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The Effect of Disordered MgSt Particle Size on Indomethacin Dissolution and Tablet Ejection Force

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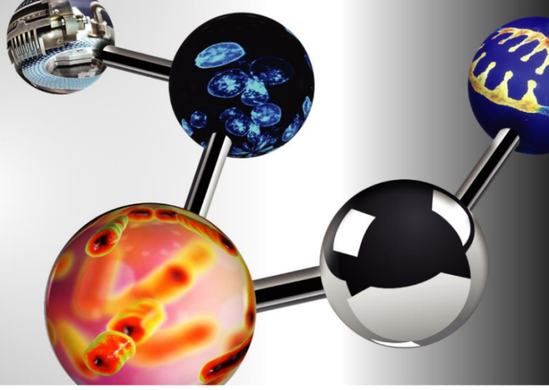
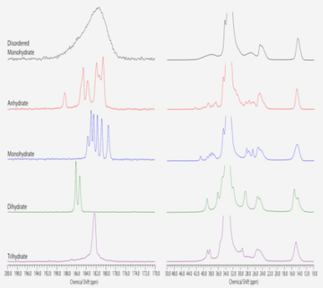


PURPOSE

Magnesium Stearate (MgSt) is the most commonly used excipient in tablet formulations. MgSt consists of multiple fatty acid salts, primarily stearate and palmitate, and has at least five crystal forms, including several hydrates. It is typically used as a tablet lubricant in the range of 0.5% to 2% of a formulation by weight. Too low a concentration of MgSt can cause manufacturing issues, while too high a concentration can slow the dissolution rate. It is generally accepted that particle size of MgSt impacts drug dissolution and tablet lubrication, with a decrease in particle size of MgSt in a formulation generally causing a slower dissolution profile. In this study, the effect and MgSt particle size fractions on the dissolution and ejection force of indomethacin tablets is explored for a commercially available disordered MgSt form.

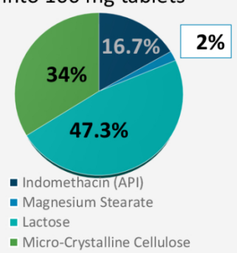
OBJECTIVES

To understand the differences in dissolution and lubrication caused by the inclusion of 'disordered' form of MgSt following sieving, mixing, and compression in formulations of indomethacin, microcrystalline cellulose, and lactose.



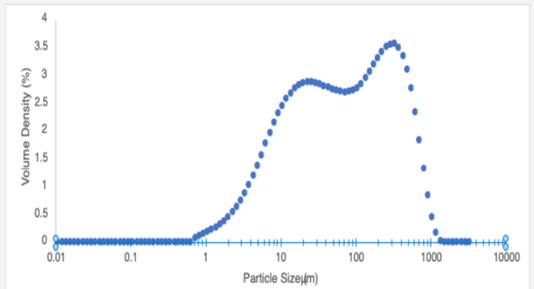
METHODS

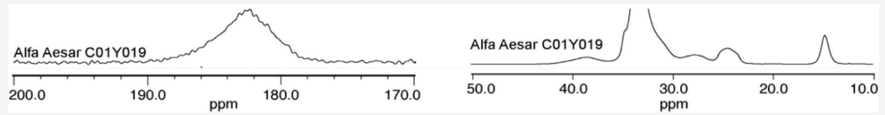
MgSt was sieved into particle size fractions greater than 425 to 250 µm, 250 to 75 µm, and 20 µm to 75 µm using a Gilson Sieve Shaker and SS-3 sieves. In all studies, MgSt was formulated at 2% by weight with indomethacin (16.7%), Avicel PH-102 (34%), and α-Lactose monohydrate (47.3%). Each particle size fraction was blended into the formulation for 60 minutes in a Turbula mixer. Tablets were compressed at 50 MPa into 100 mg tablets using a Gamlen D-500 single tablet press, and following compaction the ejection force was measured. Dissolution was performed on indomethacin tablets using a USP2 dissolution setup using Pion µDiss fiber optic probes.

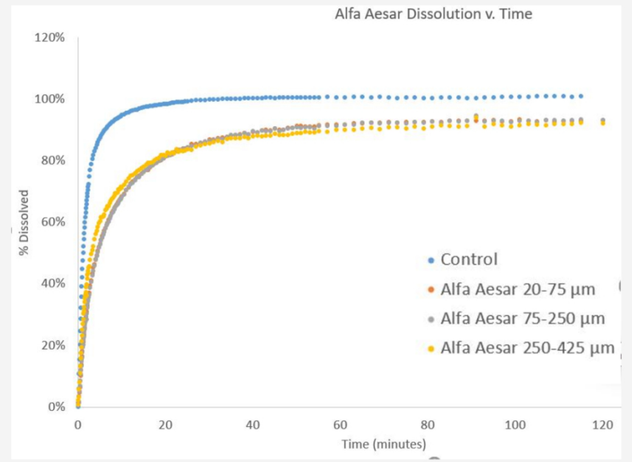


RESULTS

Variations in particle size did not show an effect on the dissolution of the Indomethacin formulation which all had 15-minute dissolutions around 80%, but the measured ejection force did appear to trend with particle size. A control indomethacin formulation tablet had released 100% of the drug at this time point. The formulations with 425 to 250 µm had an average ejection force of 1.66 MPa and a surface area of 0.5396 m^2/g. The 250 to 75 µm had an average ejection force of 1.18 MPa and a surface area of 0.5357 m^2/g. The 20 to 75 µm had an average ejection force of 0.98 MPa and a surface area of 0.8546 m^2/g.
The particle size ranges selected were used To ensure sufficient MgSt could be collected with minimal shear effect.







CONCLUSIONS

This sample of the disordered form of MgSt shown little variation in drug dissolution, but seemed to show decreasing ejection force for decreasing particle size. Having an ability to alter ejection force without altering the release of an API can offer advantages.

Sample (MgSt PS)	Surface Area (m^2/g)	Ejection Force (MPa)
425 - 250 µm	0.5396	1.66
250-75 µm	0.5357	1.18
20 to 75 µm	0.8546	0.98

FUNDING / GRANTS / REFERENCE

Delaney et al. "Characterization of Synthesized and Commercial Forms of Magnesium Stearate using DSC, TGA, PXRD and SSNMR". J Pharm Sci, 2017.

Julie Calahan, "Correlating the Physicochemical Properties of Magnesium Stearate with Tablet Dissolution and Lubrication'". 2020

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EJM discloses that he is a partial owner of Kansas Analytical Services (KAS), a company that provides solid-state NMR services to the pharmaceutical industry. The results presented here are solely from academic work and no data from KAS are presented.

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