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Polyoxyl 40 Hydrogenated Castor Oil

Polyethylene glycol 40 hydrogenated castor oil;
Polyoxyethylene 40 hydrogenated castor oil
CAS RN®: 61788-85-0.

DEFINITION

Polyoxyl 40 Hydrogenated Castor Oil contains mainly the trihydroxystearate ester of ethoxylated glycerol, with smaller amounts of polyethylene glycol hydroxystearate and the corresponding free glycols. It results from the reaction of glycerol tri-hydroxystearate with 40–45 mol of ethylene oxide.

IDENTIFICATION

• **A. Identity by Fatty Acid Composition**

Diluent: Chloroform

Standard solution 1: 0.4 mg/mL each of methyl palmitate, methyl arachidate, methyl 12-ketostearate, methyl stearate, and methyl 12-hydroxystearate, from USP Methyl Palmitate RS, methyl arachidate, methyl 12-ketostearate, USP Methyl Stearate RS, and USP Methyl 12-Hydroxystearate RS, in *Diluent*

Standard solution 2: 4 mg/mL each of methyl stearate and methyl 12-hydroxystearate from USP Methyl Stearate RS and USP Methyl 12-Hydroxystearate RS in *Diluent*

Sample solution: Transfer 140 mg of Polyoxyl 40 Hydrogenated Castor Oil to a 10-mL screw-cap test tube, add 3.0 mL of *Diluent*, and mix well. Add 0.5 mL of 0.5 M sodium methoxide in methanol,[1] and mix with the sample. Allow the reaction to proceed at room temperature for 2 h. After 2 h, add 5 mL of water, and mix. Centrifuge the test tube at 2000 × g for 10 min at 4° until a clear organic layer forms. Separate the organic layer, and remove the aqueous layer. Place an aliquot of the organic layer into an autosampler vial.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

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

Temperatures

Injection port: 240°

Detector: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)	Total Time (min)
80	0	80	1	1
80	30	140	0	3
140	20	180	5	10
180	2	250	10	55

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Carrier gas: Hydrogen

Flow rate: 5.0 mL/min, constant flow mode

Injection volume: 1.0 µL

Injection type: Split, split ratio 120:1 or 60:1

Liner: Single gooseneck liner with deactivated glass wool

Run time: 55 min

System suitability

Sample: *Standard solution 1*

[NOTE—For relative retention times, see *Table 2*.]

Table 2

Component	Relative Retention Time
Methyl palmitate (C16:0)	0.27
Methyl stearate (C18:0)	0.37
Methyl arachidate (C20:0)	0.54
Methyl 12-ketostearate	0.85
Methyl 12-hydroxystearate	1.00

Suitability requirements

Resolution: NLT 5 between any two adjacent peaks

Relative standard deviation: NMT 2.0% for the peak area ratio of methyl 12-hydroxystearate to methyl 12-ketostearate

Analysis

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

Calculate the relative response factor, *F*, for methyl 12-hydroxystearate:

$$F = (r_S/r_R) \times (C_R/C_S)$$

r_S = peak area of methyl stearate from *Standard solution 2*

r_R = peak area of methyl 12-hydroxystearate from *Standard solution 2*

C_R = concentration of USP Methyl 12-Hydroxystearate RS in *Standard solution 2* (mg/mL)

C_S = concentration of USP Methyl Stearate RS in *Standard solution 2* (mg/mL)

Correct the peak area of methyl 12-hydroxystearate in the *Sample solution* by multiplying by *F*.

Calculate the percentage of each fatty acid component in the portion of Polyoxyl 40 Hydrogenated Castor Oil taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak area of each individual fatty acid methyl ester except for the uncorrected peak area of methyl 12-hydroxystearate (or the corrected peak area of methyl 12-hydroxystearate), from the *Sample solution*

r_T = sum of all the peak areas, excluding the solvent and methyl 12-hydroxystearate peaks and including the corrected peak area of methyl 12-hydroxystearate, from the *Sample solution*

Acceptance criteria: Polyoxyl 40 Hydrogenated Castor Oil exhibits the composition profile of fatty acids shown in *Table 3*.

Table 3

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Component	Percentage (%)
Palmitic acid (C16:0)	≤4.0
Stearic acid (C18:0)	15.0–25.0
Arachidic acid (C20:0)	≤2.0
12-Ketostearic acid (or 12-oxostearic acid)	≤5.0
12-Hydroxystearic acid	50.0–70.0

• **B. Constituting Fatty Acids**

Sample: 0.1 g

Analysis: Dissolve the *Sample* in 10 mL of alcoholic potassium hydroxide TS, boil for 3 min, and evaporate to dryness. Mix the residue with 5 mL of water.

Acceptance criteria: The residue dissolves, yielding a clear solution. Add a few drops of glacial acetic acid. A white precipitate is formed.

• **C. Indication of Saturation**

Analysis: Proceed as directed in *Fats and Fixed Oils ⟨401⟩, Procedures, Iodine Value*.

Acceptance criteria: NMT 2.0

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.3%

• **Ethylene Oxide and Dioxane ⟨228⟩, *Method I***

Acceptance criteria

Ethylene oxide: NMT 1 µg/g

Dioxane: NMT 10 µg/g

Add the following:

▲• **Limit of Ethylene Glycol and Diethylene Glycol**

Diluent: Acetone

Standard solution: 25 µg/mL of USP Ethylene Glycol RS, 40 µg/mL of USP Diethylene Glycol RS, and 40 µg/mL of USP Butane-1,3-diol RS (internal standard) in *Diluent*

Sample solution: 40 mg/mL of Polyoxyl 40 Hydrogenated Castor Oil and 40 µg/mL of USP Butane-1,3-diol RS (internal standard) in *Diluent*

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 G3[2]

Temperatures

Injection port: 270°

Detector: 290°

Column: See *Table 4*.

Table 4

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	10	60	5
60	10	170	0

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Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
170	15	280	0, 60[a]

[a] Hold time was 0 min for the *Standard solution* and 60 min for the *Sample solution* and *Diluent*.

Carrier gas: Helium

Flow rate: 5.0 mL/min

Injection volume: 1.0 µL

Injection type: Split, split ratio 2:1

Liner: General purpose split/splitless, tapered, glass wool, deactivated

Run time: 26 min for the *Standard solution*; 86 min for the *Sample solution* and *Diluent*

System suitability

Sample: *Standard solution*

[NOTE—See *Table 5* for the relative retention times.]

Table 5

Name	Relative Retention Time
Ethylene glycol	0.45
Butane-1,3-diol (internal standard)	1.00
Diethylene glycol	1.25

Suitability requirements

Resolution: NLT 20 between ethylene glycol and butane-1,3-diol; NLT 20 between butane-1,3-diol and diethylene glycol

Tailing factor: 0.8–1.8 for each of the three peaks assigned to ethylene glycol; butane-1,3-diol; and diethylene glycol

Relative standard deviation: NMT 5.0% for the peak response ratio of the respective glycol (ethylene glycol or diethylene glycol) to the internal standard

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the ethylene glycol or diethylene glycol peaks in the *Sample solution* by comparison with those in the *Standard solution*.

Calculate the content of ethylene glycol or diethylene glycol, in µg/g, in the portion of test substance taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times F$$

R_U = peak response ratio of the respective glycol to the internal standard (peak response of the respective glycol/peak response of the internal standard) from the *Sample solution*

R_S = peak response ratio of the respective glycol to the internal standard (peak response of the respective glycol/peak response of the internal standard) from the *Standard solution*

C_S = concentration of the respective glycol (ethylene glycol or diethylene glycol) in the *Standard solution* (µg/mL)

C_U = concentration of the test substance in the *Sample solution* (mg/mL)

F = conversion factor (1000 mg/g)

Acceptance criteria

Ethylene glycol: NMT 620 µg/g

Diethylene glycol: NMT 1000 µg/g▲ (NF 1-May-2022)

• **LIMIT OF NICKEL**

[**CAUTION—**When using closed high-pressure digestion vessels and laboratory microwave equipment, the safety precautions and operating instructions given by the manufacturer must be followed.]

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[Note—If an alternative apparatus is used, adjustment of the instrument parameters may be necessary.]

Nickel standard stock solution: Dilute nickel standard solution TS two-fold with water. This solution contains the equivalent of 5 µg/mL of nickel.

Standard solutions: Transfer 25, 50, 75, and 100 µL of *Nickel standard stock solution* to four identical 25-mL volumetric flasks. To each flask add 0.5 mL of a 10-mg/mL solution of magnesium nitrate, 0.5 mL of a 100-mg/mL solution of monobasic ammonium phosphate, and 6.0 mL of nickel-free nitric acid. Dilute with water to volume, and mix well. [Note—Content of nickel in the nickel-free nitric acid is NMT 0.005 ppm. The *Standard solutions* contain 0.005, 0.01, 0.015, and 0.02 µg/mL of nickel, respectively.]

Sample solution: Transfer about 250 mg of Polyoxyl 40 Hydrogenated Castor Oil to a suitable high-pressure-resistant digestion vessel (fluoropolymer or quartz glass), and add 6.0 mL of nickel-free 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 to a 25-mL volumetric flask, add 0.5 mL of a 10-mg/mL solution of magnesium nitrate and 0.5 mL of a 100-mg/mL solution of monobasic ammonium phosphate. Dilute with water to volume, and mix well.

Blank solution: Place 6.0 mL of nickel-free nitric acid and 2.0 mL of 30% hydrogen peroxide in a suitable high-pressure-resistant digestion vessel. Prepare as directed in the *Sample solution*, beginning with "Place the closed vessel in a laboratory microwave oven, and digest using an appropriate program (e.g., 1000 W for 40 min)."

Zero solution: In a 50-mL volumetric flask, introduce 1.0 mL of a 10-mg/mL solution of magnesium nitrate, 1.0 mL of a 100-mg/mL solution of monobasic ammonium phosphate, and 12.0 mL of nickel-free nitric acid. Dilute with water to volume, and mix well.

Instrumental conditions

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

Mode: Atomic absorption, equipped with a graphite furnace, a background compensation system, and a coated tube resistant to pyrolysis

Analytical wavelength: 232.0 nm

Lamp: Nickel hollow-cathode

Temperature: Maintain the drying temperature of the furnace at 120° for 35 s after a 5-s ramp; maintain the ashing temperature at 1100° for 10 s after a 30-s ramp; maintain the cooling temperature at 800° for 5 s after a 5-s decrease; and maintain the atomization temperature at 2600° for 7 s. [Note—The temperature program may be modified to obtain optimum furnace temperatures.]

Analysis

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

Concomitantly determine the absorbances of the *Samples* using the *Instrumental conditions*. Use the *Zero solution* to set the instrument to zero. Plot the absorbances of the *Standard solutions* versus the concentration, in µg/mL, of nickel, and draw the straight line best fitting the plotted points. From the graph so obtained, determine the concentration, C_T, in µg/mL, of nickel in the *Sample solution*, and determine the concentration, C_B, in µg/mL, of nickel in the *Blank solution*. If necessary, dilute with the *Zero solution* to obtain a reading within the calibrated absorbance range.

Calculate the quantity, in µg, of nickel in each g of Polyoxyl 40 Hydrogenated Castor Oil taken:

$$\text{Result} = V \times [(C_T - C_B)/W]$$

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

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

C_B = concentration of nickel in the *Blank solution* (µg/mL)

W = weight of Polyoxyl 40 Hydrogenated Castor Oil taken to prepare the *Sample solution* (g)

Acceptance criteria: NMT 20 µg/g

SPECIFIC TESTS

- **Congealing Temperature ⟨651⟩:** 16°–26°
- **Fats and Fixed Oils ⟨401⟩, *Procedures, Acid Value*:** NMT 2.0
- **Fats and Fixed Oils ⟨401⟩, *Procedures, Hydroxyl Value*:** 57–80
- **Fats and Fixed Oils ⟨401⟩, *Procedures, Saponification Value*:** 45–69
- **Water Determination ⟨921⟩, *Method I*:** NMT 3.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, protected from light and moisture. Store at room temperature, and avoid exposure to excessive heat.

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Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

▲ USP Butane-1,3-diol RS
USP Diethylene Glycol RS
USP Ethylene Glycol RS▲ (NF 1-May-2022)
USP Methyl 12-Hydroxystearate RS
USP Methyl Palmitate RS
USP Methyl Stearate RS

[1] 0.5 M sodium methoxide in methanol is available from Sigma-Aldrich (www.sigmaaldrich.com), product #403067. Any other equivalent reagent can be used as well.

[2] The Restek RTX-50 brand column is suitable.

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

Topic/Question	Contact	Expert Committee
POLYOXYL 40 HYDROGENATED CASTOR OIL	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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