Carvedilol Tablets

DEFINITION
Carvedilol Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of carvedilol (C24H26N2O4).

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. ULTRAVIOLET ABSORPTION (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 0.45-µm PTFE filter.

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 0.2-µm nylon 66 filter.
Diluent: Methanol and 1 M hydrochloric acid (9:1)
Methanol solution: Methanol and 0.7% (7 mL/L)·(RB 1-Jan-2011) of hydrochloric acid (mg/mL) and water (9:1), and sonicate until dissolved. Cool to room temperature, dilute with Medium to volume, and mix well.
Diluent: 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 0.45-µm syringe filter, discard the first 5 mL, and use the filtrate as the Sample solution.
Chromatographic system
(See Chromatography (621), System Suitability.)

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 (Ct) as shown in Table 1 below.

<table>
<thead>
<tr>
<th>Label Claim (mg)</th>
<th>Ct (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>0.028</td>
</tr>
<tr>
<td>12.5</td>
<td>0.014</td>
</tr>
<tr>
<td>6.25</td>
<td>0.007</td>
</tr>
<tr>
<td>3.125</td>
<td>0.0035</td>
</tr>
</tbody>
</table>

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 as follows:

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

$$ A_{corr} = \frac{A_{corr}}{C_t} $$

$$ A_{285} = \text{absorbance of the Standard solution or the Sample solution at 285 nm} $$
Carvedilol  

\[ A_{\text{abs}} = \text{absorbance of the Standard solution at 380 nm} \]

Calculate the percentage of the carvedilol dissolved as follows:

\[ \text{Result} = (A_1/A_0) \times C_5 \times (V/L) \times 100 \]

\[ A_0 = \text{corrected absorbance from the Sample solution} \]

\[ A_1 = \text{corrected absorbance from the Standard solution} \]

\[ C_5 = \text{corrected concentration of the Standard solution (mg/mL)} \]

\[ V = \text{volume of Medium, 900 mL} \]

\[ L = \text{label claim (mg/Tablet)} \]

Tolerances: NLT 80% (Q) of the labeled amount of carvedilol (C\textsubscript{24}H\textsubscript{26}N\textsubscript{2}O\textsubscript{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


Tolerances: NLT 80% (Q) of the labeled amount of carvedilol (C\textsubscript{24}H\textsubscript{26}N\textsubscript{2}O\textsubscript{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: 30 rpm

Time: 30 min

Buffer: 2.7 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-mm; 5-μm packing L7

Temperature: 35°C

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:

\[ \text{Result} = (r_s/r_0) \times (C_s/C_0) \times V \times 100 \]

\[ r_0 = \text{peak response of each impurity from the Sample solution} \]

\[ r_s = \text{peak response of each impurity from the Standard solution} \]

\[ C_s = \text{concentration of USP Carvedilol RS in the Standard solution (mg/mL)} \]

\[ C_0 = \text{nominal concentration of the Sample solution (mg/mL)} \]

Tolerances: NLT 80% (Q) of the labeled amount of carvedilol (C\textsubscript{24}H\textsubscript{26}N\textsubscript{2}O\textsubscript{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.
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