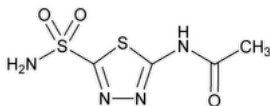


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Acetazolamide

Change to read:



$C_4H_6N_4O_3S_2$ ▲222.24▲ (USP 1-May-2024)

Acetamide, *N*-[5-(aminosulfonyl)-1,3,4-thiadiazol-2-yl]-;

N-(5-Sulfamoyl-1,3,4-thiadiazol-2-yl)acetamide CAS RN®: 59-66-5; UNII: O3FX965V0I.

DEFINITION

Acetazolamide contains NLT 98.0% and NMT 102.0% of acetazolamide ($C_4H_6N_4O_3S_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** ▲197A or▲ (USP 1-May-2024) 197K
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

• PROCEDURE

Mobile phase: Dissolve 4.1 g of [anhydrous sodium acetate](#) in 950 mL of [water](#). Add 20 mL of [methanol](#) and 30 mL of [acetonitrile](#), and mix. Adjust with [glacial acetic acid](#) to a pH of 4.0.

Standard solution: 0.1 mg/mL of [USP Acetazolamide RS](#) prepared as follows. Transfer an appropriate amount of [USP Acetazolamide RS](#) into a suitable volumetric flask, add 0.5 N [sodium hydroxide](#) equivalent to 10% of the flask volume, and dilute with [water](#) to volume.

Sample solution: 0.1 mg/mL of Acetazolamide prepared as follows. Transfer an appropriate amount of Acetazolamide into a suitable volumetric flask, add 0.5 N [sodium hydroxide](#) equivalent to 10% of the flask volume, and dilute with [water](#) to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; ▲5-μm▲ (USP 1-May-2024) packing [L1](#)

Flow rate: 2 mL/min

Injection volume: 20 μL

▲**Run time:** NLT 1.5 times the retention time of acetazolamide▲ (USP 1-May-2024)

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acetazolamide ($C_4H_6N_4O_3S_2$) in the portion of Acetazolamide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of acetazolamide from the *Sample solution*

r_S = peak response of acetazolamide from the *Standard solution*

C_S = concentration of [USP Acetazolamide RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Acetazolamide in the Sample solution (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **RESIDUE ON IGNITION (281):** NMT 0.1%
- **CHLORIDE AND SULFATE (221), Chloride**

Sample solution: Digest 1.5 g with 75 mL of [water](#) at about 70° for 5 min. Cool to room temperature, and filter.

Acceptance criteria: A 25-mL portion of the filtrate shows no more chloride than corresponds to 0.10 mL of 0.020 N [hydrochloric acid](#) (0.014%).

- **CHLORIDE AND SULFATE (221), Sulfate**

Sample solution: A 25-mL portion of the filtrate prepared in the test for *Chloride and Sulfate, Chloride*

Acceptance criteria: It shows no more sulfate than corresponds to 0.20 mL of 0.020 N [sulfuric acid](#) (0.04%).

Change to read:

- **ORGANIC IMPURITIES**

Solution A: 13.61 g/L of [monobasic potassium phosphate](#) in [water](#)

Mobile phase: [Methanol](#) and *Solution A* (10:90)

Standard stock solution: 0.4 mg/mL of [USP Acetazolamide RS](#) in *Mobile phase* prepared as follows. Transfer an appropriate amount of [USP Acetazolamide RS](#) to a suitable volumetric flask. Add 20% of the flask volume of [methanol](#), and sonicate for 15 min with occasional shaking to dissolve. Dilute with *Mobile phase* to volume.

Standard solution: 0.005 mg/mL of [USP Acetazolamide RS](#) from *Standard stock solution* in *Mobile phase*

Sensitivity solution: 0.5 µg/mL [▲] (USP 1-May-2024) of [USP Acetazolamide RS](#) from *Standard solution* in *Mobile phase*

Sample solution: 1 mg/mL of Acetazolamide in *Mobile phase* prepared as follows. Transfer an appropriate amount of Acetazolamide to a suitable volumetric flask. Add 20% of the flask volume of [methanol](#), and sonicate for 15 min with occasional shaking to dissolve. Dilute with *Mobile phase* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing [L10](#)

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 30 µL

Run time: NLT 9.5 times the retention time of acetazolamide

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[▲][NOTE—The relative retention times in [Table 1](#) are provided as information that could aid in peak assignment.]

Table 1 [▲] (USP 1-May-2024)

Name	Relative Retention Time
[▲] Acetazolamide related compound D [▲] (USP 1-May-2024) ^a	0.45
[▲] Acetazolamide related compound E [▲] (USP 1-May-2024) ^b	0.54
Acetamidothiadiazole ^c	0.82
Acetazolamide	1.0
Mercaptothiadiazole analog ^d	1.6
Chlorothiadiazole analog ^e	1.9
Acetazolamide dimer ^f	6.3

^a 5-Amino-1,3,4-thiadiazole-2-sulfonamide.
^b 5-Acetamido-1,3,4-thiadiazole-2-sulfonic acid.
^c N-(1,3,4-Thiadiazol-2-yl)acetamide.
^d N-(5-Mercapto-1,3,4-thiadiazol-2-yl)acetamide.
^e N-(5-Chloro-1,3,4-thiadiazol-2-yl)acetamide.