BRINGING NEW SOLUTIONS FOR BIOTHERAPEUTICS

BIOPHARMA

ROQUETTE

Offering the best of nature™

AN UNWAVERING COMMITMENT TO ENABLING
LIFE-SAVING PHARMACEUTICALS

Rely on Roquette's bio**logical** solutions to resolve protein stability challenges impacting your drug product development.

For biopharmaceutical formulators, the complexity and natural propensity of proteins to aggregate pose a real challenge at every stage of development. As a pioneer in the industrial development of hydroxypropyl-β-cyclodextrin and polyols, Roquette provides stabilization solutions for your biologic drug development.

Roquette offers more than just reliable material performance. Our products are contaminant-free excipients, produced in a state-of-the-art manufacturing plant (US FDA and ICH Q7 GMP compliant). Our BioPharma product portfolio is anchored by technical expertise, enabling Roquette to stand out as a premier partner in applications related to improving the stability of therapeutic proteins.

OUR LEGACY

Technical expertise is empowered by our diverse global Research and Development network.

For years, Roquette has been the market and technical leader in starches and polyols, with over 60 patents and new product launches. Now we are expanding to other excipient chemistries to provide unique solutions to the technical challenges you face.

OUR MISSION

Provide technical expertise to all stages of pharmaceutical development

Instill in our customers a sense of confidence by delivering world-class ingredients and raw materials

Remain consistent in our ability to help customers develop and elevate life-saving pharmaceuticals

UNCOMPROMISED EXPERTISE

For decades, we've been providing technical expertise supported by our signature lab in Lestrem, France. To complement our expertise in biologics formulation, in 2017 we inaugurated Roquette's Global BioPharma Center of Excellence (a 1,100 square meter state-of-the-art facility), located in Singapore.

ENDURING QUALITY

Roquette quality systems are of the highest standards. All Biopharma products for dowstream processing are manufactured under ICHQ7 and packaged under cGMP guidelines. The main manufacturing facility in Lestrem, France, also follows IPEC guidelines, ISO 9001, and offers EXCiPACT certification.

SUSTAINABLE SUPPLIER

By encouraging local supply, using geothermal energy sources, and optimizing means of transportation, we combine economic profitability with a low environmental footprint.

INSPIRED INNOVATION

Our global R&D team and pharmaceutical application experts understand the challenges you face and can readily meet your evolving needs for innovative downstream processing solutions.

The Delicate Balance of Protein Stability

Stabilizing proteins in their functional conformation is a critical challenge facing all biotherapeutic formulators. Throughout the manufacturing and storage process, protein stability is affected by multiple stress factors, including:

- temperature changes
- shearing
- shaking
- ionic strength
- impurities
- protein concentration
- solvent interaction
- presence of metal ions and additives
- morphism
- freezing/thawing

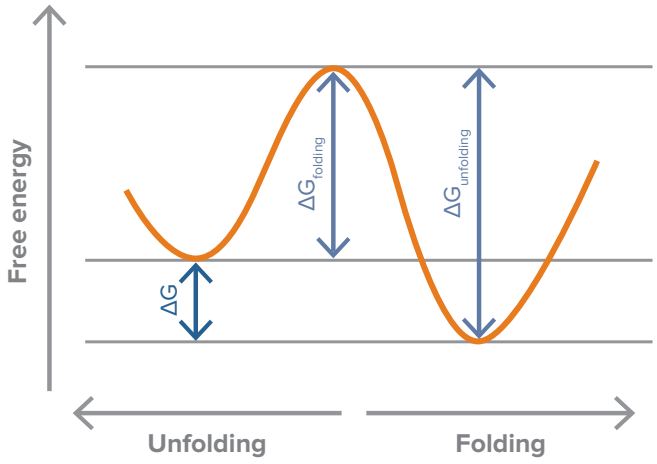
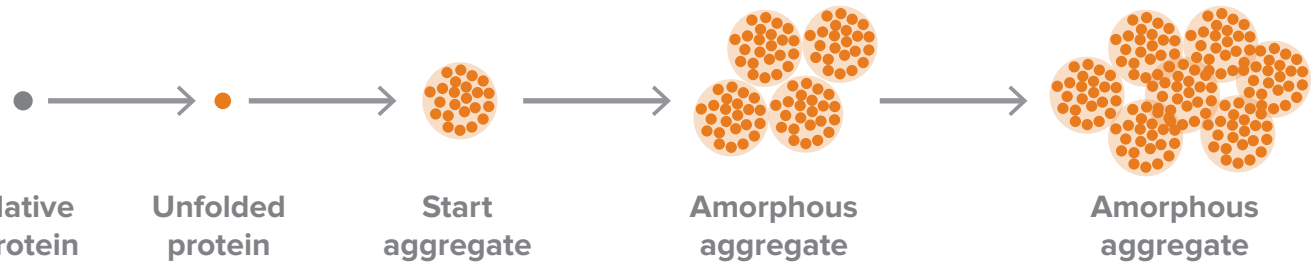


Figure 1: Protein folding/unfolding
The difference in Gibbs free energy (ΔG) between proteins' native conformation and denatured state is small.

STRESS & PROTEIN AGGREGATION



When subject to the stresses mentioned above, without protective excipients, proteins are easily susceptible to physical degradation events leading to unfolding and aggregation. Protein aggregates reduce therapeutic efficacy, and can potentially induce unwanted immunogenicity, causing harm to patients.

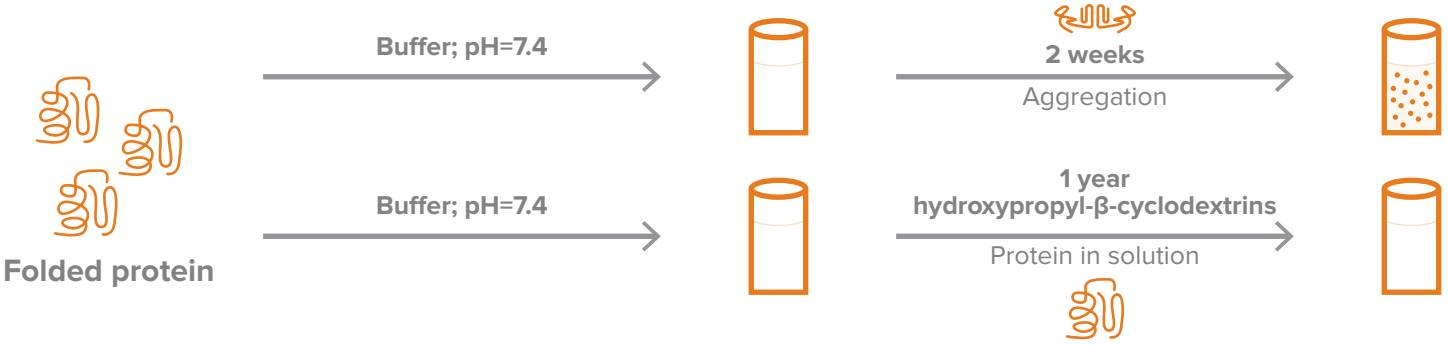
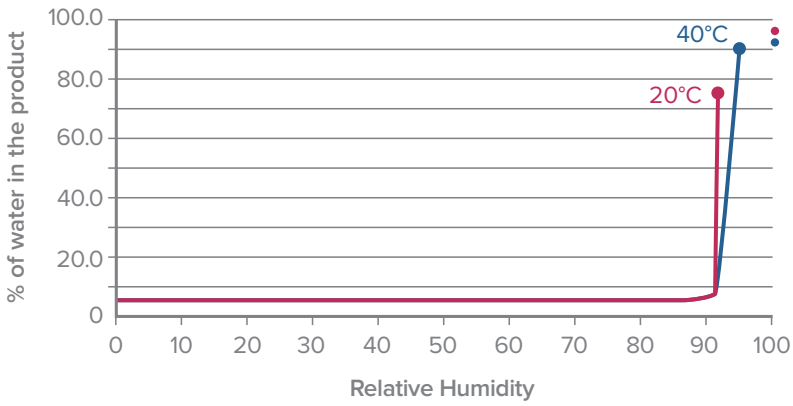


Figure 2: Stabilizing agents protect against protein aggregation[1]
Without protective stabilizing agents such as our polyols and hydroxypropyl-β-cyclodextrins, manufacturing and storage stress can lead to protein unfolding, and drive aggregation.

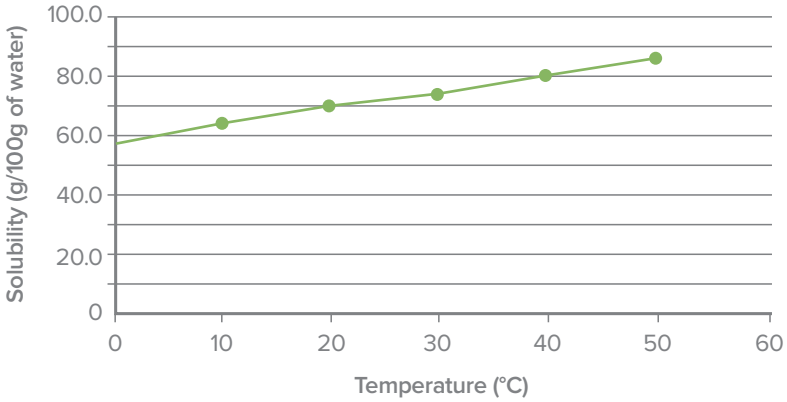
Polyol Stabilizers for Biopharmaceuticals

PEARLITOL® BIOPHARMA mannitol

Used as an excipient in over 50 commercial mAbs, protein therapeutics, and vaccines, mannitol is a proven formulation aid for biopharmaceuticals. Known for its inertness and low hygroscopicity, mannitol provides stability against humidity (see graph to the right), a particularly valuable property for freeze-dried powders. Available in a low-endotoxin level, multi-compendial grade, our PEARLITOL® BioPharma mannitol is suitable for use in biopharmaceutical development.



NEOSORB® BIOPHARMA sorbitol



Used as an excipient in over 35 commercial mAbs, therapeutic proteins, and vaccines, sorbitol is a proven formulation aid for biopharmaceuticals, known for its high water solubility (see graph on left). Available in a low-endotoxin level, multi-compendial grade, our NEOSORB® BioPharma sorbitol is suitable for use in biopharmaceutical development.

KLEPTOSE for Biopharmaceuticals

KLEPTOSE® BIOPHARMA hydroxypropyl-β-cyclodextrin†

With a hydrophobic internal cavity and hydrophilic exterior, hydroxypropyl-β-cyclodextrins exhibit the unique ability to encapsulate and shield water insoluble materials. This property can be utilized to shield exposed hydrophobic residues on aggregation-prone proteins, thereby modulating protein aggregation. Widely used as an excipient in small molecule formulations and approved for use in injectable solutions, highly soluble hydroxypropyl-β-cyclodextrins derivatives like Roquette's KLEPTOSE® HPB and HP grades show promise as multifunctional excipients suitable for biopharmaceutical applications.

The KLEPTOSE® HPB Biopharma and KLEPTOSE® HP BioPharma grades are produced in a state-of-the-art manufacturing plant conforming to US FDA and ICH Q7 GMP quality guidelines, and are suitable for use in biopharmaceutical and injectable formulations.

		KLEPTOSE® HPB	KLEPTOSE® HP
Pharmacopeia compliance		USP, Ph. Eur.	USP, Ph. Eur.
Molar degree of substitution (MS)		0.62	0.90
Molecular weight (g/mol)		~ 1390	~ 1500
Level of bacterial endotoxins		NMT 5 IU/g	NMT 5 IU/g
Solubility in water at 20°C (w/w%)		> 50 %	> 50 %
Osmolality in water at 20°C (mOsm/kg)	10 w/w%	75	70
	20 w/w%	157	163
Viscosity in water at 20°C (mPa.s)	10 w/w%	3.5	3.5
	20 w/w%	4.5	4.6

†Certain uses of this product may be covered by U.S. Patent No. 6,407,079. Such uses, if not exempt from infringement under 35 U.S.C. 271(e)(1), may require a license.

KLEPTOSE® BIOPHARMA CASE STUDY

Using a high-throughput formulation screening method (iFormulate™) paired with nanoDSF (Differential Scanning Fluorimetry), we investigated the stabilizing effects of KLEPTOSE® HPB and HP on the thermal stability of the human growth hormone (hGH) and the monoclonal antibody (mAb) Infliximab.

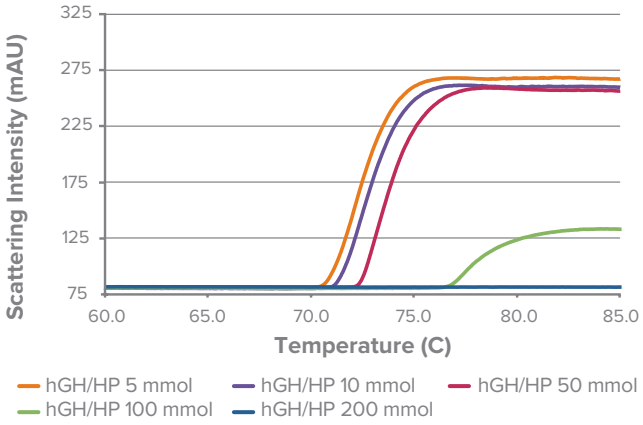


Figure 2: KLEPTOSE HP inhibits hGH aggregation
With increasing concentration of HP, we observed a positive shift in onset of aggregation (higher T_{agg}), and a decrease in relative amount of aggregation. Similar effect was observed with HPB.

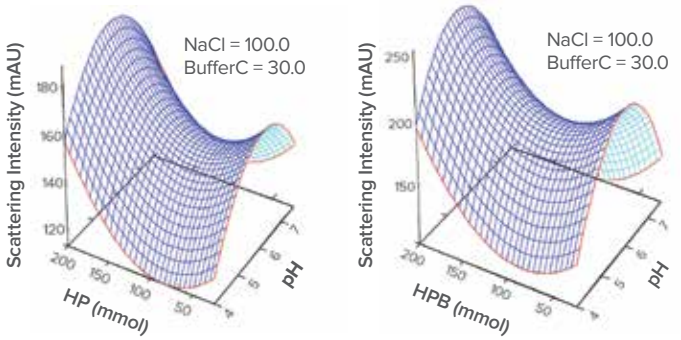
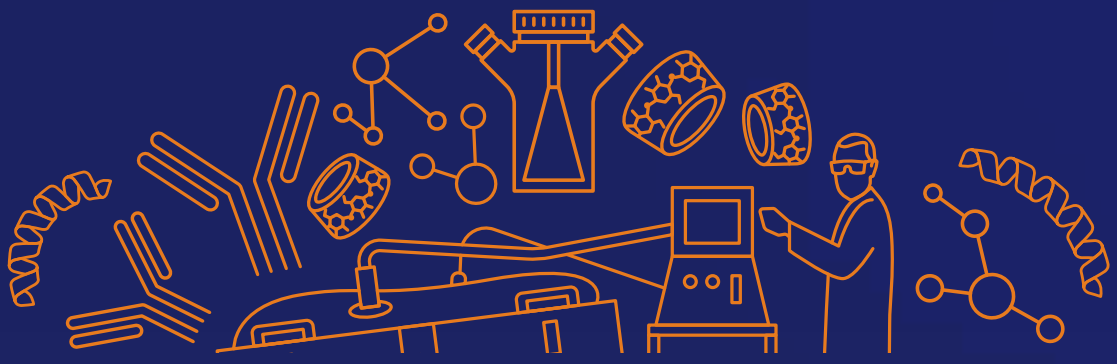


Figure 3: Effects of HP (left) and HPB (right) on Infliximab stability
Similar effects observed with KLEPTOSE HP and HPB as both reduced protein aggregation propensity at low and high pH.

The iFormulate™ Design of Experiment (DOE) approach provided a rapid evaluation of four critical formulation variables: pH, ionic strength, buffer concentration, and stabilizer concentration. Simultaneous evaluation of T_m (melting temperature) and relative degree of aggregation was performed. Our DOE-based study results demonstrate that both hydroxypropyl-β-cyclodextrins are efficient aggregation modulators (see Figures 2 and 3).

PROTEIN STABILIZATION SOLUTIONS

Product	Description	Package Size	Product Code
KLEPTOSE® HPB BioPharma	Hydroxypropylbetadex, low endotoxin, USP, EP Suitable for use in biopharmaceutical manufacturing and as an excipient for injectable dosage forms MS nominal value: 0.62	1 kg	346113101A
		10 kg	346113102B
		25 kg	346113103C
KLEPTOSE® HP BioPharma	Hydroxypropylbetadex, low endotoxin, USP, EP Suitable for use in biopharmaceutical manufacturing and as an excipient for injectable dosage forms MS nominal value: 0.90	1 kg	346105101Z
		10 kg	346105102A
		25 kg	346105103B
PEARLITOL® BioPharma	Mannitol, low endotoxin, USP, EP, JP. Suitable for use in biopharmaceutical manufacturing and as an excipient for injectable dosage forms	12 kg	450003103X
		25 kg	450003104Y
		50 kg	450003105Z
NEOSORB® BioPharma	Sorbitol, low endotoxin, USP, EP, JP. Suitable for use in biopharmaceutical manufacturing and as an excipient for injectable dosage forms	12 kg	423127103N
		25 kg	423127104P
		50 kg	423127105R



LEARN MORE ABOUT ROQUETTE BIOPHARMA

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[1] M.E. Brewster, et al. *Pharmaceutical Research*, Vol. 8, No. 6, 1991.

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