
Handbook of
PHARMACEUTICAL
EXCIPIENTS

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Polyoxyethylene Castor Oil Derivatives

1. Nonproprietary Names

Polyoxyethylene castor oil derivatives are a series of materials obtained by reacting varying amounts of ethylene oxide with either castor oil or hydrogenated castor oil. Several different types of material are commercially available the best known being the *Cremophors* (BASF Corporation). Of these, two castor oil derivatives are listed in the USP NF XVII.

USP NF: Polyoxyl 35 castor oil

USP NF: Polyoxyl 40 hydrogenated castor oil

See also Sections 2, 3, 4 and 17.

2. Synonyms

Synonyms applicable to polyoxyethylene castor oil derivatives are shown below. Table I shows synonyms for specific materials.

Arlatone; Cremothon; Mapeg; Marlowet; Simulsol.

3. Chemical Name and CAS Registry Number

Polyethoxylated castor oil [61791-12-6]

4. Empirical Formula Molecular Weight

Polyoxyethylene castor oil derivatives are complex mixtures of various hydrophobic and hydrophilic components.

In polyoxyl 35 castor oil (*Cremophor EL*) the hydrophobic constituents comprise about 83% of the total mixture, the main component being glycerol polyethylene glycol ricinoleate. Other hydrophobic constituents include fatty acid esters of polyethylene glycol along with some unchanged castor oil. The hydrophilic part (17%) consists of polyethylene glycols and glycerol ethoxylates.

In polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*), approximately 75% of the components of the mixture are hydrophobic. These comprise mainly fatty acid esters of glycerol polyethylene glycol and fatty acid esters of polyethylene glycol. The hydrophilic portion consists of polyethylene glycols and glycerol ethoxylates.

5. Structural Formula

See Section 4.

6. Functional Category

Emulsifying agent; solubilizing agent; wetting agent.

7. Applications in Pharmaceutical Formulation or Technology

Polyoxyethylene castor oil derivatives are nonionic surfactants used in oral, topical and parenteral pharmaceutical formulations. They are also used in cosmetics and animal feeds.

Polyoxyl 35 castor oil (*Cremophor EL*) is mainly used as an emulsifying and solubilizing agent, and is particularly suitable for the production of aqueous liquid preparations containing volatile oils, fat-soluble vitamins and other hydrophobic substances.^(1,2) In 1 mL of a 25% v/v aqueous polyoxyl 35 castor oil (*Cremophor EL*) solution it is possible to incorporate: approximately 10 mg of vitamin A palmitate; approximately 10 mg of vitamin D; approximately 120 mg of vitamin E acetate; or approximately 120 mg of vitamin K₁.

To solubilize fat-soluble vitamins, the active ingredient or ingredients should first be dissolved in polyoxyl 35 castor oil (*Cremophor EL*). Water should then be added very slowly with vigorous stirring. As the water is added, the viscosity increases, reaching a maximum at a water content of approximately 40% v/v. Solubilization can be facilitated by heating to approximately 60°C for a short time and in some cases by adding polyethylene glycol and/or propylene glycol. In oral formulations the taste of polyoxyl 35 castor oil (*Cremophor EL*) can be masked by a banana flavor.

Polyoxyl 35 castor oil (*Cremophor EL*) has also been used as a solvent in proprietary injections of diazepam, propanidid and alfaxalone with alfadolone acetate, see Section 14. Polyoxyl 35 castor oil (*Cremophor EL*) is also used in the production of glycerin suppositories.

In veterinary practice, polyoxyl 35 castor oil (*Cremophor EL*) can be used to emulsify cod liver oil, and oils and fats incorporated into animal feeding stuffs.

In cosmetics, polyoxyl 35 castor oil (*Cremophor EL*) is mainly used as a solubilizing agent for perfume bases and volatile oils in vehicles containing 30-50% v/v alcohol (ethanol or propan-2-ol). In hand lotions it can be used to replace castor oil.

Polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*) may be used in preference to polyoxyl 35 castor oil (*Cremophor EL*) in oral formulations since it is almost tasteless. In aqueous

Table I: Synonyms of selected polyoxyethylene castor oil derivatives.

Name	Synonym
Polyoxyl 5 castor oil	<i>Acconon CA-5</i> ; PEG-5 castor oil; polyoxyethylene 5 castor oil.
Polyoxyl 9 castor oil	<i>Acconon CA-9</i> ; castor oil POE-9; PEG-9 castor oil; polyoxyethylene 9 castor oil; <i>Protachem CA-9</i> .
Polyoxyl 15 castor oil	<i>Acconon CA-15</i> ; castor oil POE-15; PEG-15 castor oil; polyoxyethylene 15 castor oil; <i>Protachem CA-15</i> .
Polyoxyl 35 castor oil	<i>Cremophor EL</i> ; <i>Etocas 35</i> ; glycerol polyethyleneglycol ricinoleate; polyethoxylated castor oil; polyoxyethylene 35 castor oil.
Polyoxyl 40 castor oil	Castor oil POE-40; <i>Croduret 40</i> ; <i>Nonionic GR-40</i> ; PEG-40 castor oil; polyoxyethylene 40 castor oil; <i>Protachem CA-40</i> .
Polyoxyl 40 hydrogenated castor oil	<i>Cremophor RH 40</i> ; glycerol polyethyleneglycol oxystearate; hydrogenated castor oil POE-40; PEG-40 hydrogenated castor oil; polyethoxylated hydrogenated castor oil; polyoxyethylene 40 hydrogenated castor oil; <i>Nonionic GRH-40</i> ; <i>Protachem CAH-40</i> .
Polyoxyl 60 hydrogenated castor oil	<i>Cremophor RH 60</i> ; hydrogenated castor oil POE-60; PEG-60 hydrogenated castor oil; polyoxyethylene 60 hydrogenated castor oil; <i>Protachem CAH-60</i> .

alcoholic or completely aqueous solutions, polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*) can be used to solubilize vitamins, essential oils and certain drugs. Using 1 mL of a 25% v/v aqueous solution of polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*) it is possible to solubilize: approximately 88 mg of vitamin A palmitate; approximately 160 mg of vitamin A propionate. Other materials which can be solubilized are: alfadolone; alfaxalone; hexachlorophane; hexetidine; methotrimeprazine; miconazole; propanidid; and thiopentone.

In aerosol vehicles which include water, the addition of polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*) improves the solubility of the propellant in the aqueous phase. This enhancement applies both to dichlorodifluoromethane and to propane/butane mixtures.

Foam formation in aqueous ethanol solutions containing polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*) can be suppressed by the addition of small amounts of polypropylene glycol 2000.

Polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*) is also used as an emulsifier of fatty acids and alcohols.

8. Description

Polyoxyl 35 castor oil (*Cremophor EL*) occurs as a pale yellow, viscous liquid, which is clear at temperatures above 26°C. It has a slight but characteristic odor and can be completely liquefied by heating to 26°C.

Polyoxyl 40 hydrogenated castor oil (*Cremophor RH 40*) occurs as a white, semisolid paste which liquefies at 30°C. It has a very faint characteristic odor and a slight taste in aqueous solution.

Polyoxyl 60 hydrogenated castor oil (*Cremophor RH 60*) occurs as a white paste at room temperature. It has little taste or odor in aqueous solution.

9. Pharmacopeial Specifications

Test	USPNF XVII	
	Polyoxyl 35 castor oil	Polyoxyl 40 hydrogenated castor oil
Identification	+	+
Specific gravity	1.05-1.06	—
Congealing temperature	—	20-30°C
Viscosity at 25°C	650-850 mPa s	—
Water	≤ 3.0%	≤ 3.0%
Residue on ignition	≤ 0.3%	≤ 0.3%
Heavy metals	≤ 0.001%	≤ 0.001%
Acid value	≤ 2.0	≤ 2.0
Hydroxyl value	65-80	60-80
Iodine value	25-35	≤ 2.0
Saponification value	60-75	45-69

10. Typical Properties

See Tables II, III and IV.

Table II: Typical physical properties of selected commercially available polyoxyethylene castor oil derivatives.

Name	Acid value	HLB value	Hydroxyl value	Iodine number	Saponification value	Water content	Melting point (°C)	Solidification point (°C)	Cloud point for a 1% aqueous solution (°C)
Polyoxyl 35 castor oil (<i>Cremophor EL</i>)	≤ 2.0	12-14	65-78	28-32	65-70	≤ 3%	19-20	—	72.5
Polyoxyl 40 hydrogenated castor oil (<i>Cremophor RH 40</i>)	≤ 1.0	14-16	60-80	≤ 1	50-60	≤ 2%	≈ 30	21-23	95.6
Polyoxyl 60 hydrogenated castor oil (<i>Cremophor RH 60</i>)	≤ 1.0	15-17	50-70	≤ 1	40-50	≤ 2%	≈ 40	—	—

Table III: Typical physical properties of selected commercially available polyoxyethylene castor oil derivatives (continued).

Name	Density g/cm ³	pH	Refractive index at 20°C	Surface tension of 0.1% w/v aqueous solution (mN/m)	Viscosity at 25°C (mPa s)	Critical micelle concentration (%)
Polyoxyl 35 castor oil (<i>Cremophor EL</i>)	1.05-1.06	6-8	≈ 1.471	40.9	650-800	≈ 0.009
Polyoxyl 40 hydrogenated castor oil (<i>Cremophor RH 40</i>)	—	6-7	1.453-1.457	43.0	20-40 ^a	≈ 0.039
Polyoxyl 60 hydrogenated castor oil (<i>Cremophor RH 60</i>)	—	6-7	—	—	—	—

a. 30% w/v aqueous solution.

Table IV: Solubility of selected commercially available polyoxyethylene castor oil derivatives.

Name	Solubility						
	Castor oil	Chloroform	Ethanol	Fatty acids	Fatty alcohols	Olive oil	Water
Polyoxyl 35 castor oil (<i>Cremophor EL</i>)	S	S	S	S	S	S	S
Polyoxyl 40 hydrogenated castor oil (<i>Cremophor RH 40</i>)	S	S	S	S	S	S	S
Polyoxyl 60 hydrogenated castor oil (<i>Cremophor RH 60</i>)	S	—	S ^a	S	S	S	S

Key S = Soluble

a. Need to add 0.5-1.0% water to maintain a clear solution.

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