Status: Currently Official on 17-Feb-2025
Official Date: Official Prior to 2013
Document Type: NF Monographs
DocId: GUID-23120636-7157-4768-B9F6-2E9FD0FF36A6_1_en-US
DOI: https://doi.org/10.31003/USPNF_M83820_01_01
DOI Ref: zf758

Tocopherols Excipient

DEFINITION

Tocopherols Excipient is a vegetable oil solution containing NLT 50.0% of total tocopherols, of which NLT 80.0% consists of varying amounts of beta, gamma, and delta tocopherols.

IDENTIFICATION

• **A.**

Sample solution: 50 mg of Tocopherols Excipient in 10 mL of dehydrated alcohol

Analysis: To the *Sample solution* add with swirling 2 mL of nitric acid, and heat at about 75° for 15 min.

Acceptance criteria: A bright red or orange color develops.

• **B.** The retention time of the third major peak (i.e., the peak occurring just before that of the internal standard) of the *Sample solution* corresponds to that of the *Standard solution*, both relative to that of the internal standard, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: Pyridine and propionic anhydride (2:1)

Internal standard solution: 3 mg/mL of hexadecyl hexadecanoate in *Solution A*

Standard solutions: Using low-actinic glassware, add 12-, 25-, 37-, and 50-mg portions of USP Alpha Tocopherol RS to separate 50-mL conical flasks having 19/38 standard-taper ground-glass necks. Pipet 25 mL of the *Internal standard solution* into each flask, and reflux for 10 min under water-cooled condensers.

Sample solution: Using low-actinic glassware, add 60 mg of Tocopherols Excipient to a 50-mL conical flask similar to the flasks used in preparing the *Standard solutions*. Add 10.0 mL of *Internal standard solution*, and reflux for 10 min under a water-cooled condenser.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 4-mm × 2-m borosilicate glass; packed with 2%–5% liquid phase G2 on 80- to 100-mesh support S1AB using either a glass-lined sample introduction system or on-column injection

Temperatures

Column: 245°–265°, maintained isothermally

Injection port: 10° higher than the *Column* temperature

Detector: 10° higher than the *Column* temperature

Flow rate: Dry carrier gas is adjusted to obtain a hexadecyl hexadecanoate peak 30–32 min after sample introduction. [Note—Cure and condition the column as necessary.]

Injection volume: 2–5 µL

System suitability

Sample: *Sample solution*

[Note—The relative retention times for delta tocopheryl propionate, beta plus gamma tocopheryl propionate, and hexadecyl hexadecanoate are about 0.50, 0.63, and 1.00, respectively.]

Suitability requirements

Resolution: Chromatograph a sufficient number of injections to ensure that a resolution of NLT 2.5 between delta tocopheryl propionate and beta plus gamma tocopheryl propionate relative to hexadecyl hexadecanoate is met.

Analysis

Samples: *Standard solutions* and *Sample solution*

Calibration: Chromatograph each *Standard solution*, and calculate the relative response factor, *F*, for each concentration of the *Standard solution* taken:

$$F = (r_S/r_D) \times (C_D/C_S)$$

r_S = peak response of alpha tocopherol in the *Standard solution*

r_D = peak response of hexadecyl hexadecanoate in the *Standard solution*

C_D = concentration of hexadecyl hexadecanoate in the *Standard solution* (mg/mL)

C_S = concentration of USP Alpha Tocopherol RS in the *Standard solution* (mg/mL)

Chromatograph a sufficient number of injections of each *Standard solution* to ensure that *F* is constant within a range of 2.0%. Prepare a relative response factor curve by plotting *F* versus the alpha tocopheryl propionate peak response.

Inject the *Sample solution*, and measure the responses for the four major peaks occurring at relative retention times of approximately 0.50, 0.63, 0.76, and 1.00, and record the values as a_δ, $a_{\beta\gamma}$, a_α, and a_D, corresponding to delta tocopheryl propionate, beta plus gamma tocopheryl propionates, alpha tocopheryl propionate, and hexadecyl hexadecanoate, respectively.

Calculate the quantity of each tocopherol form in the Tocopherols Excipient taken:

$$\text{delta tocopherol} = (V \times C_D/F) \times (a_\delta/a_D)$$

$$\text{beta plus gamma tocopherols} = (V \times C_D/F) \times (a_{\beta\gamma}/a_D)$$

$$\text{alpha tocopherol} = (V \times C_D/F) \times (a_\alpha/a_D)$$

V = volume of *Internal standard solution* used in the *Sample solution* (mL)

F = obtained from the relative response factor curve (see *Calibration*) for each of the corresponding responses for the delta, beta plus gamma, and alpha tocopheryl propionate peaks produced by the *Sample solution*

[NOTE—The relative response factor for delta tocopheryl propionate and for beta plus gamma tocopheryl propionates has been determined empirically to be the same as for alpha tocopheryl propionate.]

Acceptance criteria: NLT 50.0% of total tocopherols, of which NLT 80.0% consists of varying amounts of beta, gamma, and delta tocopherols

SPECIFIC TESTS

- **ACIDITY**

Solution A: Alcohol and ether (50%:50%). Neutralize to phenolphthalein with 0.1 N sodium hydroxide.

Sample solution: Dissolve 1.0 g of Tocopherols Excipient in 25 mL of *Solution A*.

Analysis: To the *Sample solution* add 0.5 mL of phenolphthalein TS, and titrate with 0.10 N sodium hydroxide until the solution remains faintly pink after being shaken for 30 s.

Acceptance criteria: NMT 1.0 mL of 0.10 N sodium hydroxide is required.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, protected from light. Protect with a blanket of an inert gas.
- **LABELING:** Label it to indicate the content, in mg/g, of total tocopherols and of the sum of beta, gamma, and delta tocopherols.
- **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
TOCOPHEROLS EXCIPIENT	Documentary Standards Support	CE2020 Complex Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

Current DocID: GUID-23120636-7157-4768-B9F6-2E9FD0FF36A6_1_en-US
DOI: https://doi.org/10.31003/USPNF_M83820_01_01
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