Magnesium Stearate

Portions of the monograph text that are national *USP* text, and are not part of the harmonized text, are marked with symbols (◆◆) to specify this fact.

Octadecanoic acid, magnesium salt;
Magnesium stearate [557-04-0].

DEFINITION

Magnesium Stearate is a compound of magnesium with a mixture of solid organic acids, and consists chiefly of variable proportions of magnesium stearate and magnesium palmitate. The fatty acids are derived from edible sources. It contains NLT 4.0% and NMT 5.0% of magnesium (Mg), calculated on the dried basis.

IDENTIFICATION

- **A. IDENTIFICATION TESTS—GENERAL ⟨191⟩,** *Magnesium*
  Sample solution: Mix 5.0 g with 50 mL of peroxide-free ether, 20 mL of diluted nitric acid, and 20 mL of water in a round-bottom flask. Connect the flask to a reflux condenser, and reflux until dissolution is complete. Allow to cool, and transfer the contents of the flask to a separator. Shake, allow the layers to separate, and transfer the aqueous layer to a flask. Extract the ether layer with two 4-mL portions of water, and add these aqueous extracts to the main aqueous extract. Wash the aqueous extract with 15 mL of peroxide-free ether, transfer the aqueous extract to a 50-mL volumetric flask, and dilute with water to volume. Retain the unused portion of this solution for the chloride and sulfate impurity tests.
  Acceptance criteria: The *Sample solution* meets the requirements.
- **B.** The retention times of the peaks corresponding to stearic acid and palmitic acid of the *Sample solution* correspond to those of the *System suitability solution*, as obtained in the test for *Relative Content of Stearic Acid and Palmitic Acid*.

ASSAY

- **PROCEDURE**
  Buffer: Dissolve 5.4 g of *ammonium chloride* in water, add 20 mL of *ammonium hydroxide*, and dilute with water to 100 mL.
  Sample: 500 mg
  Analysis: To the *Sample* add 50 mL of a mixture of *butyl alcohol* and *dehydrated alcohol* (1:1), 5 mL of *ammonium hydroxide*, 3 mL of *Buffer*, 30.0 mL of *0.1 M edetate disodium VS*, and 1 or 2 drops of *eriochrome black TS*. Heat at 45°–50° until the solution is clear. Cool, and titrate the excess edetate disodium with *0.1 M zinc sulfate VS* until the solution color changes from blue to violet (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.1 M edetate disodium is equivalent to 2.431 mg of magnesium (Mg).
  Acceptance criteria: 4.0%–5.0% on the dried basis

IMPURITIES

- **CHLORIDE AND SULFATE ⟨221⟩,** *Chloride*: A 10.0-mL portion of the *Sample solution* prepared in *Identification* test *A* shows no more chloride than corresponds to 1.4 mL of 0.020 N hydrochloric acid (0.1%).
- **CHLORIDE AND SULFATE ⟨221⟩,** *Sulfate*: A 6.0-mL portion of the *Sample solution* prepared in *Identification* test *A* shows no more sulfate than corresponds to 3.0 mL of 0.020 M sulfuric acid (1.0%).

Change to read:

- **LIMIT OF CADMIUM**
  [NOTE—For the preparation of all aqueous solutions and for the rinsing of glassware before use, use water that has been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin. Select all reagents to have as low a content of cadmium, lead, and nickel as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse glassware before use by soaking in warm 8 N nitric acid for 30 min, and rinse with deionized water.]
  Matrix modifier solution: Prepare a solution containing 200 mg/mL of *monobasic ammonium phosphate* and 10 mg/mL of *magnesium nitrate*. Alternatively, use an appropriate matrix modifier as recommended by the manufacturer of the graphite furnace atomic absorption (GFAA) spectrophotometer.
  Blank: Nitric acid in water (1 in 4)
  Standard solution: 0.00825 µg/mL of *cadmium nitrate tetrahydrate* in *Blank*, corresponding to a known concentration of 0.0030 µg/mL of cadmium
  Sample stock solution: Transfer 0.100 g of Magnesium Stearate to a suitable polytetrafluoroethylene (PTFE)-lined acid-digestion bomb, and add 2.5 mL of nitric acid. Close and seal the bomb according to the manufacturer's operating instructions. [**CAUTION—**When using an acid-digestion bomb, be thoroughly familiar with the safety and operating instructions. Carefully follow the bomb manufacturer's instructions regarding care and maintenance of these acid-digestion bombs. Do not use metal-jacketed bombs or liners that have been used with hydrochloric acid because of contamination from corrosion of the metal jacket by hydrochloric acid.] Heat the bomb in an oven at 170° for 3 h. Air cool the bomb slowly to room temperature as per the bomb manufacturer's instructions. Place the bomb in a hood, and open carefully because corrosive gases may be expelled. Dilute the residue with water to 10.0 mL in a volumetric flask.
  Sample solutions: Dilute the *Sample stock solution* with *Blank* (1 in 10). Prepare mixtures of this solution, the *Standard solution*, and the *Blank* with the following proportional compositions, by volume (mL): 1.0/0/1.0, 1.0/0.5/0.5, and 1.0/1.0/0. Add 50 µL of *Matrix modifier solution* to each mixture. These *Sample solutions* contain, respectively, 0, 0.00075, and 0.0015 µg/mL of cadmium from the *Standard solution*. [NOTE—Retain the remaining *Sample stock solution* for use in the tests for *Limit of Lead* and *Limit of Nickel*.]
  Instrumental conditions
  (See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
  Mode: Atomic absorption spectrophotometry (using a suitable GFAA spectrophotometer equipped with a pyrolytic tube with platform)
  Analytical wavelength: Cadmium emission line at 228.8 nm
  Lamp: Cadmium hollow-cathode
  Temperature: Use the temperature programming recommended for cadmium by the GFAA manufacturer (for examples of temperature parameters for GFAA analysis of cadmium, see *Table 1*).

Table 1

	Drying Stage	Ashing Stage	Atomization Stage
Temperature	110°	600°	1800°
Ramp time	10 s	10 s	0 s
Hold time	20 s	30 s	5 s

Analysis: Use the *Blank* to set the instrument to zero. Plot the absorbances of the *Sample solutions* versus their contents of cadmium, in µg/mL, as furnished by the *Standard solution*, draw the straight line best fitting the three points, using a linear least-squares fit, and extrapolate the line until it intercepts the concentration axis on the negative side. From the intercept determine the concentration, *C*, in µg/mL, of cadmium in the *Sample solution* containing 0 mL of the *Standard solution*.

Calculate the content, in ppm, of cadmium in the specimen taken:

$$\text{Result} = (C/W) \times F$$

W = weight of Magnesium Stearate taken to prepare the *Sample stock solution* (g)
F = dilution factor for the sample, 200

Alternatively, the GFAA software can be used to calculate the cadmium content of the sample. For either calculation, the correlation coefficient (*r*) of the standard additions plot must be at least ■0.99.■1S (*NF34*)

Acceptance criteria: ■NMT■1S (*NF34*) 3 ppm

Change to read:

- **LIMIT OF LEAD**

[NOTE—For the preparation of all aqueous solutions and for the rinsing of glassware before use, use water that has been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin. Select all reagents to have as low a content of cadmium, lead, and nickel as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse glassware before use by soaking in warm 8 N nitric acid for 30 min, and rinse with deionized water.]

Matrix modifier solution: Prepare as directed for *Matrix modifier solution* in *Limit of Cadmium*.

Blank: Prepare as directed for *Blank* in *Limit of Cadmium*.

Standard solution: 0.1598 µg/mL of *lead nitrate* in *Blank*, corresponding to a known concentration of 0.100 µg/mL of lead. Prepare and store any solutions of lead nitrate in glass containers free from soluble lead salts.

Sample stock solution: Use a portion of the *Sample stock solution* retained from the test for *Limit of Cadmium*.

Sample solutions: Prepare mixtures of the *Sample stock solution*, the *Standard solution*, and the *Blank* with the following proportional compositions, by volume (mL): 1.0/0/1.0, 1.0/0.5/0.5, and 1.0/1.0/0. Add 50 µL of the *Matrix modifier solution* to each mixture. These *Sample solutions* contain, respectively, 0, 0.025, and 0.05 µg/mL of lead from the *Standard solution.*

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)

Mode: Atomic absorption spectrophotometry (using a suitable GFAA spectrophotometer equipped with a pyrolytic tube with platform)

Analytical wavelength: Lead emission line at 283.3 nm

Lamp: Lead hollow-cathode

Temperature: Use the temperature programming recommended for lead by the GFAA manufacturer (for examples of temperature parameters for GFAA analysis of lead, see *Table 1*).

Analysis: Use the *Blank* to set the instrument to zero. Plot the absorbances of the *Sample solutions* versus their contents of lead, in µg/mL, as furnished by the *Standard solution*, draw the straight line best fitting the three points, using a linear least-squares fit, and extrapolate the line until it intercepts the concentration axis on the negative side. From the intercept determine the concentration, *C*, in µg/mL, of lead in the *Sample solution* containing 0 mL of the *Standard solution*.

Calculate the content, in ppm, of lead in the specimen taken:

$$\text{Result} = (C/W) \times F$$

W = weight of Magnesium Stearate taken to prepare the *Sample stock solution* (g)
F = dilution factor for the sample, 20

Alternatively, the GFAA software can be used to calculate the lead content of the sample. For either calculation, the correlation coefficient (*r*) of the standard additions plot must be at least ■0.99.■1S (*NF34*)

Acceptance criteria: ■NMT■1S (*NF34*) 10 ppm

Change to read:

- **LIMIT OF NICKEL**

[NOTE—For the preparation of all aqueous solutions and for the rinsing of glassware before use, use water that has been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin. Select all reagents to have as low a content of cadmium, lead, and nickel as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse glassware before use by soaking in warm 8 N nitric acid for 30 min, and rinse with deionized water.]

Matrix modifier solution: Prepare as directed for *Matrix modifier solution* in *Limit of Cadmium*.

Blank: Prepare as directed for *Blank* in *Limit of Cadmium*.

Standard solution: 0.2477 µg/mL of *nickel nitrate hexahydrate* in *Blank*, corresponding to a known concentration of 0.050 µg/mL of nickel

Sample stock solution: Use a portion of the *Sample stock solution* retained from the test for *Limit of Cadmium*.

Sample solutions: Prepare mixtures of the *Sample stock solution*, the *Standard solution*, and the *Blank* with the following proportional compositions, by volume (mL): 1.0/0/1.0, 1.0/0.5/0.5, and 1.0/1.0/0. Add 50 µL of the *Matrix modifier solution* to each mixture. These *Sample solutions* contain, respectively, 0, 0.0125, and 0.025 µg/mL of nickel from the *Standard solution*.

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)

Mode: Atomic absorption spectrophotometry (using a suitable GFAA spectrophotometer equipped with a pyrolytic tube with platform)

Analytical wavelength: Nickel emission line at 232.0 nm

Lamp: Nickel hollow-cathode

Temperature: Use the temperature programming recommended for nickel by the GFAA manufacturer (for examples of temperature parameters for GFAA analysis of nickel, see *Table 1*).

Analysis: Use the *Blank* to set the instrument to zero. Plot the absorbances of the *Sample solutions* versus their contents of nickel, in µg/mL, as furnished by the *Standard solution*, draw the straight line best fitting the three points, using a linear least-squares fit, and extrapolate the line until it intercepts the concentration axis on the negative side. From the intercept determine the concentration, *C*, in µg/mL, of nickel in the *Sample solution* containing 0 mL of the *Standard solution*.

Calculate the content, in ppm, of nickel in the specimen taken:

$$\text{Result} = (C/W) \times F$$

W = weight of Magnesium Stearate taken to prepare the *Sample stock solution* (g)
F = dilution factor for the sample, 20

Alternatively, the GFAA software can be used to calculate the nickel content of the sample. For either calculation, the correlation coefficient (r) of the standard additions plot must be at least ■0.99.■1S (*NF34*)

Acceptance criteria: ■NMT■1S (*NF34*) 5 ppm

SPECIFIC TESTS

Change to read:

- ■◆■1S (*NF34*)**MICROBIAL ENUMERATION TESTS** ⟨**61**⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨**62**⟩**:** The total aerobic microbial count does not exceed 10^3 cfu/g, the total combined molds and yeasts count does not exceed 5×10^2 cfu/g. It meets the requirements of the tests for absence of *Salmonella* species and *Escherichia coli*.■◆ ■1S (*NF34*)
- **ACIDITY OR ALKALINITY**
  Sample solution: To 1.0 g add 20 mL of carbon dioxide-free water, boil on a steam bath for 1 min with continuous shaking, cool, and filter. Add 0.05 mL of *bromothymol blue TS* to 10 mL of the filtrate.
  Acceptance criteria: NMT 0.05 mL of *0.1 N hydrochloric acid* or *0.1 N sodium hydroxide* is required to change the color of the indicator.
- ◆**SPECIFIC SURFACE AREA** ⟨**846**⟩
  [NOTE—In cases where there are no functionality-related concerns regarding the specific surface area of this article, this test may be omitted.]
  Where the labeling states the specific surface area, determine the specific surface area value as directed in the chapter in the P/P_0 range of 0.05–0.15, and using outgassing conditions of 2 h at 40°. If the plot deviates from linearity for P/P_0 values of 0.05–0.15, then a suitable range of P/P_0 values should be validated for linearity. In this case, it is necessary to state the range of validated P/P_0 values, the increment of the P/P_0 values, and the outgassing conditions used.◆
- **LOSS ON DRYING** ⟨**731**⟩
  Analysis: Dry at 105° to constant weight.
  Acceptance criteria: NMT 6.0%
- **RELATIVE CONTENT OF STEARIC ACID AND PALMITIC ACID**
  System suitability solution: Transfer 50 mg each of USP Stearic Acid RS and USP Palmitic Acid RS to a small conical flask fitted with a suitable reflux condenser. Add 5.0 mL of a solution prepared by dissolving 14 g of *boron trifluoride* in methanol to make 100 mL, swirl to mix, and reflux for 10 min until the solids have dissolved. Add 4 mL of *chromatographic n-heptane* through the condenser, and reflux for 10 min. Cool, add 20 mL of saturated *sodium chloride* solution, shake, and allow the layers to separate. Pass the *n*-heptane layer through 0.1 g of *anhydrous sodium sulfate* (previously washed with chromatographic *n*-heptane) into a suitable flask. Transfer 1.0 mL of this solution to a 10-mL volumetric flask, and dilute with *chromatographic n-heptane* to volume.
  Sample solution: Transfer 100 mg of Magnesium Stearate to a small conical flask fitted with a suitable reflux condenser, and proceed as directed for *System suitability solution*, beginning with "Add 5.0 mL of a solution prepared by dissolving".
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: GC
  Detector: Flame ionization
  Column: 0.32-mm × 30-m fused silica capillary, bonded with a 0.5-µm layer of phase G16
  Temperatures
  Injector: 220°
  Detector: 260°
  Column: See *Table 2*.

Table 2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
70	—	70	2
70	5	240	5

  Carrier gas: Helium
  Flow rate: 2.4 mL/min
  Injection volume: 1 µL
  Injection type: Splitless injection system
  System suitability
  Sample: *System suitability solution*
  [NOTE—The relative retention times for methyl palmitate and methyl stearate are about 0.9 and 1.0, respectively.]
  Suitability requirements
  Resolution: NLT 5.0 between methyl palmitate and methyl stearate
  Relative standard deviation: NMT 3.0% for the palmitate and stearate peak areas from six replicate injections; NMT 1.0% for the peak area ratio of palmitate to stearate from six replicate injections
  Analysis
  Sample: *Sample solution*
  Measure the peak areas for all the fatty acid esters in the chromatogram.
  Calculate the percentage of stearic acid in the fatty acid fraction of the portion of Magnesium Stearate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak area of methyl stearate from the *Sample solution*
r_T = sum of the peak areas of all the fatty acid esters from the *Sample solution*

  Similarly, calculate the percentage of palmitic acid in the portion of Magnesium Stearate taken.

$$\text{Result} = (r_P/r_T) \times 100$$

r_P = peak area of methyl palmitate from the *Sample solution*
r_T = sum of the peak areas of all the fatty acid esters from the *Sample solution*

  Acceptance criteria: NLT 40% for the stearate peak. The sum of the stearate and palmitate peaks is NLT 90% of the total peak areas of all the fatty acids.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- ◆**LABELING:** Where the labeling states the specific surface area, it also indicates which method specified in *Specific Surface Area* ⟨846⟩ is used. Label to indicate that the fatty acids are derived from edible sources.◆

• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Palmitic Acid RS
USP Stearic Acid RS