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Polyglyceryl Dioleate

$R–O–(CH_2–CH(OR)–CH_2–O)_3–R$ R = H, or $CO–C_{17}H_{33}$
1,2,3-Propanetriol, homotrimer, di[(9*Z*)-9-octadecenoate];
Triglyceril dioleate;
Polyglyceryl 3 dioleate CAS RN®: 9007-48-1.$R–O–(CH_2–CH(OR)–CH_2–O)_6–R$ R = H, or $CO–C_{17}H_{33}$
1,2,3-Propanetriol, homohexamer, di[(9*Z*)-9-octadecenoate];
Hexaglyceril dioleate;
Polyglyceryl 6 dioleate
CAS RN®: 76009-37-5.

DEFINITION

Polyglyceryl Dioleate is a mixture of polyglyceryl diesters of mainly oleic acid, obtained by esterification of poly glycerin and oleic acid. The polyglycerin consists mainly of triglycerin or hexaglycerin.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197F**▲ (CN 1-May-2020)

• **B.** Meets the requirements of the test for *Content of Fatty Acids*

• **C.** Meets the requirements of the test for *Fats and Fixed Oils ⟨401⟩, Hydroxyl Value*. [Note—This test will differentiate for Polyglyceryl 3 Dioleate and Polyglyceryl 6 Dioleate.]

ASSAY

• **Content of Fatty Acids**

0.5 N methanolic sodium hydroxide solution: Dissolve 20 g of sodium hydroxide in 50 mL of water, and mix. Cool to room temperature, and add 950 mL of methanol.

Boron trifluoride methanol solution: Dissolve 14 g of boron trifluoride in methanol to make 100 mL, and mix well.[1]

Saturated sodium chloride solution: Dissolve about 375 g of sodium chloride in water to make 1000 mL.

Standard solution: Prepare the calibration ester mixture by mixing up each individual ester component (see *Table 1* for the component's composition). Dissolve 500 mg of the calibration ester mixture in *n*-heptane, and dilute with *n*-heptane to 50 mL. [Note—Commercially available mixtures of fatty acid methyl esters may also be used.]

Table 1

Component in the Calibration Ester Mixture	Composition (%)
USP Methyl Myristate RS (C14:0)	5
USP Methyl Palmitate RS (C16:0)	15
USP Methyl Palmitoleate RS (C16:1)	10
USP Methyl Stearate RS (C18:0)	10
USP Methyl Oleate RS (C18:1)	20

Component in the Calibration Ester Mixture	Composition (%)
USP Methyl Linoleate RS (C18:2)	15
USP Methyl Linolenate RS (C18:3)	10
Methyl arachidate (C20:0)	10
Methyl gadoleate (C20:1)	5

Sample solution: Introduce 100 mg of Polyglyceryl Dioleate into a 25-mL conical flask fitted with a suitable water-cooled reflux condenser and a magnetic stir bar. Add 2 mL of *0.5 N methanolic sodium hydroxide solution*, 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, each at 2 mL of water, and dry the *n*-heptane phase over anhydrous sodium sulfate.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 30-m fused-silica capillary; 0.25-µm layer of phase G16

Temperature

Detector: 250°

Injection port: 240°

Column: See temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
150	6	250	6

Carrier gas: Nitrogen

Flow rate: 1.0–1.2 mL/min

Injection size: 1 µL

Injection type: Split injection. The split ratio is about 1:80.

System suitability

Sample: *Standard solution*

[Note—See the relative retention time table below.]

Component	Relative Retention Time
Methyl myristate	0.74
Methyl palmitate	1.00
Methyl palmitoleate	1.03
Methyl stearate	1.29
Methyl oleate	1.33
Methyl linoleate	1.37[a]

Component	Relative Retention Time
Methyl linolenate	1.46[b]
Methyl arachidate	1.55
Methyl gadoleate	1.58

[a] There could be an isomer eluting at a relative retention time of 1.39.

[b] There could be two isomers eluting at relative retention times of 1.45 and 1.48.

Suitability requirements

Resolution: NLT 1.5 between the peaks due to methyl stearate and methyl oleate

Relative standard deviation: NMT 6.0% for the palmitate and stearate peak areas

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the fatty acid ester peaks of the *Sample solution* by comparing the retention times of these peaks with those of the *Standard solution*, and measure the peak areas for all of the fatty acid esters in the *Sample solution*.

Calculate the percentage of each fatty acid ester component in the test specimen:

$$\text{Result} = (A/B) \times 100$$

A = peak area of each individual fatty acid ester component

B = sum of the peak areas, excluding the solvent peak, of the *Sample solution*

Acceptance criteria: Polyglyceryl Dioleate exhibits the following composition profile of fatty acids.

Carbon-Chain Length	Number of Double Bonds	Percentage
14	0	≤5.0
16	0	2.0–16.0
16	1	≤8.0
18	0	≤6.0
18	1	65.0–88.0
18	2	5.0–18.0[a]
18	3	≤4.0[a]
Sum of fatty acids with C >18	0	≤4.0

[a] The content of C18:2 or C18:3 is the content of each fatty acid with its respective isomers.

IMPURITIES

Inorganic Impurities

• **Residue on Ignition**

Analysis: Heat a silica crucible to redness for 30 min, allow to cool in a desiccator, and weigh. Evenly distribute about 1.0 g of Polyglyceryl Dioleate in the crucible, and weigh. Dry at 100°–105° for 1 h, and ignite in a muffle furnace at 600 ± 25°, until the test substance is thoroughly charred. Perform the test for *Residue on Ignition* ⟨281⟩ on the residue obtained, starting with "Moisten the sample with a small amount (usually 1 mL) of sulfuric acid."

Acceptance criteria: NMT 1%

SPECIFIC TESTS

• **Acid Value**

Analysis: Accurately weigh (to within 0.1 mg) 5–10 g of Polyglyceryl Dioleate, add 10 mL of alcohol and 3 drops of phenolphthalein TS, and titrate with 0.1 N potassium hydroxide VS or 0.1 N sodium hydroxide VS until the solution remains faintly pink after shaking for 30 s. Proceed as directed in *Fats and Fixed Oils ⟨401⟩, Acid Value* to perform the calculation.

Acceptance criteria

Polyglyceryl 3 dioleate: NMT 6

Polyglyceryl 6 dioleate: NMT 6

• **Fats and Fixed Oils,** *Hydroxyl Value* ⟨401⟩

Acceptance criteria

Polyglyceryl 3 dioleate: 195–245, determined on a 0.7-g to 1.0-g specimen

Polyglyceryl 6 dioleate: 270–320, determined on 0.5-g to 0.7-g specimen

• **Iodine Value**

Analysis: Accurately weigh 0.15 g of Polyglyceryl Dioleate, transfer to a dry 250-mL flask with a ground-glass stopper, and add 25 mL of methylene chloride. Add 20 mL of the Wijs' solution.[2] Close the flask, and keep it in the dark for 1 h while shaking frequently. Perform the test in *Fats and Fixed Oils ⟨401⟩, Iodine Value*, starting with "Then add, in the order named, 30 mL of potassium iodide TS and 100 mL of water."

Acceptance criteria

Polyglyceryl 3 dioleate: 60–80

Polyglyceryl 6 dioleate: 50–70

• **Fats and Fixed Oils,** *Peroxide Value* ⟨401⟩**:** Use 30 mL of a mixture of glacial acetic acid and methylene chloride (3:2) to replace 30 mL of a mixture of glacial acetic acid and chloroform (3:2).

Acceptance criteria

Polyglyceryl 3 dioleate: NMT 12.5

Polyglyceryl 6 dioleate: NMT 12.5

• **Fats and Fixed Oils,** *Saponification Value* ⟨401⟩**:** Determined on 1-g specimen

Acceptance criteria

Polyglyceryl 3 dioleate: 135–155

Polyglyceryl 6 dioleate: 110–140

• **Water Determination,** *Method I* ⟨921⟩ **:** NMT 1%, determined on a 2.0-g specimen

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, protected from heat and moisture.

• **Labeling:** Label to indicate whether it is Polyglyceryl 3 Dioleate or Polyglyceryl 6 Dioleate.

• **USP Reference Standards** ⟨11⟩

USP Methyl Linoleate RS
USP Methyl Linolenate RS
USP Methyl Myristate RS
USP Methyl Oleate RS
USP Methyl Palmitate RS
USP Methyl Palmitoleate RS
USP Methyl Stearate RS
USP Polyglyceryl 3 Dioleate RS
USP Polyglyceryl 6 Dioleate RS

[1] Boron trifluoride–methanol solution (14% in methanol) is also commercially available from Sigma, B-1252, or equivalent quality.

[2] Wijs' reagent RPE for analysis from Carlo Erba Reference 491902; Wijs' solution from www.sigmaaldrich.com, or equivalent quality.

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

Topic/Question	Contact	Expert Committee
POLYGLYCERYL DIOLEATE	Documentary Standards Support	CE2020 Complex Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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