

Technical Information

December 2011

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WF-No. 117650

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Kolliphor™ RH 40

**Macrogol-Glycerolhydroxystearat Ph. Eur
Polyoxyl 40 Hydrogenated Castor Oil USP/NF**

(former Tradename Cremophor RH 40)

For the pharmaceutical industry

Kolliphor RH 40 is a solubilizer for various hydrophobic APIs, fat-soluble vitamins, and essential oils.

Generic name	Polyoxyl 40 Hydrogenated Castor Oil (USP, current edition), Macroglycerol Hydroxystearate (Ph. Eur., current edition).
Chemical nature	<p>Kolliphor RH 40 is a nonionic solubilizer and emulsifying agent obtained by reacting 1 mole of hydrogenated castor oil with 40 moles of ethylene oxide.</p> <p>The main constituent of Kolliphor RH 40 is glycerol polyethylene glycol hydroxystearate, which, together with fatty acid glycerol polyglycol esters, forms the hydrophobic part of the product. The hydrophilic part consists of polyethylene glycols and glycerol ethoxylate.</p>
Properties	<p>Kolliphor RH 40 is a white to yellowish paste at 20 °C. The HLB value lies between 14 and 16.</p> <p>Particular features are that it has very little odour and in aqueous solutions is almost tasteless.</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 stated otherwise, the analytical methods have been taken from the monographs "Macroglycerol Hydroxystearate" (Ph. Eur.) and "Polyoxyl 40 Hydrogenated Castor Oil" (USP/NF). The product fulfills the requirements of these monographs.</p>
Regulatory status	Meets the current Ph. Eur. monograph "Macrogol-Glycerolhydroxystearat" and the current USP/NF monograph "Polyoxyl 40 Hydrogenated Castor Oil".
Solubility	<p>Kolliphor RH 40 forms clear solutions in water, ethanol, 2-propanol, n-propanol, ethyl acetate, chloroform, carbon tetrachloride, toluene and xylene.</p> <p>Solutions become cloudy as the temperature increases.</p> <p>Kolliphor RH 40 can be mixed with all other Kolliphores. At elevated temperatures it forms clear mixtures with fatty acids and fatty alcohols.</p>
Stability	<p>Pure Kolliphor RH 40 is chemically very stable. Prolonged exposure to elevated temperatures can cause physical separation into a liquid and a solid phase on cooling but the product can be restored to its original form by homogenization.</p> <p>Kolliphor RH 40 is stable in aqueous alcohol and purely aqueous solutions. However, it must be noted that strong bases or acids should not be added, as otherwise the ester components may be saponified.</p> <p>Aqueous Kolliphor RH 40 solutions can be sterilized by heating to 120 °C. Allowance must be made for the fact that this can cause a slight decrease in the pH value. The phases may also separate during sterilization, but this can be remedied by agitating the solution while it is still hot.</p> <p>The preservatives normally used in the pharmaceuticals industry may be added to the aqueous solutions. The requisite concentrations should be determined in tests.</p> <p>Kolliphor RH 40 is largely insensitive to water hardness.</p>

Application

Solubilization

Aqueous solutions of vitamins A, D, E and K for oral and topical administration can be prepared with the aid of Kolliphor RH 40. The fact that the solubilizer has very little taste or odour is an asset for such applications.

In order to ensure that clear, aqueous solutions are obtained, the fatsoluble vitamins must first be intimately mixed with the solubilizer. Best results with vitamin A are obtained if it is in the form of vitamin A palmitate 1.7 million I. U./g, or vitamin A propionate 2.5 million I. U./g; or, in the case of vitamin K, if it is in the form of vitamin K₁ (phytomenadione).

As the method of preparing the solubilize is very important, the production of a 150 000 I. U./ml aqueous vitamin A palmitate solution is described in detail as a typical example:

Vitamin A palmitate 1.7 million I. U./g	8.8 g
Kolliphor RH 40	25.0 g
Water	ad 100.0 ml

The vitamin is mixed with Kolliphor RH 40 and heated to 60 – 65 °C. The water, also heated to 60 – 65 °C, is added very slowly with thorough stirring into this mixture. As a result of hydration, the solution thickens, with the viscosity attaining a maximum after about half of the water has been added. Further addition of water then decreases the viscosity again. If the first half of the water is added too quickly, the solution can become opalescent. Alternatively, the warm mixture of the vitamin and Kolliphor RH 40 can be slowly stirred into the water, which results in a smaller increase in viscosity.

The following three diagrams demonstrate the use of Kolliphor RH 40 for producing clear, highly concentrated, aqueous solutions of vitamin A palmitate, vitamin A propionate and vitamin E acetate.

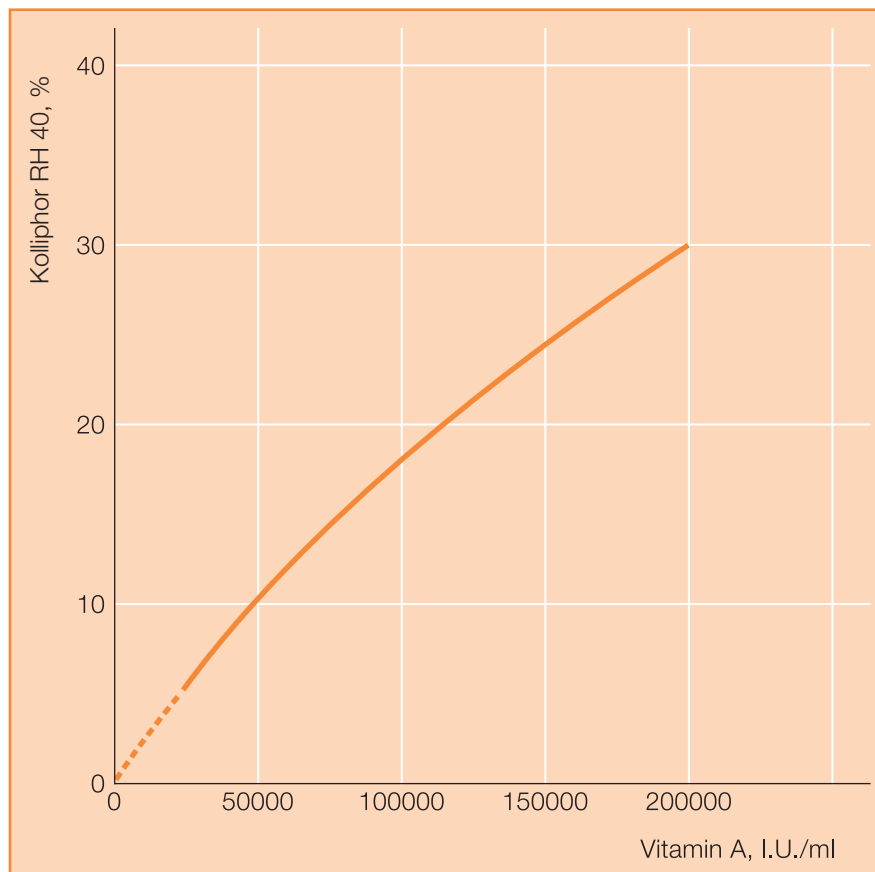


Fig. 1 Solubilization of vitamin A palmitate 1.7 million I. U./g

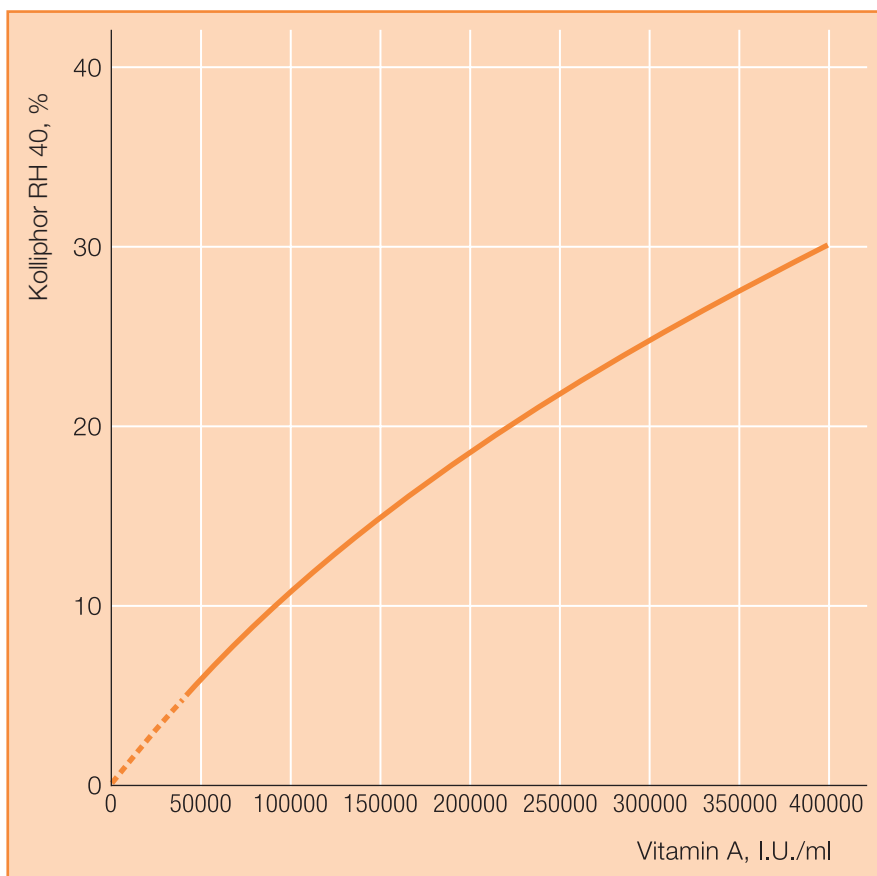


Fig. 2 Solubilization of vitamin A propionate 2.5 million I. U./g

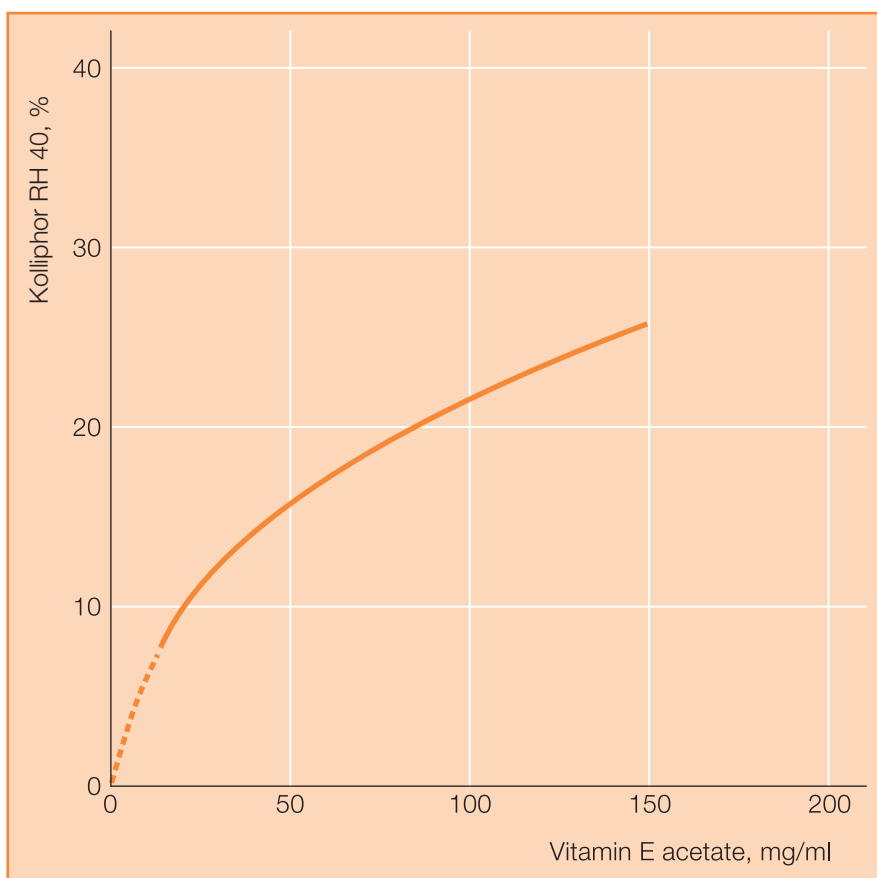


Fig. 3 Solubilization of vitamin E acetate

Likewise, the following vitamin quantities can be solubilized by a 6% Kolliphor RH 40 solution.

8 – 9 mg/ml Vitamin D₂ (400 000 I. U.), or
 5 mg/ml Vitamin D₃ (125 000 I. U.), or
 10 mg/ml Vitamin K₁

Less Kolliphor RH 40 is usually required for mixtures of vitamins.

A small addition of polyethylene glycol (Lutrol® E 400), 1,2-propylene glycol or glycerol allows the preparation temperature and sometimes also the concentration of Kolliphor RH 40 to be reduced.

Miscellaneous solubilizer applications

Clear, aqueous solutions of hydrophobic substances other than vitamins can be obtained with Kolliphor RH 40. Examples are essential oils and certain drugs for oral and topical application. A feature of the solutions thus obtained is their good stability. The following substances serve as examples:

Hexachlorocyclohexane	Miconazole
Hexeditine	Gramicidin
Levomepromazine	Eucalyptol
Thiopental	Azulene
Benzocaine	Oil of anise
Clotrimazole	Oil of sage
Diazepam	

Kolliphor RH 40 shows little tendency to foaming, which is particularly important for solutions in aqueous ethanol. Further foam suppression can be obtained by the addition of a small quantity of Polypropylene Glycol 2000.

Use as emulsifier

Kolliphor RH 40 is also very suitable as an emulsifying agent. It will emulsify a wide range of hydrophobic substances, e. g. fatty acids, fatty alcohols and drugs.

Toxicity

The toxicological abstract is available on request. Individual reports can be shared under secrecy agreement.

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.

PRD-No.	30555082
Article-No.	50254755
Packaging	PE-drums of 60 kg capacity.
Storage	<p>The drums in which Kolliphor RH 40 is stored should be kept tightly closed.</p> <p>The method of production employed for Kolliphor RH 40 ensures that it is practically sterile. If the containers are repeatedly opened, microorganisms may grow in the product, particularly if the equipment used is not sterile.</p>
Retest date	In the unopened original drums, the retest period for Kolliphor RH 40 is at least 2 years at room temperature (20 – 25 °C).
Safety Data Sheet	A Safety Data Sheet for Kolliphor RH 40 is available.
Note	<p>This document, or any answers or information provided herein by BASF, does not constitute a legally binding obligation of BASF. While the descriptions, designs, data and information contained herein are presented in good faith and believed to be accurate, it is provided for your guidance only. Because many factors may affect processing or application/use, we recommend that you make tests to determine the suitability of a product for your particular purpose prior to use. It does not relieve our customers from the obligation to perform a full inspection of the products upon delivery or any other obligation. NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, ARE MADE REGARDING PRODUCTS DESCRIBED OR DESIGNS, DATA OR INFORMATION SET FORTH, OR THAT THE PRODUCTS, DESIGNS, DATA OR INFORMATION MAY BE USED WITHOUT INFRINGING THE INTELLECTUAL PROPERTY RIGHTS OF OTHERS. IN NO CASE SHALL THE DESCRIPTIONS, INFORMATION, DATA OR DESIGNS PROVIDED BE CONSIDERED A PART OF OUR TERMS AND CONDITIONS OF SALE.</p>

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