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Diphenhydramine Hydrochloride and Ibuprofen Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb/diphenhydramine-hcl-ibuprofen-caps-20200424.

DEFINITION

Diphenhydramine Hydrochloride and Ibuprofen Capsules contain NLT 95.0% and NMT 105.0% of the labeled amounts of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) and ibuprofen ($C_{13}H_{18}O_2$).

IDENTIFICATION

• **A.** The retention times of the diphenhydramine and ibuprofen peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

• **B.** The UV absorption spectra of the diphenhydramine and ibuprofen peaks of the *Sample solution* and those of the *Standard solution* exhibit maxima at the same wavelengths of 265 and 273 nm, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (38:62)

Standard solution: 0.05 mg/mL of USP Diphenhydramine Hydrochloride RS and 0.4 mg/mL of USP Ibuprofen RS in *Mobile phase*

Sample stock solution: Nominally 0.25 mg/mL of diphenhydramine hydrochloride and 2.0 mg/mL of ibuprofen, prepared as follows. Transfer NLT 5 Capsules (including shells) to a suitable volumetric flask, add 4% of the final volume of water, and sonicate for 20 min. Dissolve and dilute with *Mobile phase* to volume. Pass a portion through a suitable filter of 0.45-µm pore size.

Sample solution: Nominally 0.05 mg/mL of diphenhydramine hydrochloride and 0.4 mg/mL of ibuprofen in *Mobile phase* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detectors

Assay: UV 220 nm

Identification B: Diode array, UV 200–400 nm

Column: 4.6-mm × 10-cm; 3-µm packing L11

Column temperature: 25°

Flow rate: 1.0 mL/min

Injection volume: 5 µL

Run time: NLT 4 times the retention time of diphenhydramine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both diphenhydramine and ibuprofen

Relative standard deviation: NMT 2.0% for both diphenhydramine and ibuprofen

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) and ibuprofen ($C_{13}H_{18}O_2$) in the portion of Capsules taken:

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

r_U = peak response of diphenhydramine or ibuprofen from the *Sample solution*

r_S = peak response of diphenhydramine or ibuprofen from the *Standard solution*

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

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Test 1**▲ (RB 1-May-2020)

Medium: Phosphate buffer, pH 7.2 (27.22 mg/mL of monobasic potassium phosphate in water and adjust with 100 mg/mL of sodium hydroxide to a pH of 7.2); 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with 100 mg/mL of sodium hydroxide to a pH of 6.6.

Mobile phase: Methanol and *Buffer* (65:35)

Standard stock solution: 0.27 mg/mL of USP Diphenhydramine Hydrochloride RS and 2.2 mg/mL of USP Ibuprofen RS, prepared as follows. Transfer known amounts of USP Diphenhydramine Hydrochloride RS and USP Ibuprofen RS to a suitable volumetric flask. Add 5% of the final volume of methanol and sonicate to dissolve. Dilute with *Medium* to volume.

Standard solution: 0.027 mg/mL of USP Diphenhydramine Hydrochloride RS and 0.22 mg/mL of USP Ibuprofen RS in *Medium* from *Standard stock solution*

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

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Column temperature: 35°

Flow rate: 1.0 mL/min

Injection volume: 5 µL

Run time: NLT 2.3 times the retention time of ibuprofen

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both diphenhydramine and ibuprofen

Relative standard deviation: NMT 2.0% for both diphenhydramine and ibuprofen

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) and ibuprofen ($C_{13}H_{18}O_2$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

r_U = peak response of diphenhydramine or ibuprofen from the *Sample solution*

r_S = peak response of diphenhydramine or ibuprofen from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim of diphenhydramine or ibuprofen (mg/Capsule)

Tolerances: NLT 75% (Q) of the labeled amounts of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) and ibuprofen ($C_{13}H_{18}O_2$) is dissolved.

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

Tier 1

0.2 M phosphate buffer pH 7.2: Dissolve 27.22 g/L of potassium phosphate, monobasic in water and add 5.52 g/L of sodium hydroxide pellets, and mix. Adjust with 0.2 N sodium hydroxide or 0.2 N hydrochloric acid to a pH of 7.2

Medium: *0.2 M phosphate buffer pH 7.2*; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Tier 2

0.2 M phosphate buffer pH 7.2 with pancreatin: 160 mg/L of pancreatin in *0.2 M phosphate buffer pH 7.2*

Medium A: *0.2 M phosphate buffer pH 7.2 with pancreatin*; 450 mL

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