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Medium-Chain Triglycerides

Glycerides, mixed decanoyl and octanoyl;
Caprylic and capric triglycerides.

DEFINITION

Medium-Chain Triglycerides consist of a mixture of triglycerides of saturated fatty acids, mainly of caprylic acid ($C_8H_{16}O_2$) and capric acid ($C_{10}H_{20}O_2$). The fatty acids are derived from the oil extracted from the hard, dried fraction of the endosperm of *Cocos nucifera* L. or from the dried endosperm of *Elaeis guineensis* Jacq. They contain NLT 95% of saturated fatty acids with 8 and 10 carbon atoms.

IDENTIFICATION

Delete the following:

▲• **A.** Meet the requirements in *Specific Tests* for *Fats and Fixed Oils ⟨401⟩, Procedures, Saponification Value*▲ (NF 1-May-2020)

Change to read:

• ▲**A.**▲ (NF 1-May-2020) Meet the requirements in *Specific Tests* for *Fats and Fixed Oils ⟨401⟩, Procedures, Fatty Acid Composition*

IMPURITIES

• **Limit of Chromium, Copper, Lead, and Nickel**

[Note—Use this test for Medium-Chain Triglycerides intended for use in parenteral nutrition.]

Internal standard solution: [Note—Prepare this solution fresh every 6 months.] Transfer 2.0 mL of a solution containing 1000 mg/L of yttrium [Note—Yttrium ICP standard solutions are commercially available.[1]] and 2.0 mL of a solution containing 1000 mg/L of lutetium [Note—Lutetium ICP standard solutions are commercially available.[2]] to a 1000-mL volumetric flask, add 10 mL of 65% ultratrace nitric acid, dilute with water to volume, and mix.

Blank standard: Transfer 1.0 mL of the *Internal standard solution* to a 100-mL volumetric flask, add 10.0 mL of 65% ultratrace nitric acid, dilute with water to volume, and mix.

Standard stock solution: Transfer 1.0 mL each of the solutions containing 1000 mg/L of chromium, copper, lead, and nickel [Note—Single-element ICP standard solutions are commercially available.[3]]to a 100-mL volumetric flask, add 10.0 mL of 65% ultratrace nitric acid, dilute with water to volume, and mix. [Note—Prepare this solution fresh monthly.]Transfer 1.0 mL of this solution to a 100-mL volumetric flask, add 10 mL of 65% ultratrace nitric acid, dilute with water to volume, and mix. The concentration of each element in this solution is 100 µg/L. [Note—Prepare this solution fresh weekly.]

Standard solutions: [Note—Prepare these solutions fresh each time.]

Into two separate 100-mL volumetric flasks, transfer 1.0 mL and 5.0 mL of the *Standard stock solution*, add 1.0 mL of the *Internal standard solution* and 10.0 mL of 65% ultratrace nitric acid, dilute with water to volume, and mix well. The concentration of each element in these solutions is 1 µg/L and 5 µg/L, respectively.

Sample solution: Transfer 3.5 g of Medium-Chain Triglycerides into a suitable quartz flask. Add 5 mL of concentrated sulfuric acid[4] and heat slowly on a hot-plate in a fume hood. At the boiling heat, carefully add 5 mL of 30% hydrogen peroxide[5] in 1-mL increments. Continue heating until the solution is clear and colorless. Otherwise, add another 3 mL of concentrated sulfuric acid and continue to add more 30% hydrogen peroxide. After cooling, cautiously add about 5 mL of water dropwise. Quantitatively transfer the flask's contents into a clean, dry, 20-mL volumetric flask, dilute with water to volume, and mix. Transfer 1.0 mL of digestion solution to a 20-mL volumetric flask, add 0.2 mL of the *Internal standard solution* and 2.0 mL of 65% ultratrace nitric acid, dilute with water to volume, and mix. Retain the remaining digestion solution for use in the test for *Limit of Tin*.

Blank solution: Prepare the blank digestion solution, following the preparation procedure for the *Sample solution*, but without using Medium-Chain Triglycerides.

Instrumental conditions

(See *Plasma Spectrochemistry ⟨730⟩*.)

Mode: ICP–MS

Spectrometer: Quadrupole mass spectrometer

Detector: Ion detector maintained under vacuum

System suitability

Samples: *Blank standard* and *Standard solutions*

Suitability requirements: Instrument performance must be verified to conform to the manufacturer's specifications for resolution and sensitivity. Before analyzing the *Sample solutions*, the instrument must pass a suitable performance check. The instrument should read all isotopes for the following elements shown in *Table 1* for the yttrium internal standard (89 amu) and the lutetium internal standard (175 amu), and should report the total element contents using the isotopes. Generate the calibration curve using the *Blank standard* and *Standard solutions* for each element. The linear regression coefficient is NLT 0.99.

Table 1

Element	Isotope (amu)
Chromium	52
Copper	63
Lead	206
Nickel	58
Tin	118

Analysis

Samples: *Blank solution* and *Sample solution*

Determine the concentration of each element in the *Blank solution* and in the *Sample solution* using the calibration curve. Calculate the quantity, in µg/g, of each element in the portion of Medium-Chain Triglycerides taken:

$$\text{Result} = (C_U - C_B)/C_S$$

C_U = concentration of each element in the *Sample solution* (µg/L)

C_B = concentration of each element in the *Blank solution* (µg/L)

C_S = concentration of Medium-Chain Triglycerides in the *Sample solution* (g/L)

Acceptance criteria: See *Table 2*.

Table 2

Element	Acceptance Criteria, NMT (µg/g)
Chromium	0.05
Copper	0.1
Lead	0.1
Nickel	0.1

• **Limit of Tin**

[Note—Use this test for Medium-Chain Triglycerides intended for use in parenteral nutrition.]

Internal standard solution, Sample solution, Blank solution, Instrumental conditions, System suitability, and **Analysis:** Proceed as directed in the test for *Limit of Chromium, Copper, Lead, and Nickel*.

Blank standard: Transfer 1.0 mL of the *Internal standard solution* to a 100-mL volumetric flask, add 10.0 mL of 30% hydrochloric acid,[6] dilute with water to volume, and mix.

Standard stock solution: Transfer 1.0 mL of a solution containing 1000 mg/L of tin [Note—Single-element ICP standard solutions are commercially available.[7]] to a 100-mL volumetric flask, add 25.0 mL of 30% hydrochloric acid, dilute with water to volume, and mix. [Note—Prepare this solution fresh monthly.] Transfer 1.0 mL of this solution to a 100-mL volumetric flask, add 25.0 mL of 30% hydrochloric acid, dilute with water to volume, and mix. The concentration of tin in this solution is 100 µg/L. [Note—Prepare this solution fresh each time.]

Standard solutions: [Note—Prepare these solutions fresh each time.] Into two separate 100-mL volumetric flasks, transfer 1.0 mL and 5.0 mL of the *Standard stock solution*, add 1.0 mL of the *Internal standard solution* and 25.0 mL of 30% hydrochloric acid, dilute with water to volume, and mix well. The concentration of tin in these solutions is 1 µg/L and 5 µg/L, respectively.

Acceptance criteria: NMT 0.1 µg/g

Change to read:

• **Alkaline Impurities**

Sample solution: Dissolve 2.0 g of Medium-Chain Triglycerides in a mixture of alcohol and ethyl ether (1.5:3.0).

Analysis: Add 0.05 mL of bromophenol blue TS to the *Sample solution*, and titrate with ▲0.01 N hydrochloric acid VS▲ (NF 1-May-2020) to a yellow endpoint.

Acceptance criteria: NMT 0.15 mL of 0.01 N hydrochloric acid ▲VS▲ (NF 1-May-2020) is required.

SPECIFIC TESTS

Delete the following:

▲• **Fats and Fixed Oils** ⟨401⟩, *Procedures, Unsaponifiable Matter*

Sample: 5.0 g

Acceptance criteria: NMT 0.5%▲ (NF 1-May-2020)

• **Specific Gravity** ⟨841⟩**:** 0.93–0.96 at 20°

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

• **Appearance**

Diluent: Hydrochloric acid and water (2.75%:97.25%)

Sample: 10 mL

Standard solution: Prepare immediately before use by mixing 2.4 mL of ferric chloride CS and 0.6 mL of cobaltous chloride CS with *Diluent* to make 10.0 mL, and diluting 5.0 mL of the solution with *Diluent* to make 10.0 mL.

Analysis: Compare the *Sample* and the *Standard solution* by viewing them downward in matched color–comparison tubes against a white surface (see *Color and Achromicity* ⟨631⟩).

Acceptance criteria: The *Sample* is clear and not more intensely colored than the *Standard solution*.

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

• **Fats and Fixed Oils** ⟨401⟩, *Procedures, Fatty Acid Composition***:** The fatty acid fraction of Medium-Chain Triglycerides exhibits the following composition as seen in *Table 3*. Disregard any peak with an area less than 0.05% of the total area.

Table 3

Carbon-Chain Length	Number of Double Bonds	Percentage (%)
6	0	≤2.0
8	0	50.0–80.0
10	0	20.0–50.0
12	0	≤3.0
14	0	≤1.0

• **Fats and Fixed Oils** ⟨401⟩, *Procedures, Hydroxyl Value***:** NMT 10

• **Fats and Fixed Oils** ⟨401⟩, *Procedures, Iodine Value***:** NMT 1.0

• **Fats and Fixed Oils** ⟨401⟩, *Procedures, Peroxide Value***:** NMT 1.0

Delete the following:

▲• **Fats and Fixed Oils** ⟨401⟩, *Procedures, Saponification Value*

Sample: 1.0 g

Acceptance criteria: 310–360▲ (NF 1-May-2020)

• **Viscosity—Capillary Methods** ⟨911⟩

Analysis: Determine at 20 ± 0.1° with a capillary viscometer.

Acceptance criteria: 25–33 mPa · s

Delete the following:

▲• **Refractive Index** ⟨831⟩**:** 1.440–1.452 at 20°▲ (NF 1-May-2020)

• **Articles of Botanical Origin** ⟨561⟩, *Methods of Analysis, Total Ash*

Sample: 2.0 g

Acceptance criteria: NMT 0.1%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, protected from light. Store at temperatures not exceeding 25°.

Change to read:

• **Labeling:** ▲Where Medium-Chain Triglycerides is intended for use in the manufacture of injectable dosage forms or parenteral nutrition therapy, it is so labeled.▲ (NF 1-May-2020)

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[1] A suitable yttrium ICP standard is available from LGC (www.lgcstandards.com) or Millipore Sigma (www.sigmaaldrich.com).

[2] A suitable lutenium ICP standard is available from LGC (www.lgcstandards.com) or Millipore Sigma (www.sigmaaldrich.com).

[3] Suitable single-element ICP standards are available from LGC (www.lgcstandards.com) or Millipore Sigma (www.sigmaaldrich.com).

[4] Suitable ultratrace concentrated sulfuric acid is available from Spectrum Chemicals (www.spectrumchemical.com) or Millipore Sigma (www.sigmaaldrich.com).

[5] Suitable ultratrace 30% hydrogen peroxide is available from Spectrum Chemicals (www.spectrumchemical.com) or Millipore Sigma (www.sigmaaldrich.com).

[6] Suitable ultratrace 30% hydrochloric acid is available from Spectrum Chemicals (www.spectrumchemical.com), Millipore Sigma (www.sigmaaldrich.com), WVR (us.vwr.com/store/) or other vendors.

[7] A suitable tin ICP standard is available from LGC (www.lgcstandards.com) or Millipore Sigma (www.sigmaaldrich.com).

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

Topic/Question	Contact	Expert Committee
MEDIUM-CHAIN TRIGLYCERIDES	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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