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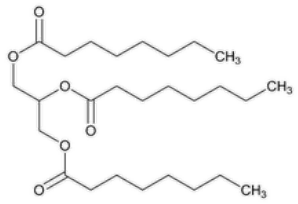
Add the following:

▲Glyceryl Tricaprylate



$C_{27}H_{50}O_6$ 470.68

Octanoic acid, 1,1',1"-(1,2,3-propanetriyl) ester;
Octanoic acid, 1,2,3-propanetriyl ester;
1,3-Di(octanoyloxy)propan-2-yl octanoate;
Glyceryl trioctanoate;

Tricapryloylglycerol CAS RN®: 538-23-8.

DEFINITION

Glyceryl Tricaprylate contains NLT 90.0% of triglycerides of saturated fatty acids, chiefly glyceryl tricaprylate ($C_{27}H_{50}O_6$).

IDENTIFICATION

• **A. Fatty Acid Composition**

Boron trifluoride methanol solution: 140 mg/mL of boron trifluoride in methanol

Saturated sodium chloride solution: Mix 1 part of sodium chloride with 2 parts of water, shake intermittently, and allow to stand. Before use, decant the solution from any undissolved substance and filter, if necessary.

Standard solution 1: 1.0 mg/mL of USP Methyl Caproate RS, 1.0 mg/mL of USP Methyl Caprylate RS, and 2.0 mg/mL of USP Methyl Caprate RS in *n*-heptane

Standard solution 2: 0.1 mg/mL of USP Methyl Caproate RS, 0.1 mg/mL of USP Methyl Caprylate RS, and 0.2 mg/mL of USP Methyl Caprate RS in *n*-heptane, diluted from *Standard solution 1*

Standard solution 3: Prepare an ester mixture by mixing a commercially available ester mixture with methyl caprylate and methyl caprate, or prepare an ester mixture by using USP Methyl Caproate RS, USP Methyl Caprylate RS, USP Methyl Caprate RS, and USP Methyl Laurate RS. Dissolve a quantity of the prepared ester mixture containing methyl caproate, methyl caprylate, methyl caprate, and methyl laurate in *n*-heptane to make a solution of about 9.0 mg/mL for methyl caprylate, 0.5 mg/mL for methyl caprate, and 0.1 mg/mL for each of methyl caproate and methyl laurate.

Sample solution: Transfer 100 mg of Glyceryl Tricaprylate to a 25-mL conical flask fitted with a suitable water-cooled reflux condenser and a magnetic stir bar. Add 2 mL of a 20-mg/mL solution of sodium hydroxide in methanol, mix, and reflux for about 30 min. Add 2 mL of *Boron trifluoride methanol solution* through the condenser and reflux for about 30 min. Add 4 mL of *n*-heptane through the condenser and reflux for 5 min. Cool, remove the condenser, add about 10 mL of *Saturated sodium chloride solution*, shake, add a quantity of *Saturated sodium chloride solution* to bring the upper layer up to the neck of the flask, and allow the layers to separate. Collect 2 mL of the *n*-heptane layer (upper layer); wash with three quantities of water, 2 mL each; and dry the *n*-heptane phase over anhydrous sodium sulfate.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m capillary bonded with a 1.0-µm layer of phase *G16*

Temperatures

Injection port: 250°

Detector: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
50	20	180	—
180	9	240	12

Carrier gas: Helium

Flow rate: 10 mL/min

Injection volume: 2 µL

Injection type: Split ratio, 4:1

System suitability

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

[NOTE—The relative retention times for methyl caproate, methyl caprylate, and methyl caprate are about 0.7, 1.0, and 1.4, respectively.]

Suitability requirements

Resolution: NLT 4.0 between the methyl caprylate and methyl caprate peaks, *Standard solution 1*

Signal-to-noise ratio: NLT 10 for the methyl caproate peak, *Standard solution 2*

Analysis

Samples: *Standard solution 3* and *Sample solution*

Measure the peak areas of the methyl esters of the fatty acids. Disregard any peaks with an area less than 0.05% of the total area and any peak due to the solvent. [NOTE—Relative retention times for several methyl esters are summarized in *Table 2*.]

Table 2

Carbon-Chain Length	Number of Double Bonds	Relative Retention Times
6	0	0.7
8	0	1.0
10	0	1.4
12	0	1.7

Take the main component in *Standard solution 3* as a reference component, and calculate the calibration factor (F_{FA}) for each fatty acid methyl ester:

$$F_{FA} = [(F_{MC} \times P_{FA1} \times A_{MC})/(P_{MC} \times A_{FA1})]$$

F_{MC} = factor for the main component, 1

P_{FA1} = percentage by weight of the fatty acid methyl ester in *Standard solution 3*

A_{MC} = peak area for the main component in *Standard solution 3*

P_{MC} = percentage by weight of the main component in *Standard solution 3*

A_{FA1} = peak area for the fatty acid methyl ester in *Standard solution 3*

Calculate the percentage of each fatty acid methyl ester by weight in the portion of Glyceryl Tricaprylate taken:

$$\text{Result} = [(A_{FA2} \times F_{FA})/A_T] \times 100$$

A_{FA2} = peak area for the fatty acid methyl ester in the *Sample solution*

F_{FA} = calibration factor, determined previously

A_T = sum of the peak areas for the fatty acid methyl esters in the *Sample solution*

Acceptance criteria: Glyceryl Tricaprylate exhibits the following composition profile of fatty acids shown in *Table 3*.

Table 3

Carbon-Chain Length	Number of Double Bonds	Percentage (w/w)
6	0	≤1.0
8	0	≥90.0
10	0	≤5.0
12	0	≤1.0

- **B. Content of Triglycerides**

Analysis: Proceed as directed in the test for *Content of Triglycerides* in the *Assay*.

Acceptance criteria: NLT 90.0% of triglycerides

- **C. Fats and Fixed Oils ⟨401⟩, *Procedures, Saponification Value*:** 340–370

ASSAY

Change to read:

- **Content of Triglycerides**

System suitability solution: 20 ▲mg/mL▲ (ERR 1-Oct-2018) each of 1-monooctanoyl-rac-glycerol and 1-monodecanoyl-rac-glycerol in tetrahydrofuran

Standard solution 1: 50 mg/mL of USP Glyceryl Monocaprylate RS in tetrahydrofuran

Standard solution 2: 50 mg/mL of USP Glyceryl Tricaprylate RS in tetrahydrofuran

Sample solution: 50 mg/mL of Glyceryl Tricaprylate in tetrahydrofuran

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 10-m bonded with a 0.1-µm layer of phase G27

Temperatures

Injection port: 350°

Detector: 370°

Column: See *Table 4*.

Table 4

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
60	—	60	3
60	8	340	12

Carrier gas: Helium

Flow rate: 2.3 mL/min

Injection volume: 1 µL

Injection type: Split ratio, 50:1

System suitability

Samples: *System suitability solution*, *Standard solution 1*, and *Standard solution 2*

[NOTE—The relative retention times for monoglycerides, diglycerides, and triglycerides are 1.0–1.2, 1.5–1.9, and 1.9–2.3, respectively, *Standard solution 1* and *Standard solution 2*.]

Suitability requirements

Resolution: NLT 5.0 between the peaks due to 1-monooctanoyl-rac-glycerol and 1-monodecanoyl-rac-glycerol, *System suitability solution*

Analysis

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

Based on the chromatograms from *Standard solution 1* and *Standard solution 2*, identify the peaks due to mono-, di-, and triglycerides in the *Sample solution*.

For the calculation of the contents of mono-, di-, and triglycerides, disregard the peaks with a retention time less than that of the monoglycerides, which are due to impurities of the solvent and to the free fatty acids.

Calculate the percentage of free fatty acids (C_A) in the portion of Glyceryl Tricaprylate taken:

$$C_A = [(I_A \times F \times M_{r1})/M_{r2}] \times 100$$

I_A = acid value for Glyceryl Tricaprylate, determined in the test for *Fats and Fixed Oils, Acid Value*

F = unit conversion factor, 10^{-3} g/mg

M_{r1} = molecular weight of caprylic acid, 144.21 g/mol

M_{r2} = molecular weight of potassium hydroxide, 56.11 g/mol

Calculate the percentage of triglycerides in the portion of Glyceryl Tricaprylate taken:

$$\text{Result} = (r_U/r_T) \times [(100 - C_A - C_W - C_G)/100] \times 100$$

r_U = peak response of the triglycerides from the *Sample solution*

r_T = sum of all the glyceride peak responses from the *Sample solution*

C_A = percentage of free fatty acids, determined previously

C_W = percentage of water, determined in the test for *Water Determination*

C_G = percentage of free glycerin, determined in the test for *Limit of Free Glycerin*

Acceptance criteria: NLT 90.0% of triglycerides

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Alkaline Impurities**

Analysis: Prepare a mixture of 2.0 g of Glyceryl Tricaprylate, 15 mL of alcohol, and 30 mL of ether. Dissolve by gently heating. Add 0.05 mL of bromophenol blue TS, and titrate with 0.01 N hydrochloric acid VS until the mixture turns yellow.

Acceptance criteria: NMT 0.4 mL of 0.01 N hydrochloric acid is required.

- **Limit of Free Glycerin**

Sample: 1.2 g

Periodic acetic acid solution: Dissolve 0.446 g of sodium periodate in 2.5 mL of a 25% (v/v) solution of sulfuric acid, and dilute with glacial acetic acid to 100.0 mL.

Potassium iodide solution: 75 mg/mL of potassium iodide

Blank: 25 mL of methylene chloride

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Residual titration

Titrant: 0.1 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 25 mL of methylene chloride. Heat to about 50°, and allow to cool. Add 100 mL of water. Shake, and add 25 mL of *Periodic acetic acid solution*. Shake again, and allow to stand for 30 min. Add 40 mL of *Potassium iodide solution,* and allow to stand

for 1 min. Add 1 mL of starch TS, and titrate the liberated iodine with *Titrant* until the aqueous phase becomes colorless. Perform a blank determination.

Calculate the percentage of free glycerol in the portion of Glyceryl Tricaprylate taken:

$$\text{Result} = \{[(V_B - V_S) \times N_A \times E \times F]/W\} \times 100$$

V_B = volume of *Titrant* consumed in the blank titration (mL)

V_S = volume of *Titrant* consumed in the *Sample* titration (mL)

N_A = actual normality of the *Titrant* (mEq/mL)

E = equivalent factor for glycerol, 23 mg/mEq

F = conversion factor, 10^{-3} g/mg

W = weight of Glyceryl Tricaprylate taken for the titration (g)

Acceptance criteria: NMT 0.5%

SPECIFIC TESTS

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states that Glyceryl Tricaprylate must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins is such that the requirement in the relevant dosage form monograph(s) in which Glyceryl Tricaprylate is used can be met.

• **Fats and Fixed Oils ⟨401⟩, *Procedures, Acid Value*:** NMT 0.2

• **Fats and Fixed Oils ⟨401⟩, *Procedures, Hydroxyl Value*:** NMT 10.0

• **Fats and Fixed Oils ⟨401⟩, *Procedures, Peroxide Value*:** NMT 1

• **Water Determination ⟨921⟩, *Method I, Method Ia*:** NMT 0.2%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at room temperature. Protect from light and moisture.

• **Labeling:** Where Glyceryl Tricaprylate must be subjected to further processing during the preparation of injectable dosage forms to ensure acceptable levels of bacterial endotoxins, it is so labeled.

• **USP Reference Standards ⟨11⟩**

USP Glyceryl Monocaprylate RS
USP Glyceryl Tricaprylate RS
USP Methyl Caprate RS
USP Methyl Caproate RS
USP Methyl Caprylate RS
USP Methyl Laurate RS

▲ (1S (NF36))

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

Topic/Question	Contact	Expert Committee
GLYCERYL TRICAPRYLATE	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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