Application Note 153

The Measurement of Pharmaceutical Lubricants Using the TriStar II Krypton Option

A major advantage for using the TriStar II with the Krypton Option is the ability to measure low surface areas. Although the TriStar II standard nitrogen system can measure surface areas as low as 0.01 m^2/g, the Krypton Option enables you to measure areas as low as 0.001 m^2/g and provides increased accuracy for materials under 1.0 m^2/g. Krypton is also useful for analyzing materials that are difficult to sample or have very low density; pharmaceutical lubricants, for example.

Advantages of Using Krypton

Isotherms are collected by measuring the amount of gas adsorbed by a material over a range of pressures at a constant temperature. The quantity of gas adsorbed by a material is determined by taking the original quantity of gas dosed into a tube (V_i) and subtracting the amount of gas remaining in the tube after equilibrium is reached (V_e). For materials with low surface areas, the difference between the original amount of gas and the amount remaining after equilibrium ($V_i - V_e$) can be substantially small and difficult to measure, resulting in increased error. Normally for materials with low surface areas, the amount of material is maximized in order to increase this difference ($V_i - V_e$). Unfortunately this approach has an upper limit depending on the size of the sample tube and the physical properties of the material. Another approach is to use an alternate analysis gas.

Krypton is an excellent choice for low surface area measurements. Nitrogen at 77 K has a saturation pressure of 760 torr, whereas krypton has a saturation pressure of only 2.5 torr. Since pressure is proportional to the number of moles or molecules in a set volume*, there are ~ 300 molecules of nitrogen for every 1 molecule of krypton. When the quantity adsorbed is significantly small, lowering the amount of molecules present by a factor of 300 substantially reduces the amount of error.

Analysis Parameters

Pharmaceutical lubricants are added to reduce the friction between a tablet and the process utilized to shape the tablets. Calcium, magnesium, and sodium stearates are typical pharmaceutical lubricants and have been chosen for analysis using the Krypton Option since they can be difficult to measure.

*Liquid nitrogen temperatures; a non-ideality factor must be used for Krypton.

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Test conditions were as follows:

Test amount:	~ 0.3 gram of each material; less than this amount produced too much variability.
Preparation:	Degassed for 48 hours at ~ 25 °C. USP method <846> suggests outgassing magnesium stearate for two hours at 40 °C; however, a lower temperature for a longer amount of time was utilized for all materials to minimize temperature damage to the materials and to ensure that all impurities were removed.
Free space:	Measured
Relative pressures:	0.05 to 0.15
Equilibration:	Relative pressure of 1.0 with an equilibration interval of 10 seconds
Backfill:	Start of analysis only; not at conclusion

Analysis Results

Surface area for the three stearates was determined using the BET multipoint analysis. One of the advantages of the TriStar II unit is the ability to run three analyses concurrently. The results for all tests are shown below. Also shown are BET plots for one of the tests.

Test	Surface Area (m^2/g)		
	Magnesium	**Sodium**	**Calcium**
1	1.7862	3.7979	1.7444
2	1.7597	3.9357	1.8402
3	1.7487	3.5191	1.8051
4	1.8089	3.6376	1.9575
5	1.7891	3.4044	2.0575
6	1.8865	3.7537	2.3472
Average	1.7965	3.6747	1.9587
Standard Deviation	0.0491	0.1940	0.2210