

Status: Currently Official on 14-Feb-2025
 Official Date: Official as of 01-May-2020
 Document Type: USP Monographs
 DocId: GUID-609C294C-FE08-40A3-AB04-6CB4136B5EC5_5_en-US
 DOI: https://doi.org/10.31003/USPNF_M2648_05_01
 DOI Ref: iyd32

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Donepezil Hydrochloride Tablets

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<https://www.uspnf.com/rb/donepezil-hcl-tabs-20200424>.

DEFINITION

Donepezil Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$).

IDENTIFICATION

Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy](#): 197U ▲ (CN 1-May-2020)

Wavelength range: 220–360 nm

Sample solution: Crush a suitable number of Tablets, and transfer an amount of powder, equivalent to 10 mg of donepezil hydrochloride, to a 100-mL volumetric flask. Add 80 mL of [0.1 N hydrochloric acid VS](#), and sonicate for 5 min. Cool the solution to room temperature, and dilute with [0.1 N hydrochloric acid VS](#) to volume. Transfer a portion of this solution to a centrifuge tube, and centrifuge for 15 min. Transfer 5 mL of the clear supernatant to a 25-mL volumetric flask, and dilute with [0.1 N hydrochloric acid VS](#) to volume.

Analysis: Using a 1-cm cell, record the UV spectrum of the *Sample solution*.

Acceptance criteria: The solution exhibits absorption maxima at 230, 271, and 315 nm.

- **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

Diluent: [Methanol](#) and [0.1 N hydrochloric acid VS](#) (75:25)

Mobile phase: Dissolve 2.5 g of [sodium 1-decanesulfonate](#) in 650 mL of [water](#), and add 1.0 mL of [perchloric acid](#) and 350 mL of [acetonitrile](#). If necessary, adjust with an additional 0.5 mL of [perchloric acid](#) to a pH of about 1.8.

System suitability solution: 0.2 mg/mL of [USP Donepezil Hydrochloride RS](#) and 0.008 mg/mL of [USP Donepezil Related Compound A RS](#). [NOTE—Dissolve in 40% of the flask volume of [methanol](#), swirl, and dilute with [water](#) to volume.]

Standard solution: 0.4 mg/mL of [USP Donepezil Hydrochloride RS](#) in *Diluent*. [NOTE—Dissolve in 60% of the flask volume of *Diluent*, swirl, and dilute with *Diluent* to volume.]

Sample solution: Nominally 0.4 mg/mL of donepezil hydrochloride prepared as follows. Dissolve a suitable number of Tablets in 75% of the flask volume of *Diluent*, and sonicate in an ultrasonic bath for 20 min. Swirl the mixture for 30 s, allow to cool to room temperature, and dilute with *Diluent* to volume. [NOTE—If necessary, add a magnetic stirring bar to the flask, and mix for 10 min on the magnetic stirrer, to aid in dissolution.] Allow a few min for the solids to settle. Pass through a suitable filter, discarding the first 2–3 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 271 nm

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

Column temperature: 35°

Flow rate: 1.4 mL/min

Injection volume: 20 μL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for donepezil related compound A and donepezil are about 0.92 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between donepezil related compound A and donepezil, *System suitability solution*

Tailing factor: NMT 1.5 for the donepezil peak, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of donepezil hydrochloride from the *Sample solution*

r_S = peak response of donepezil hydrochloride from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Test 1

Medium: [0.1 N hydrochloric acid VS](#); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Analytical procedure: Determine the amount of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$) dissolved, by using one of the following methods.

Chromatographic method

Diluent: [Methanol](#) and [0.1 N hydrochloric acid VS](#) (75:25)

Mobile phase: [Acetonitrile](#), [water](#), and [perchloric acid](#) (35: 65: 0.1)

Standard stock solution A: 1.1 mg/mL of [USP Donepezil Hydrochloride RS](#) in *Diluent*

Standard stock solution B: 0.11 mg/mL of [USP Donepezil Hydrochloride RS](#) from *Standard stock solution A* in *Medium*

Standard solution: ($L/1000$) mg/mL of [USP Donepezil Hydrochloride RS](#) from *Standard stock solution B* in *Medium*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size, discarding the first few mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 271 nm

Column: 4.6-mm $\times$ 15-cm; 5- μ m packing [L1](#)

Column temperature: 35°

Flow rate: 1.0 mL/min

Injection volume: 50 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Column efficiency: NLT 5000 theoretical plates

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Spectrometric method

Standard stock solution: 0.11 mg/mL of [USP Donepezil Hydrochloride RS](#) in [water](#)

Standard solution: ($L/900$) mg/mL of [USP Donepezil Hydrochloride RS](#) from the *Standard stock solution* in *Medium*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 230 nm**Blank:** MediumCalculate the percentage of the labeled amount of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$) dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times V \times 100$$

 A_U = absorbance of the *Sample solution* A_S = absorbance of the *Standard solution* C_S = concentration of the *Standard solution* (mg/mL) L = label claim (mg/Tablet) V = volume of *Medium*, 900 mL**Tolerances:** NLT 80% (Q) of the labeled amount of donepezil hydrochloride is dissolved.**For Tablets which contain 23 mg of donepezil hydrochloride****Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.**Medium:** pH 6.8 phosphate buffer; 900 mL**Apparatus 2:** 50 rpm**Times:** 1, 3, and 8 h**Buffer:** 5.0 g/L of monobasic ammonium phosphate in water adjusted with phosphoric acid to a pH of 2.3**Mobile phase:** Acetonitrile and Buffer (25:75)**Standard stock solution:** 0.26 mg/mL of USP Donepezil Hydrochloride RS prepared as follows. Transfer a suitable quantity of USP Donepezil Hydrochloride RS to an appropriate volumetric flask. Add 70% of the flask volume of Medium. Sonicate to dissolve and dilute with Medium to volume.**Standard solution:** ($L/900$) mg/mL of USP Donepezil Hydrochloride RS from Standard stock solution in Medium, where L is the label claim in mg/Tablet. Pass the solution through a suitable filter, discarding the first 3 mL of the filtrate.**Sample solution:** Pass a portion of the solution under test through a suitable filter, discarding the first 3 mL of the filtrate.**Chromatographic system**(See [Chromatography \(621\)](#), [System Suitability](#).)**Mode:** LC**Detector:** UV 210 nm**Column:** 4.6-mm × 15-cm; 5-μm packing L1**Column temperature:** 35°**Flow rate:** 1.5 mL/min**Injection volume:** 50 μL**Run time:** NLT 1.7 times the retention time of donepezil**System suitability****Sample:** Standard solution**Suitability requirements****Tailing factor:** NMT 1.5**Relative standard deviation:** NMT 2.0%**Analysis****Samples:** Standard solution and Sample solutionCalculate the concentration (C_i) of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$) in the sample withdrawn from the vessel at each time point (i):

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

 r_U = peak response of donepezil from the *Sample solution* r_S = peak response of donepezil from the *Standard solution* C_S = concentration of USP Donepezil Hydrochloride RS in the *Standard solution* (mg/mL)Calculate the percentage of the labeled amount of donepezil hydrochloride ($C_{24}H_{29}NO_3 \cdot HCl$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + [C_1 \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_S)]] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$