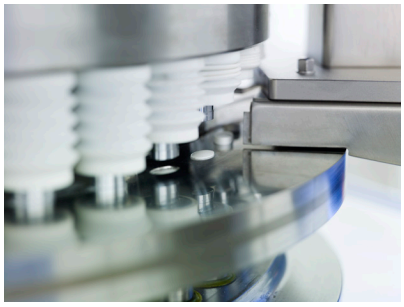
WHITEPAPER

How to Determine Size Characteristics Through Nonconventional Methods



Magnesium stearate is an inactive pharmaceutical ingredient composed of magnesium and a mix of organic acids. Magnesium stearate is used in more than two thousand five hundred pharmaceutical products as a lubricating agent to aid tablet ejection from a tablet press. In fact, magnesium stearate is the most widely used excipient among the top two hundred prescription drugs. This substance is lipophilic which coats and "waterproofs" tablets, serving as an inhibiting factor in the disintegration and dissolution of the solid tablet. Knowing the size characteristics of this ingredient is important in determining the quality of the product and predicting the behavior of the substance once it is compressed into a tablet. Particles that are too big may cause the tablet to fragment and fall apart; particles that are too small may cause clumping and hinder a manufacturing process. The surface area of magnesium stearate has a lot of variability since it exists as different hydrates. Surface area and particle size have an inverse relationship; smaller particles having greater surface area. As a result, a smaller amount of magnesium stearate with small particle size is required to do the same "work" as a grade with a larger size. Therefore it is imperative to determine accurate size characteristics of magnesium stearate for optimal performance and monitoring of product quality.

Physical properties of magnesium stearate are such that particle size cannot be determined easily through wet dispersion, dry dispersion, or sieve analysis–the three traditional methods for determining particle size. With wet dispersion, magnesium stearate floats on top of the water and has trouble wetting without the use of additional materials such as surfactants, making it difficult to make an appropriate suspension. With dry dispersion, the entire sample is so light that fines may be lost resulting in a coarser measurement since the small particles are not adequately measured. With sieve analysis, magnesium stearate clumps and will not pass through the screen mesh very easily or consistently, and can form dust in which the finer particles can be lost. So the question is: How do we determine the size characteristics of this substance without using any of the most common methods? How do we ensure a quality tablet when using magnesium stearate?

The accepted method to determine size characteristics of magnesium stearate, as specified in general chapter ‹846› in the United States Pharmacopeia (USP), is to use gas adsorption, usually with nitrogen gas. The specific surface area of magnesium stearate can be determined through measuring physical adsorption of an inert gas on the surface of the substance. Physical adsorption results from Van der waals forces among the adsorbate gas molecules and surface of the magnesium stearate. The amount of gas that is adsorbed can be determined through a volumetric or continuous flow procedure. To determine the surface area, the sample must be completely degassed to remove surface contaminants from the sample. The BET (Brunauer, Emmett, Teller) surface area can be determined through the use of a surface area analyzer instrument. The BET equation is the most accepted when calculating the surface area of magnesium stearate. Through this procedure, we can generate robust and repeatable particle size and surface area data with minimal error to ensure the quality of the grade of magnesium stearate as a raw material.

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