

# Impact of the lubricant mixing time on the compactibility and disintegration time for mannitol compacts

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## INTRODUCTION

- Impact of magnesium stearate (MgSt) mixing conditions on the compaction behavior and disintegration time for a textured mannitol compacts.
- Mannitol:
  - Synthetically produced, hydrogenation or fermentation<sup>1,2</sup>.
  - Naturally present in certain plants, extraction from algae.
  - Mainly as diluent in tablets, capsule or freeze-dried formulations, or as a drug carrier in dry powder inhalers<sup>3,4</sup>.
  - Low moisture content and non hygroscopic character, use with active ingredients that are sensitive to moisture.

### TABLET PRESS SIMULATOR:

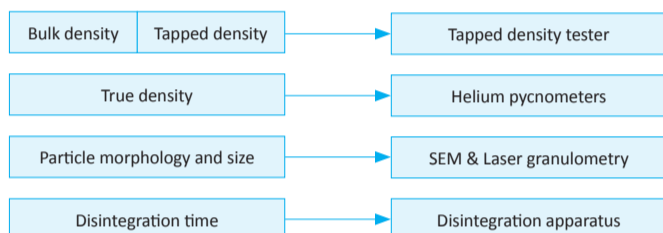
- Stylcam 200 R press simulator (MEDELPHARM FRANCE) :
  - A rotary single punch tablet press.
  - Simulate the compression profiles of various rotary tablet presses.
  - Strain gauges and potentiometric displacement transducers on the upper and lower punch.
  - Variation of the velocities of compaction.
  - Including pre-compression before the main compression.

## MATERIALS & METHODS

### PRODUCTS:

- Textured mannitol (PEARLITOL® 200 SD, Roquette Frères).
- Magnesium stearate (MgSt) (Wiga-Pharma GmbH).

### PARTICLE CHARACTERIZATION:



### COMPACTION STUDIES:

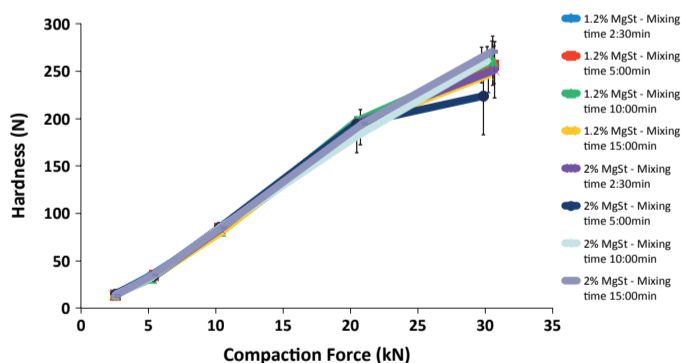
PEARLITOL® 200 SD	Magnesium Stearate	Mixing time	Punch Velocities	Tablet mass	Punch	Compression Profile
1	1.2%	2.5 min	30 tabs/min	400mg	Euro B Flat 11.28mm	STYLCAM
2	1.2%	5 min				
3	1.2%	10 min				
4	1.2%	15 min				
5	2%	2.5 min				
6	2%	5 min				
7	2%	10 min				
8	2%	15 min				

## RESULTS & DISCUSSION

Bulk density (g/cm <sup>3</sup> )	Tapped density (g/cm <sup>3</sup> )	Compressibility Index	Hausner's Index	True density (g/cm <sup>3</sup> )	Particulate size (D50 μm)
0.517	0.576	10	1.11	1.48	161.7

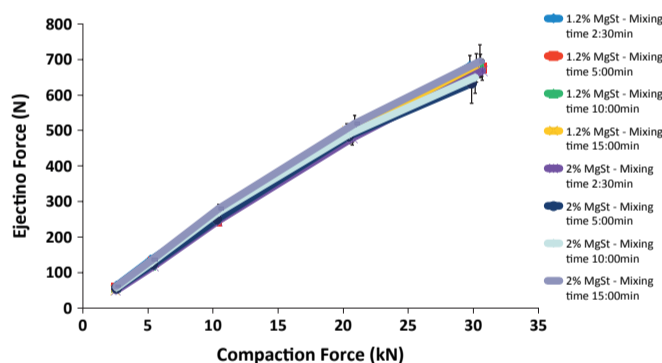
According to the European Pharmacopeia<sup>5</sup> and considering the calculated Carr's and Hausner's indexes, this powder flowability is considered as excellent.

Figure 1. Impact of lubricant mixing time on the compactibility for two lubricant ratios.

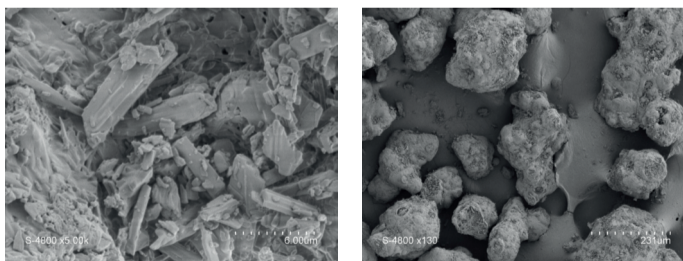


- No difference in compactibility is observed when lubricated with 1,2 or 2% MgSt.
- Furthermore, lubricant mixing time have no impact on the compactibility.
- Sample variation starts to increase at 30 kN compaction force
- MgSt doesn't hinder interparticulate interactions with PEARLITOL® 200 SD.

Figure 2. Impact of lubricant mixing time on the injection force for two lubricant ratios.

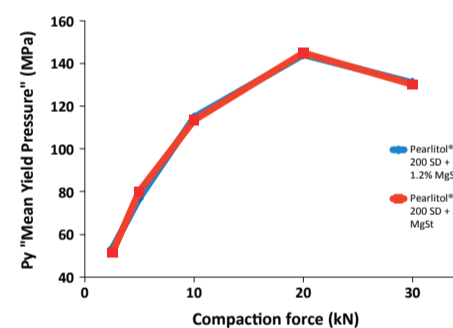


- For different ratios and mixing times, no difference in ejection forces is observed over the range of 2.5 to 30 kN.
- Minimum lubrication tested conditions (1.2% ; 2:30 min) is sufficient for good tablet ejection.



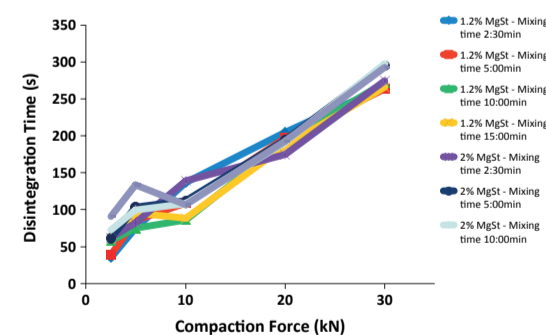
SEM's pictures show spherical particles of agglomerated mannitol crystals. Spherical morphology also contributes to the good flowability as determined previously.

Figure 3. Variations of Py vs compaction force.



- Mean yield pressure:  $P_y = 1/k$  (derived from the Heckel equation).
- Increases proportionately with compaction force up to 20 kN. After which  $P_y$  starts to decrease.
- The particles deformation of mannitol is mainly brittle with high  $P_y$  between 10 and 30 kN.
- The lack of lubricant influence and high  $P_y$  values are characteristic of brittle material.

Figure 3. Disintegration time at different lubricant mixing time and ratio.



- Disintegration time increases with compaction force.
- Lubricant mixing time and ratio doesn't have a significant impact on the disintegration time.

## CONCLUSION

A rotary press simulator (Stylcam 200R) was used to characterize a commercial grade of mannitol: PEARLITOL® 200 SD. In tested conditions, Magnesium Stearate mixing times and ratios did not influence compactibility and disintegration time of mannitol compacts. The textured mannitol compacts presented good compactibility and ejection properties. The lack of lubricant influence and high  $P_y$  values are characteristic of brittle material. The simulator proved to be a useful tool for compaction characterization and performance of pharmaceutical excipients.

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