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# Polyoxyl 20 Cetostearyl Ether

## DEFINITION

Polyoxyl 20 Cetostearyl Ether is a mixture of mono-cetostearyl (mixed hexadecyl and octadecyl) ethers of mixed polyoxyethylene diols, the average polymer length being equivalent to NLT 17.2 and NMT 25.0 oxyethylene units.

## IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197F. Use undried specimen.

## IMPURITIES

• **Residue on Ignition ⟨281⟩**

**Sample:** 25 g

**Analysis:** Weigh the *Sample* into a tared 40-mL porcelain crucible, and heat in contact with air until it ignites spontaneously or can be ignited with a glowing splint. Allow the flame to go out, place the crucible in a muffle furnace with the door partly open until the carbon is consumed, close the door, and heat at 700 ± 100° for 1 h. Cool in a desiccator, weigh, and calculate the percentage of residue. If the amount so obtained exceeds 0.4%, heat again until constant weight is attained.

**Acceptance criteria:** NMT 0.4%

• **Free Polyethylene Glycols**

**Sample solution:** Transfer 12 g to a 500-mL separator containing 50 mL of ethyl acetate. Add 50 mL of sodium chloride solution (0.29 g/mL), shake vigorously for 2 min, and allow to separate for 15 min. Drain the lower, aqueous phase into a second 500-mL separator, and extract the upper layer with a second 50-mL portion of sodium chloride solution (0.29 g/mL). To the combined aqueous layers, add 50 mL of ethyl acetate, shake vigorously for 2 min, and allow to separate as before. Drain the lower, aqueous phase into a third 500-mL separator, and extract with two 50-mL portions of chloroform by shaking for 2 min each time.

**Analysis:** Evaporate the combined chloroform extracts in a 150-mL beaker on a steam bath, with the aid of a stream of nitrogen, to apparent dryness. Redissolve in 15 mL of chloroform, and transfer to a filter, collecting the filtrate in a 150-mL beaker. Rinse the funnel with several small portions of chloroform, and evaporate the combined filtrate and rinsings, as described above, until no odor of chloroform or ethyl acetate is perceptible. Cool in a desiccator, and weigh.

**Acceptance criteria:** NMT 7.5%

• **Free Ethylene Oxide**

**Internal standard solution:** 100 mg/mL of *n*-butyl chloride in chlorobenzene. Store in a tightly closed container. Prepare fresh weekly.

**Standard stock solution**

[**Caution—**Ethylene oxide is toxic and flammable. Prepare this solution in a well-ventilated hood, using great care.]

Place 250 mL of chlorobenzene in a glass-stoppered, 500-mL conical flask. Bubble ethylene oxide through the chlorobenzene at a moderate rate for 30 min, insert the stopper, and store with protection from heat. Pipet 25 mL of a 0.5 N alcoholic hydrochloric acid solution, prepared by mixing 45 mL of hydrochloric acid with 1 L of alcohol, into a 500-mL conical flask containing 40 g of magnesium chloride hexahydrate. Shake the mixture to effect saturation. Pipet 10 mL of the ethylene oxide solution into the flask, and add 20 drops of bromocresol green TS. If the solution is not yellow (acid) at this point, add an additional volume of 0.5 N alcoholic hydrochloric acid to give an excess of 10 mL. Record the total volume of 0.5 N alcoholic hydrochloric acid added. Insert the stopper in the flask, and allow to stand for 30 min. Titrate the excess acid with 0.5 N alcoholic potassium hydroxide VS.

Perform a blank titration, using 10.0 mL of chlorobenzene instead of ethylene oxide solution, adding the same total volume of 0.5 N alcoholic hydrochloric acid, and note the difference in volumes required. Each milliliter of the difference in volumes of 0.5 N alcoholic potassium hydroxide consumed is equivalent to 22.02 mg of ethylene oxide. Calculate the concentration, in mg/mL, of ethylene oxide in the *Standard stock solution*. Standardize daily.

**Standard solution:** Transfer 5 g of Polyoxyl 20 Cetostearyl Ether to a suitable glass bottle of 60-mL capacity. Add 10 mL of chlorobenzene, exactly 50 µL of *Internal standard solution*, and a volume of *Standard stock solution* containing 0.5 mg of ethylene oxide. Insert a magnetic

stirring bar, cap the bottle tightly, and stir until homogeneity is attained.

**Sample solution:** Transfer 5 g of Polyoxyl 20 Cetostearyl Ether to a suitable glass bottle of 60-mL capacity. Add 10 mL of chlorobenzene and 50 µL of *Internal standard solution*. Add a volume of chlorobenzene equal to the volume of the *Standard stock solution* added to prepare the *Standard solution*. Insert a magnetic stirring bar, cap the bottle tightly, and stir until homogeneity is attained.

**Interference check solution:** Transfer 5 g of Polyoxyl 20 Cetostearyl Ether to a suitable glass bottle of 60-mL capacity, and add 10 mL of chlorobenzene. Add an additional volume of chlorobenzene equal to the volume of the *Standard stock solution* used to prepare the *Standard solution*. Insert a magnetic stirring bar, cap the bottle tightly, and stir until homogeneity is attained.

**Chromatographic system**

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

**Mode:** GC

**Detector:** Flame ionization

**Column:** 3-mm (OD) × 1.8-m stainless steel packed with S3

**Temperatures**

**Injection port:** 210°

**Detector:** 230°

**Column:** 160°

**Carrier gas:** Helium

**Flow rate:** 66 mL/min

**Injection volume:** 2 µL

**System suitability**

**Samples:** Chlorobenzene, *Internal standard solution*, *Standard stock solution*, and *Interference check solution*

**Interference check:** Inject a suitable volume of chlorobenzene, and allow the chromatogram to run until the solvent has eluted. Similarly inject the *Internal standard solution*, *Standard stock solution*, and *Interference check solution*. No interfering peaks are observed.

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the weight of ethylene oxide in the portion of the sample taken:

$$W_T = (W_E \times W_U \times R_U)/[(W_U \times R_S) - (W_S \times R_U)] \times F$$

$W_E$ = weight of ethylene oxide added to the *Standard solution* (mg)

$W_U$ = weight of Polyoxyl 20 Cetostearyl Ether used to prepare the *Sample solution* (g)

$R_U$ = peak area ratio of ethylene oxide to the internal standard from the *Sample solution*

$R_S$ = peak area ratio of ethylene oxide to the internal standard from the *Standard solution*

$W_S$ = weight of Polyoxyl 20 Cetostearyl Ether used to prepare the *Standard solution* (g)

$F$ = unit conversion, mg to g ($10^{-3}$)

Calculate the percentage of ethylene oxide in the portion of Polyoxyl 20 Cetostearyl Ether taken:

$$\text{Result} = (W_T/W_U) \times 100$$

$W_T$ and $W_U$ are as defined above.

**Acceptance criteria:** NMT 0.01%

**SPECIFIC TESTS**

- **Fats and Fixed Oils ⟨401⟩, *Acid Value*:** NMT 0.5
- **Fats and Fixed Oils ⟨401⟩, *Hydroxyl Value*:** 42–60
- **Fats and Fixed Oils ⟨401⟩, *Saponification Value* :** NMT 2
- **pH ⟨791⟩**

**Sample solution:** 100 mg/mL

**Acceptance criteria:** 4.5–7.5

***Change to read:***

- **Water Determination ⟨921⟩, *Method I*:** ▲NMT 3.0%▲ (NF 1-Dec-2024)

• **Average Polymer Length**

**Sample solution:** Place the Polyoxyl 20 Cetostearyl Ether in a 50° water bath overnight to melt it completely. Shake vigorously to eliminate any possibility of molecular weight gradients within it, and transfer 200 µL to a 5- × 180-mm high-resolution NMR sample tube. Add 200 µL of deuterated chloroform by means of a separate microsyringe. Add 5 drops of tetramethylsilane as an internal reference standard. Cap the tube tightly, and shake thoroughly.

**Analysis:** Place the tube in the NMR spectrometer, and record the NMR spectrum at an appropriate RF power level and a sweep time of 250 s/500 Hz (see *Nuclear Magnetic Resonance Spectroscopy ⟨761⟩, Qualitative and Quantitative NMR Analysis, Qualitative Applications*). Adjust the spectrum amplitude so that the signal at 1.1 ppm is at least 80% of full scale. Record the integral areas, from 0.4 to 2.35 ppm ($A_1$), and from 2.35 to 4.9 ppm ($A_2$), at a sweep time of 50 s/500 Hz at an integral power level such that the integral of the ethylene oxide peak at 3.5 ppm is at least 80% of full chart height. Do not change the power level during the sweep. Record the integral of each peak several times, and calculate the average integral area.

Calculate the number of oxyethylene units per molecule taken:

$$\text{Result} = [(32 \times A_2/A_1) - 3]/4$$

32 = total number of protons in the molecule not activated by oxygen, averaged for the cetyl and stearyl radicals

3 = number of oxygen-activated protons not included in the oxyethylene unit count

4 = number of protons in each oxyethylene unit

**Acceptance criteria:** 17.2–25.0

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, in a cool place.

• **USP Reference Standards ⟨11⟩**

USP Polyoxyl 20 Cetostearyl Ether RS

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| POLYOXYL 20 CETOSTEARYL ETHER | Documentary Standards Support | CE2020 Complex Excipients |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | CE2020 Complex Excipients |

**Chromatographic Database Information:** Chromatographic Database

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