SPI Pharma™
An ABF Ingredients Company

*Technical Bulletin*

# Mannogem® XL Mannitol USP/EP/JP

## Simplify Patient Friendly Dose Formulation and Production

**Background**

Drug developers consistently face more complex demands for new forms and functionality of Oral Solid Dosage Forms (OSDF). These demands come from patients requiring forms that are highly functional and pleasing. There is also regulatory focus, such as recent Guidelines from the FDA[1], emphasizing the importance of considering the patient experience with the dose form. SPI Pharma is helping formulators face the challenge. Mannogem XL Mannitol is a breakthrough for the simplification of patient friendly dosage forms. XL allows formulators to meet the demand for unique functionality or appearance, increases development output, and reduces development time, while simplifying formulation and production.

Achieving the desired critical properties such as tensile strength, friability and disintegration time can be a multifaceted challenge for applications like chewable tablets, lozenges and ODTs. Formulators meet this challenge by using many different excipients in a single formulation, adding time and complexity to both the development process and, ultimately, the production process. Mannogem XL is an innovative, spray dried, compendial mannitol that offers significant advantages such as superior tabletability[2] and rapid disintegration to enable formulators to use a single excipient to meet complex formulation requirements.

**Results**

Excipients added to enhance tabletability can detract from the organoleptics of a formulation. Specifically, HPC can be gummy and MCC has a grittiness to it. Studies were undertaken to understand whether the use of Mannogem XL could enable the removal of HPC and MCC. Removal and/or reduction of these materials would therefore be highly beneficial, provided the tabletability and disintegration targets could be maintained.

We imitated a commercially available formula of a chewable tablet and studied the effect of incorporating Mannogem XL into the mix. Substituting XL for the spray dried mannitol competitor in this formulation produced tablets with a higher tensile strength and lower friability. As demonstrated in Table 1, the number of other binding excipients in the formulation could be reduced until only 4% MCC was left in the formulation. The resulting tablet weights and tablet thicknesses were reduced by approximately 10%. To confirm the benefit, the same reduction was taken using Competitor 1 spray dried mannitol.

***Table 1- Standard formulation and formulations used in the simplified version***

| Formulation | Standard | | Simplified | |
|---|---|---|---|---|
| Product | % of Blend | mg/ Tablet | % of Blend | mg/ Tablet |
| Spray Dried Mannitol | 65% | 811.7 | 73% | 811.7 |
| Actimask® 92M | 14% | 171.8 | 15% | 171.8 |
| HPC | 4% | 49.8 | 0% | 0 |
| PH102 (MCC) | 10% | 124.5 | 4% | 47.8 |
| Crospovidone | 5% | 62.3 | 6% | 62.3 |
| Mag. Stearate | 2% | 24.9 | 2% | 24.9 |

Figure 1 shows Mannogem XL's enhanced tabletability is maintained in the simplified formulation. Figure 2 shows superior tensile strength when using Mannogem XL when compared to competitive spray dried mannitol. Competitive spray dried mannitol cannot maintain tablet robustness. Additionally, the tensile strength of the competitor's formulation only exceeds 1 MPa at high compression forces (30 kN). Such a formulation would not be acceptable for commercial manufacturing.

***Figure 1***

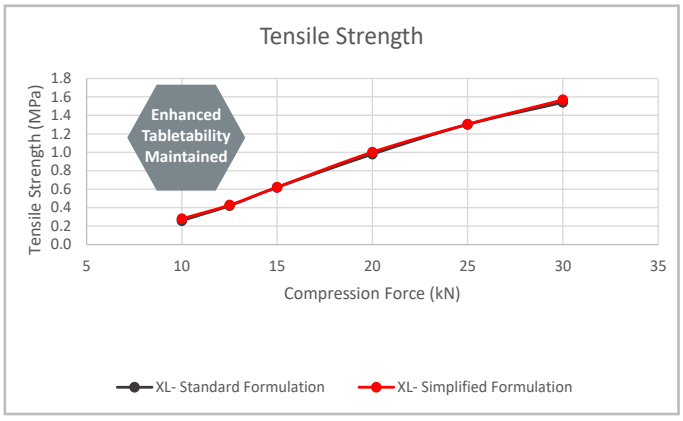



***Figure 2***

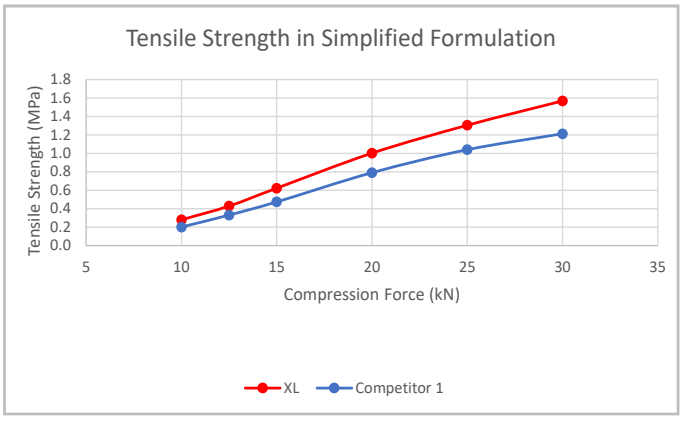


Figure 3 shows that the tablet robustness does not change in the simplified formulation while using Mannogem XL. In Figure 4, lower friability shows an increase in the tabletability of the formulation. Friability is unacceptably high for the formulation containing the competitor spray dried mannitol.

***Figure 3***

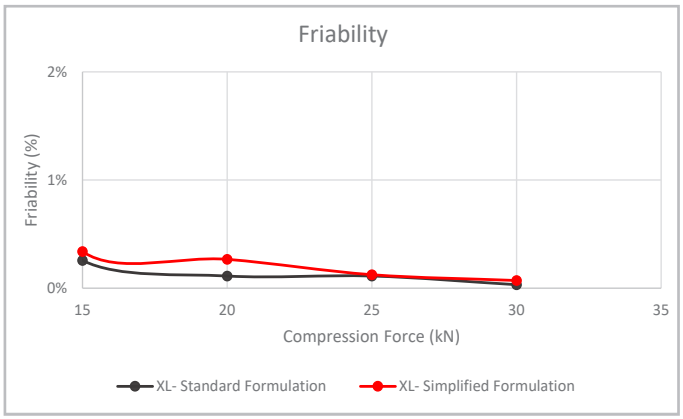
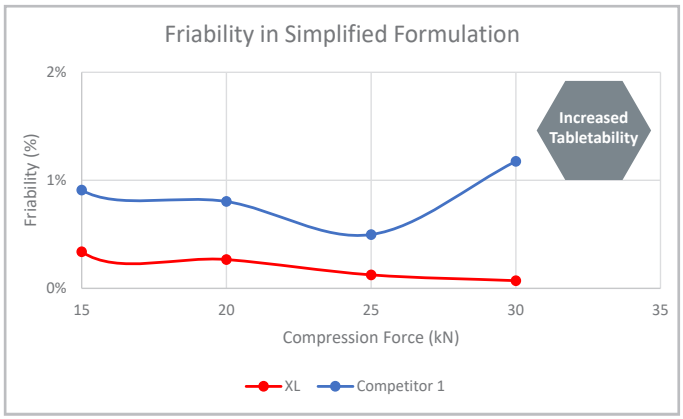



***Figure 4***




## Conclusion

This data demonstrates the potential Mannogem XL Mannitol has to be used as an excipient that can greatly simplify the formulation approaches to rapidly develop a robust tablet formulation that has all of the requisite CQAs, namely high tablet robustness, rapid disintegration, and superior organoleptics.

This simplification potential has significant advantages as it enables more rapid development cycles, eliminating wider consideration of design space required when multiple excipients and levels of excipient are needed. Mannogem XL Mannitol reduces the potential for stability issues. Stability issues increase as the number of excipients in a formulation are increased.

## References

1. Quality Attribute Considerations for Chewable Tablets. Guidance for Industry. CDER August 2018.
2. SPI Pharma Mannogem XL Superior Tabletability Technical Bulletin, January 2019.

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