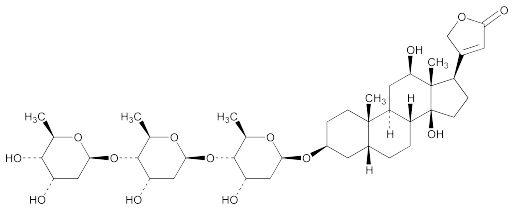
# Digoxin



$C_{41}H_{64}O_{14}$ 780.94

Card-20(22)-enolide, 3-[(*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12,14-dihydroxy-, (3β,5β,12β)-;

Digoxin;

3β-[(*O*-2,6-Dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12β,14-dihydroxy-5β-card-20(22)-enolide [20830-75-5].

## DEFINITION

***Change to read:***

Digoxin is a cardiotonic glycoside obtained from the leaves of *Digitalis lanata* •Ehrh. (Fam. Plantaginaceae, formerly Scrophulariaceae).• (IRA 1-Nov-2015) 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*.

***Delete the following:***

- **C. PROCEDURE**

**Analysis:** Examine in visible light the thin-layer chromatograph prepared as directed in the test for *Related Glycosides*.

**Acceptance criteria:** The $R_F$ value of the principal blue spot of the *Sample solution* corresponds to that of the *Standard solution*.• (IRA 1-Nov-2015)

## ASSAY

***Change to read:***

- **PROCEDURE**

**Mobile phase:** Acetonitrile and water (13:37)

**System suitability solution:** 40 µg/mL each of USP Digoxin RS and digoxigenin in diluted alcohol

**Standard solution:** 0.25 mg/mL of USP Digoxin RS in diluted alcohol. [NOTE—Use a sonic bath to aid dissolution.]

**Sample solution:** 0.25 mg/mL of Digoxin in diluted alcohol. [NOTE—Dissolve using sonication, before make-up to final volume.]

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 218 nm

**Column:** •4.6-mm × 25-cm; 5-µm packing L1•

**Column temperature:** 25°• (IRA 1-Nov-2015)

**Flow rate:** •2 mL/min• (IRA 1-Nov-2015)

**Injection volume:** 10 µL

**System suitability**

**Sample:** *System suitability solution*

**Suitability requirements**

**Resolution:** NLT 4.0 between digoxin and digoxigenin

**Column efficiency:** NLT 1200 theoretical plates for the digoxin peak

**Tailing factor:** NMT 2.0 for the digoxin peak

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of digoxin ($C_{41}H_{64}O_{14}$) in the portion of Digoxin taken:

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

$r_U$ = peak response of digoxin from the *Sample solution*

$r_S$ = peak response of digoxin from the *Standard solution*

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

$C_U$ = concentration of Digoxin in the *Sample solution* (mg/mL)

**Acceptance criteria:** 95.0%–101.0% on the dried basis

## IMPURITIES

- **RESIDUE ON IGNITION** ⟨281⟩**:** NMT 0.5%, a 100-mg specimen being used

***Change to read:***

- **RELATED GLYCOSIDES**

•**Solution A:** Acetonitrile and water (10:90)•

**Solution B:** Water and acetonitrile (10:90)

**Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 78 | 22 |
| 5 | 78 | 22 |
| 15 | 30 | 70 |
| 16 | 78 | 22 |
| 30 | 78 | 22 |

**Standard stock solution:** 0.5 mg/mL of USP Digoxin RS and USP Digitoxin 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 220 nm
**Column:** 3.9-mm × 15-cm; 5-µm packing L1
**Column temperature:** 25°
**Flow rate:** 1.5 mL/min
**Injection volume:** 10 µL
**System suitability**
**Sample:** *System suitability solution*
**Suitability requirements**
**Resolution:** NLT 1.5 between the digoxin and lanatoside C peaks
**Relative standard deviation:** NMT 2.0%, determined from the digoxin peak in replicate injections
**Analysis**
**Samples:** *Standard solution* and *Sample solution*
Calculate the percentages of the peak areas of the total impurities, gitoxin, and digitoxin, against the digoxin peak from the *Standard solution*.
**Acceptance criteria:** See *Table 2*.

**Table 2**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Digoxin (standard) | 1.00 | — |
| Gitoxin | 2.16 | 0.5 |
| Digitoxin | 2.62 | 0.5 |
| Total impurities | — | 3.5 |

● (IRA 1-Nov-2015)

• **RESIDUAL SOLVENTS** ⟨**467**⟩**:** 2000 µg/g for methylene chloride and for chloroform

**SPECIFIC TESTS**
• **LOSS ON DRYING** ⟨**731**⟩
**Analysis:** Dry under vacuum at 105° 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● (IRA 1-Nov-2015)