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# Characterization of Lubricant Distribution of Die Wall Lubricated Tablets by Scanning Electron Microscopy and Energy Dispersive X-ray Spectroscopy

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Solid oral formulations are complex mixtures of active pharmaceutical ingredients (API) and excipients. Excipients are utilized for a variety of functions such as diluent, disintegrent, lubricant, binder or glidant. Lubricants in particular play a critical role in facilitating release and ejection of the tablet from the punch and die after compression in a tablet press. The traditional approach to lubrication is to blend a lubricant with the other components before compression to facilitate tablet ejection. This approach is convenient, but can potentially reduce tablet strength and slow tablet dissolution. External or die wall lubrication is a new approach where a lubricant is sprayed directly on the tablet tooling during compression to facilitate tablet ejection. This approach directs the lubricant to the location where it is needed and reduces the levels of lubricant needed in each tablet [1, 2].
Several factors can affect lubrication effectiveness including type of lubricant, spray rate of the lubricant and vacuum pressure used to remove excess lubricant. Monitoring the quantity and distribution of the lubricant on the tablet surfaces is the best way to monitor the effectiveness of the lubrication equipment and provide guidance on selection of process parameters. Elemental analysis by scanning electron microscopy (SEM) and energy dispersive x-ray spectroscopy (EDS) has been used for monitoring excipients in solid oral formulations [3]. This system was used to measure quantity and distribution of lubricants on tablet surfaces and ultimately show the effectiveness of the lubricant system.

A systematic approach for measuring elemental magnesium from magnesium stearate and elemental sodium from sodium stearyl fumarate by SEM/EDS was used to assess relative lubricant quantity and distribution on placebo formulations. Differences in elemental distribution and quantity were measured as a function of changes in lubricant spray rate and vacuum pressure used to remove excess lubricant. Comparisons were also made between top and bottom surfaces of the tablets corresponding to upper and lower punches. SEM/EDS were also used to evaluate die wall lubricated tablets that had incomplete coatings to determine the cause of the coating defect.

Elemental analysis of magnesium on magnesium stearate lubricated tablets showed the quantity of magnesium on the surfaces of the tablets increased proportionally with increasing lubricant spray rate (Figure 1). Differences in vacuum pressure showed a dramatic effect on total magnesium concentration on tablet surfaces. Upper surfaces of tablets always had slightly lower concentrations of magnesium indicating the lubrication process was not equal on upper and lower die punches. All elemental concentrations were measured quantitatively and could also be seen qualitatively in the elemental maps (Figure 2). Elemental mapping also showed differences in the distribution of magnesium stearate and sodium stearyl fumarate, which provided an explanation for coating defects on tablets.

In conclusion, SEM/EDS is an effective tool to measure relative lubricant concentration and lubricant distribution on the surfaces of die wall lubricated tablets. This tool can also be used to find root cause of incomplete lubrication related coating defects on die wall lubricated tablets.
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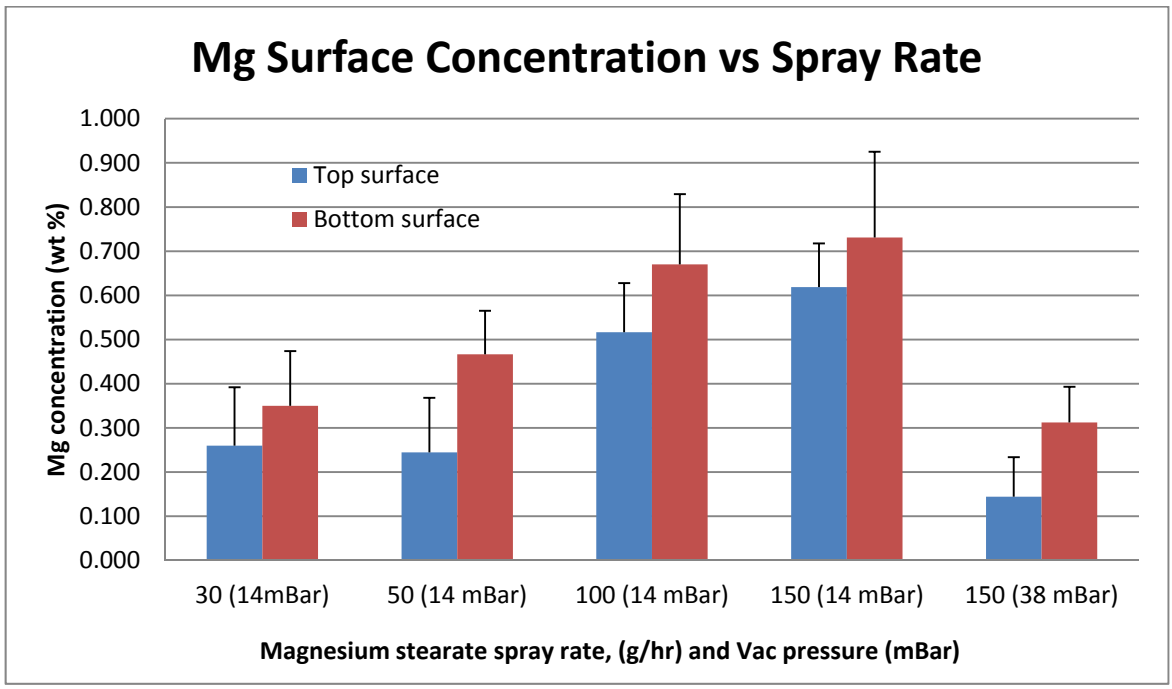


Figure 1. Quantitative concentration of magnesium on tablet surfaces based on spray rate, vacuum pressure and tablet surface.

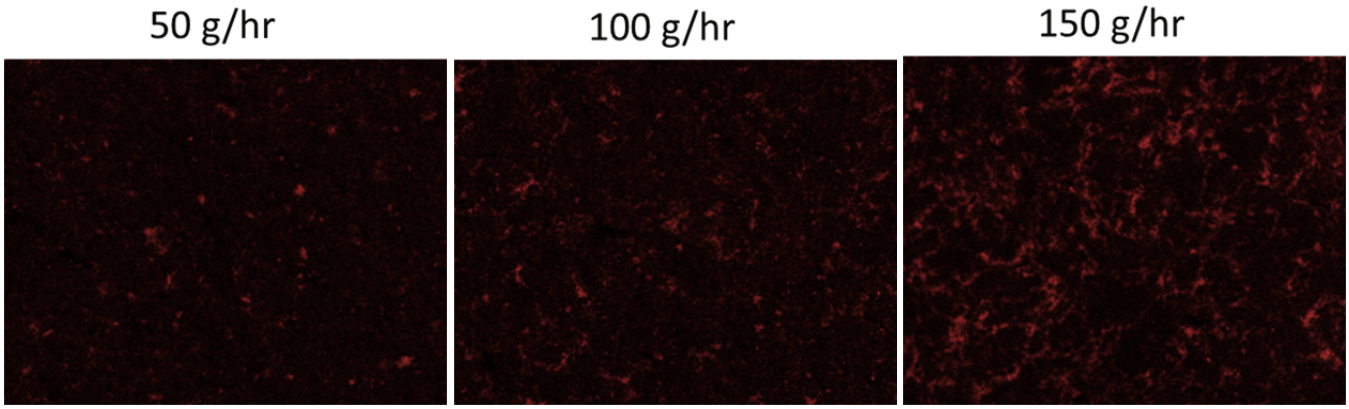


Figure 2. Elemental maps of magnesium on tablet surfaces from spray rates of 50, 100, and 150 g/hr and 14 mBar vacuum pressure.

Disclosures:
Hao Helen Hou is a former employee of AbbVie, currently employed by Allergan. All remaining authors are employees of AbbVie and may own AbbVie stock. The design, study conduct, and financial support for this research were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the publication.

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