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# Improving the hardness of dry granulated tablets containing sodium lauryl sulfate

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ABSTRACT

The impact of the addition of a wetting agent, the surfactant sodium lauryl sulfate (SLS), on the tablet hardness of a dry granulated, solid oral dosage form was investigated. In three batches, SLS was added concurrently with: (1) a poorly soluble, highly hydrophobic active pharmaceutical ingredient (API) and the other excipients prior to the initial blending step, (2) magnesium stearate prior to roller compaction, or (3) magnesium stearate prior to tableting. A fourth batch, which did not contain SLS, served as a control. The maximum hardness of 100 mg, 1/4″-SRC tablets for the four batches – SLS added initially, prior to roller compaction, prior to tableting, and no SLS – were 61 ± 3, 71 ± 3, 89 ± 5, and 86 ± 3 N, respectively, suggesting reduced processing of SLS improves tablet hardness by ∼50%. Dissolution of the tablets in 900 ml of simulated gastric fluid with paddles at 75 rpm showed that: (1) there was no impact on the insertion point of SLS into the process on API dissolution, and (2) that the presence of SLS improved dissolution by 5% compared to the control tablets. Adding SLS just prior to tableting can improve tablet hardness and yield similar dissolution performance relative to SLS addition prior to the initial blending step.



## 1. Introduction

Granulation of a pharmaceutical powder blend is often utilized prior to tableting in cases where it is necessary to: (1) improve the flow characteristics of the powder blend (Skinner et al., 1999; Habib et al., 2000), and/or (2) reduce the segregation potential of the active pharmaceutical ingredient (API) from the rest of the powder blend to improve content uniformity (am Ende et al., 2007). Dry granulation by roller compaction has several advantages relative to both wet granulation methods and dry granulation by slugging. First, dry granulation, relative to wet granulation, is preferred for APIs that degrade in the presence of elevated heat or moisture conditions during processing. Second, use of dry granulation bypasses the energy- and time-consuming drying step typically required after wet granulation (Sheskey et al., 1994; Inghelbrecht and Remon, 1998). Finally, dry granulation with roller compaction is a continuous process, which offers more streamlined manufacturing compared to dry granulation by slugging or to wet granulation, which are both batch processes (Hakanen et al., 1993; Inghelbrecht et al., 1997).

When a poorly soluble, highly hydrophobic (i.e. log $K_{O/W} > 1$) API is to be delivered with a tablet manufactured via dry granulation, the formulator may consider including a surface active wetting agent in the tablet formulation to improve the contact of the dissolving media with the API, and, thereby improve dissolution. One common wetting agent used in oral drug delivery is the surfactant, sodium lauryl sulfate (SLS) (Kassem and Ghazy, 1973; Boulenc et al., 1995; Shokri et al., 2008). By way of some examples, SLS has been shown to improve: (1) the performance of tiludronate transport across human Caco-2 monolayers (Boulenc et al., 1995), (2) the disintegration time of diiodohydroxyquinoline tablets (Kassem and Ghazy, 1973), and (3) the performance of indomethacin release from swellable elementary osmotic pump tablets (Shokri et al., 2008).

Ideally, to improve the solubility of a poorly soluble API, the formulator would like to achieve close contact between the API and the wetting agent to ensure that improved API wettability will occur as the tablet disintegrates *in vivo*. This approach would suggest the wetting agent and API should be added together in the same step of the manufacturing process. However, SLS has also been shown to possess some tablet lubrication properties, although the demonstrated degree of lubrication with SLS is typically lower than the degree of lubrication observed with magnesium stearate (Caldwell and Westlake, 1972; Lindberg, 1972; Saleh et al., 1984; Baichwal and Augsburger, 1988; Aly, 2006). Therefore, by adding SLS at the beginning of the tablet manufacturing process at the API addition step, the formulator also takes on the additional risk of

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**Table 1**
Formulation of the 100 mg standard round convex tablets.

| Item | Component | Grade | Mfg. Lot # | With SLS | No SLS |
|---|---|---|---|---|---|
| 1 | Compound X | – | – | 0.25 | 0.25 |
| 2 | MCC | Avicel PH102 | P207818621 | 62.00 | 62.67 |
| 3 | Lactose monohydrate | FastFlo 316 | 850701561 | 31.00 | 31.33 |
| 4 | SSG | Explotab | 4111054088 | 5.00 | 5.00 |
| 5 | SLS | Texapon | CS33060004 | 1.00 | 0.00 |
| 6 | IG-MgSt | HyQual | M03470 | 0.25 | 0.25 |
| 7 | EG-MgSt | HyQual | M03470 | 0.50 | 0.50 |
| Total weight | | | | 100 mg | 100 mg |

manufacturing tablets with low hardness and tensile strength associated with over-lubricating the powder blend. This risk is further compounded if a more common tablet lubricant (i.e. magnesium stearate) is added to the powder blend in downstream processing steps. Further, the over-lubrication risk would be more prominent for a manufacturing process containing a dry granulation step relative to a direct compression process, due to the additional processing steps with the former which can increase the effect of tablet lubricants on tablet hardness and tensile strength.

Presently, there is very little information on the impact of SLS on the hardness and tensile strength of immediate release tablets manufactured by roller compaction. In this investigation, then, we will examine the impact of the insertion point of SLS in the manufacturing process on the hardness and tensile strength of dry granulated tablets containing a poorly water-soluble (<10 μg/ml), highly hydrophobic (clog $K_{O/W}$ > 3) proprietary API. Specifically, the impact of adding SLS: (1) prior to the initial blend step, (2) at the intragranular (IG) lubrication step, and (3) at the extragranular (EG) lubrication step, on the tablet hardness and tensile strength relative to a control formulation without SLS, will be reported. As the results will show, the tablets with the highest hardness and tensile strength are produced when SLS is added to the dry granulation tablet manufacturing process during the extragranular lubrication step. Finally, since the manufactured tablets also contain a poorly soluble, highly hydrophobic API, it will also be shown that delaying the addition of SLS from the initial blending step to the EG lubrication step does not adversely impact the dissolution of the API.

## 2. Materials and methods

### 2.1. Materials

The materials used for the experiments, batch numbers, and per-tablet formulation are listed in Table 1. Microcrystalline Cellulose (MCC) was obtained from FMC Corporation (Philadelphia, PA), Lactose Monohydrate from Foremost Farms (Baraboo, WI), Sodium Starch Glycolate (SSG) from JRS Pharma (Rosenberg, Germany), SLS from Cognis GmbH (Monheim, Germany), and MgSt from Mallinckrodt (Hazelwood, MO). Excipient consistency was maintained within each batch, and all batches were 1.75 kg in size. Simulated gastric fluid (SGF, 900 ml) containing HCl, pepsin and NaCl was obtained from VWR (West Chester, PA) and employed as the bio-relevant dissolution media for the test.

### 2.2. Tablet manufacture

The batches were developed using a 2 min and 30 s blender pre-coat, followed by sieving and a blend-mill-blend process. The full manufacturing process is shown in Fig. 1. The studied SLS insertion points are indicated in bold text. Batches were blended for 12 min and 30 s per blend at 24 rpm in a 4-quart V-blender (Patterson-Kelly Company, East Stroudsberg, PA). Milling was performed using a Co-Mil 197 (Quadro Engineering, Waterloo, Canada) at 1900 rpm with a 0.8-mm aperture screen and a rounded impeller. The API, SLS, and MgSt were screened through a 600-micron sieve prior to their addition to the blend. Lubrication blending was performed for 3 min at 24 rpm in the same 4-Quart V-blender. Roller compaction was performed using a Gerteis Minipactor (Gerteis Maschinen, Jona, Germany), and the parameters used are listed in Table 2. 100 mg tablets were produced using a Kilian T-100 rotary tablet press (IMA S.p.A, Köln, Germany) with three sets of 1/4-inch (6.35-mm), standard round concave (SRC) tooling and a main compression dwell time of 10.6 ms. Tablets were produced with a thickness of 3.10 ± 0.20 mm.

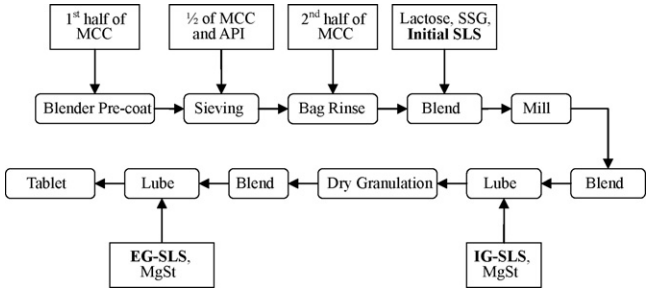


**Fig. 1.** Process flowsheet for the manufacture of the 100 mg tablets. Insertion points for SLS are presented in bold text.

### 2.3. Evaluation of tablet physical properties

Tablet hardness, thickness, diameter, and mass measurements were performed on 10 tablets per compression force using a PharmaTest rotary tablet tester (Pharma Test Apparatebau GmbH, Hainburg, Germany).

### 2.4. Calculation of tensile strength and solid fraction for SRC tablets

The tensile strength, $\sigma_T$, of the SRC tablet was calculated from the values of the hardness, thickness, and diameter of the SRC

**Table 2**
Gerteis minipactor roller compaction parameters.

| Parameter | Value |
|---|---|
| Agitator speed | 10 rpm |
| Roll gap control on/off | ON |
| Tamp/feed ratio | 200% |
| Roll type | Knurled/knurled |
| Roll configuration | Side-seals ON |
| Roll speed | 2 rpm |
| Roll pressure | 4.0–4.5 kN/cm |
| Roll gap | 2.0 mm |
| Granulator design | Pocket rotor |
| Granulator speed | 50 rpm |
| Screen size | 0.8 mm (rasping) |
| Screen to granulator distance | 1.25 mm |

tablets using the following equation (Pitt et al., 1988):

$$\sigma_T = \frac{10F}{\pi D^2}\left(2.84\frac{H}{D} - 0.126\frac{H}{H-2H_c} + 3.15\frac{H-2H_c}{D} + 0.01\right)^{-1} \quad (1)$$

where $F$ is the tablet hardness, $D$ is the diameter of the tablet, $H$ is the total thickness of the tablet, and $H_c$ is the thickness of the convex cups.

Solid fraction, SF, of the SRC tablets was calculated from the ratio of the apparent density to the true density of the powder blend (1.55 g/cm$^3$). Apparent density was calculated by dividing the mass of the SRC tablet by the volume of the SRC tablet, which was calculated using the following equation:

$$V_{SRC} = V_{band} + 2V_{cup} \quad (2)$$

where $V_{band}$ is calculated using the equation for the volume of disk:

$$V_{band} = \pi(H - 2H_c)D^2 \quad (3)$$

and $V_{cup}$ is calculated using the equation for the volume of a dome:

$$V_{cup} = \pi H_c^2\left(r_c - \frac{H_c}{3}\right) \quad (4)$$

where $r_c$, the radius of curvature for a dome, is calculated from the following equation:

$$r_c = \frac{4H_c^2 + D^2}{8H_c} \quad (5)$$

### 2.5. Tablet dissolution testing

Dissolution testing of tablets was conducted according to USP ⟨7 1 1⟩, utilizing Apparatus 2 with paddles rotating at 75 rpm. Samples were collected at 15 min, 30 min, 1 h, 2 h, 3 h, 5 h, 8 h, 22 h and 24 h using a 5 ml syringe equipped with a cannula. The 22 h time point served as the infinity time point to ensure complete dissolution from the dosage forms. After this time point, the paddle speed was increased to 150 rpm and vessels were sampled again after 2 h (i.e. 24 h time point) to ensure a complete dissolution profile. Samples were then filtered and collected in an HPLC vial for end analysis. Each manufactured batch was assayed in triplicate.

The HPLC analysis (Waters, MA) was carried out using a YMC-pack pro column (C18, 50-mm × 4.6-mm ID, 3 μm particle size) at 30 °C. The mobile phase consisted of Acetonitrile/Water/Trifluoroacetic acid (TFA) (45/55/0.5%, v/v). Samples were eluted under isocratic conditions at a flow rate of 1.0 ml/min. The injection volume was 20 μl and detection was performed by UV at 220 nm. The total run time was 5.0 min and the quantification was achieved via response comparison against an external standard.

## 3. Results

### 3.1. Impact of SLS insertion point on tablet hardness and tensile strength

Experiments were performed examining the effect on tablet hardness of relocating SLS within the manufacturing process. The four batches were produced at a ribbon solid fraction of 0.63, with 0.50% EG-MgSt, and their granulations blended at 75% blender operating capacity. The SLS insertion point was varied in three batches, and SLS was removed in the fourth batch. The hardness–compression profiles for the various SLS conditions are shown in Fig. 2. A summary of the data is also reported in Table 3. The IG SLS tablets were ~10 N (~17%) harder than initial SLS tablets between 12 and 15 kN compression force, while EG SLS tablets and tablets containing no SLS were 15–18 N (~20–25%) harder than the IG SLS tablets and 25–28 N (~40–50%) harder than initial SLS tablets

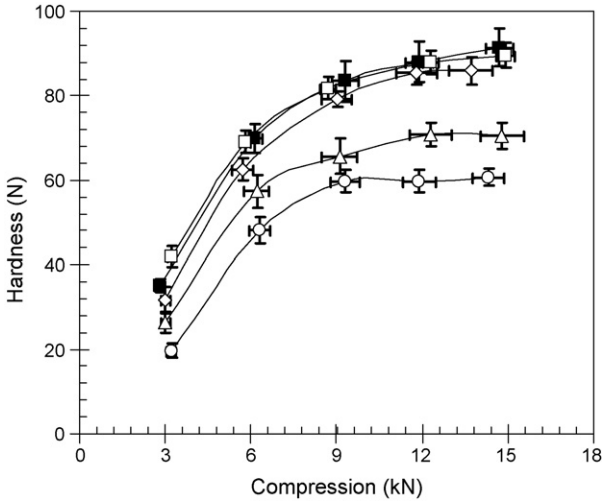


**Fig. 2.** Hardness–compression profiles for different SLS insertion points. Key: open diamonds – tablets containing no SLS; open squares – SLS added prior to tableting; open triangles – SLS added prior to roller compaction; open circles – SLS added prior to the initial blending step; and black squares – placebo formulation with SLS added prior to tableting. Errors bars: ±1 standard deviation, $n = 10$.

for this compression range. Further, to confirm that the observed differences are not due to inter-batch variability, the batch containing EG SLS was remanufactured as a placebo batch (in which the API was replaced with an equal amount of MCC) and showed no significant difference ($p > 0.1$) to the active EG SLS batch containing 0.25% API.

Fig. 3 shows the tensile strength of the tablets as a function of solid fraction. A summary table of these values is reported in Table 4. These profiles indicate the compactibility of each formulation and manufacturing method. Each point is an average of ten measurements. IG SLS addition increases the tensile strength of the formulation by 0.3 MPa (~15–20%) at 0.85 solid fraction compared to the Initial SLS formulation. EG SLS addition increases the tensile strength by 0.40 MPa (~20%) and 0.7 MPa (~40%) at 0.85 solid fraction relative to IG SLS and Initial SLS addition, respectively. The difference between the EG and No SLS formulations was negligible.

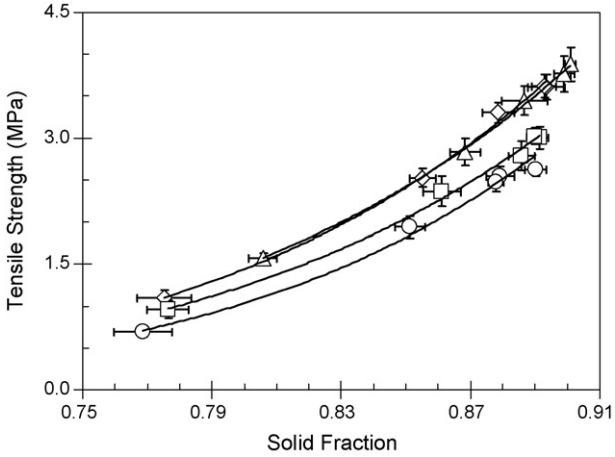


**Fig. 3.** Tensile strength vs. solid fraction curves for different SLS insertion points. Key: open diamonds – tablets containing no SLS; open squares – SLS added prior to tableting; open triangles – SLS added prior to roller compaction; and open circles – SLS added prior to the initial blending step. Errors bars: ±1 standard deviation, $n = 10$.

**Table 3**
Hardness–compression data for tablets obtained from different SLS insertion points in the manufacturing process.[a,b,c]

| Target force (kN) | No SLS | | Initial SLS | | IG SLS | | EG SLS | | EG SLS placebo | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Actual force (kN) | Hardness (N) | Actual force (kN) | Hardness (N) | Actual force (kN) | Hardness (N) | Actual force (kN) | Hardness (N) | Actual force (kN) | Hardness (N) |
| 3 | 3.0 (0.2) | 32 (3) | 3.2 (0.2) | 20 (2) | 3.0 (0.2) | 26 (3) | 3.2 (0.2) | 42 (2) | 2.8 (0.1) | 35 (2) |
| 6 | 5.7 (0.4) | 63 (3) | 6.3 (0.4) | 48 (3) | 6.2 (0.4) | 57 (4) | 5.8 (0.3) | *69 (3)* | 6.1 (0.2) | *70 (2)* |
| 9 | 9.0 (0.5) | **79 (2)** | 9.3 (0.5) | 60 (3) | 9.1 (0.6) | 66 (4) | 8.7 (0.5) | ***82 (5)*** | 9.3 (0.3) | *83 (3)* |
| 12 | 11.8 (0.7) | **85 (3)** | 11.9 (0.6) | 60 (3) | 12.3 (0.7) | 71 (3) | 12.3 (0.5) | ***88 (5)*** | 11.9 (0.3) | *88 (3)* |
| 15 | 13.7 (0.8) | 86 (3) | 14.3 (0.6) | 61 (2) | 14.8 (0.8) | 71 (3) | 14.9 (0.5) | *89 (5)* | 14.7 (0.3) | *91 (3)* |

[a] Data reported as mean (standard deviation).
[b] $N = 10$ for hardness data, $N > 100$ for compression force data.
[c] Values in bold or italics are not significantly different ($p > 0.1$).

**Table 4**
Tensile strength and solid fraction data for tablets obtained from different SLS insertion points in the manufacturing process.[a]

| No SLS | | Initial SLS | | IG SLS | | EG SLS | |
|---|---|---|---|---|---|---|---|
| Solid Fraction | Tensile Strength (MPa) | Solid Fraction | Tensile Strength (MPa) | Solid Fraction | Tensile Strength (MPa) | Solid Fraction | Tensile Strength (MPa) |
| 0.775 (0.008) | 1.10 (0.09) | 0.769 (0.009) | 0.70 (0.07) | 0.776 (0.006) | 0.96 (0.10) | 0.806 (0.004) | 1.58 (0.06) |
| 0.855 (0.004) | 2.52 (0.11) | 0.851 (0.005) | 1.94 (0.13) | 0.861 (0.006) | 2.36 (0.18) | 0.868 (0.005) | 2.83 (0.17) |
| 0.879 (0.005) | 3.31 (0.12) | 0.878 (0.002) | 2.47 (0.12) | 0.886 (0.004) | 2.79 (0.18) | 0.887 (0.007) | 3.44 (0.17) |
| 0.893 (0.004) | 3.62 (0.14) | 0.879 (0.004) | 2.55 (0.11) | 0.890 (0.002) | 3.02 (0.10) | 0.899 (0.003) | 3.77 (0.21) |
| 0.894 (0.006) | 3.61 (0.15) | 0.890 (0.003) | 2.62 (0.08) | 0.891 (0.003) | 3.00 (0.14) | 0.901 (0.002) | 3.88 (0.20) |

[a] Data reported as mean (standard deviation), $N = 10$.

**Table 5**
Dissolution data for tablets obtained from different SLS insertion points in the manufacturing process obtained in 900 ml of simulated gastric fluid with paddles at 75 rpm.[a,b,c]

| Batch | 0.25 h | 0.5 h | 1 h | 2 h | 3 h | 5 h | 8 h | 22 h | 24 h |
|---|---|---|---|---|---|---|---|---|---|
| EG SLS | 39.4 (1.0) | 53.9 (1.1) | 66.1 (1.4) | 77.3 (1.4) | 82.1 (1.1) | 86.5 (1.0) | 89.7 (1.1) | 94.5 (1.4) | 94.9 (1.3) |
| IG SLS | 41.8 (0.1) | 54.7 (0.8) | 67.3 (1.0) | 77.9 (1.0) | 82.8 (1.2) | 87.3 (1.3) | 90.1 (1.4) | 93.7 (1.1) | 94.1 (1.6) |
| Initial SLS | 37.9 (1.5) | 53.6 (1.6) | 65.7 (1.6) | 76.7 (3.0) | 80.4 (1.6) | 84.9 (1.7) | 88.1 (1.6) | 92.9 (1.8) | 93.6 (1.5) |
| No SLS | *35.6 (0.7)* | **47.7 (0.4)** | **60.7 (0.7)** | **71.4 (0.5)** | **76.8 (0.6)** | **81.9 (1.0)** | **85.2 (0.8)** | **88.6 (1.3)** | **89.2 (0.7)** |

[a] Data reported as mean percent dissolved (standard deviation).
[b] $N = 3$.
[c] Values in bold are significantly different from all SLS-containing batches, value in italics is different from EG and IG SLS batches ($p < 0.1$).

### 3.2. Impact of SLS insertion point on dissolution

Fig. 4 shows the dissolution profiles of the API from the tablets manufactured with different processes in terms of SLS insertion.

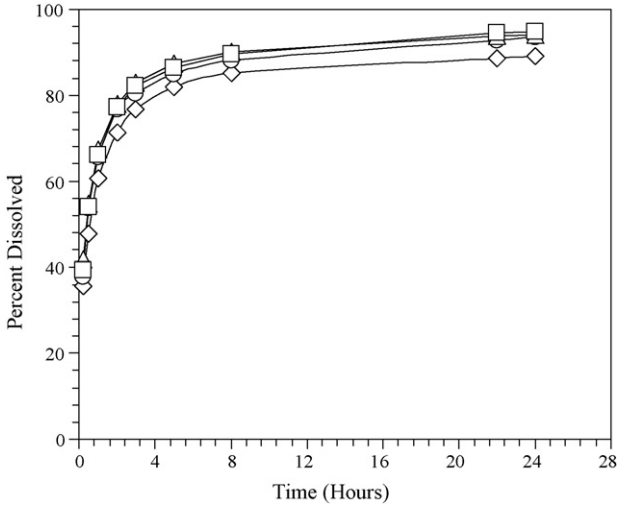


**Fig. 4.** Dissolution profiles for different SLS insertion points. Key: open diamonds – tablets containing no SLS; open squares – SLS added prior to tableting; open triangles – SLS added prior to roller compaction; and open circles – SLS added prior to the initial blending step. Errors bars: ±1 standard deviation, $n = 3$.

A summary of the dissolution data is reported in Table 5. The dissolution profiles of tablets containing SLS were not significantly different from one another ($p > 0.1$), regardless of SLS insertion point during manufacturing. Further, tablets with no SLS showed statistically slower dissolution (~5%) after 15 min ($p < 0.1$) relative to tablets containing SLS.

## 4. Discussion

From the results presented in Fig. 2, it can be seen that the insertion point of SLS in to the manufacturing process does have a significant impact on tablet hardness. As the hardness–compression profiles show, tablet hardness increases as SLS is added to the formulation later in the manufacturing process. This result suggests that tablets containing SLS become harder as the degree of processing experienced by the SLS in the formulation decreases. The increased hardness of the tablets with decreased SLS processing is due to an underlying increase in the tablet tensile strength where the same solid fraction is obtained, as shown in Fig. 3. Since tensile strength and solid fraction are both intrinsic mechanical properties of a compressed blend, the results of Fig. 3 also suggest that the differences in processing of the SLS-containing formulations result in intrinsically different materials, despite the formulations of the three SLS-containing tablets being identical.

In a sense, this observed effect for SLS is similar to the over-lubrication behavior observed for the common tablet lubricant, magnesium stearate. Several authors have demonstrated that the hardness of tablets containing magnesium stearate increases

as the mixing time during lubrication is decreased (Shah and Mlodozeniec, 1977; Bossert and Stamm, 1980; Kikuta and Kitamori, 1994; Sheskey et al., 1995) or the amount of lubricant decreases (Kikuta and Kitamori, 1994; Sheskey et al., 1995; Aly, 2006). For the SLS case, SLS added at the extragranular lubrication step undergoes minimal processing (i.e. 3 min of mixing) prior to tableting, while SLS added at the intragranular lubrication step and prior to the initial blend undergo much larger amounts of processing (i.e. 18.5 min of mixing plus dry granulation, and 43.5 min of mixing plus milling and dry granulation, respectively). The observed similarity in the hardness–compression profiles and the tensile strength vs. solid fraction profiles of the extragranular SLS blend and the blend without SLS can also be attributed to the relatively small amount of SLS processing prior to tableting for the extragranular SLS blend.

Furthermore, the degree of over-lubrication can also be quantified by the amount of compression force required to compress a tablet to a particular hardness. For the case of magnesium stearate, the amount of applied force required to produce tablets having similar hardness increases as the amount of lubrication time with magnesium stearate increases (Bossert and Stamm, 1980). For the case of SLS, an increase in the compression force required to achieve constant tablet hardness was also observed as the degree of SLS processing increased. Specifically, to produce a tablet with a hardness of 50 N, the required compression force for a formulation containing no SLS, SLS added extragranularly, SLS added intragranularly, and SLS added initially is 3.7, 4.2, 5.2, and 6.4 kN, respectively.

While tablet hardness may be reduced as a result of over-processing of SLS in a dry granulated tablet, there does not appear to be a corresponding reduction in dissolution with over-processing of SLS, which is the case of magnesium stearate (Shah and Mlodozeniec, 1977; Sheskey et al., 1995). In Fig. 4, the data shown that dissolution of the poorly soluble, highly hydrophobic API from the tablet improves if SLS is present in the formulation, while the degree of SLS processing does not appear to have an impact on dissolution. This is a notable difference in the properties of SLS and magnesium stearate, which is well-documented to retard dissolution (Shah and Mlodozeniec, 1977; Sheskey et al., 1995), especially for highly soluble APIs. This difference in the impact on dissolution is a result of the difference in the chemical properties of SLS and magnesium stearate. SLS, being a surfactant, is amphiphilic, having both hydrophilic and hydrophobic molecular domains. As a result, SLS is soluble in water, and, due to its amphiphilic nature, is attracted to interfaces while in solution. Its surface active properties can reduce surface and interfacial tension, thereby improving the spreading of water onto hydrophobic surfaces. The improved wettability imparted by having SLS in a tablet formulation can be used to improve the contact of water with hydrophobic API crystals, improving dissolution. Conversely, magnesium stearate is more hydrophobic than SLS due to: (1) the absence of the hydrophilic sulfate head group found in SLS, and (2) the presence of longer alkyl chains, and, as a result, is not soluble in water. Magnesium stearate crystals, having a plate-like structure, tend to shear apart during powder mixing and to adhere onto the surfaces of particles in pharmaceutical powder blend (Bolhuis et al., 1975; Rao et al., 2005). As the amount of magnesium stearate in the formulation increases or the amount of magnesium stearate processing increases, the amount of magnesium stearate coating the particle surface increases (Johansson and Nicklasson, 1986). When magnesium stearate coats the surface of API crystals present in the powder blend, an additional hydrophobic barrier is added, which further increases the resistance of the API crystal to solubilization in water and results in reduced rates of dissolution (Shah and Mlodozeniec, 1977; Sheskey et al., 1995).

While over-processing with magnesium stearate reduces both dissolution rates and tablet hardness, over-processing with SLS is only detrimental to tablet hardness. Therefore, if SLS is added to a formulation to improve the dissolution of a poorly soluble, highly hydrophobic API, SLS should be added to a dry granulated formulation extragranularly, just prior to the final compression step, rather than prior to the initial blending step, to minimize reduction in the hardness and tensile strength of manufactured tablets.

## 5. Conclusion

When used in a dry granulated formulation to improve the solubility of an API, addition of the wetting agent, sodium lauryl sulfate, at the extragranular lubrication step improves tablet hardness relative to addition prior to the initial blending and maintains improved dissolution performance relative to tablets which omit a wetting agent in the formulation.

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