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Vitamin E Polyethylene Glycol Succinate

DEFINITION

Vitamin E Polyethylene Glycol Succinate is a mixture formed by the esterification of *d*-alpha tocopheryl acid succinate and polyethylene glycol. The ester mixture consists primarily of mono-esterified polyethylene glycol and a small amount of di-esterified polyethylene glycol. It contains NLT 25.0% of *d*-alpha tocopherol ($C_{29}H_{50}O_2$).

IDENTIFICATION

• **A. Gas Chromatographic Identification Test**

Analysis: Proceed as directed in the test for *Content of Alpha Tocopherol*.

Acceptance criteria: The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*.

COMPOSITION

• **Content of Alpha Tocopherol**

Solvent: 0.25 mL of phenolphthalein TS in 1 L of alcohol

Internal standard solution: 12 mg/mL of ethyl arachidate in isooctane

Standard solution: Transfer 32.5 mg of USP Alpha Tocopherol RS to a suitable reaction flask. Add 2 mL of pyridine and 0.5 mL of *N,O*-bis(trimethylsilyl)trifluor oacetamide with 1% trimethylchlorosilane, and heat the flask at 100° for 10 min. Cool the flask, add 5.0 mL of *Internal standard solution* followed by 20 mL of isooctane, and shake.

Sample solution: Transfer a quantity equivalent to 0.100–0.160 g of Vitamin E Polyethylene Glycol Succinate molten at 60° to a culture tube (about 20 cm long and 2.5 cm in diameter) equipped with a screw cap. Add 40–50 mg of ascorbic acid and a few boiling chips, followed by 20 mL of *Solvent*. [Note—Reflux the solution gently without emission of contents.] Place the tube in a heating block set at 100°–150°. When the sample is fully dissolved, add 0.25 g of potassium hydroxide, and continue to reflux for 30 min. Remove the tube from heat, and while contents are still hot, add 1–2 mL of hydrochloric acid dropwise until the pink coloration disappears. [**Caution—**Exothermic reaction. Allow the acid to trickle down the inside of the tube to prevent splashing.] Cool the tube, then wash the sides of the tube with 20 mL of water. Add 5.0 mL of *Internal standard solution,* cap, and shake to ensure thorough mixing. Allow the tube to stand until two distinct layers are formed. Transfer 2.5–3.5 mL of the upper layer into a suitable reaction flask, and add 2.0 mL of pyridine followed by 2.5 mL of *N,O*-bis(trimethylsilyl)trifluoroacetamide with 1% trimethylchlorosilane. Heat the flask at 100° for 10 min. Cool, and then add 12 mL of isooctane.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.25-mm × 15-m fused-silica capillary; coated with a 0.25-µm film of phase G27

Temperature

Injector: 280°

Detector: 345°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
260	20	340	1

Carrier gas: Helium

Flow rate: 1.5 mL/min

Injection size: 1 µL

Injection type: Split ratio, 200:1

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for the alpha tocopherol peak

Relative standard deviation: NMT 2.0% for the ratio of the alpha tocopherol peak area to the internal standard peak area

Analysis

Samples: *Standard solution* and *Sample Solution*

Calculate the percentage of *d*-alpha tocopherol ($C_{29}H_{50}O_2$) in the portion of Vitamin E Polyethylene Glycol Succinate taken:

$$\text{Result} = (R_U/R_S) \times (W_S/W_U) \times 100$$

R_U = internal standard ratio (peak area of alpha tocopherol/peak area of the internal standard) from the *Sample solution*

R_S = internal standard ratio (peak area of alpha tocopherol/peak area of the internal standard) from the *Standard solution*

W_S = weight of USP Alpha Tocopherol RS used to prepare the *Standard solution* (mg)

W_U = weight of Vitamin E Polyethylene Glycol Succinate taken to prepare the *Sample solution* (mg)

Acceptance criteria: NLT 25.0%

SPECIFIC TESTS

• **Optical Rotation,** *Specific Rotation* ⟨781S⟩

[Note—This test identifies *d*-alpha tocopherol after saponification.]

Sample solution: Transfer 0.9 g of Vitamin E Polyethylene Glycol Succinate, molten at 60°, to a suitable test tube fitted with a cap, and dissolve in 10.0 mL of alcohol. Place the tube in a heating block set at 100°–105°. [Note—Reflux the solution gently without emission of contents.] When the sample is fully dissolved, add 2–3 pellets of sodium hydroxide, and continue to reflux for an additional 30 min. Remove the tube from the heat, and while contents are still hot, neutralize using phenolphthalein as the indicator by slowly adding 10 mL of a mixture of water and hydrochloric acid (1:1) until the pink color disappears. [**Caution—**Exothermic reaction. Allow the acid solution to trickle down the inside of the tube to prevent splashing.] Cool the tube, cap, and shake until contents are well mixed. Add 25.0 mL of heptane, cap, and shake for 1 min to ensure thorough mixing. Allow the tube to stand until two distinct layers are formed. Transfer the top layer to a clean, dry culture tube, then add 10.0 mL of water to the recovered solution. Cap, shake, and allow the layers to separate. Transfer the upper layer to a clean, dry tube. Add 10.0 mL of potassium ferricyanide solution, prepared by dissolving 2 g of potassium ferricyanide in 10.0 mL of 0.2 M sodium hydroxide, and replace the cap. Shake vigorously for 45 s, and allow the layers to separate for 30 min. If the top heptane layer is clear, proceed with the measurement for specific rotation; if not clear, dry over anhydrous sodium sulfate before proceeding with the test. [Note—Use the results of the test for *Content of Alpha Tocopherol* to calculate the specific rotation.]

Acceptance criteria: NLT +24.0°

• **Solubility in Water**

Sample: 20 g of melted Vitamin E Polyethylene Glycol Succinate

Analysis: Place the *Sample* in a glass container on a magnetic stirrer. Immediately add 80 mL of boiling water while stirring. Allow to cool to room temperature with constant stirring.

Acceptance criteria: The solution becomes clear within 3 h.

• **Acid Value**

Sample: 1 g of Vitamin E Polyethylene Glycol Succinate

Analysis: Dissolve the *Sample* in 25 mL of a mixture of alcohol and ether (1:1) that has been neutralized to phenolphthalein with 0.1 N sodium hydroxide. Add 0.5 mL of phenolphthalein TS, and titrate with 0.10 N sodium hydroxide until the solution remains faintly pink after shaking for 30 s.

Acceptance criteria: NMT 0.027 mEq/g, equivalent to NMT 0.27 mL of 0.10 N sodium hydroxide

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store protected from light.

• **Labeling:** The labeling indicates the *d*-alpha tocopherol content, expressed in mg/g.

• **USP Reference Standards** ⟨11⟩
USP Alpha Tocopherol RS

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

Topic/Question	Contact	Expert Committee
VITAMIN E POLYETHYLENE GLYCOL SUCCINATE	Natalia Davydova Scientific Liaison	NBDS2020 Non-botanical Dietary Supplements
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

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