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Vitamin A Oral Liquid Preparation

DEFINITION

Vitamin A Oral Liquid Preparation is an emulsion, suspension, or solution that contains retinyl acetate or retinyl palmitate in an amount equivalent to NLT 90.0% and NMT 120.0% of the labeled amount of vitamin A, as retinol ($C_{20}H_{30}O$).

IDENTIFICATION

[Note—Use low-actinic glassware.]

• **A.**

Sample solution: Equivalent to 6 µg/mL of retinol from Oral Liquid Preparation in methylene chloride

Analysis: To 1 mL of *Sample solution* add 10 mL of antimony trichloride TS.

Acceptance criteria: A transient blue color appears at once.

• **B. Thin-Layer Chromatographic Identification Test ⟨201⟩**

Standard solution: 0.5 mg/mL of retinol from USP Retinyl Acetate RS or USP Retinyl Palmitate RS in methylene chloride

Sample solution: Dissolve or extract with methylene chloride a quantity of Oral Liquid Preparation to obtain a solution with a nominal concentration of 0.5 mg/mL of retinol.

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Application volume: 10 µL, 8-mm band

Developing solvent system: Cyclohexane and ether (4:1)

Developing distance: 10 cm

Spray reagent: 0.2 g/mL of phosphomolybdic acid in alcohol. Filter, and use only the clear filtrate.

Analysis: Apply the *Sample solution* at the starting point of the chromatogram, and proceed as directed in the chapter. Allow the solvent front to move 10 cm, remove the plate, and air-dry. Spray with *Spray reagent*.

Acceptance criteria: The blue-green spot formed is indicative of the presence of retinol, and its R_F value corresponds to that of the *Standard solution*. The approximate R_F values of the predominant spots, corresponding to the different forms of retinol, are 0.1 for the alcohol form, 0.45 for the acetate form, and 0.7 for the palmitate form.

ASSAY

• **Vitamin A**

[Note—Use low-actinic glassware.]

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

For Oral Liquid Preparation in oil vehicles packaged in single-unit containers: Deliver the contents of NLT 30 single-unit containers, following the directions for use as stated in the labeling. Weigh directly the individual contents delivered from each single-unit container, and calculate the average. [Note—Do not weigh the contents delivered by difference between full containers and empty containers. Capsules intended as single-unit containers are not rinsed after expulsion of the contents.] Mix the contents to obtain a homogeneous sample. Transfer an amount of the composite to a suitable volumetric flask. Dissolve with hexane, and dilute with hexane quantitatively and stepwise, if necessary, to obtain a solution containing the equivalent of about 13 µg/mL of retinol, based on the labeled amount.

For Oral Liquid Preparation in oil vehicles packaged in multiple-unit containers: Dissolve an accurately measured volume of Oral Liquid Preparation in a suitable volume of hexane, and dilute with hexane, quantitatively and stepwise, if necessary, to obtain a solution containing the equivalent of about 13 µg/mL of retinol, based on the labeled amount.

For Oral Liquid Preparation in aqueous vehicles: Transfer a weighed quantity, or an accurately measured volume of Oral Liquid Preparation, into a separatory funnel, and extract quantitatively with hexane or other suitable solvent. Dilute with hexane, quantitatively and stepwise, if necessary, to obtain a solution containing the equivalent of about 13 µg/mL of retinol, based on the labeled amount.

Chromatographic system

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

Mode: LC

Detector: UV 325 nm

Column: 4.6-mm × 15-cm; 3-µm 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 ($C_{20}H_{30}O$), in each individual container:

$$\text{Result} = (r_U/r_S) \times (C/W) \times D \times U \times (100/L)$$

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

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

C = concentration of retinol ($C_{20}H_{30}O$) in the appropriate *Standard solution* (mg/mL)

W = weight or volume of Oral Liquid Preparation composite taken (mg or mL)

D = dilution factor (dilution volume/aliquot volume)

U = for multiple-unit containers: labeled volume of each dosage unit (mL); for single-unit containers: average mass (mg) of the contents delivered from each individual container, following the directions for use as stated in the labeling

L = label claim of vitamin A as retinol ($C_{20}H_{30}O$) (mg/dosage unit)

Acceptance criteria: 90.0%–120.0% of the labeled amount of vitamin A, as retinol ($C_{20}H_{30}O$)

PERFORMANCE TESTS

• **Deliverable Volume ⟨698⟩**

For multiple-unit containers: Meets the requirements

• **Uniformity of Dosage Units ⟨905⟩**

For single-unit containers

Analysis: Empty the single-unit containers, following the directions for use as stated in the labeling. [Note—Do not weigh the contents delivered by difference between full containers and empty containers. Capsules intended for use as single-unit containers are not rinsed after expulsion of the contents.]

Acceptance criteria: The contents so delivered, and weighed directly, meet the requirements.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight, light-resistant containers. It may be packaged in single-unit containers. It also may be suitable as single-unit containers provided they are packaged in secondary containers. ▲▲ (CN 1-May-2020)

• **Labeling:** The label states that the product is Vitamin A Oral Liquid Preparation. Label the Oral Liquid Preparation to indicate the ester form in which the vitamin is present, and to indicate the amount of vitamin A delivered in each dosage unit in terms of the equivalent amount of retinol in µg/dosage unit. Expression of the amount of vitamin A in terms of units may be added in parentheses after the mass units.[1] Capsules used as single-unit containers may be exempted from the requirements of individual labeling, provided they are packaged in an appropriately labeled secondary container, including directions for use and delivery of each dosage unit of Oral Liquid Preparation. Label the Oral Liquid Preparation packaged in multiple-unit containers to indicate the volume of each dosage unit.

• **USP Reference Standards ⟨11⟩**

USP Retinyl Acetate RS
USP Retinyl Palmitate 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 is as follows: 1 USP Vitamin A Unit = 0.3 μg of *all-trans*-retinol (vitamin A alcohol) or 0.344 μg of *all-trans*-retinyl acetate (vitamin A acetate) or 0.55 μg of *all-trans*-retinyl palmitate (vitamin A palmitate), and 1 μg of retinol (3.3 USP Vitamin A Units) = 1 retinol equivalent (RE).

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

Topic/Question	Contact	Expert Committee
VITAMIN A ORAL LIQUID PREPARATION	Natalia Davydova Scientific Liaison	NBDS2020 Non-botanical Dietary Supplements
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	NBDS2020 Non-botanical Dietary Supplements

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