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Objective

The aim of this study is to compare the compaction properties of granulated lactose with three types of superdisintegrants (with different mechanisms of actions¹) using the process of direct compression. The impact of granulometry of one of the disintegrant has also been studied.

Materials and Methods

Excipients

- **Diluant** : Granulated lactose (EXCIPRESS™ GR150, Armor Pharma)
- **Disintegrants** (JRS PHARMA) :
 - VIVAPHARM® PVPP-XL (Crospovidone, cross-linked polymer²)
 - VIVAPHARM® PVPP-XL-10 (Crospovidone, cross-linked polymer²)
 - VIVASOL® (Croscarmellose Sodium, cross-linked cellulose²)
 - EXPLOTAB® (Sodium Starch Glycolate, cross-linked starch²)
- **Lubricant** : Magnesium stearate (LIGAMED MF-3-V, Peter Greven)

Blending

Blend Name	Type of lactose	Lubricant ratio (%)	Disintegrant ratio (%)
Blend 1	EXCIPRESS™ GR150	0.5	0
Blend 2,3,4,5		0.5	3.5

Table 1. Composition of the blends

The lactose and disintegrants (blends 2 to 5) were mixed with a low-shear blender Turbula (T2F, WAB) for 5 min at 49 rpm.

All the blends were then lubricated with the Turbula for 6.5 min at 23 rpm (same conditions than lactose lubrication).

Tableting

- Compression simulator (STYL'One Nano, MEDELPHARM)
- Compression pressures: 50, 100, 200 and 300MPa
- Profile simulated: Small Rotary Press
- Punches: round flat, diameter: 11.28 mm
- Tablet weight: 500mg

Tablets Characterization

- Breaking force : MT50 Std FT (Sotax)
- Disintegration time : DT50 (Sotax), T = 37°C, Demineralized Water
- Friability : FT2 (Sotax)

Results

Lactose and Disintegrants Characterization

Granulated lactose consists of agglomerates of primary lactose fine particles.

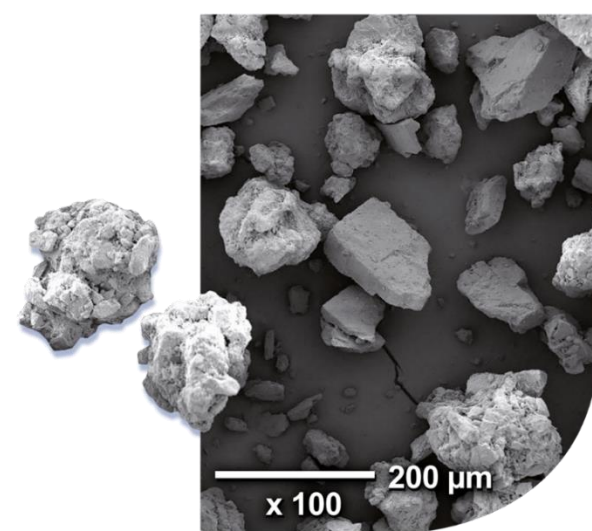


Figure 1. SEM images of Granulated lactose

The shape (Figure 1) and the Particle Size Distribution of granulated lactose (Table 2) enable a very good flowability.

Type of excipient	x ₁₀ (µm)	x ₅₀ (µm)	x ₉₀ (µm)
EXCIPRESS™ GR150	61	150	312
VIVASOL®	16	37	86
EXPLOTAB®	21	41	71
VIVAPHARM® PVPP-XL	41	120	222
VIVAPHARM® PVPP-XL-10	14	37	76

Table 2. Particle Size Distribution (Malvern 3000, wet, for information)

Tabletability

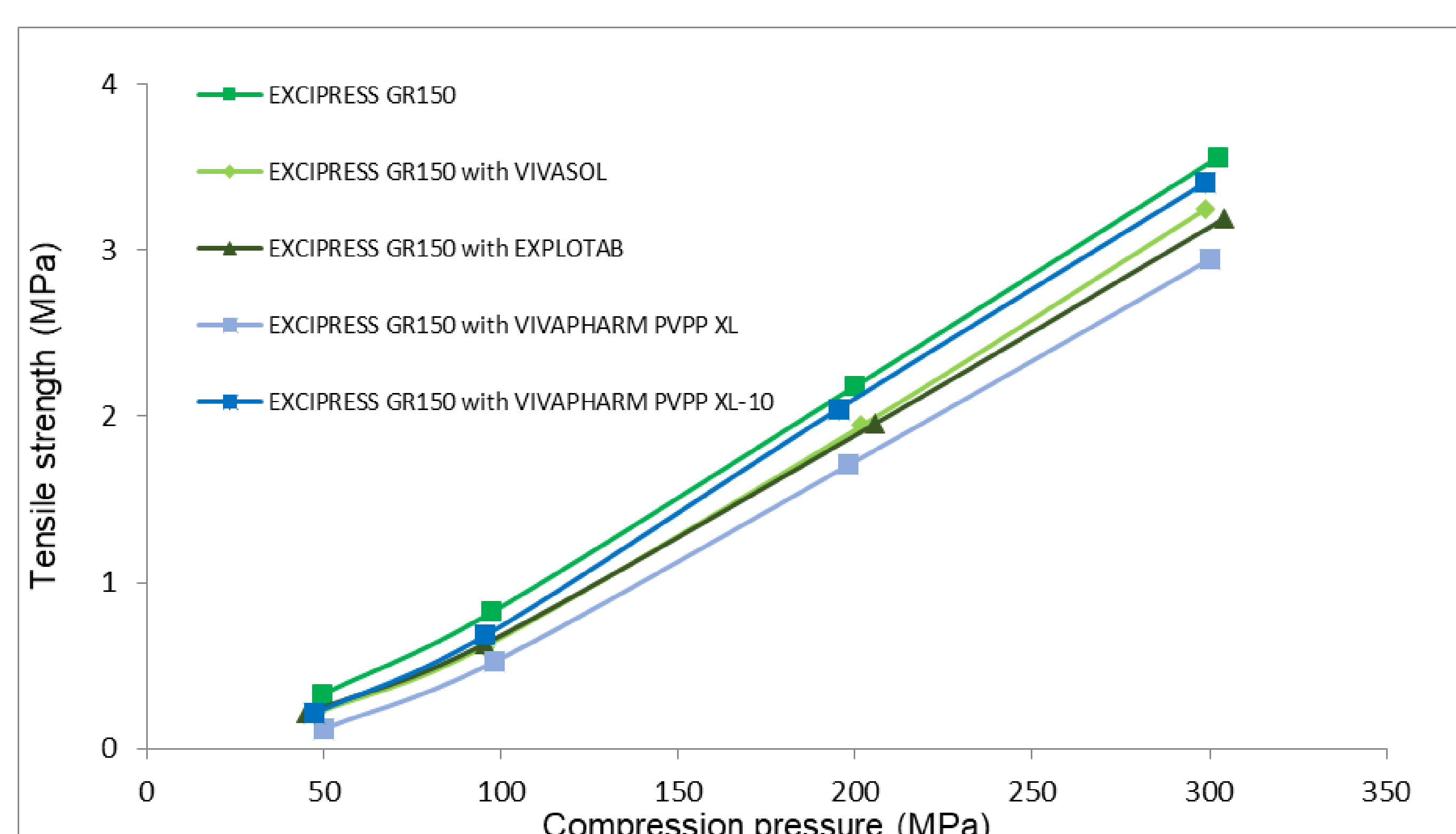


Figure 2. Tabletability profile of granulated lactose with superdisintegrants

When adding a disintegrant to granulated lactose by direct compression, the tabletability of the formulation is slightly decreasing except with VIVAPHARM® PVPP XL-10 (see Figure 2). The concentration of the disintegrant could have an impact on this phenomenon. The tabletability could be slightly lower with a higher concentration of disintegrant.

However finer particles of Crospovidone enables to maintain the same tabletability as with EXCIPRESS™ GR150 comparing to larger particles.

Disintegration time (DT)

When adding a disintegrant to granulated lactose, the disintegration time is decreasing below 2 minutes for all types of disintegrants (Table 3).

Blend Name	Disintegrant	DT 200 MPa	Friability (%) 200 MPa
Blend 1	-	4.1 min	0.5
Blend 2	VIVASOL®	1.4 min	0.6
Blend 3	EXPLOTAB®	1.9 min	0.5
Blend 4	VIVAPHARM® PVPP-XL	1.4 min	0.5
Blend 5	VIVAPHARM® PVPP-XL-10	1.9 min	0.5

Table 3. Tablets disintegration time (DT) and friability

Conclusion

At a concentration of 3.5% with a granulated lactose EXCIPRESS™ GR150 using the direct compression process, the disintegration times of the tablets with the three types of disintegrants are reduced significantly (< 2 min at 200MPa). A finer size of Crospovidone enables to keep the same tabletability as granulated lactose.

In conclusion the three types of disintegrants could be used with granulated lactose using direct compression.

REFERENCES

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2. Rowe R. C.; Sheskey P. J.; Quinn, M. E.; Handbook of Pharmaceutical Excipients, 6th Edition (2009).