# Strategies for Effective Solubilization & Bioavailability Enhancement of BCS Class Type II and Type IV APIs

## HEALTH CARE

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# Clariant has the wide product portfolio for Excipients and Polyglykols as Active Pharmaceutical Ingredients (APIs)

## OUR PROTFOLIO

**Active Pharmaceutical Ingredients**


Top quality range of Polyglykols (Polyethylene Glycols - PEGs) used as Active Pharmaceutical Ingredients (APIs) in laxatives formulations and in ophthalmic preparations

**Excipients**

Comprehensive range of excipients (Motusflex® and VitiPure®) such as Solubilizers, Emulsifiers, Solvents, Rheology Modifiers, Binders, Humectants, Plasticizers etc. for all sorts of pharmaceutical dosage formulations.

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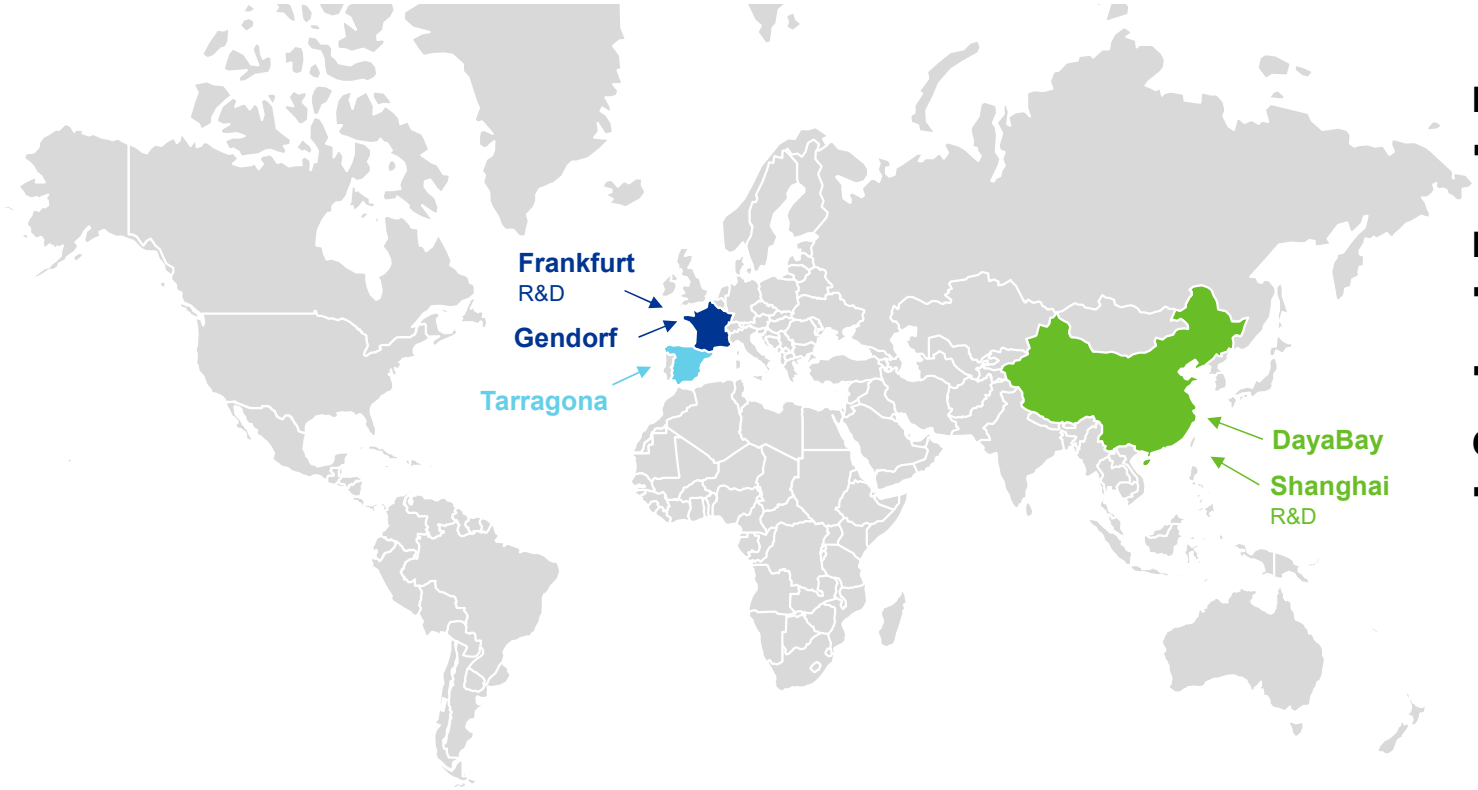
# Clariant with a worldwide Pharmaceutical Manufacturing Facilities, R&D and commercial offices




## Research & Innovation Center

- **Frankfurt** & **Shanghai**

## Pharma Manufacturing sites

- **Gendorf** & **Dayabay**: Polyglykols®, VitiPure™ mPEGs
- **Tarragona**: VitiPure™, Motusflex®

## Commercial Offices

- Across multiple countries: USA, Brazil, Germany, France, Italy, UK, UAE, Turkey, China, Singapore, India, Australia, etc.

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# Our positive and progressive track-record in the health Care industry encouraged us to become the best-in-class solution provider

## TOP SUPPLIERS BY CUSTOMER LOYALTY: SATISFACTION, LIKEHOOD TO RECOMMEND & RE-PURCHASE[1]

| Rank | Rx Pharma - Originators | Rx Generics Pharma |
|---|---|---|
| 1 | | |
| 2 | | |
| 3 | | |
| 4 | Clariant | |
| 5 | | Clariant |
| 6 | | |
| 7 | | |
| 8 | | |
| 9 | | |
| 10 | | |

Clariant in the top 5 suppliers


SOURCE: Expert interviews, Team analysis

1 Data published in ISR reports shown as the top 10 companies with the biggest loyal customer base. Loyalty is a combination of other three factors: 1. Overall satisfaction, 2. Likelihood to recommend and 3. Likelihood to use again

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# Challenges in Pharma Industry

- About 40% of NCEs are poorly water soluble
- A significant percentage cannot be absorbed effectively due to their complex chemical structures or absorption profiles”

➡ “41% of NCE developments fail due to poor bio-pharmaceutical properties”

➡ **There is an increasing need for solubilizers in Pharmaceutical industry!**

1. Oral Drug Delivery Systems. Kalorama Information, LLC 2001
2. R.A. Lipper (BMS). Modern Drug Discovery, January/February 1999, 55-60

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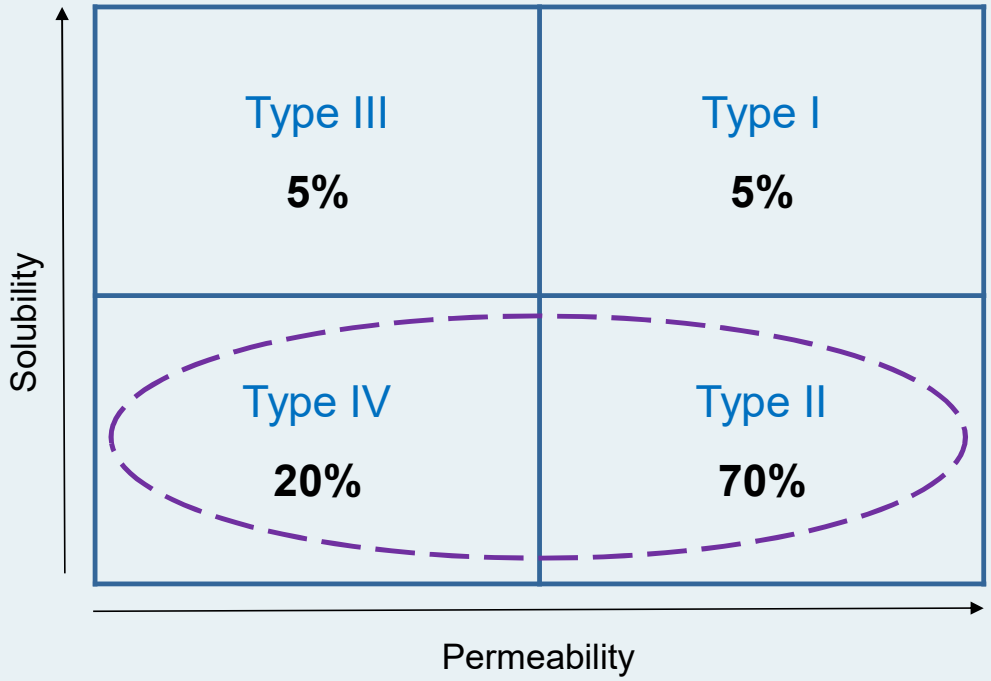
# 90% of APIs Are Poorly Soluble
## API Classification




Benet, EDAN, Leuven, March 18-20 2007

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# How Can Clariant Help You To Get A Solution?

**Using our solubilizers will increase your performance!**

Which groups of solubilizers do we offer?

1. Solvents
2. PEG- Derivatives
3. Poloxamer

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# New Solubilizers by Clariant

| | Name | Pharmacopeial name | Monograph |
|---|---|---|---|
| Solvents | VitiPure LEX 300/ 400 | Polyethylene Glycol 300/ 400<br>Macrogol 300/ 400 | USP/NF<br>Ph.Eur.<br>JP |
| PEG- Derivatives | VitiPure HCO 40 | Polyoxyl 40 Hydrogenated Castor Oil<br>Macrogolglycerol Hydroxystearate | USP/NF<br>Ph.Eur |
| | VitiPure CO 35 | Polyoxyl 35 Castor Oil<br>Macrogolglycerol Ricinoleate | USP/NF<br>Ph.Eur |
| | VitiPure L 20 | Polysorbate 20 | USP/NF<br>Ph.Eur. |
| | VitiPure O 80 | Polysorbate 80 | USP/NF<br>Ph.Eur. |
| Poloxamer | VitiPure P 188 | Poloxamer 188 | USP/NF<br>Ph.Eur. |

# VitiPure LEX 300 / 400

## Widely Used Solvent With Stringent Control of Microbial Load

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# VitiPure™ LEX 300/400 – Description

| | |
|---|---|
| ▪ GENERIC NAMES | Macrogol in Ph.Eur., JP and Polyethylene glycol in USP/NF |
| ▪ TYPE | Polyethylene Glycol 300 & Polyethylene Glycol 400 |
| ▪ APPEARANCE | Clear Liquid |
| ▪ CAS NO. | 25322-68-3 |
| ▪ SAFETY | World-wide several registered Pharmaceutical OTC and prescription medicines |
| | Listed in the inactive ingredient database of the FDA |
| ▪ RETEST PERIOD | 2 years |
| ▪ PACKAGING SIZES* | 220kg & 30kg (Stainless steel drum with PE-inliner) |
| | Sample size 0.5kg |

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# VitiPure™ LEX 300 / 400 - Key Information

**Microbial Specifications in Addition to Ph.Eur., JP and USP/NF Specifications**

| | |
|---|---|
| + Endotoxin | max. 1 IU/ml |
| + TAMC | max. 50 cfu/g |
| + TYMC | max. 50 cuf/g |
| + Salmonella | absent |
| + Staphylococcus aureus | absent |
| + Escherichia coli | absent |
| + Pseudomonas aeruginosa | absent |

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# VitiPure™ LEX 300 / 400 - Applications

- Safe and widely used pharmaceutical solvents for varieties of different APIs which are difficult to dissolve in water
- Applied in liquid and semi-solid formulations
- Excellent hygroscopicity, perfect as humectants

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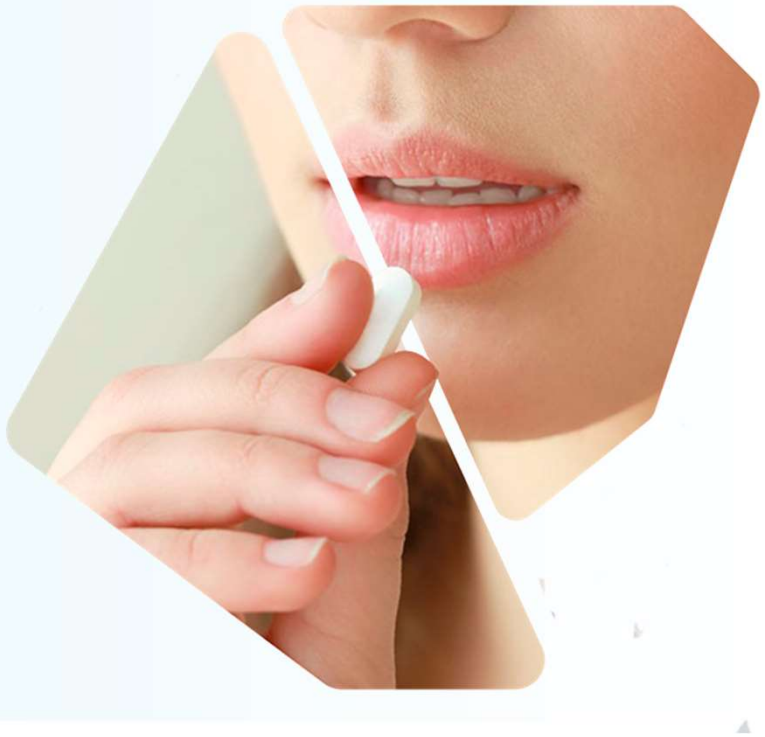
# VitiPure™ LEX 300 / 400

## DOSAGE & APPLICATIONS



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# FDA Published Applications For Polyethylene Glycol 300
## Dosage and Applications*

- **Auricular (OTIC)**
  Upto. 97.43% w/v

- **Ophthalmics****
  Upto. 0.5 – 1% w/v

- **Tablets/Capsules**
  Upto. 9 mg

- **Creams**
  Upto. 57% w/w

- **Injection****
  Upto. 65% w/v

*Published in Inactive Ingredients Database by FDA
** Requires parenteral grade

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# FDA Published Applications For Polyethylene Glycol 400
## Dosage and Applications*

- **Oral Solutions**
  upto. 74mg/1ml

- **Ophthalmics****
  upto. 4% w/v

- **Tablets/Capsules**
  upto. 324.5 mg

- **Ointment**
  upto. 65% w/w

- **Injection****
  IM: upto. 20.3% w/v
  IV: upto. 75.58% w/v

- **Suppository**
  upto. 30mg

- **Nasal**
  upto. 27mg

*Published in Inactive Ingredients Database by FDA
** Requires parenteral grade

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# VitiPure™ LEX 300 / 400 - Benefits

- Low microbial load for high-risk applications
- Surpass the current pharmacopoeia requirements
- Supports risk assessment in pharmaceutical and biopharmaceutical manufacturing

# Non-Ionic Solubilizers

## Based on PEG-Derivatives

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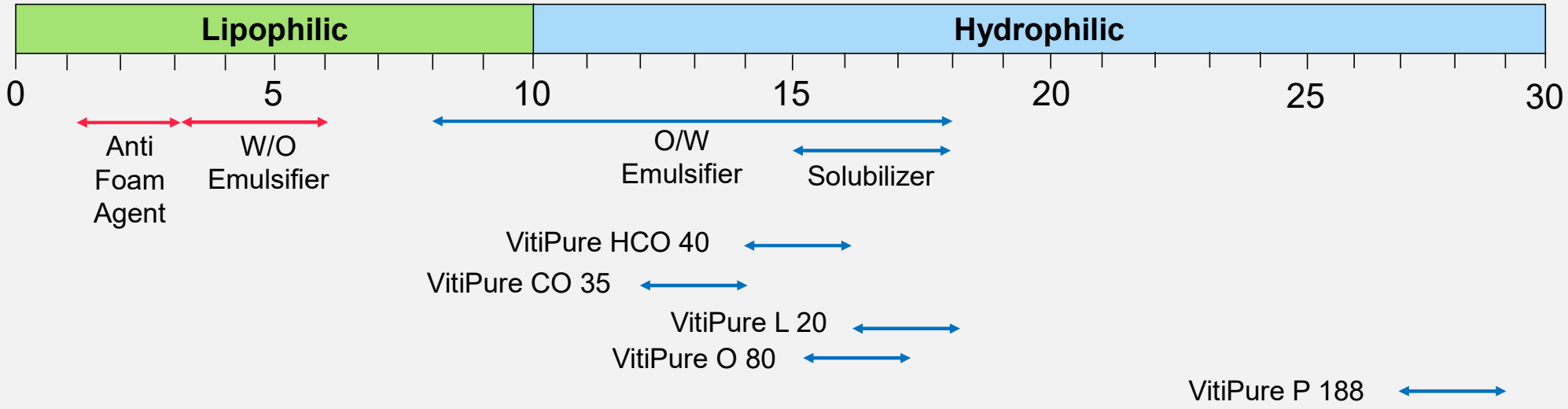
# Characterization of non-ionic solubilizers

HLB value (Hydrophilic - Lipophilic – Balance)




$$HLB = 20 \cdot \left(1 - \frac{M_o}{M}\right)$$

$M_0$ : mass of the lipophilic part
$M$ : mass of the molecule

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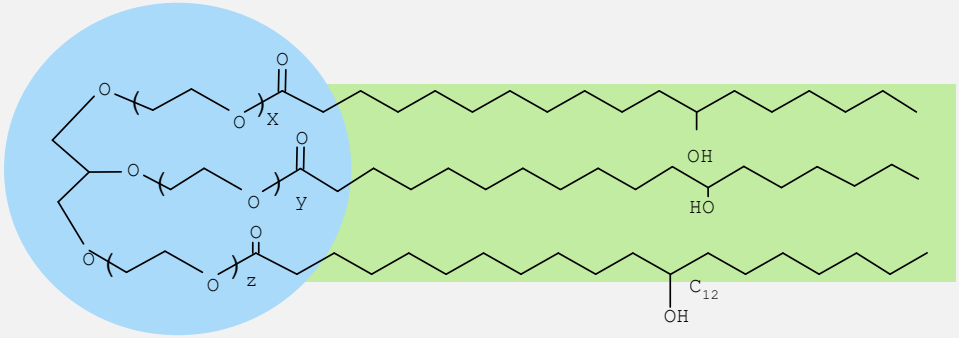
# Solubilizer – PEG - Derivatives

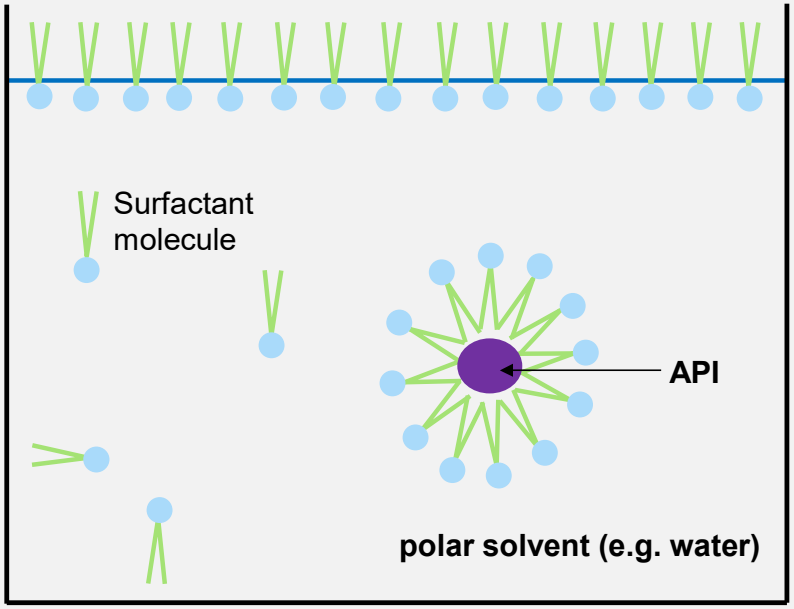
## Overview – Structure and Principle of Micellization

Hydrophilic

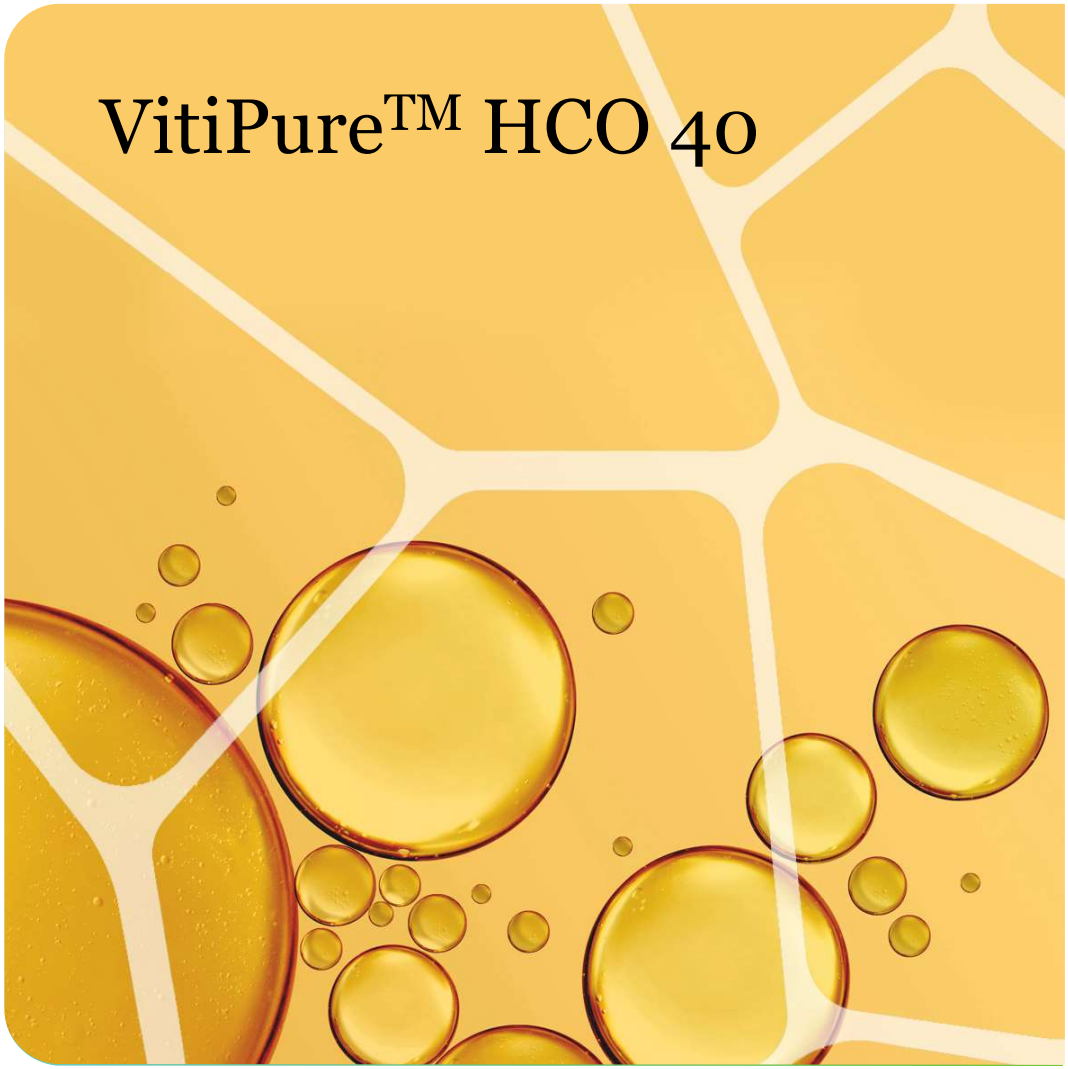
Hydrophobic




Structure: VitiPure HCO 40



# VitiPure™ HCO 40



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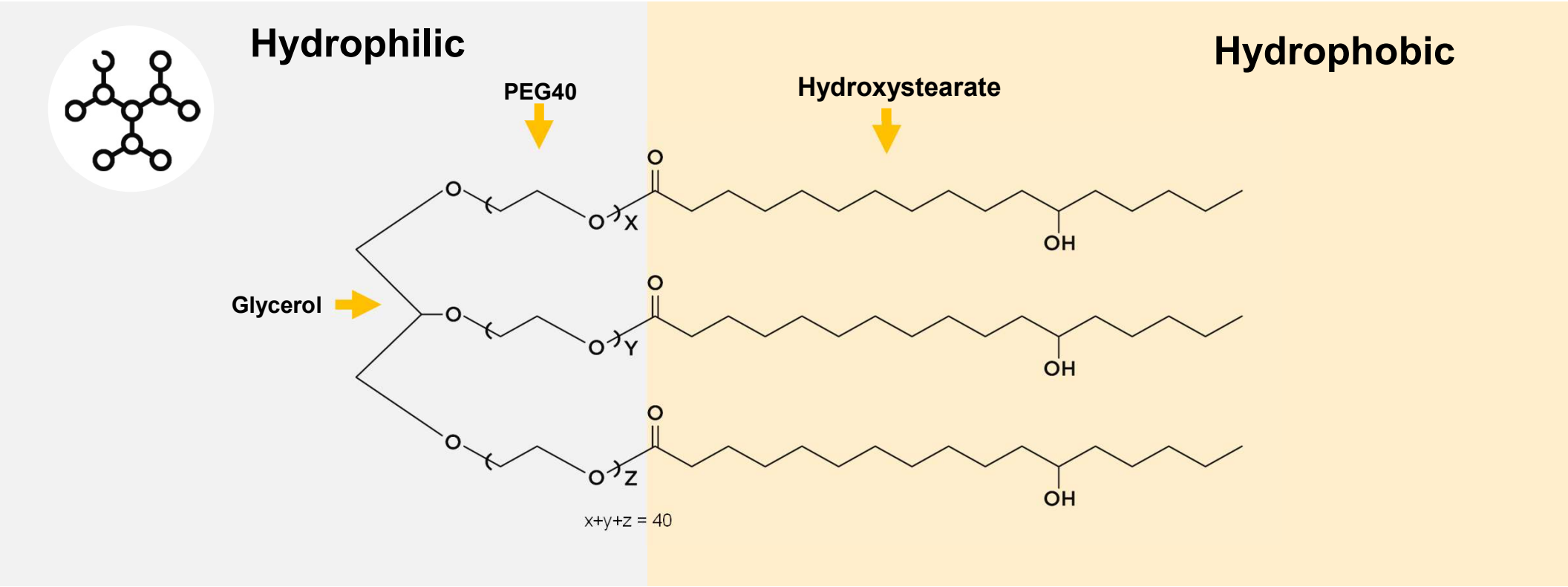
# VitiPure™ HCO 40 – Chemistry structure



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# VitiPure™ HCO 40 – Description

- GENERIC NAMES: Polyoxyl 40 Hydrogenated Castor Oil *(USP)*
  Macrogolglycerol Hydroxystearate *(Ph. Eur.)*
- TYPE: Non-ionic surfactant
- CAS NO.: 61788-85-0
- SAFETY: World-wide several registered Pharmaceutical OTC and prescription medicines
  Listed in the inactive ingredient database of the FDA
- GMP: IPEC
- RETEST PERIOD: 2 years
- PACKAGING SIZES*: 100kg steel drum (epoxy coated in-liner) and 25kg steel drum (epoxy coated in-liner)
  Sample size 0.5kg

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# VitiPure™ HCO 40 – Properties

| | |
|---|---|
| ▪ HLB VALUE | 14 - 16 |
| ▪ PHYSICAL PROPERTIES | yellowish to white paste at 20°C |
| ▪ CRITICAL MICELLE CONCENTRATION | 0.03% w/w at 37°C (in water) |
| ▪ ORGANOLEPTIC PROPERTIES | practically no odor or taste |
| ▪ SOLUBILITY | forms clear solutions in water, ethanol, 2-propanol, n-propanol, ethyl-acetate, chloroform, carbon tetrachloride, toluene and xylene |
| ▪ STABILITY | aqueous VitiPure HCO 40 solutions are stable<br>can be sterilized by heating to 120°C |

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# VitiPure™ HCO 40

## DOSAGE & APPLICATIONS

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# FDA Published Applications For PEG 40 HCO

## Dosage and Applications*

- **Oral Solutions**
  Upto. 0.5 – 45%

- **Ophthalmics**
  Upto. 0.5 – 1% w/v

- **Tablets/Capsules**
  (MDE**) 120 mg / 3319 mg

- **Creams**
  Upto. 1% w/w

- **Softgel capsules**
  Upto. 400 mg

*Published in Inactive Ingredients Database by FDA

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# Versatile Solubilizer For A Wide Range Of Applications

| Drug Form | Important Functions |
|---|---|
| Solutions / gels / cremes | ▪ Solubilization by inclusion in small micelles (→ microemulsion) |
| Emulsions | ▪ Emulsification by inclusion in big micelles (→ macroemulsion)<br>▪ Ideal solubilizer & Emulsifier for hydrophobic APIs and Vitamins |
| Suspensions | ▪ Increase of wettability<br>▪ Reduction of sedimentation |
| Tablets / capsules / suppositories | ▪ Increase of bioavailability by solubilization in the gastro-intestinal tract |

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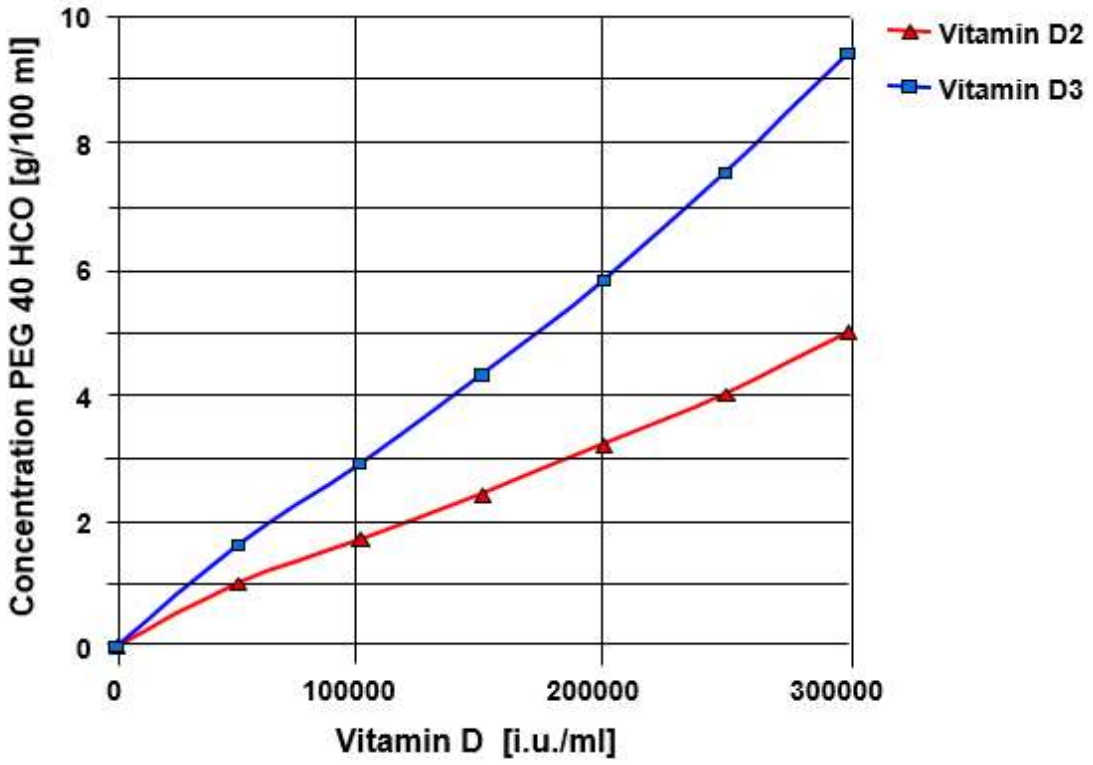
# Improving the Solubility of Fat-Soluble Vitamin D

**Aqueous solution of Vit D**

- 0.8 g Vitamin D2 (400 000 I.U.) or
- 0.5 g Vitamin D3 (125 000 I.U.)
- 100ml water
- 6g PEG 40 HCO



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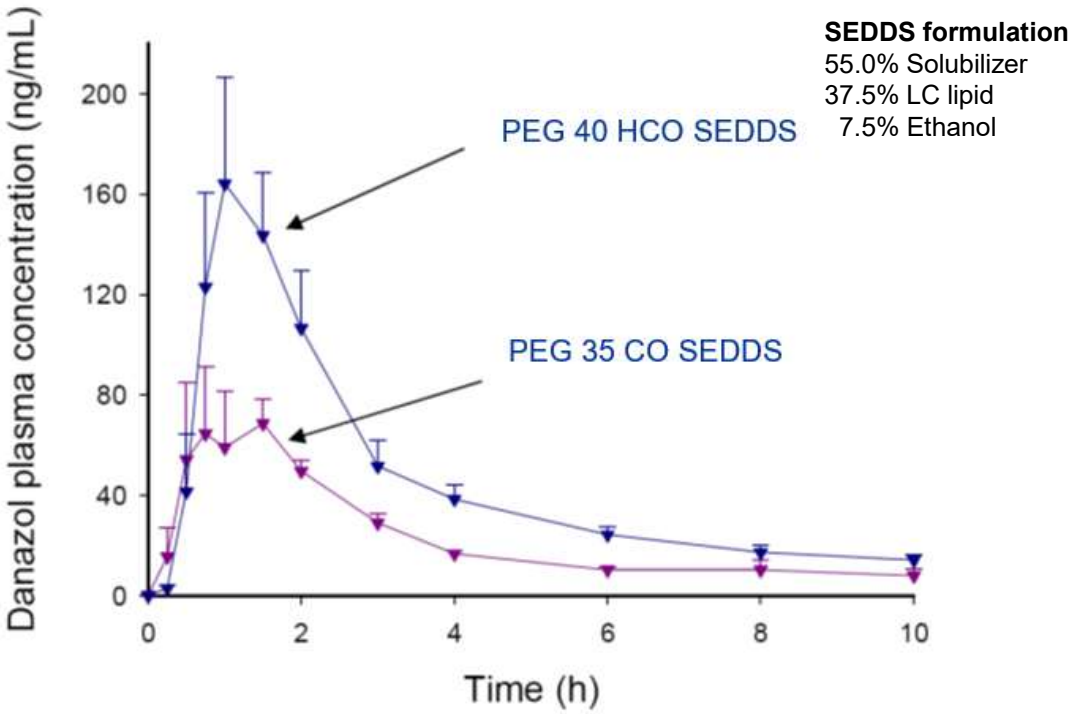
# Application of VitiPure™ HCO 40 into SEDDS

## Design of in vivo study

- Crossover (7day wash-out) study in four beagle dogs (male)
- Treatment administered in 2 x 800mg (soft gelatine capsules)
- API  Danazol at 80% saturated solubility included in formulation




Cuine et al.,Pharm. J Pharm. Sci, Vol 97, No. 2, 2008

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# VitiPure™ HCO 40 – Key benefits

- Ideal solubilizer & emulsifier for hydrophobic APIs and Vitamins
- Safety & toxicology well established via several marketed drugs world wide
- Suitable for SEDDS* and SMEDDS** formulations
- Zero taste and odour - perfect for oral applications

*SEDDS: Self-emulsifying drug delivery system **SMDDS: Self-microemulsifying drug delivery system

# VitiPure™ CO 35

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# VitiPure™ CO 35 - Description

| | |
|---|---|
| ▪ GENERIC NAMES | Polyoxyl 35 Castor Oil *(USP)*<br>Macrogolglycerol Ricinoleate *(Ph. Eur.)* |
| ▪ TYPE | Non-ionic surfactant |
| ▪ CAS NO. | 61791-12-6 |
| ▪ SAFETY | World-wide several registered Pharmaceutical OTC and prescription medicines<br>Listed in the inactive ingredient database of the FDA |
| ▪ GMP | IPEC |
| ▪ RETEST PERIOD | 2 years |
| ▪ PACKAGING SIZES* | 100kg steel drum (epoxy coated in-liner) and 25kg steel drum (epoxy coated in-liner)<br>Sample size 0.5kg |

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# VitiPure™ CO 35 – Chemistry structure

**Hydrophilic**

**Hydrophobic**

**PEG35**

**Ricinoleate**

**Glycerol**

$CH_2\text{-}O\text{-}(CH_2\text{-}CH_2\text{-}O)_x\text{-}CO\text{-}O\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}CH_2\text{-}CHOH\text{-}(CH_2)_5\text{-}(CH_3)$

$HC\text{-}O\text{-}(CH_2\text{-}CH_2\text{-}O)_y\text{-}CO\text{-}O\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}CH_2\text{-}CHOH\text{-}(CH_2)_5\text{-}CH_3$

$CH_2\text{-}O\text{-}(CH_2\text{-}CH_2\text{-}O)_z\text{-}CO\text{-}O\text{-}(CH_2)_7\text{-}CH{=}CH\text{-}CH_2\text{-}CHOH\text{-}(CH_2)_5\text{-}CH_3$

$x+y+z = 35$

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# VitiPure™ CO 35 – Properties

| | |
|---|---|
| ▪ HLB VALUE | 12 - 14 |
| ▪ PHYSICAL PROPERTIES | Pale yellow or clear liquid depending on the temperature |
| ▪ CRITICAL MICELLE CONCENTRATION | 0.02% w/w at 37°C (in water) |
| ▪ ORGANOLEPTIC PROPERTIES | Faint characteristics odor |
| ▪ SOLUBILITY | forms clear solutions in water, ethanol, 2-propanol, n-propanol, ethyl-acetate, chloroform, carbon tetrachloride, trichloroethylene, toluene and xylene |
| ▪ STABILITY | aqueous VitiPure CO 35 solutions are stable can be sterilized by heating to 120°C |

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# VitiPure™ CO 35

## DOSAGE & APPLICATIONS

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# FDA Published Applications For PEG 35 CO
## Dosage and Applications*

- **Oral Solutions**
  upto. 515 mg/1ml

- **Ophthalmics**
  upto. 5% w/v

- **Tablets/Capsules**
  upto. 599.4 mg

- **Creams**
  upto. 4% w/w

- **Injection****
  upto. 52.75%w/v
- 24945mg (MDE)

*Published in Inactive Ingredients Database by FDA per unit dose
MDE: Maximum daily exposure
**Requires parenteral grade

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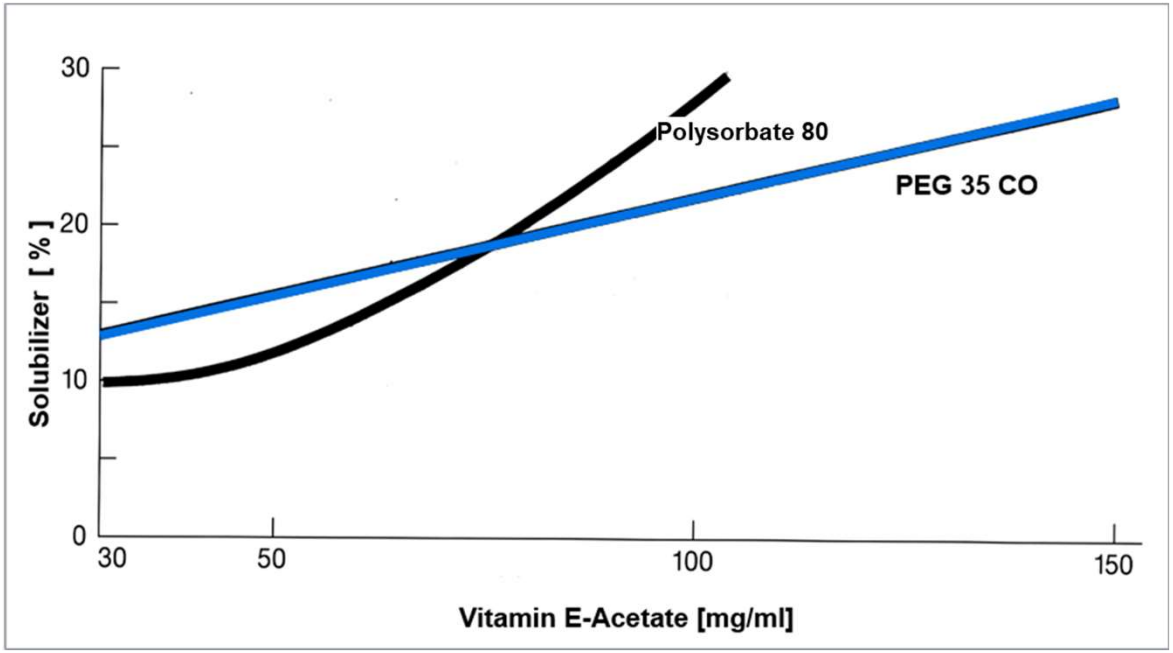
# Less VitiPure CO 35 is Required to Dissolve Equal Amount of Fat-Soluble Vitamin E Compared with Polysorbate 80

**Aqueous solution of Vit E**

- 15 g Vit E acetate
- 100ml water
- 30g Solubilizer



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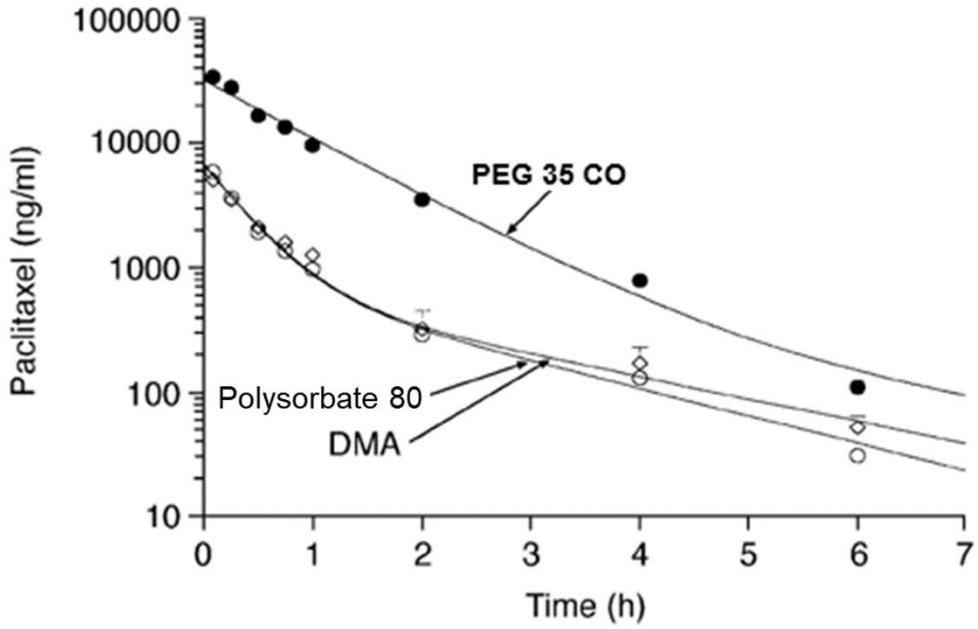
# VitiPure CO 35 - Solubilisation Capacity of Paclitaxel

Effect of the formulation vehicle on paclitaxel concentration in female mice receiving paclitaxel at a dose of 10mg/kg.

(DMA: Dimethylacetamide)




Zordan-Nudo et al, Cancer Res., Vol 56, 1996

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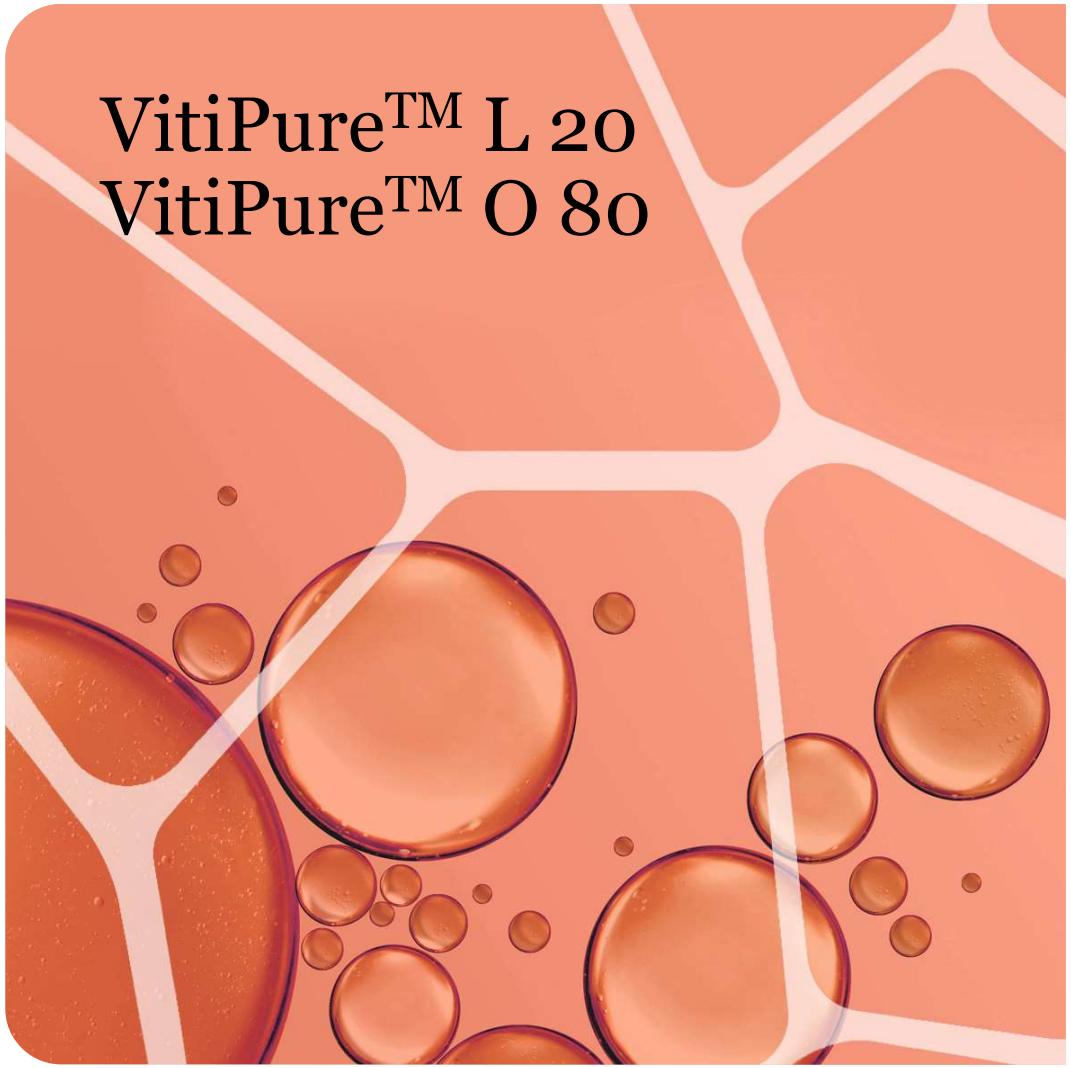
# VitiPure™ CO 35 – Key Benefits

- Emulsifies or solubilizes the fat-soluble vitamins A, D, E and K in aqueous solutions for oral and topical administration.
- Aqueous solutions of hydrophobic drugs (e.g. Miconazole, Hexedetine, Clotrimazole, Benzocaine etc.) can be prepared using VitiPure CO 35
- Safety & toxicology well established via several marketed drugs world-wide into human and veterinary medicines and nutrition.
- Increases bioavailability when used in SEDDS



# VitiPure™ L 20
# VitiPure™ O 80

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# VitiPure™ L 20 / O 80 - Description

- GENERIC NAMES: Polysorbate 20 *(USP/NF; Ph. Eur.)*<br>Polysorbate 80 *(USP/NF; Ph. Eur.)*
- TYPE: Non-ionic surfactant
- CAS NO.: VitiPure L 20 (9005-65-5); VitiPure O 80 (9005-65-6)
- SAFETY: World-wide several registered Pharmaceutical OTC and prescription medicines<br>Listed in the inactive ingredient database of the FDA
- GMP: IPEC
- RETEST PERIOD: 2 years
- PACKAGING SIZES: 100kg steel drum (epoxy coated in-liner) and 25kg steel drum (epoxy coated in-liner)<br>Sample size 0.5kg

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# VitiPure™ L 20 / O 80 – Properties

| | |
|---|---|
| ▪ HLB VALUE | 16.7 (VitiPure™ L 20) / 15.0 (VitiPure™ O 80) |
| ▪ PHYSICAL PROPERTIES | Viscous clear liquid |
| ▪ CRITICAL MICELLE CONCENTRATION | 0.006% w/w at 37°C (in water) (VitiPure™ L 20) / 0.002% w/w at (in water) (VitiPure™ O 80) |
| ▪ SOLUBILITY | It is readily soluble in water and alcohols, it is insoluble in oils. |

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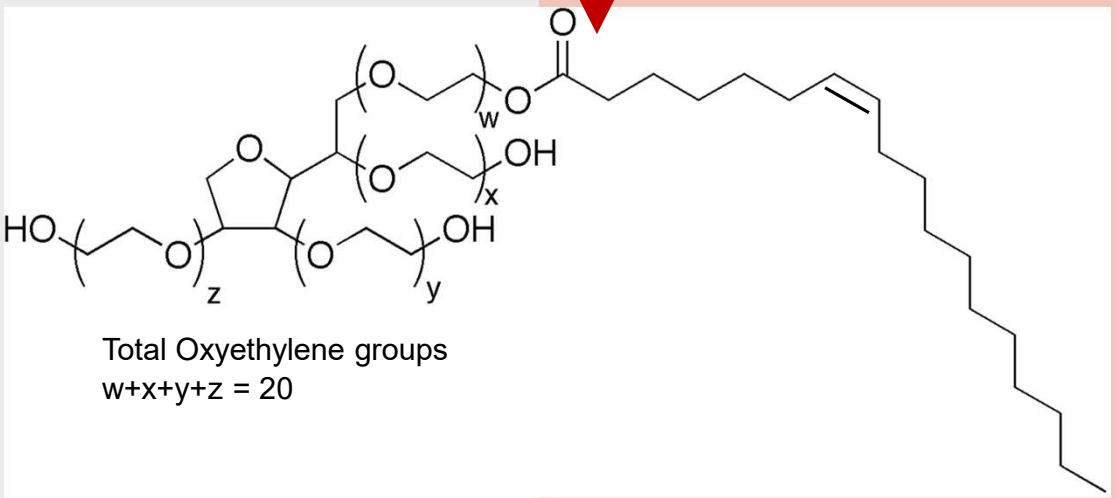
# VitiPure™ L 20 / O 80 – Chemistry structure

## Hydrophilic

## Hydrophobic

Monolaurate (VitiPure™ L 20) /
Monooleate (VitiPure™ O 80)

polyoxyethylene
(20) sorbitan




Total Oxyethylene groups
w+x+y+z = 20

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# VitiPure™ L 20 / O 80

## DOSAGE & APPLICATIONS

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# FDA Published Applications For Polysorbate 20
## Dosage and Applications*

- **Auricular (OTIC)**
  Upto. 0.1% w/v

- **Ophthalmics****
  Upto. 0.05 % w/v

- **Tablets/ Capsules**
  Upto. 4.2 mg

- **Creams**
  Upto. 7.8% w/w

- **Injection****
  IM Upto. 18mg
  IV upto 1%w/v

- **Suppository**
  upto. 64.8mg

- **Nasal**
  upto. 27mg

*Published in Inactive Ingredients Database by FDA
**Parenteral grade is required

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# FDA Published Applications For Polysorbate 80
## Dosage and Applications*

- **Auricular (OTIC)**
  Upto. 2.5% w/w

- **Ophthalmics**
  Upto. 4% w/w

- **Tablets/Capsules**
  Upto. 418.37mg

- **Creams**
  Upto. 15% w/w

- **Injection****
  IA Upto. 5mg
  IB Upto 0.04%w/v
  IL Upto 0.19%w/v
  IM Upto 5%
  IS Upto 2%
  IV Upto 69.33% w/v
  IV Upto 0.02% w/v
  SC Upto 0.3% w/v

- **Nasal**
  upto. 0.02%w/v

- **Suppository**
  upto. 72.15mg

- **Oral Solutions**
  Upto. 126mg/1ml

*Published in Inactive Ingredients Database by FDA
IA: Intra-articular; IB: Intrabursal; IL: Intralesional; IM: Intramuscular; IS: Intrasynovial; IV: Intravenous; IV:Intravitreal; SC: Subcutaneous
** Pareteral grade is required

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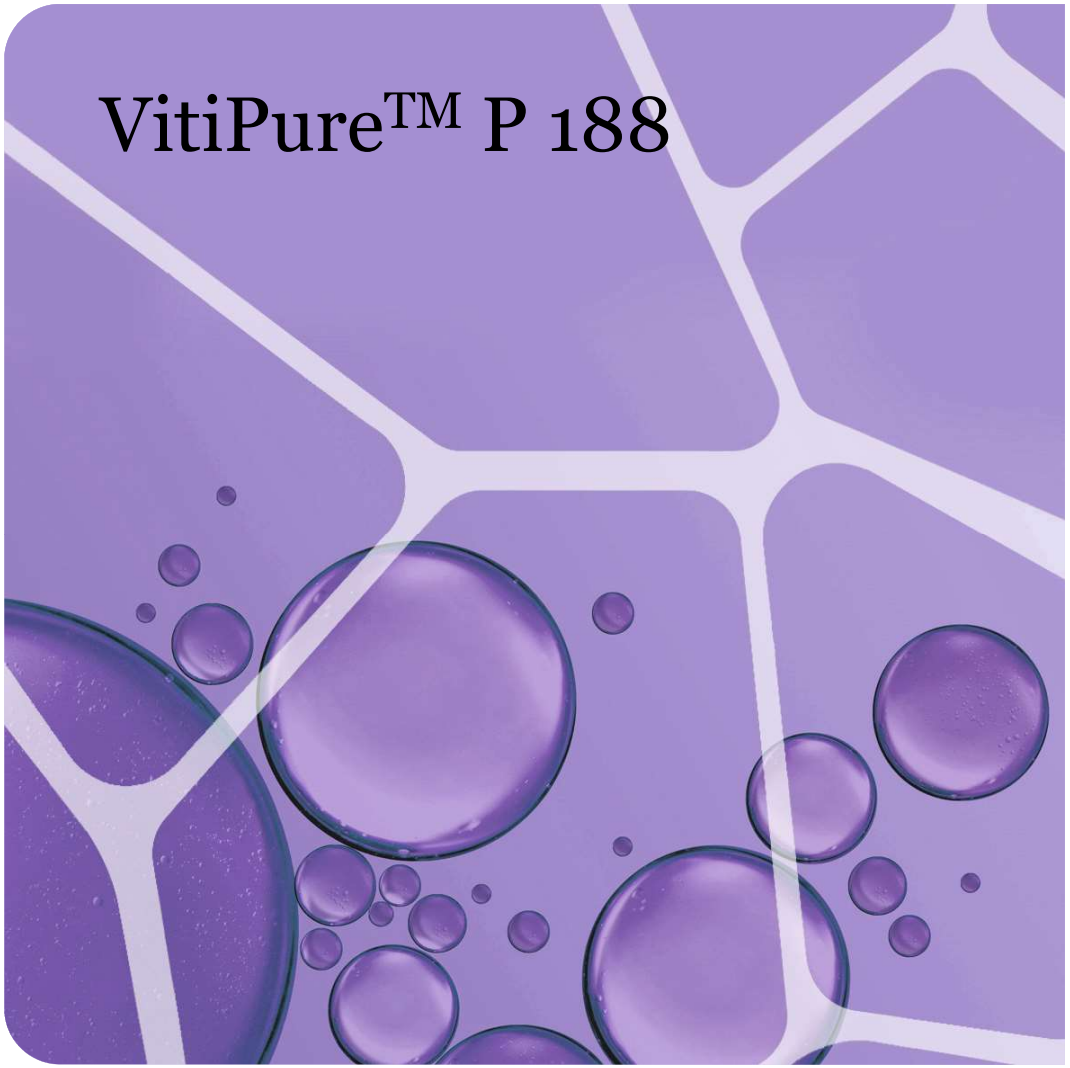
# VitiPure™ L 20 / VitiPure™ O 80 – Typical Applications

## VitiPure™ L 20 / O 80

- Solubilizer Emulsifier
- Skin Penetration enhancer
- Solubilizer in solid dispersion
- Suspension stabilizer

# VitiPure™ P 188



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# VitiPure™ P 188 – Description

- GENERIC NAMES: Poloxamer *(USP)*<br>Poloxamers *(Ph. Eur.)*
- TYPE: Non-ionic surfactant
- CAS NO.: 9003-11-6
- SAFETY: World-wide several registered Pharmaceutical OTC and prescription medicines<br>Listed in the inactive ingredient database of the FDA
- GMP: IPEC
- RETEST PERIOD: 2 years
- PACKAGING SIZES*: 100kg Plastic drums (with PE bag in-liner) and 25kg Plastic drums (with PE bag in-liner)<br>Sample size 0.5kg

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# VitiPure™ P 188 – Properties

- HLB VALUE 29
- PHYSICAL PROPERTIES Waxy Powder (Flakes)
- CRITICAL MICELLE CONCENTRATION 0.07% w/w at 37°C (in water)
- SOLUBILITY Readily soluble in water, Polar and non-polar solvents

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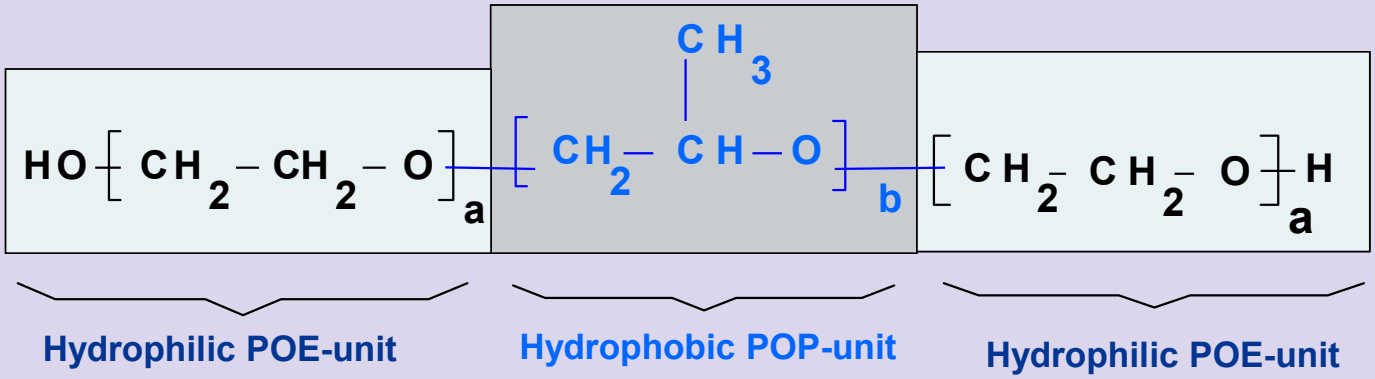
# VitiPure™ P 188 – Composition

- Poloxamers are synthetic copolymers of polyoxyethylene (POE) and polyoxypropylene (POP) units
- Chemical composition: A – B – A triblock-polymer

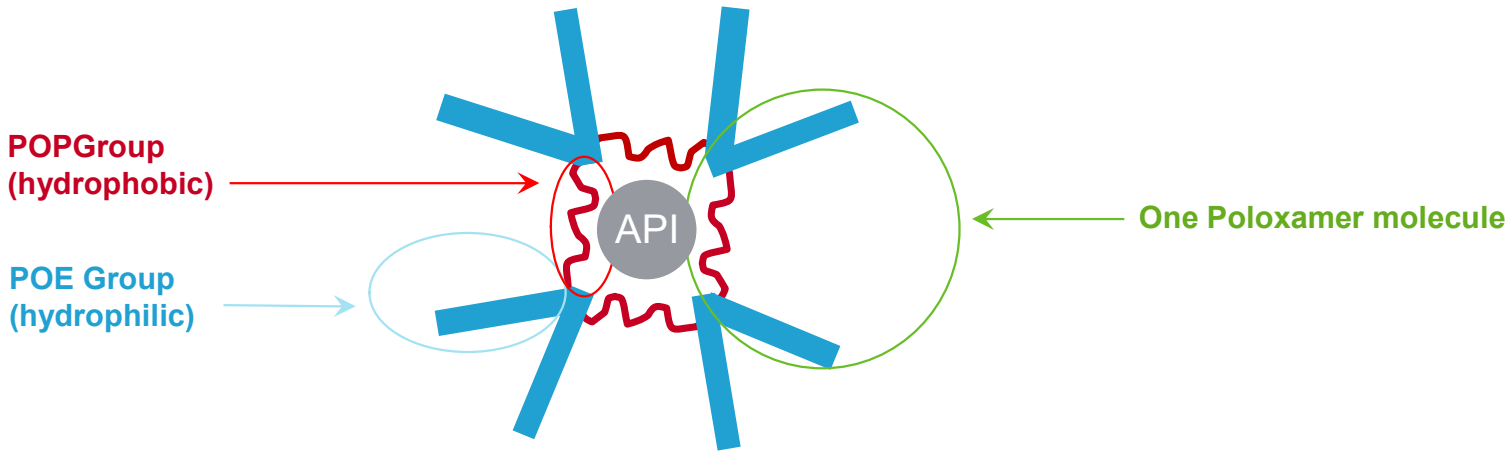



Poloxamer 188 a = ca. 79 b = ca. 28

| **Poloxamer** | **$M_W$ POP – part** [g/mol] | **POE – part** [% (m/m)] |
|---|---|---|
| Poloxamer **18** **8** | **18** x 100 = 1,800 | **8** x 10 = 80 |

CLARIANT

# Mechanism of Complexation of Poloxamers

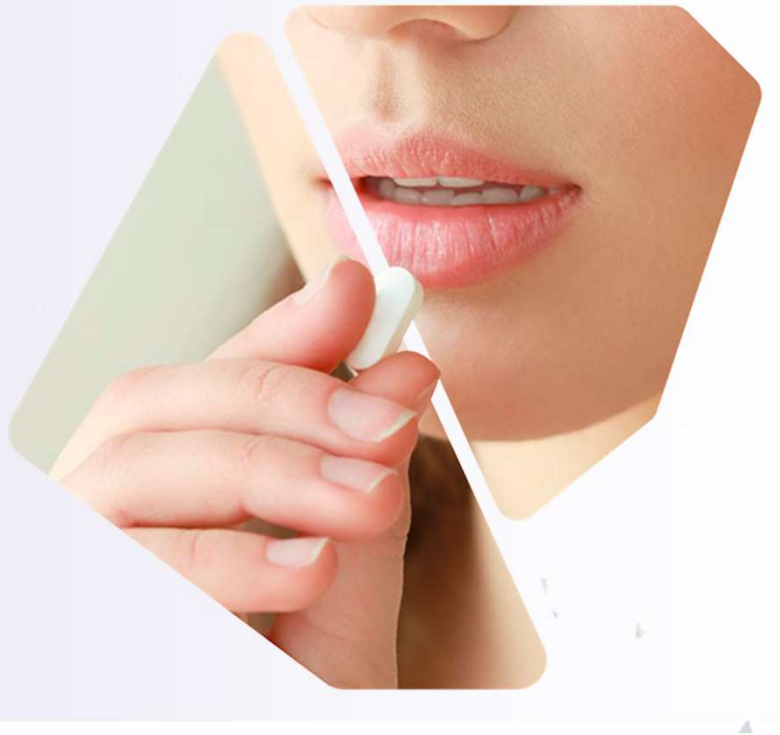



- Micelles are composed of a compact core of „insoluble“ POP blocks and a highly swollen shell of „soluble“ POE blocks.
- Micelles have spherical shape.
- Inner core radius and solubilization capacity of a specific poloxamer is dictated by the length of the POP – part of the poloxamer.

CLARIANT

# VitiPure™ P 188

## DOSAGE & APPLICATIONS



CLARIANT

# FDA Published Applications For Poloxamer 188
## Dosage and Applications*

- **Oral Solutions**
  upto 100mg/1ml

- **Ophthalmics**
  upto 0.1% w/v

- **Tablets/Capsules**
  upto 66.9 mg

- **Creams**
  upto 1% w/w

- **Injection****
  IM: 0.2% w/v
  IV: 6mg

- **Periodontal Gel**
  upto 55mg

*Published in Inactive Ingredients Database by FDA per unit dose
**Parenteral grade is required

CLARIANT

# VitiPure™ P 188 – Typical Applications

## VitiPure® P 188

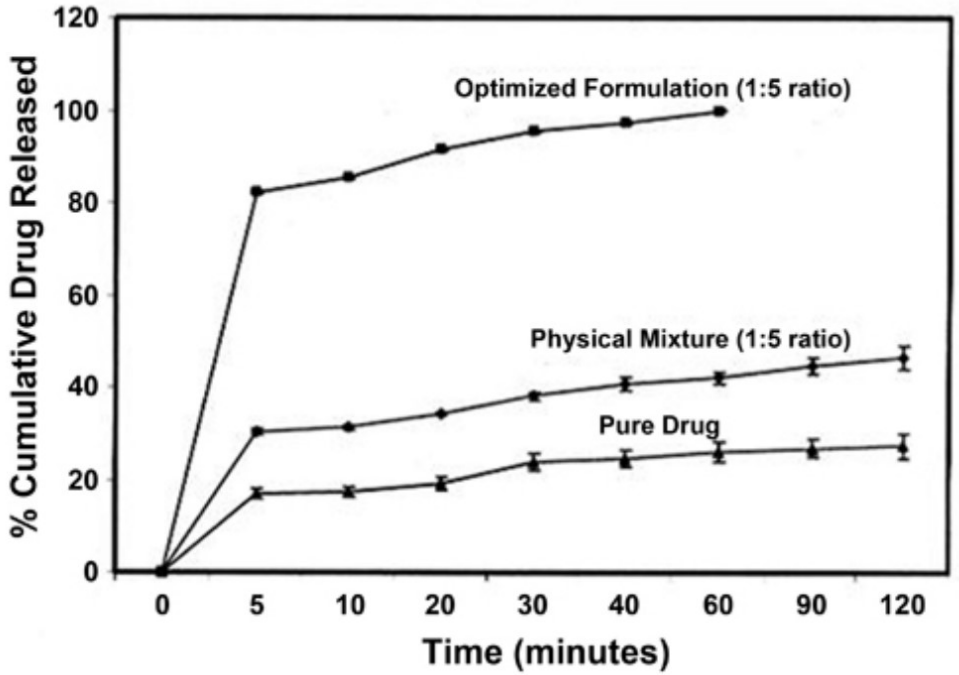
- Suspension Stabilizer
- Solubilizer Wetting Agent
- Melt / Spray Granulation
- Gel Former
- Plasticizer or Matrix Polymer in Hot Melt Extrusion

CLARIANT

# VitiPure™ P 188 – Improvement of API dissolution

Dissolution profiles of different formulations of Rofecoxib and Poloxamer 188

Optimized formulation:
solid dispersion (melt granulation)

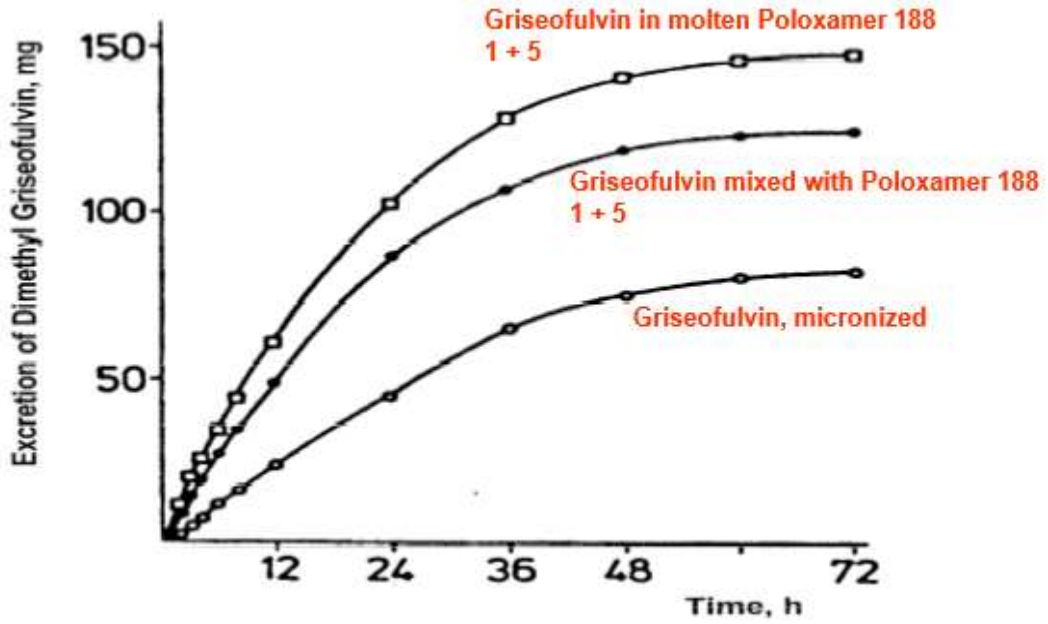



Shah et al., AAPS Pharm. Sci. Tech., Vol 8, No.2, 2007

CLARIANT

# VitiPure™ P 188 – Improvement of API dissolution

Influence of Poloxamer 188 on the bioavailability in humans of orally administered Griseofulvin (250 mg)




Heyer and Frömming, DAZ, Vol 123, No.18, 1983

CLARIANT

# VitiPure™ P 188 – Key Benefits

- Multi-talent solubilizer for variety of applications
- Safety & toxicology well established via several marketed drugs world-wide into human and veterinary medicines and nutrition.
- Suitable in solid dispersions and improves the solubility, absorption and bioavailability of low-solubility APIs in solid oral dosage forms.

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# Glossary

CLARIANT

# Glossary

*** BCS Classes:** The Biopharmaceutics Classification System is a system to differentiate the drugs on the basis of their solubility in water and intestinal permeability. This classification is limited to oral administered drugs.

**Class I - high permeability, high solubility**

Example: paracetamol. Those compounds are well absorbed and their absorption rate is usually higher than excretion.

**Class II - high permeability, low solubility**

Example: glibenclamide, bicalutamide, ezetimibe, aceclofenac.

The bioavailability of those products is limited by their solvation rate.

**Class III - low permeability, high solubility**

Example: cimetidine. The absorption is limited by the permeation rate but the drug is solvated very fast.

**Class IV - low permeability, low solubility**

Example: Bifonazole. Those compounds have a poor bioavailability. Usually they are not well absorbed over the intestinal mucosa and a high variability is expected.

CLARIANT

# Glossary

*** Bioavailability:**

Describes the fraction of an administered dose of a pre-metabolized drug that reaches the systemic circulation; one of the principal drug pharmacokinetic properties. A drug is bioavailable if the pharmaceutical form releases the API to the body in a time limit.

In the case of tablet forms, e.g, => bioavailability includes but is not limited to:

- tablet disintegration (cleavage)
- dissolution of API in the medium (solubilization),
- body absorption, linked to API permeation.

If there is no cleavage and/or no solubilization => no body absorption…

CLARIANT

# Glossary

* **Solubilization:** action of splitting in a liquid a substance into its molecular state; the result called solution is a homogenous single phase.

* **Solubility** is a physical property referring to the ability for a given substance, the solute, to dissolve in a solvent. It is measured in terms of the maximum amount of solute dissolved in a solvent at equilibrium. The resulting solution is called a saturated solution. Certain substances are soluble in all proportions with a given solvent, such as ethanol in water. This property is known as miscibility.

* **Poorly soluble drugs:** <1 mg/ml.

* **Dispersion:** action of splitting an insoluble substance into small particles in a liquid. This leads to a biphasic preparation. Some examples are: emulsions, suspensions, foam…

CLARIANT

# Glossary

*** SEDDS:** Self-emulsifying drug delivery systems (SEDDS), which are isotropic mixtures of oils, surfactants, solvents and co-solvents/surfactants, can be used for the design of formulations in order to improve the oral absorption of highly lipophilic drug compounds.

In order to effectively make such formulations, high concentrations of surfactant, oil and aqueous phase are mixed. The resultant formulations are clear, low-viscosity, isotropic and suitable for encapsulation into softgels, hard shell capsules and other liquid formulations.

Once the formulations are released inside the GIT, they emulsify into nanoscale (15 – 80 nm) droplets, which are further digested and absorbed, significantly increasing bioavailability.

CLARIANT

# Glossary

* **NCE:** New Chemical entity. It is new drug (Active pharmaceutical ingredient) which do not have market presence and is not registered.

* **SMEDDS**: A self-microemulsifying drug delivery system (SMEDDS) is a drug delivery system that uses a microemulsion achieved by chemical rather than mechanical means. SMEDDS are of particular value in increasing the absorption of lipophilic drugs taken by mouth.

* **MDE:** Maximum Daily Exposure (MDE) is the total amount of the excipient that would be taken or used in a day based on the maximum daily dose (MDD) of the drug product in which it is used. MDE is calculated as the dosage unit level of the excipient multiplied by the maximum number of dosage units recommended per day (excipient (mg) x number units). MDE may also be referred to as maximum daily intake (MDI) for oral drug products.