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Cholecalciferol Capsules

DEFINITION

Cholecalciferol Capsules contain a solution of Cholecalciferol in an edible oil or other suitable vehicle. Cholecalciferol Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of vitamin D as cholecalciferol ($C_{27}H_{44}O$).

IDENTIFICATION

• **A.** The retention time of the major peak of cholecalciferol of the *Sample solution* corresponds to that of *Standard solution A*, as obtained in the *Assay*.

ASSAY

Change to read:

• **Procedure**

[Note—Use low-actinic glassware throughout this procedure.]

Mobile phase: *n*-Hexane and isopropyl alcohol (99:1)

System suitability solution: 250 mg of USP Vitamin D Assay System Suitability RS in 10 mL of *n*-hexane. Heat this solution under reflux, at 60° for 1 h, and cool. [Note—This solution contains cholecalciferol, precholecalciferol, and *trans*-cholecalciferol.]

Standard stock solution: 50 µg/mL of USP Cholecalciferol RS in *n*-hexane. [Note—Prepare solution fresh daily.]

Standard solution A: 5 µg/mL of USP Cholecalciferol RS in *n*-hexane from the *Standard stock solution*

Standard solution B: Transfer a 5-mL volume of the *Standard stock solution* to a container having a polytef-lined screw cap. Displace the air with nitrogen and heat at 60° for 1 h under a nitrogen atmosphere, and cool. Quantitatively transfer the solution to a 50-mL volumetric flask, and dilute with *n*-hexane to volume.

Sample solution: Weigh NLT 30 Capsules in a tared weighing bottle. With a sharp blade or by other appropriate means, carefully open the Capsules, without loss of the shell material, and transfer as much as possible of the combined Capsule contents to a suitable container. Remove any adhering substance from the emptied Capsules and shell remains by washing with several small portions of *n*-hexane. Discard the washings, and allow the empty Capsules and shell remains to dry in a current of dry air until the odor of *n*-hexane is no longer perceptible. Weigh the empty Capsules and shell remains in the original tared weighing bottle, and calculate the average net weight per Capsule by difference. Dissolve a portion of the combined Capsule contents in *n*-hexane to prepare a cholecalciferol solution with a nominal concentration of 5 µg/mL.

Chromatographic system

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

Mode: LC

Detector: UV 265 nm

Column: 4.6-mm × 15-cm; 3-µm packing L8

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for precholecalciferol, *trans*-cholecalciferol, and cholecalciferol are 0.5, 0.6, and 1.0, respectively.]

Suitability requirements

Resolution: NLT ▲1.0▲ (USP 1-Aug-2019) between *trans*-cholecalciferol and precholecalciferol

Relative standard deviation: NMT 2.0% for cholecalciferol

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Cholecalciferol response factor

Calculate the *Cholecalciferol response factor* (F_C):

$$F_C = C_S/r_S$$

C_S = concentration of USP Cholecalciferol RS in *Standard solution A* (µg/mL)

r_S = peak area of cholecalciferol from *Standard solution A*

Precholecalciferol response factor

Calculate the concentration of cholecalciferol (C'_S), in µg/mL, in *Standard solution B*:

$$C'_S = F_C \times r'_S$$

F_C = *Cholecalciferol response factor*, as previously determined

r'_S = peak area of cholecalciferol from *Standard solution B*

Calculate the concentration of precholecalciferol (C'_{pre}), in µg/mL, in *Standard solution B*:

$$C'_{pre} = C_S - C'_S$$

C_S = concentration of USP Cholecalciferol RS in *Standard solution A* (µg/mL)

C'_S = concentration of cholecalciferol in *Standard solution B* (µg/mL)

Calculate the *Precholecalciferol response factor* (F_{pre}):

$$F_{pre} = C'_{pre}/r_p$$

C'_{pre} = concentration of precholecalciferol in *Standard solution B* (µg/mL)

r_p = peak response of precholecalciferol from *Standard solution B*

Vitamin D content

Calculate the percentage of the labeled amount of vitamin D as cholecalciferol ($C_{27}H_{44}O$) in the portion of Capsules taken:

$$\text{Result} = \{[(F_C \times r_C) + (F_{pre} \times r_{pre})]/C_U\} \times 100$$

F_C = *Cholecalciferol response factor*, as previously determined

r_C = peak area of cholecalciferol from the *Sample solution*

F_{pre} = *Precholecalciferol response factor*, as previously determined

r_{pre} = peak area of precholecalciferol from the *Sample solution*

C_U = nominal concentration of cholecalciferol in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Disintegration ⟨701⟩**

Buffer solution: 0.05 M acetate buffer, prepared by mixing 2.99 g of sodium acetate and 1.66 mL of glacial acetic acid with water to obtain a 1000-mL solution having a pH of 4.5 ± 0.05

Immersion fluid: *Buffer solution*

Time: 45 min

Acceptance criteria: Meet the requirements

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Change to read:

• **Labeling:** Label the Capsules to indicate the content of cholecalciferol in ▲micrograms. Expression of the amount of cholecalciferol in terms of units may be added in parentheses after the mass units.[1]▲ (USP 1-Aug-2019)

• **USP Reference Standards ⟨11⟩**
USP Cholecalciferol RS
USP Vitamin D Assay System Suitability RS

[1] Where articles are labeled in terms of units in addition to the required labeling, the relationship of the USP Units or International Units (IU) to mass units is as follows: 1 µg of cholecalciferol or ergocalciferol = 40 USP Units or IU.

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

Topic/Question	Contact	Expert Committee
CHOLECALCIFEROL CAPSULES	Natalia Davydova Scientific Liaison	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

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