GATTEFOSSÉ

Gelucire® 44/14

Self-emulsifying excipient for solubility and oral bioavailability enhancement

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Contents

ABBREVIATIONS

ATV: Atorvastatin; **API:** Active Pharmaceutical Ingredient; **AUC:** Area Under The Curve; **DSC:** Differential Scanning Calorimetry; **EP:** European Pharmacopoeia; **FDA:** Food and Drug Administration; **HLB:** Hydrophilic Lipophilic Balance; **LBF:** Lipid-Based Formulation; **PEG:** PolyEthylene Glycol; **S(M)EDDS:** Self (Micro) Emulsifying Drug Delivery System; **vs:** versus; **USP-NF:** US Pharmacopoeia/National Formulary

Product description

Gelucire® 44/14 is a non-ionic water dispersible surfactant recommended for use in lipid-based formulations to increase the aqueous solubility and oral bioavailability of poorly water soluble drugs.

A multi-component excipient

Gelucire® 44/14 is obtained by an alcoholysis reaction between coconut oil and polyethylene glycol-32 (PEG-32) under controlled conditions. It consists of glycerides and PEG esters of fatty acids of varying chain length. (Figure 1).

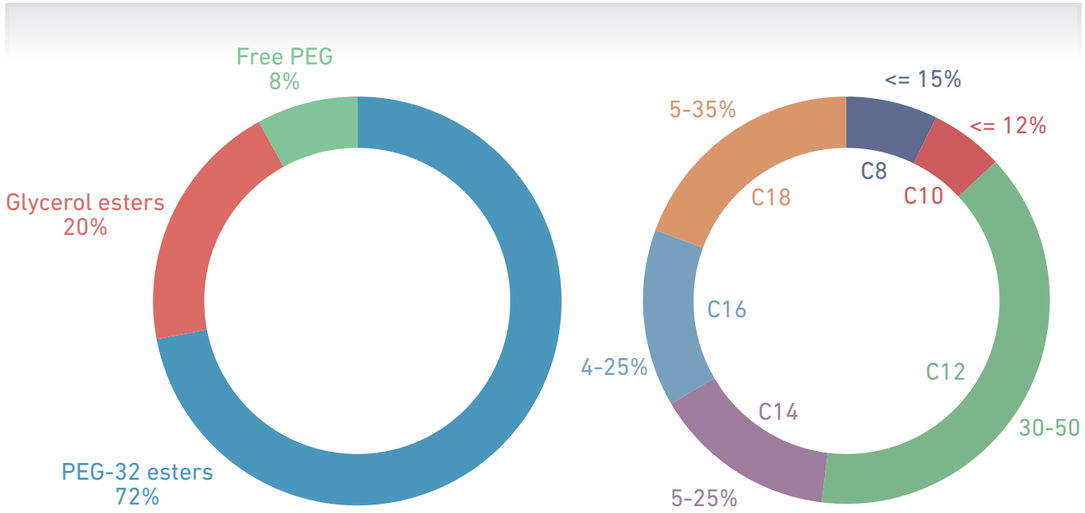


Figure 1: Schematic of Gelucire® 44/14 composition (left) and fatty acid repartition (right)

Main physicochemical properties of Gelucire® 44/14

Drop point (Mettler, °C)	45.0 ± 2.5
pH (10% in purified water)	4.4 ± 0.7
Relative density	1.023 at 50 °C
Calculated / practical HLB	14 / 11
Critical micellar concentration (g/L, 25 °C)	0.07 ± 0.05
Solubility in ethanol 96 °	Soluble
Solubility in chloroform, methylene chloride	Freely soluble
Solubility in n-hexane	Insoluble

Melt characteristics

Gelucire® 44/14 presents a broad endotherm ranging from 10 to 45°C, with an onset melting temperature of about 38°C and a peak melting temperature of about 43°C (blue line, Figure 2). This thermal behaviour is related to composition: the mono-, di- and triglyceride fraction melts first (orange line, Figure 2), followed by the PEG-ester fraction (green line, Figure 2).

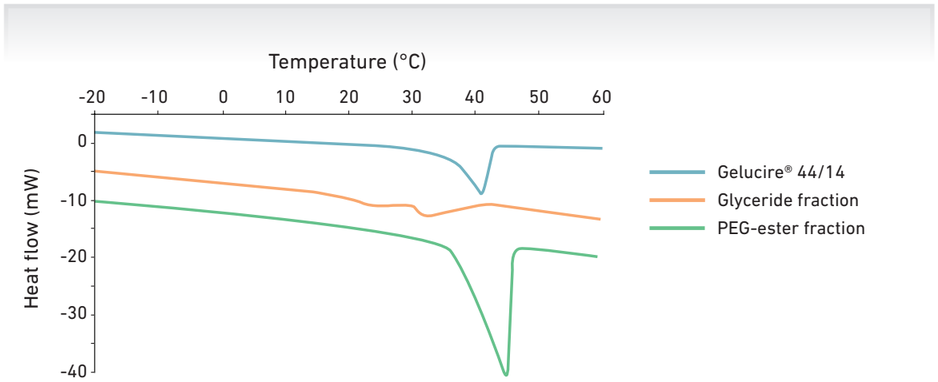


Figure 2: DSC thermogram of Gelucire® 44/14 (adapted from Jannin, 2009)

Did you know ?

Gelucire® 44/14 melting begins as low as 10 °C, meaning that at 20 – 25 °C a fraction of Gelucire® 44/14 is already liquid. This is why the product is described as 'semi-solid' and is supplied in block form.

Product functionality

Spontaneous self-emulsification in aqueous media

Gelucire® 44/14 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 and di- and triglycerides are hydrophobic.

At a concentration above the CMC (≈0.07 g/L), self-assembly results in the formation of micelles of about 10-100 nm mean diameter measured by Diffraction Light Scattering (Figure 3).

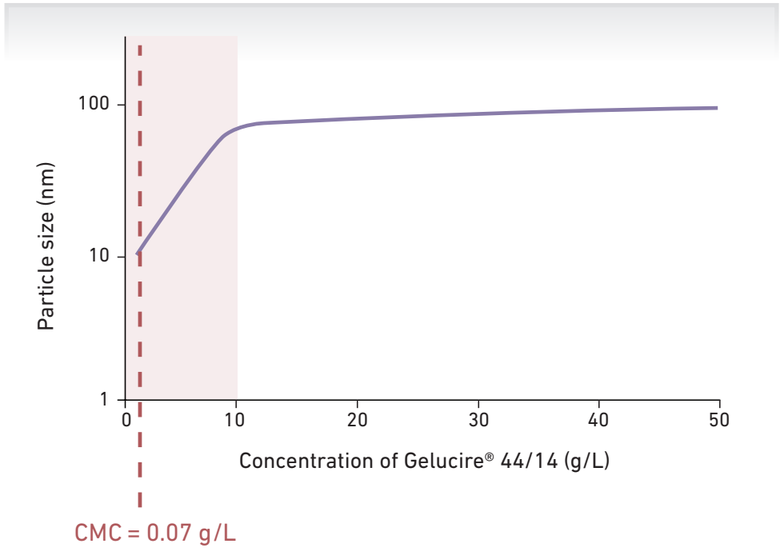


Figure 3: Size of Gelucire® 44/14 micelles at 37°C evaluated by Diffraction Light Scattering (adapted from Chamieh et al., 2015)

Did you know ?

Below 10 g/L the microemulsion appears transparent as the particle size is below 100 nm.

Above 10 g/L, the colloidal structure swells to values close to 100 nm and the microemulsion becomes translucent and bluish.

Digestion, recombination in colloidal structures and absorption

The digestion of Gelucire® 44/14 has been investigated by Fernandez et al. (2008, 2009) using an *in vitro* set-up with enzymes that simulate the gastric and duodenal phases. Each individual component of Gelucire® 44/14 was measured over time, elucidating the lipolysis of Gelucire® 44/14 and the metabolites generated (Figure 4).

During the gastric phase the glycerides fraction is digested. Triglycerides are rapidly and almost completely digested into diglycerides, monoglycerides and free fatty acids. Diglycerides are partially digested into monoglycerides and fatty acids.

During the intestinal phase, PEG esters are partially digested releasing free fatty acids and free PEG.
In vivo, free fatty acids and monoglycerides are absorbed via the enterocytes.

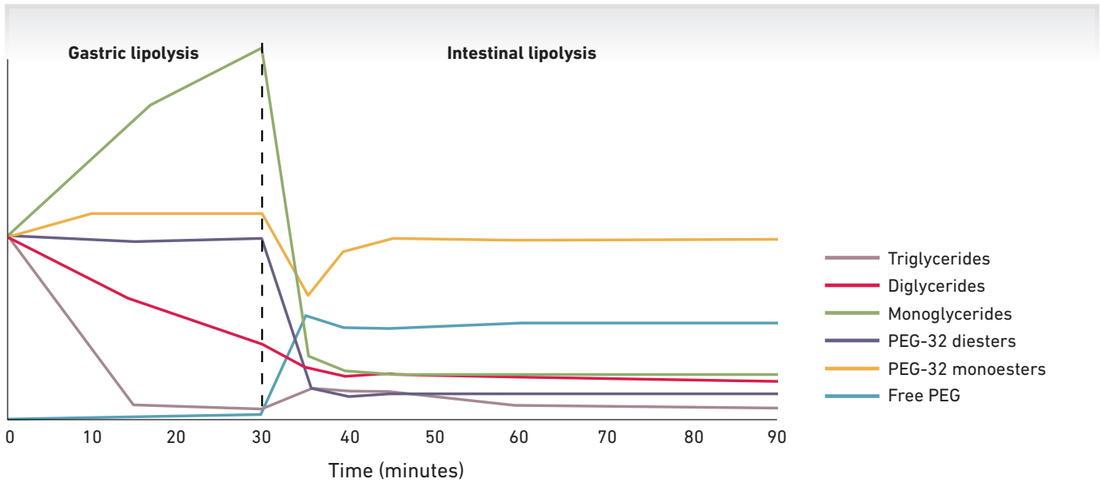
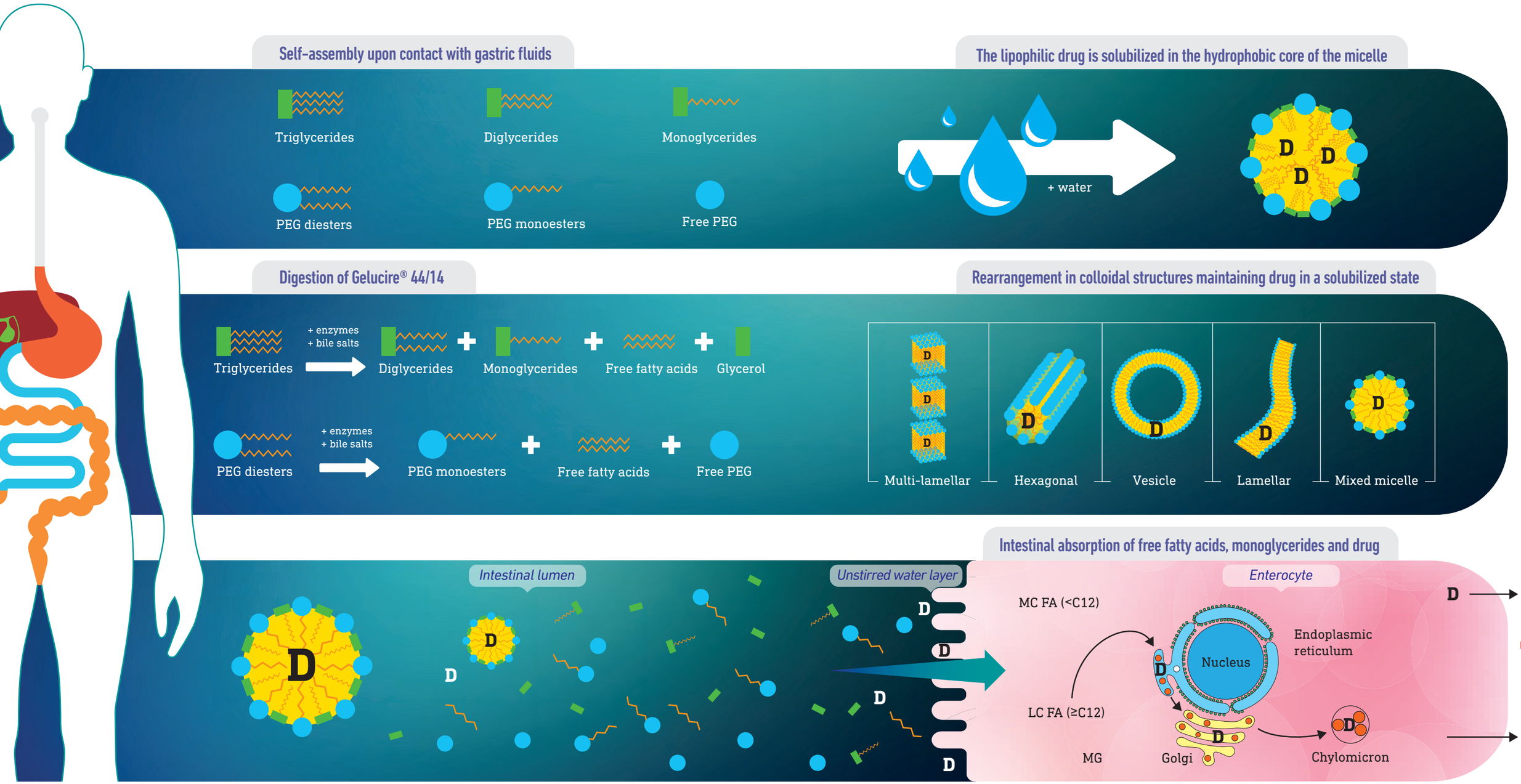


Figure 4: Variation in the concentration of Gelucire® 44/14 components as a function of time (adapted from Fernandez et al., 2009)

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® 44/14 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 (Vithani et al., 2019).

The figure on the following pages illustrates the digestion of Gelucire® 44/14 and how this actively contributes to drug solubilization and absorption.

The fate of Gelucire® 44/14 in the gastro-intestinal tract: self-emulsification, digestion and absorption



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

Handling and processing

Handling a semi-solid excipient

Gelucire® 44/14 is composed of several fractions with different densities and crystallization temperatures. After synthesis, the molten excipient is hot filled in the container. During cooling and crystallization the product stratifies resulting in a non-homogenous composition in the container. Therefore, the entire product in the original container must be **fully melted at 70 - 80°C and homogenized before sampling and use (Figure 5).**

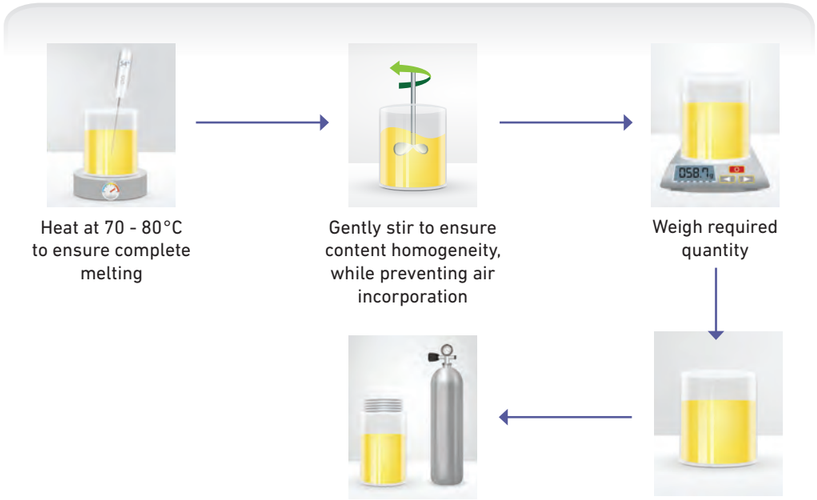


Figure 5: Gelucire® 44/14 handling

Lipids are naturally sensitive to oxidation and hydrolysis. **Gelucire® 44/14 industrial containers are opaque to light, filled under nitrogen and tightly sealed.**

Correct handling helps to preserve product integrity:

- Melt the product in a dry oven, an incubator or a microwave oven (do not use a water bath).
- After use, flush the container with nitrogen and seal tightly.
- Store the container at room temperature.

A detailed product handling sheet is available on request

Measuring API solubility in Gelucire® 44/14

The simplest method is to measure API solubility in molten Gelucire® 44/14 at about 50°C. However, the elevated temperature will generally result in an over-estimation of drug solubility.

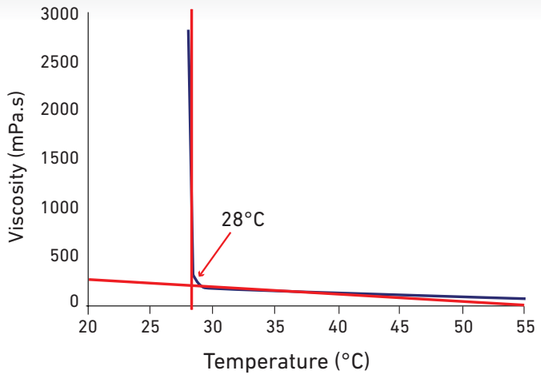
The most accurate method consists in measuring the solubility of API by Differential Scanning Calorimetry (DSC), coupled with hot stage microscopy. A detailed protocol can be provided upon request.

Processing

Gelucire® 44/14 can be used in a variety of processes however, capsule molding by filling with a molten liquid or low viscosity formulation is the most common and straightforward. Other processes such as solid dispersion by fusion, evaporation or supercritical CO_2 methods, spray drying, melt granulation, melt extrusion and 3D printing are reported in the scientific literature.

Recommendations for capsule molding

- Fully melt Gelucire® 44/14 at 70 - 80°C under gentle stirring, taking care to prevent the incorporation of air. When fully molten and homogenous, remove and weigh the required excipient quantity.
- Leave the sample to cool down to 40°C then add API and stir gently to ensure content homogeneity, again avoid exposure to air.
- Fill capsules when the temperature reaches 32 - 40°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.



Did you know ?

A thermorheogram is an essential tool to determine the appropriate capsule filling temperature.
The formulation's viscosity is plotted as a function of temperature.
The curve shows an inflexion point (28°C in the example).
The capsule filling temperature is obtained by adding 5°C to the inflexion point (28+5=33°C in the example).

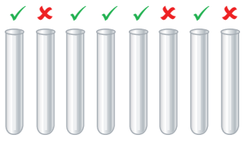
Gelucire® 44/14 is compatible with gelatin and HPMC capsule shells. A compatibility study report is available on request.

Recommendations for SEDDS formulation

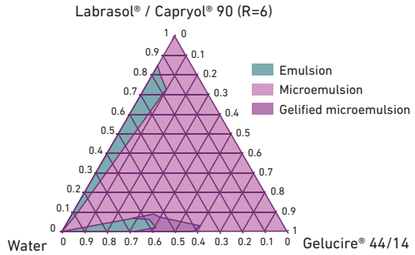
Due to its composition, Gelucire® 44/14 is a SEDDS on its own. Therefore, if a quantity corresponding to a reasonable unit dose size can solubilize the therapeutic dose of the API, there is no need to associate Gelucire® 44/14 with additional excipients. Alternatively, if the dose of API is not entirely 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 three main stages:

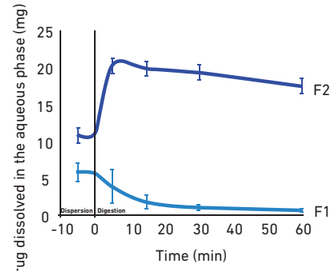
- Assessment of API solubility in individual excipients (oils, surfactants and solvents) to select the excipients with highest solubilization capacity.
- Perform miscibility, dispersion testing and ternary phase diagramming to select the best excipient combination(s) and define ratios to develop the formulations.
- 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.



Solubility screening



Diagramming



In vitro lipolysis test

Our formulation guideline for solubility and bioavailability enhancement provides extensive details on the stepwise SEDDS/SMEDDS development and characterization.

Uses of Gelucire® 44/14 for oral bioavailability enhancement

Gelucire® 44/14 is recommended for use to increase the aqueous solubility and oral bioavailability of poorly water-soluble drugs, notably BCS class II and IV. The following table summarizes key results from *in vitro* and *in vivo* studies describing the use of Gelucire® 44/14 in binary mixture with API or in combination with other excipients (Table 2).

Table 2: Uses of Gelucire® 44/14 for oral bioavailability enhancement

API	Process	Formulation details (when available)	Effect	Reference
α-tocopherol	Solid dispersion, fusion method	300 mg α-tocopherol 300 mg Gelucire®44/14	Oral bioavailability (human): 2.1 fold increase in AUC versus market reference; Cmax: 1.8 fold increase	Barker, 2003
Aceclofenac	Capsule molding, fusion method	Drug:Gelucire®44/14 (1:6) 1 % Na docusate	Improved dissolution rate *in vivo* (rats): increased anti-inflammatory activity: 80% edema reduction versus 60% for pure drug	Kalpana, 2014
Atorvastatin	Capsule molding, fusion method	80 mg atorvastatin 240 mg Gelucire®44/14	Higher drug release *in vitro*: 85% at 15 min versus 11% for pure drug Oral bioavailability (rabbits): 4.5-fold increase versus free drug and 2.5-fold increase versus market reference	Shaker, 2018
BMS-A	SEDDS	70 % Gelucire®44/14 29 % Labrasol® 1 % Tween™ 80	*In vivo* (mice): higher AUC at 10 and 300 mg/kg *In vivo* (dogs): higher AUC at 5 and 200 mg/kg	Chen, 2018
Cinnarizine	Solid SMEDDS, 3D printing	7 % drug 46.5 % Gelucire®44/14 23.3 % Gelucire® 48/16 23.2 % Kolliphor™	3D printing produces solid SMEDDS Rapid dispersion; limited effect on digestion	Vithani, 2018
Docetaxel	SEDDS	32.7 % Capryol® 90 29.4 % Gelucire®44/14 8.3 % TPGS 29.6 % Transcutol® HP	Solubility increase: up to 50 mg/mL *In vivo* (rats): 3.19-fold increase in AUC Increase in permeability and lymphatic transport Higher retention of drug in tumour	Valicherla, 2016
EMD 50733	Capsule molding, fusion method	30 mg drug 110 mg Soluphor™ 780 mg Gelucire®44/14	*In vivo* (dogs): 10 fold increase in AUC versus drug:lactose physical mixture	Schamp, 2006
Fenofibrate	Solid SMEDDS, 3D printing	7 % drug 46.5 % Gelucire®44/14 23.3 % Gelucire® 48/16 23.2% Kolliphor™	3D printing produces solid SMEDDS Rapid dispersion; limited effect on digestion	Vithani, 2018
Flurbiprofen	Solid dispersion, solvent evaporation	Ratio 1:3	Increase *in vitro* drug release: 99% in 15 min versus 35% for control tablet *In vivo* (rabbits): 1.4-fold increase in AUC; 1.3-fold increase in Cmax; Tmax 2h versus 3	Daravath, 2015
Glibenclamide	Solid dispersion, spray drying	Ratio 1:1 Silicon dioxide as carrier	*In vitro* drug dissolution improved versus physical mixture and pure drug *In vivo* (mice): higher reduction in blood glucose level compared to pure drug	Chauhan, 2005
Griseofulvin	Melt granulation	Drug: 2.5 and 5% Filler (starch or lactose) Gelucire®44/14 as a 20% binder solution HPMC: 5 % solution	Increase in drug release of granules versus physical mixture and pure drug	Yang, 2004
Lycopene	Solid dispersion, solvent evaporation	50 % Gelucire®44/14 20 % Olive oil 20 % Tween™ 85 10 % Cremophor™ RH 50 mg drug / g solid dispersion	*In vivo* (pigs): 2.37-fold increase in oral bioavailability; 2.9-fold increase in Cmax; Tmax: 2.8 h reduction versus the market reference	Faisal, 2013
LyP-1 (anti-cancer peptide)	SMEDDS	5 % Peceol™ 35 % PEG 300 60 % Labrasol®:Gelucire®44/14 (4:1)	Non cytotoxic for Caco2 cells 60% breast cancer cell death	Gürsoy, 2014
Naproxen	Solid SMEDDS, spray drying	Peceol™ : Miglyol™ (1:1) Gelucire®44/14: Solutol™ (1:1) Maltodextrin as solid carrier	Liquid and solid SMEDDS improve drug dissolution to 99% versus 64% for pure drug	Cerpnjak, 2015
Piroxicam	Solid dispersion, fusion method	20 mg piroxicam 76 mg Gelucire®44/14 304 mg Labrasol®	*In vivo* (human): 2.2-fold increase in AUC; 2.7-fold increase in Cmax; 60 min reduction in Tmax for Gelucire® solid dispersion versus pure drug	Yüksel, 2003
Progesterone	Solid dispersion, supercritical CO_2	Ratios 1:1; 1:5; 1:10 Comparison to solvent method, co-melt and physical mixture	*In vitro* drug release faster for supercritical CO_2 than cosolvent, than physical mixture than co-melt	Falconner, 2013
Valsartan	Solid SMEDDS, capsule molding	30 % Gelucire®44/14 30 % Transcutol® 40 % Solutol™ HS15 80 mg Valsartan /1g excipients	Improved *in vitro* drug release: 90% for SMEDDS vs 60% for the market reference *In vivo* (rats): 3-fold increase in AUC; 2.72-fold increase in Cmax	Zhao, 2016

Capsule molding - Atorvastatin – Gelucire® 44/14 binary mixture

The objective of this study (Shaker et al., 2018) is to increase the solubility and oral bioavailability of atorvastatin using a binary mixture of atorvastatin (80 mg) and Gelucire® 44/14 (240 mg). Atorvastatin (ATV) is added to the molten Gelucire® 44/14 and stirred to homogenize. The capsules are filled and left to cool down overnight prior to testing.

Atorvastatin solubility in water is 20.6 µg/mL and 4.37 mg/mL in Gelucire® 44/14 at 37°C.

In dissolution testing, atorvastatin solubility is significantly improved by formulating in Gelucire® 44/14: 85% for the Gelucire® 44/14 / ATV capsule versus 25% for pure drug at 120 minutes (Figure 6).

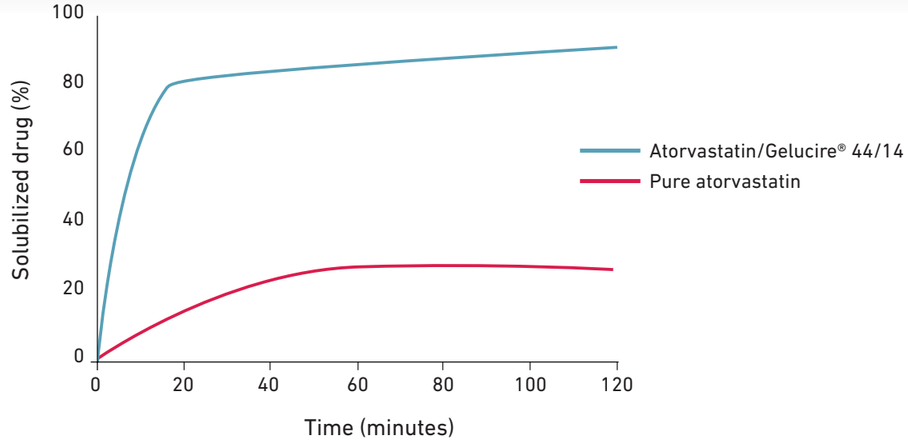


Figure 6: Dissolution of atorvastatin (adapted from Shaker et al., 2018) (80 mg ATV in 900 mL of 0.1N HCl in deionized water at 37°C; USP XXVIII paddle apparatus)

The subsequent *in vivo* pharmacokinetic study (in rabbits) shows a marked increase in oral bioavailability versus pure drug and compared with a market reference (Figure 7 and Table 3).

Table 3: Pharmacokinetic parameters after administration of 10 mg/kg oral dose to rabbits (from Shaker et al., 2018)

Parameter	Pure ATV	Market reference	Gelucire® 44/14/ATV formula
AUC (ng.h/mL)	2,545.7	4,583.7	11,393.8
Tmax (h)	1.78	2.05	3.19
Cmax (ng/mL)	527.2	652.8	1,312.2

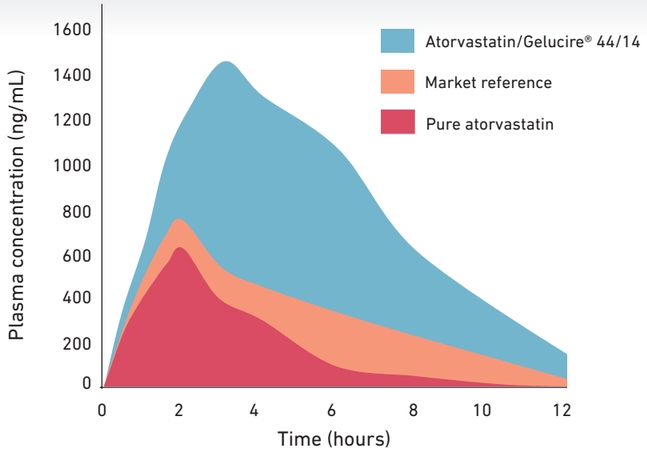


Figure 7: Atorvastatin plasma concentration in rabbits (adapted from Shaker et al., 2018)

With Gelucire® 44/14 bioavailability is improved 4.5-fold versus pure drug and 2.5-fold compared to the market reference.

The simple binary mixture Gelucire® 44/14/ATV forms a SEDDS capable of increasing drug solubility and bioavailability with excellent performance. Capsule molding is a well-established manufacturing process, conducive to faster drug development.

Did you know ?

Hard capsule molding requires a capsule filling machine equipped for hot liquid filling, which is a standard manufacturing equipment. In Europe, Solufen™ (ibuprofen) and Fenogal™ (fenofibrate) are examples of hard capsule dosage forms with Gelucire® 44/14 (Surasarang and Williams, 2016).

Multi-excipient SEDDS – Docetaxel

Valicherla et al. (2016) developed a multi-excipient SEDDS for docetaxel to increase oral bioavailability hence anti-tumour activity. Solubility screening in lipid excipients, ternary diagramming and *in vitro* performance testing were used to develop the formulas. The drug delivery efficacy of the SEDDS was assessed using *in vitro* cytotoxic activity, *in situ* single pass intestinal perfusion and *in vivo* pK studies.

Maximum solubility of docetaxel was obtained for the following single excipients:

173.13 ± 5.96 mg/mL in Transcutol® HP
54.39 ± 1.87 mg/mL in Gelucire® 44/14
47.63 ±1.56 mg/mL in Vitamin E TPGS
45.15 ± 6.03 mg/mL in Capryol® 90

A SEDDS was developed with a drug solubility of 48.35 ±1.06 mg/mL, comprising:

29.4% of Gelucire® 44/14
32.7% of Capryol® 90
8.3% of Vitamin E TPGS
29.6% Transcutol® P

About 80 % of drug was released *in vitro* from this SEDDS within 12 hours versus 43% for the pure drug (Figure 8).

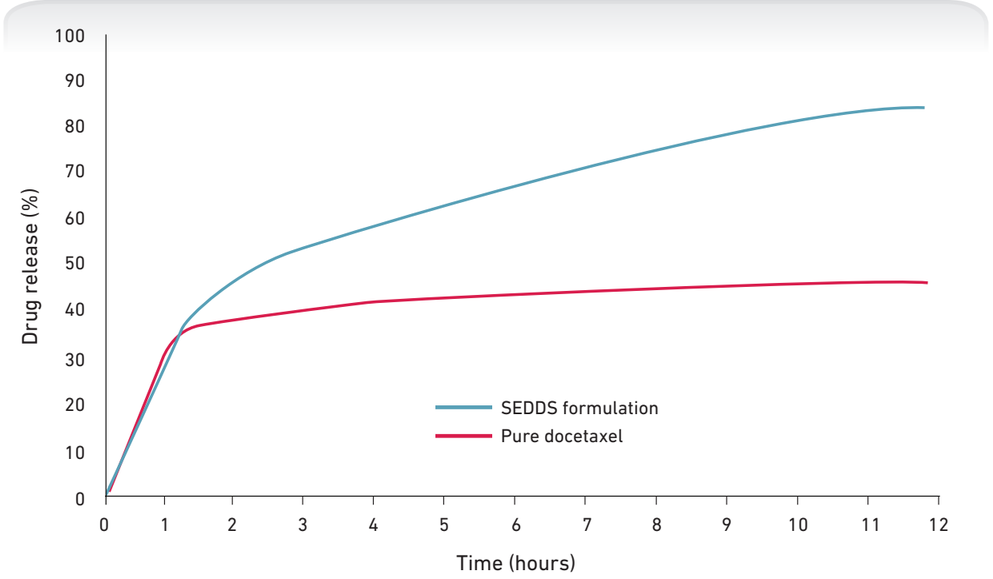


Figure 8: Docetaxel release from SEDDS vs pure drug (adapted from Valicherla et al., 2016) (2 mg of DCT – pure or in SEDDS- dispersed in 1 mL gastrointestinal fluids; dialysis through 12 kDa membrane at 37°C)

Drug efficacy was higher when delivered as a SEDDS compared to pure drug (Table 4).

- about 25-fold increase in *in vitro* cytotoxic activity on MCF -7 tumour cells
- a 5-fold increase in *in situ* effective permeability (Peff)
- a 3.19-fold increase in absolute bioavailability

Table 4: Docetaxel efficacy from SEDDS vs pure drug (from Valicherla et al., 2016)

	Free drug	Drug loaded SEDDS
In vitro tumour cell viability (IC_{50}, nM)	21	1
In situ single pass intestinal perfusion (P_{eff} 10^{-4}. cm/s)	1.04	5.71
In vivo pK studies (rats, 10 mg/kg) Cmax (ng/mL) Tmax (h) AUC (h.ng/mL)	 35.2 ± 9.7 0.25 ± 0.08 81.55 ± 17.29	 125.5 ± 2.5 0.17 260.23 ± 51.80

Multi-excipient SEDDS are formulations with high drug solubilization capacity, capable of enhancing oral bioavailability and increasing drug therapeutic efficacy.

Did you know ?

Liquid or low viscosity lipid-based formulations including SEDDS and SMEDDS are frequently filled in soft gelatin capsules.

In the USA, a calcifediol monohydrate prescription drug is available in soft gelatin capsule containing lauroyl polyoxyl-32 glycerides.

Regulatory information and precedence of use

Gelucire® 44/14 is a well-characterized, safe excipient which conforms to the USP-NF and EP pharmacopoeias (Table 5). Lauroyl polyoxylglycerides are referenced in the FDA Inactive Ingredients Database under two denominations (Table 6). Examples of marketed oral dosage forms are listed in Table 7.

Table 5: Gelucire® 44/14 regulatory summary

USP NF Name	Lauroyl polyoxyl-32 glycerides
EP Name	Lauroyl macrogol-32 glycerides
UNII Code (FDA)	H5ZC52369M
Preferred Substance Name (FDA)	Lauroyl PEG-32 glycerides
Handbook of Pharmaceutical Excipients	Polyoxylglycerides
Drug master file	US DMF 5253; Canada MF 1988-07
United States Food Additive (USFA)	21 CFR § 172.736

Table 6: US FDA inactive ingredient database references

Inactive Ingredient listed in FDA database	Dosage form	Use level (mg/unit dose)
Lauroyl PEG-32 glycerides	Capsule Tablet	3 0.15
Lauroyl polyoxylglycerides	Capsule Capsule, Hard Gelatin Tablet Tablet, Film Coated	16.58 218 0.15 0.15

Table 7: Examples of marketed oral dosage forms containing lauroyl polyoxylglycerides

Active ingredient	Indication for the product	Galenic form	Drug sales country
Calcifediol monohydrate	Vitamin D3 analogue	Soft gelatin capsule	USA
Fenofibrate	Lipid-lowering drug	Hard gelatin capsule	Canada, Europe and USA
Ibuprofen	Anti-inflammatory	Hard gelatin capsule	Europe
Lecarnidipine hydrochloride	Anti-hypertension	Tablet	Korea
Mazindol	Anti-obesity	Tablet	Korea
Mometasome furoate	Nasal decongestant	Spraying solution	Korea
Olaparib	Antineoplastic agent	Hard gelatin capsule	France and USA
Pranlukast hydrate	Cysteinyl leukotriene Receptor-1 antagonist	Soft gelatin capsule	Korea

For more information please request our Regulatory Datasheet

Technical Support

Gattefossé can provide technical support to help you with the selection of excipients for solubility enhancement, screening methods and solubility measurements, ternary phase diagram development and *in vitro* characterization assays for lipid-based formulation.

Please contact your local Gattefossé representative

Bibliography

Barker, S. A., Yap, S. P., Yuen, K. H., McCoy, C. P., Murphy, J. R., & Craig, D. Q. M. (2003)
An investigation into the structure and bioavailability of α-tocopherol dispersions in Gelucire 44/14
Journal of controlled release, 91(3), 477-488.

Čerpnjak, K., Zvonar, A., Vrečer, F., & Gašperlin, M. (2015)
Development of a solid self-microemulsifying drug delivery system (SMEDDS) for solubility enhancement of naproxen
Drug development and industrial pharmacy, 41(9), 1548-1557.

Chambin, O. and Jannin, V. (2005)
Interest of multifunctional lipid excipients: case of Gelucire® 44/14
Drug development and industrial pharmacy, 31(6), 527-534.

Chamieh, J., Davanier, F., Jannin, V., Demarne, F., & Cottet, H. (2015)
Size characterization of commercial micelles and microemulsions by Taylor dispersion analysis
International journal of pharmaceutics, 492 (1-2), 46-54.

Chauhan B, Shimpi S, Paradkar A. (2005)
Preparation and evaluation of glibenclamide-polyglycolized glycerides solid dispersions with silicon dioxide by spray drying technique
Eur J Pharm Sci. Oct; 26(2):219-30.

Chen, X. Q., Ziemba, T., Huang, C., Chang, M., Xu, C., Qiao, J. X., ... & Gudmundsson, O. (2018)
Oral Delivery of Highly Lipophilic, Poorly Water-Soluble Drugs: Self-Emulsifying Drug Delivery Systems to Improve Oral Absorption and Enable High-Dose Toxicology Studies of a Cholesteryl Ester Transfer Protein Inhibitor in Preclinical Species
Journal of pharmaceutical sciences, 107(5), 1352-1360.

Daravath B, Tadikonda RR, Vemula SK. (2015)
Formulation and pharmacokinetics of gelucire solid dispersions of flurbiprofen
Drug Dev Ind Pharm. 41(8):1254-62.

Faisal, W., Ruane-O'Hora, T., O'Driscoll, C. M., & Griffin, B. T. (2013)
A novel lipid-based solid dispersion for enhancing oral bioavailability of Lycopene–In vivo evaluation using a pig model
International journal of pharmaceutics, 453(2), 307-314.

Falconer, J. R., Wen, J., Zargar-Shoshtari, S., Chen, J. J., Farid, M., Young, S., & Alany, R. G. (2013)
Effects of supercritical carbon dioxide processing on optical crystallinity and in vitro release of progesterone and Gelucire 44/14 solid and semi-solid dispersions
Journal of Drug Delivery Science and Technology, 23(5), 477-483.

Fernandez, S., Rodier, J. D., Ritter, N., Mahler, B., Demarne, F., Carrière, F., & Jannin, V. (2008)
Lipolysis of the semi-solid self-emulsifying excipient Gelucire® 44/14 by digestive lipases
Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids, 1781(8), 367-375.

Fernandez, S., Chevrier, S., Ritter, N., Mahler, B., Demarne, F., Carrière, F., & Jannin, V. (2009)
In vitro gastrointestinal lipolysis of four formulations of piroxicam and cinnarizine with the self-emulsifying excipients Labrasol® and Gelucire® 44/14
Pharmaceutical research, 26(8), 1901-1910.

Jannin V., Michenaud M., Belotti S., Andre C., Chevrier S., Chavant Y., Voutsinas C. and Demarne F. (2013)
SELF formulation protocol: part II - excipient selection, diagram design and selection of prototype formulations
AAPS.

Jannin, V. (2009)
Lauroyl polyoxylglycerides, functionalized coconut oil, enhancing the bioavailability of poorly soluble active substances
Oléagineux, Corps gras, Lipides, 16(4-5-6), 267-272.

Kalpana M., Ramakrishna Sistla & Nalini R. Shastri (2014)
Modulating drug release profiles by lipid semi solid matrix formulations for BCS class II drug – an in vitro and an in vivo study
Drug Delivery, 22(3):418-426.

Shaker, M. A. (2018)
Dissolution and bioavailability enhancement of Atorvastatin: Gelucire semi-solid binary system
Journal of Drug Delivery Science and Technology, 43, 178-184.

Schamp, K., Schreder, S. A., & Dressman, J. (2006)
Development of an in vitro/in vivo correlation for lipid formulations of EMD 50733, a poorly soluble, lipophilic drug substance
European journal of pharmaceutics and biopharmaceutics, 62(3), 227-234.

Soraya Hengsawas Surasarang and Robert O. Williams. (2016)
Co-solvent and Complexation Systems
Pages 215-256, in Formulating Poorly water soluble drugs ISBN 2210-7371.

Gürsoy, R. N., & Çevik, Ö. (2014)
Design, characterization and in vitro evaluation of SMEDDS containing an anticancer peptide, linear LyP-1
Pharmaceutical development and technology, 19(4), 486-490.

Valicherla, G. R., Dave, K. M., Syed, A. A., Riyazuddin, M., Gupta, A. P., Singh, A., ... & Gayen, J. R. (2016)
Formulation optimization of Docetaxel loaded self-emulsifying drug delivery system to enhance bioavailability and anti-tumor activity
Scientific reports, 6, 26895.

Vithani K, Jannin V, Pouton C and Boyd B. (2019)
Colloidal aspects of dispersion and digestion of self-dispersing lipid-based formulations for poorly water-soluble drugs
Advanced Drug Delivery Reviews, ISSN 0169-409X, https://doi.org/10.1016/j.addr.2019.01.008.

Vithani K, Goyanes A, Jannin V, Gaisford S, Boyd B
A Novel Approach To Prepare Solid Self-microemulsifying Drug Delivery System Without A Solid-phase Carrier Using 3D Printing
CRS 2018 poster.

Yang D, Kulkarni R, Behme RJ, Kotiyan PN
Effect of the melt granulation technique on the dissolution characteristics of griseofulvin
Int J Pharm. 2007 Feb 1;329(1-2):72-80. Epub 2006 Aug 30.

Yüksel, N., Karataş, A., Özkan, Y., Savaşer, A., Özkan, S. A., & Baykara, T. (2003)
Enhanced bioavailability of piroxicam using Gelucire 44/14 and Labrasol: in vitro and in vivo evaluation
European journal of pharmaceutics and biopharmaceutics, 56(3), 453-459.

Zhao K, Yuan Y, Wang H, Li P, Bao Z, Li Y.
Preparation and evaluation of valsartan by a novel semi-solid self-microemulsifying delivery system using Gelucire 44/14
Drug Dev Ind Pharm. 2016 Oct; 42(10):1545-52.

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Corporate Headquarters
36 chemin de Genas - CS 70070 - 69804 Saint-Priest Cedex - **France**
+(33) 4 72 22 98 00

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