A comparative study of hydrophobic and hydrophilic lubricants for optimal combination of galenical and dissolution properties

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Purpose

In tablet production, lubricants are required to preserve tooling, prevent the tablets from sticking to punches and reduce ejection force. Typically, hydrophobic lubricants such as Magnesium stearate are used due to good lubrication efficacy. However, higher amounts of these lubricants or excessive mixing can result in particle coating. In combination with plastic-deforming binders like microcrystalline cellulose (MCC), this particle coating can reduce tablets' mechanical strength[2]. Also, hydrophobic lubricants can prolong disintegration times and reduce dissolution performance[3]. Hydrophilic lubricants, on the other hand, such as Poloxamers, although less commonly used can counteract these potential issues due to the amphiphilic nature of the polymeric structure. However, there may be concern that hydrophilic lubricants may not exhibit the same mechanical strength as their hydrophobic counterparts.

This work compared critical formulation parameters of oral solid dosage forms prepared with water-soluble Poloxamer 188 and within the more commonly used magnesium stearate, with a focus on optimizing the balance between mechanical properties and dissolution performance.

Methods

Various itraconazole tablets were prepared consisting of: directly compressible spray-granulated mannitol (MilliporeSigma, Darmstadt, Germany), a directly compressible sprayagglomerated lactose (Molkerei MEGGLE Wasserburg GmbH & Co. KG, Wasserburg am Inn, Germany) and microcrystalline cellulose (J. Rettenmaier & Söhne GmbH & Co. KG, Rosenberg, Germany) as filler/binder. Micronized Poloxamer 188 (MilliporeSigma, Darmstadt, Germany) and magnesium stearate (MilliporeSigma, Darmstadt, Germany) were used as lubricants. To prepare the mixtures, the binder, lubricant and API were sieved through a 1 mm sieve and mixed for 5 min in a tumble mixer (Willy A. Bachofen AG, Muttenz, Switzerland). The mixtures were compressed on a fully instrumented compaction simulator (MEDELPHARM, Beynost, France) at compression forces of 5, 10, 20 and 30 kN using 11 mm flat faceted tooling. Lubrication performance was determined based on the ejection force. Tablets mechanical strength were measured with a hardnesstester (Erweka, Langen, Germany). Dissolution performance was assessed with a USP Apparatus 2 online system (SOTAX AG, Aesch, Switzerland).

Results

Figure 1 shows the ejection force at each compression force.

- Mix of binder and lubricant was not optimized in this work, hence 1% lubricant is insufficient for mannitol formulations.
- With mannitol as binder, 2% of lubricant results in good ejection forces with MST and acceptable ejection forces with poloxamer.
- With Lactose and MCC as binder, all concentrations of MST result in good ejection forces. Ejection forces are higher with micronized Poloxamer 188.
- Overall, 2% of Poloxamer 188 is enough to achieve acceptable ejection forces.
- Amounts higher than 2% reduce ejection force only slightly more (MST and PLX).

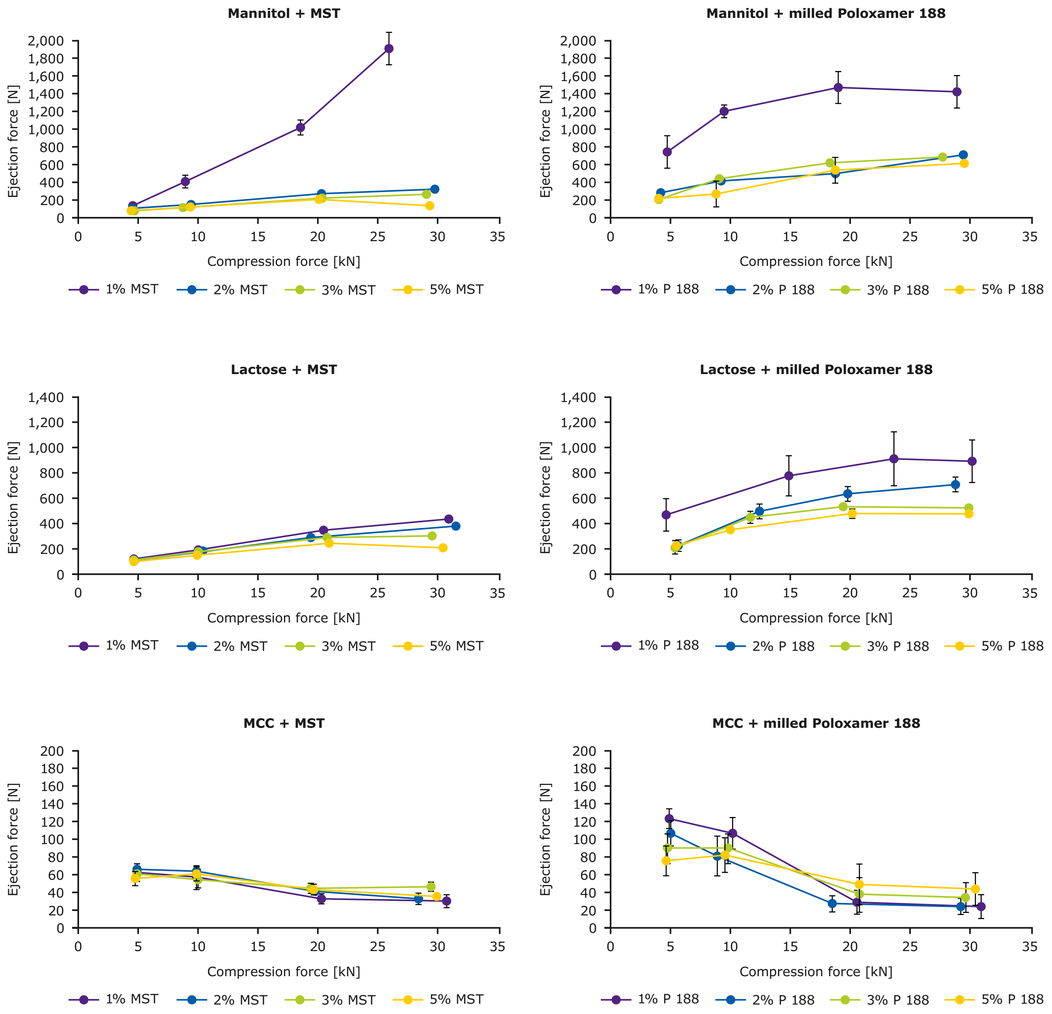

Figure 1.
Ejection forces with magnesium stearate (left) and micronized Poloxamer 188 (right) as lubricant.

Figure 2 shows the remaining hardness of MCC tablets compressed at a 10 kN compression force as a percentage compared to the hardness of tablets with 1% lubricant.

- With 5% lubricant, the remaining mechanical strength of tablets with MST is only 40%.
- With micronized poloxamer, 75% of the mechanical strength remains.
- The hardness of lactose tablets remains almost constant as the amount of lubricants is increased.
- The hardness of mannitol tablets decreases slightly with 5% MST and increases as the amount of poloxamer is increased (results not shown).

The effect of poloxamer on dissolution performance of Itraconazol can be seen in Figure 3.

- Much faster dissolution rate with Poloxamer 188.
- After 5 minutes, the dissolved amount of itraconazole from the Poloxamer 188 formulation is almost 10 times higher than for pure itraconazole.

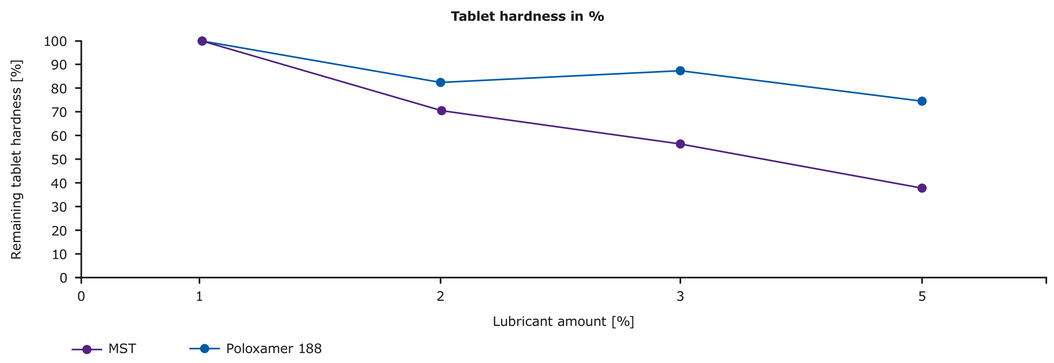

Figure 2.
Remaining tablet hardness of 10 kN MCC tablets in % compared to 1% lubricant.

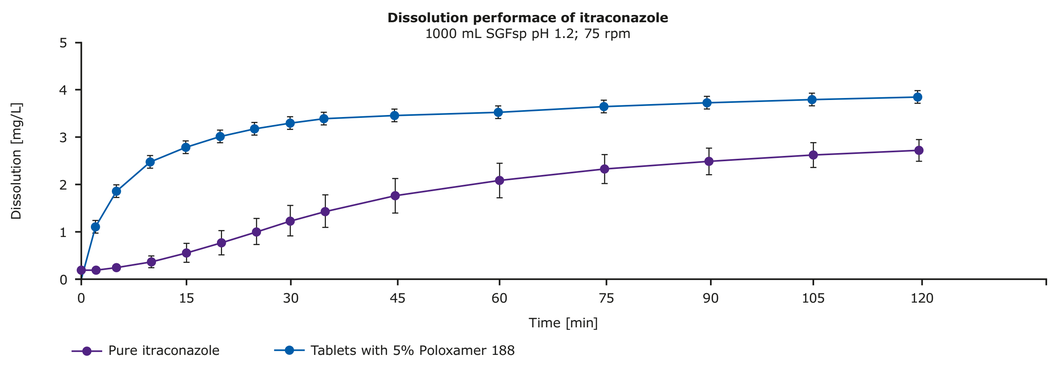

Figure 3.
Dissolution performance of pure itraconazole.

Conclusions

The lubrication efficacy of gold-standard hydrophobic MST cannot be completely matched with hydrophilic Poloxamer 188, however, good ejection forces of less than 700 N can be achieved. The negative impact on tablet hardness with plastic-deforming binders is also much less than with magnesium stearate. An additional benefit of Poloxamer 188 is its ability to significantly increase the dissolution rates of several BCS 2 drugs.

References

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