Polyoxyethylene Alkyl Ethers

1 Nonproprietary Names

The polyoxyethylene alkyl ethers are a series of polyoxyethylene glycol ethers of *n*-alcohols (lauryl, myristyl, cetyl, and stearyl alcohol). Of the large number of different materials commercially available, two types are listed in the USPNF 20, one type in the JP 2001, and four types in the PhEur 2002.

BP: Macrogol cetostearyl ether
Macrogol lauryl ether
Macrogol oleyl ether
Macrogol stearyl ether
JP: Lauromacrogol
PhEur: Macrogoli aether cetostearylicus
Macrogoli aether laurilicum
Macrogoli aether oleicum
Macrogoli aether stearylicus
USPNF: Polyoxyl 20 cetostearyl ether
Polyoxyl 10 oleyl ether

Polyoxyethylene alkyl ethers are employed extensively in cosmetics, where the CTFA names laureth-*N*, myreth-*N*, ceteth-*N*, and steareth-*N* are commonly used. In this nomenclature, *N* is the number of ethylene oxide groups, e.g., steareth-20.
See also Sections 2–5.

2 Synonyms

Polyoxyethylene alkyl ethers are nonionic surfactants produced by the polyethoxylation of linear fatty alcohols. Products tend to be mixtures of polymers of slightly varying molecular weights and the numbers used to describe polymer lengths are average values.

Two systems of nomenclature are used to describe these materials. The number '10' in the name *Texofor A10* refers to the approximate polymer length in oxyethylene units (i.e., *y*, *see* Section 5). The number '1000' in the name 'cetomacrogol 1000' refers to the average molecular weight of the polymer chain.

Synonyms applicable to polyoxyethylene alkyl ethers are shown below.

Brij; *Cremophor A*; *Cyclogol 1000*; *Empilan KB*; *Empilan KM*; *Ethylan C*; macrogol ethers; *Marlowet*; *Plurafac*; *Procol*; *Texofor A*; *Volpo*.

Table I shows synonyms for specific materials.

3 Chemical Name and CAS Registry Number

Polyethylene glycol monocetyl ether [9004-95-9]
Polyethylene glycol monolauryl ether [9002-92-0]
Polyethylene glycol monooleyl ether [9004-98-2]
Polyethylene glycol monostearyl ether [9005-00-9]

4 Empirical Formula Molecular Weight

See Sections 1, 2, and 5.

5 Structural Formula

$CH_3(CH_2)_x(OCH_2CH_2)_yOH$

In the formula, $(x + 1)$ is the number of carbon atoms in the alkyl chain, typically:
12 lauryl (dodecyl)
14 myristyl (tetradecyl)
16 cetyl (hexadecyl)
18 stearyl (octadecyl)
and *y* is the number of ethylene oxide groups in the hydrophilic chain, typically 10–60.

The polyoxyethylene alkyl ethers tend to be mixtures of polymers of slightly varying molecular weights, and the numbers quoted are average values. In cetomacrogol 1000, for example, *x* is 15 or 17, and *y* is 20–24.

6 Functional Category

Emulsifying agent; solubilizing agent; wetting agent.

Table I: Synonyms of selected polyoxyethylene alkyl ethers.

Name	Synonym
Cetomacrogol 1000	Polyethylene glycol 1000; macrocetyl ether; polyoxyethylene glycol 1000; monocetyl ether
Polyoxyl 20 cetostearyl ether	*Atlas G-3713*
Polyoxyl 2 cetyl ether	*Brij 52*; ceteth-2; *Lipocol C-2*; *Procol CA-2*
Polyoxyl 10 cetyl ether	*Brij 56*; ceteth-10; *Lipocol C-10*; *Procol CA-10*
Polyoxyl 20 cetyl ether	*Brij 58*; ceteth-20; *Lipocol C-20.*
Polyoxyl 4 lauryl ether	*Brij 30*; laureth-4; *Lipocol L-4*; *Procol LA-4*; *Tego Alkanol L4*
Polyoxyl 9 lauryl ether	Laureth 9; Lauromacrogol 400; polidocanol
Polyoxyl 23 lauryl ether	*Brij 35*; laureth-23; *Lipocol L-23*; *Procol LA-23*; *Ritox 35*; *Tego Alkanol L23 P*
Polyoxyl 2 oleyl ether	*Brij 92*; *Brij 93*; oleth-2; *Lipocol O-2*; *Procol OA-2*
Polyoxyl 10 oleyl ether	*Brij 96*; *Brij 97*; oleth-10; polyethylene glycol monooleyl ether; *Lipocol O-10*; *Procol OA-10*; *Volpo 10*
Polyoxyl 20 oleyl ether	*Brij 98*; *Brij 99*; *Lipocol O-20*; oleth-20; *Procol OA-20*; *Volpo 20*
Polyoxyl 2 stearyl ether	*Brij 72*; *Lipocol S-2*; *Procol SA-2*; steareth-2; *Tego Alkanol S2*; *Volpo S-2*
Polyoxyl 10 stearyl ether	*Brij 76*; *Lipocol S-10*; *Procol SA-10*; steareth-10; *Tego Alkanol S10*; *Volpo S-10*
Polyoxyl 20 stearyl ether	*Brij 78*; *Lipocol S-20*; *Procol SA-20*; steareth-20; *Tego Alkanol S20 P*; *Volpo S-20*
Polyoxyl 100 stearyl ether	*Brij 700*; steareth-100

7 Applications in Pharmaceutical Formulation or Technology

Polyoxyethylene alkyl ethers are nonionic surfactants widely used in topical pharmaceutical formulations and cosmetics, primarily as emulsifying agents for water-in-oil and oil-in-water emulsions.

Polyoxyethylene alkyl ethers are also used in other applications such as solubilizing agents for essential oils, perfumery chemicals, vitamin oils, and drugs of low-water solubility; gelling and foaming agents (e.g., *Brij 72* gives a quick-breaking foam, while *Brij 97* (and others) gives clear gels at 15–20% concentration); antidusting agents for powders; wetting and dispersing agents for coarse-particle liquid dispersions; and detergents, especially in shampoos and similar cosmetic cleaning preparations.

8 Description

Polyoxyethylene alkyl ethers vary considerably in their physical appearance from liquids, to pastes, to solid waxy substances. They are colorless, white or cream-colored materials with a slight odor.

9 Pharmacopeial Specifications

See Table II.

10 Typical Properties

See Tables III and IV.

11 Stability and Storage Conditions

Polyoxyethylene alkyl ethers are chemically stable in strongly acidic or alkaline conditions. The presence of strong electrolytes may, however, adversely affect the physical stability of emulsions containing polyoxyethylene alkyl ethers.

On storage, polyoxyethylene alkyl ethers can undergo autoxidation, resulting in the formation of peroxides with an increase in acidity. Many commercially available grades are thus supplied with added antioxidants. Typically, a mixture of 0.01% butylated hydroxyanisole and 0.005% citric acid is used for this purpose.

Polyoxyethylene alkyl ethers should be stored in an airtight container, in a cool, dry place.

12 Incompatibilities

Discoloration or precipitation may occur with iodides, mercury salts, phenolic substances, salicylates, sulfonamides, and tannins. Polyoxyethylene alkyl ethers are also incompatible with benzocaine and oxidizable drugs.[1]

The antimicrobial efficacy of some phenolic preservatives, such as the parabens, is reduced owing to hydrogen bonding. Cloud points are similarly depressed by phenols owing to hydrogen bonding between ether oxygen atoms and phenolic hydroxyl groups. Salts, other than nitrates, iodides, and thiocyanates (which cause an increase) can also depress cloud points.[2]

Table II: Pharmacopeial specifications for polyoxyethylene alkyl ethers.

Test	JP 2001	PhEur 2002	PhEur 2002	PhEur 2002 (Suppl 4.1)	PhEur 2002 (Suppl 4.1)	USPNF 20	USPNF 20
	Lauro-macrogol	Macrogol cetostearyl ether	Macrogol stearyl ether	Macrogol lauryl ether	Macrogol oleyl ether	Polyoxyl 20 cetostearyl ether	Polyoxyl 10 oleyl ether
Identification	+	+	+	+	+	+	+
Characters	+	+	+	+	+	—	—
Water	—	≤3.0%	≤3.0%	≤3.0%	≤3.0%	≤1.0%	≤3.0%
pH (10% solution)	—	—	—	—	—	4.5–7.5	—
Alkalinity	—	+	+	+	+	—	—
Acidity	+	—	—	—	—	—	—
Residue on ignition	≤0.20%	—	—	—	—	≤0.4%	≤0.4%
Heavy metals	—	—	—	—	—	≤0.002%	≤0.002%
Acid value	—	≤1.0	≤1.0	≤1.0	≤1.0	≤0.5	≤1.0
Hydroxyl value	—	+	+	+	+	42–60	75–95
Iodine value	—	≤2.0	≤2.0	≤2.0	+	—	23–40
Saponification value	—	≤3.0	≤3.0	≤3.0	≤3.0	≤2.0	≤3.0
Free polyethylene glycols	—	—	—	—	—	≤7.5%	≤7.5%
Free ethylene oxide	—	≤1 ppm	≤1 ppm	≤1 ppm	≤1 ppm	≤0.01%	≤0.01%
Dioxan	—	≤10 ppm	≤10 ppm	≤10 ppm	≤10 ppm	—	—
Peroxide	—	—	—	—	≤10.0	—	—
Average polymer length	—	—	—	—	—	17.2–25.0	8.6–10.4
Organic volatile impurities	—	—	—	—	—	+	+
Total ash	—	≤0.2%	—	≤0.2%	≤0.2%	—	—

Table III: Typical properties of selected commercially available grades of polyoxyethylene alkyl ethers.

Name	Physical form	Acid value	HLB value	Hydroxyl value	Iodine number	Saponification value	Density (g/cm^3) at 20°C	Water content (%)	Melting point or pour point (°C)	Cloud point (°C) for 1% aqueous solution
Brij 30	Liquid	⩽2	9.7	145–165	—	—	≈0.95	⩽1.0	—	—
Brij 35	Solid	⩽5	16.9	40–60	—	—	≈1.05	⩽3.0	33	—
Brij 52	Solid	⩽1	5.3	160–180	—	—	—	⩽1.0	33	—
Brij 56	Solid	⩽1	12.9	75–90	—	—	—	⩽3.0	31	—
Brij 58	Solid	⩽1	15.7	45–60	—	—	—	⩽3.0	38	—
Brij 72	Solid	⩽1	4.9	150–170	—	—	—	⩽1.0	43	—
Brij 76	Solid	⩽1	12.4	75–90	—	—	—	⩽3.0	38	—
Brij 78	Solid	⩽1	15.3	45–60	—	—	—	⩽3.0	38	—
Brij 93	—	⩽1	4.9	160–180	—	—	—	⩽1.0	10	—
Brij 97	—	⩽1	12.4	80–95	—	—	—	⩽3.0	16	—
Brij 99	—	⩽1	15.3	50–65	—	—	—	⩽3.0	33	—
Cremophor A6	—	⩽1	10–12	115–135	⩽1	⩽3	0.896–0.906 at 60°C	⩽1.0	41–43	—
Cremophor A25	—	⩽1	15–17	35–45	⩽1	⩽3	1.020–1.028 at 60°C	⩽1.0	44–46	—
Ethosperse 1A4	—	⩽2	—	145–160	—	—	0.95	⩽0.5	—	—
Ethosperse 1A12	—	⩽2	—	72–82	—	—	1.10	⩽1.0	—	—
Ethosperse TDA6	—	⩽1	—	118–133	—	—	0.98	⩽1.0	—	—
Ethosperse S120	—	⩽0.5	—	385–430	—	—	1.16	⩽1.0	—	—
Ethosperse G26	—	⩽2	—	133–142	—	—	1.12 at 38°C	⩽0.5	—	—
Ethylan D252	Liquid	—	5.6	—	—	—	0.903	⩽0.5	5	Insoluble
Ethylan 253	Liquid	—	7.8	—	—	—	0.930	⩽0.5	3	Insoluble
Ethylan 254	Liquid	—	9.8	—	—	—	0.948	⩽3.0	5	Insoluble
Ethylan 256	Liquid	—	11.4	—	—	—	0.972	⩽0.5	15	43
Ethylan 257	Liquid	—	12.2	—	—	—	0.974 at 40°C	⩽0.5	21	49
Ethylan 2512	Solid	—	14.2	—	—	—	1.001	⩽0.5	29	92
Ethylan 2560	Solid	—	18.6	—	—	—	—	⩽0.5	45	>100
Plurafac RA20	—	—	—	69–78	—	0.9965	⩽0.1	4	—	
Plurafac RA30	—	—	—	85–95	—	—	0.976	⩽0.1	–6	—
Plurafac RA40	—	—	—	65–75	—	—	0.978	⩽0.2	–27	—
Plurafac RA340	—	—	—	73	—	—	0.977	—	–23	—
Renex 30	Cloudy liquid	⩽1	14.5	75–85	—	—	1.0	⩽3.0	14	18.4
Renex 31	—	⩽1	15.4	60–74	—	—	1.0	⩽3.0	16	99
Renex 36	—	⩽1	11.4	118–133	—	—	1.0	⩽1.0	—	<32
Texofor A1P	Solid	—	16.2	—	—	—	1.025 at 60°C	—	40	>100
Texofor AP	—	—	—	—	—	—	0.875	—	31	Insoluble
Texofor A6	Solid	—	—	—	—	—	0.140	—	26	Insoluble
Texofor A10	Solid	—	—	—	—	—	0.970	—	30	75
Texofor A14	Solid	—	—	—	—	—	0.995	—	35	100
Texofor A30	Solid	—	—	—	—	—	1.035	—	43	>100
Texofor A45	Solid	—	—	—	—	—	1.055	—	47	>100
Texofor A60	Solid	—	—	—	—	—	1.065	—	48	>100
Volpo 10	Hazy liquid	<2	—	79–91	31–37	—	—	<1.0	—	>55
Volpo 20	Soft solid	<2	—	50–58	18–25	—	—	<1.0	—	>100
Volpo S-2	Soft solid	<1	—	150–170	—	—	—	<1.0	—	—
Volpo S-10	Soft solid	<1	—	75–90	—	—	—	<3.0	—	—
Volpo S-120	Waxy solid	<1	—	45–60	—	—	—	<3.0	—	—

Table IV: Typical properties of selected commercially available grades of polyoxyethylene alkyl ethers.

Name	Critical micelle concentration (%)	Surface tension of aqueous solution at 20°C (mN/m)			Dynamic viscosity at 25°C or pour point (mPa s)	Refractive index at 60°C	Solubility			
		(0.05%)	(0.1%)	(0.2%)			Ethanol	Fixed oils	Propylene glycol	Water
Brij 30	—	—	—	—	30	—	S	S	S	I
Brij 35	0.013	—	—	—	—	—	S	I	S	S
Brij 52	—	—	—	—	—	—	S	S	I	I
Brij 56	—	—	—	—	—	—	S	I	I	I
Brij 58	—	—	—	—	—	—	S	I	I	S
Brij 72	—	—	—	—	—	—	S	S	I	I
Brij 76	—	—	—	—	—	—	S	I	S	I
Brij 78	—	—	—	—	—	—	S	I	I	I
Brij 93	—	—	—	—	30	—	S	S	S	I
Brij 97	—	—	—	—	100	—	S	I	I	S
Brij 99	—	—	—	—	—	—	S	I	S	S
Cremophor A6	—	—	—	—	—	1.4420–1.4424	S	I	—	S
Cremophor A25	—	—	—	—	—	1.4512–1.4520	S	I	—	S
Ethosperse 1A4	—	—	—	—	30	—	S	S	—	S
Ethosperse 1A12	—	—	—	—	1000	—	S	SH	—	S
Ethosperse TDA6	—	—	—	—	80	—	S	I	—	D
Ethosperse S120	—	—	—	—	460	—	S	I	—	S
Ethosperse G26	—	—	—	—	150 at 38°C	—	S	I	—	S
Ethylan D252	—	—	—	—	—	—	—	—	—	I
Ethylan 253	—	—	—	—	—	—	—	—	—	I
Ethylan 254	—	—	—	—	—	—	—	—	—	I
Ethylan 256	—	—	—	—	—	—	—	—	—	S
Ethylan 257	—	—	—	—	—	—	—	—	—	S
Ethylan 2512	—	—	—	—	—	—	—	—	—	S
Ethylan 2560	—	—	—	—	—	—	—	—	—	S
Plurafac RA20	—	—	30.7	—	—	—	—	—	—	—
Plurafac RA30	—	—	28.6	—	—	—	—	—	—	—
Plurafac RA40	—	—	30.3	—	—	—	—	—	—	—
Plurafac RA340	—	—	30.5	—	—	—	—	—	—	—
Renex 30	—	—	—	—	60	—	S	I	—	S
Renex 31	—	—	—	—	130	—	S	I	—	S
Renex 36	—	—	—	—	80	—	S	I	—	D
Texofor A1P	0.006	42.9	—	42.3	—	—	S	—	—	S
Texofor AP	—	—	—	—	—	—	S	—	—	I
Texofor A6	—	—	—	—	—	—	S	—	—	I
Texofor A10	0.004	36.5	—	36.7	—	—	S	—	—	S
Texofor A14	—	36.9	—	36.6	—	—	S	—	—	S
Texofor A30	0.003	46.0	—	46.0	—	—	S	—	—	S
Texofor A45	0.004	47.5	—	47.0	—	—	S	—	—	S
Texofor A60	0.003	48.3	—	48.3	—	—	S	—	—	S

S = Soluble; I = Insoluble; D = Dispersible; SH = Soluble on heating.

Suppliers: ICI Surfactants (*Brij*).

13 Method of Manufacture

Polyoxyethylene alkyl ethers are prepared by the condensation of linear fatty alcohols with ethylene oxide. The reaction is controlled so that the required ether is formed with the polyethylene glycol of the desired molecular weight.

14 Safety

Polyoxyethylene alkyl ethers are used as nonionic surfactants in a variety of topical pharmaceutical formulations and cosmetics. The polyoxyethylene alkyl ethers form a series of materials with varying physical properties and manufacturers' literature should be consulted for information on the applications and safety of specific materials.

Although generally regarded as essentially nontoxic and nonirritant materials, some polyoxyethylene alkyl ethers, particularly when used in high concentration (>20%), appear to have a greater irritant potential than others.

Animal toxicity studies suggest that polyoxyethylene alkyl ethers have a similar oral toxicity to other surfactants and can be regarded as being moderately toxic. In rats, the oral LD_{50} values range from about 2–4 g/kg body-weight.

Polyoxyl 10 oleyl ether

LD_{50} (rat, oral): 2.7 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection and gloves are recommended.

16 Regulatory Status

Included in nonparenteral medicines licensed in the USA and UK.

17 Related Substances

Nonionic emulsifying wax.

18 Comments

Many other polyoxyethylene ethers, such as diethers and polyethers, are commercially available and are also used as surfactants. In addition to their surfactant properties, the series of polyoxyethylene ethers with lauryl side chains, e.g., nonoxynol 10, are also widely used as spermicides.

19 Specific References

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