Technical Information

Kolliphor® P 407

Poloxamer Ph. Eur., Poloxamer USP/NF

Poloxamer for Pharmaceutical Use

August 2019 | **WF-No. DAWF-2019-0815**

BASF

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1. Introduction

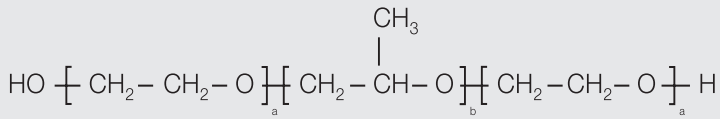
BASF's Kolliphor P grade poloxamers are white, coarse- grained powders with a waxy consistency. They contain an appropriate quantity of the antioxidant BHT.

Poloxamers are ABA-type co-polymers of poly (ethylene oxide) (PEO=A) and poly (propylene oxide) (PPO=B). The approximate relative amount of PEO and the average molecular weight of the PPO are indicated in the name of the poloxamer. For example, P 407 succeeding the word Kolliphor® indicates a poloxamer with ca. 70% m/m PEO (P 407; 7x10= 70%) and approximately average molecular weight of PPO of 4000 ((P 407; 40x100= 4000)

2. Technical properties

Structural formula

The Kolliphor® P 407 is a block copolymer that is a synthetic copolymer of ethylene oxide and propylene oxide represented by the following chemical structure:



Where the a and b blocks have the following values:

Kolliphor®	Poloxamer	a	b
P 407	407	101	56

Appearance

Kolliphor® P 407 is produced as a white to almost white prill/powder.

CAS Number

9003-11-6

Molecular Weight

The average molecular weight for Kolliphor® P 407 is 9840 to 14600 g/mol. The product contains nominally 95 to 105 ethylene oxide units and 54 to 60 propylene oxide units, with a rough concentration of oxyethylene of 71.5 to 74.9 % based on the current monograph specification. An example of the molecular weight distribution for Kolliphor® P 407 is shown below in Figure 1.

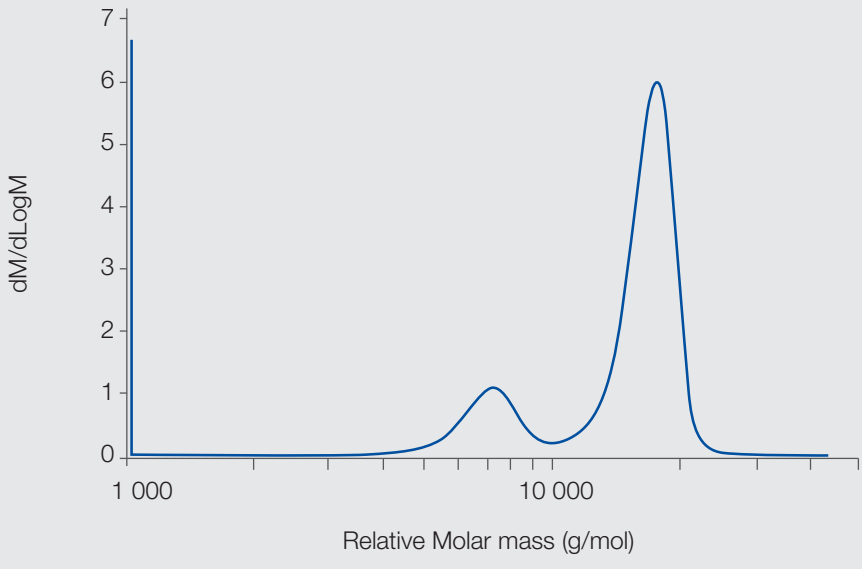


Fig. 1: The above graph was generated using size exclusion chromatography (SEC), note that the smaller peak to the left represents diblock polymers.

Viscosity

Poloxamers, and Kolliphor® P 407 exhibits a thermoreversible gelling behavior that occurs as a function of temperature. At low concentrations, aqueous concentrations exhibit Newtonian flow properties and negligible viscosity alterations to that of water, however, at higher temperatures, the solutions begin to exhibit non-Newtonian flow behavior. An example of the viscosity curve is evident in Figure 2 below with the gel points clearly noted by the sharp increase in viscosity at 10, 15 and 20 % w/w:

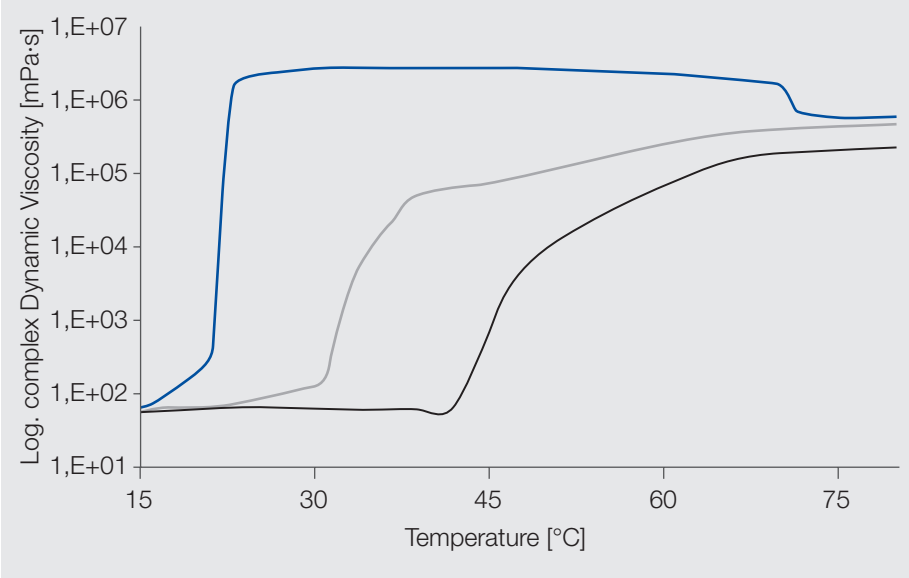


Fig. 2: Complex dynamic viscosity of aqueous Kolliphor® P 407-gels as a function of temperature. Viscosity determation was performed using a HAAKE Rheostress 6000 with a plate/plate configuration PP60Ti with an amplitude of 0.010 and a frequency of 1000/s

The dynamic viscosity of Kolliphor® P 407 gels may be affected by the addition of electrolytes, moisturizers, alcohols and surfactants. Figure 3 demonstrate the influence of sodium chloride and potassium chloride in a 20% Kolliphor® P 407-gel. The addition of electrolytes at concentrations of around 1% increases the viscosity with little or no impact on the sol-gel transition temperature. Higher concentrations demonstrate a reduced gelling temperature with increased dynamic viscosity readings. Low pH values affect the sol-gel transition temperature and the viscosity.

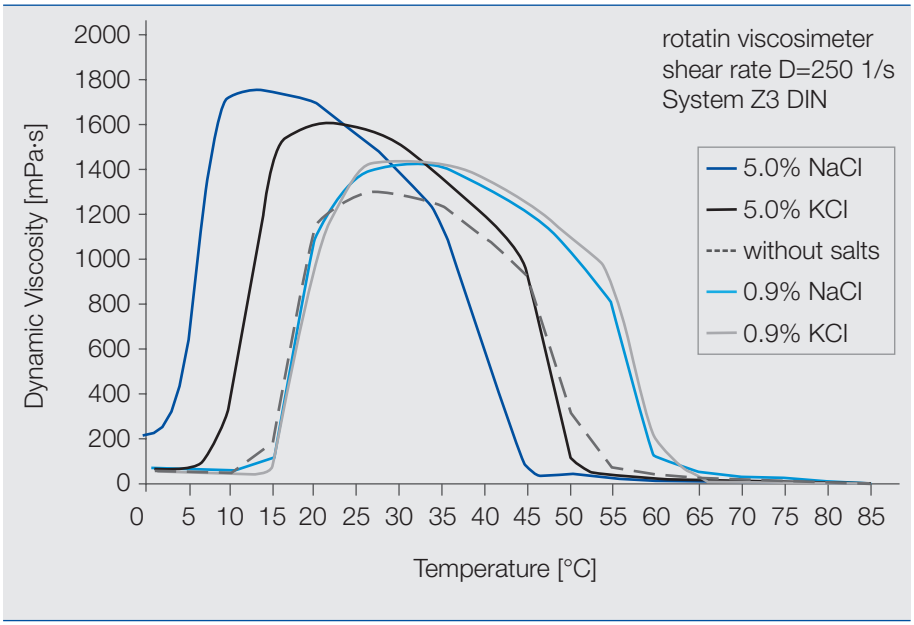


Fig. 3: Pour point of 25% aqueous Kolliphor® P 407 gels at different NaCl – or KCl – levels (temp. 25 °C)

HLB

The HLB value of Kolliphor® P407 is approximately 22.

Critical Micelle Concentration (CMC)

The critical micelle concentration for Kolliphor® P407 is published as 2.8 · 10-6 mol/L @ 37 °C (34.2 mg/L). Note that the CMC value decreases significantly as the temperature increases. Furthermore, due to the linear structure of the poloxamer, the value is difficult to ascertain as an inflection point using standard methods (such as Wilhelmy Plate Method) an example of the surface tension for Kolliphor® P407 as a function of concentration is shown below in Figure 4 (37 °C).

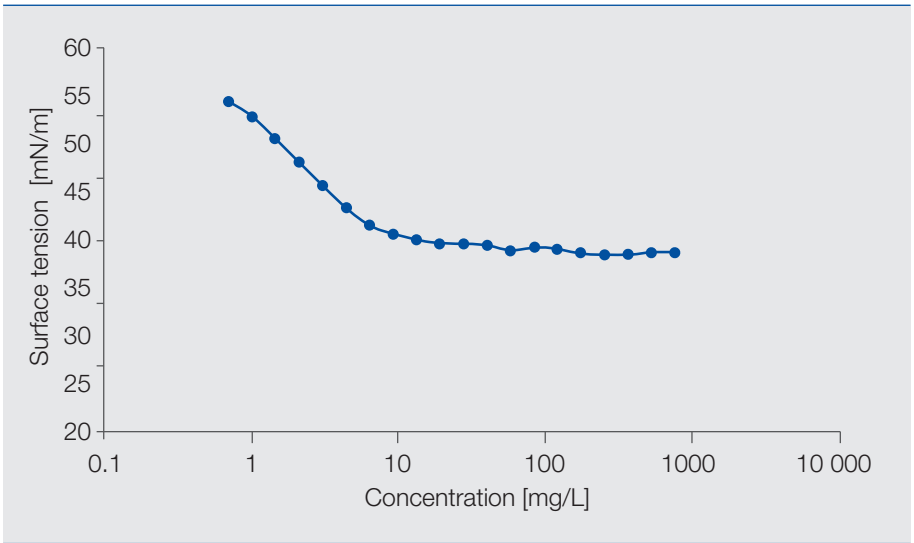


Fig. 4:

The micelle size is approximately 10-15 nm in diameter; this is shown in Figure 5 below as determined via laser diffraction:

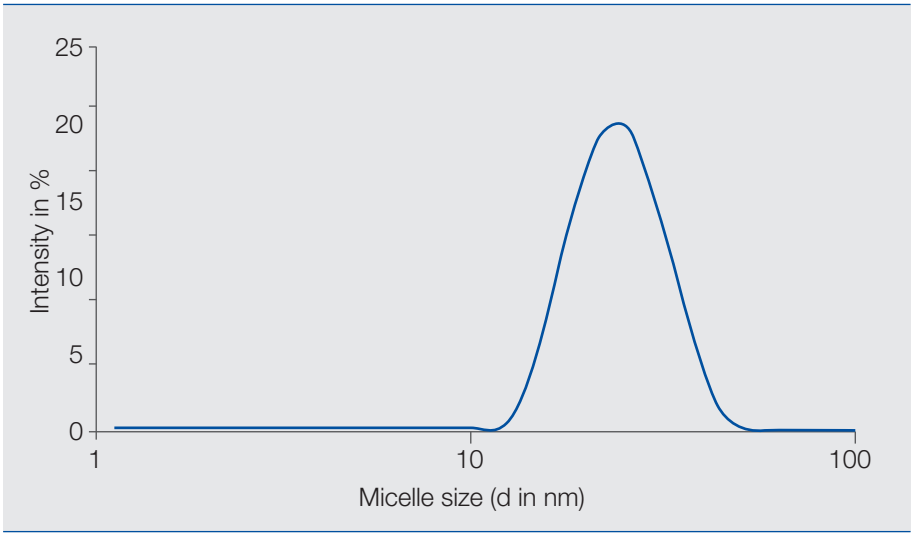


Fig. 5:

Solubility

Kolliphor® P407 is highly soluble in water and polar solvents.
Note that Kolliphor® P407 is significantly easier to dissolve in cold water.

Particle Size

Kolliphor® P407 exhibits spherical prill particles of a mean diameter of approximately 500 µm in size. An example of the size and morphology of these particles is shown in the scanning electron microscope image (SEM) show below in Figure 6.

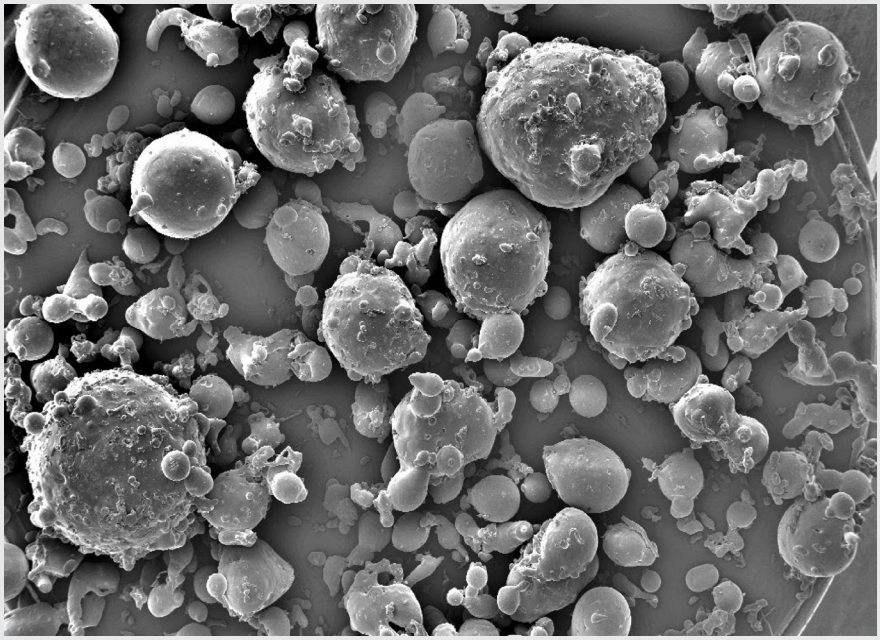


Fig. 6:

Cloud Point

The cloud point for Kolliphor® P 407 is >100 °C for a 1% and a 10% aqueous solution.

Density

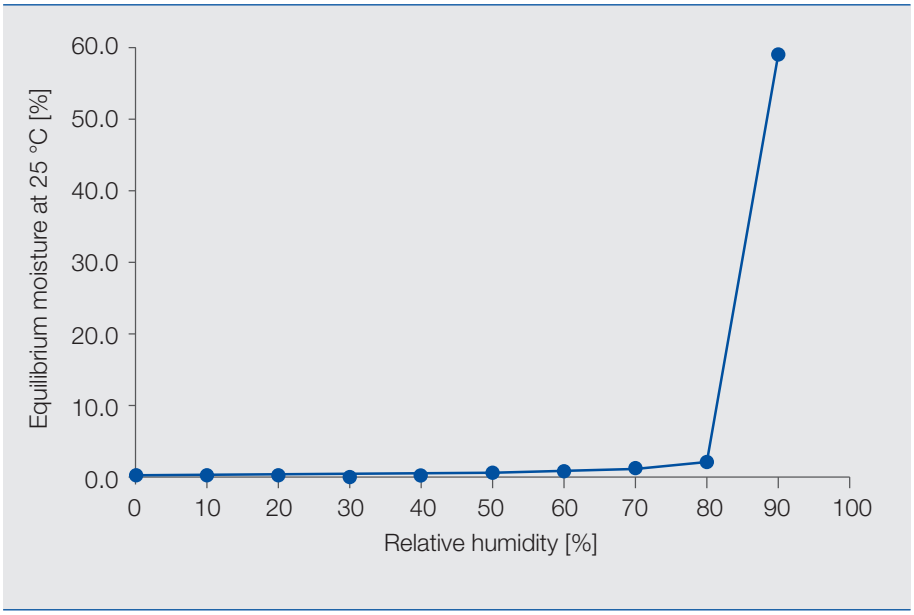
The true density of Kolliphor® P 407 is approximately 1.06 g/cm^3

The bulk density of Kolliphor® P 407 is approximately 0.50 g/cm^3.

The tapped density of Kolliphor® P 407 is approximately 0.60 g/cm^3.

Moisture Sorption

The uptake of moisture for Kolliphor® P 407 is dependent on the relative humidity of the environment, at moisture levels above 80% (RH) significant moisture uptake is possible and shown in Figure 7 below:



BHT

Poloxamers, and specifically Kolliphor® P 407 utilize 50 - 125 ppm BHT as an antioxidant – the protects the quality and performance of the P 407 in the multitude of pharmaceutical applications. The primary degradation mechanism is oxidation, and is typically monitored via the pH, hydroxyl value and molecular weight of the poloxamer.

3. Handling

Please refer to the individual Material Safety Data sheet (MSDS) for instructions on safe and proper handling and disposal.

4. Example application

Poloxamers are a widely used pharmaceutical ingredient in multitude of applications, most notably, as a dispersing agent, emulsifier, solubilizer, tablet and capsule lubricant, wetting agent, stabilizer for oral and topical suspensions, gelling agent in topical formulations.

Example Use Levels

Indication	Concentration (w/w%)
Gelling agent	15 to 50
Suspension stabilizer	0.1 to 5
Tableting	1 to 10
Wetting Agent	0.01 to 5
Emulsifier	1 to 5
Foaming agent	1 to 3
Plasticizer (matrix)	5 to 15

Solubilization

Kolliphor® P 407 can be used in a multitude of solubilization examples – more specifically the product may be a liquid solution, suspension or solid tablet. Given the low critical micelle concentration (CMC) stabilizing and solubilizing occurs at concentrations 1 to 2 orders of magnitude lower than for standard ethoxylated surfactants.

5. Skin delivery

Poloxamers as Gelling agents

Poloxamers can be used as gelling agents to build structure in a topical aqueous solution. Gels using Kolliphor® P 407 can exhibit thermoreversible behavior; they form gels which are liquids at room temperature but solidify upon contact with skin.

Phase	Ingredients	Chemical name	Description	Mass (Weight%)
A	Ethanol 200 Proof		Solvent	10
	Kollisolv® PG	Propylene Glycol	Solvent	10
	Kollicream® IPM	Isopropylmyristate	Tack reducer	2
	Glycerol		Solvent	5
B	Kolliphor® P 407	Poloxamer 407	Gelling agent	15 – 20
	Deionized Water		Solvent	53 – 58

Gelling is a function of temperature, structure, and concentration of a given poloxamer. At high enough concentrations, poloxamers form multimolecular aggregates and micelles that aid in gelling. Notably, an increase in the amount of ethanol used in a formulation increases the gelling temperature of a given formulation. Kollicream® IPM reduces tackiness, resulting in an improved sensory experience.

Emulgel

At concentrations above 15%, Poloxamers 188 and 407 can be used to make gels and viscous emulsions by both emulsifying and forming phases and networks via the hydrophobic and hydrophilic interactions driven by PPO and PEO segments of the polymer, respectively.

Phase	Ingredients	Chemical name	Description	Mass (Weight%)
A	Ethanol 200 Proof		Solvent	10
	Kollisolv® PEG 400	Polyethylene Glycol 400	Solvent	15
	Glycerol		Solvent	5
B	Kolliphor® P 407	Poloxamer 407	Gelling agent	18
C	Deionized Water		Solvent	42
D	Kollicream® 3 C	Cocoyl Caprylocaprate	Emollient	10

Kolliphor® P 407 helps emulsify the Kollicream® 3 C in this formulation, resulting in a translucent white gel with a cream-like structure visible underneath the microscope. Both Kolliphor® P 407 and Kollicream® 3 C have been shown to be very mild, in vitro and in vivo.

6. Safety data sheet

Safety data sheets are available on request and are sent with every consignment.

7. Retest date and storage conditions

Please refer to Quality & Regulatory Product Information (QRPI).

8. Stability

Please refer to Quality & Regulatory Product Information (QRPI).

9. Toxicological data

The toxicological abstract is available on request.

10. PRD and Article numbers

PRD-No.*	Product name	Article numbers	Packaging
30555080	Kolliphor® P 407	50259528	0.5 kg Plastic bottle
		50254757	25 kg Fibre drums
		50254759	90 kg fibre drums

* BASF's commercial product number.

11. Publications

http://pharmaceutical.basf.com/en.html

August 2019