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Semi-Solid Topical Formulary

High quality – reliable functionality

Topical formulations may be used to deliver active pharmaceutical ingredients (APIs) to or through the skin. These formulations typically possess a relatively soft, spreadable consistency and are often formulated as either water-in-oil or oil-in-water emulsions.

BASF offers an unparalleled portfolio of excipients for topical semi-solid formulations, enabling customers to create an ideal skin delivery solution. This booklet will serve as a guide for formulating topical semi-solid systems with detailed descriptions on processing and characterization techniques. Stable formulations using BASF pharma excipients are highlighted with detailed characterization. An additional number of formulations are included without in-depth characterization. The formulations presented in this booklet will focus on oil-in-water emulsions and demonstrate how different BASF excipients can be combined in order to achieve specific rheological and aesthetic properties.

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1. Methods for Formulating Topical Semi-Solids

Topical semi-solids are prepared via the combination of three separate phases: the oil phase, the aqueous phase, and the active pharmaceutical ingredient (API) phase. When proper processing procedures are carried out, the combination of these three phases will result in a stable emulsion containing an API.

1.1 Methods for Formulating Creams

Example Cream Formulation

Phase	Ingredients	Mass (wt%)
A (Oil)	Emollient	12.00
	Consistency Factor (Wax)	10.00
	Emulsifier	3.00
B (Aqueous)	Water	64.80
	Thickening Agent	0.20
C (Active)	Solvent	8.00
	API	1.00
	Preservative	1.00

Formulating Procedure

1. **Phase A (Oil)** – Prepare phase A by adding each excipient (emollient, consistency factor, and emulsifier) into an appropriately sized beaker. Heat the mixture to about 80°C.

2. **Phase B (Aqueous)** – Prepare phase B by blending the water and thickening agent in an appropriately sized beaker. Heat the mixture to about 80°C. NOTE: This is the phase that phases A and C will be added to so make sure to use a beaker large enough to accommodate the combination and homogenization of the phases. It is recommended to use stainless steel or aluminum beakers for homogenizing.

3. **Phase C (API)** – Prepare phase C by blending the selected API in 5–10% of solvent capable of dissolving the selected API. Heat phase C to about 80°C.

4. After the waxes and oils have completely melted and have formed a clear liquid, add phase A (oil phase) to phase B (aqueous phase) while stirring using an overhead mixer at 500 RPM.

5. Immediately homogenize the phase A and phase B mixture using a benchtop high shear mixer, set to 5000 RPM for 5–10 minutes. NOTE: The settings of the homogenizer (RPM and time) can be adjusted depending on the chemistry to achieve an improved emulsion.

6. After homogenizing, place the mixture under the overhead mixer and set to 200 RPM. While stirring, add phase C (checking that the API is fully dissolved) to the mixture. Continue to stir at 200 RPM as the formulation cools.

7. When the formulation has cooled to about 45°C, add in the preservative according to the amount recommended by the manufacturer (typically 0.5–1.0%).

8. Once the formulation has cooled to room temperature, transfer the semi-solid into an appropriate container, and wait 48 hours before analysis.

Note: Benchtop laboratory reactors are useful for formulating topical semi-solids and provide better consistency in processing and a more controlled environment.

See formulation 3.1.1 for a more detailed example.

1.2 Methods for Formulating Ointments

Example Ointment Formulation

Phase	Ingredients	Mass (wt%)
A	Kollisolv® PEG 400	50.00
	Kollisolv® PEG 3350*	30.00
B	Kollisolv® PG	18.00
	API	1.00
C	Preservative	1.00

Formulating Procedure

1. Heat phase B (API + solvent) until all of the API has dissolved.
2. Prepare phase A by blending the high and low molecular weight PEGs into an appropriately sized beaker. Heat the mixture to 60°C and continue heating until the mixture has completely melted. Try to minimize the heating time as much as possible.
3. Once all the components have melted, place phase A underneath an overhead mixer. Stir at a low shear rate and add phase B.
4. Add phase C (preservative) when the formulation has cooled to about 45°C. Continue stirring until the ointment has solidified.
5. After solidification, place the ointment in an airtight container and wait 48 hours before analysis.

See formulation 3.2.2 for a more detailed example.

*Kollisolv® PEG 3350 is commercially available only in the USA and Canada.

1.3 Methods for Formulating Gels

Example Gel Formulation

Phase	Ingredients	Mass (wt%)
A	Kollisolv® PG	10.00
	Ethanol	10.00
	Glycerin	5.00
	API	1.00
B	Kolliphor® Poloxamer	18.00
	Deionized Water	55.00
C	Preservative	1.00

Formulating Procedure (Cold Process)

1. Leave phase B refrigerated at 5°C for 24 hours, or until all of the Kolliphor® has dissolved in the water (gels can be prepared with Kolliphor® P 188, P 338, and P 407).

2. Add phases A and C to phase B. Stir slowly until the poloxamer has gelled, being careful not to mix in excess air.

Formulating Procedure (Hot Process)

1. Prepare phase B by adding the poloxamer to water which has been preheated to 70°C. Stir this mixture for at least 1 hour to ensure proper dissolution of the poloxamer.

2. As the poloxamer cools, add phases A and C until a robust gel is formed.

1.4 Methods for Formulating Aerosol Foams

Example Aerosol Foam Formulation

Phase	Ingredients	Mass (wt%)
A	API	5.00
	Deionized Water	84.00
	Emulsifier	3.00
	Wax	3.00
B	Propellant	5.00

Formulating Procedure

1. Mix all the phase A ingredients in a beaker, using slight heating if necessary to ensure a uniform distribution.
2. Transfer the contents of the beaker into an appropriate aerosol container.
3. Charge the container with the desired propellant.

See formulation 3.3.1 for a more detailed example.

1.5 Methods for Formulating Non-Aerosol Foams

Example Non-Aerosol Foam Formulation

Phase	Ingredients	Mass (wt%)
A	API	5.00
	Deionized Water	92.00
	Emulsifier (e.g. Kolliphor® P 188)	3.00

Formulating Procedure

1. Mix all the phase A ingredients in a beaker, using slight heating if necessary to ensure a uniform distribution.
2. Transfer the contents of the beaker into an appropriate foam pump bottle.

See formulation 3.3.3 for a more detailed example.

1.6 Methods for Formulating Film-Forming Sprays

Example Film-Forming Formulation

Phase	Ingredients	Mass (wt%)
A	Film-Former	3.00
B	Ethanol	85.00
	Deionized Water	10.00
C	Preservative	1.00
	Plasticizer	1.00

Formulating Procedure

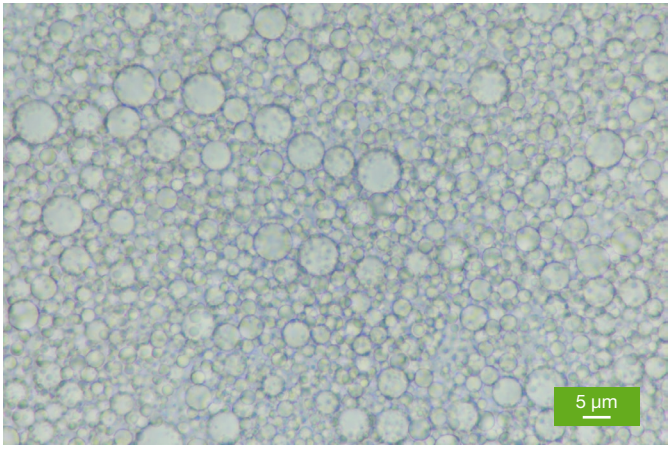
1. Mix phase B at a medium shear rate using an overhead mixer.
2. Slowly add phase A (film-forming polymer) to phase B and continue to stir until the polymer is completely dissolved.
3. Add Phase C and mix until uniform.
4. Transfer the formulation into a high viscosity spray container.

2. Methods of Characterizing Topical Semi-Solids

Key attributes to consider when formulating topical semi-solids include: viscosity and rheological behavior, microstructure of the emulsion and dispersed API, transdermal delivery of the API, sensory profile, and stability.

A. Microscopy

The microstructure of a topical semi-solid is highly sensitive to processing conditions and excipient selection and can impact API delivery, activity, and performance. Additionally, microstructure analysis is an effective way to predict the stability of semi-solid emulsions. Optical light microscopes are a powerful and efficient tool for the characterization of semi-solid microstructure. An example of a semi-solid formulation evaluated using a light microscope at 400x magnification is shown to the right. Microscopy can be used to evaluate the types of structures, networks, and crystallinity that may be present in the semi-solid formulation.

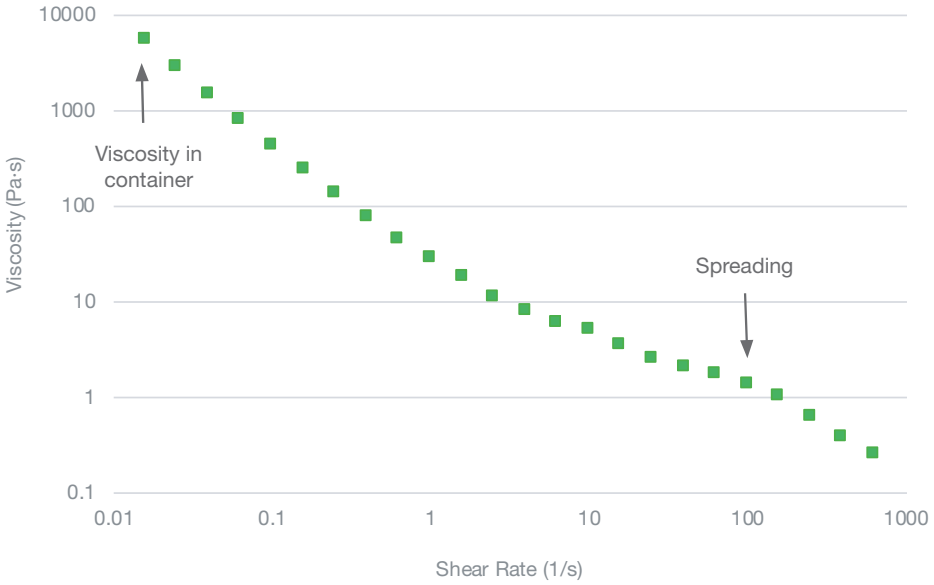


Diclofenac Sodium Emulgel Microstructure, Bright Field (400x magnification)

B. Rheology

The rheological properties of a topical semi-solid directly influence the formulation's sensory properties and API diffusion rate. Changes in the viscosity over time are indicators of the stability of the emulsion. Typically for lotions and creams, a parallel plate rheometer is used in which the product is dispensed between the two parallel plates. The upper tool shears the product and measures its viscosity, while the lower tool remains stationary and controls the temperature of the experiment. Known as a "dynamic sheer sweep," this rheological experiment increases the shear rate applied to the product and measures its viscosity as a function of shear. From this test, a viscosity profile is gathered. This viscosity profile not only provides valuable information about the viscosity of the semi-solid, but also identifies how the viscosity changes with applied force (i.e., spreadability of the product) will affect product behavior during application to the skin.

Viscosity Profile of Semi-Solid Cream

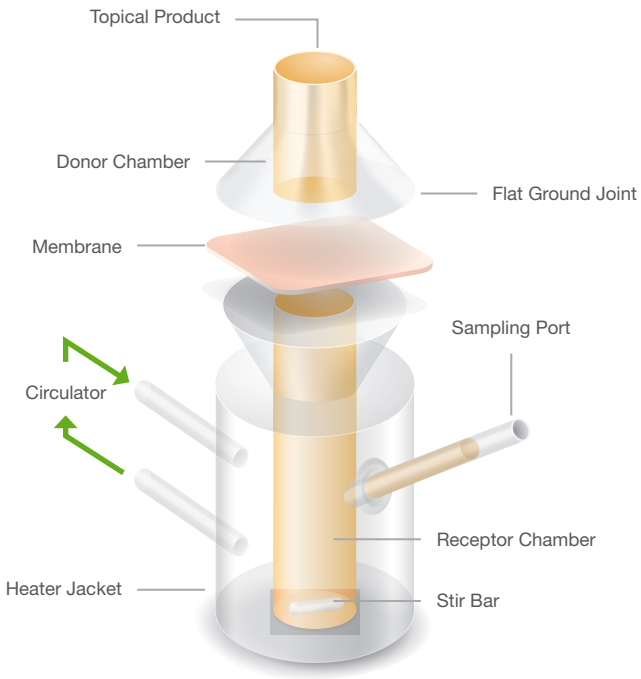


C. *In Vitro* Release Testing using Franz Diffusion Cells

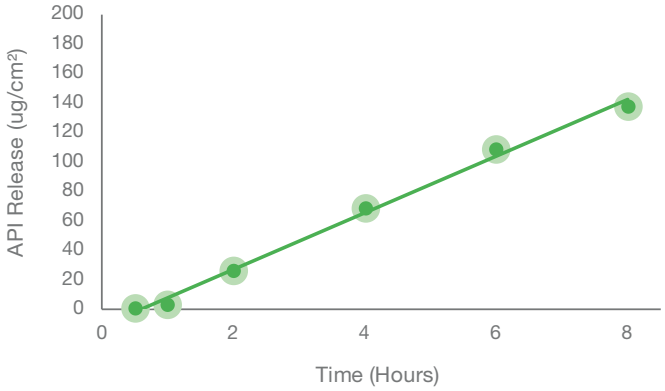
The *in vitro* release/diffusion of an API in a topical semi-solid formulation can be measured using Franz diffusion cells in combination with spectroscopic methods such as HPLC and UV-vis. Synthetic membranes are used in the cells (such as Strat-M®) to simulate delivery through the skin. A Franz diffusion cell consists of a donor chamber and membrane (where the topical is applied), a receptor chamber filled with a buffer solution, a heater/circulator jacket, a sampling port, and a stir bar.

When conducting Franz diffusion cell experiments, it is critical to choose the appropriate buffer solution. When the correct buffer is used, the receptor chamber of the cell will create "sink" conditions that will aid in the diffusion of the API through the membrane. At specific time intervals, samples are extracted from the sampling port of the receptor chamber and discharged into glass vials for spectroscopic analysis. By plotting the amount of API in the receptor chamber as a function of time, a diffusion profile of the topical can be generated.

Typically, six diffusion cells will run in unison (n=6) in order to generate statistically significant data.



Franz Diffusion Cell



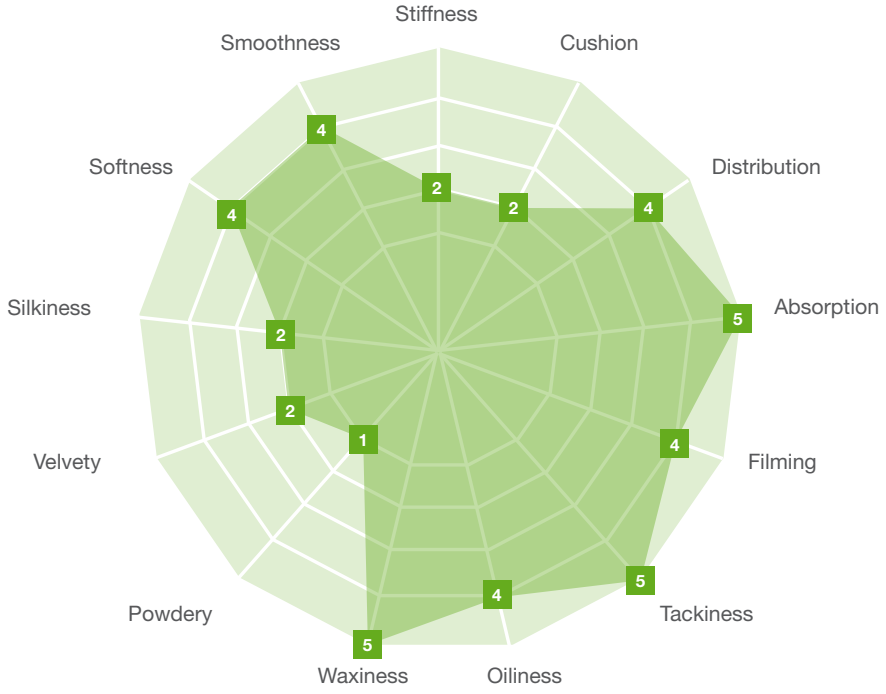
Diffusion Plot – API Containing Cream

D. Sensory Properties

Sensory properties are of critical importance when evaluating topical semi-solids. When developing a new semi-solid formulation, a panel is typically used to evaluate and distinguish different sensory properties. Panels are usually composed of untrained volunteers (large numbers), trained panelists (8–12 people), or an experienced customer panel (16–24 people) calibrated with reference points. For the sensory analysis presented in this formulary, the monadic method was used with a trained sensory panel of 11 subjects.

Monadic Method

The Monadic Method evaluates the effects of varying excipients on sensory properties using a scaling factor. In the diagram below, a panelist compares the test formulation to the reference formulation. Each sensory property is compared to baseline and rated on a scale of 0 to 5.



E. Stability Evaluation

The stability of a topical formulation can be in part determined by "matching" the chemistry of the oil and emulsifier to achieve the proper hydrophilic lipophilic balance (HLB). Typically, stability should be evaluated for at least six months under accelerated conditions to ensure a stable emulsion. When evaluating the stability of an emulsion, the following key characteristics should be monitored over time:

- **pH** – Significant variations in pH over time indicate the occurrence of chemical reactions and are indicative of instability.
- **Viscosity** – An increase or decrease in the viscosity of a semi-solid emulsion over time may also indicate changes in the chemistry, phase behavior, or microstructure. Viscosity of a stable emulsion should remain relatively consistent for several months.
- **Microstructure** – Significant variations in the microstructure of a semi-solid emulsion such as coalescence of oil droplets and/or variations in the size and distribution of the droplets is demonstrative of an unstable emulsion.
- **Phase Separation** – Visual (macro-scale) phase separation such as "weeping" is indicative of an unstable emulsion.

In a complete stability evaluation, formulations are monitored under varying environmental conditions to better predict the stability. The pH, viscosity, microstructure, and phase behavior of a topical semi-solid should be monitored approximately every 2 weeks under the following conditions:

- 25°C and 60% Relative Humidity
- 30°C and 65% Relative Humidity
- 40°C and 75% Relative Humidity

Phase Separation of Two Creams: When emulsion oil droplets coalesce into larger droplets, they migrate upwards causing the underlying layer to appear darker. This is called "creaming."

3. Model Formulations

Model formulations are presented featuring BASF skin delivery excipients. Microstructure, rheology and sensory properties are presented for select formulations.

Selection of the Lipidic Fluid

It is important to choose the right lipidic fluid to not only achieve the desired sensory properties, but to also maintain critical qualities for solubilization and delivery of the active ingredient.

		Spreading				
Emollient	**Chemical Name**	**mPa·s**	**MW**	**mm²/10min**	**Class**	**Emollience**
Kollicream® IPM	Isopropyl myristate	5–6	270	**1200**	**Fast**	**Dry, Light**
Kollicream® 3C	Coco-caprylate/capate	11	335	**800**		
Kollicream® OA	Oleyl alcohol	33	270	**700**		
Kollicream® DO	Decyl oleate	15.9	415	**700**		
Kollicream® OD	Octyl dodecanol	58–64	300	**600**		
Kollisolv® MCT 70	Medium-chain triglycerides	25–33	500	**550**		
Kollicream® CP 15	Cetyl palmitate	(s)	480	**Solid**	**Slow** (molten)	**Rich**

3.1 Model Cream Formulations

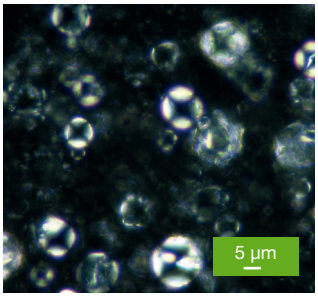
3.1.1 Rich Cream

The rich cream formulation utilizes Kolliwax® CSA 70 and Kolliphor® PS 60 to create a very stiff cream that offers a slow spread and cushioned feeling when applied to the skin. Kollicream® IPM is a fast spreading oil for topical semi-solid formulations that results in a smooth finish.

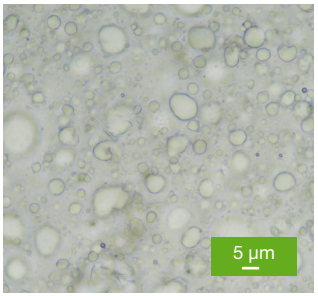
Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kolliwax® CSA 70	Cetostearyl Alcohol	Viscogen, consistency factor	7.00
	Kolliwax® GMS II	Glycerol Monostearate 40-55 (Type II)	Consistency factor, co-emulsifier	2.50
	Kolliphor® PS 60	Polysorbate 60	Emulsifier	4.20
	Kollisolv® MCT 70	Medium Chain Triglycerides	Emollient	11.50
	Kollicream® IPM	Isopropyl Myristate	Emollient	1.30
B	Deionized Water		Solvent	69.20
	Glycerin		Solvent	3.30
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Rich Cream

Kolliwax® CSA 70 is a useful consistency factor where a thicker cream profile (41 Pa·s @1s^{-1}) is desired. Kollicream® IPM is used as a light emollient with broad penetration enhancement properties and as a solubilizer for lipophilic drugs. Kollicream® IPM is a medium polarity emollient which may be used to improve stability.



Microstructure, Polarized
(400x magnification)



Microstructure, Bright Field
(400x magnification)

3.1.2 Light Cream

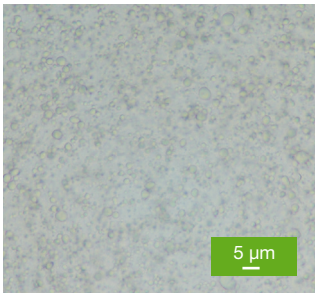
Kollicream® IPM is a medium polarity emollient which may be used to improve stability. Kolliphor® CS 12 and Kolliphor® CS 20 are both non-ionic emulsifiers which are stable in a broad pH range.

Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kolliwax® CSA 50	Cetostearyl Alcohol	Viscogen, consistency factor	4.00
	Kolliwax® GMS II	Glycerol Monostearate 40-55 (Type II)	Consistency factor, co-emulsifier	5.00
	Kolliphor® CS 20	Macrogol Cetostearyl Ether 20	Emulsifier	2.00
	Kolliphor® CS 12	Macrogol Cetostearyl Ether 12	Emulsifier	0.80
	Kollicream® CP 15	Cetyl Palmitate 15	Emollient	0.80
	Kollicream® IPM	Isopropyl Myristate	Emollient	7.40
B	Deionized Water		Solvent	74.00
	Glycerin		Solvent	5.00
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Light Cream

The light cream is a smooth cream with easy distribution, medium viscosity (50 Pa·s @1s^{-1}), and a glossy finish. The hydrophilic-lipophilic balance (HLB) resulting from the blend of Kolliphor® CS 12 and Kolliphor® CS 20 can be adjusted to maximize emulsion stability.

Macrostructure



Microstructure, Bright Field
(400x magnification)

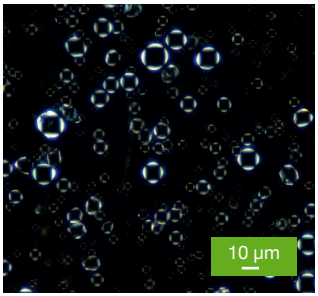
3.1.3 Kollicream® 3C + Kolliphor® CS 12

Kollicream® 3C is a moderately fast spreading oil that offers pleasing sensory properties during application and may also function as a potential penetration enhancer for dermal drug delivery. In clinical studies conducted on highly sensitive patients, Kollicream® 3C was demonstrated to be both mild and non-irritating.

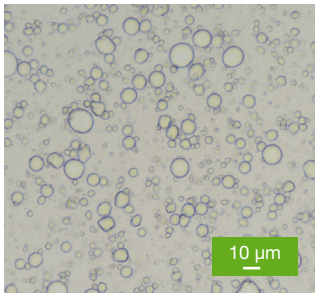
Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollicream® 3C	Cocoyl Caprylocaprate	Emollient	9.00
	Kolliwax® GMS II	Glycerol Monostearate 40-55 (Type II)	Consistency factor, co-emulsifier	0.70
	Kolliwax® S	Stearic Acid 50	Viscogen, consistency factor	0.10
	Kolliwax® CSA 50	Cetostearyl Alcohol	Viscogen, consistency factor	7.50
	Kolliphor® CS 12	Macrogol Cetostearyl Ether 12	Emulsifier	2.70
B	Deionized Water		Solvent	79.00
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Kollicream® 3C + Kolliphor® CS 12

Stable formulations containing Kollicream® 3C were prepared with Kolliphor® CS 12 as the emulsifier and Kolliwax® GMS II as the co-emulsifier. Kolliwax® S, Kolliwax® CSA 50, and Kolliwax® GMS II function as viscogens and consistency factors, yielding a moderate viscosity formulation (19 Pa·s @1s^{-1}) that glides easily on skin and leaves behind a slightly oily finish.



Microstructure, Polarized
(200x magnification)



Microstructure, Bright Field
(200x magnification)

3.1.4 Kollicream® OA + Kolliphor® CS 20 (10% Emollient)

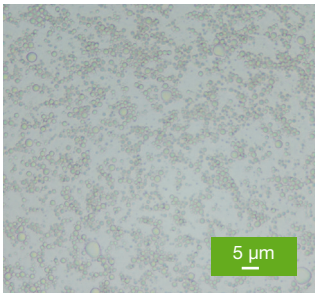
Kollicream® OA is a suitable solubilizer for lipophilic drugs and can also improve the spreadability of semi-solid formulations. Kollicream® OA may also improve dermal penetration due to the unsaturated alkene or alkane chain which can disorder the stratum corneum lipid organization.

Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollicream® OA	Oleyl Alcohol	Emollient	10.00
	Kolliwax® GMS II	Glycerol Monostearate 40-55 (Type II)	Consistency factor, co-emulsifier	0.80
	Kolliphor® CS 20	Macrogol Cetostearyl Ether 20	Emulsifier	2.60
	Kolliwax® S	Stearic Acid 50	Viscogen, consistency factor	0.10
	Kolliwax® CSA 50	Cetostearyl Alcohol	Viscogen, consistency factor	7.50
B	Deionized Water		Solvent	78.00
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Kollicream® OA + Kolliphor® CS 20

The viscosity, microstructure, and sensory properties of the sample formulation were tailored by changing the chemistry of the emulsifier. The combination of the emulsifier and co-emulsifier, Kolliphor® CS 20 and Kolliwax® GMS II, respectively, yields a formulation with a creamy texture (25 Pa·s @1s^{-1}) and some residual tackiness.

Macrostructure



Microstructure, Bright Field
(400x magnification)

3.1.5 Kollicream® OD + Kolliphor® CS 20 (12% Emollient)

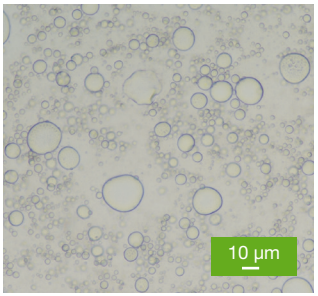
Kollicream® OD is a low polarity, medium spreading, non-ester emollient that is widely used in creams and lotions. Kollicream® OD is a solubilizer for lipophilic actives and offers good skin tolerance. Kollicream® OD is stable against acid and base hydrolysis, and may function to enhance skin penetration.

Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollicream® OD	Octyldodecanol	Emollient	12.00
	Kolliphor® CS 20	Macrogol Cetostearyl Ether 20	Emulsifier	3.10
	Kolliwax® S	Stearic Acid 50	Viscogen, consistency factor	0.10
	Kolliwax® CSA 50	Cetostearyl Alcohol	Viscogen, consistency factor	7.50
	Kolliwax® GMS II	Glycerol Monostearate 40-55 (Type II)	Consistency factor, co-emulsifier	0.50
B	Deionized Water		Solvent	75.80
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Kollicream® OD + Kolliphor® CS 20

The viscosity, microstructure, and sensory properties of Kollicream® OD based topical semi-solids are similar to those of formulations containing a combination of Kollicream® OA and Kolliphor® CS 20. The combination of Kollicream® OD and Kolliphor® CS 20 yields a medium viscosity (19 Pa·s @1s^{-1}), formulation with a non-greasy finish.

Macrostructure



Microstructure, Bright Field
(200x magnification)

3.1.6 Kolliphor® PS 80

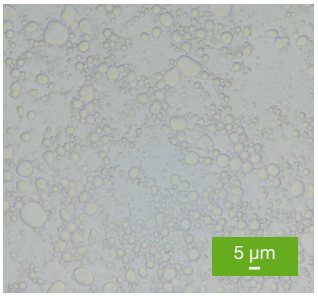
Kolliphor® PS 80 can be used as a solubilizer for APIs that are poorly soluble in water. It can also aid in the stabilization of emulsions.

Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollicream® 3C	Cocoyl Caprylocaprate	Emollient	20.00
	Kolliphor® PS 80	Polysorbate 80	Solubilizer, emulsifier	3.00
	Kolliwax® GMS II	Glycerol Monostearate 40-55 (Type II)	Consistency factor, co-emulsifier	3.00
	Kolliwax® CSA 70	Cetostearyl Alcohol	Viscogen, consistency factor	5.00
B	Deionized Water		Solvent	68.00
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Kolliphor® PS 80

Polysorbates are mainly used as solubilizers, emulsifiers, or suspension stabilizers in pharmaceutical applications. Kolliphor® PS 80 and PS 20 have also been found to increase the skin penetration of certain APIs. All polysorbate products have a wide pH range of effective use. This formulation yields a cream with a medium viscosity (14 Pa·s @1s^{-1}) and smooth feel.

Macrostructure



Microstructure, Bright Field
(400x magnification)

3.1.7 Kolliphor® CS A

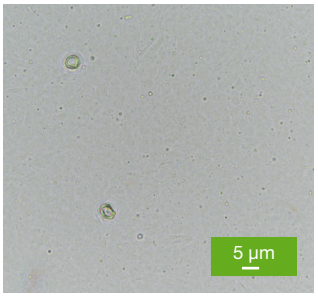
Kolliphor® CS A is self-emulsifying, providing body and thickness to a cream. This property is useful for minimizing the number of ingredients needed in a cream. An emollient such as Kollicream® 3C can also be added to provide a softer feel in addition to increasing the spreadability.

Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kolliphor® CS A	Cetostearyl Alcohol (Type A), emulsifying	Consistency factor, emulsifier	8.00
	Kollisolv® PG	Propylene Glycol	Solvent	4.00
B	Deionized Water		Solvent	87.00
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Self-Emulsifying Cream

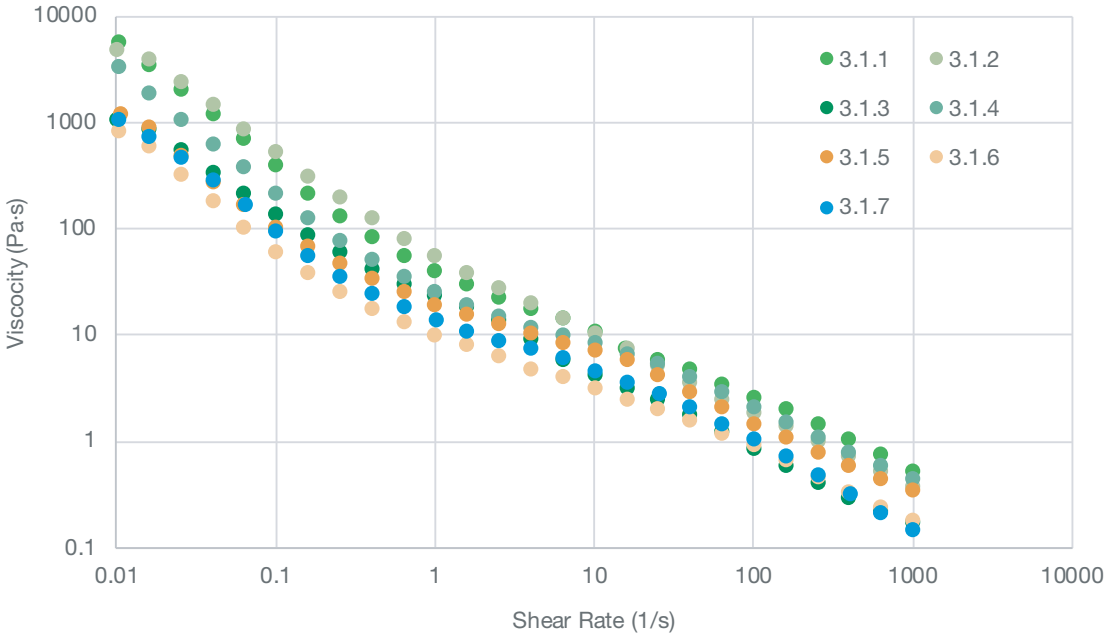
Self-emulsifying excipients such as Kolliphor® CS A demonstrate the ability to structurally organize a cream without the aid of other components. When mixed with water, Kolliphor® CS A yields a translucent semi-solid that has a viscous nature (37 Pa·s @1s^{-1}). The physical stability of the cream is aided by the formation of multilamellar onion-like phases in addition to the extended gel network. It is recommended that an emollient is added in the final formulation for a more robust cream.

Macrostructure



Microstructure, Bright Field
(400x magnification)

Compiled Rheology of Presented Creams at 25°C



3.2 Model Ointment Formulations

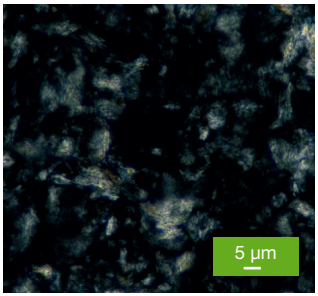
3.2.1 Kollisolv® PEG Ointment

Kollisolv® PEG ointments can be used as an alternative to traditional petrolatum-based ointment formulations. By pairing different amounts of high and low molecular weight chains, PEG ointments can be tuned for desirable rheological profiles and sensory properties.

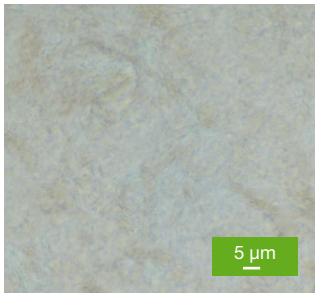
Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollisolv® PEG 400	Polyethylene Glycol 400	Solvent	50.00
	Kollisolv® PEG 3350*	Polyethylene Glycol 3350	Viscogen, consistency factor	30.00
B	Kollisolv® PG	Propylene Glycol	Solvent	20.00

Model Formulation: Kollisolv® PEG Ointment

Low molecular weight liquid PEG 400 can be an excellent solvent for substances that do not readily dissolve in water. PEG 400 formulations offer a slightly slick residue following application to the skin. To ensure API integrity, it is recommended that tests should always be performed to account for variations in API stability and solubility.



Microstructure, Polarized
(400x magnification)



Microstructure, Bright Field
(400x magnification)

*Kollisolv® PEG 3350 is commercially available only in the USA and Canada.

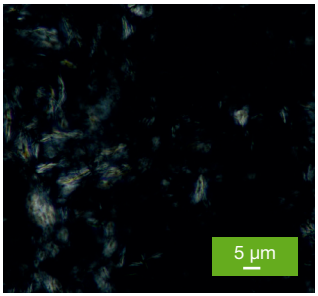
3.2.2 Novata® Ointment

The Novata® ointment has a rich feel when applied to the skin, leaving behind a slightly oily residue. The use of several emollients in addition to waxes and hard fats leads to a balanced ointment with good shear and sensory properties.

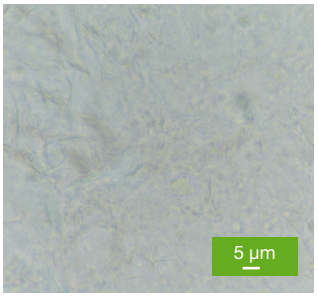
Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kolliwax® HCO	Hydrogenated Castor Oil	Consistency factor	2.00
	Kolliwax® GMS II	Glycerol Monostearate 40-55 (Type II)	Consistency factor	4.00
	Kollicream® 3C	Cocoyl Caprylocaprate	Emollient, solvent	19.00
	Kollicream® OD	Octyldodecanol	Emollient, solvent	19.00
	Novata® BC PH	Hard Fat	Solubilizer, consistency factor	20.00
	White Wax		Consistency factor, viscogen	10.00
	Kollicream® CP 15	Cetyl Palmitate 15	Emollient, solvent	7.00
	Kollicream® IPM	Isopropyl Myristate	Emollient, solvent	10.00
	Kollisolv® MCT 70	Medium Chain Triglycerides	Emollient, solvent	9.00

Model Formulation: Novata® Ointment

Commonly used in suppositories, Novata® hard fats also offer desirable functionalities in ointment formulations including improved solubilization of some APIs and enhanced sensory properties due to their low melting ranges. The Novata® line complies with the European Pharmacopoeia monograph for "hard fat."

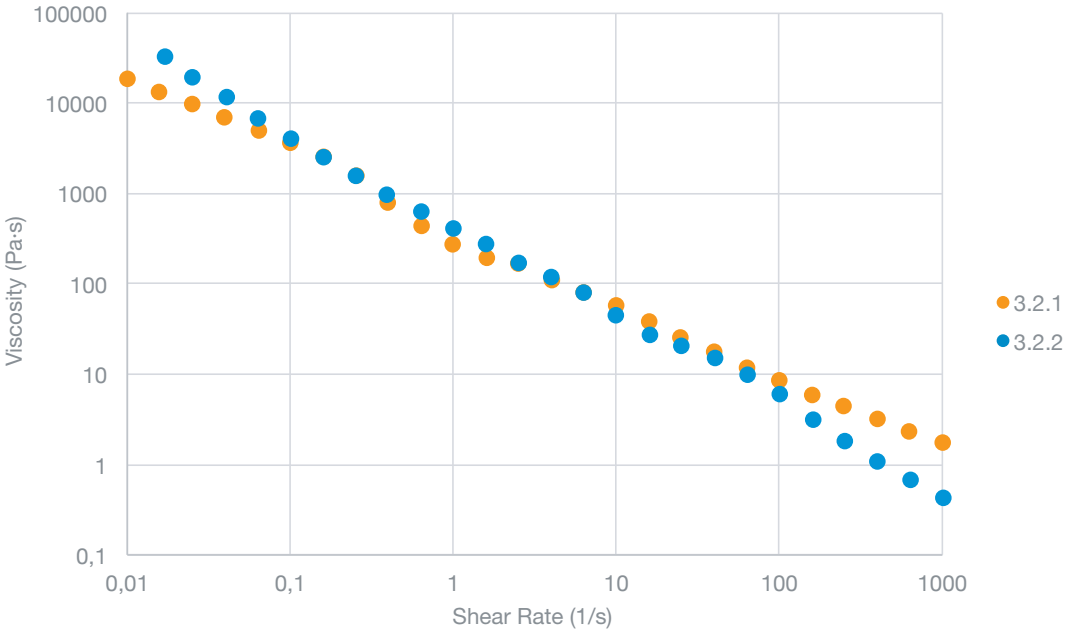


Microstructure, Polarized
(400x magnification)



Microstructure, Bright Field
(400x magnification)

Compiled Rheology of Presented Ointments at 25°C



3.3 Model Foam Formulations

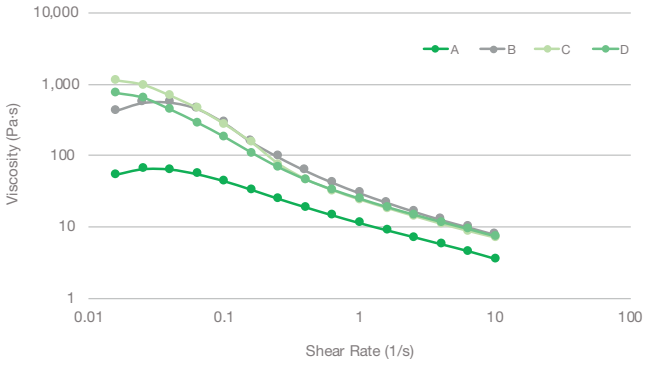
3.3.1 General Aerosol Foams

Growing in popularity, topical foams can sometimes be preferred over a cream due to their pleasing sensory application. The four foam formulations below retain their shape upon application to the skin, spreading easily and drying quickly.

Ingredients	Chemical Name	Role	A (wt%)	B (wt%)	C (wt%)	D (wt%)
Kolliwax® CSA 50	Cetostearyl Alcohol	Foam stabilizer	3.00	3.00	3.00	3.00
Kolliphor® CS 12	Macrogol Cetostearyl Ether 12	Foaming agent, emulsifier	0.00	0.00	6.00	5.00
Kolliphor® CS 20	Macrogol Cetostearyl Ether 20	Foaming agent, emulsifier	5.00	6.00	0.00	0.00
Kollicream® 3C	Cocoyl Caprylocaprate	Emollient, solubilizer	3.00	3.00	3.00	3.00
Kolliphor® P 188	Poloxamer 188	Foaming agent	1.00	0.00	0.00	1.00
Deionized Water		Solvent	82.00	82.00	82.00	82.00
A-46	Propane/Isobutane	Propellant, solvent	6.00	6.00	6.00	6.00

Model Formulation: Kolliphor® Emulsification

Foams made with Kolliphor® CS 12 tend to demonstrate a higher viscosity and stiffness than foams formulated with Kolliphor® CS 20. To create richer, creamier foams, poloxamers such as Kolliphor® P 188 or Kolliphor® P 407 can be added to the formulations as needed. The incorporation of an aerosol propellant can further enhance foam richness.



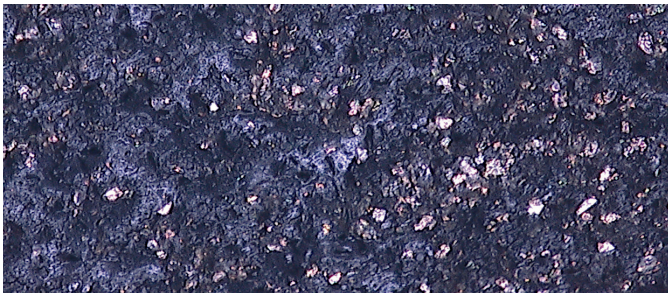
3.3.2 Kollidon® 90 F Film-Forming Foam

Kollidon® 90 F foam formulations yield smooth, cohesive films on the skin with excellent API retention and good bioadhesion. Kollidon® 90 F foams are easily applied to the skin from an aerosol dispenser and can be used to treat very large surface areas.

Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollicream® 3C	Cocoyl Caprylocaprate	Emollient, solubilizer	3.00
	Kolliwax® CSA 50	Cetostearyl Alcohol	Foam Stabilizer	3.00
B	Deionized Water		Solvent	73.00
	Kolliphor® CS 20	Macrogol Cetostearyl Ether 20	Foaming agent	5.00
C	Kollidon® 90 F	Polyvinylpyrrolidone	Film Former	10.00
D	A-46	Propane/Isobutane	Propellant, solvent	6.00

Model Formulation: Kollidon® 90 F

Kollidon® 90 F yields rich foams with favorable sensory properties and fast dry times. Most of the BASF film-forming excipients offered in BASF's skin delivery portfolio can be utilized in aerosol foams. In topical foam formulations, high molecular weight polymers are necessary to achieve cohesive films on the skin from a topical foam formulation. Kollidon® 90 F foams are stable for up to 3+ months in ambient conditions.



Kollidon® 90 F Film + Faux API on Human Skin

3.3.3 Kolliphor® P 188 Povidone-Iodine Foam

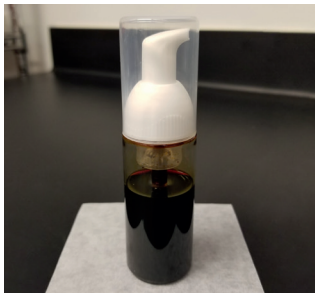
Kolliphor® P 188 acts as an effective emulsifier in the formation of non-aerosol foams for topical use. Foams of various strength can be created by altering the mass percent of the API.

Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	PVP Iodine 30	Povidone-Iodine	API	5.00–10.00
	Deionized Water		Solvent	87.00–92.00
	Kolliphor® P 188	Poloxamer 188	Emulsifier, foaming agent	3.00

Model Formulation: PVP-I Foam

A poloxamer foam with PVP-I is an effective antiseptic that does not require an aerosol. As a foam, it can be spread over a wide area of skin. Poloxamers such as Kolliphor® P 188 can help decrease overall droplet size and prevent the aggregation of large molecules.

Macrostructure (5% PVP-I)



5% PVP-I foaming liquid

3.4 Model Film-Forming Spray Formulations

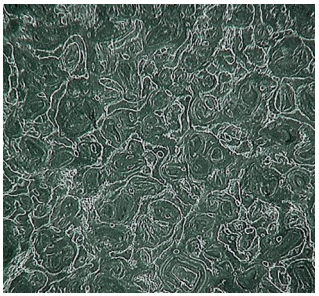
3.4.1 Kollidon® 90 F Film-Forming Spray

Kollidon® 90 F spray formulations yield smooth, cohesive films on the skin with excellent API retention and good bioadhesion. Kollidon® 90 F film formers are easily applied to the skin from a high viscosity spray container and can be used to treat very large surface areas.

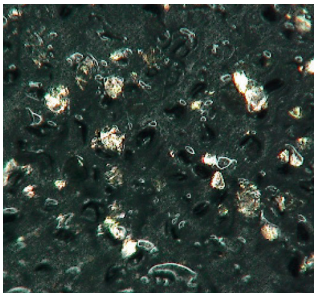
Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollidon® 90 F	Polyvinylpyrrolidone	Film former	3.00
B	Deionized Water		Solvent	9.70
	Ethanol		Solvent	86.30
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Kollidon® 90 F

Kollidon® 90 F yields sprays with fast dry times and some moisture resistance. Kollidon 90 F films can be removed from the skin with soap and warm water. Kollidon® 90 F sprays are stable for up to 3+ months in accelerated conditions.



Neat Vitro Skin Substrate



Vitro Skin Substrate with Kollidon® 90 F

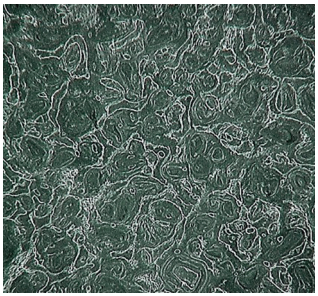
3.4.2 Kollicoat® SR 30 D Film-Forming Spray

Kollicoat® SR 30 D sprays yield smooth, cohesive films on the skin with fast dry times (20–30 seconds). Kollicoat® SR 30 D films demonstrate excellent water resistance, but still allow for removal from the skin's surface with soap and warm water.

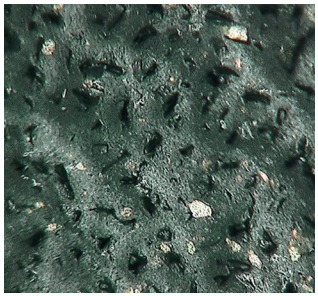
Phase	Ingredients	Chemical Name	Role	Mass (wt%)
A	Kollicoat® SR 30 D	Polyvinyl acetate	Film former	13.33
B	Ethanol		Solvent	85.67
C	Euxyl® PE 9010	Phenoxyethanol	Preservative	1.00

Model Formulation: Kollicoat® SR 30 D

Microscopic analysis reveals excellent API retention on the skin (based on faux API gold pigment). Using a high viscosity spray nozzle, Kollicoat® SR 30 D films are easily sprayed onto the skin. For localized application to smaller surface areas, Kollicoat® SR 30 D films can also be brushed onto the skin.



Neat Vitro Skin Substrate



Vitro Skin Substrate with Kollicoat® SR 30 D

3.5 Model Gel Formulations

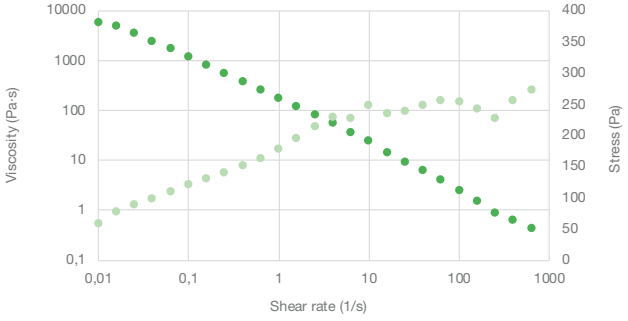
3.5.1 Poloxamers as Gelling Agents

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 liquid at room temperature but solidify upon contact with skin.

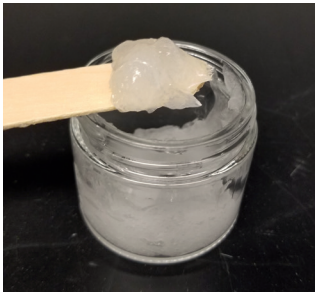
Phase	Ingredients	Chemical Name	Description	Mass (wt%)
A	Ethanol		Solvent	10.00
	Kollisolv® PG	Propylene Glycol	Solvent	10.00
	Kollicream® IPM	Isopropyl Myristate	Tack reducer, emollient	2.00
	Glycerin		Solvent	5.00
B	Kolliphor® P 407	Poloxamer 407	Gelling agent	15.00–20.00
	Deionized Water		Solvent	53.00–58.00

Model Formulation: Kolliphor® P 407

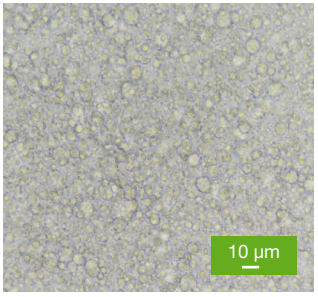
Gelling of a given poloxamer is a function of temperature, structure, and concentration. At high enough concentrations, poloxamers form multimolecular aggregates and micelles that aid in gelling. Increasing the amount of ethanol used in a formulation results in an increased gelling temperature. To reduce tackiness and improve the sensory profile of a gel, an emollient such as Kollicream® IPM can be incorporated into the formulation.



Gel Behavior at 32°C



Macrostructure



Microstructure, Bright Field
(200x magnification)

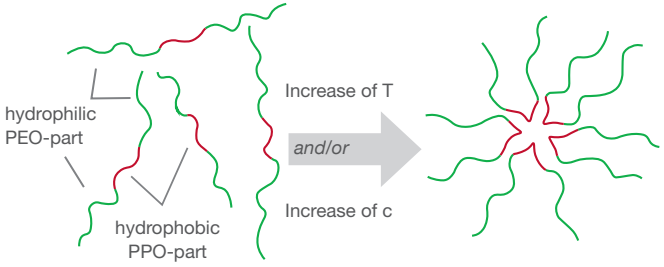
3.5.2 Emulgel

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; these hydrophobic and hydrophilic interactions are driven by the PPO and PEO segments of the polymer, respectively.

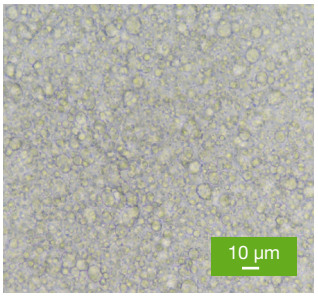
Phase	Ingredients	Chemical Name	Description	Mass (wt%)
A	Ethanol		Solvent	10.00
	Kollisolv® PEG 400	Polyethylene Glycol 400	Solvent	15.00
	Glycerin		Solvent	5.00
B	Kolliphor® P 407	Poloxamer 407	Gelling agent	18.00
	Deionized Water		Solvent	42.00
C	Kollicream® 3C	Cocoyl Caprylocaprate	Emollient	10.00

Model Formulation: Emulgel

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

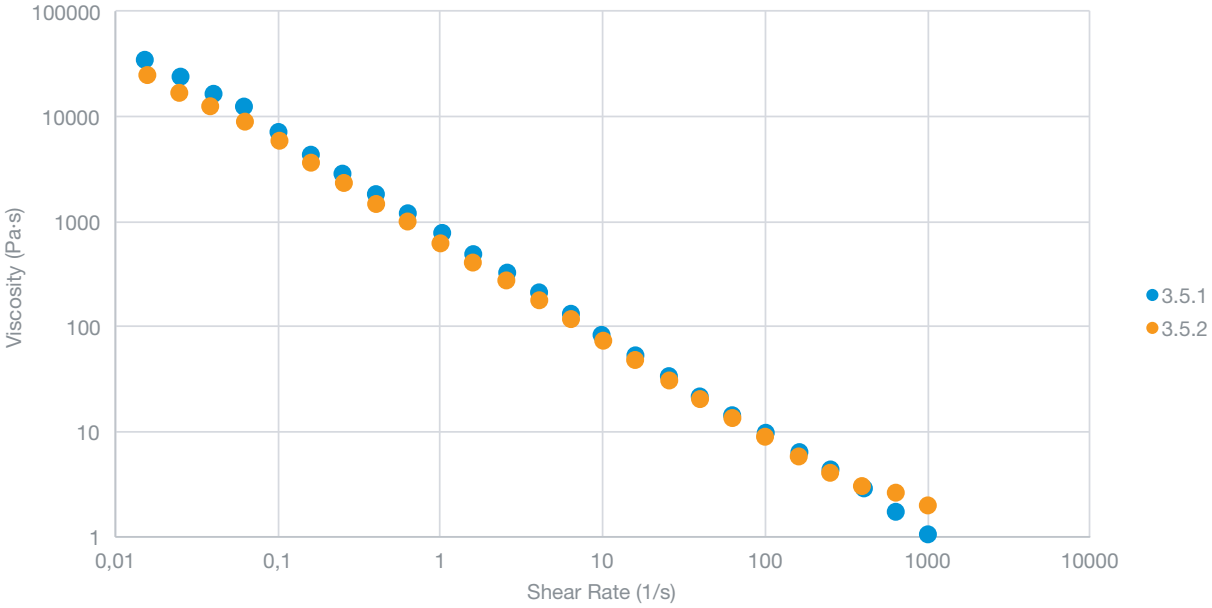


Macrostructure



Microstructure, Bright Field
(200x magnification)

Compiled Rheology of Presented Gels at 25°C



3.6 Additional Formulations*

Kollicream® 3C + Kolliphor® CSL			
Phase	**Ingredients**	**Description**	**Mass**
A	Kollicream® 3C	Emollient	20.00
	Kolliphor® CSL	Emulsifier, consistency factor	5.00
B	Deionized Water	Solvent	73.80
	Xanthan Gum	Viscogen	0.20
C	Euxyl® PE 9010	Preservative	1.00

Kollicream® IPM + Kolliphor® CSL			
Phase	**Ingredients**	**Description**	**Mass**
A	Kollicream® IPM	Emollient	20.00
	Kolliphor® CSL	Emulsifier, consistency factor	5.00
B	Deionized Water	Solvent	73.80
	Xanthan Gum	Viscogen	0.20
C	Euxyl® PE 9010	Preservative	1.00

*Cream formulations showing stability after a year of ambient conditions are displayed in the following pages.

Kollisolv® MCT 70 + Kolliphor® CS A

Phase	Ingredients	Description	Mass
A	Kollisolv® MCT 70	Emollient	20.00
	Kolliphor® CS A	Emulsifier, consistency factor	5.00
B	Deionized Water	Solvent	73.80
	Xanthan Gum	Viscogen	0.20
C	Euxyl® PE 9010	Preservative	1.00

Kollicream® IPM + Kolliphor® CS A

Phase	Ingredients	Role	Mass
A	Kollicream® IPM	Emollient	8.00
	Kolliphor® CS A	Emulsifier, consistency factor	10.00
B	Deionized Water	Solvent	80.80
	Xanthan Gum	Viscogen	0.20
C	Euxyl® PE 9010	Preservative	1.00

Kollicream® OA + Kolliphor® CS A

Phase	Ingredients	Description	Mass
A	Kollicream® OA	Emollient	20.00
	Kolliphor® CS A	Emulsifier, consistency factor	5.00
B	Deionized Water	Solvent	73.80
	Xanthan Gum	Viscogen	0.20
C	Euxyl® PE 9010	Preservative	1.00

Kollicream® OA + Kolliphor® CSL			
Phase	**Ingredients**	**Description**	**Mass**
A	Kollicream® OA	Emollient	20.00
	Kolliphor® CSL	Emulsifier, consistency factor	5.00
B	Deionized Water	Solvent	73.80
	Xanthan Gum	Viscogen	0.20
C	Euxyl® PE 9010	Preservative	1.00

Kollicream® OD + Kolliphor® CSL			
Phase	**Ingredients**	**Description**	**Mass**
A	Kollicream® OD	Emollient	20.00
	Kolliphor® CSL	Emulsifier, consistency factor	5.00
B	Deionized Water	Solvent	73.80
	Xanthan Gum	Viscogen	0.20
C	Euxyl® PE 9010	Preservative	1.00

4. BASF Skin Delivery Excipients*

A select list of skin delivery ingredients for emulsions, ointments, and gels.

Functionality	Product	Description
Emollients & Solvents	Kollicream® 3C	Medium spreadability. Extremely mild. Solvent for lipophilic drugs. Enhances skin penetration.
	Kollicream® CP 15	Solid, slow spreading with rich feeling. Solvent for lipophilic drugs.
	Kollicream® IPM	Fast spreading with light and fresh feeling. Solvent for lipophilic drugs. Enhances skin penetration.
	Kollicream® OA	Medium spreadability. Solvent for lipophilic drugs. Enhances skin penetration.
	Kollicream® OD	Medium spreadability. Solvent for lipophilic drugs. Enhances skin penetration. Effective in exceptionally wide pH range.
	Kollisolv® MCT 70	Oily solvent for some lipophilic drugs. Water barrier-repairing, emollient film-former on skin.
Consistency Factors & Viscosity Enhancement	Kolliwax® S	Structure-building consistency factor with dry feel; forms crystalline barrier on skin.
	Kolliwax® SA	Structure-building consistency factor for semi-solids. Viscosity regulator. Higher melting point.
	Kolliwax® CSA 50	Structure-building consistency factor for semi-solids. Viscosity regulator.
	Kolliwax® GMS II	Structure-building consistency factor for semi-solids. Can mitigate stickiness or greasiness.
Emulsification	Kolliphor® CS 12	Nonionic emulsifier for O/W emulsions.
	Kolliphor® CS 20	Nonionic emulsifier for O/W emulsions.
	Kolliphor® PS 60	Nonionic emulsifier for O/W emulsions; foam stabilizer.
	Kolliphor® CS A	Anionic emulsifier and consistency factor combination for creams & lotions.
	Kolliwax® GMS II	Co-emulsifier and low HLB surfactant. Stabilizes surfactant phases & emulsion droplets.

*This list is to serve a a brief summary of commonly utilized excipients offered in the BASF Skin Delivery portfolio. For complete list of excipients, visit www.pharma.basf.com.

Form				Monography Name*/Chemical Name
Emulsions & Creams	Ointments	Gels	Foams	
■	■	■	■	Ph. Eur.: Cocoyl caprylocaprate, Coco-caprylate/caprate
■	■			Ph. Eur.: Cetyl Palmitate 15
■	■	■	■	Ph. Eur., USP-NF: Isopropyl Myristate
■	■	■	■	Ph. Eur., USP-NF: Oleyl Alcohol
■	■	■	■	Ph. Eur., USP-NF: Octyldodecanol
■	■	■	■	Ph. Eur.: Medium Chain Triglycerides, USP-NF: Triglycerides, Medium Chain
■	■	■		Ph. Eur., USP-NF, JP: Stearic Acid 50
■	■	■		Ph. Eur., USP-NF, JP: Stearyl Alcohol
■	■	■		Ph. Eur., USP-NF, JP: Cetostearyl Alcohol 50
■	■	■	■	Ph. Eur.: Glycerol Monostearate 40-55 (Type II), USP-NF: Mono- and Di-Glycerides
■			■	Ph. Eur.: Macrogol Cetostearyl Ether 12
■			■	Ph. Eur.: Macrogol Cetostearyl Ether 20, USP-NF: Polyoxyl 20 Cetostearyl Ether
■		■	■	Ph. Eur., USP-NF, JP: Polysorbate 60
■				Ph. Eur.: Cetostearyl Alcohol (Type A), Emulsifying
■	■	■	■	Ph. Eur.: Glycerol Monostearate 40-55 (Type II), USP-NF: Mono- and Di-Glycerides

*Monograph references were updated at time of printing. Please visit us online for the latest status.

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