

Technical Information

March 2012
Supersedes issue dated December 2011

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WF-No. 118491

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Kolliphor™ HS 15

Macrogol 15 Hydroxystearate Ph. Eur.
Polyoxyl 15 Hydroxystearate USP

(former Tradename Solutol HS 15)

A nonionic solubilizer

Generic name	Macrogol 15 Hydroxystearate, Polyoxyl 15 Hydroxystearate
Chemical nature	Kolliphor HS 15 is a nonionic solubilizer and emulsifying agent obtained by reacting 15 moles of ethylene oxide with 1 mole of 12-hydroxy stearic acid.
Description	<p>Kolliphor HS 15 is a yellowish white paste at room temperature that becomes liquid at approx. 30 °C.</p> <p>The hydrophilic-lipophilic balance lies between 14 and 16.</p> <p>The critical micelle concentration (CMC) lies between 0.005 and 0.02%.</p>
Specification	<p>See separate document: "Standard Specification (not for regulatory purposes)" available via BASF's WorldAccount: https://worldaccount.basf.com (registered access).</p> <p>Unless otherwise stated, the determination methods have been taken from the current European Pharmacopoeia.</p>
Composition	<p>Kolliphor HS 15 consists of polyglycol mono- and di-esters of 12-hydroxystearic acid (= lipophilic part) and of about 30% of free polyethylene glycol (= hydrophilic part). The free polyethylene glycol can be determined by HPLC. The method is available on request.</p> <p>The main components of the lipophilic part have the following chemical structures:</p> <div style="border: 1px solid black; padding: 10px; margin: 10px 0;"> </div>
Solubility	<p>Kolliphor HS 15 is soluble in water, ethanol and 2-propanol to form clear solutions.</p> <p>Its solubility in water decreases with increasing temperature. It is insoluble in liquid paraffin.</p>

Stability

Kolliphor HS 15 has high chemical stability. The prolonged action of heat may induce physical separation into a liquid and a solid phase after cooling, which can be reversed by subsequent homogenization.

Kolliphor HS 15 is stable for at least 24 months if stored in the unopened original containers at room temperature (max. 25 °C).

Aqueous solutions of Kolliphor HS 15 can be sterilized by heating them to 121 °C. The pH may drop slightly during heating and this should be taken into account. Separation into phases may also occur here, but this can be reversed by agitating the hot solution.

Aqueous solutions can be stabilized with the usual preservatives used in pharmaceuticals.

Recommendations for product handling and sampling

For proper product handling and sampling homogenization of the drum content is necessary. The new drums allow the repeated liquefaction of their content at around 60 °C. It is recommended to use electrical drum heaters, heating covers or a heating chamber.

Regulatory status

Meets current "Macrogol 15 Hydroxystearate" Ph. Eur. and "Polyoxyl 15 Hydroxystearate" USP monographs.

A CEP was already issued. For further information see the EDQM homepage.

Applications

Please note:

Prior to sampling, filling or processing part of the contents of a drum, the contents must be homogenised. This is done by completely melting the product and stirring it.

The product is used for manufacturing aqueous parenteral preparations with vitamins A, D, E and K, and a number of other lipophilic pharmaceutical active agents, such as

Propanidid, Nifedipine,
Miconazole, Piroxicam.
Alfadolone,
Alfaxalone,

The graphs overleaf show the amount of solubilizer required over a range of concentrations of vitamins A palmitate, A propionate, E acetate and K₁.

The procedure is described below for vitamin A palmitate, as an example.

Vitamin A palmitate 1.7 million I. U./g	8.3 g
Kolliphor HS 15	25.0 g
Water, dist.	ad 100.0 ml

Mix the vitamin with Kolliphor HS 15 and heat the mixture to 60 – 65 °C. Heat the water to the same temperature and stir it thoroughly into the mixture. Thickening occurs initially due to hydration and reaches a maximum when half of the water has been added. The viscosity decreases as more water is added.

If the first half of the water is added too quickly, the solution may turn cloudy.

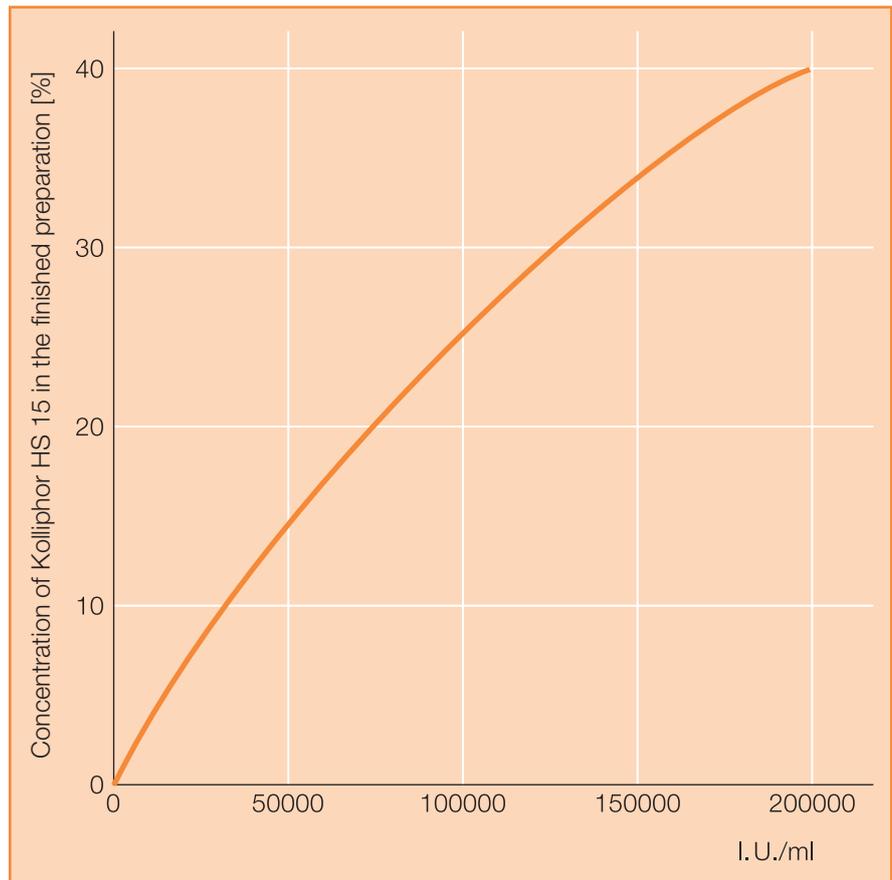


Fig. 1: Solubilization of vitamin A palmitate 1.7 million I. U./g

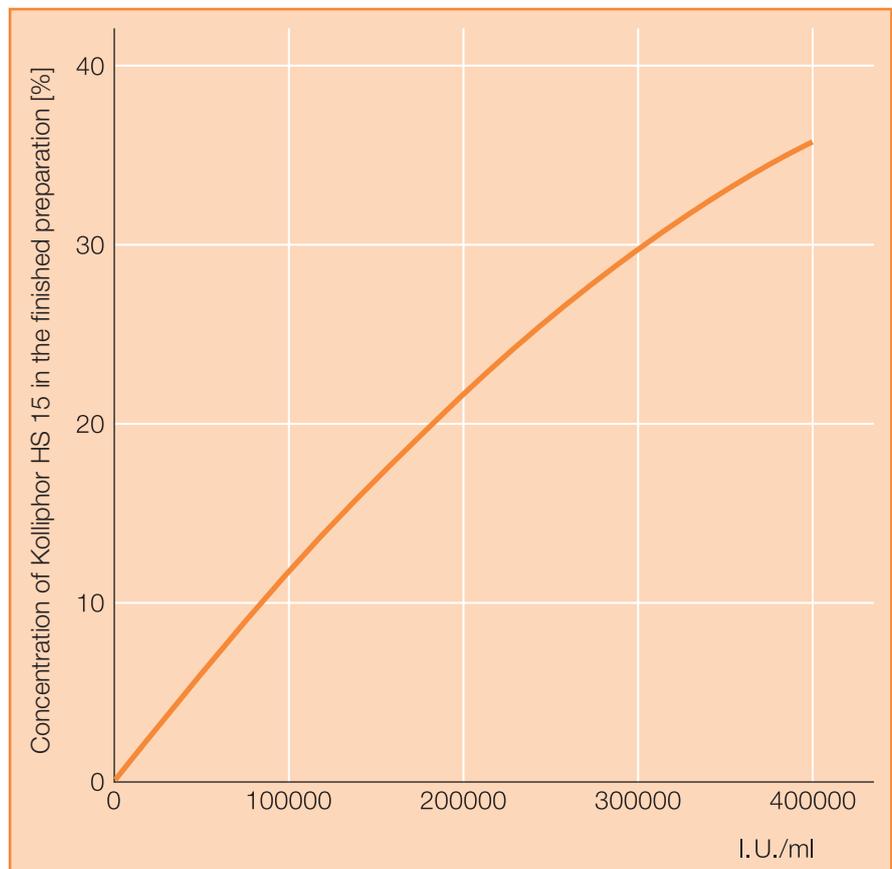


Fig. 2: Solubilization of vitamin A propionate 2.5 million I. U./g

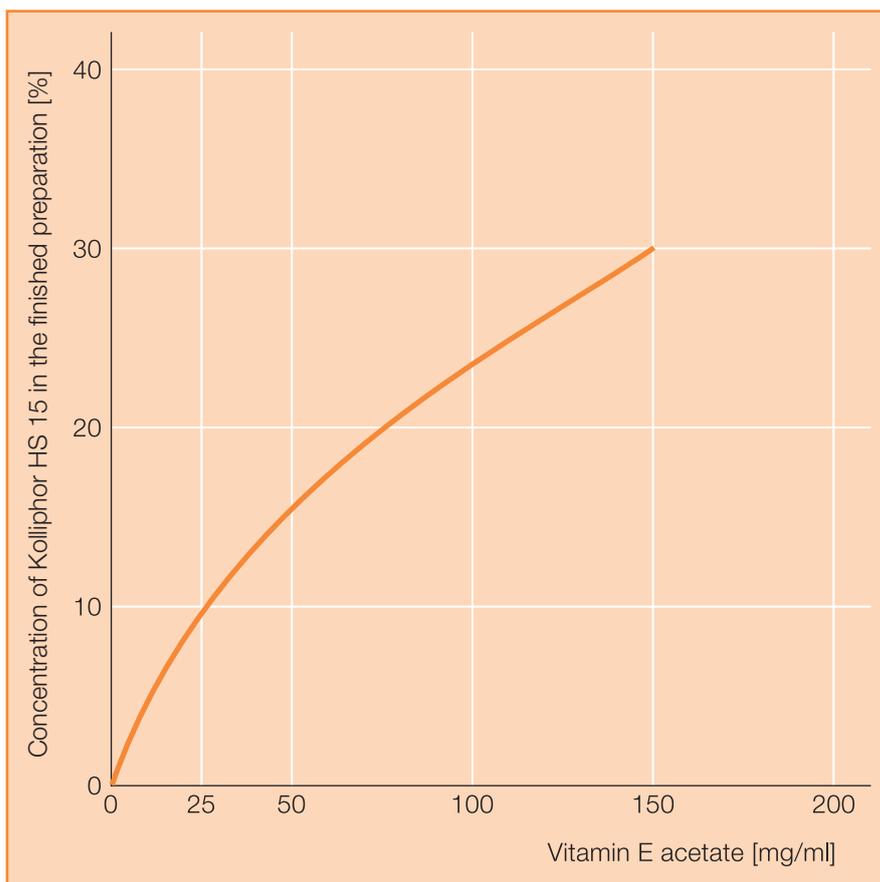


Fig. 3: Solubilization of vitamin E acetate

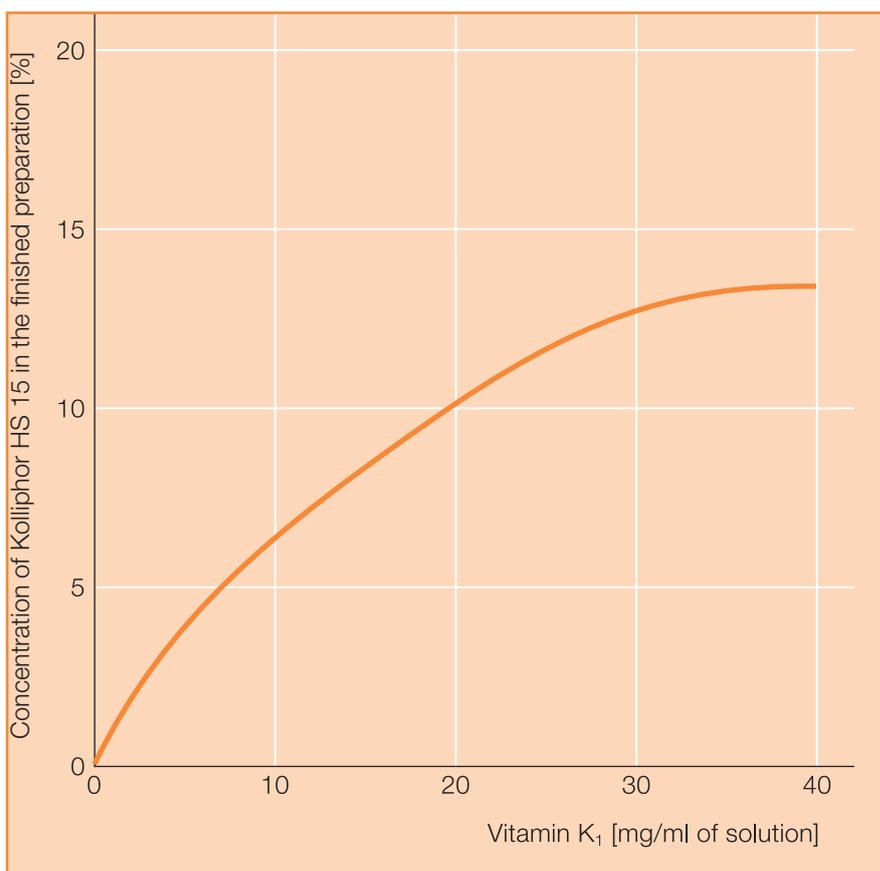


Fig. 4: Solubilization of vitamin K₁

The solubilizer is also suitable for manufacturing an injection emulsion of the following composition:

Vitamin A propionate	2.5 million I. U./g	23.0 g
Vitamin D ₃	40 million I. U./g	0.2 g
Vitamin E acetate		5.5 g
Kolliphor HS 15		15.0 g
Butylhydroxytoluene		1.5 g
Benzyl alcohol		1.0 g
Water for injections		ad 100 ml

An injection emulsion of this kind has good chemical and physical stability.

The question is often raised as to the dependency of micelle size on charge and temperature during solubilization. Photon correlation spectroscopy has provided the following results.

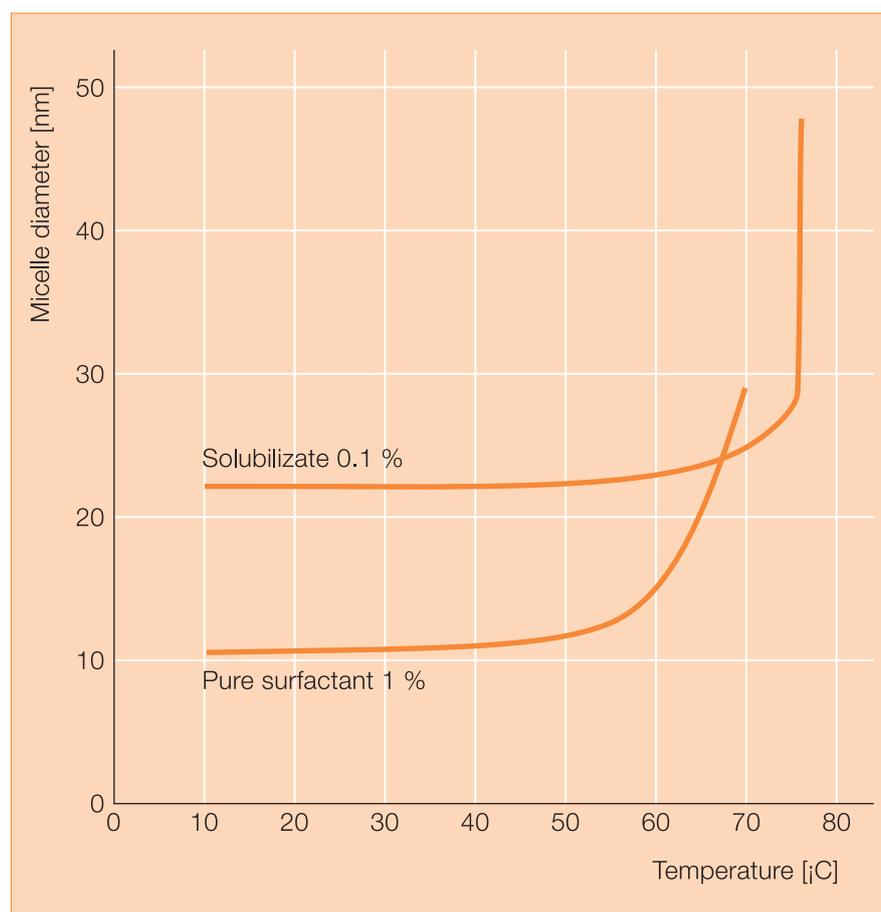


Fig. 6: Dependency of micelle size on temperature

Toxicology

For information on toxicological issues please refer to the tox abstract which can be supplied on request.

More/detailed toxicological information for Kolliphor HS 15 is available on request under Secrecy Agreement.

Packaging

50 kg removable-head PE-drum.

PRD-No.	30554050
Article-No.	50253404
Retest date	Kolliphor HS 15 should be stored in tightly closed containers protected from light. Under these conditions the retest period is 2 years.
Safety data sheet	A Safety Data Sheed is available for Kolliphor HS 15.
Literature	<ol style="list-style-type: none">(1) K. Buszello, S. Harnisch, R. H. Müller, B. W. Müller Eur. J. Pharm. Biopharm 49, 143 (2000)(2) K. Woodburn, E. Sykes, D. Kessel Int. J. Biochem. Cell Biol. 27, 693 (1995)(3) K.-H. Frömming, C. Kraus, W. Mehnert Acta Pharm. Technol. 36, 214 (1990)(4) C. von Corswant, P. Thoren, S. Engström J. Pharm. Sci. 87, 200 (1998)(5) J. S. Coon et al. Cancer Res. 51, 897 (1991)(6) D. B. Smith et al. Br. J. Cancer 57, 623 (1988)

Note

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March 2012

