

Medium-chain Triglycerides

1 Nonproprietary Names

BP: Medium-chain triglycerides
PhEur: Triglycerida saturata media

2 Synonyms

Bergabest; caprylic/capric triglyceride; *Captex 300*; *Captex 355*; *Crodamol GTC/C*; glyceryl tricaprylate/caprate; *Labrafac CC*; MCT oil; *Miglyol 810*; *Miglyol 812*; *Myritol*; *Neobee M5*; *Nesatol*; oleum neutrale; oleum vegetable tenue; thin vegetable oil; *Waglinol 3/9280*.

3 Chemical Name and CAS Registry Number

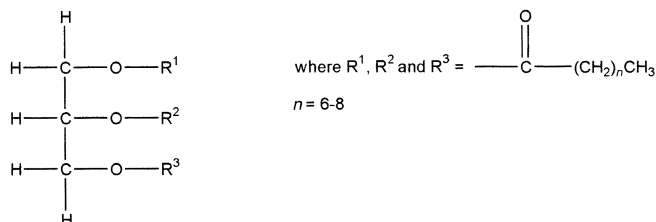
Medium-chain triglycerides [73398-61-5]

4 Empirical Formula Molecular Weight

≈ 500 (average)

The PhEur 2002 (Suppl 4.3) describes medium-chain triglycerides as the fixed oil extracted from the hard, dried fraction of the endosperm of *Cocos nucifera* L. or from the dried endosperm of *Elaeis guineensis* Jacq. They consist of a mixture of triglycerides of saturated fatty acids, mainly of caprylic acid and of capric acid. They contain not less than 95% of saturated fatty acids.

5 Structural Formula



See also Section 4.

6 Functional Category

Emulsifying agent; solvent; suspending agent; therapeutic agent.

7 Applications in Pharmaceutical Formulation or Technology

Medium-chain triglycerides have been used in a variety of pharmaceutical formulations including oral, parenteral, and topical preparations.

In oral formulations, medium-chain triglycerides are used as the base for the preparation of oral emulsions, microemulsions, self-emulsifying systems, solutions, or suspensions of drugs that are unstable or insoluble in aqueous media, e.g., calciferol. Medium-chain triglycerides have also been investigated as intestinal-absorption enhancers⁽¹⁾ and have addition-

ally been used as a filler in capsules and sugar-coated tablets, and as a lubricant or antiadhesion agent in tablets.

In parenteral formulations, medium-chain triglycerides have similarly been used in the production of emulsions, solutions, or suspensions intended for intravenous administration.^(2,3) Medium-chain triglycerides have been particularly investigated for their use in total parenteral nutrition (TPN) regimens in combination with long-chain triglycerides.⁽³⁾

In cosmetics and topical pharmaceutical preparations, medium-chain triglycerides are used as a component of ointments, creams, and liquid emulsions.⁽⁴⁾ In rectal formulations, medium-chain triglycerides have been used in the preparation of suppositories containing labile materials.

Therapeutically, medium-chain triglycerides have been used as nutritional agents.⁽⁵⁾ Diets containing medium-chain triglycerides are used in conditions associated with the malabsorption of fat, such as cystic fibrosis, since medium-chain triglycerides are more readily digested than long-chain triglycerides. Medium-chain triglycerides provide 35 kJ (8.3 kcal) of energy per gram.

Although similar to long-chain triglycerides, medium-chain triglycerides have a number of advantages in pharmaceutical formulations, which include better spreading properties on the skin; no impedance of skin respiration; good penetration properties; good emollient and cosmetic properties; no visible film on the skin surface; good compatibility; good solvent properties; and good stability against oxidation.

8 Description

A colorless to slightly yellowish oily liquid that is practically odorless and tasteless. It solidifies at about 0°C. The oil is free from catalytic residues or the products of cracking.

9 Pharmacopeial Specifications

See Table I.

10 Typical Properties

Acid value:

≤ 0.1 for *Crodamol GTC/C*

≤ 0.1 for *Miglyol 810*

≤ 0.1 for *Miglyol 812*

≤ 0.05 for *Neobee M5*

Cloud point:

≤ 5°C for *Crodamol GTC/C*

≈ 10°C for *Miglyol 810*

≈ 10°C for *Miglyol 812*

Color:

≤ 60 (Hazen color index) for *Crodamol GTC/C*

≤ 90 (Hazen color index) for *Miglyol 810*

≤ 60 (Hazen color index) for *Miglyol 812*

≤ 100 (Hazen color index) for *Neobee M5*

Density:

0.94–0.96 g/cm³ for *Crodamol GTC/C* at 20°C

0.94–0.95 g/cm³ for *Miglyol 810* at 20°C

0.94–0.95 g/cm³ for *Miglyol 812* at 20°C

0.94 g/cm³ for *Neobee M5* at 20°C

Table I: Pharmacopeial specifications for medium-chain triglycerides.

Test	PhEur 2002 (Suppl 4.3)
Identification	+
Characters	+
Appearance	+
Alkaline impurities	+
Relative density	0.93–0.96
Refractive index	1.440–1.452
Viscosity	25–33 mPa s
Acid value	≤0.2
Hydroxyl value	≤10
Iodine value	≤1.0
Peroxide value	≤1.0
Saponification value	310–360
Unsaponifiable matter	≤0.5
Composition of fatty acids	
Caproic acid	≤2.0%
Caprylic acid	50.0–80.0%
Capric acid	20.0–50.0%
Lauric acid	≤3.0%
Myristic acid	≤1.0%
Heavy metals ^(a)	≤10 ppm
Water	≤0.2%
Total ash	≤0.1%
Chromium	≤0.05 ppm
Copper ^(a)	≤0.1 ppm
Lead ^(a)	≤0.1 ppm
Nickel ^(a)	≤0.2 ppm
Tin ^(a)	≤0.1 ppm

^(a) For medium-chain triglycerides intended for use in parenteral nutrition, the test for heavy metals is replaced by the tests for chromium, copper, lead, nickel, and tin.

Freezing point: –5°C for *Neobee M5*

Hydroxyl value: ≤8 for *Neobee M5*

Iodine number:

≤1.0 for *Crodamol GTC/C*

≤0.5 for *Miglyol 810*

≤0.5 for *Miglyol 812*

≤0.5 for *Neobee M5*

Moisture content:

≤0.15% w/w for *Crodamol GTC/C*

≤0.10% w/w for *Miglyol 810*

≤0.10% w/w for *Miglyol 812*

≤0.15% w/w for *Neobee M5*

Peroxide value:

≤1.0 for *Miglyol 810*

≤1.0 for *Miglyol 812*

≤0.5 for *Neobee M5*

Refractive index:

1.4485–1.4500 for *Crodamol GTC/C* at 20°C

1.4485–1.4505 for *Miglyol 810* at 20°C

1.4490–1.4510 for *Miglyol 812* at 20°C

1.4480–1.4510 for *Neobee M5* at 20°C

Saponification value:

325–345 for *Crodamol GTC/C*

335–355 for *Miglyol 810*

325–345 for *Miglyol 812*

335–360 for *Neobee M5*

Solubility: soluble in all proportions at 20°C in acetone, benzene, 2-butanone, carbon tetrachloride, chloroform, dichloromethane, ethanol, ethanol (95%), ether, ethyl acetate, petroleum ether, special petroleum spirit (boiling

range 80–110°C), propan-2-ol, toluene, and xylene. Miscible with long-chain hydrocarbons and triglycerides; practically insoluble in water.

Surface tension:

32.2 mN/m for *Crodamol GTC/C* at 25°C

31.0 mN/m for *Miglyol 810* at 20°C

31.1 mN/m for *Miglyol 812* at 20°C

32.3 mN/m for *Neobee M5* at 25°C

Viscosity (dynamic):

27–30 mPa s (27–30 cP) for *Miglyol 810* at 20°C

28–32 mPa s (28–32 cP) for *Miglyol 812* at 20°C

23 mPa s (23 cP) for *Neobee M5* at 25°C

11 Stability and Storage Conditions

Medium-chain triglycerides are stable over the wide range of storage temperatures that can be experienced in tropical and temperate climates. Ideally, however, they should be stored at temperatures not exceeding 25°C and not exposed to temperatures above 40°C for long periods.

In the preparation of microemulsions and self-emulsifying systems, emulsions, or aqueous suspensions of medium-chain triglycerides, care should be taken to avoid microbiological contamination of the preparation, since lipase-producing microorganisms, which become active in the presence of moisture, can cause hydrolysis of the triglycerides. Hydrolysis of the triglycerides is revealed by the characteristic unpleasant odor of free medium-chain fatty acids.

Medium-chain triglycerides may be sterilized by maintaining at 170°C for 1 hour.

At low temperatures, samples of medium-chain triglycerides may become viscous or solidify. Samples should therefore be well melted and mixed before use, although overheating should be avoided.

Medium-chain triglycerides should be stored protected from light in a well-filled and well-closed container. When stored dry, in sealed containers, medium-chain triglycerides remain stable for many years.

12 Incompatibilities

Preparations containing medium-chain triglycerides should not come into contact with polystyrene containers or packaging components since the plastic rapidly becomes brittle upon contact. Low-density polyethylene should also not be used as a packaging material as the medium-chain triglycerides readily penetrate the plastic, especially at high temperatures, forming an oily film on the outside. High-density polyethylene is a suitable packaging material. Closures based on phenol resins should be tested before use for compatibility with medium-chain triglycerides. Polyvinyl chloride packaging should also be tested for compatibility since medium-chain triglycerides can dissolve some plasticisers, such as phthalates, out of the plastic.

Materials recommended as safe for packaging medium-chain triglycerides are low-density polyethylene, polypropylene, glass, and metal.

13 Method of Manufacture

Medium-chain triglycerides are obtained from the fixed oil extracted from the hard, dried fraction of the endosperm of *Cocos nucifera* L. Hydrolysis of the fixed oil followed by distillation yields the required fatty acids, which are then re-esterified to produce the medium-chain triglycerides.

Although the PhEur 2002 (Suppl 4.3) specifies that medium-chain fatty acids are obtained from coconut oil, medium-chain triglycerides are also to be found in substantial amounts in the kernel oils of certain other types of palm-tree, e.g., palm kernel oil and babassu oil. Some animal products, such as milk-fat, also contain small amounts (up to 4%) of the medium-chain fatty acid esters.

14 Safety

Medium-chain triglycerides are used in a variety of pharmaceutical formulations including oral, parenteral, and topical products and are generally regarded as essentially nontoxic and nonirritant materials.

In acute toxicology studies in animals and humans, no irritant or other adverse reactions have been observed; for example, when they were patch-tested on more than 100 individuals, no irritation was produced on either healthy or eczematous skin. Medium-chain triglycerides are not irritating to the eyes.

Similarly, chronic toxicology studies in animals have shown no harmful adverse effects associated with medium-chain triglycerides following inhalation or intraperitoneal, oral, and parenteral administration.

In humans, administration of 0.5 g/kg body-weight medium-chain triglycerides to healthy individuals produced no change in blood or serum triglycerides compared to subjects receiving the same dose of the long-chain triglyceride triolein.

In patients consuming diets based on medium-chain triglycerides, adverse effects reported include abdominal pain and diarrhea.

LD₅₀ (mouse, IV): 3.7 g/kg
LD₅₀ (mouse, oral): 29.6 g/kg
LD₅₀ (rat, oral): 33.3 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

16 Regulatory Status

GRAS listed. Included in the FDA Inactive Ingredients Guide (topical preparations). Included in nonparenteral and parenteral medicines licensed in Europe.

17 Related Substances

Suppository bases, hard fat.

18 Comments

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19 Specific References

- 1 Swenson ES, Curatolo WJ. Intestinal permeability enhancement for proteins, peptides and other drugs: mechanisms and potential toxicity. *Adv Drug Del Rev* 1992; 8: 39–92.
- 2 Bach A, Guisard D, Metais P, Debry G. Metabolic effects following a short and medium-chain triglycerides load in dogs I: infusion of an emulsion of short and medium-chain triglycerides. *Arch Sci Physiol* 1972; 26: 121–129.
- 3 Hatton J, Record KE, Bivins BA, *et al.* Safety and efficacy of a lipid emulsion containing medium-chain triglycerides. *Clin Pharm* 1990; 9: 366–371.
- 4 Adams U, Neuwald F. Comparative studies of the release of salicylic acid from medium-chain triglyceride gel and paraffin ointment bases: *in vitro* and *in vivo*. *Pharm Ind* 1982; 44: 625–629.
- 5 Ruppin DC, Middleton WRJ. Clinical use of medium-chain triglycerides. *Drugs* 1980; 20: 216–224.

20 General References

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21 Author

MJ Lawrence.

22 Date of Revision

25 October 2002.