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Diphenhydramine Citrate and Ibuprofen Tablets

DEFINITION

Diphenhydramine Citrate and Ibuprofen Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of diphenhydramine citrate ($C_{17}H_{21}NO \cdot C_6H_8O_7$) and ibuprofen ($C_{13}H_{18}O_2$).

IDENTIFICATION

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

ASSAY

• PROCEDURE

Buffer A: 6.9 g/L of monobasic sodium phosphate in water

Buffer B: 6.9 g/L of monobasic sodium phosphate in water. Adjust with triethylamine to a pH of 7.2.

Mobile phase: Acetonitrile, triethylamine, glacial acetic acid, and *Buffer A* (45:0.2:0.2:55)

Diluent: Acetonitrile and *Buffer B* (3:2)

Standard solution: 1.1 mg/mL of [USP Diphenhydramine Citrate RS](#) and 5.7 mg/mL of [USP Ibuprofen RS](#) in *Diluent*. [NOTE—Sonicate as necessary.]

Sample solution: Transfer 10 Tablets into a suitable volumetric flask, add 350 mL of *Diluent*, and shake with a rotary shaker for 20 min.

Sonicate for 20 min with intermediate shaking to obtain a solution containing about 1.1 mg/mL of diphenhydramine citrate and 5.7 mg/mL of ibuprofen. Centrifuge an aliquot at 4000 rpm for 10 min, and use the supernatant. [NOTE—Do not dilute to volume.]

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Flow rate: 1.2 mL/min

Injection size: 20 μL

Run time: 1.3 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 citrate ($C_{17}H_{21}NO \cdot C_6H_8O_7$) and ibuprofen ($C_{13}H_{18}O_2$) in the portion of Tablets taken:

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

r_U = peak response of the corresponding analyte from the *Sample solution*

r_S = peak response of the corresponding analyte from the *Standard solution*

C_S = concentration of the appropriate USP Reference Standard in the *Standard solution* (mg/mL)

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



Acceptance criteria: 90.0%–110.0% for both diphenhydramine citrate and ibuprofen

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: pH 6.5 phosphate buffer (Transfer 250 mL of 0.2 M monobasic potassium phosphate and 58 mL of 0.2 M sodium hydroxide to a 1000-mL volumetric flask, and dilute with water to volume.); 900 mL, deaerated

Apparatus 2: 50 rpm

Time: 30 min

Buffer solution: 6.9 g/L of sodium dihydrogen phosphate monohydrate in water

Ibuprofen standard stock solution: 1.1 mg/mL of [USP Ibuprofen RS](#) in acetonitrile

Diphenhydramine citrate standard stock solution: 1.1 mg/mL of [USP Diphenhydramine Citrate RS](#) in water

Standard solution: Transfer 5 mL of the *Ibuprofen standard stock solution* and 1 mL of *Diphenhydramine citrate standard stock solution* to a 25-mL volumetric flask, and dilute with *Medium* to volume.

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

Mobile phase: Acetonitrile, triethylamine, glacial acetic acid, and *Buffer solution* (45:0.2:0.2:55)

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm, 5-μm packing L1

Flow rate: 1.2 mL/min

Injection size: 20 μL

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 diphenhydramine and ibuprofen dissolved:

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

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

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

C_S = concentration of ibuprofen or diphenhydramine in the *Standard solution*

L = label claim for ibuprofen or diphenhydramine (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amounts of diphenhydramine and ibuprofen are dissolved.

• [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

• ORGANIC IMPURITIES

Buffer A: 1 mL of phosphoric acid in 1 L of water. Adjust with triethylamine to a pH of 3.2.

Buffer B: 1 mL of phosphoric acid and 1.0 g of monobasic potassium phosphate in 1 L of water. Adjust with triethylamine to a pH of 3.7.

Solution A: Acetonitrile and *Buffer A* (1:4)

Solution B: Acetonitrile and *Buffer B* (1:1)

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

Table 1