



DELIVERING SECURE SUPPLY WITH THE RIGHT PARTNER

CASE STUDY | BIOPHARMA

KLEPTOSE® BIOPHARMA as a potential functional alternative to surfactants within biologic formulations

CHALLENGE

Therapeutic proteins are inherently unstable and are sensitive to temperature change, shearing, shaking, solvents, ionic strength, purity, protein concentration, pressure and freeze/thaw-drying cycles. Of all the various degradation pathways possible, aggregation is one of the most common and a cause for great concern. Formulation is a key component that is required in order to produce a stable and efficacious biologic medicine.

Many excipients are used within biologic drug formulations, including a range of surfactants called polysorbates. As a potential functional alternative to surfactants within biologic formulations, KLEPTOSE® can act as an inhibitor of protein aggregation in liquid formulations by:

- ◆ Shielding hydrophobic interactions to block potential protein-protein interaction which causes aggregation
- ◆ Displacing proteins induced by air-water interface

EXPERIMENT

Objective: To benchmark KLEPTOSE® HP/HPB against polysorbates in commercial mAb formulations

Experiments used two techniques - NanoDSF and SEC-HPLC

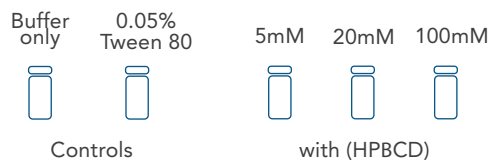


Model proteins: Immunoglobulin G (IgG) is the most abundant immunoglobulin in plasma.



Bevacizumab is a recombinant humanized monoclonal antibody (IgG1) used to treat a number of types of cancers.

Human plasma IgG:



Bevacizumab:



* CF = Commercial Formulation



1) NanoDSF

- ◆ Aggregation onset temperature
- ◆ Relative amount of aggregation

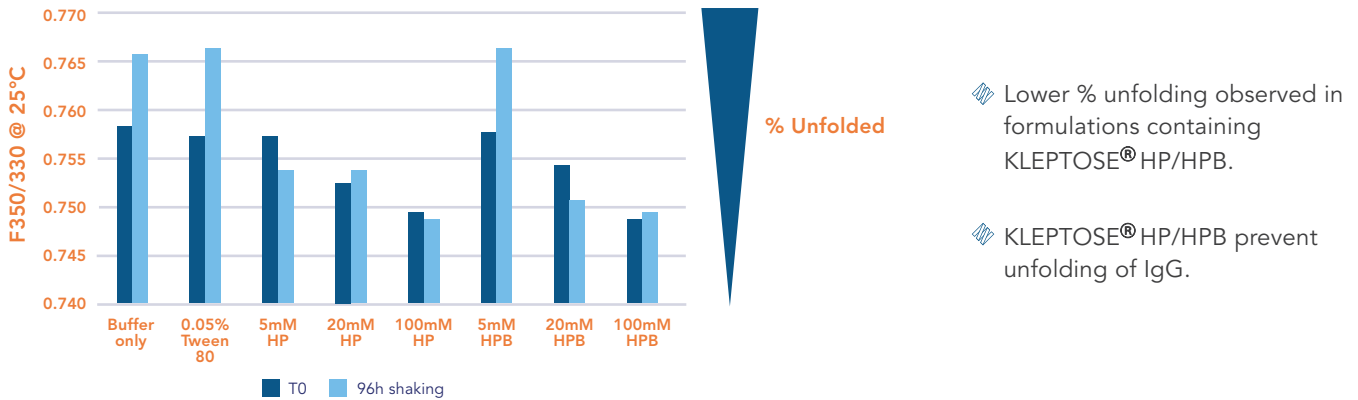


2) SEC-HPLC

- ◆ % soluble monomers, aggregates & fragments

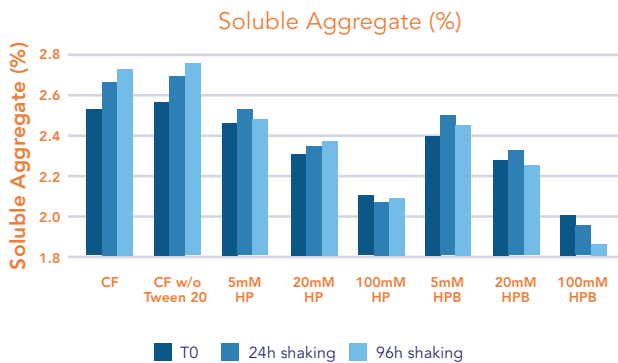
RESULTS NanoDSF results for IgG protein

Effect of agitation stress on Protein Unfolding

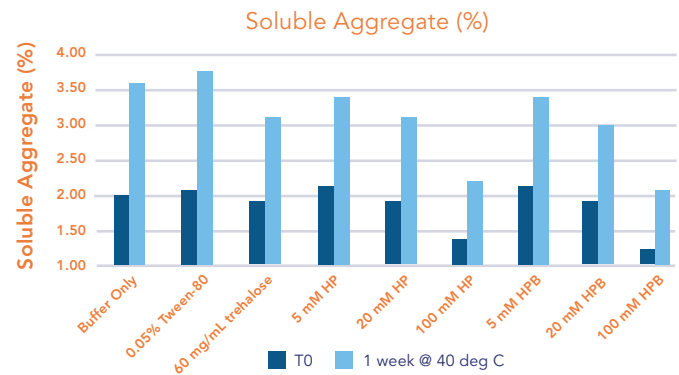


SEC-HPLC results for Bevacizumab

Agitation-Induced Aggregation



Heat-Induced Aggregation



- ❖ The rate of aggregation was lower in formulations containing KLEPTOSE® HP/HPB, when compared to the commercial formulation containing polysorbates.
- ❖ KLEPTOSE® HP/HPB may have the ability to interfere with the reversible self-association of protein monomers.

- ❖ KLEPTOSE® HP and HPB reduce heat-induced aggregation in a concentration-dependent manner.
- ❖ KLEPTOSE® HP and HPB when used at optimized concentrations can be as effective as trehalose in inhibiting protein aggregation.

CONCLUSIONS

We have shown that KLEPTOSE® BioPharma (hydroxypropyl beta cyclodextrin) represents a promising alternative to surfactants commonly used within biologic formulations, such as polysorbates Tween 20 and 80. Formulations containing KLEPTOSE® BioPharma perform better than the reference formulations containing polysorbates, when subjected to stress conditions of shaking (1400 rpm) and temperature (40°C). It represents a functional alternative to surfactants within biologic formulations.

KLEPTOSE® BioPharma is a potential alternative to Tween 20/80

- ❖ The product can also be used synergistically with polysorbates.
- ❖ A multi-functional excipient, providing anti-aggregation stabilization and surfactant properties all in one.
- ❖ Able to extend the shelf-life of therapeutic protein formulations.

Life-cycle management

- ❖ KLEPTOSE® BioPharma represents a new tool to be used during the life-cycle management of biologic formulation.
- ❖ Biosimilars represent a promising area of formulation with KLEPTOSE® BioPharma due to the large number (>70%) of products containing polysorbates.

LEARN ABOUT ROQUETTE BIOPHARMA PRODUCTS AT

www.roquette.com | pharma@roquette.com

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