Evaluation of a Co-processed Self-Lubricating Compressible Excipient

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Introduction

Anhydrous Lactose is widely used as an excipient in tabletting applications due to inert chemical properties, as well as its superior compression and compaction characteristics. Direct tabletting is widely used in the pharmaceutical industry due to it's simplicity versus other methods (ie. wet granulations, dry granulations, encapsulations, etc.). For direct tabletting, the materials are simply blended together and compressed to form the tablets. However, prior to tabletting, a lubricant, typically Magnesium Stearate, must be blended into the formulation. This ensures proper release of the tablets from the tablet press and without it, sticking occurs. This causes tablet deformities, such as capping, chipping, pitting, weight variations, and other issues.

Magnesium stearate gives excellent lubrication properties to ensure tablet release but can lead to an array of other problems. Since it is water insoluble, it can cause an increase in tablet disintegration. It can also interfere with compression and cause reduced tablet hardness. Over blending the formulation with Magnesium Stearate exemplifies the increases in tablet disintegration time and decreased tablet hardness. Also, to work as a lubricant, the material must be very fine, which causes poor flowability and dustiness. The material tends to coat equipment and is difficult to clean.

Sheffield Bio-Science has launched a co-processed lubricated Anhydrous Lactose excipient that was designed to eliminate the need for adding a separate lubricant to a formulation. The use of this excipient was evaluated to determine if the lubricant (Magnesium Stearate) and its blending step could be eliminated.

Materials

Starting Materials:
Materials. The excipient evaluated in this study was Sheffield Pharma's new LubriTose AN (co-processed Anhydrous Lactose with Glyceryl Monostearate).
Sheffield's Anhydrous Lactose DT and Magnesium Stearate were used for the control.

Preparation of Blends and Tablets. For blending steps, a standard V-shell blender was used without an I-bar.
For tablets made with the LubriTose AN, they were compressed as is, since the product is co-processed with the lubricant. For the tablets with Lactose and Magnesium Stearate only, dry blends of Lactose (99%) and Magnesium Stearate (1%) were prepared.
At the tablet press settings used, tablets were typically about 0.400 grams.
Tabletting was completed by adding the material to the hopper of a Globe Pharma 10 Station Instrumented Rotary Tablet Press.

Methods

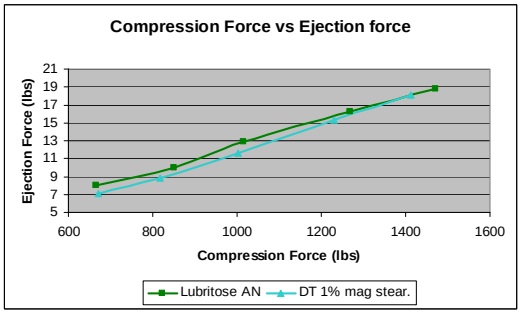
Evaluation of Tablets:
Tablet Hardness. Tablet hardness testing was performed using a PharmaTest PTB 311/511E Automated Tablet Testing Instrument. The hardness is stated as tablet break point in Newtons. For each set of data, five tablets were tested for hardness and average.

Tablet Disintegration. Tablet disintegrations were performed using a Copley DIS600 Disintegration Tester. The vessel was filled with E-pure water and the unit was set to 37ºC.

Results & Discussions

Lubrication Properties. Tablets were produced using LubriTose AN as is and were compared to a blend of Anhydrous Lactose with 1% Magnesium Stearate. A compression versus ejection force profile was created using the tablet press. Ejection force gives an indication of lubrication properties as a high ejection force is equivalent to poor lubrication. Figure 1 shows the ejection force comparison.

Figure 1: Ejection Force Comparison of LubriTose AN versus Lactose/Magnesium Stearate



Tablet Hardness Properties. Tablet hardness profiles are shown in Figure 2 and 3 below. The effects of blending using Magnesium Stearate were compared to blending using just LubriTose AN. As expected, the tablet hardness was significantly reduced with increased blending using Magnesium Stearate. Over blending LubriTose AN did not cause a significant reduction in tablet hardness.

Figure 2: Lactose/Magnesium Stearate Blend Tablet Hardness Data

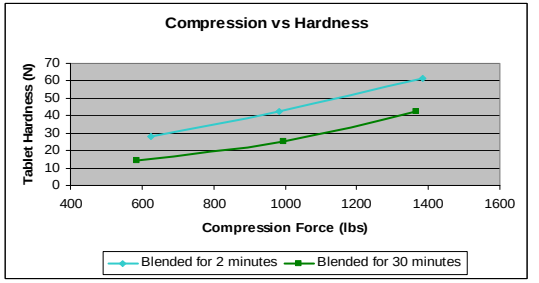
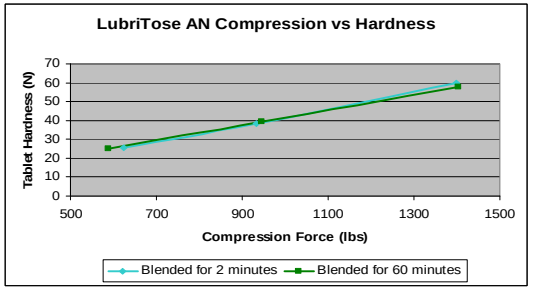


Figure 3: LubriTose AN Blend Tablet Hardness Data



Tablet Disintegration Properties. Tablet disintegration profiles are shown in Figure 4 and 5. The effects of blending using Magnesium Stearate were compared to blending using just LubriTose AN. As expected, the tablet disintegration time was significantly increased with increased blending using Magnesium Stearate. Over blending LubriTose AN did not cause a significant increase in tablet disintegration time. Note: Timer was stopped after 2500 seconds.

Figure 4: Lactose/Magnesium Stearate Blend Tablet Disintegration Data

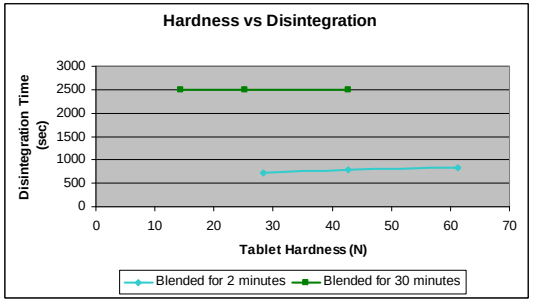
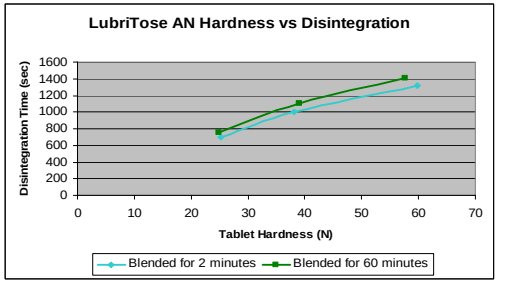


Figure 5: LubriTose AN Blend Tablet Disintegration Data



Conclusions

The direct tabletting method of producing tablets is widely used in the pharmaceutical industry. In nearly all cases, Magnesium Stearate is used as the tablet lubricant of choice. As observed in this study and many others, using Magnesium Stearate in the tabletting operations, while providing excellent lubrication, can have negative effects on tablet hardness and disintegration. This study evaluated a co-processed excipient consisting of Anhydrous Lactose and Glyceryl Monostearate, which was designed to replace compressible excipients and lubricant in one product.

Lubrication of press dies not only ensures optimal tablet appearance but also is important for press tooling lifespan. With inadequate lubrication, tooling will need to be replaced more often resulting in higher manufacturing costs. The LubriTose AN excipient was equal in lubrication properties to the Lactose with Magnesium Stearate, showing that it can effectively replace the compressible excipient and lubricant.

It is widely understood that if Magnesium Stearate is over blended, tablet hardness is reduced. This was shown in Figure 2. This was not observed when using LubriTose even when it was blended for 60 minutes. This shows that tablet hardness will not be affected with LubriTose AN.

It is also widely understood that another result of over blending Magnesium Stearate is increased tablet disintegration. This can be observed in Figure 4. This was not observed when using LubriTose AN even when blended for 60 minutes.

This paper shows that LubriTose AN can be used to replace the compressible excipient and lubricant in a tablet formulation without the effects observed when using Magnesium Stearate.

The results clearly show that the product met the design expectation and that it is a highly reliable choice in direct tabletting operations.

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