Providing Solutions for Dissolution

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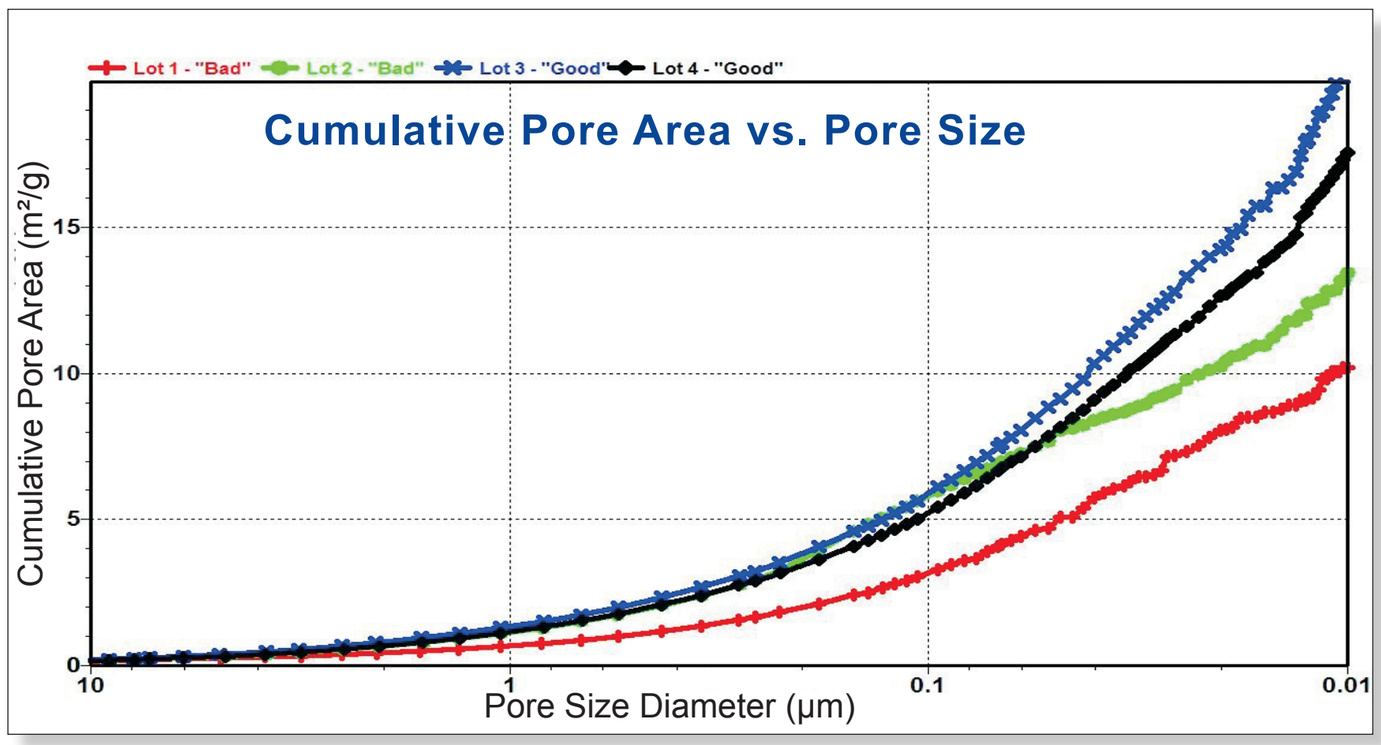
Background

Pharmaceutical manufacturers create formulations and tablets designed to dissolve at a specific rate after ingestion. There are many factors that can affect this rate including, but not limited to: a) the chemical species of the component materials, b) the chemical interaction between these materials, c) the physical properties of the material, and d) the physical properties of the final product.



Case Study

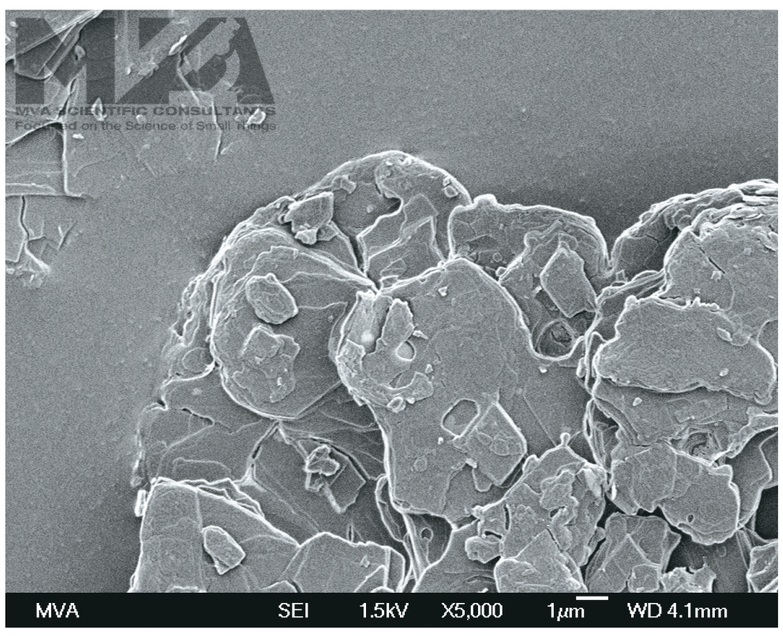
Recently, Micromeritics Analytical Services was contacted by a pharmaceutical customer asking if we could determine why the dissolution rate of their product had changed even though the formulation and raw materials were the same.

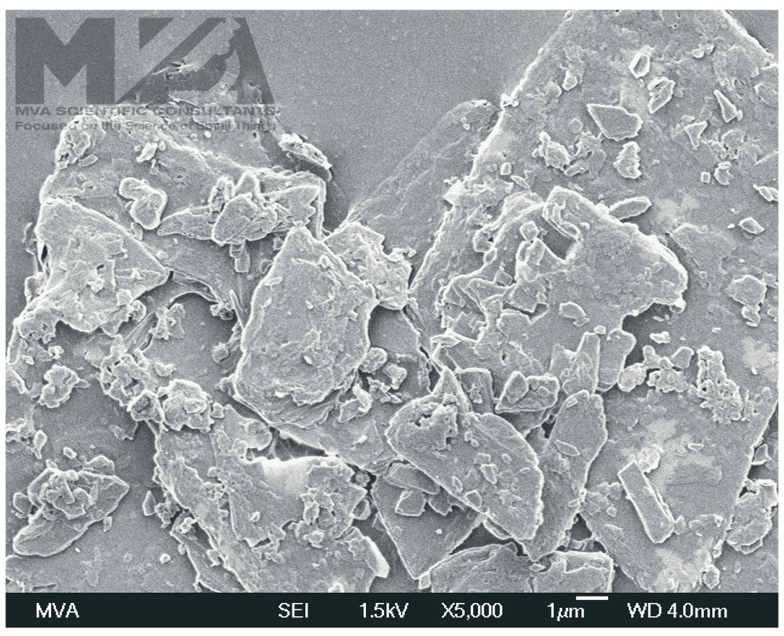
It was decided that a combination of tests should be run to fully characterize certain raw materials used in the formulation, namely magnesium stearate and dextrose. The tests chosen were BET surface area, mercury porosimetry, polarized light microscopy (PLM), and scanning electron microscopy (SEM).

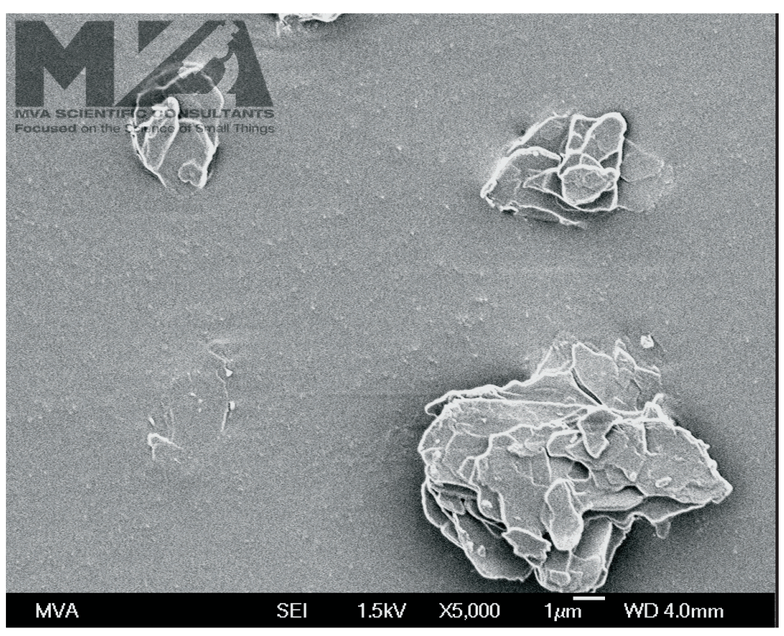
All the dextrose lots appeared to be fairly consistent in the measured characteristics. Analysis of the magnesium stearate revealed clear differences between the lots tested. Lots 1 and 2, used to produce product that failed Q/A, were found to have a BET surface area between $6m^2/g$ and $8m^2/g$. The lots that produced product with desired dissolution rate were found to have BET surface area between $16m^2/g$ and $20m^2/g$.

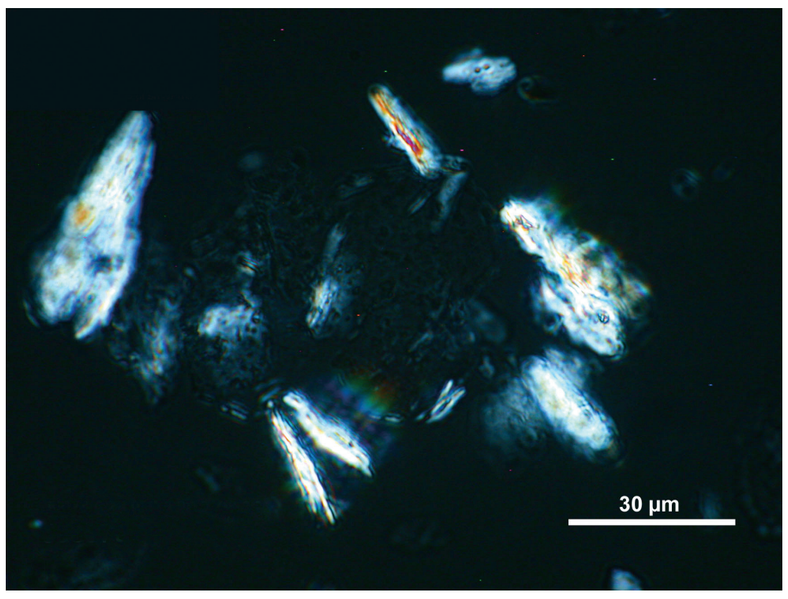
Differences between lots 1 and 2, and lot 3 also were seen using mercury porosimetry. The cumulative pore area curve to the left clearly shows differences between lots.

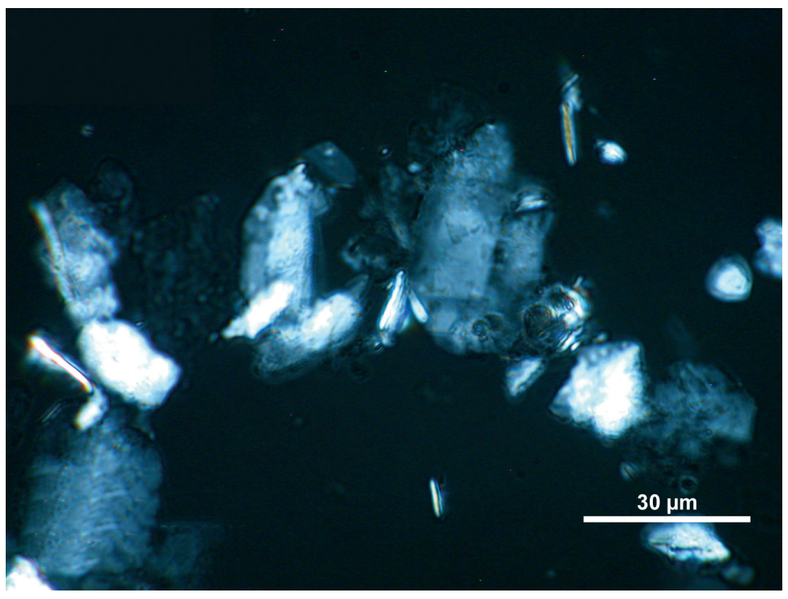
The PLM and SEM images (courtesy of Rich Brown, MVA Scientific Consultants) revealed differences in morphology that correlated to the BET surface area and mercury porosimetry.

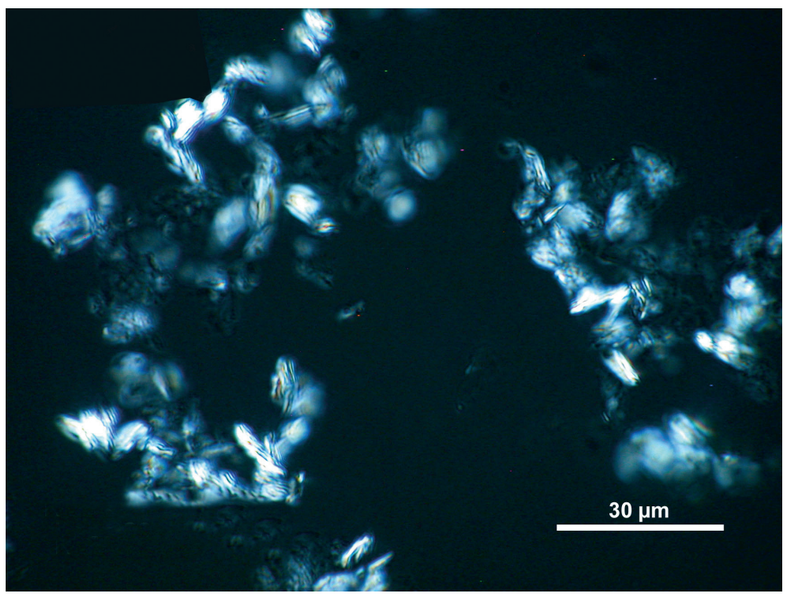












Lot 1 | Lot 2 | Lot 3

Summary

It was clear that two separate lots of magnesium stearate were received that had specific physical characteristics that negatively affected this particular formulation. The combination of BET surface area and mercury porosimetry provided quantitative measurements of the physical characteristics of the magnesium stearate powders.

Imaging the same powders using a combination of polarized light microscopy and scanning electron microscopy provided direct visual information to relate surface area and porosimetry data to particle morphology. A BET surface area specification for the raw material now could be created to assure that this problem does not recur.

Surface area and mercury porosimetry results courtesy of Micromeritcs Analytical Services using a Micromeritics Tristar 3000 and AutoPore 9520, respectively.

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