Aspirin, Alumina, and Magnesia Tablets

DEFINITION
Aspirin, Alumina, and Magnesia Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of aspirin (C9H8O4), the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of aluminum hydroxide [Al(OH)₃], and NLT 90.0% and NMT 110.0% of the labeled amount of magnesium hydroxide [Mg(OH)₂].

IDENTIFICATION

Change to read:

- A. The retention time of the aspirin peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay for Aspirin.

- B. IDENTIFICATION TESTS—GENERAL

Sample solution: To a 0.7-g portion of finely powdered Tablets, add 20 mL of 3 N hydrochloric acid and 5 drops of methyl red TS, heat to boiling, and add 6 N ammonium hydroxide until the color of the solution changes to deep yellow. Continue boiling for 2 min, and filter. Use the filtrate for analysis and use the precipitate in Identification C.

Acceptance criteria: Meet the requirements

C. IDENTIFICATION TESTS—GENERAL

Sample solution: Wash the precipitate obtained in Identification B with a hot solution of ammonium chloride (1 in 50), and dissolve the precipitate in hydrochloric acid.

Acceptance criteria: Meet the requirements

ASSAY

Change to read:

- ASPIRIN

Mobile phase: Dissolve 225 mg of tetrabutylammonium hydroxide pentahydrate and 200 mg of sodium 1-octanesulfonate in 700 mL of water. Add 150 mL of methanol, 150 mL of acetonitrile, and 1.0 mL of glacial acetic acid, and stir.

Diluent: To 2 g of anhydrous citric acid add 990 mL of acetonitrile, 990 mL of chloroform, and 20 mL of formic acid, and stir for about 30 min. Allow to settle, and use the decanted clear solution.

Internal standard solution: 2 mg/mL of phenacetin in Diluent

Salicylic acid stock solution: 1 mg/mL of USP Salicylic Acid RS in Diluent

Standard solution: 6.5 mg/mL of USP Aspirin RS and 0.2 mg/mL of each of USP Salicylic Acid RS and phenacetin prepared as follows. Transfer, accurately weighed, about 325 mg of USP Aspirin RS to a 50-mL volumetric flask. Add 10.0 mL of Salicylic acid stock solution and 5.0 mL of Internal standard solution, dilute with Diluent to volume, and mix.

Sample solution: Normally 6.5 mg/mL of aspirin prepared as follows. Transfer a quantity equivalent to about 325 mg of aspirin from NLT 20 finely powdered Tablets to a screw-capped, 120-mL bottle. Add 5.0 mL of Internal standard solution and 45.0 mL of Diluent, mix, and sonicate for 2–5 min. Centrifuge, and use the resultant clear solution.

Chromatographic system
(See Chromatography (621), System Suitability.)

Mode: LC
Detector: UV 280 nm
Column: 4-mm × 30-cm; 10-μm packing L1
Flow rate: 2 mL/min
Injection volume: 5 μL

System suitability
Sample: Standard solution

[NOTE—The relative retention times for salicylic acid, aspirin, and phenacetin are about 0.3, 0.6, and 1.0, respectively. Record each chromatogram until the chloroform peak appears at the relative retention time of about 1.8.]

Suitability requirements
Resolution: NLT 2.0 between two adjacent peaks for salicylic acid, aspirin, and phenacetin
Tailing factor: NMT 2.0 for each peak
Relative standard deviation: NMT 3.0%

Analysis
Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of aspirin (C9H8O4) in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{R_s}{R_u} \times \frac{C_u}{C_s} \right) \times 100
\]

\[ R_u = \text{peak response ratio of aspirin to phenacetin from the Sample solution} \]

\[ R_s = \text{peak response ratio of aspirin to phenacetin from the Standard solution} \]

\[ C_s = \text{concentration of USP Aspirin RS in the Standard solution (mg/mL)} \]

\[ C_u = \text{nominal concentration of aspirin in the Sample solution (mg/mL)} \]

Acceptance criteria: 90.0%–110.0%

- ALUMINUM HYDROXIDE

Sample solution: Nominally 1.25 mg/mL of aluminum hydroxide prepared as follows. To a portion of NLT 20 powdered Tablets, equivalent to 250 mg of aluminum hydroxide in 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, and transfer to a 200-mL volumetric flask. Wash the beaker with water, adding the washings to the flask, dilute with water to volume, and mix.

Titrimetric system
Mode: Residual titration
Titrant: 0.05 M edetate disodium VS
Back titrant: 0.05 M zinc sulfate VS
Blank: Water, 50 mL
Endpoint detection: Visual

Analysis: To 50 mL of Sample solution add, in the order named and with continuous stirring, 25.0 mL of the Titrant and 20 mL of acetic acid–ammonium acetate buffer TS, and heat the solution near the boiling temperature for 5 min. Cool, and add 50 mL of alcohol and 2 mL of dithizone TS. Titrate with Back titrant until the color changes from green-violet to rose-pink. Perform a blank determination, substituting 50 mL of water for the Sample solution, and make any necessary corrections. Each mL of Titrant consumed is equivalent to 3.900 mg of aluminum hydroxide [Al(OH)₃].

Acceptance criteria: 90.0%–110.0%

- MAGNESIUM HYDROXIDE

Indicator solution: Dissolve by mixing 200 mg of eriochrome black T in a mixture of 15 mL of triethanolamine and 5 mL of dehydrated alcohol

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

**LIMIT OF FREE SALICYLIC ACID**

Mobile phase, Diluent, Internal standard solution, Salicylic acid stock solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay for Aspirin.

**System suitability solution**: Transfer about 325 mg of USP Aspirin RS to a 50-mL volumetric flask. Add 10.0 mL of Salicylic acid stock solution and 5.0 mL of Internal standard solution, dilute with Diluent to volume, and mix.

**Standard solution**: 0.2 mg/mL of USP Salicylic Acid RS prepared as follows. Transfer 10.0 mL of Salicylic acid stock solution and 5.0 mL of Internal standard solution to a 50-mL volumetric flask, dilute with Diluent to volume, and mix.· (IRA 1-Jan-2017)

**System suitability**

**Samples**: System suitability solution and Standard solution

**Acceptance criteria**: NMT 3.0%, Standard solution

**Relative standard deviation**: NMT 3.0%, Standard solution

**Analysis**

Samples: Standard solution and Sample solution

Calculate the percentage of salicylic acid in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{R_d}{R_s} \right) \times \left( \frac{C_s}{C_d} \right) \times 100 \]

- \( R_d \) = peak response ratio of salicylic acid to phenacetin from the Sample solution
- \( R_s \) = peak response ratio of salicylic acid to phenacetin from the Standard solution
- \( C_s \) = concentration of USP Salicylic Acid RS in the Standard solution (mg/mL)
- \( C_d \) = nominal concentration of aspirin in the Sample solution (mg/mL)

**Acceptance criteria**: NMT 3.0%

**SPECIFIC TESTS**

**Acid-Neutralizing Capacity (301)**: NLT 1.9 mEq of acid is consumed for each 325 mg of aspirin in the Tablets.

**ADDITIONAL REQUIREMENTS**

**Packaging and Storage**: Preserve in tight containers.

**USP Reference Standards (11)**

USP Aspirin RS
USP Salicylic Acid RS