Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Dec-2017
Document Type: USP Monographs
DocId: GUID-09472A27-C9BE-4037-AAEC-588CDDA0DC27_1_en-US
DOI: https://doi.org/10.31003/USPNF_M6300_01_01
DOI Ref: j4j2v

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 ($C_9H_8O_4$), 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

• **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 ⟨191⟩, *Magnesium***

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 ⟨191⟩, *Aluminum***

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

• **Aspirin**

Mobile phase: Dissolve 225 mg of tetramethylammonium 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 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: Nominally 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 ($C_9H_8O_4$) in the portion of Tablets taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of aspirin to phenacetin from the *Sample solution*

R_S = peak response ratio of aspirin to phenacetin from the *Standard solution*

C_S = concentration of USP Aspirin RS in the *Standard solution* (mg/mL)

C_U = 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*.

Titrimetric system

Mode: Direct titration

Titrant: 0.05 M edetate disodium VS

Blank: Water, 50 mL

Endpoint detection: Visual

Analysis: To a volume of *Sample solution*, equivalent to 80 mg of magnesium hydroxide, add 200 mL of water, 20 mL of triethanolamine, 50 mL of ammonia–ammonium chloride buffer TS, and 2 drops of *Indicator solution*. Cool the solution to between 3° and 4° by immersion in an ice bath, then remove, and titrate with *Titrant* until the color changes to pure blue. Perform a blank determination, substituting for the *Sample solution* a volume of water equal to the volume of *Sample solution* used, and make any necessary corrections. Each mL of *Titrant* is equivalent to 2.916 mg of magnesium hydroxide [$Mg(OH)_2$].

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **Dissolution** ⟨711⟩

Medium: 0.05 M acetate buffer, prepared by mixing 2.99 g of sodium acetate (trihydrate) and 1.66 mL of glacial acetic acid with water to obtain 1000 mL of solution with a pH of 4.50 ± 0.05; 900 mL

Apparatus 2: 75 rpm

Time: 45 min

Standard solution: A known concentration of USP Aspirin RS in *Medium*. Prepare the *Standard solution* at the time of use. [Note—A quantity of methanol NMT 1% of the total volume of the *Standard solution* may be used to dissolve the Reference Standard into solution prior to dilution with *Medium*.]

Sample solution: Pass a portion of the solution under test through a suitable filter, and dilute with *Medium*, if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: 265 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the percentage of the labeled amount of aspirin ($C_9H_8O_4$) dissolved from UV absorbances at the isosbestic point of aspirin and salicylic acid at about 265 nm.

Tolerances: NLT 75% (*Q*) of the labeled amount of aspirin ($C_9H_8O_4$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩, *Weight Variation* and *Content Uniformity*:** Meet the requirements for weight variation with respect to aluminum hydroxide and to magnesium hydroxide. Meet the requirements for content uniformity with respect to aspirin.

IMPURITIES

• **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.

System suitability

Samples: *System suitability solution* and *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, *System suitability solution*

Tailing factor: NMT 2.0, *System suitability 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:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = 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_U = 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

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

Topic/Question	Contact	Expert Committee
ASPIRIN, ALUMINA, AND MAGNESIA TABLETS	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 42(4)

Current DocID: GUID-09472A27-C9BE-4037-AAEC-588CDDA0DC27_1_en-US

DOI: https://doi.org/10.31003/USPNF_M6300_01_01

DOI ref: j4j2v