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Acetazolamide Extended-Release Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-acetazolamide-erc-20240628.

DEFINITION

Acetazolamide Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of acetazolamide ($C_4H_6N_4O_3S_2$).

IDENTIFICATION

- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **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

PROCEDURE

Buffer: 1.38 g/L of [sodium phosphate monobasic](#), prepared as follows. Transfer a suitable quantity of [sodium phosphate monobasic](#) to an appropriate volumetric flask. Dissolve in 95% of the flask volume of [water](#). Adjust with 2 M [phosphoric acid](#) to a pH of 3.0 and dilute with [water](#) to volume.

Mobile phase: [Acetonitrile](#) and *Buffer* (10:90)

Diluent: [Methanol](#) and *Buffer* (90:10)

Standard stock solution: 0.4 mg/mL of [USP Acetazolamide RS](#) in *Diluent*. Sonicate to dissolve.

Standard solution: 0.02 mg/mL of [USP Acetazolamide RS](#) in *Mobile Phase*, from the *Standard stock solution*

Sample stock solution: Nominally 0.4 mg/mL of acetazolamide, prepared as follows. Transfer a portion of the contents from NLT 10 Capsules to a suitable volumetric flask. Add about 60% of the flask volume of *Diluent*. Sonicate for NLT 30 min with intermittent shaking and maintain at room temperature. Dilute with *Diluent* to volume. Pass the solution through a suitable filter.

Sample solution: Nominally 0.02 mg/mL of acetazolamide in *Mobile phase*, from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 265 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-μm packing [L1](#)

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 25 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetazolamide ($C_4H_6N_4O_3S_2$) in the portion of Capsules 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 = nominal concentration of acetazolamide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Test 1

Medium: Acetate buffer, pH 4.5 with 2.2% polysorbate 20,¹ prepared as follows. Dissolve 3.0 g of ▲[sodium acetate](#)▲ (RB 1-Jul-2024) in 900 mL of [water](#). Add 22 mL of polysorbate 20, and adjust with [glacial acetic acid](#) to a pH of 4.5. Dilute with [water](#) to 1000 mL; 900 mL.

Apparatus 2: 75 rpm

Times: 0.5, 2, 5, and 12 h

Standard stock solution: 0.28 mg/mL of [USP Acetazolamide RS](#) prepared as follows. Transfer [USP Acetazolamide RS](#) to a suitable volumetric flask. Add 10% of the flask volume of [methanol](#), and sonicate to dissolve. Dilute with *Medium* to volume.

Standard solution: 0.017 mg/mL of [USP Acetazolamide RS](#) in *Medium*, from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute the filtrate with *Medium*, if necessary. Replace the amount of solution withdrawn at each time point with the same volume of *Medium*.

Blank: *Medium*

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 265 nm

Cell: 1.0 cm

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of acetazolamide ($C_4H_6N_4O_3S_2$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor of the *Sample solution*, if necessary

Calculate the percentage of the labeled amount of acetazolamide ($C_4H_6N_4O_3S_2$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{[(C_3 \times V) + [(C_2 + C_1) \times V_S]]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{[(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]]\} \times (1/L) \times 100$$

C_i = concentration of acetazolamide in the portion of the sample withdrawn at time point i (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See [Table 1](#).

Table 1

Time Point (i)	Time (h)	Amount Dissolved (%)
1	0.5	NMT 35

Time Point (i)	Time (h)	Amount Dissolved (%)
2	2	40–65
3	5	70–90
4	12	NLT 85

The percentages of the labeled amount of acetazolamide ($C_4H_6N_4O_3S_2$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: Acetate buffer, pH 4.5 with 2.2% [polysorbate 20](#), prepared as follows. Weigh and transfer 2.99 g of [sodium acetate](#) into a 1000-mL volumetric flask. Add 14.0 mL of 2 N [acetic acid](#) and dilute with [water](#) to volume. The measured pH should be 4.5. Transfer the resulted solution to a suitable container and add about 22.0 mL of [polysorbate 20](#). Shake vigorously and further sonicate for about 10–15 min; 900 mL.

Apparatus 2: 75 rpm

Times: 1, 2, and 7 h

Standard stock solution: 0.22 mg/mL of [USP Acetazolamide RS](#) prepared as follows. Transfer a suitable amount of [USP Acetazolamide RS](#) to a suitable volumetric flask. Add 5% of the flask volume of [methanol](#), and sonicate to dissolve if necessary. Dilute with *Medium* to volume.

Standard solution: 0.022 mg/mL of [USP Acetazolamide RS](#) from the *Standard stock solution* in *Medium*. [NOTE—The *Standard solution* may be stable for 22 h at room temperature.]

Sample solution: At the specified time points, withdraw a suitable volume of the solution under test. Pass through a suitable filter of 0.45- μ m pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Dilute 1.0 mL of the filtrate with *Medium* to 25 mL. Replace the amount of solution withdrawn at each time point with the same volume of *Medium*. [NOTE—The *Sample solution* may be stable for 22 h at room temperature.]

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 265 nm

Cell: 0.5 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of acetazolamide ($C_4H_6N_4O_3S_2$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S \times D$$

A_U = absorbance from the *Sample solution*

A_S = absorbance from the *Standard solution*

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

D = dilution factor of the *Sample solution*

Calculate the percentage of the labeled amount of acetazolamide ($C_4H_6N_4O_3S_2$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of acetazolamide in the portion of the sample withdrawn at time point i (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

