

**ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON
PHARMACOPOEIAL PRODUCT
DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory**

Antacid Suspension with Oxetacaine & Simethicone

Analytical Profile No.: ATO S 074/075/AP019

Antacid Suspension with Oxetacaine & Simethicone contains not less than 90% and not more than 115% of the stated amount of Dried Aluminium Hydroxide gel and Magnesium Hydroxide and not less than 90% and not more than 110% of the stated amount of Oxetacaine & Simethicone.

1. Identification:

1.1 Magnesium

Dissolve an amount of suspension containing about 0.8 g of anhydrous magaldrate in 20 ml of 3M hydrochloric acid, dilute with water to 50 ml, add 3 drops of methyl red solution and heat to boiling. Add dilute ammonia solution until the color changes to just yellow, continue boiling for 2 minutes and filter; the filtrate gives the reaction of magnesium salt. For reaction of magnesium salt, follow latest IP.

1.2 Aluminium

Wash the precipitates obtained in the test 1.1 with 50 ml of hot 2% solution of ammonium chloride, then dissolve the precipitate in 15 ml of 3 M hydrochloric acid; the solution gives the reaction of aluminium salt. For reaction of aluminium salt, follow latest IP.

1.3 Oxetacaine

In the Assay, the principle peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

1.4 Simethicone (As per USP 2018)

2. pH: 7.0 to 8.6

3. wt/ml: As per manufacturer's specification

4. Acid-neutralizing capacity

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4.1 Test Solution:

Shake the container until the contents are uniform, and determine the density. Transfer an accurately weighed quantity of the uniform mixture, equivalent to 10 ml to a 250 ml beaker; add water to make a total volume of about 70 ml, and mix on the magnetic stirrer for 1 minute.

4.2 Procedure:

Pipette 30 ml of 1.0 N hydrochloric acid VS into the test solution while continuing to stir with the magnetic stirrer. Stir for 15 minutes, accurately timed, after the addition of the acid, begin to titrate immediately, and in a period not to exceed and additional 5 minutes, titrate the excess hydrochloric acid with 0.5 N sodium hydroxide VS to attain a stable (for 10 to 15 seconds) pH of 3.5. Calculate the number of mEq of acid consumed by the formula:

$$\text{Total mEq} = (30 \times \text{Normality of HCl}) - (\text{Volume of NaOH} \times \text{Normality of NaOH})$$

Theoretical mEq value: $[0.55 \times (0.0385 \text{ A})] + [0.8 \times (0.0343 \times \text{M})]$

Where, 0.0385 and 0.0343 are the theoretical acid neutralizing capacity in mEq of Aluminium Hydroxide and Magnesium Hydroxide, and A and M are quantities in mg of Aluminum hydroxide and Magnesium hydroxide, based on the label claim.

Note: All tests shall be conducted at 37 °C ± 3 °C

4.3 Limit: NLT 5 mEq

5. Assay

5.1 Aluminum Hydroxide

5.1.1 Reagent preparation

Acetic acid ammonium acetate Buffer: Dissolve 77.1 g of ammonium acetate in water and add 57 ml of glacial acetic acid and dilute with water to 1000 ml.

Disodium Edetate, xM: Solution of any molarity xM may be prepared by dissolving 372.2x g of disodium edetate in sufficient water to produce 1000 ml.

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Zinc Sulphate, xM: Solution of any molarity xM may be prepared by dissolving 289x g of zinc sulphate in sufficient water to produce 1000 ml.

Dithizone solution: A 0.05% w/v solution of dithizone in chloroform.

5.1.2 Test Solution

Weigh the sample equivalent to 250 mg of Dried Aluminium Hydroxide gel in a 100 ml volumetric flask, add 10 ml water, shake and add slowly 5 ml of HCl. Heat gently, if necessary, and dilute to 100 ml with water.

5.1.3 Procedure

Pipette 20 ml of the assay preparation into a 250 ml conical flask, add 20 ml of water and then with stirring 25.0 ml of 0.05 M disodium edetate, mix and add 20 ml of acetic acid-ammonium acetate buffer, and heat near the boiling temperature for 5 minutes. Cool and add 40 ml ethanol (95%) and add 2 ml of dithizone solution and titrate with 0.05 M zinc sulphate to a bright rose-pink color. Repeat the procedure without the substance being examined. The difference between the titrations represents the amount of disodium edetate required.

Each ml of 0.05 M disodium edetate is equivalent to 0.0039 g of $\text{Al}(\text{OH})_3$.

5.2 Magnesium Hydroxide

5.2.1 Reagent Preparation

Ammonium- Ammonium Chloride Buffer: Dissolve 67.5 g of ammonium Chloride in about 200 ml of water, add 570 ml of strong ammonia solution and dilute with water to 1000 ml.

5.2.2 Test Solution

Prepare as directed in the assay for aluminum hydroxide

5.2.3 Procedure

Pipette 20 ml of the sample obtained in the assay preparation of aluminium hydroxide, add 40 ml of water and 20 ml of triethanolamine and stir. Add 10 ml of ammonia-ammonium chloride buffer

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and 3 drops of an erichrome black T solution. Cool the solution to between 3° and 4° C by immersion of the flask in an ice bath, then remove and titrate with 0.05 M disodium edetate to blue color. Repeat the procedure without the substance being examined.

The difference between the titration represents the amount of disodium edetate required.

Each ml of 0.05 M disodium edetate is equivalent to 0.002916 g of Mg(OH)₂.

5.3 Oxetacaine: Determine by liquid chromatography

5.3.1 Test Solution:

Weigh accurately about the sample equivalent to 5 mg of Oxetacaine in 100 ml volumetric flask. Dissolve with mobile phase by sonicating for about 10 minutes and make up the volume to 100 ml with mobile phase. Centrifuge or filter the resulting sample. Dilute 5 ml of the clear solution to 25 ml with mobile phase.

5.3.2 Reference Solution:

Weigh accurately about 25 mg of Oxetacaine WS and transfer into 100 ml volumetric flask. Dissolve with mobile phase and make up the volume to 100 ml with mobile phase. Dilute 2 ml of the resulting solution to 50 ml with mobile phase.

5.3.3 Chromatographic Condition

Column: C18, (150*4.6 mm), 5 µm column

Oven temperature: 30 °C

Mobile Phase: A mixture of 78 volumes of Acetonitrile and 22 volumes of Buffer (78:22).

Buffer: 0.01 M Potassium hydrogen phosphate and pH adjusted to pH 6.5 ± 0.1 with orthophosphoric acid.

Flow rate: 1.0 ml/min

Detector: UV Detector

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Wavelength: 220 nm

Injection volume: 50 µl

5.3.4 Procedure:

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates. The tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0%.

Inject the reference solution and the test solution.

Calculate the content of Oxetacaine in the suspension.

5.4 Simethicone (Polydimethylsiloxane)

By IR Spectrophotometry as per USP 2018 (Simethicone oral suspension).

5. Other tests: As per pharmacopoeial requirement