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WHITE PAPER

Cleaning Ultrafiltration Membranes with Pharmaceutical Detergents

Data shows pharmaceutical detergents can reduce process inefficiencies and extend usable membrane life.

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Ultrafiltration membranes are an expensive yet vital component in the biopharmaceutical manufacturing process. They enable the concentration and purification of the necessary harvest material. Routine cleaning of the membrane ensures proper function and longer usable life.

This white paper reviews an experimental study comparing the performance of a pharmaceutical detergent to sodium hydroxide and concludes that using a formulated detergent offers many advantages.

A Data-Driven Comparison Focused on Cleanability, Compatibility, and Rinsability

Ultrafiltration steps are used in biopharmaceutical manufacturing processes to concentrate and purify harvest material. In the downstream process, ultrafiltration steps may be performed two to six times. Multiple filtration steps during the manufacturing process help with the following:

- Concentrate the solution using a pore size of 0.001-0.01 µm.
- Filter based on the molecular weight cut off (MWCO).
- Provide buffer exchange.
- Reduce the volume of harvest material to a manageable level for the subsequent chromatography step.

For example, in the blood and plasma fractionation industry ultrafiltration membranes help concentrate albumin and may filter out viruses. The expensive nature of the membranes, frequency of filtration in the downstream process, and length of time required for purification make ultrafiltration a critical step, but also a bottleneck, in the manufacturing process. Therefore, it is important to maintain and clean the ultrafiltration membrane.

Challenges with Cleaning Ultrafiltration Membranes

Historically, membrane manufacturers recommend sodium hydroxide for cleaning these membranes based on material compatibility, not what product cleans efficiently. Using a pharmaceutical detergent that is both compatible and effective may:

Improve product yield

Minimize risk for microbial contamination

Reduce process wastes

STERIS has evaluated the use of a pharmaceutical detergent compared to sodium hydroxide (NaOH) on cleaning select ultrafiltration membranes. In the study outlined below, the cleanability, compatibility, and rinsability of STERIS's CIP 150™ Alkaline Process & Research Cleaner and NaOH on ultrafiltration membranes is explored.

Study Methods

For this study, a 30 kDa polyethersulfone (PES) coupon was used as a representative membrane substrate commonly used in the biopharmaceutical industry on a lab scale ultrafiltration membrane system. The membrane was rinsed with MilliQ water and equilibrated with phosphate buffer solution (PBS), a common industry buffer, prior to use. Bovine serum albumin (BSA) was used at a consistent concentration for membrane soiling.

Cleanability

Normalized Water Permeability (NWP) measures the flux of water through a membrane in liters per meter squared per hour. The industry standard is to continue using a membrane with an NWP level of ≥ 60% when compared to the initial NWP. The higher the percentage, the more water can pass through the membrane, which indicates the effectiveness of cleaning. Cleanliness was tested by soiling the PES membrane with BSA, then calculating the NWP after three cycles.

Table 1. Results of lab scale NWP % using different cleaning solutions after three cycles.

Cleaning Solution	NWP %	Average Rinse Water Required (mL)
1% v/v CIP 150	81.5	750
0.1 N NaOH	65.1	1050
0.5 N NaOH	66.6	2100

The 1% CIP 150 detergent maintained a higher NWP % after three cycles compared to sodium hydroxide in Table 1. Additionally, 30-65% less water was required to rinse with the alkaline detergent. Water savings is also demonstrated during the rinsability assessment when comparing the alkaline detergent and NaOH.

Compatibility Testing

Compatibility testing was conducted with 10 cleaning cycles. The NWP was calculated between each cleaning cycle. In addition to indicating the cleanliness of the membrane, the NWP percentage can indicate the compatibility of the cleaning solution over time. As illustrated in Figure 1, both cleaning solutions performed comparably for compatibility with the PES membrane.

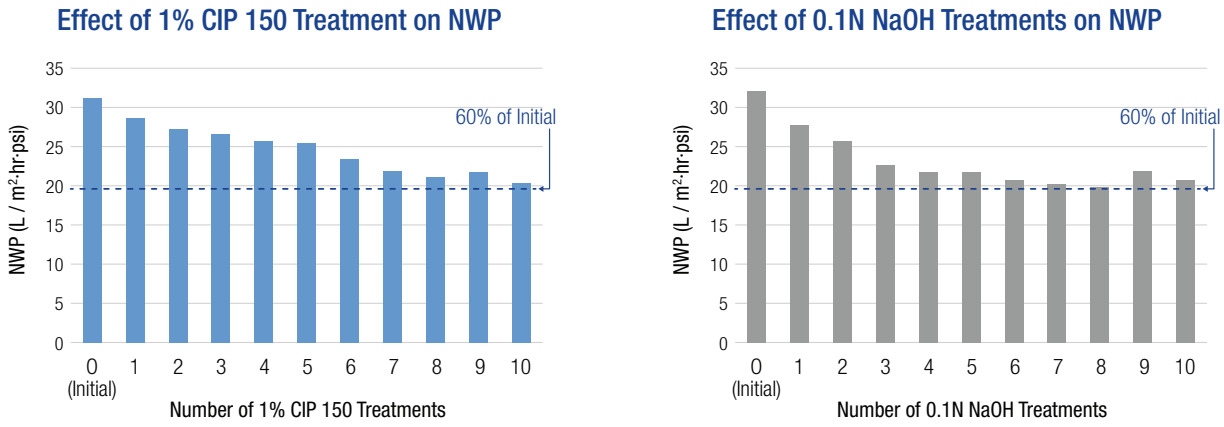

Figure 1. NWP results after 10 cycles for different cleaning solutions on a PES coupon.

Rinsability

Rinsability refers to a cleaning solutions ability to rinse off a surface with ease. A third study was performed to compare the rinse volume required after the cleaning cycle for each cleaning solution.

Table 2 demonstrates a water savings of 40% for a lab scale ultrafiltration membrane when using 1% v/v CIP 150 detergent compared to 0.1 N NaOH. A pharmaceutical detergent is engineered to contain components to improve rinsability, resulting in time and water savings in the cleaning process. In addition to water savings, a pharmaceutical detergent that cleans more efficiently and effectively may reduce the amount of time and energy required to clean.

Table 2. Results of rinse water study for two cleaning solutions.

Cleaning Solution	Average Rinse Volume Required (mL)
1% v/v CIP 150	521
0.1 N NaOH	827

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Summary

While not always included on the manufacturers cleaning recommendations, a pharmaceutical detergent may be an advantageous alternative for cleaning ultrafiltration membranes. In addition to cleaning soils more effectively, a pharmaceutical detergent may increase the lifespan of the membrane and decrease process inefficiencies.

For more information on cleaning ultrafiltration membranes, contact your local STERIS account representative or Ask the Experts at https://www.sterislifesciences.com/education-and-training/meet-the-experts/ask-the-experts.

References

Kroeger, B., Lopolito, P., Smith, T., & Deal, A. (2019, March/April). Challenges and Advances in Cleaning Ultrafiltration Membranes used in Bioprocessing. *PharmaHorizon*, 37, 2, 60-63. Chemistry Today.

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The Pharmaceutical Detergent Advantage

FIVE WAYS
cleaning ultrafiltration membranes with a pharmaceutical detergent can
SAVE YOU MONEY

Five ways cleaning ultrafiltration membranes with a pharmaceutical detergent improves business results:

1. Lower life-cycle costs – Cleaning an ultrafiltration membrane with a pharmaceutical detergent rather than NaOH can lengthen membrane life, reducing the need for frequent replacement.
2. Greater yield – Cleaning with a pharmaceutical detergent enables greater throughput and more productive operation.
3. Formulated to be free-rinsing, pharmaceutical detergents require less rinse water when cleaning.
4. Reduced contamination risk – Pharmaceutical detergents are designed to clean more thoroughly, which helps avoid contamination.
5. Scientific expertise and support – A formulated detergent like STERIS CIP 150™ Alkaline Process & Research Cleaner comes with technical literature and expert support to keep your operation running efficiently.