Croda Pharma

Super Refined™ Polysorbates for biopharma applications

Super Refined Polysorbates solubilise and stabilise the most sensitive APIs (active pharmaceutical ingredients) across dosage forms including injectable and oral.

Super Refining removes polar impurities (including primary and secondary oxidation products) from an excipient without altering its chemical composition, helping to reduce negative API interaction and degradation.

Our range of **Super Refined Polysorbates** include:

- **Super Refined Polysorbate 20**
- **Super Refined Polysorbate 80**
- **Super Refined Polysorbate 80 POA**

Benefits

- Improve API stability and finished formulation integrity
- Reduce potential for cellular irritation
- Prevents protein aggregation
- Highly effective protein interfacial clearing
- Batch to batch consistency

Monograph compliance

- PhEur, NF, JP/JPE, ChP

Smart science to improve lives™

CRODA

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Protein aggregation study

In this assay protein aggregation was defined as the concentration of GuHCl (Guanidine Hydrochloride) added which caused a particle size of > 200nm for more than 3% of the mass reading. The results in Figure 1 show that the Super Refined and High Purity polysorbates successfully prevented aggregation of the IgG protein.

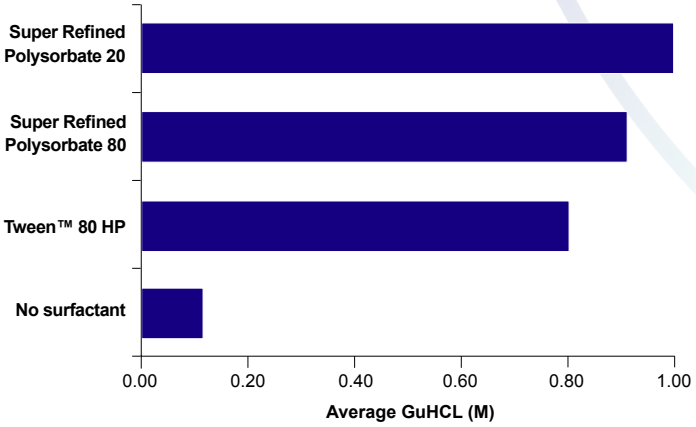

Figure 1: The aggregation of Bovine IgG 0.05% w/w with or without 0.005% w/w Polysorbate species

Cellular irritation

Super Refined Polysorbate 80 displayed a significantly lower irritation potential at all concentrations tested. There was up to a 40% decrease in irritation potential with the Super Refined Polysorbate 80 as compared to standard pharmaceutical grade Polysorbate 80. Based on the data, it can be concluded that polysorbate purity is critical for minimising cellular irritation.

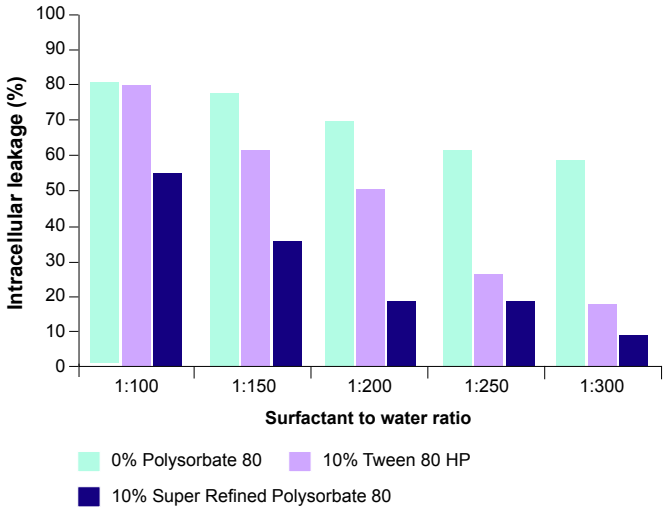

Figure 2: Comparison of intracellular leakage using High Purity and Super Refined Polysorbate 80 at varying concentrations

Batch to batch consistency

The controls in place during the Super Refined manufacturing process ensure that there is limited differences in species distribution across multiple batches. The consistency of these distributions can be seen in Figure 3 below:

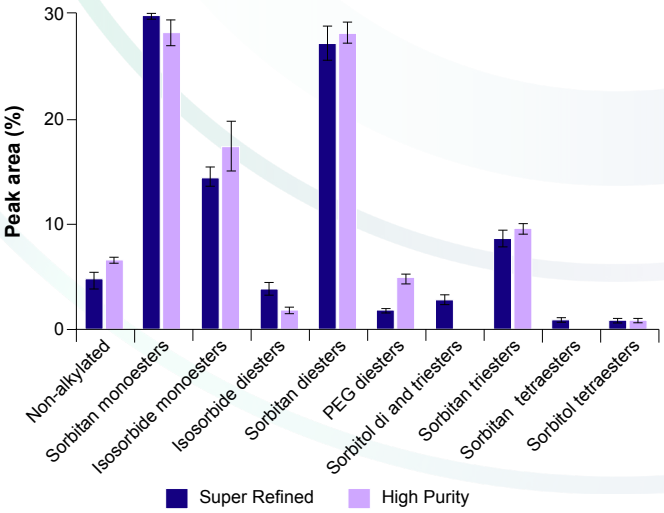

Figure 3: Species distribution from six batches of Super Refined and six batches of High Purity Polysorbate 80

A high level of consistency across multiple batches shows that final formulation performance will not be affected when using Super Refined or High Purity Polysorbate 80. The results in Figure 4 show that measured micelle diameter and surface tension are consistent across multiple different manufactured batches.

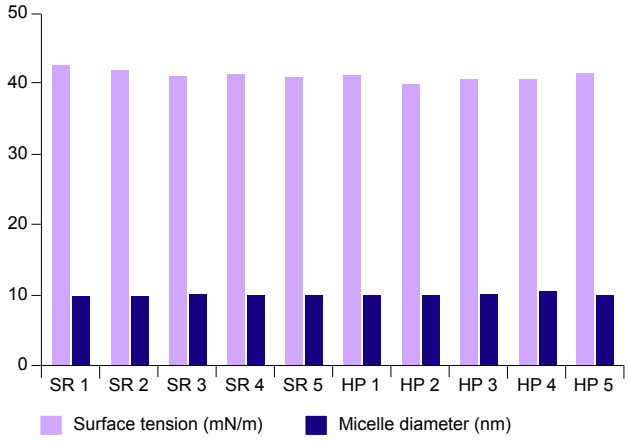

Figure 4: Measured micelle diameter and surface tension comparing different batches of Super Refined and High Purity Polysorbate 80

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Polysorbate enzymatic degradation

Enzymatic degradation has become an area of interest, as esterases carried over from monoclonal antibody manufacture can cause degradation of the polysorbate. This could lead to polysorbate loss and therefore loss of API stability in the final formulation. The study in Figure 5 uses LC-ELSD in the presence of a model lipase to track the degradation of individual polysorbate species.

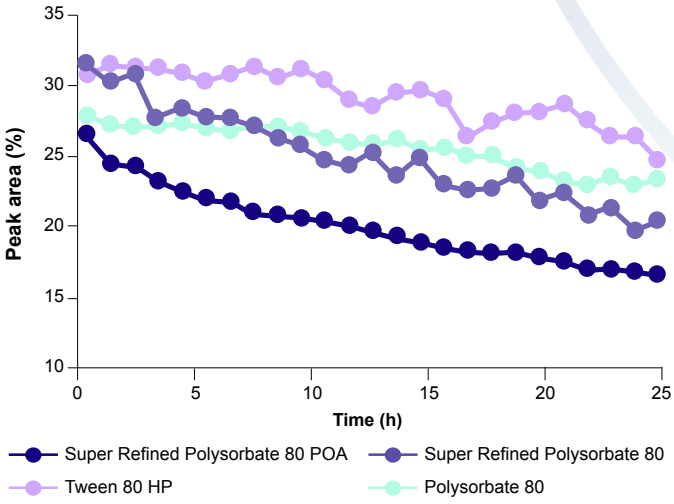

Figure 5: Change in ethoxylated sorbitan diesters peak area % in Polysorbate 80 via enzymatic hydrolysis over 24 hours

In a comparable study in terms of polysorbate level and lipase concentration, over 3 days we can see that the micelle size of the polysorbate increases.

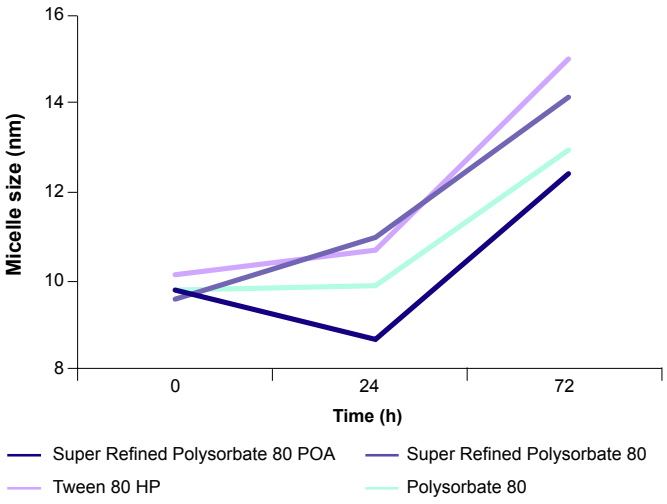

Figure 6: Micelle size of polysorbate measured over 72 hours

Protein interfacial clearance

Understanding how a surfactant interacts with solid surfaces (eg glass vials) in the presence of high protein concentration is important when considering the effect of surfactants in biopharma formulations. To model this, interfacial rheology was measured using the double wall attachment on a TA Instruments DHR-3 rheometer. Bovine Serum Albumin (BSA) 10% w/w was added to the vessel and then surfactant added as 10% aqueous solution of polysorbate species to give an overall dose of 0.0005% w/w – 0.02% w/w. This was added at 3 minutes and the change to the surface elasticity monitored for 2 hours.

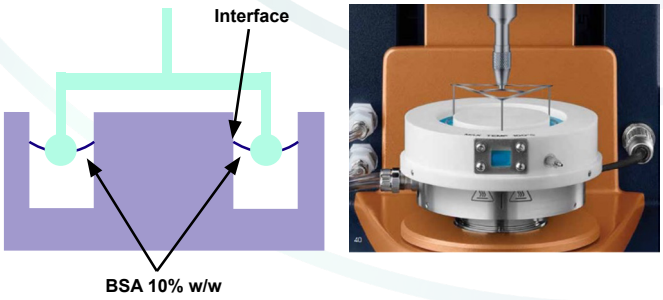

Figure 7 : Double wall interfacial attachment

The results in Figure 8 show that Super Refined Polysorbate 20 is very good at clearing the interface, almost immediately reducing the elasticity to that of water. Both Super Refined Polysorbate 20 and 80 are shown to outperform the Poloxamer 188 competitor product.

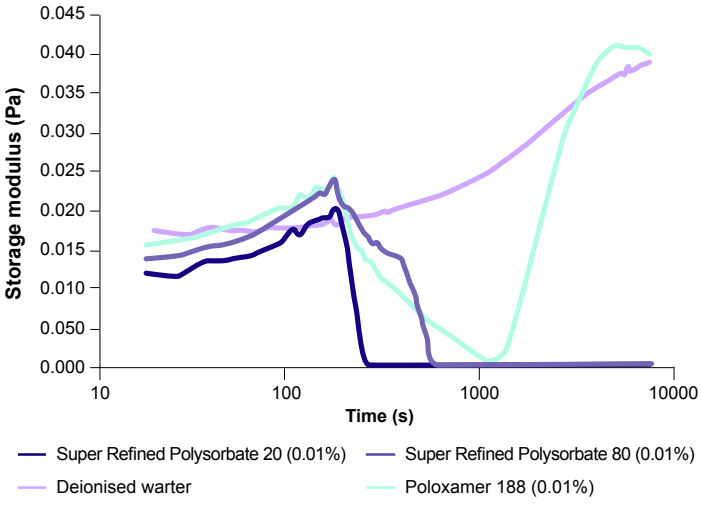

Figure 8: Super Refined Polysorbate 20 and 80 performance measured against deionised water and Poloxamer 188

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