



Utilization of Cell Optimizer System® to Determine Optimal Growth Conditions of Mammalian and Insect Cells

Abstract

The optimization of growth and production parameters is one of the more critical concerns of cell culture research. Although the most important optimization efforts are directed to the production of desired cellular products, the next most important concern is the production of the maximum number of cells. The Cell Optimizer System® was used to determine the optimal pH growth conditions for the HFN 7.1 hybridoma cell line.

Materials and Methods

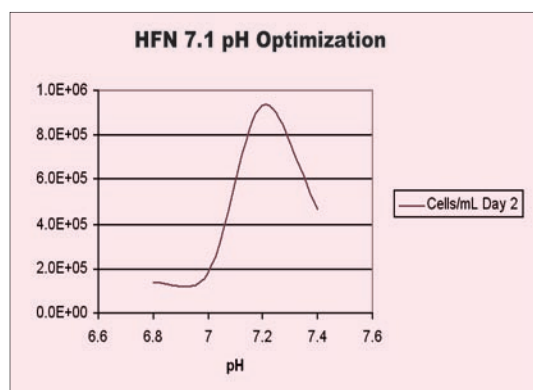
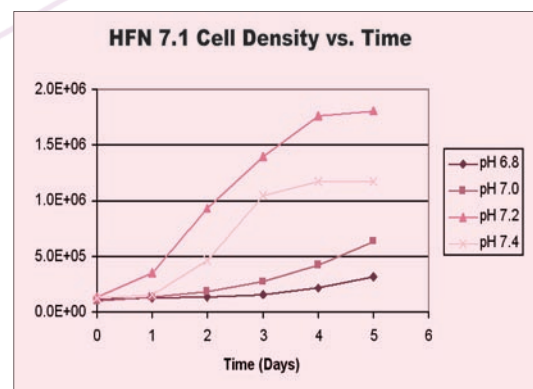
The Cell Optimizer System® was used for the experiments described below. The Cell Optimizer System® is a small (250 mL to 3 L) stirred tank bioreactor. The experimental parameters of pH, temperature, and DO were regulated and controlled using the Control Tower™ equipped with a 4-gas control system. The vessel was stirred with a flat-blade PTFE impeller, using a manually set stirring rate. Data was collected at 10 minute intervals using the BioPro™ data acquisition software.

The HFN 7.1 hybridoma cell line (ATCC, CRL 1606) was used to evaluate a pH optimization protocol. This line was propagated in DMEM/F12 (1:1) (Paragon Biotech, Baltimore, MD) containing 2% FBS (fetal bovine serum). Seed cultures were propagated continually in T-75 flasks in the same medium. The Cell Optimizer System® was filled with 900 mL medium. The environmental parameters were allowed to equilibrate to the following values: 37°C; 50% DO; 50 RPM. The pH was set specific to the study. All cultures were seeded at $\sim 10^5$ cells/mL. Each study was run for 5 days. Cell densities were determined using a hemacytometer.

Results

Optimization of pH for HFN 7.1

HFN 7.1 shows a pH shift of 0.8 to 1 pH units towards acid from a starting pH of 7.4. The cell line appears stable at this low pH, causing some users of this cell line to assume that the optimum pH for this cell line to be pH 6.8. To determine the optimal pH, this cell line was cultured at four pH values ranging from pH 6.8 to 7.4 in 0.2 pH unit increments. The data showed that pH 7.2 provided the maximum growth rate and cell density.



Conclusion

The Cell Optimizer System® can easily be used to design and execute culture optimization protocols, avoiding elaborate setup problems that exist with other bioreactors. This system provides simplicity, but also possesses the full complement of environmental controls. The Cell Optimizer System® was also able to maintain the pH of the culture system, despite the tendency of the culture to shift to a more acidic pH mentioned earlier.