



BET specific surface area test method for
pharmaceutical excipients

— Magnesium Stearate



The specific surface area plays an important role in the purification, processing, mixing, tableting, and packaging capabilities of pharmaceuticals in tablet form. It also has an influence on the expiry date, dissolution rate, and efficacy.

1 Introduction

Magnesium Stearate [MS] (CAS: 557-04-0) is a common pharmaceutical excipient. MS is a white, fine powder with fluffy texture, low bulk density, poor fluidity, and soft to the touch. It has a slight odor and is insoluble in water, ethanol and ether. Magnesium is compounded with stearic acid. Calculated as dry product, the magnesium content should be 4%-5%.

Magnesium stearate is often used as a lubricant in the production of capsules and tablets, which can reduce the friction between particles and between the contact surfaces of the particles and the manufacturing equipment (such as tablet punches and dies). An important variable in lubricating performance is the specific surface area. The larger the specific surface area, the easier it is to distribute evenly during the mixing process.

Magnesium stearate can transition into an amorphous state or crystalline hydrate after absorbing water. Hydrate includes: monohydrate, dihydrate and trihydrate. Darren P et al. [1] pointed out that during the heating process, magnesium stearate's free water is removed below 40°C, bound water is removed between 70-105°C, and MS is melted above 110°C.

The 2020, several international pharmacopoeias stipulated that magnesium stearate should be marked with a specific surface area value, and the US Pharmacopeia stipulated that the degassing condition of magnesium stearate should be 40°C under vacuum for 2 hours [2]. This article aims to explore the precautions and procedures for magnesium stearate in the specific surface area test process.

2 Specific surface area test program

Test sample: Magnesium stearate;

Test instrument: AMI-Meso 112 specific surface area and pore size analyzer



Fig. 1 photo of AMI-Meso 112

2.1 Pretreatment and general requirements

a. Sampling amount:

The US Pharmacopeia stipulates that nitrogen is used as adsorbate, and the area to be tested is $> 1\text{m}^2$.

b. Gas:

High-purity nitrogen, purity $> 99.999\%$;

High purity helium.

c. Pretreatment:

Before the test, the magnesium stearate sample was degassed by heating under vacuum.

Magnesium stearate is light in weight, fluffy, and has a low bulk density. When pumping a vacuum, you need to pay attention to prevent it from dislodging. In the vacuum option of AMI-PAS software, the vacuum pumping speed is divided into "Fine Powder", "Powder" and "Particles" according to the material type. For the magnesium stearate samples, select "Fine Powder" to avoid any sample being pulled into the vacuum system.

2.2 Sample test

The steps of the static volume method to test specific surface area are as follows:

- a. Weigh the sample: use a one-tenths balance, first weigh the mass of the empty tube, record mass₁, then weigh an appropriate amount of sample, pour it into the sample tube, record the sample + the mass of the empty tube mass₂; (Note: Weigh 1.2g in this experiment)
- b. Pretreatment: Put the sample tube in the pretreatment position or degasser for degassing, set the degassing temperature and degassing time (Note: the degassing condition of this experiment is 40°C for 2h);
- c. Review mass: After the pretreatment is completed, the weight the sample again and record it as mass₃;
- d. Start experiment: put the sample tube in the test position, set the test conditions, put the Dewar flask filled with liquid nitrogen in the tray corresponding to the test position, and click to start the experiment;
- e. After the experiment is completed, export the report.

2.3 Results for a specific sample

BET specific surface area test data

Single-point BET specific surface area at p/p_0 0.20000: 3.99427 m²/g

BET specific surface area: 4.94369 m²/g

Slope: 0.82547

Intercept: 0.05496 cm³/g STP

Monolayer saturated adsorption capacity V_m : 1.13580 cm³/g STP

C value: 16.01841

Linear factor C_c : 0.99985

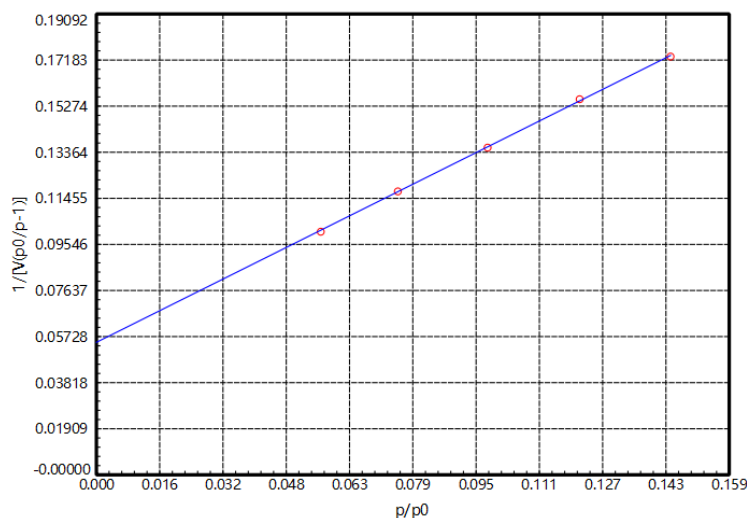


Figure 2

The United States Pharmacopoeia stipulates that the specific surface area of magnesium stearate should be determined in the range from P/P0 0.05-0.15, and the linear factor of the specific surface is $C_c > 0.9975$. It can be seen from [Figure 2] that in the BET test result of magnesium stearate, the linear factor C_c satisfies > 0.999 . $C > 0$, which means that the BET test result is reliable.

3 Conclusion

Guidelines for testing the specific surface area and pore diameter of magnesium stearate:

- (1) Magnesium stearate is light, fluffy, and has a low bulk density. Use "AMI-PAS" software, select the "Fine Powder" vacuum option.
- (2) Use nitrogen (purity > 99.999%) as the adsorbate, and the area to be measured is at least 1m².
- (3) The specific surface area selection range of magnesium stearate is P/P0: 0.05-0.15, and the linear factor of the specific surface area should be greater than 0.9975.

The AMI-Meso series specific surface area and pore size analyzer is a fast and economical instrument that can meet multiple pharmaceutical test methods. This instrument can not only reliably test ultra-low specific surface area samples, but it can also help determine product performance and even help predict the promise of a specific sample's application. In addition, rapid determination of specific surface area and other parameters can easily enable manufacturers to focus on quality control in order to yield better a better pharmaceutical product.

Reference

[1]Darren P. Lapham, Julie L. Lapham. Gas adsorption on commercial magnesium stearate: Effects of degassing conditions on nitrogen BET surface area and isotherm characteristics[J]. International Journal of Pharmaceutics, 2017,530:364-376.

[2]The United States Pharmacopoeia. Magnesium Stearate, 2012:1850.