

 **BASF**

We create chemistry

Expediting topical semi-solid development with self-emulsifying systems



 BASF_Pharma

 BASF Pharma Solutions

www.pharma.basf.com

Inspiring Medicines for Better Lives

Introduction

At BASF Pharma Solutions, we know that innovation, speed-to-market, and cost-effectiveness are essential to pharmaceutical companies. Committed to delivering on all three accounts, we use our expertise across the entire pharmaceutical value chain to drive the development of various dosage forms.

By supplying both high-quality products and RSPO-certified, lipid-based excipients, we work alongside our customers to resolve formulation challenges, while also addressing strong sustainability values in the evolving marketplace. Partner with BASF to be supported by our best-in-class regulatory, quality, and technical teams.

Included in this formulary are exemplary semi-solid, topical formulations composed of Kolliphor® ready-to-use cream base products. Utilize these versatile excipients to expedite the formulation development process.



Disclaimer:
The following formulations are exemplary. Formulating procedures are recommendations based on established laboratory conditions and may require alterations dependent on the final application. NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, 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, DESCRIPTIONS, DESIGNS, DATA OR INFORMATION MAY BE USED WITHOUT INFRINGING THE INTELLECTUAL PROPERTY RIGHTS OF OTHERS.

Table of contents

Introduction	2
<hr/>	
Kolliphor® cream bases and ionic emulsifiers	4
<hr/>	
Processing methods	5
Direct conventional method	6
Liquid crystalline lamellar gel method	7
<hr/>	
Cream formulations	8
Rich or heavy-weight	8
Medium-weight	14
Light-weight and soft	18



Kolliphor® cream bases and ionic emulsifiers

BASF offers a broad portfolio of functional materials including our pharmaceutical grade Kolliphor® cream bases. Composed of both emulsifiers and structuring agents, these materials are easy-to-use, self-emulsifying systems that are ideal for simplifying the development of topical semi-solids.

With consistent quality and reliable supply, Kolliphor® cream bases are especially designed with the formulator in mind.

Product information

Cream bases

	Chemical name	CAS number	Regulatory status
Kolliphor® CS A	Cetostearyl alcohol (Type A)	67762-27-0 68955-20-4	Ph. Eur.
Kolliphor® CS L	Mixture of cetyl stearyl alcohol, sodium lauryl sulfate, and sodium cetyl stearyl sulfate	67762-27-0 151-21-3 68955-20-4	N/A

Ionic emulsifiers

	Chemical name	CAS number	Regulatory status
Kolliphor® CSS	Sodium cetostearyl sulfate	68955-20-4	Ph. Eur.

Typical properties

	HLB value	Usage concentration	pH working range
Kolliphor® CS A	7	0.5 – 5%	6 – 12
Kolliphor® CS L	7.5	0.5 – 5%	6 – 12
Kolliphor® CSS	>40	0.5 – 2%	7 – 12

Processing methods

Topical semi-solids are complex mixtures composed of various functional excipients including structuring agents, emulsifiers, and emollients. Because the development of topical semi-solids is influenced by not only excipient selection but also processing parameters, these two inputs have a significant effect on the overall stability of the system. To stabilize a two-phase emulsion, formulators will typically employ the following processing methods: phase-inversion technique, direct conventional method, or the liquid crystalline lamellar gel method.

As cream bases, Kolliphor® CS A and CSL are composed of both a structuring agent and emulsifier in a singular product. These excipients are best suited to be processed via the direct conventional method or liquid crystalline lamellar gel method. While the direct conventional method allows for the formation of liquid crystals around the emulsion droplets, the liquid crystalline lamellar gel method promotes the development of liquid crystals in the aqueous phase.

Both processing methods are utilized in this formulary and have been shown to allow for the formation of stable, sensorially pleasing emulsions.



Direct conventional method

Phase	Ingredient
A	Water
	Preservative
B	Xanthan gum
	Kollisolv® PEG
	Kolliwax® structuring agent
C	Kolliphor® cream base or emulsifier
	Kollicream® emollient

When processing using the direct conventional method, the hydrophilic (A/B) and lipophilic (C) phases are heated separately to approximately 75 to 80 °C. The inner phase is then added to the outer phase and sheared at a high rate to promote emulsification. After being cooled to room temperature, the semi-solid can be briefly homogenized to form an opaque, glossy emulsion.

Liquid crystalline lamellar gel method

Phase	Ingredient
A	Water
	Xanthan gum
B	Kollisolv® PEG
	Preservative
C	Kolliwax® structuring agent
	Kolliphor® cream base or emulsifier
D	Kollicream® emollient

To process a semi-solid using the liquid crystalline lamellar gel method, water (A) is first heated to approximately 80 °C. After the water has reached the appropriate temperature, the remaining water-soluble excipients (B) are added to the pre-heated water and heated until phase A/B reaches approximately 80 °C. Phase C is then added to Phase A/B and is mixed under low shear; the heat of the water phase (A/B) is used to melt the oil phase (C). To determine if the lamellar crystalline structure has formed, a spatula can be inserted into the heated liquid mixture. If upon cooling the sample on the spatula forms a grainy texture, the mixture should continue to be heated until a consistent, semi-solid texture is formed. Phase A/B/C should then be cooled to at least 45 °C. Once cooled, Kollicream® emollient should be slowly dribbled into Phase A/B/C under low shear to form an opaque, glossy emulsion.



Topical cream L4.5

A thick, substantial cream suitable for multipurpose applications

Phase	Ingredient	Chemical name	Wt/wt%
A	Water	Water	68.3
	Euxyl® K 712	Sodium benzoate (and) potassium sorbate (and) aqua (water)	1.5
B	Kollisolv® PEG 300	Polyethylene glycol	10
	Xanthan gum	Xanthan gum	0.3
C	Kolliphor® CSL	Mixture of cetyl stearyl alcohol, sodium lauryl sulfate, and sodium cetyl stearyl sulfate	4.0
	Kolliwax® SA	Stearyl alcohol	0.5
	Kolliwax® GMS II	Glyceryl monostearate (type II); Mono- and di-glycerides	0.4
	Kollicream® IPM	Isopropyl myristate	15

Procedure: Direct conventional method

1. Heat phases A and C separately to 75 to 80 °C.
2. Premix phase B then add to phase A. Using the overhead mixer, mix until uniform. Heat phase A/B to approximately 75 to 80 °C.
3. Add phase C to phase A/B under overhead mixer with fast, sharp-bladed stirring.
4. Continue mixing until fully combined, cooling the emulsion to room temperature.
5. Homogenize briefly if needed to achieve an opaque, glossy emulsion.

Leveraging Kolliwax® SA to enhance yield stress

Kolliwax® SA (stearyl alcohol) is a C₁₈ fatty alcohol that is commonly used as a structuring agent, providing consistency and stability in topical formulations. As a high melting range fatty alcohol (57 – 60 °C), Kolliwax® SA has a notable effect on critical quality attributes such as physical stability and rheological properties.

Rheology studies have indicated that factors affecting spreadability, such as yield stress, are influenced by the fatty alcohol composition in the formulation. Formulations composed of mixed fatty alcohol chain lengths (Kolliwax® CSA 50 and 70; C₁₆, C₁₈) yielded a higher yield stress in contrast to creams composed of a singular fatty alcohol chain length (Kolliwax® CA; C₁₆). The difference in yield stress can be attributed to the blend of high and low melting range structuring agents which improves emulsion stability. The addition of stearyl alcohol to cetyl alcohol blends can enhance yield stress, resulting in better rheological performance.

Fatty alcohol	Stearyl alcohol present	Yield stress (Pa)
Kolliwax® CSA 50	●	16
Kolliwax® CSA 70	●	13
Kolliwax® CA	-	9



Topical cream L6.5

A heavy, care-feeling cream perfect for both body and face application

Phase	Ingredient	Chemical name	Wt/wt%
A	Water	Water	71.3
	Euxyl® K 712	Sodium benzoate (and) potassium sorbate (and) aqua (water)	1.5
B	Kollisolv® PEG 400	Polyethylene glycol	10
	Xanthan gum	Xanthan gum	0.3
C	Kolliphor® CSL	Mixture of cetyl stearyl alcohol, sodium lauryl sulfate, and sodium cetyl stearyl sulfate	5
	Koliwax® CA	Cetyl alcohol	0.4
	Koliwax® GMS II	Glyceryl monostearate (type II); Mono- and di-glycerides	0.5
	Kollicream® IPM	Isopropyl myristate	11

Procedure: Direct conventional method

1. Heat phases A and C separately to 75 to 80 °C.
2. Premix phase B then add to phase A. Using the overhead mixer, mix until uniform. Heat phase A/B to approximately 75 to 80 °C.
3. Add phase C to phase A/B under overhead mixer with fast, sharp-bladed stirring.
4. Continue mixing until fully combined, cooling the emulsion to room temperature.
5. Homogenize briefly, if needed, to achieve an opaque, glossy emulsion.

An efficacious yet mild penetration enhancer: Kollicream® IPM

Kollicream® IPM (isopropyl myristate) is a low viscosity, fast spreading oil suitable for topical applications requiring light emollience, such as lotions, creams, and emulgels. As a light emollient, Kollicream® IPM offers formulators with a dual effect, also functioning as a skin penetration enhancer that can improve dermal penetration of some drugs.

While some skin penetration enhancers can be irritating to the skin, patch testing conducted on 500 allergy-prone patients have indicated that Kollicream® IPM has minimal allergy or irritation potential. With its relatively benign mildness profile, Kollicream® IPM can be used to formulate mild topical formulations, reducing the risk of eliciting irritation reactions.

In addition to Kollicream® IPM, the following materials have been indicated to have minimal allergy or irritation potential:



Product name	Chemical name	Functionality
Kollicream® 3 C	Cocoyl caprylocaprato	
Kollicream® OD	Octyldodecanol	Penetration enhancer, emollient, solvent
Kollicream® DO	Decyl oleate	
Kollicream® OA	Oleyl alcohol	
Kollicream® CP 15	Cetyl palmitate 15	Emollient
Kollisolv® PEG 300	Polyethylene glycol	Solubilizer
Soluplus®	Polyvinyl caprolactam – polyvinyl acetate – polyethylene glycol graft copolymer	Solubilizer
Kolliphor® PS 60	Polysorbate 60	Emulsifier, surfactant, solubilizer
Kolliphor® CS 20	Macrogol cetostearyl ether 20; Polyoxyl 20 cetostearyl ether	Emulsifier, surfactant
Kolliphor® P 407	Poloxamer 407	Gelling agent, surfactant, solubilizer
Koliwax® CA	Cetyl alcohol	Structuring agent
Koliwax® SA	Stearyl alcohol	
Koliwax® CSA 50	Cetostearyl alcohol	
Koliwax® S	Stearic acid 50	

Topical cream S6.5

A silky smooth, thick formula intended for easy spreadability

Phase	Ingredient	Chemical name	Wt/wt%
A	Water	Water	70.4
	Euxyl® K 712	Sodium benzoate (and) potassium sorbate (and) aqua (water)	1.5
B	Kollisol® PEG 400	Polyethylene glycol	10
	Xanthan gum	Xanthan gum	0.1
	Kolliphor® CSS	Sodium cetostearyl sulfate	2
C	Kolliwax® CA	Cetyl alcohol	3.5
	Kolliwax® GMS II	Glyceryl monostearate (type II); Mono- and di-glycerides	2.5
D	Kollicream® DO	Decyl oleate	10

Procedure: Liquid crystalline lamellar gel method

1. Heat phase A to 80 °C.
2. Premix phase B then add to phase A. Using the overhead mixer, mix until uniform. Heat phase A/B to 80 °C.
3. Add phase C to phase A/B under overhead mixer, mixing slowly with propeller or paddle blade to ensure no bubbles are formed.
4. Continue mixing with gentle stirring under heat until fully combined.
5. Once fully combined, cool the emulsion to 45 °C or room temperature.
6. Slowly add phase D under slow, gentle shear until uniform.

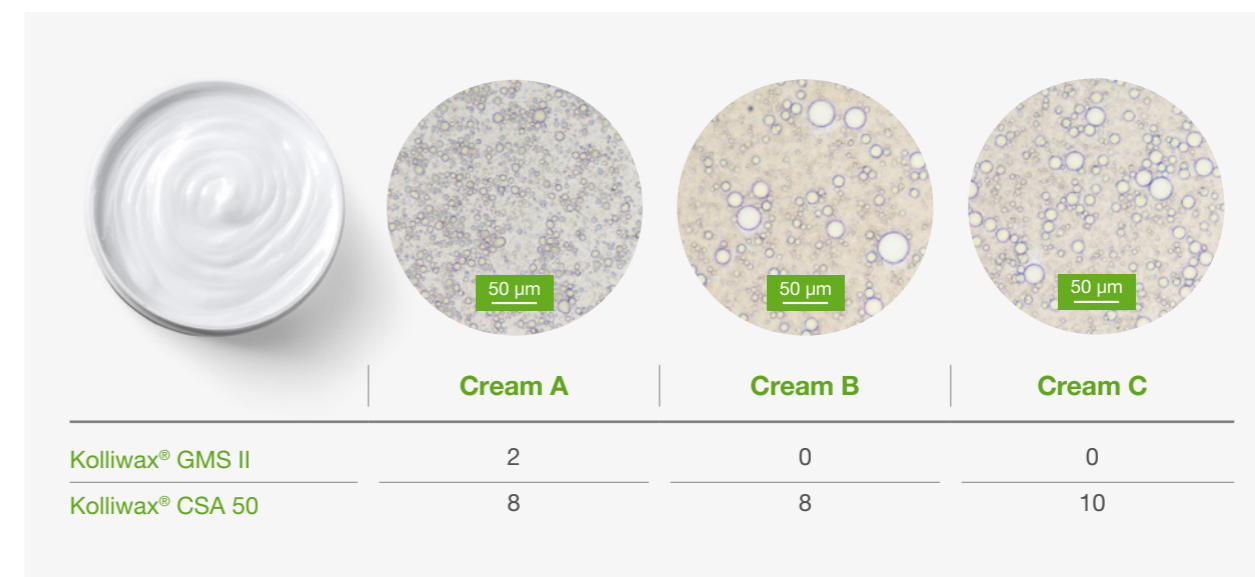
Improving formulation stability with Kolliwax® GMS II

Kolliwax® GMS II (glycerol monostearate 40-55 [type II], mono- and di-glycerides) is a mixture consisting predominantly of 1-glycerol monostearate and 2-glycerol monostearate. Used primarily as a consistency factor or structuring agent in topical applications, this material also functions as a co-emulsifier to enhance formulation stability. Kolliwax® GMS II has a melting point of 54 – 64 °C, allowing this multifunctional material to act as a stabilizing agent in topical formulations such as foams and creams.

To study the effect of Kolliwax® GMS II on cream stability, microscopic analysis was conducted on three creams composed of varying amounts of Kolliwax® GMS II and Kolliwax® CSA 50 (cetostearyl alcohol). Creams stabilized with Kolliwax® GMS II demonstrated smaller droplet size, better droplet dispersion, and stronger emulsification compared to creams composed of Kolliwax® CSA 50 as the lone structuring agent. These differences in droplet size and uniformity can be attributed to Kolliwax® GMS II's amphiphilic character which allows this excipient to offer co-emulsification benefits to reinforce emulsion stability.



Figure 1. Creams composed of variable amounts of structuring agents and co-emulsifiers.



Topical cream A6.5

A protective-feeling, medium thick cream perfect for facial and body applications

Phase	Ingredient	Chemical name	Wt/wt%
A	Water	Water	70.3
	Euxyl® K 712	Sodium benzoate (and) potassium sorbate (and) aqua (water)	1.5
B	Kollisol® PEG 400	Polyethylene glycol	10
	Xanthan gum	Xanthan gum	0.3
C	Kolliphor® CS A	Cetostearyl alcohol (type A), emulsifying	5.0
	Kolliwax® CSA 50	Cetostearyl alcohol	0.4
	Kolliwax® GMS II	Glyceryl monostearate (type II); Mono- and di-glycerides	0.5
	Kollicream® 3 C	Cocoyl caprylocaprate	12

Procedure: Direct conventional method

1. Heat phases A and C separately to 75 to 80 °C.
2. Premix phase B then add to phase A. Using the overhead mixer, mix until uniform. Heat phase A/B to approximately 75 to 80 °C.
3. Add phase C to phase A/B under overhead mixer with fast, sharp-bladed stirring.
4. Continue mixing until fully combined, cooling the emulsion to room temperature.
5. Homogenize briefly, if needed, to achieve an opaque, glossy emulsion.

Kolliwax® CSA 50: Enhancing formulation stability

Fatty alcohols such as Kolliwax® CSA 50 are commonly used as structuring agents in topical formulations. Found in a variety of dosage forms including, but not limited to, creams, lotions, and ointments, Kolliwax® CSA 50 (cetostearyl alcohol) is a fatty alcohol mixture composed primarily of C₁₆ and C₁₈-chain fatty alcohols. When used in tandem with emulsifiers, the combination of the two functionalities can synergistically enhance the formation of viscoelastic lamellar gel networks in oil-in-water creams, stabilizing and promoting size uniformity of oil droplets.

To adjust pickup and rubout following product application, the structuring agent of the formulation can be tuned as needed. Selecting the ideal BASF's Kolliwax® fatty alcohol is essential to achieve desired aesthetics.

Product name	Chemical name	Carbon chain length	Melting point (°C)
Kolliwax® MA	Myristyl alcohol	C ₁₄	36 – 42
Kolliwax® CA	Cetyl alcohol	C ₁₆	46 – 52
Kolliwax® SA	Stearyl alcohol	C ₁₈	57 – 60
Kolliwax® CSA 50	Cetostearyl alcohol	C ₁₆ , C ₁₈	49 – 56
Kolliwax® CSA 70	Cetostearyl alcohol	C ₁₆ , C ₁₈	49 – 56



Topical cream A9.5

A medium thick, emollient cream with light after-feel and suitable for facial and body applications

Phase	Ingredient	Chemical name	Wt/wt%
A	Water	Water	72.3
	Euxyl® K 712	Sodium benzoate (and) potassium sorbate (and) aqua (water)	1.5
B	Kollisol® PEG 400	Polyethylene glycol	10
	Xanthan gum	Xanthan gum	0.3
C	Kolliphor® CS A	Cetostearyl alcohol (type A), emulsifying	4
	Kolliwax® CA	Cetyl alcohol	0.5
	Kolliwax® GMS II	Glyceryl monostearate (type II); Mono- and di-glycerides	0.4
	Kollicream® IPM	Isopropyl myristate	11

Procedure: Direct conventional method

1. Heat phases A and C separately to 75 to 80 °C.
2. Premix phase B then add to phase A. Using the overhead mixer, mix until uniform. Heat phase A/B to approximately 75 to 80 °C.
3. Add phase C to phase A/B under overhead mixer with fast, sharp-bladed stirring.
4. Continue mixing until fully combined, cooling the emulsion to room temperature.
5. Homogenize briefly, if needed, to achieve an opaque, glossy emulsion.



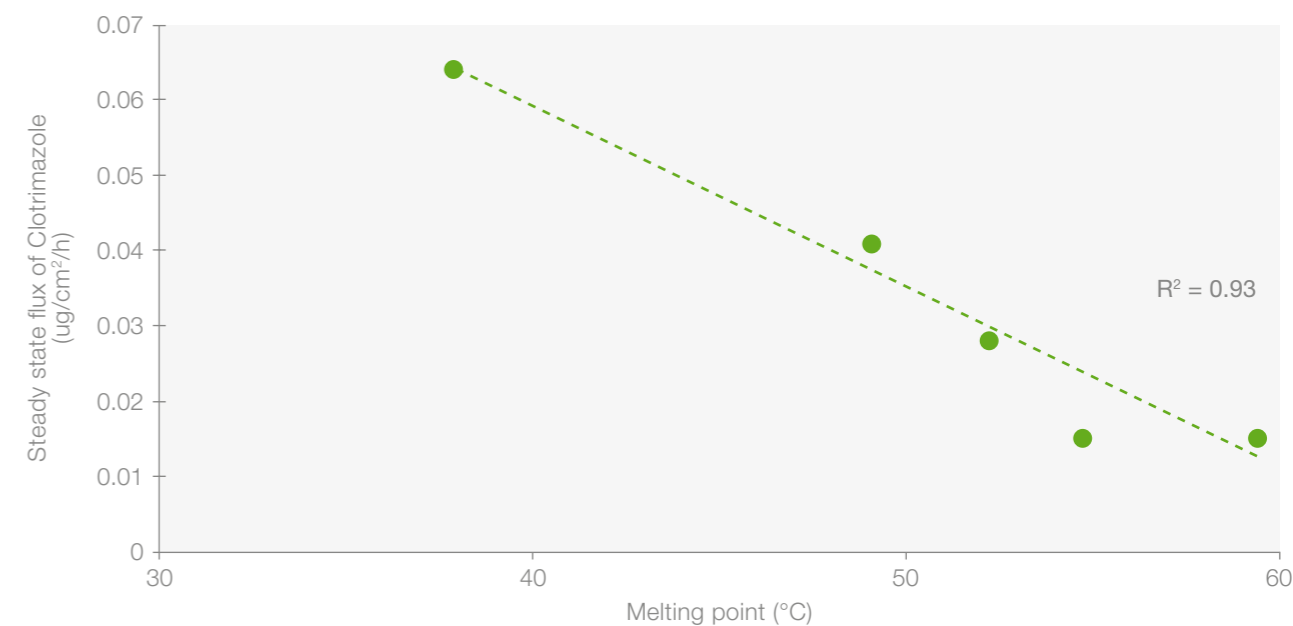
Providing more than just structure: Kolliwax® CA

C₁₆ fatty alcohol Kolliwax® CA (cetyl alcohol) is a versatile material. While it is predominantly known for its functionality as a structuring agent, this lipophilic viscosity factor has been found to influence dermal drug penetration. To study the effect of fatty alcohol composition on dermal drug penetration, IVPT was conducted on clotrimazole creams composed of variable fatty alcohol compositions.

In comparison to the creams composed of higher melting range cetostearyl (C₁₆, C₁₈) or stearyl (C₁₈) alcohol, the formulations composed of Kolliwax® MA (myristyl alcohol) and Kolliwax® CA demonstrated the greatest steady state flux. While Kolliwax® MA's steady state flux was slightly greater than that of Kolliwax® CA, Kolliwax® CA can be used as a singular structuring agent; in comparison, Kolliwax® MA is best suited to be formulated in combination with a higher melting point structuring agent to achieve stable emulsions.

Fatty alcohol	Melting point	Steady state flux (µg/cm ² /h)
Kolliwax® MA	38.0	0.064 ± 0.028
Kolliwax® CA	49.3	0.041 ± 0.021
Kolliwax® CSA 50	52.0	0.028 ± 0.011
Kolliwax® CSA 70	54.3	0.015 ± 0.004
Kolliwax® SA	59.5	0.015 ± 0.004

Figure 2. Inverse relationship of clotrimazole steady state flux and fatty alcohol melting point.



Topical cream SA4.5

An easy-to-apply, low viscosity cream ideal for lightweight applications

Phase	Ingredient	Chemical name	Wt/wt%
A	Water	Water	69
	Euxyl® K 712	Sodium benzoate (and) potassium sorbate (and) aqua (water)	1.5
B	Kollisol® PEG 300	Polyethylene glycol	10
	Xanthan gum	Xanthan gum	0.3
C	Kolliphor® CS A	Cetostearyl alcohol (type A), emulsifying	4
	Kolliphor® CSS	Sodium cetostearyl sulfate	1
	Kolliwax® CSA 50	Cetostearyl alcohol	0.5
	Kolliwax® GMS II	Glyceryl monostearate (type II); Mono- and di-glycerides	0.7
	Kollicream® OD	Octyldodecanol	8
	Kollicream® 3 C	Cocoyl caprylocaprates	5

Procedure: Direct conventional method

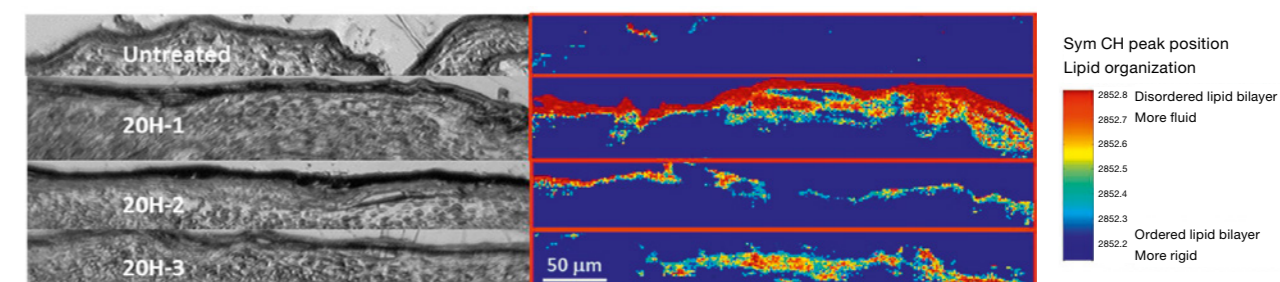
1. Heat phases A and C to 80 °C.
2. Premix phase B then add to phase A. Using the overhead mixer, mix until uniform. Heat phase A/B to approximately 75 to 80 °C.
3. Add phase C to phase A/B under overhead mixer with fast, sharp-bladed stirring.
4. Continue mixing until fully combined, cooling the emulsion to room temperature.
5. Homogenize briefly if needed to achieve an opaque, glossy emulsion.

Enhancing topical drug delivery with Kollicream® OD

Kollicream® OD (octyldodecanol) is a medium spreadability solvent, emollient, and skin penetration enhancer. Suitable for both alkaline and acidic formulations due to its resistance to hydrolysis, Kollicream® OD is a multifunctional excipient that can be formulated into various topical dosage forms.

As a lipidic excipient, Kollicream® OD is a skin penetration enhancer that may improve transdermal drug delivery of some APIs. To visualize the effects of Kollicream® OD on the stratum corneum of the skin, spectroscopic evaluations were conducted. Kollicream® OD was found to be capable of disrupting the highly organized lipids in the stratum corneum via ATR-FTIR (attenuated total reflectance-Fourier transform infrared spectroscopy). As shown in Figure 3 below, Kollicream® OD was detectable up to 40 µm deep in the skin, penetrating inside the stratum corneum and epidermis. The coloring of the skin cross section can be used to understand the intensity of Kollicream® OD penetration in the skin (red = higher Kollicream® OD concentration, blue = lower Kollicream® OD concentration).

Figure 3. ATR-FTIR images showing the CH₂ (~2850 cm⁻¹) peak position.





We create chemistry

For more information visit us at

www.pharma.basf.com

For sample requests contact us at

pharma-solutions@basf.com

This document, or any information provided herein does not constitute a legally binding obligation of BASF and has been prepared in good faith and is believed to be accurate as of the date of issuance. Unless expressly agreed otherwise in writing in a supply contract or other written agreement between you and BASF:

- (a) To the fullest extent not prohibited by the applicable laws, BASF EXPRESSLY DISCLAIMS ALL OTHER REPRESENTATIONS, WARRANTIES, CONDITIONS OR GUARANTEES OF ANY KIND, WHETHER EXPRESS OR IMPLIED, WRITTEN OR ORAL, BY FACT OR LAW, INCLUDING ANY IMPLIED WARRANTIES, REPRESENTATIONS OR CONDITIONS OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, SATISFACTORY QUALITY, NON-INFRINGEMENT, AND ANY REPRESENTATIONS, WARRANTIES, CONDITIONS OR GUARANTEES, ARISING FROM STATUTE, COURSE OF DEALING OR USAGE OF TRADE and BASF HEREBY EXPRESSLY EXCLUDES AND DISCLAIMS ANY LIABILITY RESULTING FROM OR IN CONNECTION WITH THIS DOCUMENT OR ANY INFORMATION PROVIDED HEREIN, including, without limitation, any liability for any direct, consequential, special, or punitive damages relating to or arising therefrom, except in cases of (i) death or personal injury to the extent caused by BASF's sole negligence, (ii) BASF's willful misconduct, fraud or fraudulent misrepresentation or (iii) any matter in respect of which it would be unlawful for BASF to exclude or restrict liability under the applicable laws;
- (b) Any information provided herein can be changed at BASF's sole discretion anytime and neither this document nor the information provided herein may be relied upon to satisfy from any and all obligations you may have to undertake your own inspections and evaluations;
- (c) BASF rejects any obligation to, and will not, automatically update this document and any information provided herein, unless required by applicable law; and
- (d) The user is responsible for confirming that the user has retrieved the most current version of this document from BASF as appropriate

RegXcellence® is a registered trademark of BASF. © March 2023 BASF Corporation. All Rights Reserved.

If you have any further questions or need additional support, please contact your BASF representative.

MarComm-2023-00127

