

Difco TC Yeastolate ultra-filtered (TCY UF) in scale-up optimization

Increasing titer to optimize productivity, delivering over 100% improvement

Situation

A customer asked us to replace a chemically defined CHO medium with a higher-performing medium and feed pairing strategy to optimize their results. The goal of this study was to meet or exceed the current baseline titer (control) established in bioreactors. Confirmation of scalability in bioreactors was also a requirement.

Solution

A basal medium and feeds were developed after traditional spent media analyses. Following development, a variety of peptones were tested in the basal medium and as feed supplements to improve performance. Process development work was also done to optimize productivity and confirm results in a bioreactor platform.

Results

- A basal medium, Medium 1, was developed with a ~25% improvement over the control using Gibco™ **PD-Express Services** (Figure 1, Medium 1)
- When combined with Gibco™ Difco™ TC Yeastolate ultra-filtered (TCY UF) for supplementation, Medium 1 yielded >50% improvement in titer over the control (Figure 1, Medium 1 with TCY UF)
- Feed strategy was optimized by evaluating various concentrations and additional time points of Difco TCY UF; the optimal condition for this experiment was identified as 3 g/L of Difco TCY UF fed at day 5 and collected on day 14, resulting in a ~70% increase in titer over control (Figure 2, CD-1000 (no feed) vs. day 5 feed of 3 g/L of Difco TCY UF)
- By adding Difco TCY UF to the feed, more than 100% improvement was seen over the feeds designed based on spent media analyses (Figure 3, Medium 1 with TCY UF and AA feed and Medium 1 with TCY UF and NA feed vs. Medium 1 with TCY UF and TCY UF feed)
- Process was successfully scaled to a bench-scale bioreactor with similar results as a shake flask study (Figure 1, Medium 1 with TCY UF and feed vs. Medium 1 with TCY UF and feed in bioreactor)



~25% improvement of the control media using Gibco Custom Media Services



>50% increase in titer using Gibco™ Difco™ peptones alone



~70% increase in titer with optimized feed strategy compared to control medium



Over 100% improvement in titer yield with TCY UF feed compared to traditional feed design



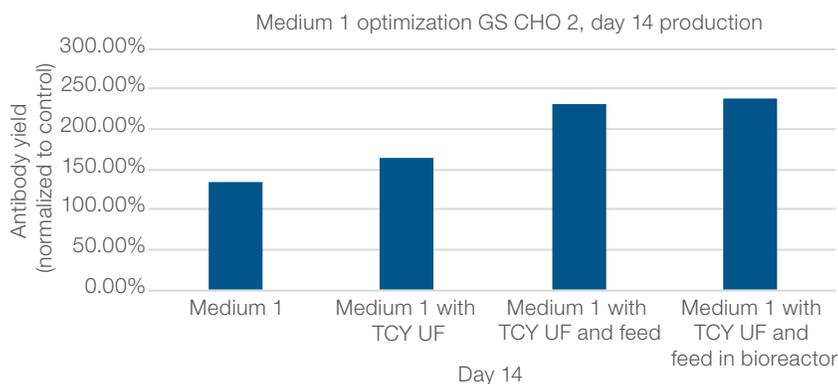


Figure 1. CHO culture can benefit from Difco TCY UF addition to basal media and supplemented as a feed. Here we see that Medium 1, optimized through the media design service, performs better than CD-1000 (control). By simply supplementing Medium 1 with 3 g/L of Difco TCY UF, there was an increase in titer performance. When an additional 3 g/L of Difco TCY UF was fed on day 5, there was a further performance boost, and these results were replicated in a bench-scale bioreactor.

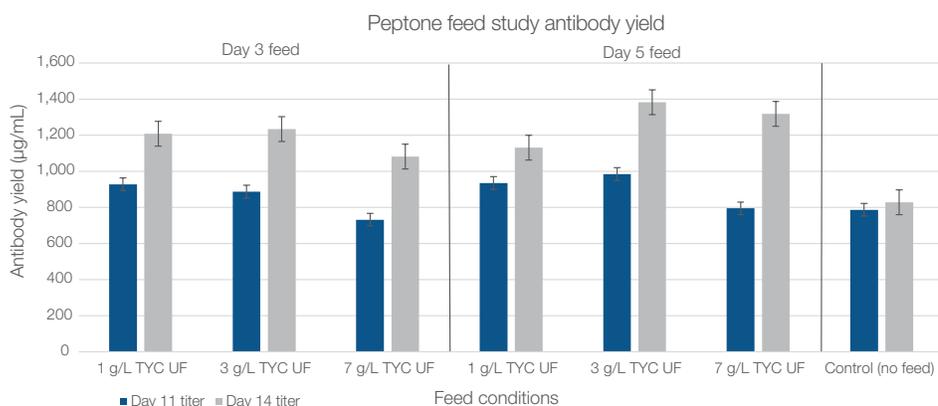
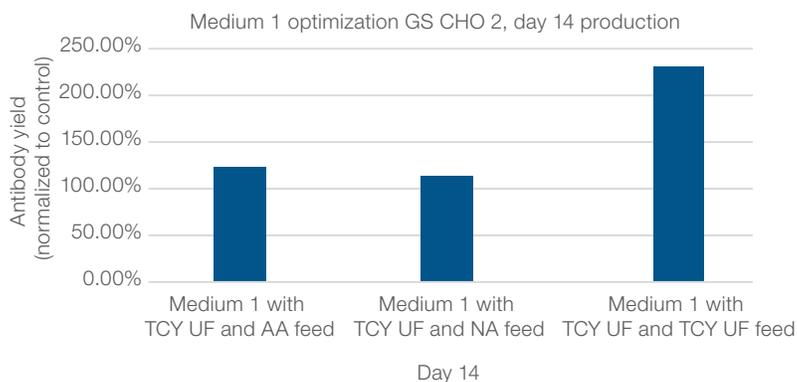


Figure 2. Peptone optimization: feed amount and timing. This experiment demonstrates the importance of optimizing your feeding strategy. The amount of peptone fed and the timing of the feed both impact product titer. This graph shows the three different feed concentrations (1 g/L, 3 g/L, and 7 g/L) fed at day 3 and day 5 of the study. Here, the top condition is 3 g/L of Difco TCY UF fed at day 5 and collected at day 14. If these different feed time points had not been investigated, ~20% productivity would have been lost when comparing day 3 to day 5 feeds.



Use	Product
Control medium	CD-1000 Medium
Medium 1	Optimized version of CD-1000 developed with Gibco PD-Express Media Development Services
Feed	AA feed—amino acid internal formulation designed as part of media design service
Feed	NA feed—nucleic acid internal formulation designed as part of media design service

Figure 3. Traditional feed design compared to Difco TCY UF feed. This demonstrates the superior performance of peptones when compared to feeds developed as part of a media design service. Difco TCY UF feed is superior to both the designed amino acid (AA) and nucleic acid (NA) feeds.

Ordering information

Product	Cat. No.
Difco TC Yeastolate, ultra-filtered (UF)	670079, 292804, 292805

Find out more at thermofisher.com/peptones