Polyoxyl 20 Cetostearyl Ether

» 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 not less than 17.2 and not more than 25.0 oxyethylene units.

Packaging and storage— Preserve in tight containers, in a cool place.

USP Reference standards ⟨ 11 ⟩ **—** *USP Polyoxyl 20 Cetostearyl Ether RS*.

Identification, *Infrared Absorption* ⟨ 197F ⟩, on undried specimen.

Acid value ⟨ 401 ⟩: not more than 0.5.

Hydroxyl value ⟨ 401 ⟩: between 42 and 60.

Saponification value ⟨ 401 ⟩: not more than 2.

pH ⟨ 791 ⟩: between 4.5 and 7.5, determined in a solution (1 in 10).

Water, *Method I* ⟨ 921 ⟩: not more than 1.0%.

Residue on ignition— Weigh accurately about 25 g 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 hour. Cool in a desiccator, weigh, and calculate the percentage of residue. If the amount so obtained exceeds 0.4%, again heat until constant weight is attained: the limit is 0.4%.

Heavy metals, *Method II* ⟨ 231 ⟩: 0.002%.

Free ethylene oxide—

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

Standard 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 about 30 minutes, insert the stopper, and store protected from heat. Pipet 25 mL of 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, accurately measured, of 0.5 N alcoholic hydrochloric acid to give an excess of about

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 minutes. 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 mL 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 per mL, of ethylene oxide in the *Standard solution*. Standardize daily.

Standard preparation— Transfer about 5 g of *USP Polyoxyl 20 Cetostearyl Ether RS* to a suitable glass bottle of about 60-mL capacity, and add 10 mL of chlorobenzene, exactly 50 µL of *Internal standard solution*, and an accurately measured volume of *Standard solution* containing about 0.5 mg of ethylene oxide. Insert a magnetic stirring bar, cap the bottle tightly, and stir until homogeneity is attained.

Test preparation— Transfer about 5 g of Polyoxyl 20 Cetostearyl Ether, accurately weighed, to a suitable glass bottle of about 60-mL capacity, and add 10 mL of chlorobenzene and 50 µL, accurately measured, of *Internal standard solution*. Insert a magnetic stirring bar, cap the bottle tightly, and stir until homogeneity is attained.

Chromatographic system— Under typical conditions, the instrument is equipped with a flame-ionization detector, and contains a 1.8-m × 3-mm (OD) stainless steel column packed with S3. The injector port and detector block are maintained at about 210° and 230°, respectively, and the column at about 160°. Helium is used as the carrier gas at a flow rate of 66 mL per minute.

Interference check— Inject a suitable volume of chlorobenzene into the gas chromatograph, and allow the chromatogram to run until the solvent has eluted. Similarly inject and chromatograph the *Internal standard solution*, the *Standard solution*, and a solution prepared according to the directions for the *Test preparation*, but omitting the internal standard. No interfering peaks are observed.

Procedure— Inject about 2 µL of the *Standard preparation* into a suitable gas chromatograph, and record the chromatogram. Similarly, inject about 2 µL of the *Test preparation*, and record the chromatogram. Calculate the quantity, in mg, of ethylene oxide in the portion of Polyoxyl 20 Cetostearyl Ether taken by the formula:

$$W_S (R_U / R_S),$$

in which W_S is the weight, in mg, of ethylene oxide in the portion of *Standard solution* taken, and R_U and R_S are the area ratios of ethylene oxide to internal standard in the chromatograms for the *Test preparation* and the *Standard preparation*, respectively. The limit is 0.01%.

Free polyethylene glycols— Transfer about 12 g, accurately weighed, to a 500-mL separator containing 50 mL of ethyl acetate. Add 50 mL of sodium chloride solution (29 in 100), shake vigorously for 2 minutes, and allow to separate for 15 minutes. 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 (29 in 100). To the combined aqueous layers add 50 mL of ethyl acetate, shake vigorously for 2 minutes, 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 minutes each time. 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 about 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: the limit is 7.5%.

Organic volatile impurities, *Method I* ⟨ 467 ⟩ : meets the requirements.

Average polymer length— Place the Polyoxyl 20 Cetostearyl Ether in a 50° water bath overnight, in order 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. Place the tube in the NMR spectrometer, and record the NMR spectrum at an appropriate RF power level and a sweep time of 250 seconds per 500 Hz (see *Qualitative scans* under *Nuclear Magnetic Resonance* ⟨ 761 ⟩). 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 ppm to 2.35 ppm (A_1), and from 2.35 ppm to 4.9 ppm (A_2) at a sweep time of 50 seconds per 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, *n*, per molecule taken by the formula:

$$n = (32A_2 / A_1 - 3) / 4,$$

in which 32 is the total number of protons in the molecule not activated by oxygen, averaged for the cetyl and stearyl radicals, 3 is the number of oxygen-activated protons not included in the oxyethylene unit count, 4 is the number of protons in each oxyethylene unit.

Residual solvents ⟨ 467 ⟩ **:** meets the requirements.
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