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Acebutolol Hydrochloride Capsules

DEFINITION
Acebutolol Hydrochloride Capsules contain the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of acebutolol ($C_{18}H_{28}N_2O_4$).

IDENTIFICATION
• **A.** The UV absorption spectra of the major peak of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the corresponding peak 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: Dissolve 2.4 g of sodium 1-decanesulfonate in 1000 mL of water. Adjust with glacial acetic acid to a pH of 3.5.

Mobile phase: Methanol and *Buffer* (60:40)

Standard solution: 0.22 mg/mL of USP Acebutolol Hydrochloride RS in methanol. [Note—This is equivalent to 0.2 mg/mL of acebutolol.]

Sample stock solution: Nominally 1 mg/mL of acebutolol prepared as follows. Transfer an equivalent to 200 mg of acebutolol, from the contents of NLT 20 Capsules, to a 200-mL volumetric flask. Add 180 mL of methanol, and stir by mechanical means for 30 min. Dilute with methanol to volume.

Sample solution: Nominally 0.2 mg/mL of acebutolol in methanol from *Sample stock solution*

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

Mode: LC

Detector: UV 254 nm. For *Identification A*, use a diode-array detector in the range of 200–400 nm.

Column: 3.9-mm × 15-cm; 4-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acebutolol ($C_{18}H_{28}N_2O_4$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

C_U = nominal concentration of acebutolol from the *Sample solution* (mg/mL)

M_{r1} = molecular weight of acebutolol, 336.43

M_{r2} = molecular weight of acebutolol hydrochloride, 372.89

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS
• **Dissolution ⟨711⟩**

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: A known concentration of USP Acebutolol Hydrochloride RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 232 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acebutolol ($C_{18}H_{28}N_2O_4$) dissolved:

$$(A_U/A_S) \times C_S \times V \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

M_{r1} = molecular weight of acebutolol, 336.43

M_{r2} = molecular weight of acebutolol hydrochloride, 372.89

Tolerances: NLT 80% (Q) of the labeled amount of acebutolol ($C_{18}H_{28}N_2O_4$) is dissolved.

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

IMPURITIES

- **Organic Impurities**

Test 1

Buffer: Prepare as directed in the *Assay*.

Mobile phase: Methanol and *Buffer* (44:56)

Diluent: Methanol and *Buffer* (50:50)

Standard stock solution: 0.6 mg/mL of USP Acebutolol Hydrochloride RS prepared as follows. To a suitable amount of USP Acebutolol Hydrochloride RS in a suitable volumetric flask, add methanol, about 24% of the flask volume, swirl to dissolve, and dilute with *Diluent* to volume.

Standard solution: 1.4 µg/mL of USP Acebutolol Hydrochloride RS in *Diluent* from *Standard stock solution*

Sample stock solution: Nominally 2.5 mg/mL of acebutolol prepared as follows. Transfer a portion of the contents of 20 opened Capsules, equivalent to 250 mg of acebutolol, to a 100-mL volumetric flask. Add 25 mL of methanol and shake by mechanical means for 15 min. Dilute with *Diluent* to volume. Centrifuge a portion of this solution and use the supernatant.

Sample solution: Nominally 250 µg/mL of acebutolol in *Diluent* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Flow rate: 1 mL/min

Injection volume: 35 µL

Run time: NLT 2 times the retention time of acebutolol

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 6.0%

Analysis

Samples: *Diluent*, *Standard solution*, and *Sample solution*

Calculate the percentage of each impurity eluting before the acebutolol peak in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

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

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

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

M_{r1} = molecular weight of acebutolol, 336.43

M_{r2} = molecular weight of acebutolol hydrochloride, 372.89

Acceptance criteria: NMT 0.5% of any individual impurity. Disregard any peaks from the *Diluent*.

Test 2

Buffer and **System suitability:** Proceed as directed in *Test 1*.

Mobile phase: Methanol and *Buffer* (50:50)

Standard stock solution: 0.6 mg/mL of USP Acebutolol Hydrochloride RS prepared as follows. To a suitable amount of USP Acebutolol Hydrochloride RS in a suitable volumetric flask, add methanol, about 24% of the flask volume, swirl to dissolve, and dilute with *Mobile phase* to volume.

Standard solution: 1.4 µg/mL of USP Acebutolol Hydrochloride RS in *Mobile phase* from *Standard stock solution*

Sample stock solution: Nominally 2.5 mg/mL of acebutolol prepared as follows. Transfer a portion of the contents of 20 opened Capsules, equivalent to 250 mg of acebutolol, to a 100-mL volumetric flask. Add 25 mL of methanol and shake by mechanical means for 15 min. Dilute with *Mobile phase* to volume.

Sample solution: Nominally 250 µg/mL of acebutolol in *Diluent* from *Sample stock solution* prepared as follows. Centrifuge a portion of *Sample stock solution*, and transfer 10.0 mL of the clear supernatant to a 100-mL volumetric flask. Dilute with *Mobile phase* to volume.

Chromatographic system

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

Proceed as directed in *Test 1* except for the *Injection volume* and *Run time*.

Injection volume: 70 µL

Run time: NLT 3 times the retention time of acebutolol

Analysis

Samples: *Mobile phase*, *Standard solution*, and *Sample solution*

Calculate the percentage of each impurity eluting after the acebutolol peak in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

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

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

C_U = nominal concentration of acebutolol from the *Sample solution* (µg/mL)

M_{r1} = molecular weight of acebutolol, 336.43

M_{r2} = molecular weight of acebutolol hydrochloride, 372.89

Acceptance criteria

Test 2: NMT 0.5% of any individual impurity. Disregard any peaks from the *Mobile phase*.

Sum of impurities from *Test 1* and *Test 2*: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**
  USP Acebutolol Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
ACEBUTOLOL HYDROCHLORIDE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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