

Kolliphor[®] Grades – Emulsifier for topical pharmaceutical applications

® = Registered trademark of BASF
in many countries.

Rebranding

As a result of the integration of former Cognis excipients in the BASF portfolio a rebranding was conducted. The rebranding should increase the reliability and compliance for the supply of pharmaceutical excipients. The following table shows a comparison of old versus new trade names.

Tradename	Former Tradename
Kolliphor® CS 12	Eumulgin B1 PH
Kolliphor® CS 20	Eumulgin B2 PH
Kolliphor® CSS	Lanette E PH
Kolliphor® CS A	Lanette N PH
Kolliphor® CSL	Lanette SX PH

Table 1: New Tradenames – Old Tradenames

PRD-No., Article-No. and CAS.-No.

Tradename	PRD-No.	Article-No.	CAS.-No.
Kolliphor® CS 12	30554458	50253256	68439-49-6
Kolliphor® CS 20	30554459	50253257	68439-49-6
Kolliphor® CSS	30554486	50253269	68955-20-4
Kolliphor® CS A	30554487	50253281	67762-27-0 68955-20-4
Kolliphor® CSL	30554435	50253856	67762-27-0 151-21-3 68955-20-4

Table 2: PRD and Article and CAS number of the Kolliphor® Grades

Specifications

See separate documents: “Standard Specification” (not for regulatory purposes) available via BASF’s WorldAccount: <https://worldaccount.basf.com> (registered access).

Regulatory Status

In table 3 you can find all the monographs for the Kolliphor® Grades.

New Name	Monograph Tests
Kolliphor® CS 12	Ph. Eur. : Macrogol Cetostearyl Ether 12
Kolliphor® CS 20	Ph. Eur. : Macrogol Cetostearyl Ether 20 USP/NF: Polyoxyl 20 Cetostearyl Ether
Kolliphor® CSS	Ph. Eur. : Sodium Cetostearyl Sulphate
Kolliphor® CS A	Ph. Eur. : Cetostearyl Alcohol (Type A), Emulsifying
Kolliphor® CSL	not monographed

Table 3: Compendial names

Product groups

An emulsion is a dispersion of droplets of a non-miscible liquid in a continuous phase. The polar (hydrophilic) aqueous phase and the non-polar (lipophilic) oil phase of an emulsion cannot be combined in a stable and homogenous way without a surface-active additive.

Emulsifiers are interfacial active substances that reduce the interfacial tension between the oil and the water phase. The emulsifier is adsorbed at the interface, giving a film between both phases, which prevents coalescence of droplets.

Due to its amphiphilic structure, the polar part of the emulsifier has an affinity to the water phase and the non-polar part of the emulsifier to the oil phase.

Emulsifiers can be defined according to their hydrophilic/lipophilic characteristics. In 1949 W.C. Griffin proposed the HLB (Hydrophilic- Lipophilic Balance) system in which non-ionic surfactants have been classified on a scale from 0 to 20. Emulsifiers with a strong lipophilic character have low HLB values between 3 to 8 and tend to form W/O emulsions. Emulsifiers of the HLB range of 8 to 18 are hydrophilic and form O/W emulsions.

HLB values from 12 to 18 are most favorable for solubilization to enhance bio-availability of active ingredients.

Emulsifiers can be classified according the chemical structure in non-ionic and ionic emulsifiers or emulsifying waxes.

Non-Ionic Emulsifier

Ethoxylates

Chemical structure

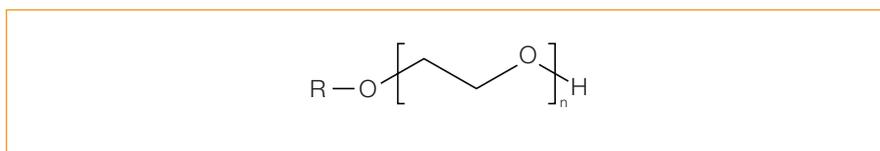


Figure 1: Chemical structure Kolliphor® CS 12 and Kolliphor® CS 20

Typical Properties

Product	R-Lipo-phil	N-Hydro-phil	Appearance	HLB value	Usage concentration	pH working range
Kolliphor® CS 12	C ₁₆ , C ₁₈	12x EO	White or yellowish white waxy powder	13	0.5 – 5%	2 – 12
Kolliphor® CS 20	C ₁₆ , C ₁₈	20x EO	White or yellowish white waxy powder	15	0.5 – 5%	2 – 12

Table 4: Typical properties Kolliphor® CS 12 and Kolliphor® CS 20

Ionic Emulsifier

Kolliphor® CSS

Chemical Structure

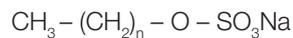


Figure 4: Chemical structure Kolliphor® CSS ($n=15$ or 17)

Typical properties

Product	Appearance	HLB value	Usage concentration	pH working range
Kolliphor® CSS	White or pale yellow amorphous or crystalline powder	>40	0.5 – 2%	7 – 12

Table 5: Typical properties of Kolliphor® CSS

Cream-bases/Emulsifying Waxes

Emulsifying Waxes (Cream-bases) are a combination of a consistency factor (eg. Fatty alcohols) and an emulsifier. They are especially designed to enable an effective and short development time of a topical pharmaceutical formulation.

Typical properties

Product	Ingredients	Appearance	HLB value	Usage concentration	pH working range
Kolliphor® CS A	Cetostearyl Alcohol Sodium Cetostearyl Sulphate	White or pale yellow, waxy pellets	7.0	0.5 – 5%	6 – 12
Kolliphor® CSL	Cetostearyl Alcohol Sodium Lauryl Sulfate Sodium Cetearyl Sulfate	Pellets with a faint characteristic odor	7.5	0.5 – 5%	6 – 12

Table 6: Typical property of the creambases/emulsifying waxes

Application

The choice of emulsifiers for specific applications depends on the desired properties of the formulation (e.g. stability, viscosity, skin feel and API), or on the desired processing technology (e.g. PIT, Hot or cold processing).

The traditional processing technology for emulsion is the so called hot process, where you combine both water and oil phase at a temperature of 70 – 85 °C. With this technology you are very flexible in the ingredients you can choose in your emulsion.

Beside the well-known hot process of emulsification, there is also the possibility to formulate an emulsion with a processing temperature at room temperature.

The processing of O/W emulsions at room temperature has several significant benefits. For example, it is no longer necessary to heat the water and oil phase to 70 – 80 °C. This saves considerable amounts of energy and reduces the production time as the cooling step is eliminated.

Another very important advantage is that heat-sensitive APIs can be added to the emulsions at any point.

On the other hand the possible ingredients are limited as there is not melting step of the oil phase. In the BASF portfolio of emulsifier for topical pharmaceutical applications only Kolliphor® PS 60 is suitable for this kind of processing technology.

Another very interesting processing technology is the Phase Inversion Technology (PIT) as it leads to water thin emulsions with a very small droplet sizes and thus these emulsions are very stable. This processing technology uses the temperature dependency of the HLB value of non-ionic emulsifiers as this kind of emulsifier change solubility behavior with elevated temperature. This can be used for pharmaceutical applications where a very thin emulsion is needed, which is easy to distribute over the skin (e.g. sprayable wound sprays etc.).

Product	Ph. Eur.	W/O Emulsifier	O/W Emulsifier	Solubilizer	Non-ionic emulsifier	Ionic emulsifier	Creambase	Phase Inversion Technology (PIT)	Suitable for creams and lotions	Suitable for gel creams	Hot-process	Cold-process	Broad pH range
Kolliphor® CS 12	Marcrogol Cetostearyl Ether 12		x		x			x	x	x	x		x
Kolliphor® CS 20	Marcrogol Cetostearyl Ether 20		x		x			x	x	x	x		x
Kolliphor® CS A	Cetostearylalcohol (Type A), Emulsifying		x			x	x		x		x		
Kolliphor® CSS	Sodium Cetostearyl Sulphate		x			x			x		x		
Kolliphor® CSL			x			x	x		x		x		

Table 7: Application fields in topical pharmaceutical formulations of the Kolliphor® grades

Skin Tolerance	All Kolliphor® types have a good skin tolerance.
Raw material origin	All Kolliphor® grades are based on vegetable and synthetic raw materials.
Toxicology	The toxicological abstracts are available on request. Individual reports can be shared under secrecy agreement.
Stability and storage	In originally sealed containers all Kolliphor® types can be stored for at least two years. It is important that they are protected from moisture and stored at less than 30 °C.
Handling and Disposal	Please refer to the individual Material Safety Data Sheet (MSDS) for instructions on safe and proper handling and disposal
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