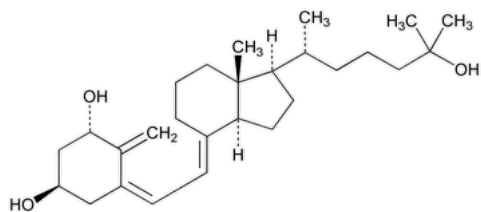


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Calcitriol



$C_{27}H_{44}O_3$ 416.64

$C_{27}H_{44}O_3 \cdot H_2O$ 434.65

9,10-Secosteroid-5,7,10(19)-triene-1,3,25-triol, (1 α ,3 β ,5Z,7E)-;

(5Z,7E)-9,10-Secosteroid-5,7,10(19)-triene-1 α ,3 β ,25-triol CAS RN®: 32222-06-3.

Monohydrate CAS RN®: 77326-95-5.

DEFINITION

Calcitriol is anhydrous or contains 1 molecule of hydration. The anhydrous form contains NLT 97.0% and NMT 103.0% of calcitriol ($C_{27}H_{44}O_3$), calculated on the solvent-free basis. The monohydrate form contains NLT 97.0% and NMT 103.0% of calcitriol ($C_{27}H_{44}O_3$), calculated on the anhydrous basis.

[CAUTION]—Care should be taken to prevent inhaling particles of calcitriol, and exposing the skin to it.]

IDENTIFICATION

Change to read:

- **A.** ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Infrared Spectroscopy*: 197A or 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

Carry out the procedure as rapidly as possible, and protect all solutions containing calcitriol from light.

Buffer: 1.0 mg/mL of [tris\(hydroxymethyl\)aminomethane](#) in [water](#), adjusted with [phosphoric acid](#) to a pH of 7.0–7.5 before final dilution

Mobile phase: Acetonitrile and *Buffer* (55:45)

Standard solution: 0.1 mg/mL of [USP Calcitriol RS](#) prepared as follows. Transfer an appropriate amount of [USP Calcitriol RS](#) to a suitable volumetric flask, dissolve in acetonitrile, using 55% of the final volume, then dilute with *Buffer* to volume.

System suitability solution: Heat 2.0 mL of the *Standard solution* at 80° for 30 min.

Sample solution: 0.1 mg/mL of Calcitriol prepared as follows. Transfer an appropriate amount of Calcitriol to a suitable volumetric flask, dissolve in acetonitrile, using 55% of the final volume, then dilute with *Buffer* to volume.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5- μ m packing [L7](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 50 μ L

Run time: NLT 2 times the retention time of calcitriol

System suitability

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

[NOTE—The relative retention times for pre-calcitriol and calcitriol are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.5 between the pre-calcitriol and calcitriol peaks, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of calcitriol (C₂₇H₄₄O₃) in the portion of Calcitriol taken:

Result = (r_U/r_S) × (C_S/C_U) × 100

r_U = sum of the peak responses of calcitriol and pre-calcitriol from the *Sample solution*

r_S = sum of the peak responses of calcitriol and pre-calcitriol from the *Standard solution*

C_S = concentration of [USP Calcitriol RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria

Anhydrous form: 97.0%–103.0% on the solvent-free basis

Monohydrate form: 97.0%–103.0% on the anhydrous basis

IMPURITIES

• **ORGANIC IMPURITIES**

Carry out the procedure as rapidly as possible, and protect all solutions containing calcitriol from light.

Buffer, Mobile phase, System suitability solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Analysis

Sample: *Sample solution*

Calculate the percentage of any individual impurity in the portion of Calcitriol taken:

Result = (r_U/r_T) × 100

r_U = peak response of any individual peak other than the main calcitriol peak and the pre-calcitriol peak from the *Sample solution*

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See [Table 1](#). The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Triazoline adduct of pre-calcitriol ^a	0.43	0.1
<i>trans</i> -Calcitriol ^b	0.96	0.25
Calcitriol	1.0	—
1β-Calcitriol ^c	1.15	0.1
Methylene calcitriol ^d	1.5	0.25
Any unspecified impurity	—	0.1
Total impurities	—	1.0

^a (6aR,7R,9aR)-11-[(3S,5R)-3,5-Dihydroxy-2-methylcyclohex-1-enyl]-7-[(R)-6-hydroxy-6-methylheptan-2-yl]-6a-methyl-2-phenyl-4a,5,6,6a,7,8,9,9a-octahydrocyclopenta[*f*][1,2,4]triazolo[1,2-*a*]cinnoline-1,3(2*H*,11*H*)-dione.

^b (5*E*,7*E*)-9,10-Secocholesta-5,7,10(19)-triene-1α,3β,25-triol.

^c (5*Z*,7*E*)-9,10-Secocholesta-5,7,10(19)-triene-1β,3β,25-triol.

^d (5*Z*,7*E*)-1α,3β-Dihydroxy-17-[(R)-7-hydroxy-7-methyloctan-2-yl]-9,10-secoandrosta-5,7,10(19)-triene.

SPECIFIC TESTS

- [WATER DETERMINATION \(921\), Method I, Method Ic](#): 3.5%–5.5%, where it is labeled as a monohydrate