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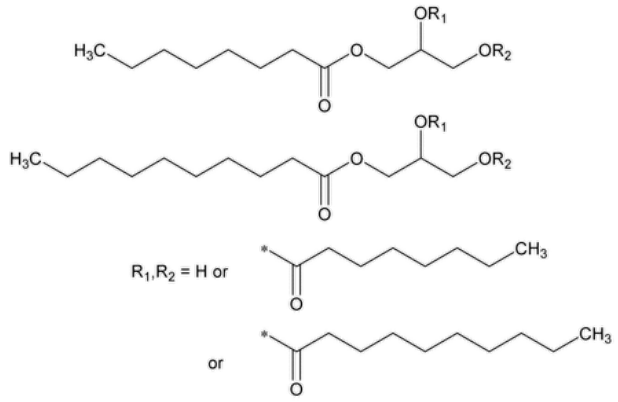
Add the following:

▲Glyceryl Mono and Dicaprylocaprate

(Title for this monograph—not to become official until May 1, 2025) (Prior to May 1, 2025, the current practice of labeling the article of commerce with the name Glyceryl Monocaprylocaprate Type I may be continued. Use of the name Glyceryl Mono and Dicaprylocaprate will be permitted as of May 1, 2020; however, the use of this name will not be mandatory until May 1, 2025. The 60-month extension will provide the time needed by manufacturers and users to make necessary changes.)



Octanoic acid, monoester and diester with 1,2,3-propanetriol and decanoic acid, monoester and diester with 1,2,3-propanetriol;
Caprylic acid monoglyceride and diglyceride and capric acid monoglyceride and diglyceride;
Glyceryl mono and dioctanoate and glyceryl mono and didecanoate;
Glycerides, $C_{8\text{-}10}$ monoglycerides and diglycerides;
$C_{8\text{-}10}$ mono- and diglycerides
CAS RN®: 85536-07-8.

DEFINITION

Glyceryl Mono and Dicaprylocaprate is a mixture of glyceryl monoesters and diesters, mainly mono- and di-*O*-octanoylglycerol and mono- and di-*O*-decanoylglycerol, containing variable quantities of triesters of fatty acids composed predominately of caprylic acid and capric acid. The requirements for monoester, diester, and triester content are: Monoesters: 40.0%–75.0%; Diesters: 20.0%–50.0%; and Triesters: NMT 15.0%.

IDENTIFICATION

• **A. Fatty Acid Composition**

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

Saturated sodium chloride solution: Mix 1 part sodium chloride with 2 parts 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: 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 either by mixing a commercially available ester mixture with methyl caprylate and methyl caprate, or by using USP Methyl Caproate RS, USP Methyl Caprylate RS, USP Methyl Caprate RS, USP Methyl Laurate RS, and USP Methyl Myristate RS. Dissolve a quantity of the prepared ester mixture containing methyl caproate, methyl caprylate, methyl caprate, methyl laurate, and methyl myristate in *n*-heptane to make a solution of about 5.0–9.0 mg/mL for methyl caprylate, 1.0–5.0 mg/mL for methyl caprate, and 0.1–0.3 mg/mL for each of the other methyl esters.

Sample solution: Transfer 100 mg of Glyceryl Mono and Dicaprylocaprate 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 each of 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: 0.53-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 injection; 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 1.3, respectively.]

Suitability requirements

Resolution: NLT 4.0 between 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 for 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—The 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	1.3
12	0	1.6

Carbon-Chain Length	Number of Double Bonds	Relative Retention Times
14	0	1.9

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 of the main component from *Standard solution 3*

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

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

Calculate the percentage of the fatty acid methyl ester by weight in the portion of Glyceryl Mono and Dicaprylocaprate taken:

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

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

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

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

Table 3

Carbon-Chain Length	Number of Double Bonds	Percentage (%, w/w)
6	0	≤3.0
8	0	50.0–90.0
10	0	10.0–50.0
12	0	≤3.0
14	0	≤1.0

- **B. Glyceride Content:** It meets the requirements of the test for *Content of Monoglycerides, Diglycerides, and Triglycerides* in the *Assay*.
- **C. Fats and Fixed Oils ⟨401⟩, *Procedures, Saponification Value*:** 250–280

ASSAY

- **Content of Monoglycerides, Diglycerides, and Triglycerides**

System suitability solution: 20 mg/mL each of 1-monooctanoyl-rac-glycerol and 1-monodecanoyl-rac-glycerol in tetrahydrofuran

Standard solution: 50 mg/mL of USP Glyceryl Mono and Dicaprylocaprate RS in tetrahydrofuran

Sample solution: 50 mg/mL of Glyceryl Mono and Dicaprylocaprate 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 injection; split ratio, 50:1

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The typical relative retention times for monoglycerides, diglycerides, and triglycerides are 1.0–1.2, 1.5–1.9, and 2.0–2.3, respectively, *Standard solution*.]

Suitability requirements

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

Analysis

Samples: *Standard solution* and *Sample solution*

Based on the chromatogram from the *Standard solution*, identify the peaks due to monoglycerides, diglycerides, and triglycerides in the *Sample solution*.

For the calculation of the contents of monoglycerides, diglycerides, and triglycerides, disregard the peaks with retention times less than those of the monoglycerides, which are due to impurities of the solvent and to the free fatty acids.

Calculate the percentage content of free fatty acids (C_A):

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

I_A = acid value for Glyceryl Mono and Dicaprylocaprate, determined from the test for *Acid Value*

F = 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 monoglycerides, diglycerides, or triglycerides in the portion of Glyceryl Mono and Dicaprylocaprate taken:

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

r_U = peak response of the monoglycerides, diglycerides, or 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 above

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

C_G = percentage of free glycerin, determined from the test for *Limit of Free Glycerol*

Acceptance criteria

Monoesters: 40.0%–75.0%

Diesters: 20.0%–50.0%

Triesters: NMT 15.0%

IMPURITIES

• **Total Ash**

Sample: 1.0 g

Analysis: Heat a silica or platinum crucible to redness for 30 min, allow to cool in a desiccator, and weigh. Evenly distribute the *Sample* in the crucible. Dry at 100°–105° for 1 h and ignite to constant weight in a muffle furnace at 600 ± 25°, allowing the crucible to cool in a desiccator after each ignition. Flames should not be produced at any time during the procedure. If after prolonged ignition the ash still contains black particles, take up with hot water, pass through an ashless filter paper, and ignite the residue and the filter paper. Combine the filtrate with the ash, carefully evaporate to dryness, and ignite to constant mass.

Acceptance criteria: NMT 0.5%

• **Limit of Free Glycerol**

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 M 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 Mono and Dicaprylocaprate taken:

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

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

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

N = 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 Mono and Dicaprylocaprate taken for the titration (g)

Acceptance criteria: NMT 3.0%

SPECIFIC TESTS

• **Fats and Fixed Oils** ⟨401⟩, *Procedures, Acid Value*: NMT 3.0

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

• **Water Determination** ⟨921⟩, *Method I, Method Ia*: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at room temperature. Protect from moisture.

• **USP Reference Standards** ⟨11⟩

USP Glyceryl Mono and Dicaprylocaprate RS [Note—May also be labeled as USP Glyceryl Monocaprylocaprate RS (Type I) until May 1, 2025.]
USP Methyl Caprate RS
USP Methyl Caproate RS
USP Methyl Caprylate RS
USP Methyl Laurate RS
USP Methyl Myristate RS▲ (NF 1-May-2020)

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

Topic/Question	Contact	Expert Committee
GLYCERYL MONO AND DICAPRYLOCAPRATE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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