Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-Nov-2024
Document Type: USP Monographs
DocId: GUID-5E9DB10F-4720-4599-A1D0-70B64397A7EE_3_en-US
DOI: https://doi.org/10.31003/USPNF_M25160_03_01
DOI Ref: h4ivm

Dicyclomine Hydrochloride Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-dicyclomine-hcl-tabs-20241025.

DEFINITION

Dicyclomine Hydrochloride Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$).

IDENTIFICATION

• **A.**

Sample: Transfer a portion of finely powdered Tablets, equivalent to 100 mg of dicyclomine hydrochloride, to a separator containing 10 mL of water and 1 mL of hydrochloric acid. Extract the aqueous acid solution with two 30-mL portions of chloroform, transfer the chloroform extracts to a second separator containing 20 mL of water and 1 mL of sodium hydroxide solution (1 in 10), and shake. Filter the chloroform layer through anhydrous sodium sulfate into a suitable container. Add 3 mL of a freshly prepared 1-in-20 solution of acetyl chloride in anhydrous methanol, prepared by cautiously adding acetyl chloride dropwise to anhydrous methanol with stirring. Evaporate under reduced pressure at room temperature until the residue has been thoroughly dried. Use the residue so obtained to prepare a potassium bromide dispersion.

Standard: Use a similarly prepared potassium bromide dispersion of USP Dicyclomine Hydrochloride RS.

Acceptance criteria: The IR absorption spectrum of the *Sample* exhibits maxima and minima at the same wavelengths as those of the *Standard*.

• **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 2.72 g of monobasic potassium phosphate in 900 mL of water, adjust with 10% sodium hydroxide to a pH of 7.5 ± 0.1, and dilute with water to 1000 mL.

Mobile phase: Acetonitrile and *Buffer* (70:30)

Diluent: Acetonitrile and water (70:30)

Standard solution: 0.4 mg/mL of USP Dicyclomine Hydrochloride RS in *Diluent*. [Note—This solution is stable for at least 2 days.]

Sample solution: Transfer NLT 20 Tablets to a tared container, and determine the average Tablet weight. Grind the Tablets to a fine powder using a glass mortar and pestle. Transfer a portion of the powder, equivalent to 20 mg of dicyclomine hydrochloride, to a 50-mL volumetric flask, add 2.0 mL of water, and sonicate for at least 2 min to disperse the sample. Add 35 mL of acetonitrile, sonicate for at least 5 min, and shake by mechanical means for at least 30 min. Add 10 mL of water, allow the solution to equilibrate to room temperature, then dilute with water to volume. Centrifuge a portion of this solution in a 15-mL glass centrifuge tube for at least 5 min. Use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak area of dicyclomine from the *Sample solution*

r_S = peak area of dicyclomine from the *Standard solution*

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

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Test 1**▲ (RB 1-Nov-2024)

Medium: 0.01 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 45 min

Determine the amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$) dissolved by employing the following method.

Buffer: Dissolve 2.72 g of monobasic potassium phosphate in 450 mL of water, adjust with 10% sodium hydroxide to a pH of 7.5 ± 0.1, and dilute with water to 500 mL.

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

Diluent: Acetonitrile and *Buffer* (1:1)

Standard stock solution: 40 µg/mL of USP Dicyclomine Hydrochloride RS in *Medium*

Standard solution: Mix 25.0 mL of *Standard stock solution* and 25.0 mL of *Diluent*.

Sample solution: Pass a portion of the solution under test through a glass microfiber filter of 0.7-µm pore size. Transfer 5.0 mL of the filtrate to a suitable flask, and add 5.0 mL of *Diluent*.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 250 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$) dissolved:

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

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

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

D = dilution factor for the *Sample solution*

Tolerances: NLT 75% (*Q*) of the labeled amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$) is dissolved.

▲**Test 3:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: Dissolve 2.72 g of potassium phosphate, monobasic in 450 mL of water, adjust with 10% sodium hydroxide to a pH of 7.5 and dilute with water to 500 mL.

Mobile phase: Acetonitrile and *Buffer* (70:30)

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

Standard stock solution: 0.04 mg/mL of USP Dicyclomine Hydrochloride RS in *Medium*. Sonicate to dissolve, if necessary.

Standard solution: 0.02 mg/mL of USP Dicyclomine Hydrochloride RS from *Standard stock solution* in *Diluent*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Dilute the solution to a concentration similar to that of the *Standard solution* in *Diluent*.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 250 µL

Run time: NLT 1.7 times the retention time of dicyclomine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$) dissolved:

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

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

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

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

V = volume of *Medium*, 500 mL

D = dilution factor for the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of dicyclomine hydrochloride ($C_{19}H_{35}NO_2 \cdot HCl$) is dissolved.▲ (RB 1-Nov-2024)

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

IMPURITIES

• **Limit of Dicyclomine Related Compound A**

Buffer: Dissolve 2.72 g of monobasic potassium phosphate in 900 mL of water, adjust with phosphoric acid to a pH of 3.5, and dilute with water to 1000 mL.

Solution A: Acetonitrile and *Buffer* (55:45)

Solution B: Acetonitrile and *Buffer* (80:20)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
20	100	0
20.1	0	100
40	0	100
40.1	100	0
50	100	0

Diluent: Acetonitrile and water (70:30)

Standard stock solution: 0.1 mg/mL of USP Dicyclomine Related Compound A RS in *Diluent*. Sonication may be used.

Standard solution: 4.0 µg/mL of USP Dicyclomine Related Compound A RS in *Diluent* from *Standard stock solution*

Sensitivity solution: 2.0 µg/mL of USP Dicyclomine Related Compound A RS in *Diluent* from *Standard solution*

Sample solution: Nominally 2.0 mg/mL of dicyclomine hydrochloride in *Diluent* prepared as follows. Transfer NLT 20 Tablets to a tared container, and determine the average Tablet weight. Grind the Tablets to a fine powder using a glass mortar and pestle. Transfer a portion of the powder, equivalent to 200 mg of dicyclomine hydrochloride, to a 100-mL volumetric flask, add about 10 mL of water, and sonicate for at least 2 min to disperse the sample. Add 70 mL of acetonitrile, sonicate for at least 5 min, and shake by mechanical means for at least 30 min. Add 10 mL of water, allow the solution to equilibrate to room temperature, then dilute with water to volume. Centrifuge a portion of this solution, and use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 100 µL

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dicyclomine related compound A in the portion of Tablets taken:

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

r_U = peak response of dicyclomine related compound A from the *Sample solution*

r_S = peak response of dicyclomine related compound A from the *Standard solution*

C_S = concentration of USP Dicyclomine Related Compound A RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.2%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

Add the following:

▲• **Labeling:** The labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 1-Nov-2024)

• **USP Reference Standards ⟨11⟩**

USP Dicyclomine Hydrochloride RS

USP Dicyclomine Related Compound A RS

[1,1'-Bi(cyclohexane)]-1-carboxylic acid.

$C_{13}H_{22}O_2$ 210.32

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

Topic/Question	Contact	Expert Committee
DICYCLOMINE HYDROCHLORIDE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(6)

Current DocID: GUID-5E9DB10F-4720-4599-A1D0-70B64397A7EE_3_en-US

DOI: https://doi.org/10.31003/USPNF_M25160_03_01

DOI ref: h4ivm