Technical Information

Kolliwax® GMS II

Glycerol Monostearate

Functional excipient for semi-solid formulations and solid oral dosage forms.

April 2019 | Supersedes issue dated February 2016 | WF-No. 137110

BASF
We create chemistry

1. Introduction

Our Kolliwax® portfolio includes a total of ten products, most of them being predominantly used as consistency factors in topical applications. While the fatty acid and alcohol based products are summarized in the general Technical Information sheet on the Kolliwax® grades, two products (namely Kolliwax® HCO and Kolliwax® GMS II) are provided with their own, dedicated technical information sheet due to the broad application areas: this document focuses on Kolliwax® GMS II, our pharmaceutical grade glycerol monostearate, which covers a broad range of pharmaceutical applications ranging from a consistency factor and (co-)emulsifier in topical applications (i.e. lotions and creams), to solid oral dosage forms, where it can be used e.g. as a lubricant in the tableting process, and/or as an anti-tacking agent for coatings.

Kolliwax® GMS II complies with the following compendial monographs:

Ph. Eur.: Glycerol monostearate 40-55 (type II)

USP/NF: Mono- and Diglycerides

For further details please refer to the product specification sheet, as well as the quality and regulatory product information (QRPI).

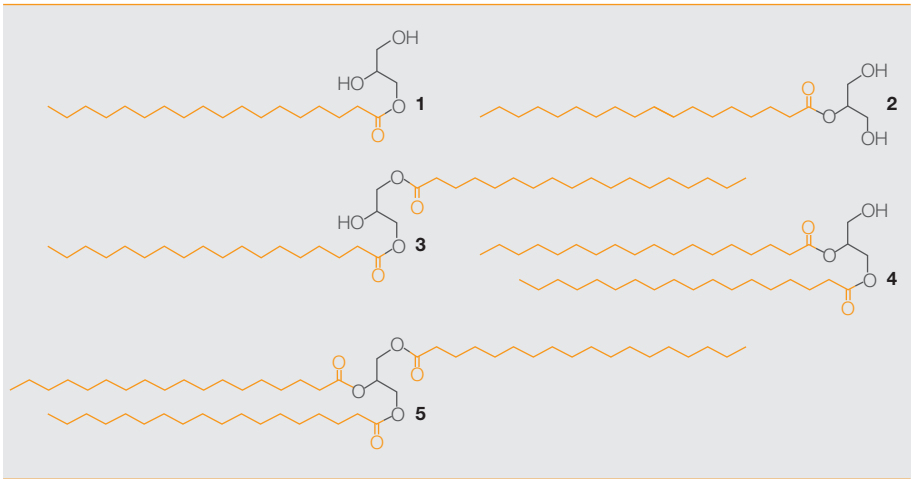

Figure 1: Chemical Structures of the major components that make up for Kolliwax® GMS II. Lead components are the two monoglyceride compounds 1-glycerol monostearate (1), and 2-glycerol monostearate (2); according to the Ph.Eur. monography, these must make up for 40 – 55% of the mixture (hence the name).
The product also contains the 1,3 and 1,2 diglycerides (3 and 4, respectively), as well as the triglyceride (5). Please refer to the products specification sheet for details on the distribution of the compounds, as well as possible ratios of C_{16}/C_{18} fatty acids. For simplicity reasons, only stearic acid (C_{18}) is shown in this scheme as the hydrophobic moiety.

2. Technical properties

Description

Kolliwax® GMS II is an off-white to slightly yellowish, waxy substance derived from natural resources such as coconut- and palm kernel oil. It contains mostly mono- and diesters of mainly stearic (C_{18}), but also palmitic (C_{16}) acid with glycerol (Fig. 1). Kolliwax® GMS II is practically insoluble in water, but soluble in hot ethanol (> 50% at 60 °C).

Owing to free hydroxyl groups on the glycerol end of the molecule, the product exhibits an amphiphilic character that is reflected in the HLB value of approx. 3.8, and a melting point of 54 – 64 °C, which is significantly higher than that of the respective triglycerides (please refer to the documents on our Novata® Grades for further information).

Appearance

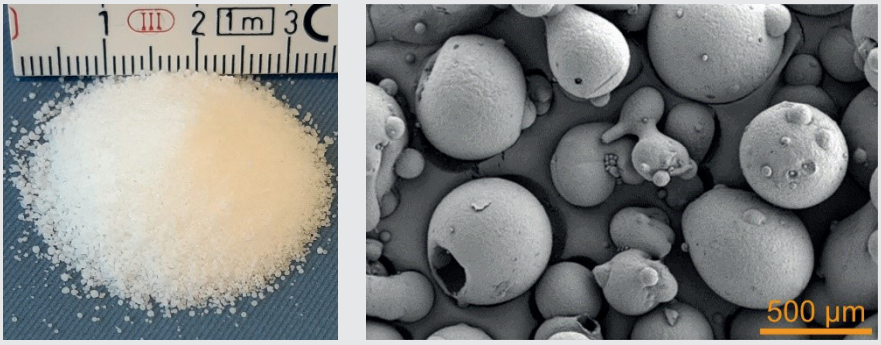

Figure 2: Kolliwax® GMS II is provided as a free-flowing powder (left), consisting of spherical particles that are formed during the spray crystallization process. These structures can be seen in the scanning electron microscope image (right).

Powder Characteristics

The following values are typical for a representative sample of Kolliwax® GMS II. However, as they are not part of the product specification, the values are for guidance only:

Particle size distribution

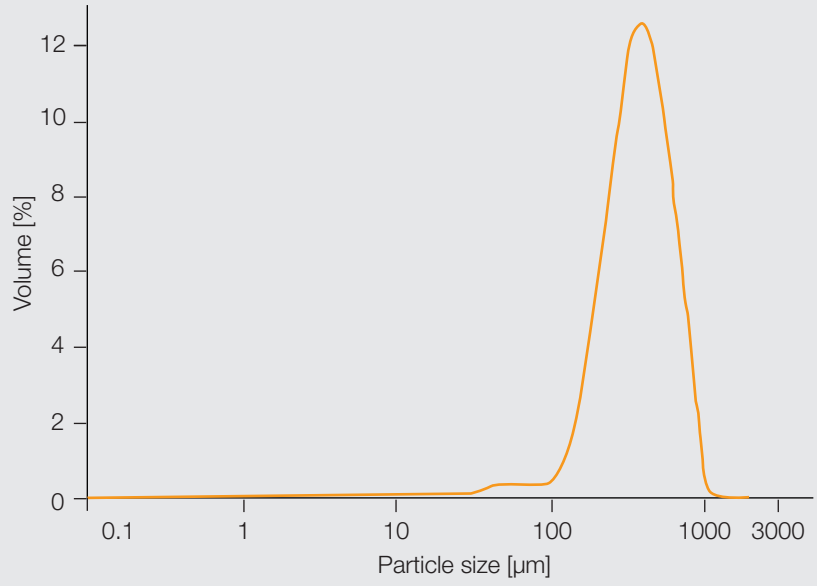

Figure 3: Typical particle size distribution of a Kolliwax® GMS II sample.

d_{10}	198 µm
d_{50}	383 µm
d_{90}	676 µm
Bulk density	0.52 g/cm³
Tapped density	0.61 g/cm³
Hausner factor	1.17
Angle of response	30.1°
BET surface	1.0 m²/g

Differential Scanning Calorimetry

Differential Scanning Calorimetry (DSC) was performed using 6.5 mg of sample material. At a rate of 10 °C/min, the sample was heated to 120 °C, cooled to 20 °C, and reheated to 120 °C. The DSC plot reveals that the melting point measured at the second melting incident has shifted to smaller temperatures compared to the initial value. This effect, commonly referred to as post-hardening, is known from other glycerides and can be explained by polymorphism: while the product predominantly crystallizes in its alpha form, ageing leads to a partial transformation into its beta form that has a slightly higher melting point.

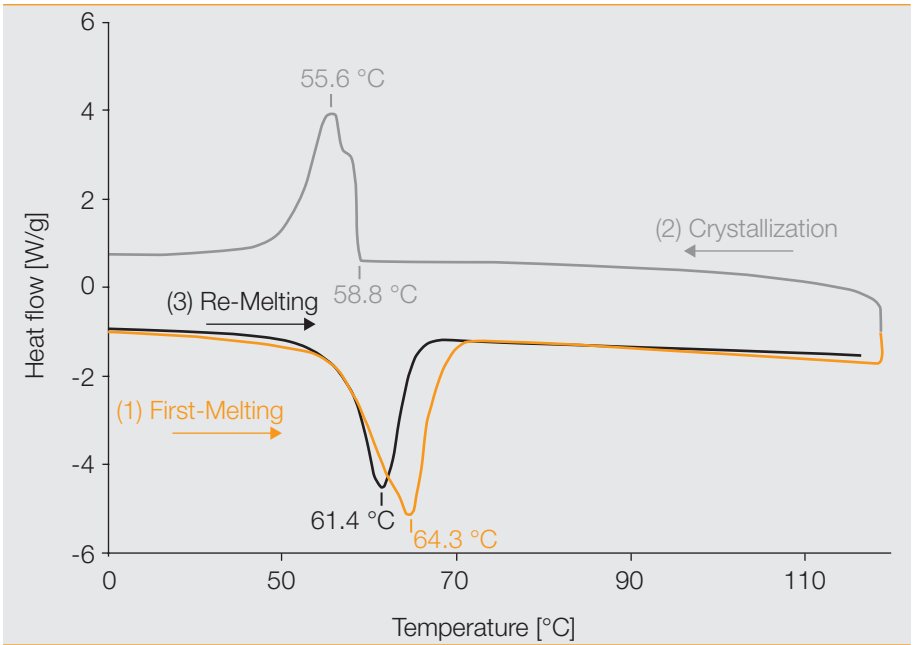

Figure 4: DSC plot of Kolliwax® GMS II. The sample was heated (orange), subsequently cooled (gray), and reheated (black).

3. Application

Overview

Kolliwax® GMS II is a versatile pharmaceutical formulation aid, featuring a broad range of applications, some of which are listed in the following table.

Solid oral dosage forms	Alternative for inorganic materials (e. g. Talc): • Lubricant in the (direct compression) tableting process • Anti-tacking agent for coatings
Skin delivery	Consistency factor/(co-)emulsifier for topical formulations (creams and gels)
Suppositories	Matrix former/melting point correction factor
LBDDS	Lipophilic surfactant in lipid based drug delivery systems

Lubricant in the Tableting Process

In the tableting process for solid oral dosage forms, lubricants are generally added to the solid formulation to prevent ingredients from clumping to undesired aggregates and from sticking to the tablet punches or capsule filling machine. Lubricants such as Kolliwax® GMS II can reduce friction during tabletting, and also reduce the ejection force.

In the example shown below, tablets were made from Ludipress®, our lactose-based direct compression excipient. Mixing was performed in a tubular blender at 5 min blending time, 10 mm flat tablets with 300 mg mass were then prepared with a Korsch XL 100 rotary press.

When tableting is performed without any lubricant, the formulation tends to stick onto the punch faces, whereby the compression force is limited to approx. 5 kN. This, in return, results in tablets of very low hardness (merely 18 N, values are not shown in fig. 5). Kolliwax GMS II acts as an efficient lubricant at concentrations as low as 1.5 %, and has no measurable influence on hardness and disintegration time of the tablets (fig. 5).

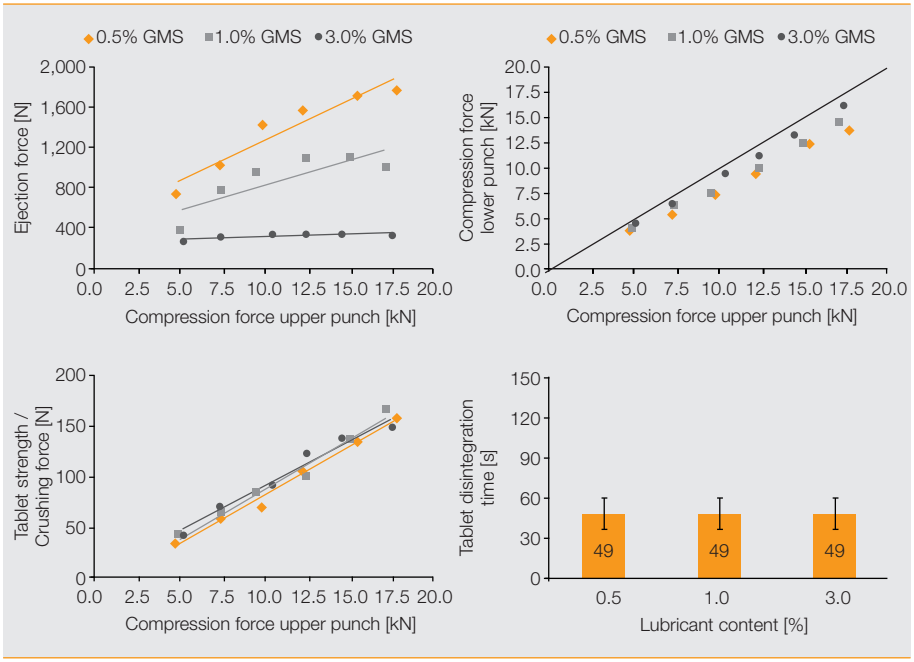

Figure 5: Top: Kolliwax® GMS II reduces the ejection force (left), while raising the compression force of the lower punch (right).
Bottom: The addition of Kolliwax® GMS II to the formulation has no measurable influence on tablet strength (left), as well as dissolution time (right).

Anti-Tacking Agent for Coatings

Kolliwax® GMS II can be used as anti-tacking agent in the spray-coating process of tablets, pellets, and crystals. It will eliminate the need for talc, which is generally subject to sedimentation, which in return can lead to separation in the tubing system, clogging of the spraying nozzles, and inhomogeneous films.

The following formulation example shows the use of Kolliwax® GMS II in an enteric coating formulation based on Kollicoat® MAE 30 DP. The core specimens, round-shaped tablets with 9.0 mm diameter, were comprised of:

Name	Chemistry	Role	Conc. [wt.-%]
Ludipress® LCE	Lactose-based direct compression excipient	Filler	74.0
Caffeine	(gran. 0.2 – 0.5)	API	15.5
Kollidon® CL-F	Crospovidone	Disintegrant	5.0
Kollidon® VA 64	VP / VA Copolymer	Dry binder	5.0
Mg-Stearate		Lubricant	0.5

Coating of the 9.0 mm round-shaped tablets was performed in a batch size of 4.0 kg using a vented pan coater (Manesty XL Lab 01) equipped with a middle-sized drum (480 mm) running at drum speed of 12 rpm. The inlet air quantity was set to 450 m³/h at a temperature of 55 °C. A spray rate of 13 g/min was achieved by employing an OptiCoat spray gun with a bore diameter of 0.8 mm, with atomizing- and pattern air pressures set to 1.8 bar.

Exemplary enteric coating formulation (1 kg) using Kolliwax® GMS II as anti-tacking agent (see Fig. 6 for preparation procedure):

Step	Name	Function	Amount [g]
1	Water (first 50 %)	Solvent	200
	Kolliphor® PS 80	Polysorbate Emulsifier	3.0
2	Kolliwax® GMS II	Anti-Tacking Agent	8.0
	Triethyl Citrate	Plasticizer	25.0
3	Water (remaining amount)	Solvent	208
4	Kollicoat® MAE 30 DP (30 % solid content)	Enteric Coating Dispersion	556

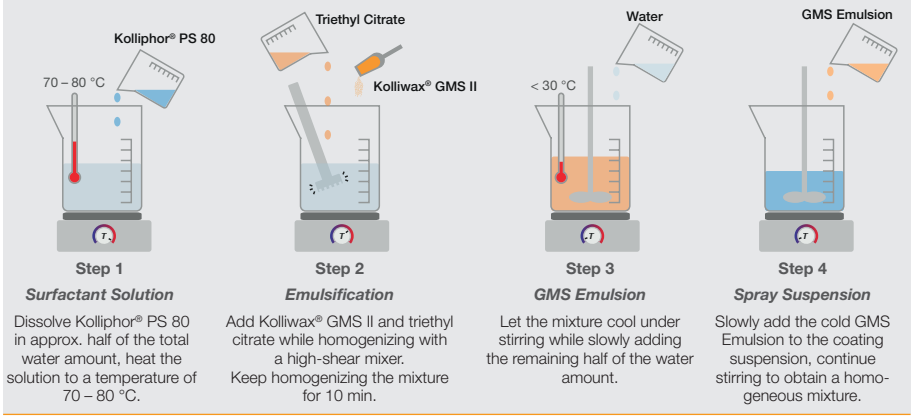

Figure 6: Procedure for the preparation of a coating suspension containing Kolliwax® GMS II as anti-tacking agent. Pigments can be dispersed into the remaining water amount and added accordingly in step 3. Before spraying, the suspension should be passed through a 0.5 mm sieve.

As the dissolution curves show (Fig. 7), Kolliwax® GMS II has no measurable influence on dissolution. However, its anti-tacking effectiveness at concentrations as low as 4% (relative with respect to the dry matter of polymer) in combination with the stability of the suspension towards sedimentation make it a powerful additive in this application field.

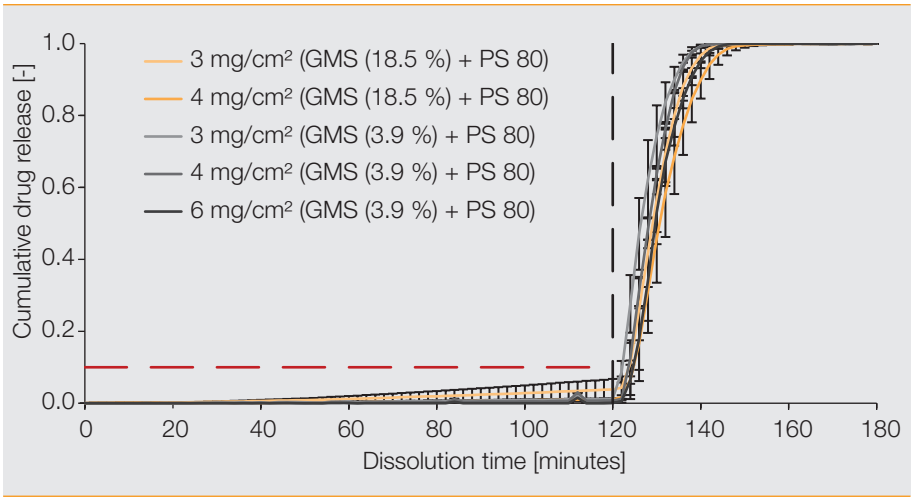

Figure 7: Dissolution profiles of cores coated with different Kollicoat® MAE 30 DP formulations with Kolliwax® GMS II as insoluble component. Dissolution tests were performed at a paddle speed of 50 rpm, at (37 ± 0.5) °C; 0 – 2 h 880 mL (0.08 mol/L HCl, pH = 1.1), 2 – 4 h 900 mL (phosphate buffer, pH = 6.8). Given value: mean (n = 3) ± std. dev.

Consistency Factor/(Co-)Emulsifier in Topical Formulations

A topical (semi solid) formulation is a complex mixture of ingredients with varying functionalities. The majority of these formulations are based on o/w or w/o emulsions, where several different emulsifiers are typically required to achieve proper stabilization of the two-phase system. Depending on the nature of the API, the formulation needs to be adapted to deliver APIs that are either soluble in water, or in oil.

The main function of Kolliwax® GMS II in topical formulations is a (co-)emulsifier or consistency factor, which enhances the viscosity of the formulation. It is typically added in concentrations ranging from 0.1 to 15%. Glycerol monostearate is compatible with most vegetable and animal waxes and can therefore be used in combination with fatty alcohols and other consistency factors. Its relatively high melting point can aid increasing the high-temperature storage stability of an emulsion.

Procedure for the preparation of example formulations:

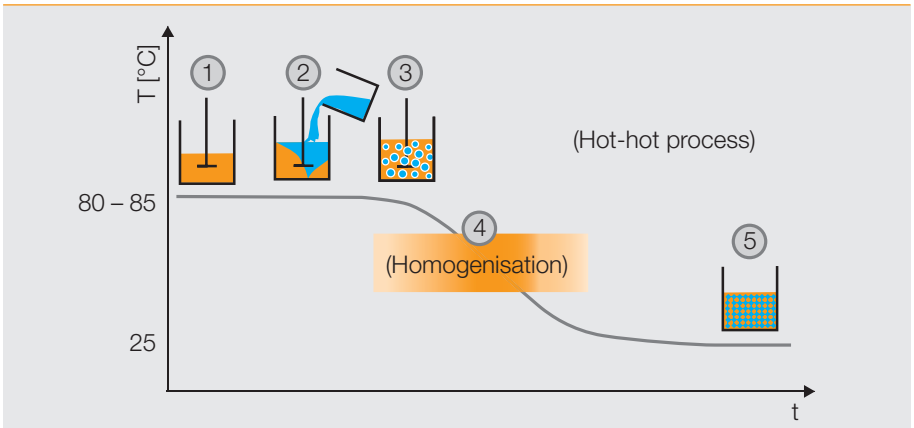

Figure 8: Scheme for the preparation of a topical formulation via the hot-hot process.

The following formulation can be prepared by the procedure outlined above. The emulsifier system comprised of Kolliphor® PS 80 and Kolliwax® GMS II with our versatile Emollient Kollicream® 3 C yields a cream of medium viscosity (14 Pa·s @ 1 s^{-1}) with a smooth feel.

Phase	Ingredients	Chemical name	Role	Mass [wt%]
A	Kollicream® 3 C	Cocoyl Caprylocaprate	Emollient	20.00
	Kolliphor® PS 80	Polysorbate 80	Solubilizer, emulsifier	3.00
	Kollwax® 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
	Euxyl PE 9010	Phenoxyethanol	Preservative	1.00

Especially when used at high concentrations, Kolliwax® GMS II may tend to crystallize, resulting in the formulations to “weep” or “bleed” (a phenomenon called syresis), and take on a dull appearance as well as a grainy texture. This effect can be prevented by adding stearic acid (Kolliwax® S, or Kolliwax® S Fine) to the formulation, or by increasing its content.

4. Handling & Safety

Please refer to the individual material safety data sheet (MSDS) for instructions on safe and proper handling and disposal. Material safety data sheets (MSDS) are available on BASF WorldAccount*, or from your local BASF sales representative.

5. Product specification

The current version of the product specification is available on BASF WorldAccount* or from your local BASF sales representative.

6. Regulatory & Quality

Please refer to the individual document quality & regulatory product information (QRPI) which is available on BASF WorldAccount* and from your local sales representative. **The QRPI covers all relevant information including retest dates, and storage conditions.**

* https://worldaccount.basf.com

7. PRD and Article numbers

PRD-No.*	Product name	Article numbers	Packaging
30554444	Kolliwax® GMS II	50263842	0.5 kg Plastic bottle**
		50264282	25 kg Plastic film bags

* BASF's commercial product number.

** Free non-GMP samples (0.5 kg) for testing purposes are available on request.

8. Publications

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

April 2019