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Alumina, Magnesia, and Simethicone Chewable Tablets

DEFINITION

Alumina, Magnesia, and Simethicone Chewable Tablets contain the equivalent of NLT 90.0% and NMT 115.0% of the labeled amounts of aluminum hydroxide [$Al(OH)_3$] and magnesium hydroxide [$Mg(OH)_2$], and an amount of polydimethylsiloxane ([$-(CH_3)_2 SiO-]_n$) that is NLT 85.0% and NMT 115.0% of the labeled amount of simethicone.

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197S**▲ (CN 1-May-2020)

  Sample solution: Prepare as directed in the *Assay* for *Polydimethylsiloxane*.

  Analysis: Proceed as directed using a 0.5-mm cell.

  Acceptance criteria: Meet the requirements

- **B.** **Identification Tests—General, *Magnesium* ⟨191⟩**

  Sample solution: To a portion of finely powdered Chewable Tablets, equivalent to 600 mg of magnesium hydroxide, add 25 mL of 3 N hydrochloric acid and 25 mL of water, and mix. Boil gently for 2 min. Allow to cool, and filter. Add 5 drops of methyl red TS, heat to boiling, and add 6 N ammonium hydroxide until the color of the solution just turns to deep yellow. Continue boiling for 2 min, and filter.

  Acceptance criteria: Meet the requirements

- **C.** **Identification Tests—General, *Aluminum* ⟨191⟩**

  Sample solution: Wash the precipitate from *Identification* test *B* with hot ammonium chloride solution (1 in 50), and dissolve the precipitate in hydrochloric acid. Divide this solution into two portions.

  Analysis 1: Add, dropwise, 6 N ammonium hydroxide to one portion of the *Sample solution*.

  Acceptance criteria 1: A gelatinous white precipitate, which does not dissolve in an excess of 6 N ammonium hydroxide, is obtained.

  Analysis 2: Add, dropwise, 1 N sodium hydroxide to the second portion of the *Sample solution*.

  Acceptance criteria 2: A gelatinous white precipitate, which dissolves in an excess of 1 N sodium hydroxide, leaving some turbidity, is obtained.

ASSAY

- **Aluminum Hydroxide**

  Edetate disodium titrant: Prepare and standardize as directed in *Reagents, Volumetric Solutions*, *Edetate Disodium, Twentieth-Molar (0.05 M)*.

  Sample solution: Weigh and finely powder NLT 20 Chewable Tablets. Transfer a portion of the powder, equivalent of 800 mg of aluminum hydroxide, to a 150-mL beaker. Add 20 mL of water, stir, and slowly add 30 mL of 3 N hydrochloric acid. Heat gently, if necessary, to aid solution, cool to room temperature, and filter into a 200-mL volumetric flask. Wash the filter with water into the flask, and add water to volume.

  Analysis: Pipet 10 mL of the *Sample solution* into a 250-mL beaker, add 20 mL of water, then add, in the order named and with continuous stirring, 25.0 mL of *Edetate disodium titrant* and 20 mL of acetic acid–ammonium acetate buffer TS, and heat the solution near the boiling temperature for 5 min. Cool, add 50 mL of alcohol and 2 mL of dithizone TS. Titrate the excess edetate disodium with 0.05 M zinc sulfate VS until the color changes from green-violet to rose-pink. Perform a blank determination, substituting 10 mL of water for the *Sample solution*, and make any necessary correction. Each mL of *Edetate disodium titrant* consumed is equivalent to 3.900 mg of aluminum hydroxide [$Al(OH)_3$].

  Acceptance criteria: 90.0%–115.0%

- **Magnesium Hydroxide**

  Sample solution: Prepare as directed in the *Assay* for *Aluminum Hydroxide*.

  Analysis: Pipet a volume of the *Sample solution*, equivalent to 40 mg of magnesium hydroxide, into a 400-mL beaker, add 200 mL of water and 20 mL of triethanolamine, and stir. Add 10 mL of ammonia–ammonium chloride buffer TS and 3 drops of an eriochrome black indicator solution (prepared by dissolving 200 mg of eriochrome black T in a mixture of 15 mL of triethanolamine and 5 mL of dehydrated alcohol, and mixing). Cool the solution to between 3° and 4° by immersion of the beaker in an ice bath, then remove, and titrate with 0.05 M edetate disodium VS to a blue endpoint. Perform a blank determination, substituting water for the *Sample solution*, and make any necessary correction. Each mL of 0.05 M edetate disodium consumed is equivalent to 2.916 mg of magnesium hydroxide [$Mg(OH)_2$].

  Acceptance criteria: 90.0%–115.0%

- **Polydimethylsiloxane**

  Standard solution: Prepare similarly to the *Sample solution* below, using 33 mg of USP Polydimethylsiloxane RS.

Sample solution: Weigh and finely powder NLT 20 Chewable Tablets. Transfer a portion of the powder, equivalent of 33 mg of simethicone, to a suitable round, narrow-mouth, screw-capped, 120-mL bottle. Add 40 mL of 0.1 N sodium hydroxide, and swirl to disperse. Add 20.0 mL of toluene, close the bottle securely with a cap having an inert liner, and shake for 30 min on a reciprocating shaker (e.g., 200 oscillations/min and a stroke of 38 ± 2 mm). Transfer the mixture to a 125-mL separator, and allow to separate. Remove the upper, organic layer to a screw-capped, centrifuge tube containing 2 g of anhydrous sodium sulfate. Close the tube with a screw-cap having an inert liner, agitate vigorously, and centrifuge the mixture until a clear supernatant is obtained.

Blank: Mix 10 mL of toluene with 1 g of anhydrous sodium sulfate, and centrifuge to obtain a clear supernatant.

Analysis: Concomitantly determine the absorbances of the *Standard solution* and *Sample solution* in 0.5-mm cells at the wavelength of maximum absorbance at about 7.9 µm (1265.8 cm^{-1}), with a suitable IR spectrophotometer, using the *Blank* to set the instrument. Calculate the percentage of polydimethylsiloxane ($[-(CH_3)_2\ SiO-]_n$) in the portion of Chewable Tablets taken:

$$\text{Result} = (A_U/A_S) \times (W_S/W_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

W_S = weight of USP Polydimethylsiloxane RS taken to prepare the *Standard solution* (mg)

W_U = nominal amount of simethicone in the portion of the Chewable Tablets taken to prepare the *Sample solution* (mg)

Acceptance criteria: 85.0%–115.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements for *Weight Variation* with respect to aluminum hydroxide and to magnesium hydroxide

SPECIFIC TESTS

• **Acid-Neutralizing Capacity ⟨301⟩**

Acceptance criteria: The acid consumed by the minimum single dose recommended in the labeling is NLT 5 mEq, and NLT the number of mEq calculated by the formula:

$$\text{Result} = 0.55 \times (F_A \times A) + 0.8 \times (F_M \times M)$$

F_A = theoretical acid-neutralizing capacity of aluminum hydroxide $[Al(OH)_3]$, 0.0385 mEq

A = amount of aluminum hydroxide $[Al(OH)_3]$ in the specimen tested, based on the labeled quantity (mg)

F_M = theoretical acid-neutralizing capacity of magnesium hydroxide $[Mg(OH)_2]$, 0.0343 mEq

M = amount of magnesium hydroxide $[Mg(OH)_2]$ in the specimen tested, based on the labeled quantity (mg)

• **Sodium Content**

Potassium chloride solution: 38 mg/mL of potassium chloride

Sodium chloride stock solution: 25.42 µg/mL of sodium chloride (previously dried at 105° for 2 h) in water. The solution contains 10 µg/mL of sodium.

Standard solutions: On the day of use, transfer 4.0 mL of 1 N hydrochloric acid and 10.0 mL of *Potassium chloride solution* to each of two 100-mL volumetric flasks. To the respective flasks add 5.0 and 10.0 mL of *Sodium chloride stock solution*. Dilute with water to volume. The resulting *Standard solutions* contain 0.5 and 1.0 µg/mL of sodium (Na), respectively.

Sample solution: Weigh and finely powder NLT 20 Chewable Tablets. Transfer a portion of the powder, equivalent to the average weight of 1 Chewable Tablet, to a 100-mL volumetric flask. Add 50 mL of 1 N hydrochloric acid, boil for 15 min, cool to room temperature, and dilute with water to volume. Filter, discarding the first few mL of the filtrate. Transfer 5.0 mL of the filtrate to a 100-mL volumetric flask containing 10.0 mL of *Potassium chloride solution*, and dilute with water to volume.

Blank solution: Combine 4.0 mL of 1 N hydrochloric acid and 10.0 mL of *Potassium chloride solution* in a 100-mL volumetric flask, and dilute with water to volume.

Analysis

Samples: *Standard solution* and *Sample solution*

Concomitantly determine the absorbances of the *Standard solutions* and the *Sample solution* at the sodium emission line at 589.0 nm with a suitable atomic absorption spectrophotometer (see *Atomic Absorption Spectroscopy ⟨852⟩*) equipped with a sodium hollow–cathode lamp and an air–acetylene flame, using the *Blank solution* as the blank. Plot the absorbances of the *Standard solutions* versus concentration, in µg/mL, of sodium, and draw a straight line between the plotted points. From the graph so obtained, determine the concentration, *C*, in µg/mL, of sodium in the *Sample solution*.

Calculate the quantity, in mg, of sodium (Na) in each Chewable Tablet taken:

$$\text{Result} = C \times D \times F$$

C = concentration of sodium in the *Sample solution* (µg/mL)

D = dilution factor for the *Sample solution*, 2000

F = conversion factor, 0.001 mg/µg

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **Labeling:** Label the Chewable Tablets to indicate that they are to be chewed before being swallowed. Label the Chewable Tablets to state the sodium content if it is greater than 5 mg/Tablet. The Chewable Tablets may be labeled to state the aluminum hydroxide content in terms of the equivalent amount of dried aluminum hydroxide gel, on the basis that each mg of dried gel is equivalent to 0.765 mg of aluminum hydroxide [$Al(OH)_3$].

• **USP Reference Standards** ⟨11⟩

USP Polydimethylsiloxane RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ALUMINA, MAGNESIA, AND SIMETHICONE CHEWABLE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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