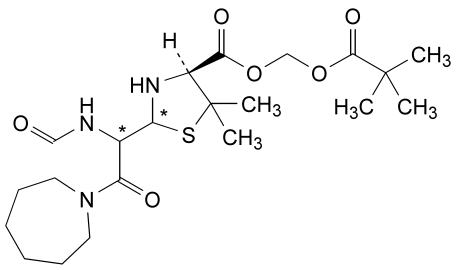


D. methylene 2,2-dimethylpropanoate (4*S*)-2-[1-(formylamino)-2-(hexahydro-1*H*-azepin-1-yl)-2-oxoethyl]-5,5-dimethylthiazolidin-4-carboxylate.

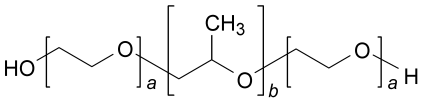
01/2005:1464

POLOXAMERS

Poloxamera

DEFINITION

Synthetic block copolymer of ethylene oxide and propylene oxide, represented by the following general formula:



Poloxamer type	Ethylene oxide units (a)	Propylene oxide units (b)	Content of oxyethylene (per cent)	Average molecular mass
124	10 - 15	18 - 23	44.8 - 48.6	2090 - 2360
188	75 - 85	25 - 30	79.9 - 83.7	7680 - 9510
237	60 - 68	35 - 40	70.5 - 74.3	6840 - 8830
338	137 - 146	42 - 47	81.4 - 84.9	12 700 - 17 400
407	95 - 105	54 - 60	71.5 - 74.9	9840 - 14 600

A suitable antioxidant may be added.

CHARACTERS

Appearance: colourless or almost colourless liquid (poloxamer 124); white or almost white, waxy powder, microbeads or flakes.

Solubility: very soluble in water and in alcohol, practically insoluble in light petroleum (50-70 °C).

mp: about 50 °C for poloxamers 188, 237, 338 and 407.

IDENTIFICATION

First identification: A, B.

Second identification: B, C.

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: chemical reference substance of the Ph. Eur. corresponding to the type of poloxamer to be examined.

B. It complies with the test for average molecular mass (see Tests).

C. It complies with the test for oxypropylene:oxyethylene ratio (see Tests).

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* and dilute to 100 ml with the same solvent.

Appearance of solution. Solution S is not more intensely coloured than reference solution BY_7 (*2.2.2, Method II*).

pH (*2.2.3*): 5.0 to 7.5 for solution S.

Ethylene oxide, propylene oxide and dioxan. Head-space gas chromatography (*2.2.28*).

Ethylene oxide stock solution. Introduce 0.5 g of *ethylene oxide solution R5* in a vial and dilute to 50.0 ml with *dimethyl sulphoxide R1*. Mix carefully.

Ethylene oxide solution. Dilute 1.0 ml of ethylene oxide stock solution to 250 ml with *dimethyl sulphoxide R1*.

Propylene oxide stock solution. Introduce about 7 ml of *methylene chloride R* in a volumetric flask and add 0.500 g (*m*) of *propylene oxide R*. Dilute to 10.0 ml with *methylene chloride R*. Dilute 0.5 ml of this solution to 50.0 ml with *dimethyl sulphoxide R1*. Mix carefully. Calculate the exact concentration of propylene oxide in mg/ml using the following expression:

$$\frac{m \times 1000 \times 0.5}{10 \times 50}$$

Propylene oxide solution. Dilute 1.0 ml of propylene oxide stock solution to 50.0 ml with *dimethyl sulphoxide R1*.

Calculate the exact concentration of propylene oxide in µg/ml using the following expression:

$$\frac{C \times 1000 \times 1}{50}$$

C = concentration of the propylene oxide stock solution in mg/ml.

Dioxan solution. Introduce 0.100 g (*m*) of *dioxan R* in a flask and dilute to 50.0 ml with *dimethyl sulphoxide R1*. Dilute 2.50 ml of this solution to 100.0 ml with *dimethyl sulphoxide R1*.

Calculate the exact concentration of dioxan in µg/ml using the following expression:

$$\frac{m \times 2.50 \times 1000 \times 1000}{50 \times 100}$$

Mixture solution. Dilute a mixture of 6.0 ml of ethylene oxide solution, 6.0 ml of propylene oxide solution and 2.5 ml of dioxan solution to 25.0 ml with *dimethyl sulphoxide R1*.

Test solution. To 1.000 g of the substance to be examined in a head-space vial, add 4.0 ml of *dimethyl sulphoxide R1* and close the vial immediately.

Reference solution. To 1.000 g of the substance to be examined in a head-space vial, add 2.0 ml of *dimethyl sulphoxide R1* and 2.0 ml of the mixture solution. Close the vial immediately.

Column:

- *material*: fused silica,
- *size*: *l* = 50 m, Ø = 0.32 mm,
- *stationary phase*: *poly(dimethyl)(diphenyl)siloxane R* (film thickness 5 µm).

Carrier gas: *helium for chromatography R*.

Flow rate: 1.4 ml/min.

Static head-space conditions:

- *equilibrium temperature*: 110 °C,
- *equilibration time*: 30 min,
- *transfer-line temperature*: 140 °C,
- *pressurisation time*: 1 min,
- *injection time*: 0.05 min.

Temperature:

	Time (min)	Temperature (°C)
	0 - 10	70
Column	10 - 27	70 → 240
Injection port		250
Detector		250

Detection: flame ionisation.

Injection: inject a suitable volume of the gaseous phase, for example 1 ml.

Relative retention with reference to ethylene oxide (retention time = about 6 min): propylene oxide = about 1.3; methylene chloride = about 1.6; dioxan = about 3.0; dimethyl sulphoxide = about 3.7.

Limits:

- *ethylene oxide*: not more than half the area of the corresponding peak in the chromatogram obtained with the reference solution (1 ppm),
- *propylene oxide*: not more than half the area of the corresponding peak in the chromatogram obtained with the reference solution (5 ppm),
- *dioxan*: not more than half the area of the corresponding peak in the chromatogram obtained with the reference solution (10 ppm).

Average molecular mass. Weigh 15 g (*m*) of the substance to be examined into a 250 ml ground-glass-stoppered flask, add 25.0 ml of *phthalic anhydride solution R* and a few glass beads and swirl to dissolve. Boil gently under a reflux condenser for 1 h, allow to cool and add 2 quantities, each of 10 ml, of *pyridine R*, through the condenser. Add 10 ml of *water R*, mix and allow to stand for 10 min. Add 40.0 ml of *0.5 M sodium hydroxide* and 0.5 ml of a 10 g/l solution of *phenolphthalein R* in *pyridine R*. Titrate with *0.5 M sodium hydroxide* to a light pink endpoint that persists for 15 s and record the volume of sodium hydroxide used (*S*). Prepare a blank in the same manner but omitting the substance to be examined. Record the volume of sodium hydroxide used (*B*).

Calculate the average molecular mass using the expression:

$$\frac{4000m}{B-S}$$

Oxypropylene:oxyethylene ratio. Nuclear magnetic resonance spectrometry (*2.2.33*).

Use a 100 g/l solution of the substance to be examined in *deuterated chloroform R*. Record the average area of the doublet appearing at about 1.08 ppm due to the methyl groups of the oxypropylene units (A_1) and the average area of the composite band from 3.2 ppm to 3.8 ppm due to CH_2O groups of both the oxyethylene and oxypropylene units and the CHO groups of the oxypropylene units (A_2) with reference to the internal standard.

Calculate the percentage of oxyethylene, by weight, in the sample being examined using the following expression:

$$\frac{3300\alpha}{33\alpha+58}$$

$$\text{where } \alpha = \frac{A_2}{A_1} - 1$$

Water (*2.5.12*): maximum 1.0 per cent, determined on 1.000 g.

Total ash (*2.4.16*): maximum 0.4 per cent, determined on 1.0 g.

STORAGE

In an airtight container.

LABELLING

The label states:

- the type of poloxamer,
- the name and concentration of any added antioxidant.

01/2005:0733

POLYACRYLATE DISPERSION 30 PER CENT

Polyacrylatis dispersio 30 per centum

DEFINITION

Polyacrylate dispersion 30 per cent is a dispersion in water of a copolymer of ethyl acrylate and methyl methacrylate having a mean relative molecular mass of about 800 000. It may contain a suitable emulsifier. The residue on evaporation is not less than 28.5 per cent *m/m* and not more than 31.5 per cent *m/m*.

CHARACTERS

An opaque, white, slightly viscous liquid, miscible with water, soluble in acetone, in ethanol and in 2-propanol.

IDENTIFICATION

First identification: A.

Second identification: B, C, D, E.

A. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the *Ph. Eur. reference spectrum of polyacrylate.*

B. To 1 g add 5 ml of *water R* and mix; the mixture remains opaque. Take three 1 g portions and mix separately with 5 g each of *ethanol R*, *acetone R* and *2-propanol R*. Transparent solutions are obtained.

C. To 1 g add 10 ml of *0.1 M sodium hydroxide*. The mixture remains opaque.

D. It complies with the test for appearance of a film (see Tests).

E. Dry 4 g in a Petri dish at 60 °C in an oven for 4 h and transfer the resulting clear film to a small test-tube (100 mm × 12 mm). Heat over a flame and collect the fumes that evolve in a second test-tube held over the mouth of the first tube. The condensate gives the reaction of esters (*2.3.1*).

TESTS

Relative density (*2.2.5*): 1.037 to 1.047.

Apparent viscosity. Determine the viscosity (*2.2.10*) using a rotating viscometer at 20 °C. At a shear rate of 10 s^{-1}, the apparent viscosity is not more than 50 mPa·s.

Appearance of a film. Pour 1 ml on a glass plate and allow to dry. A clear elastic film is formed.

Particulate matter. Filter 100.0 g through a tared stainless steel sieve (90). Rinse with *water R* until a clear filtrate is obtained and dry at 80 °C to constant mass. The mass of the residue is not more than 0.500 g.

Residual monomers. Not more than 100 ppm, determined by liquid chromatography (*2.2.29*).

Test solution. Dissolve 1.00 g of the substance to be examined in *tetrahydrofuran R* and dilute to 50.0 ml with the same solvent. To 5.0 ml of a 35 g/l solution of *sodium perchlorate R* add 10.0 ml of the solution dropwise