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Carvedilol Tablets

DEFINITION
Carvedilol Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of carvedilol ($C_{24}H_{26}N_2O_4$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** **Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

Wavelength range: 250–400 nm

Cell: 0.2 cm

Sample solution: 0.125 mg/mL of carvedilol prepared as follows. Place 10 Tablets in a 150-mL polypropylene tube, and disintegrate the Tablets in methanol (100 mL for the Tablet strengths 3.125, 6.25, and 25 mg, and 50 mL for the Tablet strength 12.5 mg) using a mechanical homogenizer. Transfer the homogenate to an appropriate volumetric flask, and dilute with methanol to volume. Pass through a suitable PTFE filter of 0.45-µm pore size.

ASSAY

- **Procedure**

Buffer: Dissolve 0.7 g of anhydrous monobasic potassium phosphate in 500 mL of water, and add 10 mL of triethylamine. Adjust with phosphoric acid to a pH of 3.0 ± 0.1.

Mobile phase: Dissolve 1.04 g of sodium dodecyl sulfate in 150 mL of *Buffer* in a 2-L volumetric flask, and sonicate. Add 720 mL of acetonitrile, and dilute with water to volume. Pass through a nylon 66 filter of 0.2-µm pore size.

Diluent: Methanol and 1 M hydrochloric acid (9:1)

Methanol solution: Methanol and water (1:1)

Standard solution: 0.0125 mg/mL of USP Carvedilol RS prepared as follows. Dissolve a quantity of USP Carvedilol RS in a mixture of *Diluent* and water (9:1), and sonicate until the solution is clear. Dilute with *Methanol solution* to obtain the required final concentration.

Sample stock solution: Transfer a portion of the powdered Tablets (NLT 20), equivalent to 25 mg of carvedilol, to a 100-mL volumetric flask. Add 10 mL of water, shake by hand, then add 70 mL of *Diluent*, and sonicate for 30 min. Shake on a mechanical shaker for about 30 min, and dilute with *Diluent* to volume to prepare a 0.25-mg/mL solution. Centrifuge an appropriate amount (about 50 mL) at 2000 rpm for 10 min.

Sample solution: 0.0125 mg/mL of carvedilol in *Methanol solution* from the *Sample stock solution*. Pass a portion of the solution through a suitable syringe filter of 0.45-µm pore size, discard the first 5 mL, and use the filtrate as the *Sample solution*.

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 50-mm; packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Run time: 30 min

Injection size: 25 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 carvedilol ($C_{24}H_{26}N_2O_4$) in the portion of Tablets taken:

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

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)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.7% (7 mL/L) of hydrochloric acid, adjusted with 50% (w/w) sodium hydroxide to a pH of 1.45 ± 0.2; 900 mL; deaerated

Apparatus 2: 50 rpm

Time: 30 min

Standard stock solution: Transfer about 7 mg of USP Carvedilol RS to a 250-mL volumetric flask. Add 5 mL of methanol, and sonicate until dissolved. Cool to room temperature, dilute with *Medium* to volume, and mix well.

Standard solution: On the basis of the label claim and using the *Standard stock solution*, prepare a solution of USP Carvedilol RS in *Medium* having an appropriate concentration (C_S), as shown in *Table 1*.

Table 1

Label Claim (mg)	C_S (mg/mL)
25	0.028
12.5	0.014
6.25	0.007
3.125	0.0035

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

Analytical wavelengths: 285 and 380 nm

Path length: 1 cm

Blank: *Medium*

Analysis: Calculate the corrected absorbance of the *Standard solution* and the *Sample solution*:

$$A_{corr} = A_{285} - A_{380}$$

A_{corr} = corrected absorbance of the *Standard solution* or the *Sample solution*

A_{285} = absorbance of the *Standard solution* or the *Sample solution* at 285 nm

A_{380} = absorbance of the *Standard solution* at 380 nm

Calculate the percentage of carvedilol dissolved:

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

A_U = corrected absorbance from the *Sample solution*

A_S = corrected absorbance from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of carvedilol ($C_{24}H_{26}N_2O_4$) is dissolved.

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

Medium: Simulated gastric fluid without enzymes; 900 mL

Apparatus 2, Time, Standard stock solution, Standard solution, Sample solution, and **Analysis:** Proceed as directed in *Test 1*.

Tolerances: NLT 80% (Q) of the labeled amount of carvedilol ($C_{24}H_{26}N_2O_4$) is dissolved.

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

Medium: Simulated gastric fluid with pepsin, pH 1.45 (dissolve 12.0 g of sodium chloride and 19.2 g of purified pepsin (porcine origin, activity 800–2500 Units/mg of protein) in 18 mL of hydrochloric acid and sufficient water to make 6 L; adjust with hydrochloric acid to a pH of 1.45); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: 2.72 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.0 ± 0.05.

Mobile phase: *Buffer* and acetonitrile (650:350)

Standard stock solution: 1.4 mg/mL of USP Carvedilol RS in methanol

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (*L*/900) mg/mL, where *L* is the Tablet label claim, in mg.

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

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × ▲15-cm▲ (ERR 1-Feb-2024); 5-µm packing L7

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3500 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis: Calculate the percentage of carvedilol 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

Tolerances: NLT 80% (*Q*) of the labeled amount of carvedilol ($C_{24}H_{26}N_2O_4$) is dissolved.

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

Buffer, Mobile phase, Diluent, Methanol solution, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Sample solution: 0.25 mg/mL of carvedilol prepared as follows. Place 1 Tablet into a volumetric flask of appropriate size, based on the label claim. Add water to the flask up to about 10% of volume, and shake by hand to disintegrate the Tablet. Fill the flask up to 75% of volume with *Diluent*, and sonicate for 30 min to obtain complete disintegration. Shake on a mechanical shaker for 30 min, allow to cool, and dilute with *Diluent* to volume. Centrifuge an appropriate amount of this solution for 10 min at 2400 rpm, and transfer 4 mL of supernatant into a 100-mL volumetric flask. Fill the flask to about 85% of volume with *Methanol solution*, and sonicate for 20 min, with intermittent shaking. Dilute with *Methanol solution* to volume, and pass through a suitable syringe filter of 0.45-µm pore size.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of carvedilol ($C_{24}H_{26}N_2O_4$) in the Tablet taken:

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

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)

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

IMPURITIES

• **Organic Impurities**

Buffer, Mobile phase, Diluent, Methanol solution, and **Sample stock solution:** Prepare as directed in the *Assay*.

Standard stock solution: Use the *Standard solution* from the *Assay*.

Standard solution: 1.25 µg/mL USP Carvedilol RS in a mixture of *Diluent* and water (1:1) from the *Standard stock solution*

Sample solution: Dilute with water to volume, 25 mL of the supernatant from the *Sample stock solution* in a 50-mL volumetric flask. Pass a portion of the solution through a suitable syringe filter of 0.45-µm pore size.

Chromatographic system: Proceed as directed in the *Assay*, except for *Injection size*.

Injection size: 15 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each 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 impurity from the *Sample solution*

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

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

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

Acceptance criteria

Individual impurities: NMT 0.2% (specified or unspecified)

Total impurities: NMT 1.0%

[Note—Disregard any peaks with a relative retention time less than or equal to 0.04 and peaks with less than 0.05% of the nominal carvedilol peak response in the *Sample solution*.]

ADDITIONAL REQUIREMENTS

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

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.

• **USP Reference Standards** ⟨11⟩

USP Carvedilol RS

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

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

Chromatographic Database Information: Chromatographic Database

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