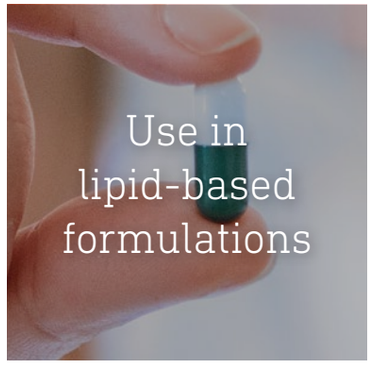
GATTEFOSSÉ

People make our name

Gelucire® 59/14

Solid surfactant for oral bioavailability enhancement



Gelucire® 59/14 in a nutshell »

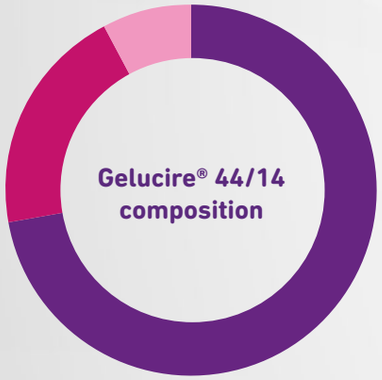
Product description

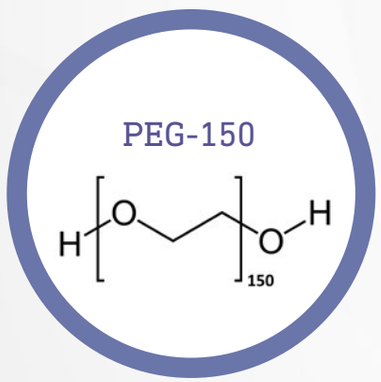
- Composition
- A solid excipient at 25°C, available as pellets
- Physico-chemical properties
- Miscibility at 25°C with common excipients

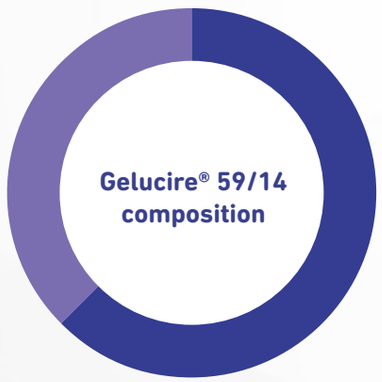
Composition

Gelucire® 44/14 + PEG-150 (= PEG 6000) = Gelucire® 59/14

Gelucire® 59/14 is a mixture of self-emulsifying excipient Gelucire® 44/14 (lauroyl PEG-32 glycerides) and PEG-150. It has been designed to benefit from Gelucire® 44/14 power for oral bioavailability enhancement, while being solid at room temperature.







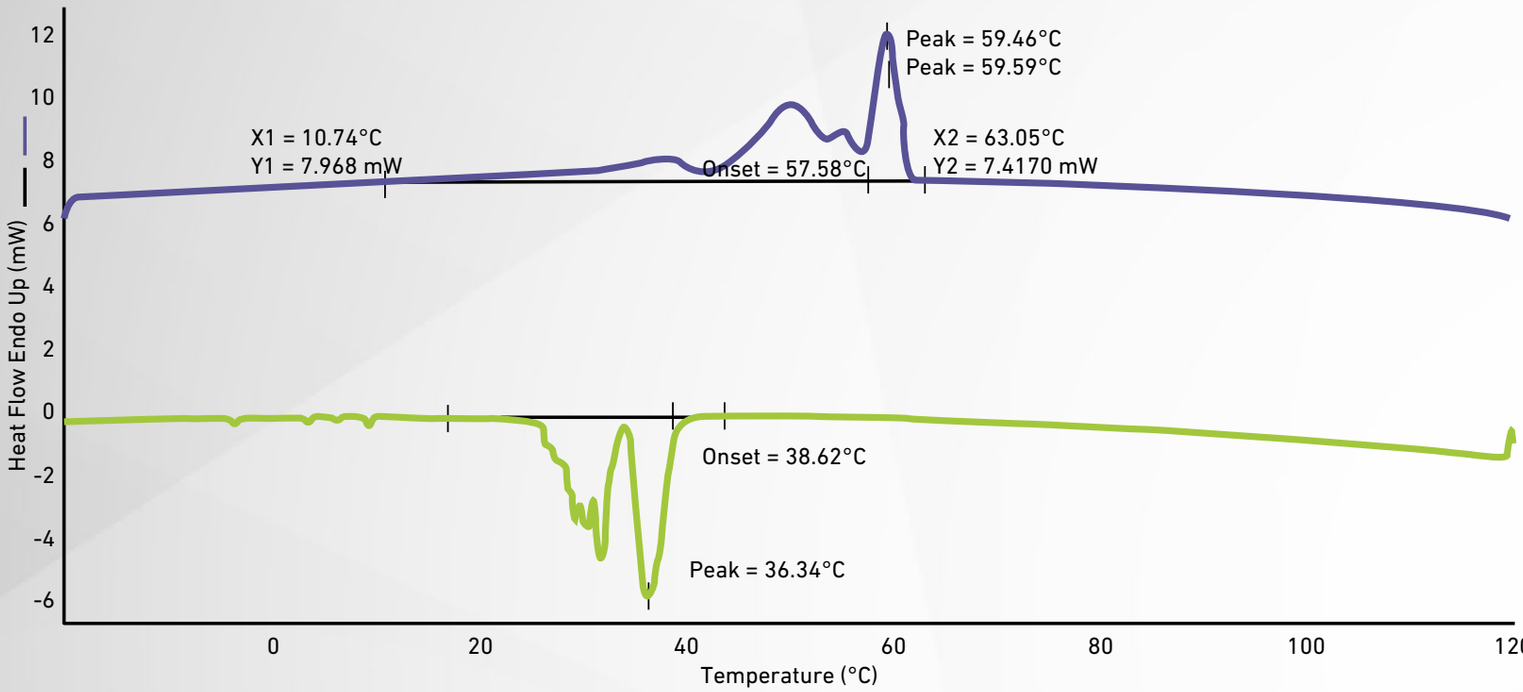
Product handling

Heat above 80°C before use to fully melt the product

N_2

Flush the container with nitrogen after use

A solid excipient at 25°C, available as pellets



DSC thermogram of Gelucire® 59/14

The DSC thermogram clearly shows two peaks both on fusion and recrystallization, reflecting the dual composition of Gelucire® 59/14.

The melting point of Gelucire® 59/14 is about 59°C (peak temperature, fusion - blue line), and upon recrystallization two peaks can be seen at around 36 and 26°C (peak temperatures, recrystallization – green line).

Storage recommendations

Store below 35°C to prevent pellet agglomeration

Physico-chemical properties

Gelucire® 59/14 is a water dispersible surfactant due to its HLB of 14 ± 1

HLB	14 ± 1
Melting point (°C)	59

Miscibility with solvents (25°C)	
Acetonitrile	Non-miscible
Ethanol 96°	≥ 90%
Methanol	≥ 90%
Water	≥ 90%

Miscibility at 25°C with common excipients used in lipid-based formulations

Miscible Non-miscible

% Gelucire® 59/14

		10	20	30	40	50	60	70	80	90
Oils	Maisine® CC									
	Peceol™									
	Labrafac™ Lipophile WL 1349									
Water insoluble surfactants	Capryol® 90									
	Labrafac™ MC60									
	Lauroglycol™ 90									
	Plurol® Oleique CC 497									
Water dispersible surfactants	Labrafil® M 1944 CS									
	Labrafil® M 2125 CS									
Solvents	Transcutol® HP									
	Water									

Product functionality

- Self-emulsifying excipient
- Oral bioavailability enhancer

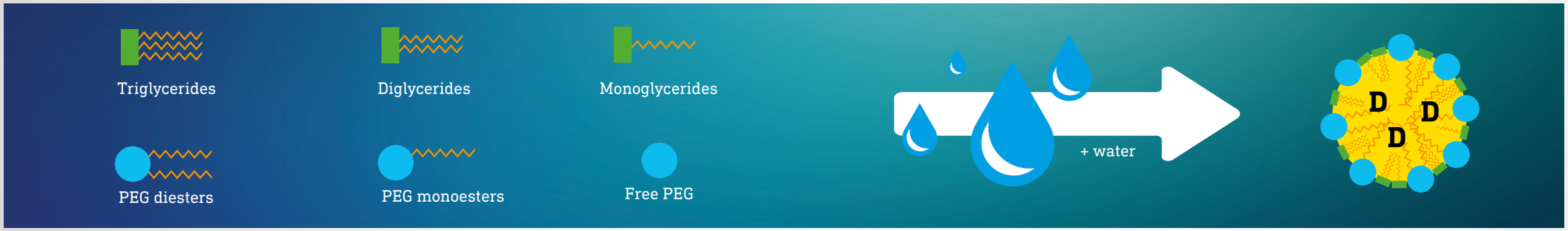
Self-emulsifying excipient

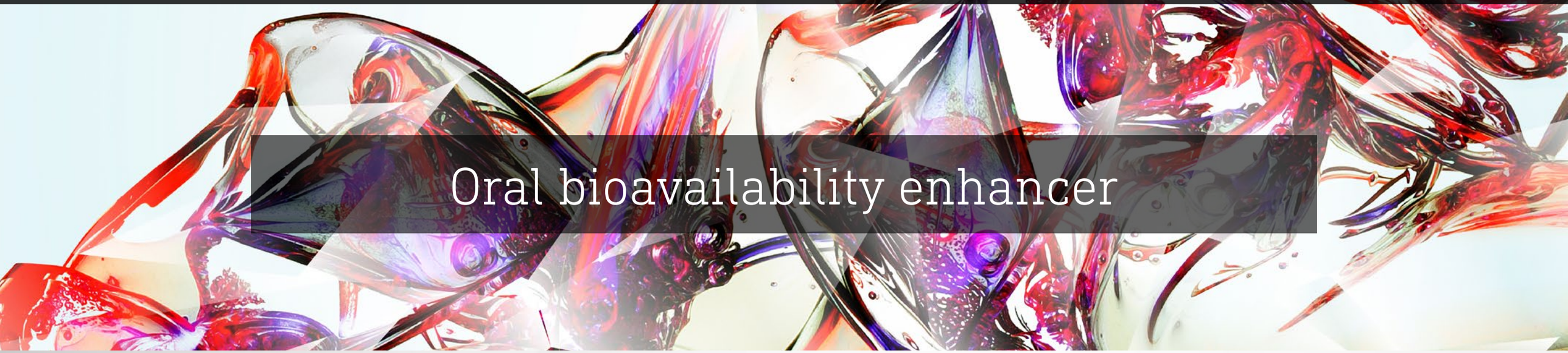
Gelucire® 59/14 is a self-emulsifying system: upon contact with aqueous / digestive media it spontaneously forms a fine dispersion.

The different components self-assemble as a function of their affinity for water:

- PEGs are water-soluble
- PEG esters and monoglycerides are amphiphilic
- di- and triglycerides are hydrophobic.

Self-assembly results in the formation of micelles, wherein the drug is solubilized.





Oral bioavailability enhancer

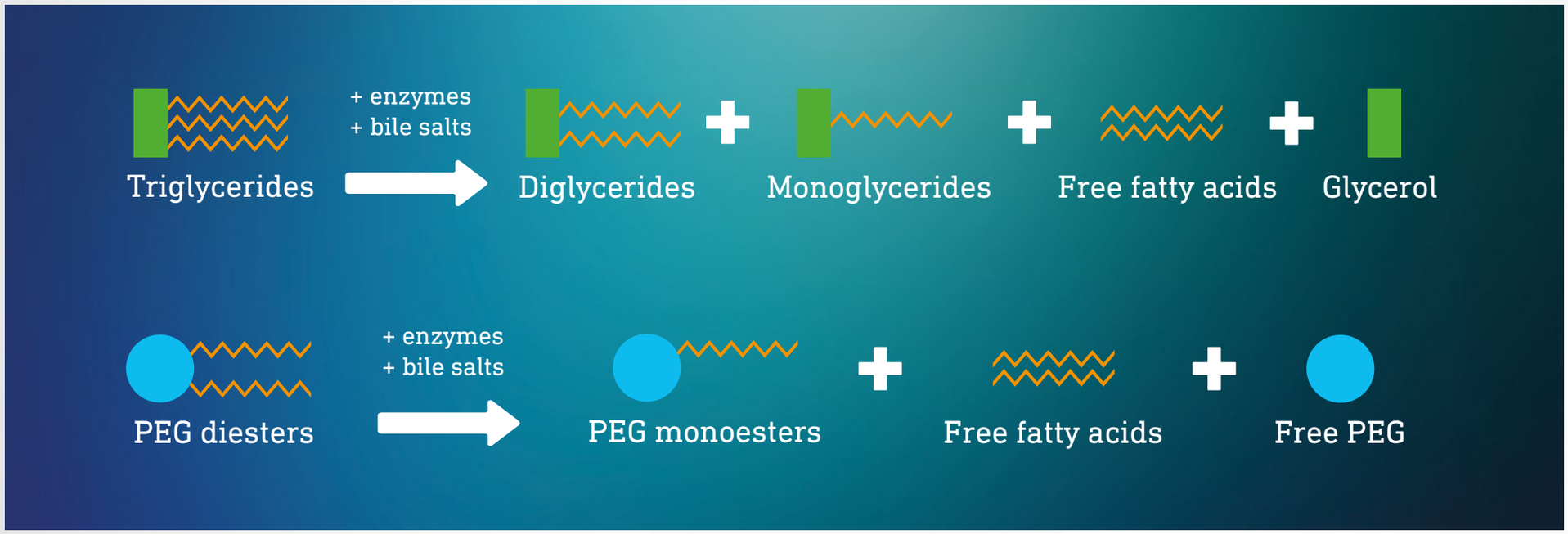
When entering the digestive system, the various components of the self-emulsifying excipient are digested.

In the stomach

- Triglycerides are rapidly and almost completely digested into diglycerides, monoglycerides and free fatty acids.
- Diglycerides are partially digested into monoglycerides and fatty acids.

In the intestine

- PEG esters are partially digested releasing free fatty acids and free PEG.
- Free fatty acids and monoglycerides are absorbed via the enterocytes.

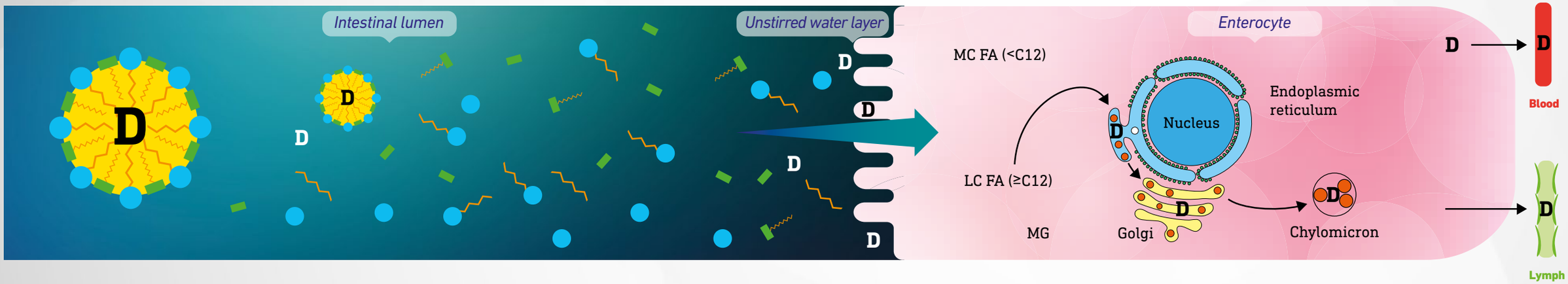


Oral bioavailability enhancer

The digestion products self-assemble into colloidal structures that maintain the drug in solubilized state until absorption.

The digestion of lipids stimulates the secretion of bile salts, phospholipids and cholesterol by the gallbladder. These amphiphilic compounds associate with the components of Gelucire® 59/14 digestion and self-assemble into different colloidal structures: multi-lamellar, vesicles, mixed micelles and micelles.

These structures have variable solubilizing capacities and contribute to maintaining the drug in solubilized state throughout the on-going digestion process. Ultimately, the fatty acids, monoglycerides and drug partition out of the mixed micelles and are absorbed in the enterocyte.



D drug; MC FA medium chain fatty acid; LC FA long chain fatty acid; MG monoglyceride

Regulatory information and precedence of use

- Multicompendial excipient
- Maximum potency per unit dose (IID)

Multi-compendial excipient

USP-NF	Lauroyl polyoxyl-32 glycerides Polyethylene Glycol 6000
European Pharmacopoeia	Lauroyl macrogol-32 glycerides Macrogols 6000

Maximum potency per unit dose (IID)

Individual components of Gelucire® 59/14 are both listed in the FDA Inactive ingredient database.

LAUROYL PEG-32 GLYCERIDES (UNII: H5ZC52369M)

Administration route	Dosage form	Maximum Potency per unit dose	Maximum Daily Exposure (MDE)
Oral	Capsule	NA	7200mg
	Tablet	0.15mg	NA

POLYETHYLENE GLYCOL 6000 (UNII:30IQX730WE)

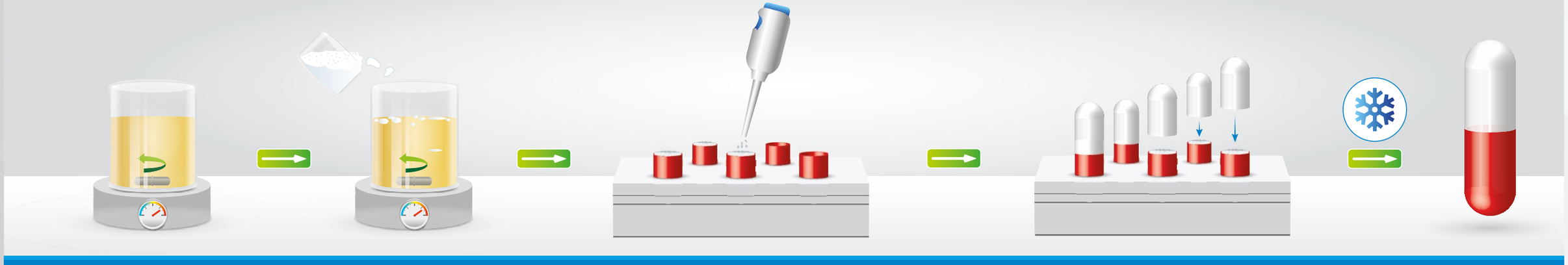
Administration route	Dosage form	Maximum Potency per unit dose	Maximum Daily Exposure (MDE)
Oral	Capsule	NA	3600 mg
	Tablet	NA	250 mg
Buccal	Tablet	70 mg	NA
Sublingual	Tablet	70 mg	NA
Rectal	Suppository	128 mg	NA
Topical	Cream	5% w/w	NA

Use in lipid-based formulations

- Capsule molding process
- Capsule filling temperature
- Case study with Gelucire® 59/14 and piroxicam
- SEDDS formulation development

Capsule molding process

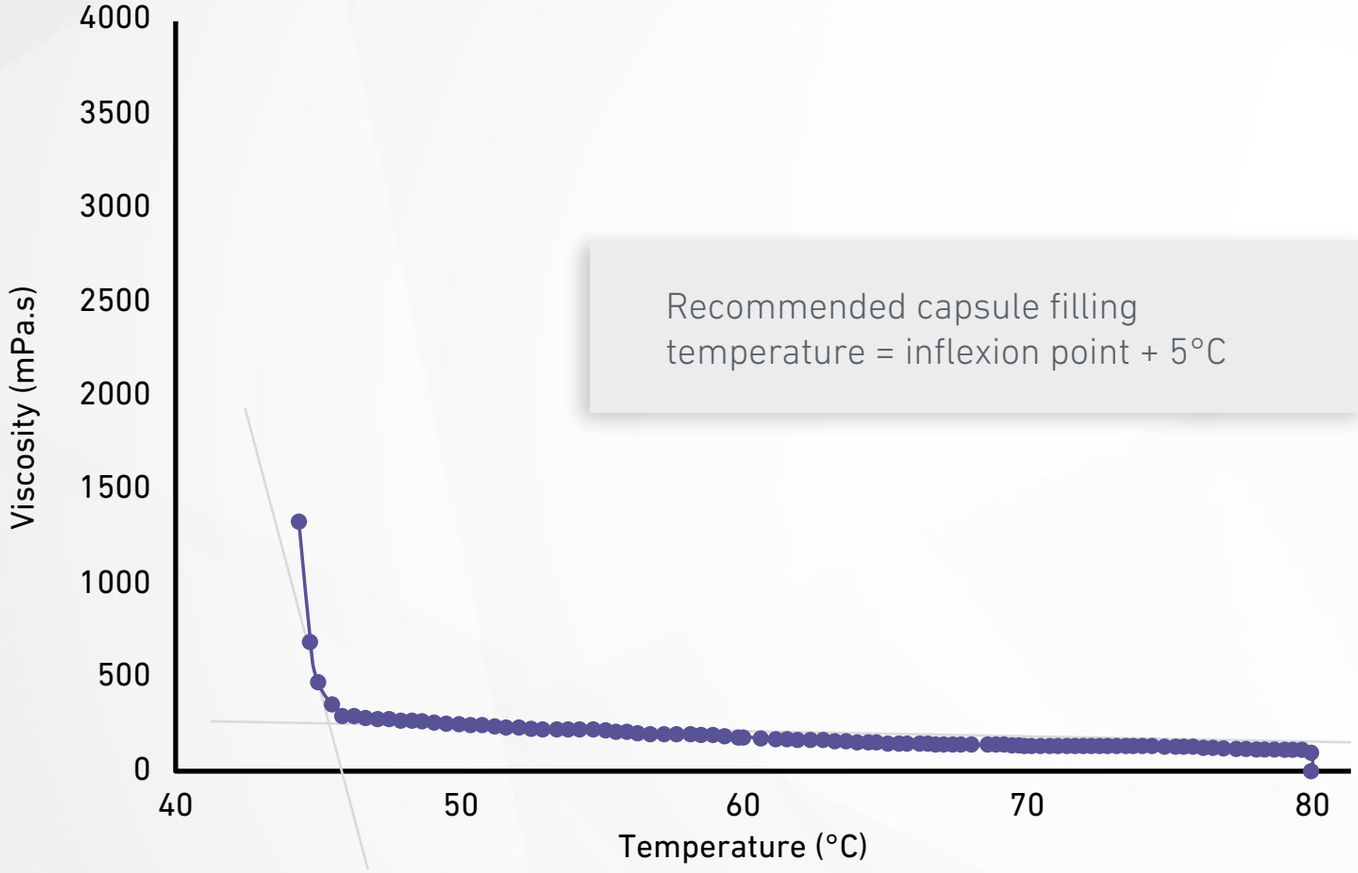
Simple formulation can be developed using Gelucire® 59/14 and a capsule molding process.



Melt the lipid excipient	Add the API	Fill the capsules with the molten mixture	Cool down to room temperature for 24h before analysis
Weigh the required Gelucire® 59/14 quantity and allow to melt at 80°C, under gentle stirring, taking care to prevent the incorporation of air.	Leave the sample to cool down then add the API and stir gently to ensure content homogeneity, again avoid exposure to air.	Fill capsules when the temperature reaches 50-55°C; the exact filling temperature should be determined with a thermorheogram.	Leave the capsules to cool down and equilibrate for 24 hours at ambient temperature before characterization

Capsule filling temperature

A thermorheogram is an essential tool to determine the appropriate capsule filling temperature. It should be performed on the complete formulation (excipients and API).



Thermorheogram of Gelucire ® 59/14 alone: inflexion point ≈ 46°C

Case study with Gelucire® 59/14 and piroxicam

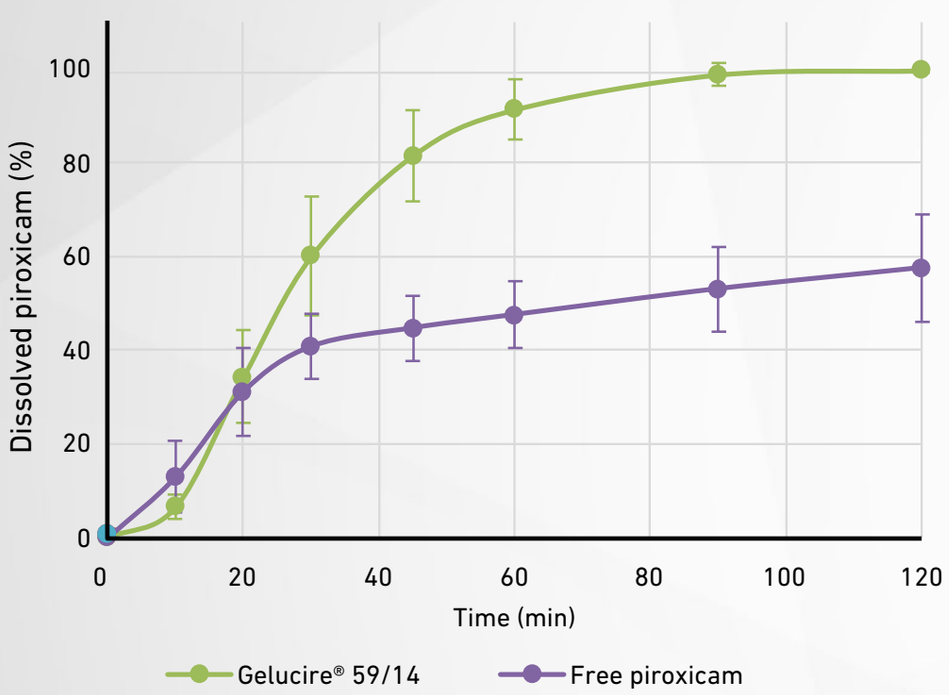
Drug characteristics

- Log P = 2.2
- Water solubility: 0.143 mg/mL
- Solubility in Gelucire® 59/14: 25 mg/g
- Commercial product strength: 10 to 20 mg

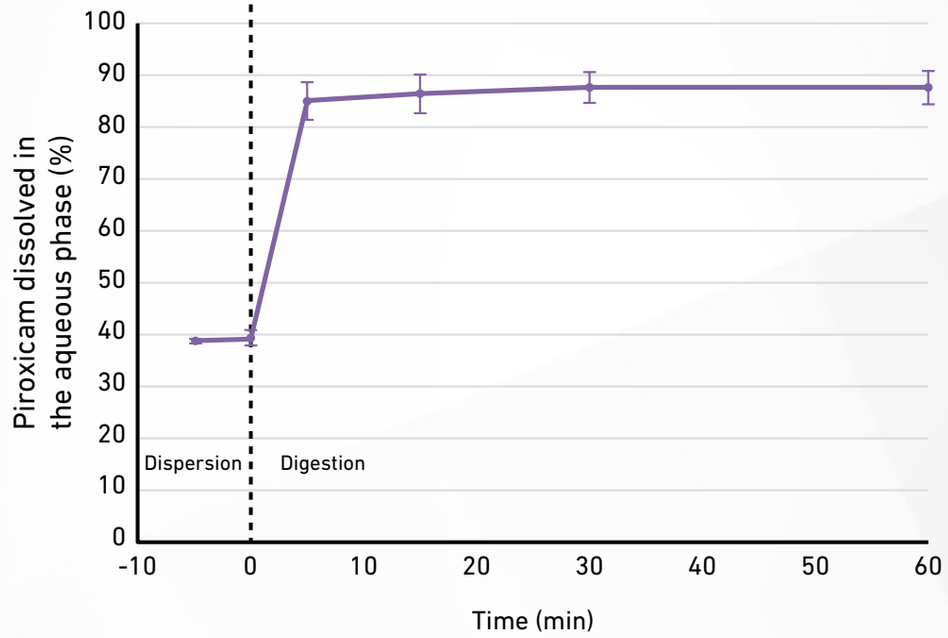
SEDDS formulation

- 660 mg Gelucire® 59/14
- 20 mg piroxicam

In vitro dissolution test at 37°C



In vitro lipolysis test at 37°C



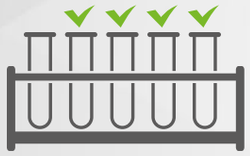
In this SEDDS formulation, Gelucire® 59/14 alone was able to successfully maintain piroxicam in solution during lipolysis

SEDDS formulation development

Due to its composition, Gelucire® 59/14 is a SEDDS on its own. Therefore, if a quantity corresponding to a reasonable unit dose size can solubilize the therapeutic dose of the API, there is no need to associate Gelucire® 59/14 with additional excipients. Alternatively, if the dose of API is not entirely solubilized, other standard SEDDS/SMEDDS excipients, such as oil, surfactant, co-surfactant and solvent, may be required.

Multi-excipient SEDDS and SMEDDS are developed in a stepwise approach following these main stages:

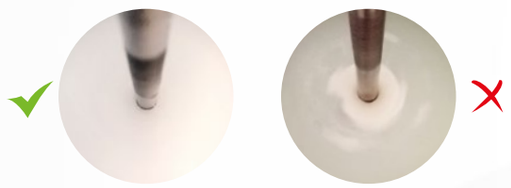
Select excipients with highest solubilizing capacity in various classes: oily vehicles, surfactants and solvents



Assess API solubility in individual excipients (oils, surfactants and solvents) to select the excipients with highest solubilization capacity.

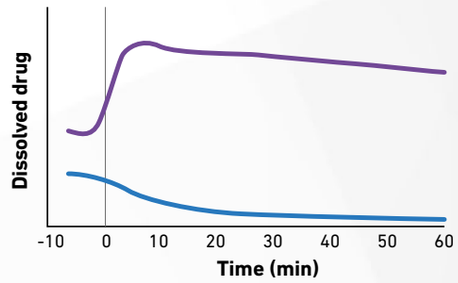
Miscibility screening of binary mixtures of excipients

Dispersability testing of mixtures of excipients without and with API



Perform miscibility and dispersion testing to select the best excipient combination(s) and define ratios to develop the formulations.

***In vitro* lipolysis test**



Undertake in vitro lipolysis testing to assess if the drug is maintained in a solubilized state throughout the digestion process and select the best formulation for further development.

More information on SEDDS development

Technical support

A long-established company

A pioneer in lipid-based formulations

A worldwide presence

A long tradition of knowledge sharing

High quality, functional excipients

A network of application laboratories

For technical support
and more information

www.gattefosse.com

Contact us

Gelucire® 59/14 in a nutshell

- A self-emulsifying excipient
- Available as pellets, for easy handling
- Oral bioavailability enhancer
- Solubilizer of a wide range of molecules
- Surfactant, HLB=14
- Mixture of lauroyl PEG-32 glycerides EP/NF and PEG 6000 EP/NF

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