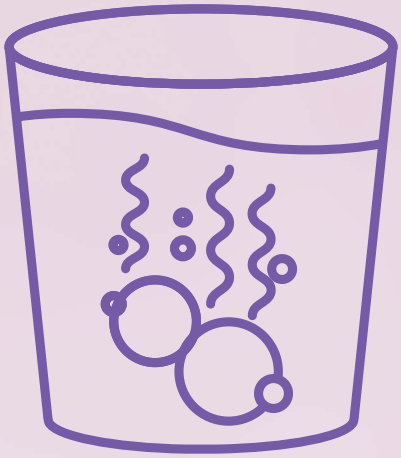
DELIVERING CONFIDENCE WITH THE RIGHT PARTNER



SOLUBILITY IMPROVEMENT SOLUTIONS

ROQUETTE
Offering the best of nature™

AN UNWAVERING COMMITMENT TO ENABLING
LIFE-SAVING PHARMACEUTICALS

Don’t let poor bioavailability hold you back. Advance your oral dosage forms with our versatile solubilizing solutions.

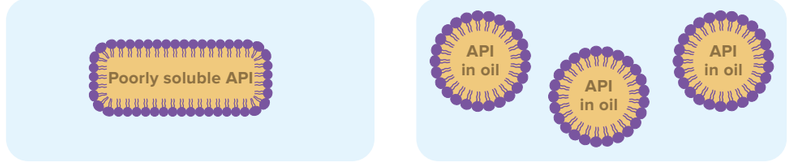
For several decades, formulators have trusted us to help them efficiently overcome the challenge of API insolubility. The consistency of their formulations’ performance is why they do. Roquette offers versatile solubility enhancers that adapt to the demands of your formulations’ characteristics.

Engineered to deliver functional reliability, our solutions deliver repeatable dissolution profiles batch after batch. It’s a quality our customers have come to expect. No matter the drug characteristics or process strategy, we provide a range of products suited to enhance API solubility in your oral dosage forms.

Overcoming Insolubility

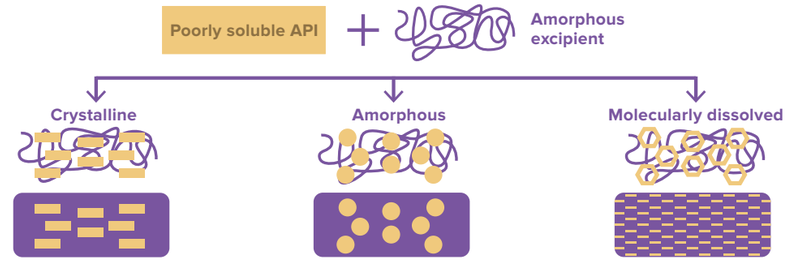
EMULSION/WETTING

The use of surfactants, known as emulsifying or wetting agents, can alleviate solubility issues by either speeding up dissolution via the molecule’s hydrophobicity or promoting stable lipidic formulations. This mechanism provides protection against drug precipitation in the gastrointestinal tract and ensures delivery by solubilizing the API in oil.



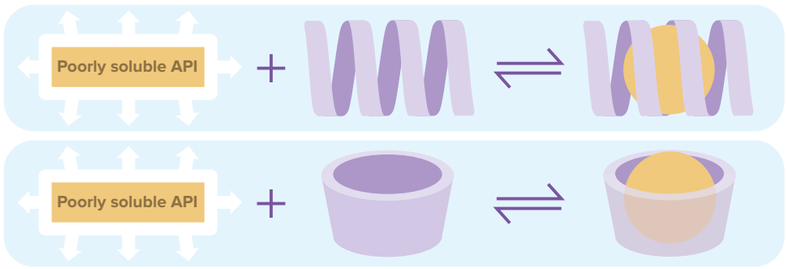
SOLID DISPERSION

The physical state of the dispersion of poorly soluble drugs in an excipient matrix can vary (see the different types below) depending on the API, the excipient, their degree of interaction and the process of obtention of this solid dispersion. Reducing particle size, preventing agglomeration or stabilizing API in an amorphous state will deliver solubility improvement.



ENCAPSULATION/COMPLEXATION

This mechanism involves a reversible, affinity-based complexation of the guest (API) in the host molecule. The bonds created at the molecular level are strong enough to provide the stability your formulation needs, while still able to release the drug. When formed, the complex will ultimately undergo solid dispersion.



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	KLEPTOSE® range	KLEPTOSE® HPB and HP range	KLEPTOSE® Linecaps	CLEARGUM® CO range
Composition	Betacyclodextrin	Hydroxypropyl betacyclodextrin	Pea maltodextrin	Octenyl succinate starch
Main mechanism	Molecular encapsulation	Molecular encapsulation	Molecular encapsulation	Surfactant/emulsifier or matrix (solid dispersion*)
Moisture content	4% to 10%	5%	5%	5%
Solubility	1.85%	>50% (viscosity is a limiting factor)	>50% (viscosity is a limiting factor)	>50% (viscosity is a limiting factor)
Recommended application	Pharmaceutical, Nutraceutical	Pharmaceutical	Pharmaceutical, Nutraceutical	Pharmaceutical, Nutraceutical
Regulatory	EP, USP**	EP, USP**	EP, USP**	USP**

*Solid dispersion can also be obtained with less specific ingredients such as our polyols and polymer range.
**Compliance to other Pharmacopeias available upon request depending on product grade.

The encapsulation process with KLEPTOSE, KLEPTOSE HPB, KLEPTOSE HP and KLEPTOSE Linecaps allows for any of the different strategies of solubilization improvement including jet or ball milling, spray drying, extrusion, lyophilization, and in a few cases simple blending.

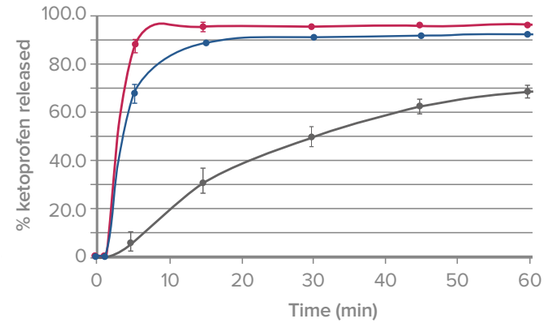
KLEPTOSE® AND KLEPTOSE® HPB AND HP RANGE

The rigid truncated cone shape of the KLEPTOSE structure decreases the interaction between hydrophobic parts of the API and surrounding aqueous environment (as shown in the bottom of the third mechanism on page 2).

KLEPTOSE (native betacyclodextrin) grades are mainly recommended for solid dosage forms due to their low aqueous solubility. A variety of grades are available based on particle size, water content and compactibility.

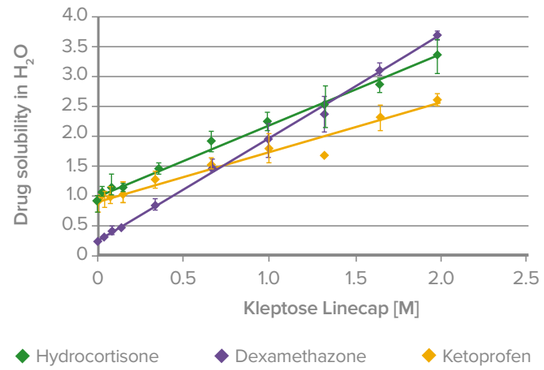
Due to their high solubility, KLEPTOSE HPB and HP (hydroxypropyl betacyclodextrin) grades are specifically equipped to handle liquid dosage forms or any form requiring complete solubilization.

The graph on the right shows solubilization via HPBCD addition is independent of the presence of water. KLEPTOSE facilitates process flexibility, allowing for adjustments based on the sensitivity of your API.



A. Colin, et al. Precellys(R)-24 as a useful screening tool in preformulation for evaluation of cyclodextrin complexation with small quantities of poorly water-soluble pharmaceutical compound. Poster presented at: AAPS Annual Meeting; 2012 Oct 14-18; Chicago, IL.

KLEPTOSE® LINECAPS



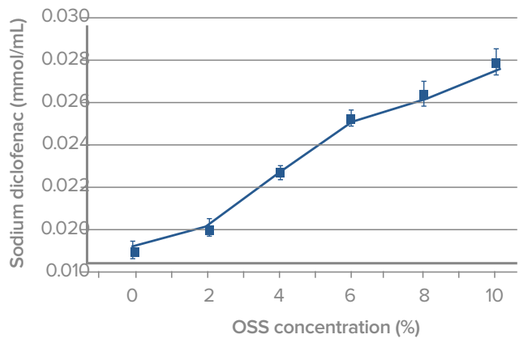
With a helicoidal structure, KLEPTOSE Linecaps (pea maltodextrin) offers encapsulation similar to betacyclodextrin. Compared to cyclodextrin, the helix structure is flexible and less sensitive to steric factor (as shown in the top of the third mechanism on page 2). Thus, KLEPTOSE Linecaps has the potential to encapsulate a larger population of molecules. Without recommendation of daily intake, this special maltodextrin is the obvious option to address even the most sensitive patient population like pediatrics.

CLEARGUM® CO RANGE

We offer the CLEARGUM CO (octenyl succinate starch) range, which are amphiphilic polymers providing multiple functions:

- Decreases surface tension for the stability of your emulsions (liquid or solid)
- Increases wettability of your API and speed of dissolution
- Improves directly API solubility in water via its stabilization

Saturation concentrations for sodium diclofenac depending on octenyl succinate starch concentration



L. Baydoun, C.C. Mueller-Goymann. Proceed. 3rd World Meeting on Pharmaceutics, Biopharmaceutics, Pharmaceutical Technology, APGI/APV, Berlin, 3-6. April, 2000, p. 801-802. Amphiphilic starch as a new excipient for pharmaceutical applications (abstract).

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KLEPTOSE® RANGE

	KLEPTOSE® 10	KLEPTOSE® 200 F	KLEPTOSE®	KLEPTOSE® 7%	KLEPTOSE® 4%	KLEPTOSE® DC
Product description	Beta-cyclodextrin	Beta-cyclodextrin	Beta-cyclodextrin	Beta-cyclodextrin	Beta-cyclodextrin	Beta-cyclodextrin
Particle size (µm) Mouth feel/suspension	10	Approx. 80	Approx. 110	Approx. 80	Approx. 80	Approx. 80
Moisture content Moisture sensitive API	10%	10%	10%	7%	4%	12%
Solubility Dosage form / mouth feel	1.85%	1.85%	1.85%	1.85%	1.85%	1.85%
Tabletability	–	+	+	–	–	+++

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KLEPTOSE® HPB & HP

	KLEPTOSE® HPB ORAL GRADE	KLEPTOSE® HP ORAL GRADE
Product description	Hydroxypropyl Beta-cyclodextrin	
Hydroxypropylation (DS) Affinity / encapsulation	0.62	0.9
Residual BCD Stability	0.60%	0.10%
Moisture content Moisture sensitive API	5%	5%
Solubility Dosage form / mouth feel	>50% (viscosity is a limiting factor)	>50% (viscosity is a limiting factor)

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CLEARGUM® CO RANGE

	CLEARGUM® CO A1	CLEARGUM® CO 01	CLEARGUM® CO 03
Product description	Octenyl Succinate Starch		
Viscosity Process requirements (spray drying)	Low	Medium	Low
Cold water solubility Solid /liquid	>98%	100%	100%
Oragnoleptic properties	+	+++	+++

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LEARN MORE ABOUT ROQUETTE SOLUBILITY PRODUCTS AT

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