Digoxin

Digoxin is a cardiotonic glycoside obtained from the leaves of *Digitalis lanata* Ehrh. (Fam. Plantaginaceae, formerly Scrophulariaceae). It contains NLT 95.0% and NMT 101.0% of digoxin (C_{41}H_{64}O_{14}), calculated on the dried basis. [CAUTION—Handle Digoxin with exceptional care, because it is extremely poisonous.]

**IDENTIFICATION**
- **A. INFRARED ABSORPTION (197K)**
- **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**

**Change to read:**
- **PROCEDURE**
  - **Mobile phase:** Acetonitrile and water (13:37)
  - **System suitability solution:** 40 \( \mu g/mL \) each of USP Digoxin RS and digoxigenin in diluted alcohol
  - **Sample solution:** 0.25 mg/mL of Digoxin in diluted alcohol. [NOTE—Use a sonic bath to aid dissolution.]
  - **Chromatographic system**
    (See Chromatography (621), System Suitability.)

**Table 1**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>15</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>16</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>30</td>
<td>78</td>
<td>22</td>
</tr>
</tbody>
</table>

Standard stock solution: 0.5 mg/mL of USP Digoxin RS and USP Digoxigenin RS in methanol
Standard solution: Dilute 1.0 mL of Standard stock solution with methanol to 100 mL System suitability solution: Dissolve 50 mg of lanatoside C in methanol, and dilute with methanol to 100 mL. To 1.0 mL of this solution add 1.0 mL of Standard stock solution, and dilute with methanol to 20 mL Sample solution: Accurately weigh 25 mg of Digoxin, transfer into a 50-mL volumetric flask, and dilute with methanol to volume.

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

**Mode:** LC  
**Detector:** UV 218 nm  
**Column:** 4.6-mm \( \times 25-cm \); 5-\( \mu m \) packing L1  
**Column temperature:** 25°  
**Flow rate:** 2 mL/min  
**Injection volume:** 10 \( \mu L \)

**IMPURITIES**
- **RESIDUE ON IGNITION (281):** NMT 0.5%, a 100-mg specimen being used
- **RELATED GLYCOSIDES**
  - **Solution A:** Acetonitrile and water (10:90)
  - **Solution B:** Water and acetonitrile (10:90)
  - **Mobile phase:** See Table 1,
Mode: LC
Detector: UV 220 nm
Column: 3.9-mm × 15-cm; 5-µm packing L1
Column temperature: 25 °C
Flow rate: 1.5 mL/min
Injection volume: 10 µL

**Specific Tests**

**Residual Solvents** (467): 2000 µg/g for methylene chloride and for chloroform

**Loss on Drying** (731)
Analysis: Dry under vacuum at 105 °C for 1 h.
Acceptance criteria: NMT 1.0%

**Additional Requirements**

**Packaging and Storage:** Preserve in tight containers.

**Change to read:**

**USP Reference Standards** (11)
USP Digoxin RS
USP Digitoxin RS

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**Table 2**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin (standard)</td>
<td>1.00</td>
<td>—</td>
</tr>
<tr>
<td>Gitoxin</td>
<td>2.16</td>
<td>0.5</td>
</tr>
<tr>
<td>Digitoxin</td>
<td>2.62</td>
<td>0.5</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>3.5</td>
</tr>
</tbody>
</table>

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