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Benazepril Hydrochloride and Hydrochlorothiazide Tablets

DEFINITION

Benazepril Hydrochloride and Hydrochlorothiazide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of benazepril hydrochloride ($C_{24}H_{28}N_2O_5 \cdot HCl$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectra of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Buffer: Dissolve 3.45 g of sodium phosphate, monobasic in 1000 mL of water. Add 2.0 mL of triethylamine. Adjust with phosphoric acid to a pH of 6.8.

Mobile phase: Acetonitrile and *Buffer* (32:68)

Diluent: Acetonitrile and water (50:50)

Standard solution: Concentrations of USP Benazepril Hydrochloride RS and USP Hydrochlorothiazide RS in *Diluent*, prepared as directed in *Table 1*. Sonicate to dissolve if needed.

Table 1

Tablet Strength Benazepril Hydrochloride/ Hydrochlorothiazide (mg/mg)	Concentration of USP Benazepril Hydrochloride RS (mg/mL)	Concentration of USP Hydrochlorothiazide RS (mg/mL)
5/6.25	0.10	0.125
10/12.5	0.10	0.125
20/25	0.10	0.125
20/12.5	0.10	0.0625

Sample stock solution: Transfer a quantity of Tablets (NLT 10) to a 200-mL volumetric flask. Add 10% of the flask volume of water and shake mechanically until the Tablets are disintegrated and well dispersed. Add another 10% of the flask volume of acetonitrile, sonicate for 20 min, then mechanically shake for an additional 20 min. Dilute with *Diluent* to volume.

Sample solution: Dilute the *Sample stock solution* with *Diluent* to obtain nominal concentrations of benazepril hydrochloride and hydrochlorothiazide as directed in *Table 1*. Pass a portion through a suitable filter and discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm. For *Identification B*, use a diode array detector in the range of 210–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of benazepril

System suitability

Sample: *Standard solution*

[Note—The relative retention times for hydrochlorothiazide and benazepril are about 0.4 and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 2.0 for benazepril and hydrochlorothiazide

Relative standard deviation: NMT 2.0% for benazepril and hydrochlorothiazide

Analysis

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Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benazepril hydrochloride ($C_{24}H_{28}N_2O_5 \cdot HCl$) in the portion of Tablets taken:

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

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

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

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

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

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 of hydrochlorothiazide from the *Sample solution*

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

C_S = concentration of USP Hydrochlorothiazide RS in 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⟩

Test 1

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

Standard stock solution A: 0.1 mg/mL of USP Benazepril Hydrochloride RS in *Medium*. Sonicate to dissolve if needed.

Standard stock solution B: 0.125 mg/mL of USP Hydrochlorothiazide RS in *Medium*. Sonicate to dissolve if needed.

Standard solution: USP Benazepril Hydrochloride RS and USP Hydrochlorothiazide RS in *Medium*, prepared as directed in *Table 2* from *Standard stock solution A* and *Standard stock solution B*

Table 2

Tablet Strength Benazepril Hydrochloride/ Hydrochlorothiazide (mg/mg)	Concentration of USP Benazepril Hydrochloride RS (mg/mL)	Concentration of USP Hydrochlorothiazide RS (mg/mL)
5/6.25	0.01	0.0125
10/12.5	0.02	0.025
20/12.5	0.04	0.025
20/25	0.04	0.05

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 234 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 0.9 mL/min

Injection volume

For Tablet strength of 5/6.25 mg: 100 µL

For Tablet strengths of 10/12.5, 20/12.5, and 20/25 mg: 25 µL

Run time: NLT 2 times the retention time of benazepril

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System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for hydrochlorothiazide and benazepril are about 0.5 and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 2.0 for benazepril and hydrochlorothiazide

Relative standard deviation: NMT 2.0% for benazepril and hydrochlorothiazide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benazepril hydrochloride ($C_{24}H_{28}N_2O_5 \cdot HCl$) dissolved:

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

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

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Calculate the percentage of the labeled amount of hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) dissolved:

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

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

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (Q) of the labeled amount of benazepril hydrochloride ($C_{24}H_{28}N_2O_5 \cdot HCl$) and hydrochlorothiazide ($C_7H_8ClN_3O_4S_2$) is dissolved.

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

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Buffer: 3.75 g/L of potassium phosphate, dibasic in water. Adjust with phosphoric acid to a pH of 2.1.

Mobile Phase: Acetonitrile and *Buffer* (35:65)

Standard stock solution: 0.25 mg/mL of USP Hydrochlorothiazide RS, prepared as follows. Transfer a suitable amount of USP Hydrochlorothiazide RS to a volumetric flask. Add a volume of acetonitrile equivalent to 5% of the total flask volume and, if necessary, sonicate to dissolve. Dilute with *Medium* to volume.

Standard solution: (L_2/500) mg/mL of USP Hydrochlorothiazide RS from *Standard stock solution* and (L_1/500) mg/mL of USP Benazepril Hydrochloride RS diluted in *Medium*, where L_1 is the label claim for benazepril hydrochloride in mg/Tablet and L_2 is the label claim for hydrochlorothiazide in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate. [NOTE—It is recommended to avoid using stainless steel cannula when sampling.]

Chromatographic system

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

Mode: LC

Detector: UV 240 nm for benazepril and UV 275 nm for hydrochlorothiazide

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of benazepril

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for benazepril at 240 nm and hydrochlorothiazide at 275 nm

Relative standard deviation: NMT 2.0% for benazepril at 240 nm and hydrochlorothiazide at 275 nm

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