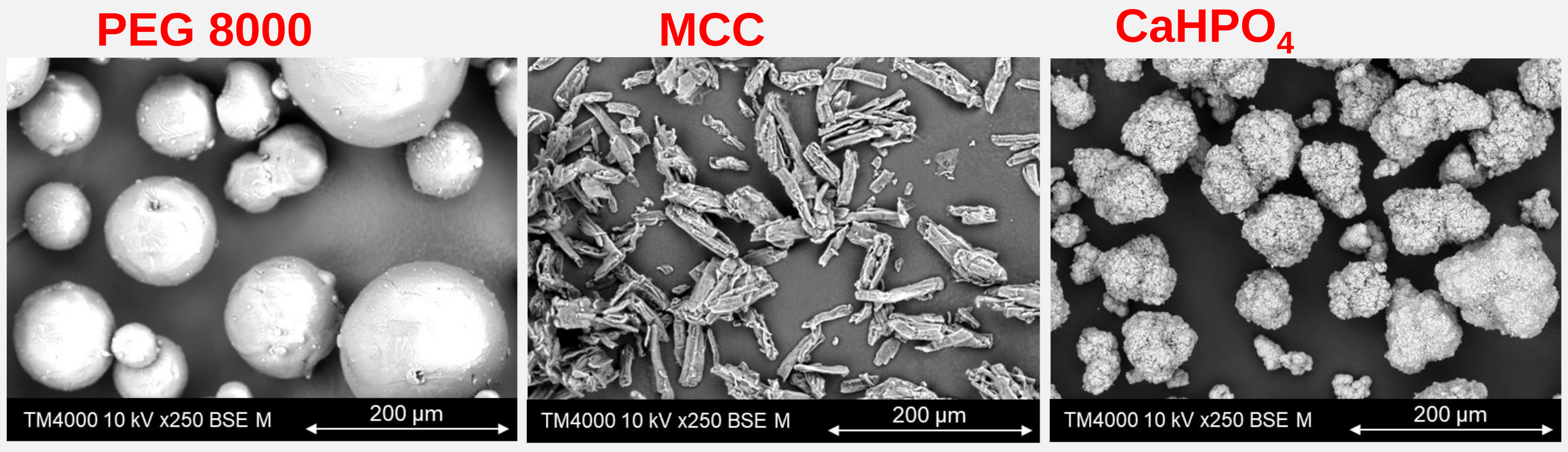
Materials

- MCC - **CEOLUS UF-711** (Asahi Kasei, Japan); $CaHPO_4$ - **DI-CAFOS A60** (Budenheim KG, Germany); PEG 8000 - **Kollisolv®** (BASF SE, Germany)
- Silica dioxide - **SYLOID® 244FP** (Grace GmbH, Germany) and Sodium stearyl fumarate - **PRUV®** (JRS Pharma, Germany) were used for directly compressed tablets (**DC**) where PEG 8000 was not used [1-2].

Methods [1-2]

- **Twin-Screw Melt Granulation** was carried out using a **Pharma 11** Extruder without nozzle, a Volumetric Mini Feeder, and a Conveyor (Thermo Electron Corp., Germany). The part of barrel that was used had a flighted length of 259mm and a diameter of 11mm with a length/diameter ratio (L/D) of 23.5:1. The screw design consisted of 1 L/D feed screw elements
- Ungranulated (incl. SYLOID® 244FP and PRUV®; without PEG 8000) [**1**] and melt granulated (**Table 1** [**2**]) tablets (D 11.28mm; flat punches; 500 mg) were prepared using a compaction simulator (**Styl'One Nano**, Medelpharm, France) simulating small rotary tablet press at 70 rpm; 50 MPa pre-compaction pressure and 100-250 MPa compaction pressure.
- The tablet thickness, diameter, and hardness, 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 on the true density (ρt) of components and their shares (x, w/w): $\rho t = (\rho_1 \cdot x_1) + (\rho_2 \cdot x_2) + \cdots + (\rho_i \cdot x_i)$
- For in-die Heckel plot, the relative density ***ln(1/ε)*** was calculated with Alix software (Medelpharm). The relative density and compaction pressure were plotted in accordance with the Heckel eq.: $ln(1/\varepsilon) = MPaK \cdot P + ln(1/\varepsilon 0) = K \cdot P + A$
- **Scanning Electron** (TM4000 Plus, Hitachi, Japan) and **optical** (BA410E, Motic, China) **microscopy** were used

PEG 8000 | MCC | $CaHPO_4$



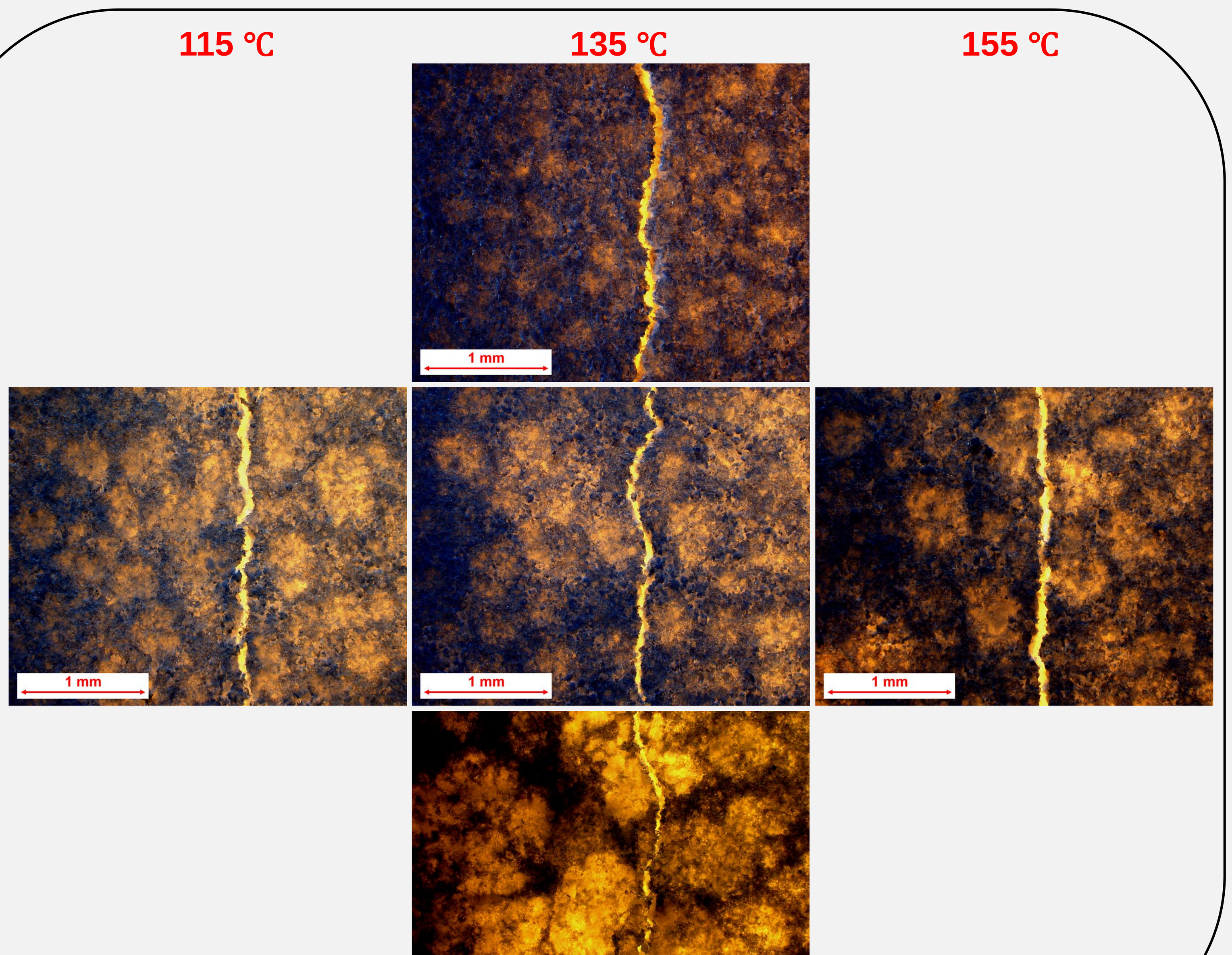


Fig. 2

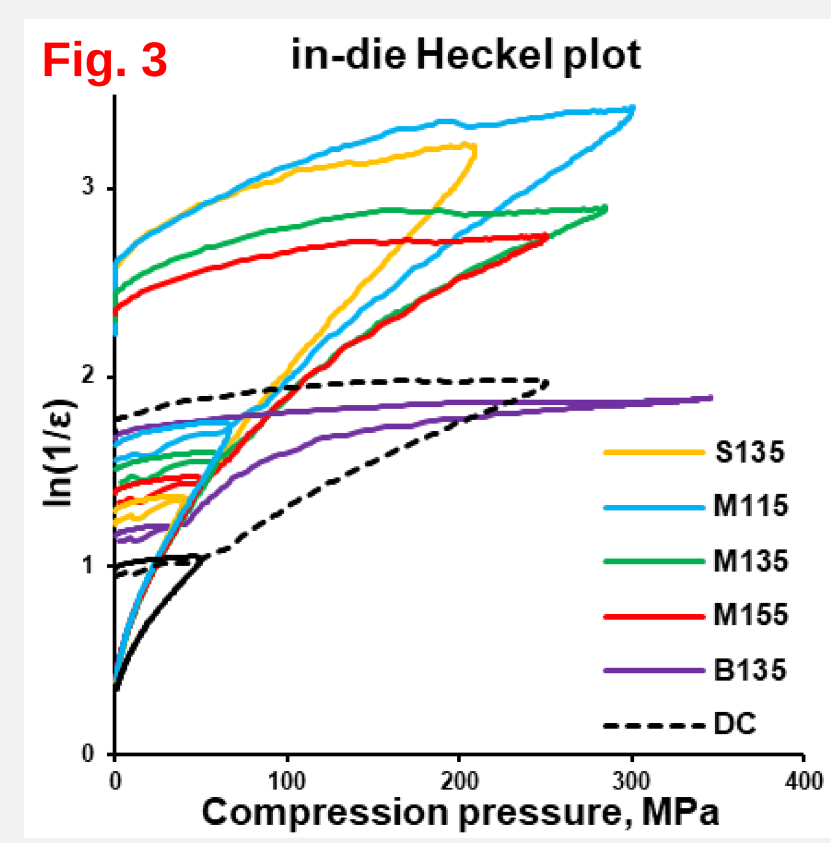


Fig. 3

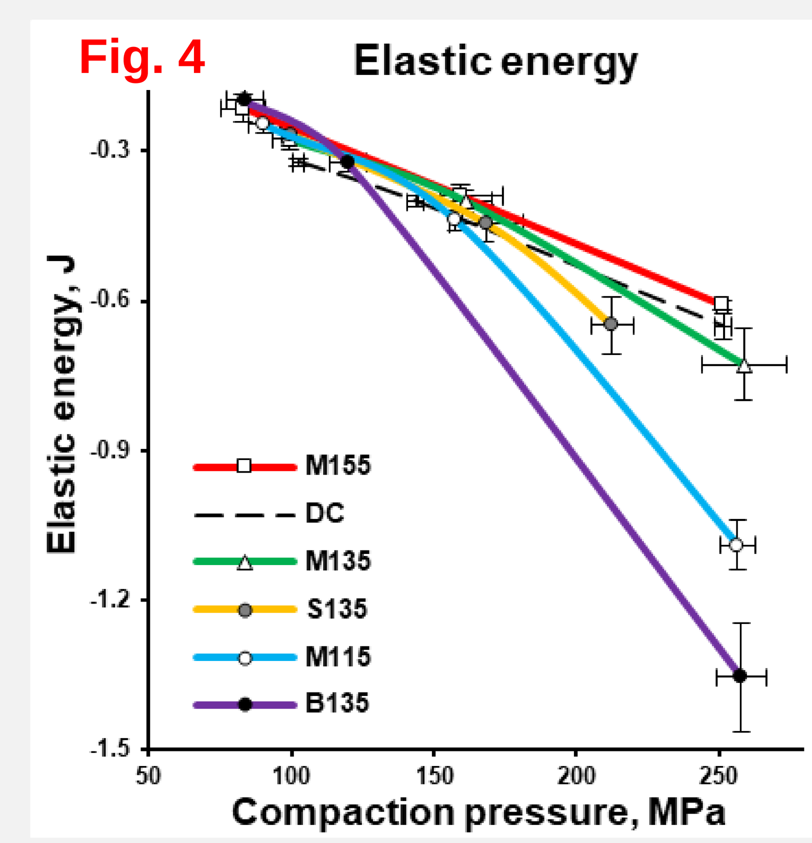


Fig. 4

Table 1

		S135	M115	M135	M155	B135
Formulation	MCC (wt.%)	56				
	$CaHPO_4$ (wt.%)	34				
	PEG 8000 0-200 µm (wt.%)	10	-	-	-	-
	PEG 8000 200-400 µm (wt.%)	-	10	10	10	-
	PEG 8000 400-500 µm (wt.%)	-	-	-	-	10
Processing parameters	Zone 1 (°C)	20				
	Zone 2 (°C)	80	70	80	90	80
	Zone 3 (°C)	**135**	**115**	**135**	**155**	**135**
	Zone 4 (°C)	**135**	**115**	**135**	**155**	**135**
	Zone 5 (°C)	60	60	60	60	60
	Feed rate (g/min)	1.582				
	Screw speed (rpm)	120				
	Torque (%)	2				

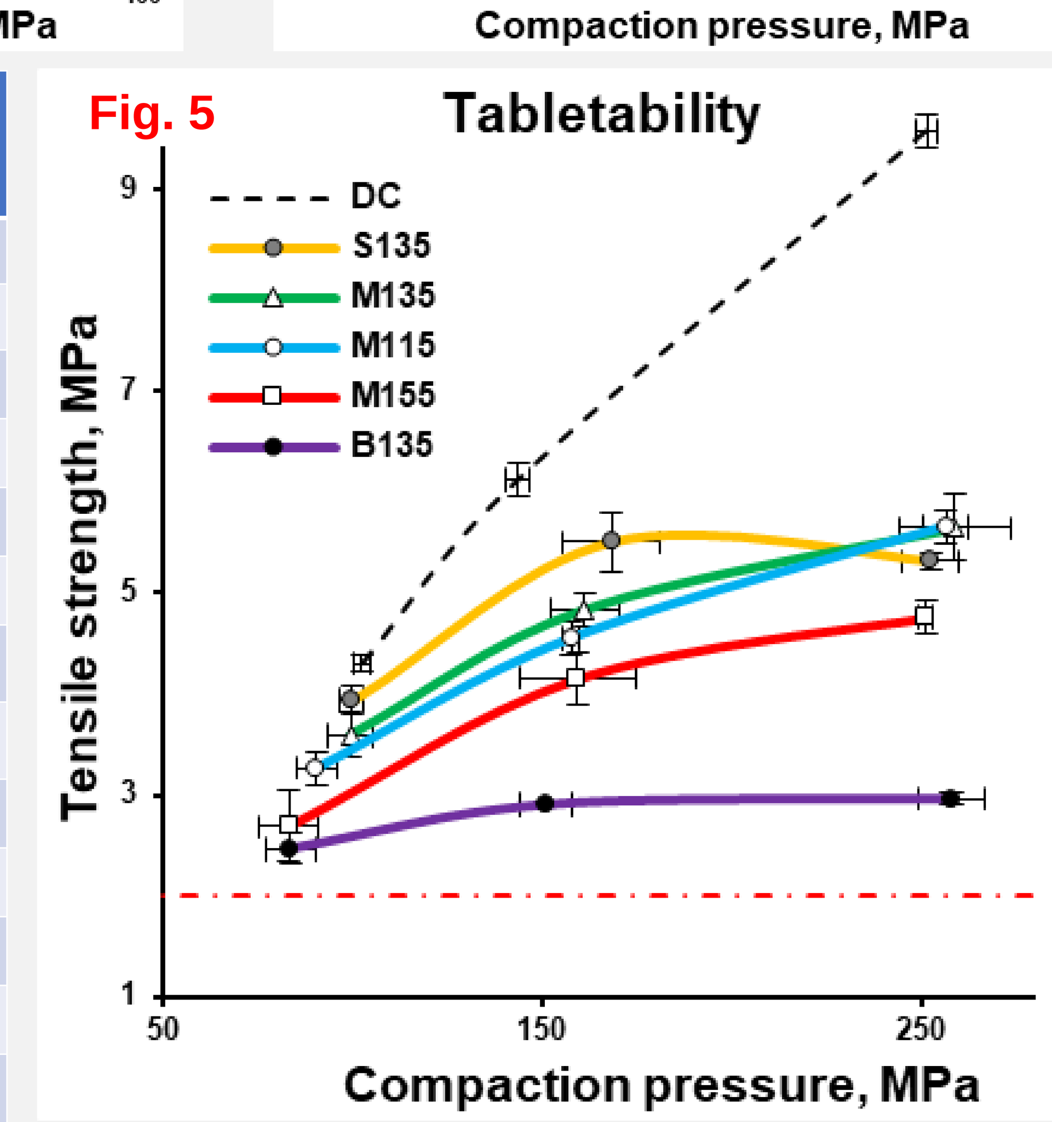


Fig. 5

Results

- The size of granules increased with increasing PEG 8000 particle size and granulation temperature
- Optical microscopy of tablets revealed the individual granules and their points of contact (**Fig. 2**)
- Raman mapping confirmed the location of components and their conformation according to the optical microscope images in **Fig. 2**.
- The plasticity of formulations increased with decreasing PEG 8000 particle size and with decreasing granulation temperature (**Fig. 3**).
- The elastic energy of formulations increased with increasing PEG 8000 particle size and granulation temperature (**Fig. 4**).
- Tabletability decreased with increasing PEG 8000 particle size and with increasing granulation temperature (**Fig. 5**).
- Tabletability of ungranulated material was higher than that of melt granulated.

Conclusion

- PEG 8000 particle size and granulation T℃ influenced the granule's properties
- Structure of granules influenced tablet structure (**Fig. 2**) & formulation plasticity (**Fig. 3**)
- Structure of granules, their plasticity, and structure of tablets influenced their mechanical properties (**Fig. 3-5**).
- Most plastic melt granulated formulations showed best tabletability (**Fig. 3, 5**).
- Melt-granulated formulations showed lower tensile strength compared to ungranulated directly compressed tablets (**Fig. 5**).

Ref.1: Mohylyuk V, Paulausks A, Radzins O, Lauberte L. *The Effect of Microcrystalline Cellulose–$CaHPO_4$ Mixtures in Different Volume Ratios on the Compaction and Structural–Mechanical Properties of Tablets*. Pharmaceutics. 2024;16(3), DOI: 10.3390/pharmaceutics16030362.
Ref.2: Horváth ZM, Lauberte L, Mohylyuk V. *Twin-Screw Melt Granulation with PEG 8000: effect of binder particle size and processing temperature on the granule and tablet properties*. Adv Powder Technol, 2024. 35(9), DOI: 10.1016/j.apt.2024.104585..

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