FACULTY OF PHARMACEUTICAL SCIENCES

LABORATORY OF PHARMACEUTICAL TECHNOLOGY

EFFECT OF BINDER TYPE AND LUBRICATION METHOD ON THE BINDER EFFICACY FOR DIRECT COMPRESSION

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1. Introduction

- Addition of a **binder** to a direct compression formulation to increase tablet tensile strength and prevent tablets defects.
- **Internal blending of magnesium stearate** (MgSt) is often associated with decreasing tensile strengths and increasing disintegration times.
  ➔ Minimizing these negative effects with **external lubrication.**

2. Objective

- Investigation of the **effect** of different **binders** and **lubrication method** on ejection force, tablet tensile strength and disintegration time of tablets produced through direct compression.
- Linking **binder properties** to tablet tensile strength and disintegration behavior, applying partial least square (PLS) analysis.

3. Material & Methods

STYL'One Evolution compaction simulator (Medelpharm)

- **Formulations: filler + binder**
  - Fillers: anhydrous dicalcium phosphate (DCP), lactose monohydrate and microcrystalline cellulose (MCC)
  - Binders:

Binder	Brand name	Abbreviation
Hydroxypropyl cellulose	Klucel® EF	KEF
Hydroxypropyl cellulose	Klucel® EXF	KEXF
Povidone	Kollidon® K30	K30
Copovidone	Kollidon® VA64	VA64
Copovidone	Kollidon® VA64F	VA64F
Microcrystalline cellulose	Avicel® PH105	PH105
Microcrystalline cellulose	Avicel® PH200	PH200
Hydroxypropyl methylcellulose	Methocel® E15	E15
Partially pregelatinized maize starch	Starch1500®	S1500
Native maize starch	/	NMSt

Table 1. Overview of the used binders.

  - Binder concentration: 0 (pure filler), 10, 20 and 30%
  - Lubrication method:
    - Internal lubrication (IL) (0.75% MgSt)
    - External lubrication (EL) using MgSt as lubricant

- **Raw material characterization**
  - Particle size distribution: dv10, dv50, dv90
  - Powder density and porosity: bulk density (ρb), tapped density (ρt), Hausner Ratio (HR), compressibility index (CI), true density (ρtrue), powder bed porosity (ε_p)
  - Ring shear tester: flow function coefficients (ffc, ffp, ffrho), wall friction angle (WFA)
  - Loss on drying (LOD)
  - Compaction properties: specific work of compaction (SpecWComp), plasticity factor (PF), elasticity, cohesion index, tablet porosity (ε_t), tablet brittleness index (TBI)
  - Wettability: contact angle (CA) (CA_t0, CA_t30)
  - Water binding capacity (WBC)

- **Responses**
  - Ejection force
  - Tensile strength
  - Disintegration time (pure filler and filler + 20% binder)

4. Results

Pure fillers

Tensile strength:

➢ Lactose and MCC: reduced tensile strength when applying internal lubrication
⇔ no effect of lubrication method for DCP ➔ Use of DCP to study lubricant sensitivity of binders

➢ Lubricant sensitivity can be explained by the compaction properties (brittle versus ductile deformation).

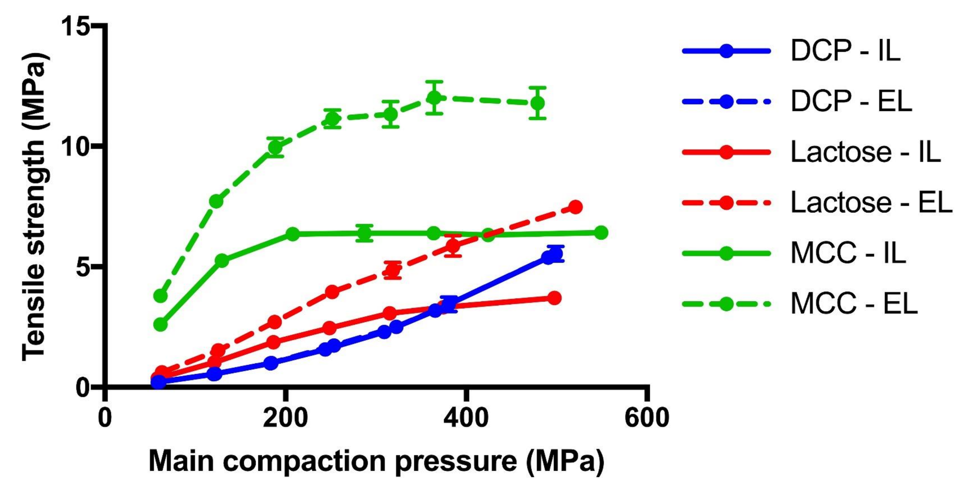

Figure 1. Tensile strength (right) of MCC (green), lactose (red) and DCP (blue), applying internal (solid line) and external lubrication (dashed line).

Filler	SpecWComp (J/g)	TBI
DCP	18	237
Lactose	24	123
MCC	32	37

Table 2. Compaction properties of the fillers.

Filler + binder

Ejection force:

➢ Inclusion of a binder: reduction of the ejection forces compared to tablets composed of pure filler.

➢ Higher binder concentration: further decrease in ejection forces.

➢ Similar ejection forces were obtained for internal and external lubrication.

Tensile strength:

➢ Effective binder concentration was depending on filler, binder type and lubrication method.

➢ Lubricant sensitivity was observed for all binders but to a different extent.

➢ The highest tensile strength was obtained with VA64F and PH105 whereas low tensile strengths were observed for E15 and S1500.

➢ PLS analysis and interpretation of the raw material dataset revealed that compaction properties (i.e. SpecWComp, PF, elasticity and cohesion index) and particle size were the most predominant factors affecting the tensile strength.

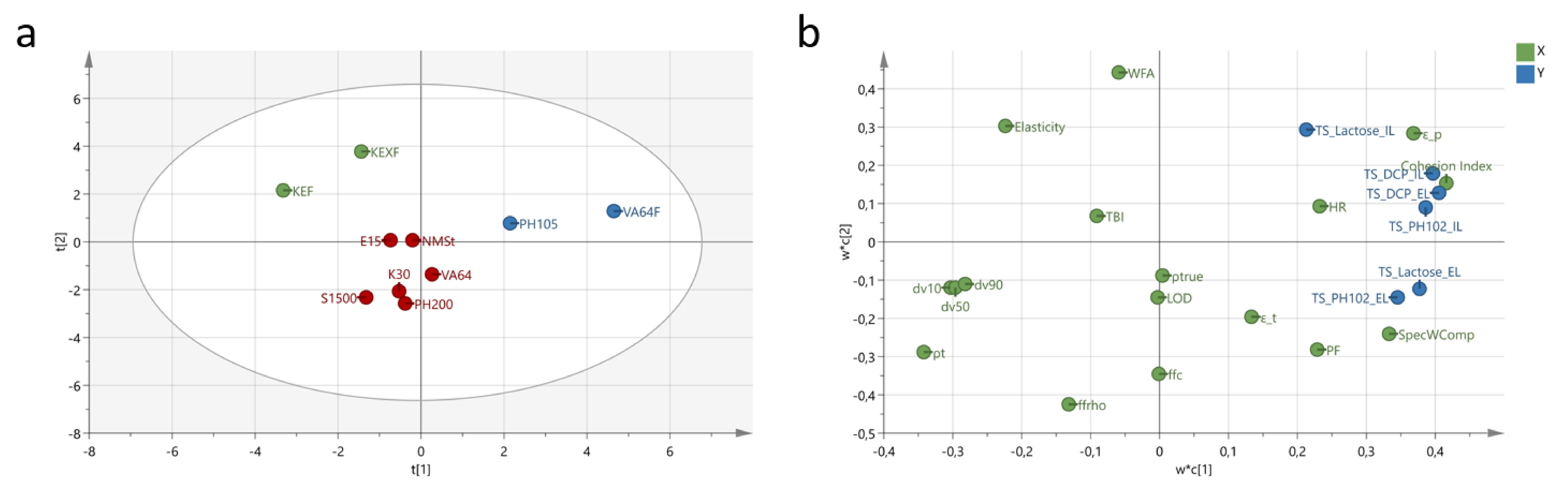

Figure 2. PC1 versus PC2 score scatter plot (a) and loading scatter plot (b) of the tensile strength (TS) model. Binder clusters are visualized in different colors.

Disintegration time:

➢ Filler and binder type were most predominant on disintegration while the effect of lubrication method was limited.

➢ Three binder clusters were identified through PLS analysis:
(i) S1500, NMSt, PH105 and PH200, (ii) K30, VA64, VA64F and E15 and (ii) KEF and KEXF corresponding to fast, slightly delayed and delayed disintegration, respectively. Similar binder clusters can be distinguished in Figure 3.

➢ Wettability measurements correlated well with the disintegration behavior of the binders and can therefore be used as an indicative measurement for disintegration.

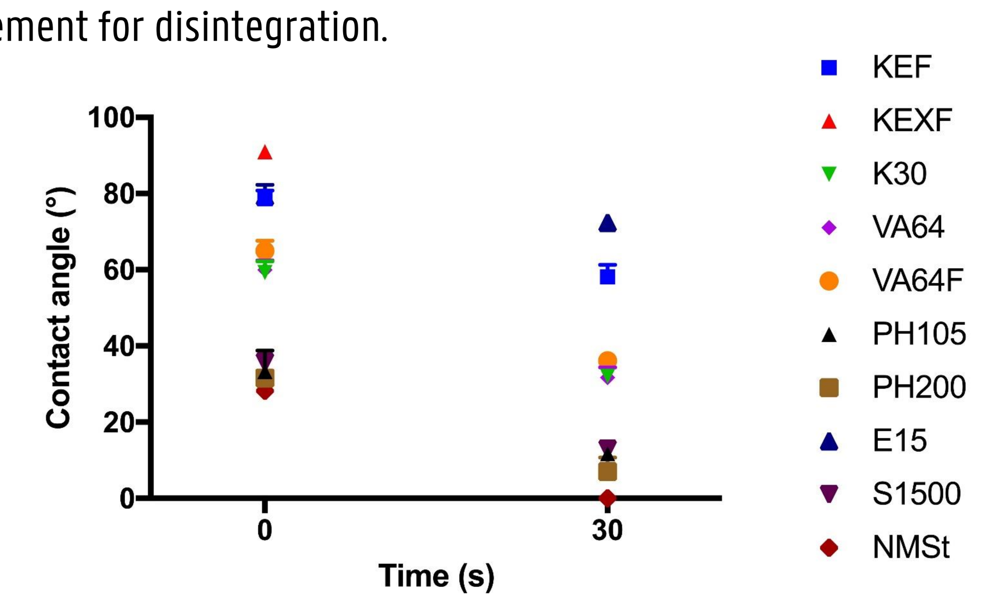

Figure 3. Contact angle (CA) of the pure binder tablets measured immediately after a drop of demineralized water touched the tablet surface (CA_t0) and after 30 s (CA_t30).

5. Conclusion

- Addition of a binder to a direct compression formulation impacted the ejection forces, tensile strength and disintegration.
- Compaction properties (high SpecWComp, high cohesion index, low elasticity) and smaller particle size were the most influential properties for increasing the tensile strength. Poor wettability (high CA) was indicative for prolonged disintegration.
- The choice of binder type for direct compression should be carefully selected as the effect on tensile strength and disintegration time will be different based on the binder properties.

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