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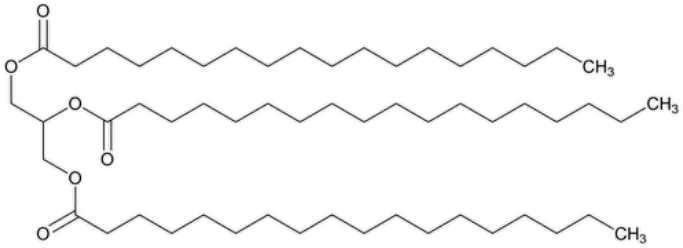
Glyceryl Tristearate



$C_{57}H_{110}O_6$ 891.48

Octadecanoic acid, 1,1',1"-(1,2,3-propanetriyl) ester;

Octadecanoic acid, 1,2,3-propanetriyl ester;

Glycerol trioctadecanoate;

Tristearoylglycerol CAS RN®: 555-43-1.

DEFINITION

Glyceryl Tristearate contains NLT 90.0% of triglycerides of saturated fatty acids, chiefly glyceryl tristearate ($C_{57}H_{110}O_6$).

IDENTIFICATION

• **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 from time to time, and allow to stand. Before use, decant the solution from any undissolved substance and filter, if necessary.

Standard solution 1: 0.5 mg/mL of USP Methyl Myristate RS, 2.0 mg/mL of USP Methyl Stearate RS, and 2.0 mg/mL of USP Methyl Oleate RS in *n*-heptane

Standard solution 2: 0.05 mg/mL of USP Methyl Myristate RS, 0.2 mg/mL of USP Methyl Stearate RS, and 0.2 mg/mL of USP Methyl Oleate RS in *n*-heptane, diluted from *Standard solution 1*

Standard solution 3: Dissolve a quantity of an ester mixture[1] containing methyl hexanoate, methyl caprylate, methyl caprate, methyl laurate, methyl myristate, methyl palmitate, methyl palmitoleate, methyl stearate, methyl oleate, methyl linoleate, and methyl arachidate in *n*-heptane to make a solution of about 9.0 mg/mL for methyl stearate and 0.1–0.2 mg/mL for each other methyl ester.

Sample solution: Transfer 100 mg of Glyceryl Tristearate 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*, and 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 (the 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 myristate, methyl stearate, and methyl oleate are about 0.70, 1.00, and 1.01, respectively.]

Suitability requirements

Resolution: NLT 1.5 between methyl stearate and methyl oleate, *Standard solution 1*

Signal-to-noise ratio: NLT 5 for methyl myristate, *Standard solution 2*

Analysis

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

Measure the areas for the peaks of the methyl esters of the fatty acids. Disregard any peak 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
12	0	0.58
14	0	0.70
16	0	0.83
18	0	1.00
18	1	1.01
20	0	1.14

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

$$\text{Result} = (F_{MC} \times P_{FA1} \times A_{MC})/(P_{MC} \times A_{FA1})$$

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 of the main component in *Standard solution 3*

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

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

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

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

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

F_{FA} = calibration factor

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

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

Table 3

Carbon-Chain Length	Number of Double Bonds	Percentage (w/w)
6, 8, 10	0	0.0–0.3
12	0	0.0–0.5
14	0	0.0–0.5
16	0	0.0–2.0
16	1	0.0–0.1
18	0	≥97
18	1	0.0–0.5
18	2	0.0–0.5
20	0	0.0–1.0

ASSAY

• **Content of Triglycerides**

Mobile phase: Tetrahydrofuran

System suitability solution: 40 mg/mL of USP Glyceryl Distearate RS in *Mobile phase*

Sample solution: 8 mg/mL of Glyceryl Tristearate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 7.5-mm × 60-cm; 3-µm or 5-µm 100-Å packing L21

Temperatures

Column: 40°

Detector: 40°

[Note—Two or three 7.5-mm × 30-cm L21 columns may be used in place of the one 60-cm column, provided that system suitability requirements are met. The column temperature may be lowered to ambient temperature, although working at 40° provides stable separation conditions and ensures better sample solubility.]

Flow rate: 1 mL/min

Injection volume: 40 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for triglycerides, diglycerides, monoglycerides, and glycerin are 0.78, 0.81, 0.86, and 1.00, respectively.]

Suitability requirements

Resolution: NLT 1.0 between the diglycerides and the monoglycerides

Relative standard deviation: NMT 2.0%, determined for the monoglycerides peak

Analysis

Samples: *System suitability solution* and *Sample solution*

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

Result = $(r_U/r_T) \times 100$

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

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

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 Tristearate, 15 mL of alcohol, and 30 mL of ether. Dissolve by gentle 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 Nickel**

[**Caution**—When using closed high-pressure digestion vessels and laboratory microwave equipment, be familiar with the safety and operating instructions given by the manufacturer.]

Magnesium nitrate solution: 10 mg/mL of magnesium nitrate in water

Ammonium dihydrogen phosphate solution: 100 mg/mL of ammonium dihydrogen phosphate in water

Standard stock solution: Transfer 5.0 mL of nickel standard solution TS to a 10-mL volumetric flask, and dilute with water to make a solution containing 5 µg/mL of nickel.

Standard solutions: To four identical 25-mL volumetric flasks, each containing 6 mL of nitric acid, transfer 25, 50, 75, and 100 µL, respectively, of the *Standard stock solution*. To each flask add 0.5 mL of *Magnesium nitrate solution* and 0.5 mL of *Ammonium dihydrogen phosphate solution*, and dilute with water to volume. These solutions contain 0.005, 0.01, 0.015, and 0.02 µg/mL, respectively, of nickel.

Sample solution: Transfer 0.25 g of Glyceryl Tristearate to a suitable high-pressure-resistant digestion vessel (fluoropolymer or quartz), and add 6.0 mL of nitric acid and 2.0 mL of 30% hydrogen peroxide. Place the closed vessel in a laboratory microwave oven, and digest using an appropriate program (e.g., 1000 W for 40 min). Allow the digestion vessel to cool before opening. Add 2.0 mL of 30% hydrogen peroxide, and repeat the digestion step. Allow the digestion vessel to cool before opening. Quantitatively transfer the contents to a 25-mL volumetric flask, add 0.5 mL of *Magnesium nitrate solution* and 0.5 mL of *Ammonium dihydrogen phosphate solution*, dilute with water to volume, and mix.

Blank solution: Add 6.0 mL of nitric acid and 2.0 mL of 30% hydrogen peroxide to a high-pressure-resistant digestion vessel, and proceed as directed for the *Sample solution*.

Zero solution: Into a 50.0-mL volumetric flask, introduce 1.0 mL of *Magnesium nitrate solution*, 1.0 mL of *Ammonium dihydrogen phosphate solution*, and 12.0 mL of nitric acid. Dilute with water to volume, and mix.

Instrumental conditions

(See *Atomic Absorption Spectroscopy ⟨852⟩*.)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Maximum absorbance at 232.0 nm

Detection: Graphite furnace

Lamp: Nickel hollow-cathode

Tube: Pyrolytically coated

Other: Background compensation system

Furnace program: See *Table 4*.

[Note—The temperature program may be modified to obtain optimum furnace temperatures.]

Table 4

Step	Dry	Ash	Cool	Atomize
Temperature (°)	120	1100	800	2600
Ramp time (s)	5	30	5	—
Hold time (s)	35	10	5 (decrease)	7

Analysis

Samples: *Standard solutions*, *Sample solution*, and *Blank solution*

Use the *Zero solution* to set the instrument to zero. Concomitantly determine the absorbances of the *Samples* at least three times each. Record the average of the steady readings for each of the solutions. If necessary, dilute the *Sample solution* with the *Zero solution* to obtain a reading within the calibrated absorbance range.

Plot the absorbances versus the concentrations of nickel, in µg/mL, in the *Standard solutions*. On the basis of the calibration curve, determine the concentrations of nickel, in µg/mL, in the *Sample solution* and the *Blank solution* from the corresponding absorptions. Obtain the correct concentration of nickel, C_C, in µg/mL, in the *Sample solution*.

Calculate the content of nickel, in µg/g (ppm), in the portion of Glyceryl Tristearate taken:

[NOTE—If the *Sample solution* is diluted with the *Zero solution*, apply an appropriate correction factor for dilution.]

$$\text{Result} = (C_C \times V)/W$$

C_C = concentration of nickel in the *Sample solution* (µg/mL)

V = volume of the *Sample solution*, 25 mL

W = weight of Glyceryl Tristearate taken to prepare the *Sample solution* (g)

Acceptance criteria: NMT 1 µg/g (ppm)

SPECIFIC TESTS

- **MELTING RANGE OR TEMPERATURE ⟨741⟩, *Procedures, Procedure for Class II*:** 69°–73°
- **FATS AND FIXED OILS ⟨401⟩, *Acid Value*:** NMT 1.0
- **FATS AND FIXED OILS ⟨401⟩, *Hydroxyl Value*:** NMT 5.0
- **FATS AND FIXED OILS ⟨401⟩, *Saponification Value*:** 186–192
- **FATS AND FIXED OILS ⟨401⟩, *Peroxide Value*:** NMT 3
- **FATS AND FIXED OILS ⟨401⟩, *Unsaponifiable Matter*:** NMT 0.5%
- **WATER DETERMINATION ⟨921⟩, *Method I, Method Ia*:** NMT 0.1%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at room temperature. Protect from moisture.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Glyceryl Distearate RS
USP Methyl Myristate RS
USP Methyl Oleate RS
USP Methyl Stearate RS

[1] Ester mixture can be obtained commercially from Nu-Chek-Prep, Inc., P.O. Box 295, Elysian, MN 56028, or from Sigma-Aldrich; or it can be prepared by mixing a commercially-available ester mixture with methyl stearate.

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

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

Chromatographic Database Information: Chromatographic Database

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