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Hydrochlorothiazide Tablets

DEFINITION

Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

IDENTIFICATION

• **A. Infrared Absorption**

Sample: Transfer an amount, equivalent to 50 mg of hydrochlorothiazide from finely powdered Tablets, to a 50-mL volumetric flask. Add 20 mL of sodium hydroxide solution (1 in 125), and shake vigorously for 15 min. Dilute with the same solvent to volume, mix, and filter, discarding the first few mL of the filtrate. Transfer 5 mL of the filtrate to a 125-mL separator, and add 5 mL of hydrochloric acid (1 in 10). Extract with 50 mL of ether, pass the ether extract through a small, dry, folded filter paper, and evaporate to dryness. Add 5 mL of alcohol, and again evaporate to dryness.

Acceptance criteria: The IR absorption spectrum of a potassium bromide dispersion of the residue obtained from the *Sample* exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydrochlorothiazide RS previously dissolved in alcohol and recovered by evaporating the solution to dryness.

• **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**

Mobile phase: Acetonitrile and 0.1 M monobasic sodium phosphate (1:9). Adjust with phosphoric acid to a pH of 3.0 ± 0.1, and filter.

System suitability solution: 0.15 mg/mL of chlorothiazide and 0.15 mg/mL of USP Hydrochlorothiazide RS in *Mobile phase*. [Note—A volume of acetonitrile not exceeding 10% of the total volume of solution may be used to dissolve the USP Reference Standard.]

Standard solution: 0.15 mg/mL of USP Hydrochlorothiazide RS in *Mobile phase*

Sample solution: Nominally 0.15 mg/mL of hydrochlorothiazide prepared as follows. Equivalent to 30 mg of hydrochlorothiazide from finely powdered Tablets (NLT 20) in a 200-mL volumetric flask. Add 20 mL of *Mobile phase*, sonicate for 5 min, and add 20 mL of acetonitrile. Sonicate for 5 min, add 50 mL of *Mobile phase*, and shake by mechanical means for 10 min. Dilute with *Mobile phase* to volume, mix, and filter, discarding the first 10 mL of the filtrate.

Chromatographic system

(See *Chromatography (621), System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for chlorothiazide and hydrochlorothiazide are about 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between chlorothiazide and hydrochlorothiazide, *System suitability solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

C_U = nominal concentration of hydrochlorothiazide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 60 min

Standard solution: USP Hydrochlorothiazide RS at a known concentration in *Medium*

Sample solution: Pass a portion of solution under test through a suitable filter. Dilute with *Medium* as necessary in comparison with the *Standard solution*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: About 272 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: NLT 60% (*Q*) of the labeled amount of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Mobile phase, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Standard solution: 1.5 µg/mL of USP Benzothiadiazine Related Compound A RS in *Mobile phase*. [Note—A volume of acetonitrile not exceeding 10% of the total volume of the solution may be used to dissolve the USP Reference Standard.]

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of benzothiadiazine related compound A in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Benzothiadiazine Related Compound A RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of hydrochlorothiazide in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards ⟨11⟩**

USP Benzothiadiazine Related Compound A RS

4-Amino-6-chloro-1,3-benzenedisulfonamide.

$C_6H_8ClN_3O_4S_2$ 285.73

USP Hydrochlorothiazide RS

Topic/Question	Contact	Expert Committee
HYDROCHLOROTHIAZIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

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