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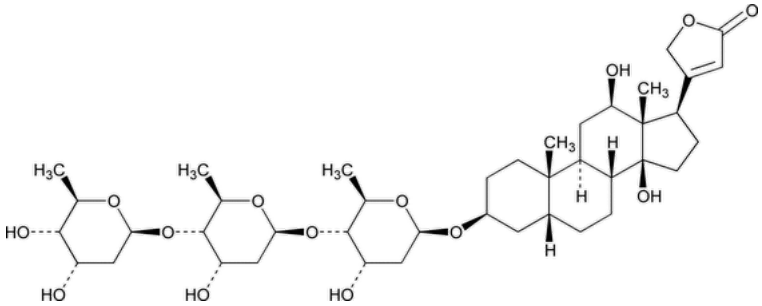
Digoxin



$C_{41}H_{64}O_{14}$ 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 CAS RN®: 20830-75-5; UNII: 73K4184T59.

DEFINITION

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

Change to read:

• **A.** ▲**SPECTROSCOPIC IDENTIFICATION TESTS ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-MAY-2020)

• **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**

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°

Flow rate: 2 mL/min

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
- **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

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

Suitability requirements

Resolution: NLT 1.5 between the digoxin and lanatoside C peaks, *System suitability solution*

Relative standard deviation: NMT 2.0%, determined from the digoxin peak in replicated injections, *Standard solution*

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	—

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

• **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.

• **USP Reference Standards ⟨11⟩**

USP Digoxin RS

USP Digitoxin RS

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

Topic/Question	Contact	Expert Committee
DIGOXIN	Nam-Cheol Kim Scientific Liaison	BDSHM2020 Botanical Dietary Supplements and Herbal Medicines

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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