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Oil-Soluble Vitamins Oral Solution

DEFINITION

Oil-Soluble Vitamins Oral Solution contains two or more of the following oil-soluble vitamins: Vitamin A, as retinol or esters of retinol in the form of retinyl acetate or retinyl palmitate; Vitamin D, as ergocalciferol (Vitamin D₂) or cholecalciferol (Vitamin D₃); Vitamin E, as alpha tocopherol, alpha tocopheryl acetate, or alpha tocopheryl acid succinate; Phytonadione (Vitamin K₁); and beta carotene. It contains NLT 90.0% and NMT 150.0% of the labeled amounts of vitamin A, as retinol equivalent (C₂₀H₃₀O); vitamin D, as cholecalciferol (C₂₇H₄₄O) or ergocalciferol (C₂₈H₄₄O); vitamin E, as alpha tocopherol (C₂₉H₅₀O₂), alpha tocopheryl acetate (C₃₁H₅₂O₃), or alpha tocopheryl acid succinate (C₃₃H₅₄O₅); phytonadione (C₃₁H₄₆O₂); and beta carotene (C₄₀H₅₆).

STRENGTH

• VITAMIN A

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

Mobile phase: *n*-Hexane

Standard solution 1: 13 µg/mL of retinol from [USP Retinyl Acetate RS](#) in *n*-hexane

Standard solution 2: 13 µg/mL of retinol from [USP Retinyl Palmitate RS](#) in *n*-hexane

System suitability solution: Mix equal volumes of *Standard solution 1* and *Standard solution 2*.

Sample solution: Equivalent to 13 µg/mL of retinol from an accurately measured volume of Oral Solution in *n*-hexane

Chromatographic system

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

Mode: LC

Detector: UV 325 nm

Column: 4.6-mm × 15-cm; packing L8

Flow rate: 1 mL/min

Injection volume: 40 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 10 between all-*trans*-retinyl acetate and all-*trans*-retinyl palmitate

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution 1* or *Standard solution 2* and *Sample solution*

Calculate the percentage of the labeled amount of vitamin A, as retinol (C₂₀H₃₀O), in the portion of Oral Solution taken:

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

r_U = peak area of the all-*trans*-retinyl ester from the *Sample solution*

r_S = peak area of the all-*trans*-retinyl ester from the appropriate *Standard solution*

C_S = concentration of retinol in the appropriate *Standard solution* (µg/mL)

C_U = nominal concentration of vitamin A, as retinol, in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–150.0% of the labeled amount of vitamin A as retinol equivalent (C₂₀H₃₀O)

• VITAMIN D

[NOTE—Where vitamin D (cholecalciferol or ergocalciferol) is specified in the following procedure, use the chemical form present in the formulation and the relevant USP Reference Standard. Use low-actinic glassware throughout this procedure.]

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

Standard solution: 2 µg/mL of [USP Cholecalciferol RS](#) or [USP Ergocalciferol RS](#) in *n*-hexane

System suitability solution: Heat a volume of the *Standard solution* at 60° for 1 h to partially isomerize vitamin D (cholecalciferol or ergocalciferol) to its corresponding precursor.

Sample stock solution: Equivalent to 20 µg/mL of cholecalciferol or ergocalciferol from an accurately measured volume of Oral Solution in *n*-hexane

Sample solution: Transfer 5.0 mL of the *Sample stock solution* to a container having a polytetrafluoroethylene-lined screw cap and heat, with constant shaking, for 1 h in a water bath maintained at 60° to obtain a solution containing vitamin D (cholecalciferol or ergocalciferol) and its corresponding precursor. Cool, and dilute with *n*-hexane to obtain a solution containing 2 µg/mL of cholecalciferol or ergocalciferol.

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: 100 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 10 between the vitamin D form present and its corresponding precursor

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Measure the peak areas for vitamin D. Calculate the percentage of the labeled amount of cholecalciferol ($C_{27}H_{44}O$) or ergocalciferol ($C_{28}H_{44}O$) in the portion of Oral Solution taken:

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

r_U = peak area of cholecalciferol or ergocalciferol from the *Sample solution*

r_S = peak area of cholecalciferol or ergocalciferol from the *Standard solution*

C_S = concentration of [USP Cholecalciferol RS](#) or [USP Ergocalciferol RS](#) in the *Standard solution* (µg/mL)

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

F = correction factor to account for the average amount of pre-vitamin D present in the *Sample solution*, 1.09

Acceptance criteria: 90.0%–150.0% of the labeled amount of vitamin D as cholecalciferol ($C_{27}H_{44}O$) or ergocalciferol ($C_{28}H_{44}O$)

• VITAMIN E

[NOTE—Where vitamin E (alpha tocopherol, alpha tocopheryl acetate, or alpha tocopheryl acid succinate) is specified in the following procedure, use the chemical form present in the formulation and the relevant USP Reference Standard. Use low-actinic glassware throughout this procedure.]

Solution A: Phosphoric acid solution in water (1 in 100)

Mobile phase: Methanol and *Solution A* (19:1)

Standard solution: 2 mg/mL of [USP Alpha Tocopherol RS](#), [USP Alpha Tocopheryl Acetate RS](#), or [USP Alpha Tocopheryl Acid Succinate RS](#) in methanol

Sample solution: Equivalent to 2.0 mg/mL of alpha tocopherol, alpha tocopheryl acetate, or alpha tocopheryl acid succinate from an accurately measured volume of Oral Solution in methanol

Chromatographic system

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

Mode: LC

Detector: UV 291 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min