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ORIGINAL ARTICLE

An experimental investigation of the effect of the amount of lubricant on tablet properties

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Abstract

Background: Magnesium stearate (MgSt) is widely used as a lubricant in the production of tablets. However, the amount added to a formulation is often too high or it is poorly mixed, which can lead to the production of tablets whose properties are out of specifications. *Method*: The objective of this work was to investigate by means of a new method based on gamma-ray flux measurement and to study the impact of the amount of MgSt on the mass, thickness, hardness, friability, and disintegration time of tablets containing a 50 : 50 wt.% microcrystalline cellulose and spray-dried lactose pre-blend. Other blends were lubricated with sodium lauryl sulfate (SLS) to compare the performance of the two lubricants in equal amounts. *Results*: It was observed that, contrary to SLS, a greater amount of MgSt increased the variability of the tablet mass. The tablet hardness decreased with an increasing amount of MgSt, whereas it remained relatively unaffected by the presence of SLS. No solid conclusion could be drawn concerning the relationship between the lubricant concentration and the tablet friability. *Conclusion*: An amount of 0.25 wt.% MgSt and 0.75 wt.% SLS were found to be sufficient amounts of lubricants to obtain a proper compression.

Key words: disintegration, friability, hardness, magnesium stearate, tablet compression, thickness

Introduction

Magnesium stearate (MgSt) has been widely used for the past 40 years as a lubricant in tablet production. The small size of MgSt particles makes it possible for them to be adsorbed into the pores of larger excipients and API particles, thus forming a lubricating film. Over the years, there have been many reports that extending this film, through either an increase in the amount of MgSt or a longer mixing time, has a negative effect on the hardness, friability, and disintegration time of the tablets[1–6]. Because the bonds between MgSt particles are weaker than those between unlubricated excipient particles, a more extensive coverage of the excipient particles by MgSt will lead to a decrease in tablet hardness. This decrease in hardness may also lead to an increase in tablet friability, but the link between this parameter and MgSt is less clear. Most friability studies have involved wet-granulation formulations, in which friability is very dependent on the final humidity of the granules and the amount of granulating fluid used[7], which makes it difficult to isolate the effect of MgSt. Along with a decrease in tablet hardness, most authors report that an increase in the amount of MgSt leads to an increase in tablet disintegration time[8]. This is due to the hydrophobic nature of the MgSt molecule and, by extension, of the lubricant film, which hinders the penetration of water in the tablet.

Sodium lauryl sulfate (SLS) is commonly used in tablet formulation as a surfactant during granulation. SLS is used almost exclusively as a surfactant in the production of tablets, but its possible use as a lubricant has also been investigated[9,10]. The fact that the size of an average SLS particle is higher than that of an MgSt particle implies a different lubrication mechanism. Hölzer and Sjögren[10] observed that one of its most interesting properties as a lubricant is that it does not negatively affect the tablet disintegration time because of its hydrophilic nature. A quick summary of the link between the amount of lubricant and the tablet hardness and disintegration time reported in the literature is shown in Table 1. Aside from Aly's experiments with SLS lubrication, the

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Table 1. Relationship between tablet hardness and disintegration time for an increasing amount of lubricant, as reported in the literature.

Authors	Major excipient	Lubricant amount	Hardness	Disintegration time
Bolhuis et al.[1]	Amylose V	0.01–0.5% MgSt	Decrease	N/A
Bolhuis et al.[1]	NaCl	0.01–0.5% MgSt	Decrease	N/A
Ragnarsson et al.[12]	NaCl	0–2.5% MgSt	Decrease	Increase
Ragnarsson et al.[12]	Anhydrous lactose	0.25–2.5% MgSt	Decrease	Increase
Ragnarsson et al.[12]	Calcium citrate	0.5–2.5% MgSt	Decrease	Increase
Lindberg[9]	Aluminium hydroxide-magnesium carbonate	0.25–5.0% MgSt	Decrease	Increase
Lindberg[9]	Aluminium hydroxide-magnesium carbonate	0.5–5.0% SLS	Increase	Decrease
Aly[8]	Lactose	0.5–3.0% MgSt	Decrease	Increase
Aly[8]	Lactose	0.5–3.0% SLS	Decrease	Increase
Aly[8]	Microcrystalline cellulose	0.5–3.0% MgSt	Decrease	Increase
Aly[8]	Microcrystalline cellulose	0.5–3.0% SLS	Decrease	Increase

results reported in the literature are very consistent with the theory over a broad range of excipients.

It must be pointed out that the target physical properties of a tablet are interrelated and that only the tablet mass, press rotation speed, and compression force can be controlled on the press. An increase of either parameter will lead to an increase in tablet hardness if the other one remains constant. Hardness is directly linked to friability because USP ⟨1216⟩ specifies that the tablet weight loss from the friability test must not exceed 1%[11]. If it does, the hardness must be increased. The tablet disintegration time and the dissolution profile are dictated by the pharmacological activity of the API. If the hardness increases, the disintegration time will increase as well because of slower water penetration in the tablet. In other words, a small modification to the formulation or to the tablet press settings is expected to affect all tablet physical properties to some degree.

To properly study the influence of a lubricant on the physical properties of tablets, it should first be verified that the lubricant particles are homogenously mixed to the rest of the formulation. This is not necessary in the study of the link between the lubricant mixing time and the physical properties of the tablets[8,12]. However, to the best of our knowledge, no investigation of the effect of the lubricant on the physical properties of the tablets in which the mixing time is fixed includes a verification of the quality of mixing of the lubricant. If the lubricant particles can be shown to be uniformly distributed throughout the powder bed, then the physical properties of the tablets sampled are representative of those of the rest of the tablets in the batch and it becomes possible to optimize the amount of lubricant needed to obtain a proper compression. This way, the deleterious effect of lubricants such as MgSt on tablet properties can be minimized.

The objective of this work is to study, for a predetermined formulation, the impact of the amount of a well-mixed lubricant on tablet mass, thickness, hardness, friability, and disintegration time. More specifically, this work aims at determining an adequate amount of lubricant required for the production of large quantities of specific tablets at a laboratory scale. The experiments were made with the same amounts of MgSt and SLS to compare the influence of the two lubricants on tablet properties when used under the same conditions.

Materials and methods

Equal quantities of MCC PH101 (JRS Vivapur, Germany) and spray-dried lactose (FlowLac 100, Meggle GmbH, Germany) were mixed in an 8-qt V-blender for 10 minutes at 26 rpm. These excipients were chosen because they are compressible, to a certain extent, without lubricant. This makes it easier to investigate the influence of very small amounts of lubricant on the tablet properties. No API was added to the formulation to make the results of this study as widely applicable as possible. In addition, no disintegrant was added to clearly show the effects of the lubricants on the properties of the tablets. Both MgSt (Peter–Greven Fett–Chemie GmbH, Germany) and SLS (Texapon K12P, Cognis, France) were used as lubricants. The particle size distributions of the excipients and the lubricants are presented in Figure 1 and Table 2.

The fill volume of the blender was set at 70%, which corresponds to a total mass of approximately 2200 g. The homogeneity of these pre-blends was assessed by extracting 20 samples and determining the MCC amount through vacuum filtration. As lactose is soluble in water whereas MCC is not, one phase of the pre-blend can be completely recovered and the other completely removed, which allows a precise assessment of the composition of the sample. The relative standard deviation (RSD) of the recovered fraction of MCC reflects the homogeneity of the pre-blend; it was deemed homogeneous if the RSD value was inferior to 1%. The proportions of MgSt added to the pre-blends were set at 0.25%, 0.5%, and 0.75%. In this work, 0.75% SLS was also mixed to the pre-blends in the same manner. A robust protocol to study the mixing of lubricants based on radioactivity and the measurement of the gamma-ray flux emitted by the lubricant particles has been described in a previous paper[13]. The lubricants were made radioactive in the SLOWPOKE nuclear reactor of École Polytechnique de Montréal prior to mixing. During mixing, the blender was stopped at regular intervals and a number of samples were

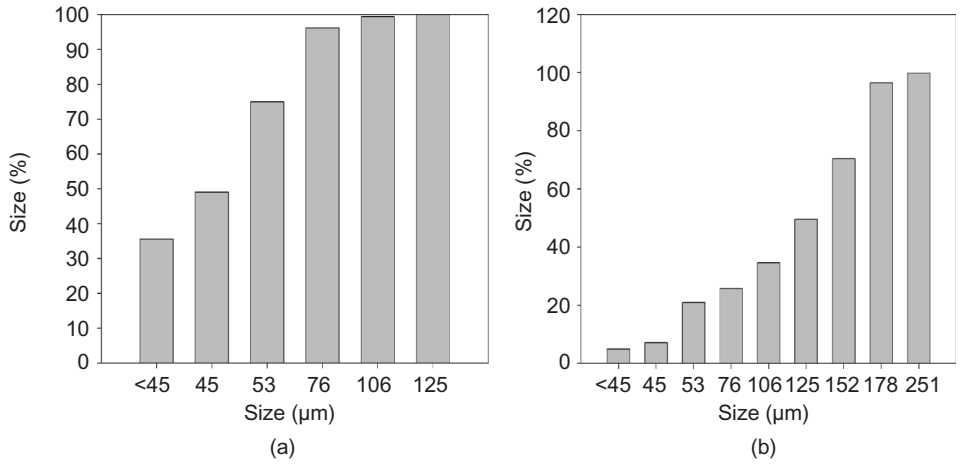

Figure 1. Cumulative particle size distributions of MCC and lactose grades used in blends. (a) MCC PH101 and (b) Spray-dried lactose.

Table 2. Cumulative particle size distributions of the lubricants used in the blends.

Lubricant	d_{10} (μm)	d_{50} (μm)	d_{90} (μm)
MgSt	3	8	24
SLS	56	258	512

extracted. Because the lubricant was radioactive, it could be detected with a scintillation detector and quantified with a calibration curve. The RSD of the lubricant concentration in every sample collected reflects the homogeneity of the blend at the corresponding time. Using this protocol, the mixing time required to adequately mix the lowest amount of lubricant was determined and this mixing time was used for the preparation of the other blends.

Using a 10-station Piccola tablet press (Riva Piccola, Argentina) with five punches and five dummies as well as a gravity-fed hopper, 100-mg round tablets were compressed from each of the five powder blends. The press was run at a speed of 35 rpm for 84 minutes, which corresponds to a tablet production of approximately 1470 g or two-thirds of each powder blend. The tablets are biconvex with straight-through bisect and have a diameter of approximately 6.35 mm, as shown in Figure 2. All tablets were produced at a similar compression force, which is related to the punch displacement.

Using a standard operating procedure, twelve 10-tablet samples and three 75-tablet samples were collected at regular intervals during the compression run to measure

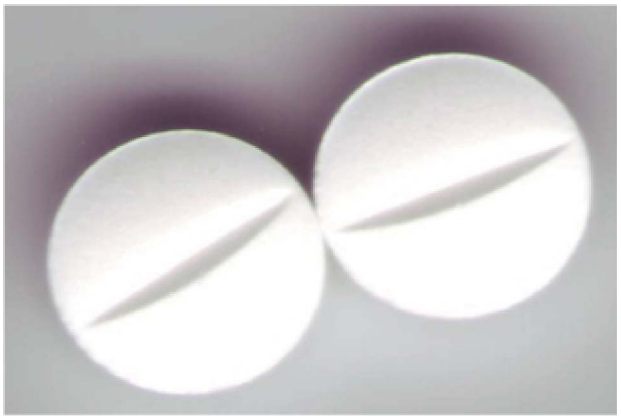

Figure 2. Examples of compressed tablets. Their shape is biconvex with straight-through bisect and their diameter is approximately 6.35 mm.

the relevant physical properties of the tablets produced. These properties, as well as the tests performed to measure them, are described in Table 3. The tablet average mass, thickness, and hardness were measured from the 10-tablet samples. The individual mass, friability and disintegration time of the tablets were measured from the 75-tablet samples. The hardness was measured by compressing the tablets between two slowly moving jaws until they are crushed. The friability corresponds to the total mass lost by approximately 65 tablets after 100 rotations in a drum and the disintegration time refers to the time required for a tablet suspended in warm water

Table 3. Tablet physical properties measured and reference standards used.

Physical property	Reference standard	Instrument
Mass (average)	In-house standard	Balance (Denver instruments)
Mass (individual)	Ph.Eur. 2.9.5	Balance (Denver instruments)
Thickness	N/A	Micrometer (Mitutoyo Canada)
Friability	USP ⟨1216⟩	Friability Tester (Electrolab, India)
Hardness	USP ⟨1217⟩	Hardness Tester (Dr. Schleuniger, USA)
Disintegration time	USP ⟨701⟩	DT-3 Disintegration Tester (Sotax AG)

to break down into pieces which can all pass through a 0.25-inch mesh screen.

Results and discussion

Before linking the amount of lubricant to the physical properties of the tablets, it should be mentioned that the compression of an unlubricated blend of MCC and spray-dried lactose quickly led to punch fouling. In this case, only one 10-tablet sample and one 75-tablet sample were collected, as opposed to a total of 15 samples for the results described below. This indicates that a minimum amount of lubricant is required to obtain an acceptable compression, even though direct-compression-grade excipients are used. The single 10-tablet sample collected from the unlubricated blend contained three outliers, whose presence is most likely due to poor powder flow in the hopper of the press. The three amounts of MgSt allowed the production of tablets that were ejected normally from the press. When 0.25% SLS was added to the formulation, the hardness of the tablets was higher than that of tablets made from unlubricated excipients. However, they could not be properly ejected from the press because of their adhesion to the lower punch. For this reason, the compression run was aborted and only one 10-tablet sample and one 75-tablet sample were collected in that case.

Mass and thickness

Figures 3a and b display the evolution of the average tablet mass with respect to time and the SD on each value. The horizontal lines represent the maximum and minimum mass according to the standards of the European Pharmacopeia.

Figure 3a shows that the mass of tablets lubricated with MgSt varies little during compression, with an average SD lower than 2% for each amount. This indicates that MgSt acts as a glidant as well as a lubricant in this case, a property well documented in the literature[8,14]. The improvement of the powder flow has been studied by mixing MgSt to MCC, the most cohesive of the two excipients used in the pre-blends, and by measuring the flow of the resulting blend (FT300 Flow Tester, Sotax AG, Switzerland). The results shown in Table 4 indicate that the glidant effect of MgSt is mainly felt when very small amounts are added to the formulation. Figure 3b indicates that the average mass of tablets produced from excipients lubricated with SLS is similar to that of tablets produced with an identical amount of MgSt. This suggests that SLS has glidant properties similar to those of MgSt despite the fact that the SLS particles do not adsorb themselves of the larger excipients.

The effect of MgSt and SLS on the tablet mass can be studied in greater detail by comparing the SD on each amount with Student's *t*-tests, which can be used to determine whether there is a statistically significant difference between them. The null hypothesis, which is rejected in this case if the *P*-value is lower than 0.05, is that the average SD are equal. The results of these tests are shown in Table 5.

The small *P*-values of Table 5 indicate that the SD increases with the amount of MgSt and that the SD of the tablets lubricated with 0.75% SLS is much lower than that of the tablets lubricated with the same amount of MgSt. This explains why the difference between SD is statistically significant for all relevant comparisions. The results indicate that when higher amounts of lubricant are required, SLS may be preferable to MgSt because it ensures a good powder flow with less variability of the tablet mass.

Table 4. Evaluation of the flowability of MCC PH101 in relation to the amount of MgSt added. Measurement value increases with flowability.

MgSt added (%)	Flowability measurement
0	0.21
0.5	0.39
1	0.42

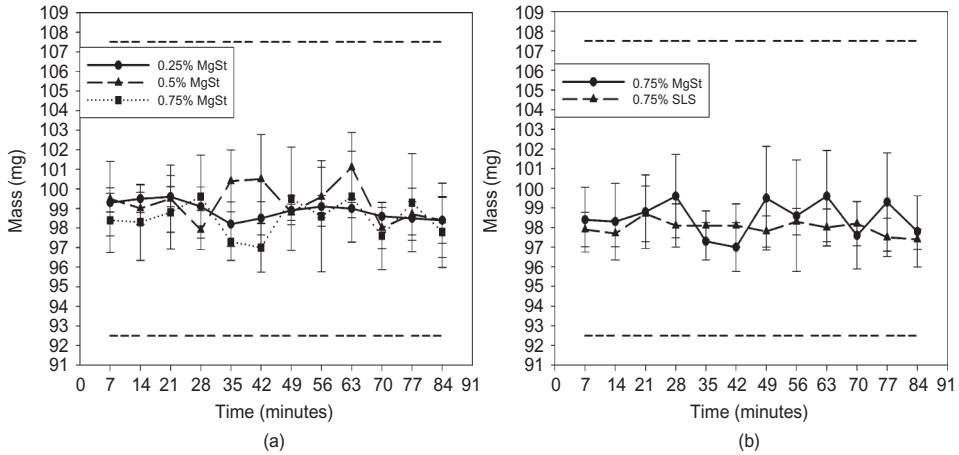

Figure 3. (a) Average tablet mass of tablets lubricated with 0.25%, 0.5%, and 0.75% MgSt. (b) Comparison of the effect of 0.75% of both lubricants on the tablet mass.

Table 5. Description and results of Student's *t*-test (P = 0.05) performed on SD calculated from the average tablet masses. The normality of the distributions of the SD has been verified for all lubricant amounts.

1	2	Average SD 1	Average SD 2	*P*-value
0.25% MgSt	0.5% MgSt	0.765	1.440	0.0006
0.25% MgSt	0.75% MgSt	0.765	1.966	$1{\cdot}10^{-6}$
0.5% MgSt	0.75% MgSt	1.44	1.966	0.0271
0.75% MgSt	0.75% SLS	1.966	0.911	$5{\cdot}10^{-6}$

In addition to the twelve 10-tablet samples used to measure the average mass, the individual mass of 20 tablets was measured from each of the three 75-tablet samples collected during a compression run. The single 75-tablet sample in which no lubricant was used contained tablets whose mass was as low as 57 mg and seven tablets failed to meet the specifications of the European Pharmacopeia. This reflects the very poor flow of the blend in the absence of lubricant, as shown in Table 4. The distribution of the masses in each completed run is shown in Figure 4.

The distributions show that the individual masses of the tablets tend to be inferior to the target mass of 100 mg for MgSt levels below 0.75%. When the amount of MgSt reaches 0.75%, the individual tablet mass increases as shown by the median, but each distribution becomes much broader, in accordance with the average SD reported in Table 5. Because Table 4 shows that there is no significant improvement in the flow properties of MCC between 0.5% and 0.75%, the explanation may lie in the flow behavior of the lubricated excipients rather than in their flow rate. A comparison of the masses of the tablets lubricated with identical amounts of MgSt and SLS shows that although the medians are similar, the distribution of the masses of SLS tablets is much more narrow. Because the tablets are produced in the same manner in both cases, a possible explanation may be that both lubricants improve the flow of the excipients, but that the flow of MgSt-lubricated excipients is irregular.

The true importance of the thickness as a physical property lies in the fact that the diameter of the tablet corresponds to the diameter of the dies and can therefore be considered constant. As a result, the thickness directly reflects the volume of the tablets. Knowing the tablet mass, one can then readily evaluate a 'modified density' of the tablets, which can be used as a rough indicator of their composition. Figure 5a shows that the SD of the thickness of the tablets lubricated with MgSt is lower than 1% for each of the three amounts. This implies that the tablet density varies little as well, as shown in Figure 6a and b. Such small variations may indicate that an increase in the amount of MgSt does not lead to a segregation of the blend in the hopper prior to compression and that the composition of the tablets is unaffected. Figure 5b shows that the thickness of tablets produced with SLS varies slightly more than that of the tablets produced with MgSt. One can also observe that the thickness of tablets produced from SLS is noticeably higher than that of the tablets produced with MgSt. As the densities of the SLS and MgSt used are 0.15 and 0.37 g/mL, respectively, and the same mass of lubricant is used in both cases, the difference in thickness can be attributed to the larger volume occupied by the SLS particles within the tablets.

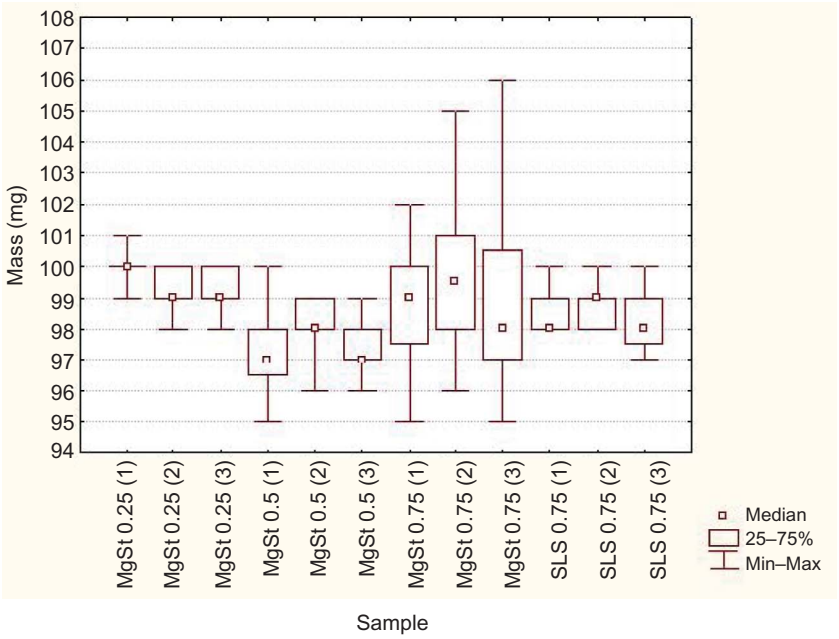

Figure 4. Box-and-whisker plots of the individual masses measured for all 75-tablet samples. The plots show the median, the 25th and 75th percentiles, and the range of the measurements.

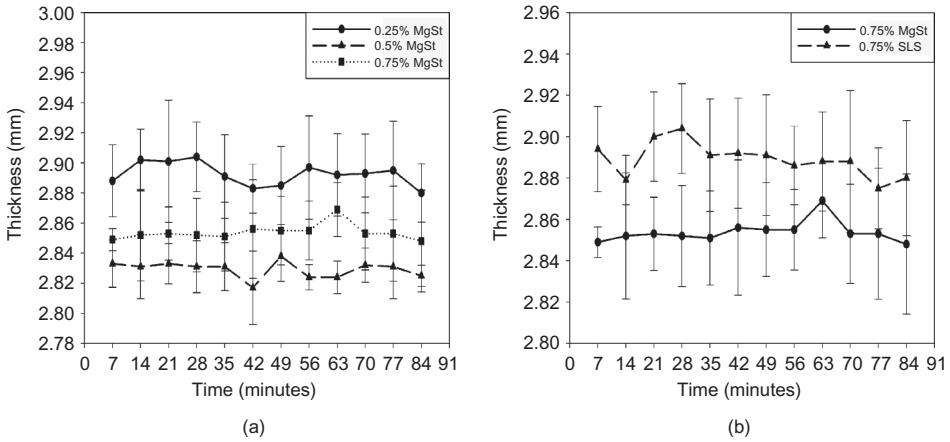

Figure 5. (a) Average thickness of tablets lubricated with 0.25%, 0.5% and 0.75% of MgSt. (b) Comparison of the effect of 0.75% of both lubricants on the tablet thickness.

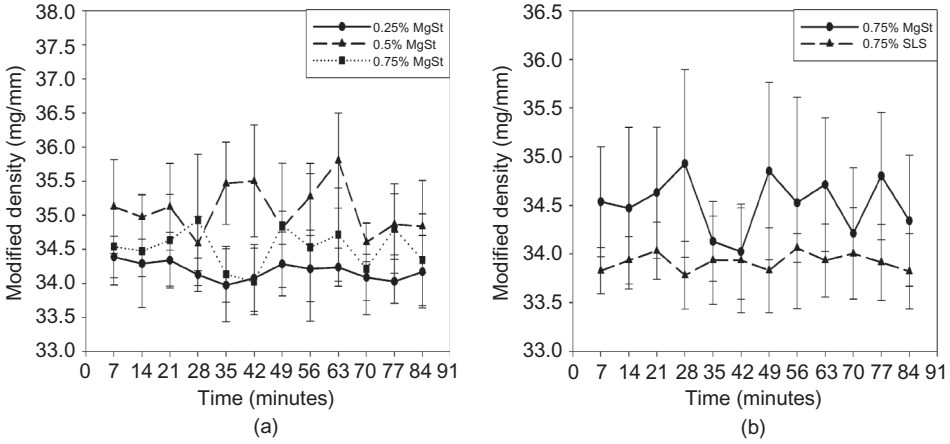

Figure 6. (a) Average modified density of tablets lubricated with 0.25%, 0.5%, and 0.75% of MgSt. (b) Comparison of the effect of 0.75% of both lubricants on the modified density of the tablets.

Table 6. Description and results of Student's *t*-test (P = 0.05) performed on SDs calculated from the average tablet thicknesses. The normality of the distributions of the SDs has been verified for all lubricant amounts.

1	2	Average SD 1	Average SD 2	*P*-value
0.25% MgSt	0.5% MgSt	0.027	0.015	0.0002
0.25% MgSt	0.75% MgSt	0.027	0.024	0.363
0.5% MgSt	0.75% MgSt	0.015	0.024	0.005
0.75% MgSt	0.75% SLS	0.024	0.024	0.961

Just as in the case of the tablet mass, the SD of the average thickness can be compared with Student's *t*-tests. The results of these tests are shown in Table 6.

The *P*-values of Table 6 indicate that the link between the amount of MgSt and the SD of the thickness is not as clear as the one concerning the SD of the mass, as evidenced by the fact that the difference between the SD of tablets lubricated with 0.25% MgSt and those of the tablets lubricated with 0.75% MgSt is not statistically significant. It is interesting to note that the difference between the SDs of the thickness of tablets lubricated with equal amounts of MgSt and SLS be insignificant as well, despite the fact that the thickness itself is clearly different in Figure 5b.

Hardness, friability, and disintegration time

These three parameters are studied together because of their known sensitivity to the presence of MgSt[6]. Furthermore, when using identical amounts of SLS in the production of sodium chloride tablets, Hölzer and Sjögren[10] observed a disintegration time nearly 5 times shorter and a tensile strength 3 times higher than those observed in the case of MgSt-lubricated ones.

Figure 7a shows that the difference in tablet hardness between the blends lubricated with 0.25% and 0.5% MgSt is almost negligible. However, there is a drop of approximately 25% in tablet hardness as the amount of MgSt increases from 0.50% to 0.75%. This could indicate that the excipient particles must be saturated to a certain extent with MgSt before a decrease in hardness can be

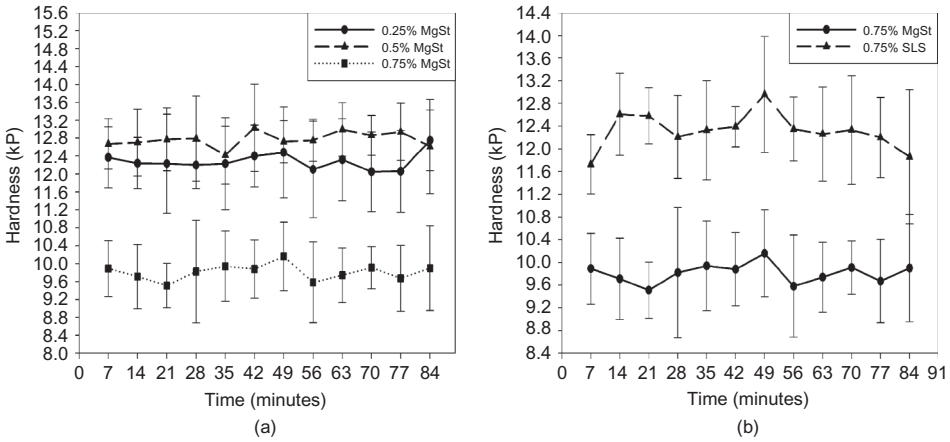

Figure 7. (a) Average hardness of tablets lubricated with 0.25%, 0.5%, and 0.75% of MgSt. (b) Comparison of the effect of 0.75% of both lubricants on the tablet hardness.

felt. Similar results have been reported in the literature[15], but the relationship between the amount of MgSt and the hardness of the tablets seems to depend mostly on the physical properties of the excipients used.

The hardness of tablets lubricated with 0.75% MgSt and 0.75% SLS are compared in Figure 7b, which shows that the SLS, contrary to the MgSt, does not lower the hardness of the tablets in this case. This lack of effect on the tablet hardness may be partly due to the fact that, contrary to MgSt, the lubrication mechanism of SLS does not involve the formation of a film around excipient particles and has therefore little impact on the strength of interparticle bonds. The SD of the hardness of tablets lubricated with SLS appears to vary slightly more than that of tablets lubricated with the same amount of MgSt, as is the case with tablet thickness in Figure 5b. Note that Lindberg[9] observed that, in the case of tablets made from lubricated granules containing antacid and corn starch, the tablet hardness remained constant when the SLS concentration was increased. This stands in contrast to the decrease of tablet hardness with increasing MgSt amounts reported by most authors[1].

The results of the comparison of the average SD of the tablet hardnesses by means of Student's *t*-tests are shown in Table 7. In all cases, the difference between the SDs is insignificant, despite of the considerable difference between the average hardness of tablets lubricated with 0.75% MgSt and that of tablets containing an equal amount of SLS or 0.50% MgSt.

Table 7. Description and results of Student's *t*-test (P = 0.05) performed on SDs calculated from the average tablet hardnesses. The normality of the distributions of the SDs has been verified for all lubricant amounts.

1	2	Average SD 1	Average SD 2	*P*-value
0.25% MgSt	0.5% MgSt	0.841	0.687	0.079
0.25% MgSt	0.75% MgSt	0.841	0.737	0.212
0.5% MgSt	0.75% MgSt	0.687	0.737	0.546
0.75% MgSt	0.75% SLS	0.737	0.746	0.921

Table 8. Measured values of tablet individual mass, friability, and disintegration time in the case of unlubricated and lubricated blends, for each 75-tablet sample collected during a typical compression run.

			Disintegration time (seconds)	
Lubricant	Amount	Friability (%)	Min	Max
MgSt	0.25 (1)	0.17	530	1490
MgSt	0.25 (2)	0.21	361	721
MgSt	0.25 (3)	0.06	510	3240
SLS	0.25	0.08	530	2437
MgSt	0.5 (1)	0.38	1995	4140
MgSt	0.5 (2)	0.03	705	2140
MgSt	0.5 (3)	0.04	516	2227
MgSt	0.75 (1)	0.14	300	3460
MgSt	0.75 (2)	0.09	250	790
MgSt	0.75 (3)	0.11	253	530
SLS	0.75 (1)	0.08	780	>3300
SLS	0.75 (2)	0.15	490	>3300
SLS	0.75 (3)	0.08	1420	>3300

Table 8 indicates that the average friability of tablets lubricated with MgSt amounts of 0.25%, 0.50%, and 0.75% are 0.15%, 0.15%, and 0.11%, respectively. Considering that the average friability of the tablets lubricated with 0.75% SLS is approximately 0.10%, and in spite of the fact that a rather important variability can be noticed in each case, the results seem to indicate that the lubricant, whether MgSt or SLS, has little to no influence on tablet friability. This is interesting because there is a clear link between the hardness of the tablets and the amount of MgSt, as shown in Figure 7a, and because the hardness and the friability are both related to the strength of the interparticle bonds. But the results also show that they are not affected to the same extent by the amount of MgSt, making the link between them unclear. Previous reports in the literature have indicated that an increase in MgSt fraction is expected to lead to an increase in tablet friability through a decrease

in tablet hardness[8,15], but the results presented therein also show that the extent of this increase may be affected by other related parameters.

In theory, the disintegration time should increase with the amount of MgSt because of the hydrophobic nature of the film[8], but this is not the case here. Instead, as shown in Table 8, the disintegration time seems to decrease with the amount of MgSt when this amount is higher than 0.50%. A possible explanation for this behavior would be the overriding influence of the strength of the interparticule bonds on the disintegration time of the tablets as well as on their hardness and friability. One must still be cautious when interpreting the disintegration time data because the large differences between the results obtained for the same amount of MgSt indicate that the standard disintegration test did not provide reproducible results.

Even though an increase in the concentration of SLS is expected to lead to a decrease in tablet hardness, as in the case of MgSt, and thus a shorter disintegration time because of its hydrophilic nature[9], the counterintuitive results of Table 8 clearly show that a larger amount of SLS increases the tablet disintegration time. Furthermore, these results indicate that the disintegration time of tablets lubricated with 0.75% SLS is longer than that of the tablets lubricated with the same amount of MgSt. The fact that neither lubricant has the expected effect on the disintegration time supports the explanation that this parameter is not dependent on the behavior of the lubricant with regard to water as much as its influence on the strength of the bonds between particles. The lack of influence of SLS on the strength of interparticle bonds, which can be seen in the hardness of tablets made with this lubricant, may also explain the higher disintegration times observed in comparison to those of the tablets containing MgSt. By contrast, when MgSt was used, an increase in the amount of lubricant from 0.50% to 0.75% led to a decrease in the strength of the interparticule bonds that facilitated the penetration of water within the tablets and lowered the disintegration time. The lack of influence of SLS on the interparticule bonds is due to the fact that SLS particles are too large to adsorb on excipient particles. The interactions between excipient particles are then similar whether SLS is present or not.

Conclusion

A mixture of equal parts of MCC PH101 and spray-dried lactose was lubricated with three different concentrations of MgSt to assess the impact of this lubricant on the final tablet properties with the knowledge that the lubricant and the excipients are homogeneously mixed. Two preblends were also lubricated with 0.25% and 0.75% SLS to determine whether SLS can be used as a lubricant in this case and if so, how its impact on tablet properties compares to that of MgSt. Results show that a minimum of lubricant is required to improve powder flowability and prevent punch fouling. On the whole, it can be concluded from Figures 3 and 7a as well as from Table 8 that an MgSt amount of 0.25% is sufficient to produce large quantities of tablets and that any increase in the amount of MgSt beyond this level does not lead to an improvement in the physical properties studied. It should be noticed that this proportion of MgSt is identical to that reported in the previous works regarding the flow of MCC[14]. In this case, the minimum amount of MgSt needed may even be lower than 0.25%, the lowest fraction of MgSt considered for our experiments. The statistical analysis of the tablet mass by means of Student's *t*-tests and box-and-whisker plots indicates that an increase in the amount of MgSt will lead to a greater variability of the mass, which may lead to the production of tablets that do not meet the required specifications.

Results also indicate that the minimal amount of SLS required to obtain a proper compression is higher than that of MgSt, and that the SLS does not weaken the interparticle bonds as much as MgSt, as evidenced by the higher disintegration times recorded with SLS. In the case of both MgSt and SLS, no solid conclusion could be drawn concerning the relationship between the lubricant concentration and the tablet friability.

The conclusions drawn in this work are limited by the difficulty of compressing suitable tablets at very low lubricant levels, particularly in the case of SLS. The decision not to include a disintegrant in the preblend came at the cost of a high variance in the disintegration time measurements, which complicated their interpretation. Further work should include additional friability and disintegration tests on tablets of the same composition as those tested in this article to draw stronger conclusions on the link between the amount of lubricant and tablet friability and disintegration time. This analysis would also be strengthened by analyzing tablets produced from blends lubricated with for instance 0.10% MgSt and 0.35% SLS or preblends with different MCC : lactose ratios than the one used in this work.

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Declaration of interest

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References

1. Aly S. (2006). The resistance to compression index as a parameter to evaluate the efficiency of lubricants in pharmaceutical tabletting. J Drug Deliv Sci Technol, 16(2):151–5.
2. Bolhuis G, Lerk C, Zijlstra H, De Boer A. (1975). Film formation by magnesium stearate during mixing and its effect on tabletting. Pharm Weekbl, 110:317–25.
3. Bossert J, Stamm A. (1980). Effect of mixing on the lubrication of crystalline lactose by magnesium stearate. Drug Dev Ind Pharm, 6(6):573–89.
4. Chowhan ZT, Amaro A. (1988). Optimization of tablet friability, maximum attainable crushing strength, weight variation and in vitro dissolution by establishing in-process variable controls. Drug Dev Ind Pharm, 14(8):1079–106.
5. De Boer A, Bolhuis G, Lerk C. (1978). Bonding characteristics by scanning electron microscopy of powders mixed with magnesium stearate. Powder Technol, 20:75–82.
6. Gordon M. (1994). Process considerations in reducing tablet friability and their effect on in vitro dissolution. Drug Dev Ind Pharm, 20(1):11–29.
7. Hölzer A, Sjögren J. (1981). Evaluation of some lubricants by the comparison of friction coefficients and tablet properties. Acta Pharm Suec, 18(1):139–48.
8. Lindberg N-O. (1972). Evaluation of some tablet lubricants. Acta Pharm Suec, 3(1):207–14.
9. Otsuka M, Yamane I, Matsuda Y. (2004). Effects of lubricant mixing on compression properties of various kinds of direct compression excipients and physical properties of the tablets. Adv Powder Technol, 15(4):477–93.
10. Perrault M, Bertrand F, Chaouki J. (2010). An investigation of magnesium stearate blending in a v-blender through gamma-ray detection. Powder Technol, 200(3):234–45.
11. Podczeck F, Miah Y. (1996). The influence of particle size and shape on the angle of internal friction and the flow factor of unlubricated and lubricated powders. Int J Pharm, 144(1):187.
12. Ragnarsson G, Hölzer A, Sjögren J. (1978). The influence of mixing time and colloidal silica on the lubricating properties of magnesium stearate. Int J Pharm, 3:127–31.
13. Roblot L, Puisieux F, Duchêne D. (1983). Étude de la lubrification par le stéarate de magnésium: Influence des proportions de lubrifiant et du procédé de mélange sur les caractéristiques des comprimés. Labo-Pharma, Probl Tech, 31(336):843–7.
14. Shah A, Mlodozeniec A. (1977). Mechanism of surface lubrification: Influence of duration of excipient mixing on processing characteristics of powders and properties of compressed tablets. J Pharm Sci, 66(10):1377–82.
15. United States Pharmacopeia. (2008). USP 31 - NF 28. 31st ed. Washington, DC: Port City Press.