PBS BIOTECH®
Innovative Bioprocess Solutions

Application Note

PBS Air-Wheel™ bioreactor offers seamless transition from stirred-tanks in fed-batch CHO process

Introduction

Chinese hamster ovary (CHO) cells have been used extensively for large scale recombinant protein production over the last 20 years. As animal cells, CHO cells offer advantages over other expression systems in that they secrete desired products with accurate glycosylation patterns that have undergone proper protein folding. The added benefits that CHO cells offer are that they are well-characterized with a solid track record for meeting the strict regulatory requirements for biopharmaceuticals, in addition to their high productivity (cell growth and protein expression levels) and their robustness to culturing in suspension in conventional stirred-tank bioreactor systems.

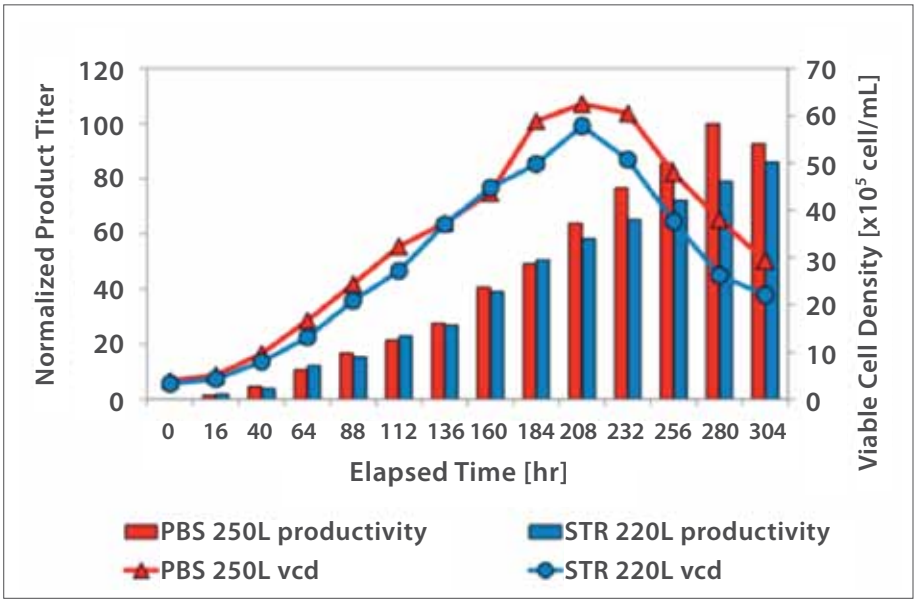

Figure 1. *Cell growth and product titer profiles of PBS (250L w.v.) and stirred-tank (220L w.v.) systems. The growth and titer profiles achieved in the PBS system were very comparable to those of the stirred-tank system, but slightly higher peak viable cell density and titer were attained in the PBS.*

The novel, low shear single-use bioreactor system from PBS Biotech® has the potential to offer unmatched performance in shear-sensitive applications involving microcarriers and viral production, but we show here that processes developed and optimized in a traditional stainless steel stirred-tank system can be easily transferred over to the PBS platform with at least equivalent results and the potential for better performance.

Experimental Procedure

In this study, a CHO-S cell line expressing an Fc-fusion protein was cultured in fed-batch mode over a span of 13 days at typical operating conditions in the PBS bioreactor at 250L working volume, in parallel to a stainless steel stirred-tank bioreactor at 220L working volume. Concentrated glucose and glutamine solutions were fed to the bioreactors as needed in pre-determined amounts. The desired protein was purified and analyzed upon harvest.

Results

In this study, cell culture performance was evaluated based on the viable cell density profile and a full-breadth of analyses on the product, including titer, yield, purity, glycosylation, and in-vitro bioactivity.

As shown in Figure 1, comparable cell growth and product titer profiles were demonstrated over the course of the run in both the PBS bioreactor system and the stirred-tank bioreactor. Product yield and impurities data from the harvests were also comparable (Table 1), and similar product quality data were attained in both systems, based on reduced SDS-PAGE and IEF (Figure 2). Equivalent *in vitro* bioactivity profiles were also achieved in both systems (Figure 3), confirming all other assay results.

Conclusions

This experiment demonstrated that existing processes developed in traditional stainless steel bioreactor can be seamlessly transferred to the PBS Biotech® single-use bioreactor system platform, expecting results equivalent to stirred-tank systems in the production of biopharmaceuticals. The PBS Biotech bioreactors, while offering gentle and low-shear mixing suitable for shear-sensitive applications, provides the level of performance expected in conventional stirred-tank bioreactors even for processes involving robust cell lines.

Table 1. *Product yield and impurities data from the PBS (250L w.v.) and stirred-tank (220L w.v.). The product yield from downstream processing was comparable between the PBS and stirred-tank (47% vs. 44%, respectively). The impurities data were also comparable between the two systems, when considering the variability expected from this process as seen in historical runs.*

	Yield (%)	Polymer (%)	HCP (ppm)	Host DNA (pg/mg)
PBS (250L w.v.)	47	1.15	7.22	0.8
Stirred-tank (220L w.v.)	44	0.92	4.81	9.5

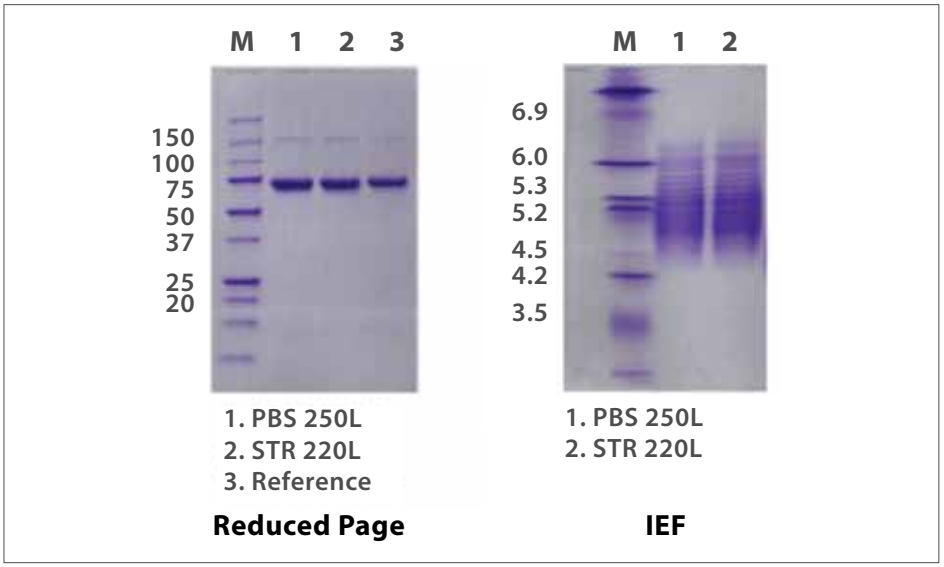

Figure 2. *Product quality profiles of products from PBS (250L w.v.) and stirred-tank (220L w.v.) systems. Similar size distribution of proteins is demonstrated by the SDS-PAGE on the left, while similar electric charge distribution is evidenced by Isoelectric Focusing (IEF) technique.*

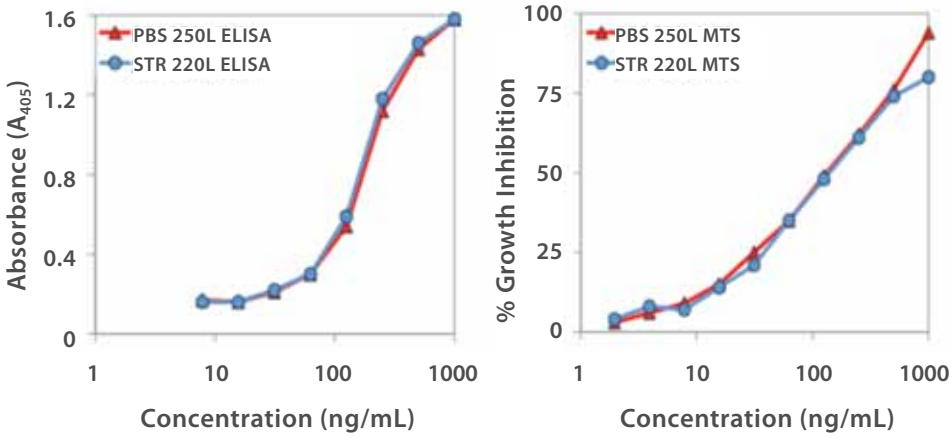

Figure 3. *In vitro bioactivity assay results of products from PBS (250L w.v.) and stirred-tank (220L w.v.) systems. Equivalent bioactivity was demonstrated by the ELISA assay (left) and MTS assay utilizing L929 mouse myeloma cells (right).*

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