Magnesium Stearate

Solving the Surface Area Problem

by: **Martin A. Thomas Ph.D.**, Director of Business Development
Quantachrome Instruments (martin.thomas@quantachrome.com)

Magnesium stearate (MgSt), a waxy, lamellar (platey) solid, is the most widely used solid excipient in pharmaceutical technology [1]. Primarily, MgSt is added to a formulation in order to lubricate powder flow and compaction [2], but it also imparts certain hardness, disintegration and dissolution characteristics to tablets. This excipient's performance depends, at least to some extent, on chemical purity, density, particle size, particle shape, and surface area. The least understood of these properties, and exactly how to measure it, is surface area -despite it being required in the USP MgSt monograph. The established USP method for Specific Surface Area includes a specified pass/fail criterion (strangely perhaps, it is not an actual surface area value). That method is General Chapter 846 based on low-temperature gas adsorption and the BET calculation [3]. Specific experimental conditions, including those for pretreatment, appear in the MgSt monograph.

Meeting Surface Area Specifications

Wide variability in surface area (3-54m^2/g) [4,5,6] is not surprising given that MgSt may exist as a number of hydrates [7]! Further variability (in measured surface area values) can be imparted by different outgassing, or pretreatment conditions, particularly that of temperature. 40ºC was formally adopted in the monograph since there was evidence that (cf 30ºC) it improved the BET *correlation coefficient* for some commercial samples [8]. The correlation coefficient (goodness of fit of the BET adsorption model to experimental data) was recently given greater importance, more than both outgassing conditions and experimental data range. USP28/NF23 allows the analyst to adjust both said variables in order to achieve a correlation coefficient greater than 0.9975, i.e. that which is required to "pass" 846 . Perhaps then, the appropriate relative pressure (P/P_o) range might have to be determined for each sample analyzed, since data at $0.05 < P/P_o < 0.15$, per the original monograph's strict requirements [9] may not always be valid. It is recommended therefore, that at least 5-7 data points be acquired in the relative pressure range 0.03 to 0.23. A need for unique data point selection is evidenced by a gradual decrease in slope in the BET plot. This may or may not be accompanied by a short linear region at lower relative pressures… if it is, use that linear range. Those higher P/P_o values that clearly do not lie on the straight line can be safely discarded from the multipoint surface area calculation.

Good Scientific Practice (GSP)

Be careful, however. The correctness of the BET model is not proven if a plot of the data according to the BET equation merely gives a straight line. It is also necessary that the other evaluated constant, the so-called BET C value, should be reasonable [10]. The average value of C is about 14; A straight line which meets the correlation coefficient requirement (>0.9975) of USP 846 but which yields a C value outside a range say from 10 to 18 for practical purposes should still be considered suspicious. If there is no truly linear region, then it can be said that the BET model is invalid for that particular sample. However, this does not necessarily mean that the sample would prove to be problematical in manufacture, even though it would fail USP grade. On the contrary, this behavior could be a desirable attribute [11]. Furthermore, there is some evidence [12] that certain grades of metal stearates undergo a morphological change when cooled to liquid nitrogen temperature, which results in a distinct change in measured surface area.

Summary

The BET equation is the most widely adopted for the calculation of surface area, most commonly using data from nitrogen adsorption at liquid N_2 temperature. However, its success (in terms of an unequivocal surface area value) cannot be guaranteed when analyzing excipient grade MgSt. Outgassing, or pretreatment, of the sample plays a vital role due to the varied and ill-defined chemistry of commercially available material. The appropriate relative pressure range may be dictated by sample morphology, with some samples not being amenable to the BET method whatsoever. Further insight into the problem, and additional experimental guidelines to improve the quality of the data to achieve the desired correlation coefficient, can be obtained by contacting the surface area experts at Quantachrome Instruments. ■

References

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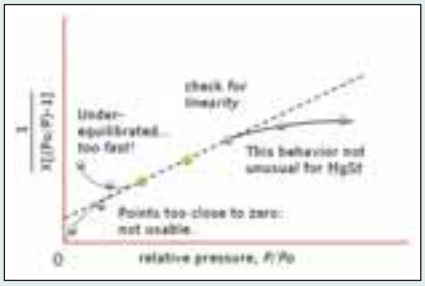
To receive a detailed white paper on this subject, email Dr. Thomas at Martin.Thomas@quantachrome.com.

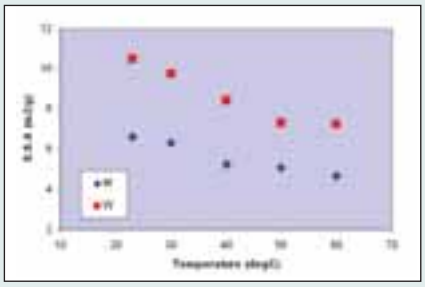
Surface areas of MgSt and other pharmaceutical ingredients are measured by gas adsorption at cryogenic temperatures. The NOVAe series from Quantachrome features multiple sample capability and optional IQ/OQ/PQ & 21CFR Part 11 compliance packages.

Evaluating Quality of Data by the BET method.



Where "X" is the amount of gas absorbed at a given relative pressure.

MgSt Surface Area as Function of Degas Temperature [13]



Two brands of MgSt show similar trends in surface area loss as function of increasing degas temp.

Converting MgSt Single-Point Values to Multipoint Values.

Sample No.	Multipoint BET (m^2/g) [14]	Original Single-point (m^2/g) [14]	Initial Difference (%)	Corrected Single-point (m^2/g)	Final Difference (%)
1	4.92	4.24	-13.9	4.85	+0.51
2	4.29	3.66	-14.5	4.28	-0.26
3	8.06	6.87	-14.8	8.01	-0.56
4	5.96	5.19	-12.8	6.06	+1.73

Single-point BET values are often evaluated at P/Po = 0.3 . Single-point values can be converted to multi-point values by the multiplier C/(C-2), i.e 1.167 based on the premise that the average BET C value for typical excipient grade magnesium stearate is 14.

References

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For More Information about surface analyzers: Contact Quantachrome Instruments by phone: (561) 731.4999, fax: (561) 732.9888, email: QC.pharma@ quantachrome.com or visit www.quantachrome.com.

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