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Levalbuterol Inhalation Solution

DEFINITION

Levalbuterol Inhalation Solution is a sterile, aqueous solution of Levalbuterol Hydrochloride, prepared with Sodium Chloride. It contains NLT 90.0% and NMT 110.0% of the labeled amount of levalbuterol (C₁₃H₂₁NO₃).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the test for *Limit of S-Albuterol*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the major peak of the *System suitability solution*, as obtained in the test for *Limit of S-Albuterol*.

ASSAY

• **PROCEDURE**

Solution A: Dilute 1 mL of [phosphoric acid](#) with [water](#) to 1 L.

Solution B: [Acetonitrile](#), [methanol](#), and [water](#) (35:35:30). To each liter of the solution add 1 mL of [phosphoric acid](#).

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	91.5	8.5
15	91.5	8.5
15.01	0	100
20	0	100
20.01	91.5	8.5
30	91.5	8.5

Diluent: Dissolve 9.0 g of [sodium chloride](#) in 950 mL of [water](#). Adjust with dilute [sulfuric acid](#) to a pH of 4.0, and dilute with [water](#) to 1000 mL.

Standard solution: 0.1 mg/mL of [USP Levalbuterol Hydrochloride RS](#) in *Diluent*

Sample solution: Nominally 0.1 mg/mL of levalbuterol hydrochloride (equivalent to 0.087 mg/mL of levalbuterol free base) in *Diluent* from an appropriately diluted volume of Inhalation Solution

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.3

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of levalbuterol ($C_{13}H_{21}NO_3$) in the portion of Inhalation Solution taken:

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

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

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

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

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

M_{r1} = molecular weight of levalbuterol (free base), 239.31

M_{r2} = molecular weight of levalbuterol hydrochloride, 275.77

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meets the requirements

IMPURITIES

Change to read:

- **LIMIT OF S-ALBUTEROL**

Mobile phase: [Acetonitrile](#) and [methanol](#) (50:50). To each liter of the solution add 3 mL of [acetic acid](#) and 1 mL of [triethylamine](#).

Diluent: Prepare as directed in the Assay.

System suitability solution: 0.10 mg/mL of [USP Levalbuterol Hydrochloride RS](#) and 0.04 mg/mL of [USP Albuterol RS](#) in *Diluent*

Sample solution: Inhalation Solution

Chromatographic system

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

Mode: LC

Detector: UV 225 nm. For *Identification B* use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-μm packing [L63](#)

Flow rate: 1 mL/min

Injection volume: 40 μL

Run time: NLT 1.5 times the retention time of levalbuterol

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for levalbuterol and (S)-albuterol are 1.0 and 1.16, respectively.]

Suitability requirements

Resolution: NLT 3.0 between levalbuterol and (S)-albuterol

Tailing factor: NMT 1.6 for levalbuterol and NMT 2.0 for (S)-albuterol

Analysis

Sample: *Sample solution*

Calculate the percentage of (S)-albuterol in the portion of Inhalation Solution taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of (S)-albuterol from the *Sample solution*

r_T = sum of the peak responses of levalbuterol and (S)-albuterol from the *Sample solution*

Acceptance criteria: NMT 2.50% of (S)-albuterol ▲▲ (IRA 1-Nov-2022)

Change to read:

- **ORGANIC IMPURITIES**

Solution A, Solution B, Diluent, and Sample solution: Prepare as directed in the Assay.

Mobile phase: See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	100	



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