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Alumina, Magnesia, Calcium Carbonate, and Simethicone Chewable Tablets

DEFINITION

Alumina, Magnesia, Calcium Carbonate, and Simethicone Chewable Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of aluminum hydroxide [$Al(OH)_3$], magnesium hydroxide [$Mg(OH)_2$], and calcium carbonate ($CaCO_3$), 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

• **A.** **Identification Tests—General, *Calcium*⟨191⟩**

Sample solution: Cut a Chewable Tablet into pieces, add 50 mL of 1 N sulfuric acid, stir until the pieces disintegrate, and heat on a steam bath for 10 min. Cool, add 50 mL of alcohol, and stir. Place in an ice bath for 30 min. Filter while cold, retaining the filtrate for *Identification* test *B*. Wash the precipitate with 50 mL of 0.75 N sulfuric acid, and discard the washings. Dissolve the precipitate in 3 N hydrochloric acid, filter, and use the filtrate.

Acceptance criteria: Meet the requirements

• **B.** **Identification Tests—General, *Aluminum*⟨191⟩**

Sample solution: To the filtrate obtained in *Identification* test *A*, add 5 drops of methyl red TS, and heat to boiling. Add 6 N ammonium hydroxide until the color of the solution changes to deep yellow, continue boiling for 2 min, and filter through hardened filter paper. (Retain the filtrate for *Identification* test *C*.) Wash the precipitate with 350 mL of a hot solution containing 20 mg/mL of ammonium chloride, discarding the washings. Dissolve the precipitate so obtained in 3 N hydrochloric acid.

Acceptance criteria: Meet the requirements

• **C.** **Identification Tests—General, *Magnesium*⟨191⟩**

Sample solution: The filtrate obtained in *Identification* test *B*

Acceptance criteria: Meet the requirements

Change to read:

• **D.** ▲**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

ASSAY

• **Aluminum Hydroxide**

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

Sample solution: Transfer a number of Chewable Tablets, equivalent of about 665 mg of aluminum hydroxide, to a suitable beaker. Add 15 mL of hydrochloric acid, and swirl to dissolve the Chewable Tablets. Add 80 mL of water, and filter into a 200-mL volumetric flask. Wash the filter with water into the flask, and add water to volume.

Analysis: Pipet 20 mL of the *Sample solution* into a 250-mL beaker, 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 20 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 $Al(OH)_3$.

Acceptance criteria: 90.0%–110.0%

• **Magnesium Hydroxide**

Lanthanum chloride solution: Transfer 17.6 g of lanthanum chloride to a 200-mL volumetric flask, add 100 mL of water, and carefully add 50 mL of hydrochloric acid. Allow to cool, and dilute with water to volume.

Dilute hydrochloric acid: Dilute 226 mL of hydrochloric acid to 1000 mL with water.

Potassium chloride solution: 30 mg/mL in water

Magnesium stock solution: Transfer 1.000 g of magnesium metal to a 1000-mL volumetric flask containing 10 mL of water, slowly add 10 mL of hydrochloric acid, and swirl to dissolve the metal. Dilute with water to volume. Transfer 1.0 mL of this solution to a 100-mL volumetric flask to obtain a solution containing 10 µg/mL of magnesium (Mg).

Standard solutions: To three separate 100-mL volumetric flasks each containing 5.0 mL of *Lanthanum chloride solution*, add 1.0, 2.0, and 3.0 mL, respectively, of the *Magnesium stock solution*. Dilute each with water to volume. These solutions contain 0.1, 0.2, and 0.3 µg/mL of magnesium (Mg), respectively.

Sample stock solution: Transfer a number of Chewable Tablets, equivalent of 250 mg of magnesium hydroxide (100 mg of magnesium), to a 1000-mL volumetric flask. Add 500 mL of *Dilute hydrochloric acid*, and swirl to dissolve the Chewable Tablets. Add 100.0 mL of *Potassium chloride solution*, and dilute with water to volume. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, and dilute with water to volume.

Sample solution: Transfer 2.0 mL of *Sample stock solution* to a second 100-mL volumetric flask, add 5.0 mL of *Lanthanum chloride solution*, and dilute with water to volume.

Blank: Add 50 mL of *Dilute hydrochloric acid* and 10.0 mL of *Potassium chloride solution* to a 100-mL volumetric flask, and dilute with water to volume. Transfer 10.0 mL of this solution to a second 100-mL volumetric flask, and dilute with water to volume. Transfer 2.0 mL of this solution to a third 100-mL volumetric flask, add 5.0 mL of *Lanthanum chloride solution*, and dilute with water to volume.

Analysis: Concomitantly determine the absorbances of the *Standard solutions* and the *Sample solution* at the magnesium emission line at 285.2 nm, with a suitable atomic absorption spectrophotometer (see *Atomic Absorption Spectroscopy* ⟨852⟩) equipped with a magnesium hollow-cathode lamp and an air–acetylene flame, using the *Blank* to set the instrument. Plot the absorbances of the *Standard solutions* versus concentration, in µg/mL, of magnesium, and draw the straight line best fitting the three plotted points. From the graph so obtained, determine the concentration, *C*, in µg/mL, of magnesium in the *Sample solution*.

Calculate the percentage of the labeled amount of magnesium hydroxide [$Mg(OH)_2$] in the portion of Tablets taken:

$$\text{Result} = (C/C_U) \times (M_r/A_r) \times 100$$

C = concentration of magnesium in the *Sample solution*, as determined above (µg/mL)

C_U = nominal concentration of magnesium hydroxide in the *Sample solution* (µg/mL)

M_r = molecular weight of magnesium hydroxide, 58.34

A_r = atomic weight of magnesium, 24.305

Acceptance criteria: 90.0%–110.0%

- **Calcium Carbonate**

Sample solution: Transfer a number of Chewable Tablets, equivalent of about 665 mg of aluminum hydroxide, to a suitable beaker. Add 15 mL of hydrochloric acid, and swirl to dissolve the Chewable Tablets. Add 80 mL of water, and filter into a 200-mL volumetric flask. Wash the filter with water into the flask, and add water to volume.

Analysis: Pipet a volume of the *Sample solution*, equivalent to 50 mg of calcium carbonate, into a 400-mL beaker, and add 200 mL of water, a volume of sodium hydroxide solution (1 in 2) equivalent to the volume of the *Sample solution* taken, and 250 mg of hydroxy naphthol blue. Stir with a magnetic stirrer, and titrate immediately with 0.05 M edetate disodium VS until the solution is distinctly blue. Perform a blank determination, substituting a volume of water equivalent to the volume of the *Sample solution* taken, and make any necessary correction. Each mL of 0.05 M edetate disodium is equivalent to 5.004 mg of calcium carbonate ($CaCO_3$).

Acceptance criteria: 90.0%–110.0%

- **Polydimethylsiloxane**

Dilute hydrochloric acid: Dilute 400 mL of hydrochloric acid with sufficient water to make 1000 mL.

Standard solution: Transfer 60 mg of USP Polydimethylsiloxane RS to a separator, add 30.0 mL of chloroform and 60 mL of *Dilute hydrochloric acid*, shake for 30 s, and allow the phases to separate. Remove 10 mL of the lower, organic layer to a screw-capped, 15-mL test tube containing 0.5 g of anhydrous sodium sulfate. Close the tube with a screw-cap having an inert liner, agitate vigorously, and centrifuge the mixture to obtain a clear supernatant.

Sample solution: Weigh and finely powder NLT 20 Chewable Tablets. Transfer a portion of the powder, equivalent of 60 mg of simethicone, to a suitable screw-capped bottle. Add 30.0 mL of chloroform and 60 mL of *Dilute hydrochloric acid*, and allow to stand, with frequent shaking, until the Chewable Tablets are dissolved. Transfer the contents of the bottle to a separator, shake, and allow the phases to separate. Remove 10 mL of the lower, organic layer to a screw-capped, 15-mL test tube containing 0.5 g of anhydrous sodium sulfate. Close the tube with a screw-cap having an inert liner, agitate vigorously, and centrifuge the mixture to obtain a clear supernatant.

Blank: Place 30.0 mL of chloroform and 60 mL of *Dilute hydrochloric acid* in a separator, shake for 30 s, and allow the phases to separate. Remove 10 mL of the lower, organic layer to a screw-capped, 15-mL test tube containing 0.5 g of anhydrous sodium sulfate. Close the tube with a screw-cap that has an inert liner, agitate vigorously, and centrifuge the mixture to obtain a clear supernatant.

Analysis: Concomitantly determine the absorbances of the *Standard solution* and the *Sample solution* in 0.5-mm cells at the wavelength of maximum absorbance at about 7.9 µm, 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 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 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, to magnesium hydroxide, and to calcium carbonate.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count is NMT 2×10^2 cfu/g, the total combined molds and yeasts count is NMT 2×10^2 cfu/g, and the Chewable Tablets meet the requirements of the test for the absence of *Salmonella* species and *Escherichia coli*.

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

Sample solution: Dissolve an accurately counted number of Chewable Tablets, equivalent to about 120 mEq of acid-neutralizing capacity, in 400 mL of water. Transfer the mixture to a 500-mL volumetric flask, and dilute with water to volume.

Analysis: Proceed as directed in the section *Procedure for Powders, Effervescent Solids, Suspensions and Other Liquids, Lozenges Nonchewable Tablets, Chewable Tablets, and Capsules* using 75.0 mL of the *Sample solution*.

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:

$$\text{Result} = 0.55 \times (F_A \times A) + 0.8 \times (F_M \times M) + 0.9 \times (F_C \times C)$$

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)

F_C = theoretical acid-neutralizing capacity of calcium carbonate ($CaCO_3$), 0.02 mEq

C = amount of calcium carbonate ($CaCO_3$) in the specimen tested, based on the labeled quantity (mg)

• **Sodium Content**

Potassium chloride solution: 30 mg/mL of potassium chloride

Dilute hydrochloric acid: Dilute 226 mL of hydrochloric acid with sufficient water to make 1000 mL.

Standard stock solution: Transfer 2.5420 g of sodium chloride, previously dried at 105° for 2 h, to a 1000-mL volumetric flask, and dissolve in and dilute with water to volume. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, and dilute with water to volume. Transfer 10.0 mL of this solution to a second 100-mL volumetric flask, and dilute with water to volume.

Standard solutions: To three separate 100-mL volumetric flasks, each containing 10.0 mL of *Potassium chloride solution* and 3.0 mL of *Dilute hydrochloric acid*, add 10.0, 20.0, and 30.0 mL, respectively, of the *Standard stock solution*. The resulting *Standard solutions* contain 1.0, 2.0, and 3.0 µg/mL of sodium (Na), respectively.

Sample stock solution: Weigh 10 Chewable Tablets, and determine the average weight, *A*, in mg. Cut 4 Chewable Tablets into pieces, combine the pieces, and weigh them. Transfer the combined pieces to a 500-mL volumetric flask, add 150 mL of *Dilute hydrochloric acid*, and swirl gently to dissolve the pieces. Dilute with water to volume.

Sample solution: Transfer 10.0 mL of the *Sample stock solution* to a 100-mL volumetric flask, add 10.0 mL of *Potassium chloride solution*, and dilute with water to volume.

Blank solution: Combine 3.0 mL of *Dilute 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 the straight line best fitting the three 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:

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

A = average weight of each Tablet (mg)

W = weight of the portion of Chewable Tablets taken to prepare the *Sample solution* (mg)

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

D = dilution factor for the *Sample solution*, 5000

F = conversion factor, 0.001 mg/µg

Acceptance criteria: Chewable Tablets contain NMT 5 mg/Tablet of sodium, except when labeled as containing more than 5 mg/Tablet of sodium; then they contain NMT 110% of the labeled amount.

ADDITIONAL REQUIREMENTS

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

• **Labeling:** The labeling indicates that the Chewable Tablets are to be chewed before swallowing. Label the Chewable Tablets to state the sodium content, if it is greater than 5 mg/Chewable Tablet.

• **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, CALCIUM CARBONATE, AND SIMETHICONE CHEWABLE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

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