

# Effects of Magnesium Stearate on Tablet Properties

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## Abstract

This experiment tested the influence of the lubricant magnesium stearate on the effectiveness of the drug acetaminophen in a mixture of glidants and excipients. There are many factors that can cause variation in the effectiveness of drugs in tablet form. Chief among them are the lubrication and glidant percentages, shear rate, tablet hardness and hydrophobicity. In order to allow the powder to flow through the tablet press without building up a static charge, glidant must be added and regulated in proper amounts to ensure that the hydrophobicity of the powder does not cause an undesirably long dissolution rate. Lubricant must be added to prevent the adhesion to and then the damaging of the Rotary Tablet Press. Too much lubricant, however, will cause the powder to form globules and to resist proper cohesion. This would fail to provide both full bioavailability and quick relief of symptoms.

The effects of glidant/lubricant concentration were studied on the prior enumerated factors. The powders were mixed, blended to homogeneity, sheared, and compressed into tablets. Then the resulting tablets were tested for hydrophobicity, tablet hardness, tablet weight, and dissolution. It was found that including the glidant and lubricant was vital to counteract static and press adherence. However, the percentage of their concentrations must be kept at approximately 1% to avoid altering the

powder and tablet properties as well as decreasing the dissolution rate. Following these guidelines, the tablets will maintain optimal hydrophobicity and percentage of drug release.

## Introduction

The surface properties of the componential particles have a tendency to affect both the characteristics and behavior of the finished product. Adhesive forces between surfaces of acetaminophen, the flowing agents (glidants and lubricants), and the excipients can unfavorably affect properties of the tablet and dissolution [1].

A prominent portion of the blend is not devoted to function as the actual drug, as the general public might think. On the other hand, it is to avoid complications while using the Rotary Tablet Press, the machine that compresses the powders into tablets at a force of twelve kilo-newtons. Adhesive forces between the powder and the press can lead to partially compacted tablets. This can also cause jams in the machine, which can not only halt production but also be potentially dangerous to both the machine workers and the manufacturing equipment. Lubricants are added to remedy these problems. The objective is to investigate the correct percentage of lubricant to add without offsetting the unique tablet properties and to determine whether the efficiency of magnesium stearate as a lubricant changes when in concentrations beyond 1%.

Subsequently, other methods of drug transport might seem like more attractive alternatives. These include soluble powders, aerosol, and intravenous methods. Although these alternative means yield a faster activation rate or drug release, they are more expensive, less mobile, and imprecise in dosage. Tablets are very cost-effective, easy to transport, and simple to administer in accurate dosages.

Were it not for the slow dissolution rate, tablets would be the premiere mode of medical drug use. The focus of the research project, of which these investigations are a part, is designed to eventually develop a means of tablet manufacturing that will enable nearly instant bioavailability. The time between consuming the pill and receiving its effects will be less than five minutes.

Previous work has shown that drug release rates slowed astonishingly in the presence of colloidal silica and magnesium stearate [1]. Because this counter-acts the goal of the entire project, investigations to find the optimal amount of lubricant must be conducted.

The study depicted in this paper investigates the lubrication efficiency of magnesium stearate at various lubricant concentrations in the presences of colloidal silica. Because different levels of magnesium stearate affect the bioavailability of the drug, it is essential to find the appropriate concentration that allows for functional production of the pills but does not hinder the effects of the active ingredient or lessen its bioavailability.

A previous study showed that the concentration of magnesium stearate altered not only the powder properties,

but also the tablet properties. For example changing the tablet properties may impact the drug release [2]. An increased mixing time of magnesium stearate was found to prolong the time of drug liberation, decrease hardness and increase drug disintegration time. Clearly, the concentration of magnesium stearate in a tablet blend has the power to make or break the successfulness of tablet production. It must be closely monitored so that an opportune amount can be established. By testing tablet weight, hardness, dissolution, and hydrophobicity, this amount can be successfully determined.

## **Background**

This experiment focused mainly on the effect of the concentration of lubricant in tablets. Magnesium stearate has a chemical formula of  $Mg(C_{18}H_{35}O_2)_2$  or MgSt. Commonly used, it is found in many mixtures that are safe for human consumption. However, the appropriate amount for the proper lubrication of powders to preserve the properties of the drug still needs to be specified. The glidant used in this experiment was Colloidal Silica (referred to as Cab-o-Sil or CS) a thin, finely-grained silica that has a large surface area. The glidant reduces static collection within the particles and facilitates a smooth flow of powders.

Other less active ingredients are the excipients, Pharmatose and Avicel, which are simply biodegradable carriers for the active ingredient. The excipients make up the majority of the tablets by mass. The pills that we used for these tests were Acetaminophen-based. Found in Tylenol™ and in many cough medicines, Acetaminophen is a minor

pain-reliever, fever reducer, and headache treatment.

Processes involved in the preparation/testing of the tablets include some generally obscure concepts such as mixing order, shear, electrostatic and adhesion forces, hydrophobicity, solvent penetration rate, bioavailability, and dissolution.

Mixing order is the order in which ingredients are added to the blend. Different mixing orders have been shown to affect the tablet's rate of dissolution [2]. Because different components of the blend will mix differently when combined with certain elements rather than others, mixing order is an important aspect of tablet production.

Uniformity and weight variability were two key aspects that had to be taken into consideration when dealing with tablet production. The blends were composed of five starkly different yet visibly similar white powders. Added in different amounts, each ingredient had very distinctive physical properties. If the components of the blends were not uniformly distributed, the tablets would each have drastically different compositions and be ineffective at best and harmful at worst. Free flow of powders in a blender is necessary for complete homogeneity. Weight variation is an efficient method to examine the uniformity of the tablets due to varying densities among the ingredients. Low weight variability depicts a uniform blend.

Shear is the separation of particles in which the particles slide past one another and are decreased in size. Shearing the powder blends allows for free flow of the powder, gross

homogeneity, and a decreased particle size. Varying the shear rate and time are also possible approaches to quicken the rate of dissolution, and are currently being examined.

Electrostatic forces in powder flow are quite dangerous. For example, an electrostatic build-up in a pipe or a part of a machine could cause an explosion that could injure numerous factory workers. These electrical charges are caused by friction, can generate a significant amount of electricity, and are dissimilar from adhesion forces that cause the particles to stick together. Adhesion forces are caused by inter-particulate attractions between the surfaces of the powder particles.

Glidants and lubricants can greatly increase hydrophobicity (the resistance of a particle to absorb water), which lowers the solvent penetration rate (speed of absorption). When a tablet does not allow solvents to penetrate, it will have a slow dissolution, or dissolving rate. Tablets exhibiting this dilemma will have a high activation delay-time and their bioavailability (availability of a drug for use by the body) can be decreased.

## **Methodology**

In order to run the necessary tests, the blends first had to be prepared. This process involved mixing the powders, using a V-Blender, a Modified Couette Shear Cell, and a Rotary Tablet Press. The tablets were then subjected to a number of test including tablet weight, tablet hardness, hydrophobicity and dissolution.

*Mixing:* In this experiment, micronized Acetaminophen was used because its particle size was the smallest available.

Acetaminophen had been the active ingredient in similar studies that have also been working toward the eventual decrease in drug activation delay time. The active ingredient was held at a constant 9% in all three blends tested. The percentage of the glidant, Cab-o-Sil (1%), was also kept constant. An equal amount of Pharmatose and Avicel (45% without MgSt, but equally decreased based on the percentage of MgSt added) was used so that despite the changing percentages of MgSt, the active ingredients could be kept at constant concentrations. The first blend contained 1% MgSt, the second contained 2% MgSt, and the third contained 3% MgSt. The blends were primed in this order and concurrently tested.

After weighing each powder, the different layers were mixed together and sifted through a sieve to ensure that there were no clumps. The clustering of powder would cause weight variability and allow irregularity in the blend. The uneven distributions caused by such agglomerations would have severely skewed the results found after tablet testing.

This section of the process leaves the most room for possible sources of error due to the properties of the powders and the most opportunity for human error by means of measurement inaccuracy and spills. As mentioned earlier, the components of the powder blends have strong adhesive forces, even when mixed with lubricants and glidants. The powder had an inclination to stick to the sides of measuring containers and thus add a slight variability to the measurements.

*V-Blender:* After sifting, two and a half kilograms of the blend were placed in a

V-blender (a rotating V-shaped mixer) for ten minutes. It was subsequently sieved yet again before further processing. It was necessary to make certain that the mixture was fully blended and free of clusters so that all of the ingredients would be equally distributed. If the ingredients are not pre-blended, different parts of the blend will have different concentrations of the lubricant or the active ingredient, etc.

*Shear Cell Rheometer:* After the essential blending, the powder was transferred to batches of 0.8L each. The powder batches were then sheared for eight minutes at a rate of eighty rotations per minute and a shear strain of six-hundred and forty revolutions. Because dispersion is the primary axial macro-mixing method in the machine, displacement around the central axis of rotation is very slow. Pre-blending in the V-Blender mitigates this problem. The shear compartments limit the sample to two-hundred grams per run.

*Rotary Tablet Press:* Finally, five-hundred grams of the finished powder were converted into tablet form using a rotary tablet press. The powder was fed into the machine through a feed tube. It was then redirected into shafts, out of which the tablets were compressed. Released onto a rotating platform, the tablets were then expelled from the machine and into a collecting bag. The tablet press applied a desired force of twelve kilo-newtons of compression. Although many tablets were made, only the middle one-hundred tablets were tested. This is because tablets produced at the start and end of the process tend to differ in consistency due to unstable compression forces. This instability accounted for a seemingly large amount of wasted powder, as most if not all the

powder at the beginning and end of the run was piled up around the machine or made into pitiful half-tablets to be discarded.

*Testing:* Out of these one-hundred tablets, fifty were weighed on an electric balance and then tested for hardness with a machine that measures the number of newtons applied before the tablets fractured.

Thirty grams of the sheared powder was tested for hydrophobicity. A column of the blend suspended over a saturated solution of acetaminophen was used, after freeing all the remnants of the blend from the side of the column with a machine called the Autotap. Calculating the mass of liquid that penetrated the powder over thirty minutes simply involved calculating the change in weight of the powder column. These parameters were then inserted into the Washburn equation

$$t = \eta / (C\rho^2 \gamma \cos\theta) * m^2$$

in which  $t$ =time,  $\eta$ = liquid viscosity,  $C$  = geometric factor,  $\rho$ =liquid density,  $\gamma$ =surface tension,  $\theta$ = contact angle between solid and liquid, and  $m$ =mass of liquid that had penetrated by capillarity. Hydrophobicity was then determined by calculating the slope of a graph of  $m^2$  vs. time.

Lastly, the tablets were tested for dissolution. The dissolution apparatus (a Vankel VK7010 USP II) consists of eight cuvettes, or cups, which are filled with nine-hundred milliliters of phosphate buffer solution that has a pH of 5.8. Each cuvette contains paddles that spin at fifty rpm for the large part of the test, but in the first step they are allowed to run at one-hundred rpm for thirty minutes while the solution was

heated to thirty-seven degrees Celsius. The weight and thickness of each tablet was recorded at that point.

In the second step, the tablets were dropped into the solution with the paddles running at their normal speed (50rpm) and a total test time of ninety minutes. The apparatus took automatic readings of the absorbance every two minutes. A final spin cycle at two-hundred and fifty rpm was run for 5 minutes at the end of the test. The weight was then used in conjunction with the percentage of active concentration and the amount released at each time point to derive a percentage release profile. The Weibull function was used to find the difference in dissolution profiles. Dissolution determines the percentage of drug released.

## Results

After completion of all production and experimentation, the data was collected and revealed a number of interesting trends.

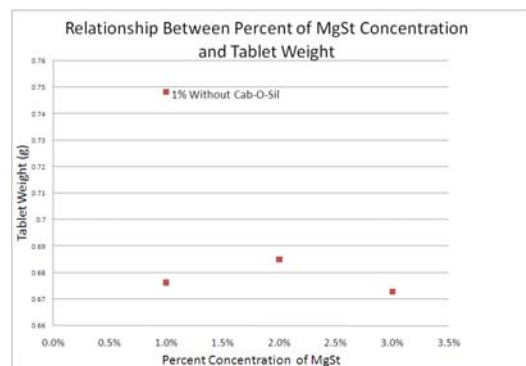


Figure 1: Concentration of MgSt vs. Tablet Weight

*Tablet Weight:* In the blend composed of Acetaminophen, Avicel, Pharmatose, and 1% MgSt, excluding Cab-O-Sil, the average tablet weight was found to be 0.7482 grams (see Figure 1). When Cab-

O-Sil was added to another blend with the same concentration of MgSt, the tablet weight dropped by approximately 10% and was found to be 0.6762 grams. Upon increasing the concentration of MgSt to 2%, the average weight was found to slightly increase. However, at concentrations greater than 2%, the average tablet weight decreased.

The addition of Cab-O-Sil to 1% MgSt caused an interaction between particulate forces of glidant and lubricant. This functioned to increase the lubrication and cause more flow freedom in the blend and thus yielded a lighter mass. Increasing the concentration of MgSt from 1% to 2% slightly increased the tablet weight. This amount of lubrication provided conditions that allowed for essential granular interactions, which increased the average weight. Concentrations greater than 2% caused a decrease in relative standard deviation of tablet weight from the mean and improved powder flow due to over-lubrication. Such increments of concentration of MgSt do not contribute to tablet weight, but alter the interactions between the powder particles and affect blend uniformity. When the particles are over-lubricated, they begin to acquire a waxy coating that decreases viscosity and decreases uniformity.

**Tablet Hardness:** The data indicated that an increase in concentration of MgSt decreased the hardness of the tablets, see *Table 1*. This is due to the altered physical properties caused by the lubricant that created a waxy covering and prohibited inter-particulate forces from bonding.

% MgSt	1	2	3
Hardness	175.88	154.52	127.38

Table 1: Tablet hardness vs. MgSt concentration

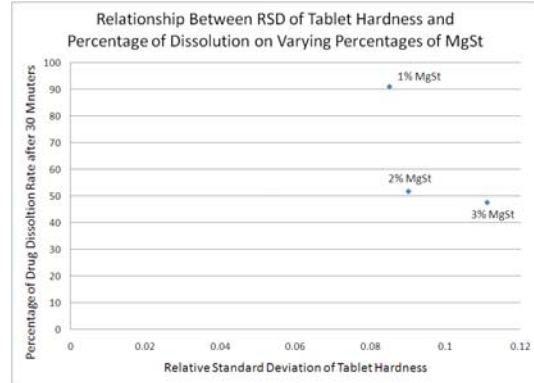


Figure 2: RSD Tablet Hardness vs. Percent Dissolution.

When the relative standard deviation of tablet hardness is compared to the rate of dissolution after 30 minutes (see *Figure 2*), it is clear that the tablets containing 1% magnesium stearate had the least deviation from the mean and the most uniformity in composition.

**Hydrophobicity:** Using the Washburn equation, the data showed that 1% MgSt blend displayed the least hydrophobicity. The solvent penetration weight decreased as the percentage of MgSt concentration increased. As a non-soluble lubricant, MgSt does not allow water to flow through the waxy covering of the powders.

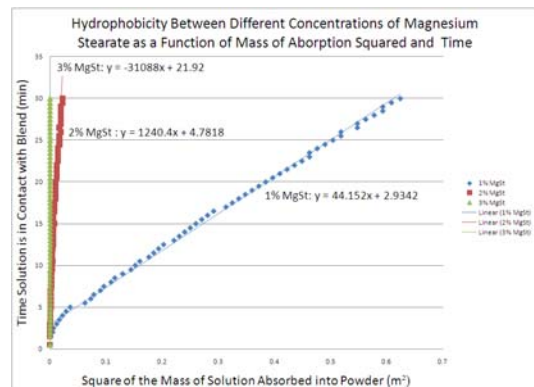


Figure 3: Hydrophobicity of varying concentrations of MgSt

When the percent of dissolution is compared to hydrophobicity, the data produces a clear trend (see *Figure 4*). If

the percentage of dissolution is high, then the blend is less hydrophobic.

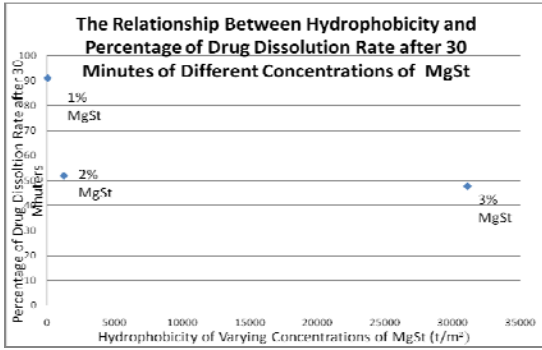
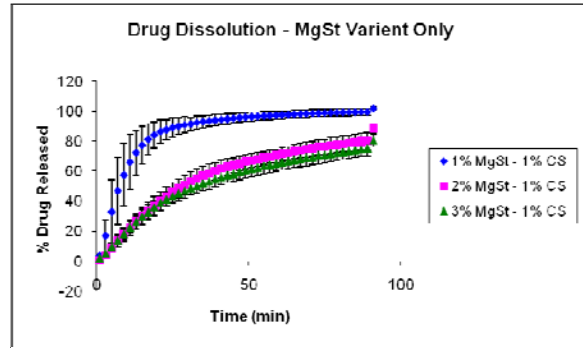


Figure 4: Hydrophobicity vs. Dissolution

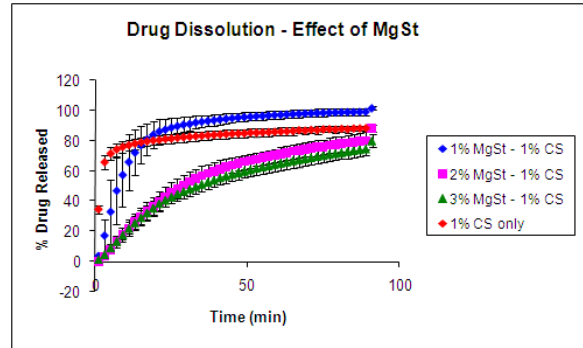
**Dissolution:** The dissolution test determined how efficiently the tablet could dissolve over time, which was the ultimate aim of this investigation. Based on the data (see Figure 5a), the tablets containing 1% of MgSt and 1% of CS had a much higher percentage of drug released than those containing 2-3% MgSt and 1% CS.

Ample water penetration, not permitted by the lubricant, is necessary to break down and dissolve the tablet thus releasing the active drug ingredient. Figure 5b shows the effect MgSt has on the dissolution by comparing a blend containing only 1% CS and no MgSt. Over time, the amount of dissolution of this blend (shown in red) remains relatively constant. CS alters the surface energies, a process which prohibits the rate of drug release to exceed much more than 80%. The higher the percentage of drug released, the more effective the drug.

5a.



5b.



5c.

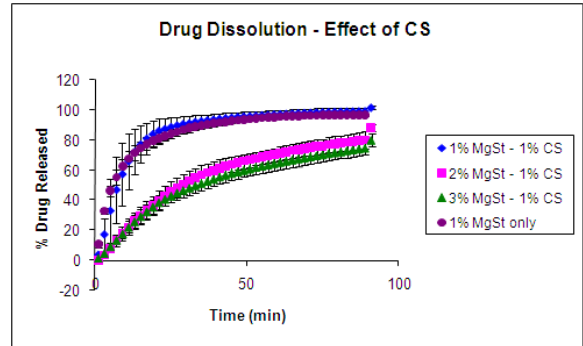


Figure 5: Dissolution of Tablets

The plot depicted by Figure 5c exhibits the effects of CS on the dissolution of the blend by comparing the results of the original three blends with one containing only 1% MgSt and no CS. These data points are nearly identical with those of the 1% MgSt and 1% CS blend, which indicates that CS has little to no effect on the dissolution of the blend at 1% of MgSt.

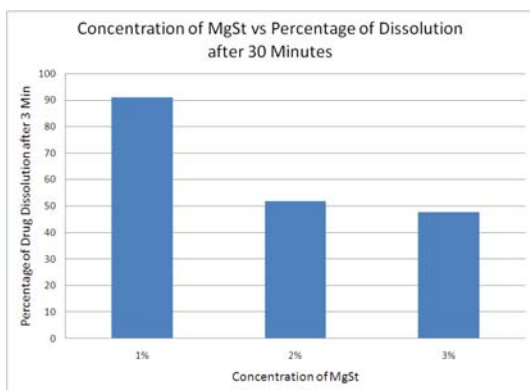


Figure 6: MgSt vs. Dissolution Percent after 30 min

Figure 6 displays the rates of dissolution after 30 minutes for each of the three blends 1%, 2% and 3% MgSt respectively. After 30 minutes, more than 90% of the drug has been released in the 1% blend, while the other two are nearer to 50% dissolution. Therefore more time is necessary for release of the active ingredient when the tablet contains more concentrated amounts of MgSt lubricant.

### Related Work

This study was sparked by the many findings about MgSt. In prior works, others have found that it has very good flow properties and lubrication effectiveness [3]. Yet, it is known that lubricants can have adverse effects on tablet adhesion strength as well as other tablet properties [4, 2]. This also leads to a decrease in tablet hardness [2]. Studies have shown that addition of MgSt decreases tablet cohesion and crushing strength, but it also increases dissolution rates [5, 6]. The deficiency in these works, however, is that they fail to examine the relationships between these many factors. They also do not go as far as to identify an optimal concentration of MgSt. For this reason, it was necessary to rectify these situations through our

own research toward a further goal of tablet dissolution speed and efficiency.

Furthermore, these other tests were not done utilizing acetaminophen. This can be a drawback in that acetaminophen is a highly used yet simple drug that often requires quick bio-availability. It is paramount that these tests be done in order to optimize the usefulness of tablets and this specific drug. This study's findings are, not only, useful on their own, but highly important for further tablet engineering.

### Conclusion

The properties of tablets, powder mixtures, and pharmaceutical drugs are significantly affected by their components, especially by lubricants such as magnesium stearate. This study investigated the influence of different concentrations of MgSt on a number of variables including tablet weight, tablet hardness, hydrophobicity, and most importantly dissolution. While processing and producing powders or tablets, there are a number of ideal properties that serve to increase the functionality of the drug. These include low hydrophobicity, low weight variability, uniformity in mixture, a high hardness factor, and a high percentage of drug released/dissolution.

This paper investigates the lubrication efficiency of MgSt at concentrations beyond 1% in powder blends (without altering the concentration of silica). The lubricant must overcome the adhesive forces between the particles of the powders without disrupting properties of the tablet or decreasing the dissolution. The results showed that the efficiency of MgSt begins to fall after 1% concentration and most assuredly after

2% concentration. The blend that contained 1% MgSt had the lowest hydrophobicity, the highest percentage of drug released in a set time frame, the most dissolution, and therefore the most uniformity, and the least relative standard deviation from the mean.

The future of this research project will focus on determining which among a number of other variables including mixing order, shear settings, glidant concentration, solvent penetration rate, impedance, internal friction angle, and bioavailability, are ideal with the intent of increasing dissolution and drug release rates in the shortest amount of time.

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