Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2024
Document Type: USP Monographs
DocId: GUID-168A7982-1998-4772-BC63-F810EFDC61D2_2_en-US
DOI: https://doi.org/10.31003/USPNF_M26358_02_01
DOI Ref: q4hq5

Diltiazem Hydrochloride Tablets

DEFINITION
Diltiazem Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$).

IDENTIFICATION
- **A.** The UV-Vis spectrum of the major peak of the *Sample solution* corresponds to that 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**

Solution A: 0.79 g/L of ammonium bicarbonate in water. Adjust with diluted ammonia solution to a pH of 8.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
2.0	95	5
5.0	60	40
13.0	60	40
16.0	30	70
20.0	30	70
20.1	95	5
25.0	95	5

Diluent: Acetonitrile and water (40:60)

Standard solution: 0.05 mg/mL of USP Diltiazem Hydrochloride RS in *Diluent*

Sample stock solution: Nominally 0.5 mg/mL of diltiazem hydrochloride from Tablets in *Diluent* prepared as follows. Transfer an appropriate portion of finely powdered Tablets (NLT 20) to a suitable volumetric flask. Add *Diluent* equivalent to 80% of the flask volume, and sonicate for 60 min. Dilute with *Diluent* to volume. Centrifuge the solution for 20 min. Use the supernatant.

Sample solution: Nominally 0.05 mg/mL of diltiazem hydrochloride in *Diluent* from *Sample stock solution*

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

Mode: LC

Detector: UV 240 nm. For *Identification* test *A*, use a diode-array detector in the range of 190–400 nm.

Column: 2.1-mm × 15-cm; 1.7-µm packing L1

Flow rate: 0.3 mL/min

Injection volume: 2.0 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Water; 900 mL

Apparatus 2: 75 rpm

Time: 30 min and 3 h

Detector: UV 237 nm

Standard solution: USP Diltiazem Hydrochloride RS in *Medium*

Sample solution: Sample per *Dissolution ⟨711⟩*. Dilute with *Medium* to a concentration that is similar to the *Standard solution*.

Tolerances: See *Table 2* for the 30-min time point. Use the criteria in *Dissolution ⟨711⟩*, *Acceptance Table 1* for the 3-h time point. NMT 60% (*Q*) of the labeled amount of diltiazem hydrochloride ($C_{22}H_{26}N_2O_4S \cdot HCl$) is dissolved in 30 min, and NLT 75% (*Q*) is dissolved in 3 h.

Table 2

Stage	Acceptance Criteria
S_1	No unit is more than *Q*.
S_2	Average value is equal to or less than *Q*, and no unit is greater than *Q* + 10%.
S_3	Average value is equal to or less than *Q*, and NMT 2 units are more than *Q* + 10%, and no unit is more than *Q* + 25%.

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

IMPURITIES

• **Organic Impurities**

Solution A, Solution B, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 2.5 µg/mL each of USP Desacetyl Diltiazem Hydrochloride RS and USP Diltiazem Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.5 mg/mL of diltiazem hydrochloride from Tablets in *Diluent* prepared as follows. Transfer an appropriate portion of the powdered Tablets (NLT 20) to a suitable volumetric flask. Add *Diluent* equivalent to 80% of the flask volume, and sonicate for 60 min. Dilute with *Diluent* to volume. Centrifuge the solution for 20 min. Use the supernatant.

System suitability

Sample: *Standard solution*

[Note—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between desacetyl diltiazem and diltiazem

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of desacetyl diltiazem in the portion of Tablets taken:

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

r_U = peak response of desacetyl diltiazem from the *Sample solution*

r_S = peak response of desacetyl diltiazem from the *Standard solution*

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

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

Calculate the percentage of any individual unspecified impurity in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: See *Table 3*. The disregard limit is 0.05%.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Diltiazem related compound H[a,h]	0.44	—
Diltiazem related compound G[b,h]	0.52	—
Diltiazem related compound C[c,h]	0.58	—
Diltiazem related compound D[d,h]	0.61	—
Diltiazem related compound E[e,h]	0.66	—
Desacetyl diltiazem	0.75	1.5
Diltiazem related compound A[f,h]	0.83	—
Diltiazem related compound B[g,h]	0.89	—
Diltiazem	1.0	—
Any individual unspecified impurity	—	0.2
Total impurities	—	2.0

[a] (2*S*,3*S*)-5-(2-Aminoethyl)-3-hydroxy-2-(4-hydroxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5*H*)-one.

[b] (2*S*,3*S*)-3-Hydroxy-2-(3-methoxyphenyl)-5-[2-(methylamino)ethyl]-2,3-dihydrobenzo[*b*][1,4]thiazepin-4(5*H*)-one.

[c] (2*S*,3*S*)-5-[2-(Dimethylamino)ethyl]-2-(4-hydroxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepin-3-yl acetate.

[d] (2*S*,3*S*)-2-(4-Methoxyphenyl)-5-[2-(methylamino)ethyl]-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate.

[e] (2*S*,3*S*)-3-Hydroxy-2-(4-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepine-4(5*H*)-one.

[f] (2*R*,3*S*)-5-[2-(Dimethylamino)ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate.

[g] (2*S*,3*S*)-2-(4-Methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-3-yl acetate.

[h] These are impurities related to the drug substance. They are not to be reported for the drug product and should not be included in the total impurities.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Desacetyl Diltiazem Hydrochloride RS	$C_{20}H_{24}N_2O_3S \cdot HCl$	▲408.94▲ (CN 1-Dec-2024)
USP Diltiazem Hydrochloride RS		

Topic/Question	Contact	Expert Committee
DILTIAZEM HYDROCHLORIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 41(1)

Current DocID: GUID-168A7982-1998-4772-BC63-F810EFDC61D2_2_en-US

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