Pregelatinized Starch as a Binder in Wet Granulation: Optimization of the Incorporation Rate

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INTRODUCTION

In wet granulation, pregelatinized starches are preferred to starches (which require a cooking step), and when coupled with new generation high shear equipment leads to faster and consistent granules production due to a homogeneous binder and granulation liquid distribution[1,2]. It is common practice to use up to 15% of pregelatinized starches[3] in a formulation. The objective of this study is to evaluate the optimum amount of LYCATAB® PGS (pregelatinized maize starch) as a binder and granulation process conditions in order to get mannitol-based tablet with desired properties.

MATERIALS AND METHODS

PEARLITOL® 50 C crystalline mannitol powder, Extra White maize starch, and LYCATAB® PGS pregelatinized maize starch are from Roquette Frères, France. Vegetal magnesium stearate is from Baerlocher, Germany.

Granulation trials: 1500 g of mannitol and maize starch (80/20) were granulated in a high shear mixer Diosna P1-6 (Diosna, Germany) (impeller at 250 rpm and chopper at 1800 rpm) with LYCATAB® PGS as binder at different incorporation rate (0, 3, 6, 9 and 15%) and 300 g of demineralized water. Mannitol, maize starch and LYCATAB® PGS were mixed together for 5 minutes (impeller and chopper rotation speeds at respectively 250 rpm and 1800 rpm); water was sprayed for 4 minutes, and mixing continued for 4 additional minutes. Generated granules were dried in an Aeromatic Strea-1TM (Aeromatic, UK) at 50°C and calibrated with an Erweka oscillating calibrator (1000µm) (Erweka, Germany).

Tableting trials: 600 g of granules (99.5%) and magnesium stearate (0.5%) mixed in a Turbula mixer (WAB, Switzerland) for 5 minutes. Tablets were made with Korsch XP1 single punch tablet press (Korsch AG, Germany) equipped with D13R13 concave punches at 20 tablets/min and 5 compression forces (5, 10, 15, 20, 25 kN). Tablet characterization: weight, thickness, diameter, hardness were evaluated with a Pharmatron® ST50 (Sotax AG, Switzerland). Disintegration times were measured with a Pharmatron® DT50 (Sotax AG, Switzerland). Tablets friability were measured with an Erweka TAR220 (Erweka, Germany).

RESULTS AND DISCUSSION

1. Impeller torque profiles can be separated into three steps:
   - Step 1 (0 – 300 s): homogenization of the blend;
   - Step 2 (300 – 540 s): spray of the granulation liquid;
   - Step 3 (540 – 840 s): homogenization of the granules.

   It clearly appears that the impeller torque decreases with the increase of the binder amount up to 9% of LYCATAB® PGS in the formulation. No difference is observed between the trial at 9% and 15% of LYCATAB® PGS.

2. According to the physical characteristics shown in table 1, all granules were suitable for compaction.

Binder quantity	Moisture content (%)	Flow time (s)	Bulk density (g/ml)	Tapped density (g/ml)
0 %	1.22	5	0.633	0.855
3 %	1.67	5	0.602	0.720
6 %	2.63	4	0.602	0.758
9 %	2.69	5	0.625	0.775
15 %	2.19	5	0.606	0.730

Table 1. Granules main characteristics.

3. Granules with 3% - 15% LYCATAB® PGS (figure 1) lead to tablets with a similar hardness for a given compression force in comparison with granules made without binder.

4. All the formulations produced tablets with a friability lower than 1% as soon as their hardness is higher than 20 – 30 N (figure 2). Formulations containing LYCATAB® PGS facilitate tablets' production with a friability lower than 0.2% at a hardness exceeding 50 N.

5. For tablets prepared with 3%, 6% and 9% of LYCATAB® PGS, disintegration time is not dependent of compression force while for 15% LYCATAB® PGS disintegration time increases with the compression force increase (figure 3).

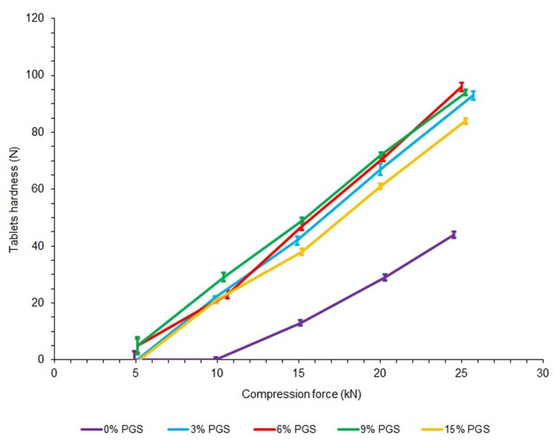

Figure 1. Granules tabletability.

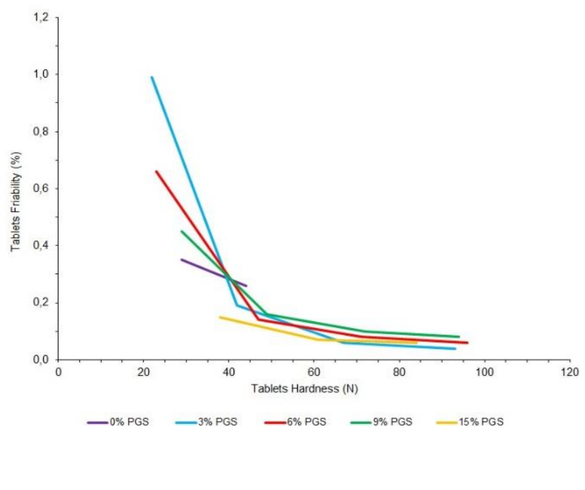

Figure 2. Tablet friability.

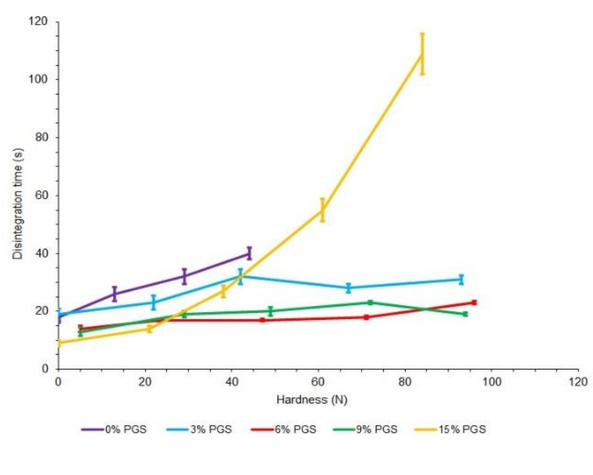

Figure 3. Tablet disintegration time.

CONCLUSION

The optimization of starches' binding capacities combined with the performance of modern high shear granulation equipment permits fine tuning formulation in order to obtain tablets with the desired properties. LYCATAB® PGS pregelatinized maize starch at a ratio between 3% - 9% enables compliant physical properties in tablet manufacturing.

REFERENCES

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