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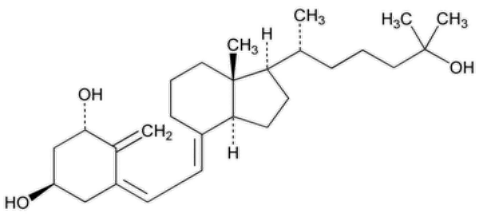
# Calcitriol




$C_{27}H_{44}O_3$ 416.64
$C_{27}H_{44}O_3 \cdot H_2O$ 434.65
9,10-Secocholesta-5,7,10(19)-triene-1,3,25-triol, (1α,3β,5*Z*,7*E*)-;
(5*Z*,7*E*)-9,10-Secocholesta-5,7,10(19)-triene-1α,3β,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-µm packing L7

**Column temperature:** 40°

**Flow rate:** 1 mL/min

**Injection volume:** 50 µL

**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 ($C_{27}H_{44}O_3$) in the portion of Calcitriol taken:

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

$r_U$ = 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:

$$\text{Result} = (r_U/r_T) \times 100$$

$r_U$ = 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 |
| *trans*-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] (6a*R*,7*R*,9a*R*)-11-[(3*S*,5*R*)-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

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store as per labeling instructions.
- **Labeling:** Where it is a monohydrate form, the label so indicates.
- **USP Reference Standards** ⟨11⟩
  USP Calcitriol RS

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| CALCITRIOL | Documentary Standards Support | SM32020 Small Molecules 3 |

**Chromatographic Database Information:** Chromatographic Database

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