Lactose Anhydrous DT High Velocity Tabletting Properties

Introduction

Direct tabletting 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. Although the operation is simple, results may vary tremendously due to the properties of the Lactose. The Lactose must flow well to ensure even blending and even die filling, which lead to more uniform tablets (tablet weight and active ingredient distribution). The Lactose must compact well to form hard tablets (high hardness and low friability). Lastly, the tablets, although hard, should still dissolve and release the active in a timely manner (dissolution). While other properties may be relevant in complex formulations, these are the most important in direct tabletting, standard release solid dose forms.

Sheffield™ Brand Lactose Anhydrous DT High Velocity from Kerry Bioscience was designed to optimize the tabletting operation. It has high flowability and a low percentage of fines that should lead to uniform tablet weights, uniform active distribution, harder tablets, and steady dissolution. For this study, tests were performed to evaluate this new product by comparing it against existing standard Direct Tabletting Lactose products.

Material

Starting Materials:

Materials. The excipients used in this study were Sheffield™ Pharma's new Lactose Anhydrous DT High Velocity, Sheffield's™ standard DT Lactose, one industry standard brand of DT Lactose, and two industry standard brands of Monohydrate Lactose (not all were used for each part of the study). Potassium Iodide (KI) was used as the active ingredient in the tablets and Magnesium Stearate was used as the lubricant.

Tablets were made using Lactose and Magnesium Stearate only for the tablet hardness and weight uniformity parts of the study, and tablets were made with the Lactose, KI, and Magnesium Stearate for the active uniformity and dissolution parts of the study.

Preparation of Tablets. For the tablets with Lactose and Magnesium Stearate only, dry blends of Lactose (99.5%) and Magnesium Stearate (0.5%) were prepared to equal 50 grams of material. The Lactose and Magnesium Stearate were blended in a V-blender for 1 minute. At the tablet press settings used, tablets are typically about 0.400 grams (see tablet press information below). Ten tablets of each blend were produced.

For the tablets with Lactose, KI, and Magnesium Stearate, dry blends of Lactose (94.5%), Potassium Iodide (KI) (5%), and Magnesium Stearate (0.5%) were prepared to equal 50 grams of material. At the tablet press settings used, tablets are typically about 0.400 grams (see tablet press information below). Therefore, each tablet would contain about 20 mg of KI, depending on the actual tablet weight. The Lactose and KI were blended in a V-blender for 5 minutes, and then the Magnesium Stearate was added and blended for 1 minute. Ten tablets of each blend were produced.

Tabletting was completed by adding the material to the hopper of a TDP-30 Motorized Single Punch Tablet Press. The press was set at 3KN of force and 8 tablets per minute, using a 8mm die set.

Methods

Evaluation of Tablets:

Tablet Weight. All tablets were weighed on a Shimadzu AY220 Balance with a d=0.1mg resolution. Ten tablets of each of the Lactose and Magnesium Stearate blends were weighed for tablet uniformity (function of Lactose flowability and density).

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. Ten tablets of each of the Lactose and Magnesium Stearate blends were tested for hardness.

Tablet Dissolution. Tablet dissolutions were performed using a Copley DIS6000 Dissolution Tester. The vessels were filled with 900ml of E-pure water and the unit was set to 37ºC with paddle attachments turning at 50 rpm's (USP specifications for KI tablets). A standard KI absorbance versus concentration (at 227nm, USP specification for KI tablets) curve was prepared prior to the dissolutions. The tablet blends were prepared so that tablets would contain approximately 20mg of KI and the final solution that they would be dissolved in would be 900ml. Therefore, the standard curve was prepared by reading the absorbances of KI dilutions from 0 to 25mg in 900ml. Then, during the dissolutions, absorbances were read every 2 minutes and using the standard curve, converted to amount of KI released from the tablet. Dissolution curves were prepared from this data to show dissolution. Also, the final mg of KI dissolved (when tablet is completely dissolved) was recorded. This data is a function of active ingredient uniformity in the blend/tablet (if final absorbance number shows varying amounts of KI released, then the blends/tablets are not uniform).

Results & Decisions

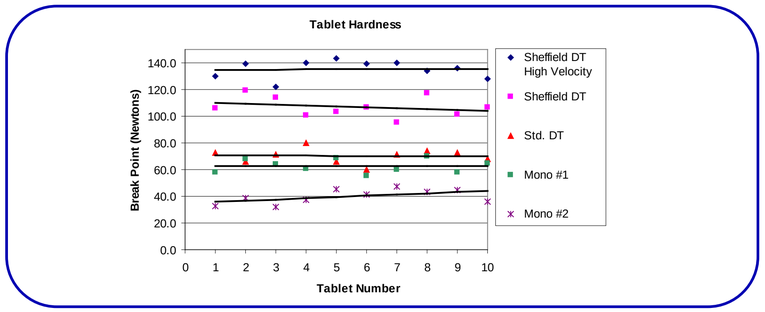
Tablet Weight. Tablet weights are listed in Table 1. Included is the new Sheffield Pharma DT High Velocity, standard Sheffield™ Pharma DT Lactose, one industry standard brand of DT Lactose, and two industry standard brands of Monohydrate Lactose used for tabletting. Ten tablets for each brand are listed along with the tablet weights, Mean, Standard Deviation, and Relative Standard Deviation (RSD) of the data. The DT High Velocity had the second lowest RSD, however, also had a mean that was exactly on target for the tablet based on the amount of blended material (0.4000mg).
Note: Tablets contained Lactose and Magnesium Stearate as listed in Materials & Methods Section.

Table 1: Lactose/Magnesium Stearate Blend Tablet Weights

Tablet #	Sheffield™ DT High Velocity	Sheffield™ DT	Standard DT #2	Standard Mono #1	Standard Mono #2
1	0.4009	0.3878	0.3820	0.3580	0.3520
2	0.4020	0.3860	0.3665	0.3571	0.3578
3	0.3999	0.3878	0.3912	0.3648	0.3548
4	0.3980	0.3915	0.3458	0.3572	0.3557
5	0.4006	0.3891	0.3866	0.3586	0.3640
6	0.3970	0.3840	0.3877	0.3657	0.3633
7	0.4030	0.3894	0.3846	0.3595	0.3666
8	0.4023	0.3865	0.3860	0.3615	0.3568
9	0.3997	0.3877	0.3860	0.3645	0.3625
10	0.3965	0.3895	0.3867	0.3640	0.3556
Mean	**0.4000**	**0.3879**	**0.3803**	**0.3611**	**0.3589**
St. Dev.	0.002231	0.002109	0.013829	0.003409	0.004817
RSD	**0.557843**	**0.543723**	**3.636347**	**0.944165**	**1.341983**

Tablet Hardness. Tablet hardness is shown in Figure 1. Included is the new Sheffield™ Pharma DT High Velocity, standard Sheffield™ Pharma DT Lactose, one industry standard brand of DT Lactose, and two industry standard brands of Monohydrate Lactose used for tabletting. Tablet hardness was measured for all ten tablets for each Lactose product. A trendline was also added to the chart, just to verify that the tabletting conditions were not changing significantly during the run. The DT High Velocity resulted in the hardest tablets, and with the least amount of capping (voids in the tablet due to the Lactose fines being pushed out of the die, or due to the Lactose sticking to the die). With the Monohydrates, the press had to be stopped after tablet #5 to clean the die surfaces as the tablets began to show capping.
Note: Tablets contained Lactose and Magnesium Stearate as listed in Materials & Methods Section.

Figure 1: Lactose/Magnesium Stearate Blend Tablet Hardness Data



Tablet Dissolution. Tablet dissolution data is shown in Figure 2. Dissolution data was only compared for the anhydrous brands of Lactose. Sheffield™ Pharma DT released KI the fastest and also released fast in the beginning that slowed near the end. DT High Velocity and DT Lactose #2 had similar dissolution profiles, and had a more steady release. As expected based on the tablet weight uniformity studies, the endpoint of the dissolution (all KI released) showed more uniformity with DT High Velocity.
Note: Tablets contained Lactose, KI, and Magnesium Stearate as listed in Materials & Methods Section.

Table 2 shows the final amount of KI released from the two trials for each product. Ideally, each tablet would contain the same amount of KI.

Figure 2: Lactose/KI/Magnesium Stearate Tablet Dissolution Data

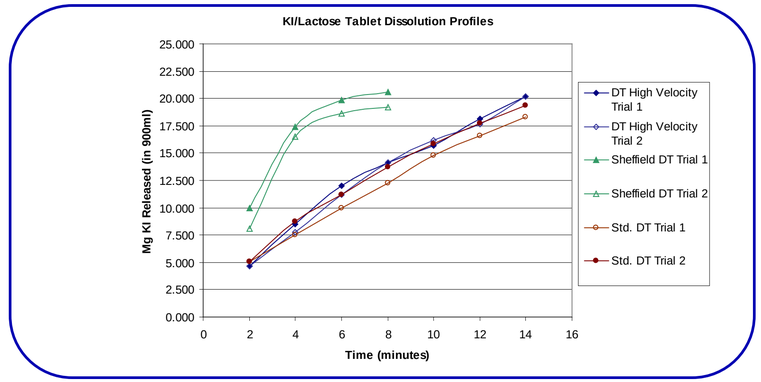


Table 2: Final Amount of KI Released

Product	Final Amount of KI Released (mg)	Theoretical (from initial blend and tablet weight)
Sheffield™ DT High Velocity Trial 1	20.210	20.00
Sheffield™ DT High Velocity Trial 2	20.182	20.00
Sheffield™ DT Trial 1	20.575	19.40
Sheffield™ DT Trial 2	19.215	19.40
Standard DT Trial 1	19.776	19.02
Standard DT Trial 2	20.813	19.02

Conclusions

The most important issues in direct tabletting operations are tablet weight control, active ingredient uniformity, tablet hardness, and tablet dissolution. As observed in this study and many others, the excipient used in the tabletting operations greatly affects these properties. Lactose Anhydrous DT High Velocity was specifically designed to facilitate precise tabletting operations.

For tablet weight control, it resulted in uniform tablet weights, with an RSD of 0.558 for ten tablets. Also, the mean weight of the ten tablets was exactly at the target weight of 0.400 based on the initial blend of ingredients. This was expected since this Lactose flows very well and contains a low percentage of fines. These properties lead to even press filling and less tablet capping. All of the anhydrous lactose outperformed the monohydrates. This is due to the lower moisture content that helps prevent the lactose from sticking to the dies as was observed with the monohydrates.

DT High Velocity had the highest tablet hardness of all products tested. This is important, as the tablet press can be set to a lower compression force, which lessens die wear and tear. With the monohydrates, tablet hardness was very low so when using these products, compression force has to be maximized to produce acceptable tablets.

Dissolution was the fastest with the Sheffield™ Pharma Standard DT product. Dissolution with the DT High Velocity was equal to the industry standard DT product, despite the much higher tablet hardness. Also, the dissolution was steady versus Sheffield™ Pharma Standard DT, which begins with a very fast dissolution and levels off near the end.

Although the data was limited, the DT High Velocity exhibited the best active ingredient uniformity in the tablets. This is based on the final amount of KI released into the dissolution solution (amount of KI released should equal the total amount that was in the tablet). With the two runs using this lactose, the final amounts of KI released were 20.210 mg and 20.182 mg.

In summary, Lactose DT High Velocity was specifically designed to facilitate precise direct tabletting operations by producing uniform tablets, hard tablets, and tablets that meet dissolution expectations.

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