

# Nonionic Surfactants

A surfactant is a compound that can reduce the interfacial tension between 2 immiscible phases. This is because the molecule contains 2 localised regions, one hydrophilic in nature and the other hydrophobic. Nonionic surfactants differ from anionic surfactants (p.2138) by the absence of charge on, or ionisation of, the molecule; they are generally less irritant than anionic or cationic surfactants.

Hydrophilic groups include the oxyethylene group ( $-O.CH_2.CH_2-$ ) and the hydroxyl group ( $-OH$ ). By varying the number of these groups in a hydrophobic molecule, such as a fatty acid, substances are obtained that range from strongly hydrophobic and water-insoluble compounds, such as glyceryl monostearate, to strongly hydrophilic and water-soluble compounds, such as the macrogols. These 2 extreme types are not satisfactory as emulsifying agents, though they are useful stabilisers in the presence of efficient emulsifying agents. Between these extremes are the nonionic emulsifying agents in which the proportions of hydrophilic and hydrophobic groups are more evenly balanced; these include some of the macrogol esters and ethers, and sorbitan derivatives. Nonionic surfactants may be classified according to their *hydrophilic-lipophilic balance* (HLB). This is an arbitrary scale of values denoting the relative affinity of the surfactant for oil and water. Lipophilic surfactants have low HLB values (less than 10) and are generally used as antifoaming agents, water-in-oil emulsifying agents, and as wetting agents; hydrophilic surfactants have higher HLB values (greater than 10) and are generally used as oil-in-water emulsifying agents and solubilising agents.

Nonionic surfactants also have applications in the food, cosmetic, paint, pesticide, and textile industries as well as being used as oil slick dispersants. Some macrogol ethers such as nonoxinol 9 are used as spermicides.

By virtue of the processes used in their manufacture, nonionic surfactants are usually mixtures of related compounds; the properties of a particular material may vary from one manufacturer to another and there may be variation in batches from an individual source. Since nonionic surfactants do not ionise to any great extent in solution, they are generally compatible with both anionic and cationic substances, but they reduce the antimicrobial action of many preservatives.

The range of nonionic surfactants used in pharmaceutical practice is large and their classification can be varied and complex. The principal groups of nonionic surfactants are outlined below.

**Glycol and glycerol esters** are a group of nonionic surfactants consisting of fatty acid esters of glycols and glycerol. Hydrophobic properties predominate and these compounds are poor emulsifying agents if used alone, though they are useful stabilisers for both oil-in-water and water-in-oil emulsions. If a small amount of soap, sulfated fatty alcohol, or other surfactant is added to the esters, a 'self-emulsifying' product is formed, which is capable of producing satisfactory oil-in-water emulsions. **Acetoglycerides** are mixed glyceryl esters in which the glycerol is esterified partly with a fatty acid and partly with acetic acid.

**Macrogol esters** are polyoxyethylene esters of fatty acids, mainly stearates. The hydrophilic properties of the oxyethylene group are weaker than those of the hydroxyl group but by introducing a sufficient number into a fatty acid molecule, substances are produced in which the hydrophilic and hydrophobic properties are sufficiently well balanced for the esters to act as efficient oil-in-water emulsifying agents. They may also be used as wetting and solubilising agents. Since the ester linkage is prone to hydrolysis, these compounds are less resistant to acids and alkalis than the macrogol ethers.

**Macrogol ethers** are condensation products prepared by reaction between fatty alcohols or alkylphenols and ethylene oxide. The ether linkage confers good stability to acids and alkalis. Macrogol ethers are widely used in the preparation of oil-in-water emulsions and as wetting and solubilising agents.

**Sorbitan derivatives** are derivatives of the cyclic mono- or di-anhydrides of sorbitol. They consist of *sorbitan esters*, which are prepared by esterification of one or more of the hydroxyl groups in the anhydrides with a fatty acid such as stearic, palmitic, oleic, or lauric acid, and *polysorbates*, which are polyoxyethylene derivatives of the sorbitan esters. Sorbitan esters are oil-soluble, water-dispersible, nonionic surfactants and are effective water-in-oil emulsifiers. Polysorbates are more hydrophilic, water-soluble compounds and are used as oil-in-water emulsifying agents. By varying the number of oxyethylene groups in the molecule, and the type of fatty acid in the sorbitan ester, surfactants with a wide range of properties may be obtained.

**Poloxamers** are copolymers of polyoxyethylene and polyoxypropylene. They are used as oil-in-water emulsifiers and as solubilising and wetting agents in pharmaceutical preparations intended for internal use.

Other nonionic compounds with surface activity such as the higher fatty alcohols are covered in the chapter on Paraffins and Similar Bases (p.2028).

## Diacetylated Monoglycerides

Monoglicéridos diacetilados.

Моноглицериды Диацетилированные

**Pharmacopoeias.** In *USNF*.

**USNF 26** (Diacetylated Monoglycerides). Consists of glycerol esterified with edible fat-forming fatty acids and acetic acid. A clear liquid. Very soluble in alcohol 80%, in vegetable oils, and in mineral oils; sparingly soluble in alcohol 70%. Store in airtight containers. Protect from light.

### Profile

Diacetylated monoglycerides have been used as plasticisers, pharmaceutical excipients, and food additives.

## Diethylene Glycol Monopalmitostearate

Diethylene Glycol Monostearate; Diéthylène Glycol (Stéarate de); Diéthylèneglycol, palmitostéarate de; Diéthylenglycoli Monopalmitostearas; Diéthylenglycoli palmitostearas; Diéthylenglykol monopalmitostearát; Diéthylenglykol palmito stearát; Diéthyleni Glycoli Stearas; Diethylenglicol, monopalmitoestearato de; Diethylenglikolio palmitostearatas; Diethylenglikol-monopalmitát és monosztearát; Diethylene glykolipalmitostearaatti; Diethylenglykolpalmitostearat; Diglycol Stearate.

Диэтиленгликоля Монопальмитостеарат

CAS — 106-11-6 (diethylene glycol monostearate); 36381-62-1 (diethylene glycol monopalmitate).

**Pharmacopoeias.** In *Eur.* (see p.vii). *USNF* includes Diethylene Glycol Stearates.

**Ph. Eur. 6.2** (Diethylene Glycol Palmitostearate). A mixture of diethylene glycol mono- and di-esters of stearic and palmitic acids produced by esterification of diethylene glycol and stearic acid of vegetable or animal origin. It contains 45.0 to 60.0% of monoesters and 35.0 to 55.0% of diesters, and a maximum of 2.5% of free diethylene glycol. A white or almost white, waxy solid. Practically insoluble in water; soluble in hot alcohol and in acetone. M.p. 43° to 50°. Protect from light.

**USNF 26** (Diethylene Glycol Stearates). A mixture of diethylene glycol mono- and di-esters of stearic and palmitic acids. It contains not less than 45.0% of monoesters produced from the condensation of ethylene glycol and stearic acid of vegetable or animal origin. A white or almost white, waxy solid. Practically insoluble in water; soluble in hot alcohol and in acetone. M.p. 43° to 50°. Store in airtight containers.

### Profile

Diethylene glycol monopalmitostearate has similar properties and uses to glyceryl monostearate or self-emulsifying glyceryl monostearate (p.1915). Diethylene glycol monolaurate and mono-oleate have also been used.

## Ethylene Glycol Monopalmitostearate

Ethylene Glycol Monostearate; Ethylene Glycol Stearate; Éthylène Glycol (Stéarate d'); Éthylèneglycol, monopalmitostéarate d'; Ethylèneglycoli Monopalmitostearas; Ethylenglycoli monopalmitostearas; Ethylenglycoli Monostearas; Ethylenglykol-monopalmitostearát; Ethyleni Glycoli Stearas; Etilenglicol, monopalmitoestearato de; Etilenglikolio monopalmitostearatas; Etilénglikol-monopalmitát és monosztearát; Etyleniglykolmonopalmitostearaatti; Etylenglykolmonopalmitostearat.

Этиленгликоля Монопальмитостеарат

CAS — 111-60-4 (ethylene glycol monostearate); 4219-49-2 (ethylene glycol monopalmitate).

**Pharmacopoeias.** In *Eur.* (see p.vii). *USNF* includes Ethylene Glycol Stearates.

**Ph. Eur. 6.2** (Ethylene Glycol Monopalmitostearate). A mixture of ethylene glycol mono- and di-esters of stearic and palmitic acids. It contains not less than 50% of monoesters produced from the condensation of ethylene glycol and stearic acid and not more than 5% of free ethylene glycol. A white or almost white, waxy solid. Practically insoluble in water; soluble in hot alcohol and in acetone. M.p. 54° to 60°. Protect from light.

**USNF 26** (Ethylene Glycol Stearates). A mixture of ethylene glycol mono- and di-esters of stearic and palmitic acids. It contains not less than 50% of monoesters produced from the condensation of ethylene glycol and stearic acid of vegetable or animal origin. A white or almost white, waxy solid. Practically insoluble in water; soluble in hot alcohol and in acetone. M.p. 54° to 60°. Store in airtight containers.

### Profile

Ethylene glycol monopalmitostearate has similar properties and uses to glyceryl monostearate or self-emulsifying glyceryl monostearate (p.1915). Ethylene glycol monolaurate and mono-oleate have also been used.

## Glycerol Behenate

Glicerol, behenato de.

Глицерил Бегенат

**Pharmacopoeias.** In *USNF. Eur.* (see p.vii) includes Glycerol Dibehenate.

**Ph. Eur. 6.2** (Glycerol Dibehenate; Glyceroli Dibehenas). A mixture of diacylglycerols, mainly dibehenoylglycerol, together with variable quantities of mono- and triacylglycerols. It contains 15 to 23% of monoacylglycerols, 40 to 60% of diacylglycerols, and 21 to 35% of triacylglycerols, obtained by esterification of glycerol and behenic acid. A hard, waxy mass or powder or white or almost white, unctuous flakes. Practically insoluble in water; partly soluble in hot alcohol; soluble in dichloromethane. M.p. 65° to 77°.

**USNF 26** (Glycerol Behenate). A mixture of glycerides of fatty acids, mainly behenic acid. A fine powder with a faint odour. M.p. about 70°. Practically insoluble in water and in alcohol; soluble in chloroform. Store in airtight containers at a temperature not exceeding 35°.

### Profile

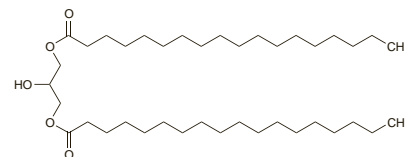
Glycerol behenate is used as a lubricant and binder in tablet-making.

## Glycerol Distearate

Glicerín-disztearát; Glicerol, diestearato de; Glicerolio distearatas; Glycerol Distearate; Glicérol, distéarate de; Glyceroldistearat; Glycerol-distearát; Glyceroli distearas; Glyceroldistearaatti.

Глицерилдистеарат

CAS — 1323-83-7.



**Pharmacopoeias.** In *Eur.* (see p.vii). Also in *USNF*.

**Ph. Eur. 6.2** (Glycerol Distearate). A mixture of diacylglycerols, mainly distearoylglycerol, together with variable quantities of mono- and triacylglycerols. It contains 8 to 22% of monoacylglycerols, 40 to 60% of diacylglycerols, and 25 to 35% of triacylglycerols, obtained by partial glycerolysis of vegetable oils containing triacylglycerols of palmitic or stearic acid or by esterification of glycerol with stearic acid. The fatty acids may be of vegetable or animal origin.