



Production of recombinant monoclonal antibody (rMAb) in Chinese hamster ovary cells using CDM4CHO medium and Cell Boost™ 2 feed supplement

One of the most important cell lines used in the production of recombinant proteins is the Chinese hamster ovary (CHO) cell line. Regulatory concerns surrounding the use of animal-derived components in the production of therapeutic proteins is a major driver for the development of chemically defined and animal-derived component-free (ADCF) media for CHO cell growth and protein production. This application note demonstrates the performance of the chemically defined HyClone™ CDM4CHO base medium optimized for CHO cells. To increase process yield, the CHO cell culture was supplemented with HyClone Cell Boost 2.

Introduction

CDM4CHO is a CHO cell culture medium free of protein and animal-derived components. This regulatory-friendly medium is developed to increase process yields for the industrial manufacture of recombinant proteins using a variety of CHO cell clones. CDM4CHO medium has been successfully tested in a variety of culture systems, including T-flasks, shaker flasks, and bioreactors including fed-batch and perfusion culturing. In this study, an rMAb-producing CHO cell clone was cultured in a stirred-tank bioreactor.

To optimize process yields with the CDM4CHO medium, the culture was fed Cell Boost 2 supplement. Cell Boost 2 supplement is designed to provide nutrients such as carbohydrates, amino acids, and vitamins as part of a fed-batch culture strategy. Cell Boost 2 has been developed for recombinant protein production with various cell lines including CHO cells.

Materials and methods

An rMAb-producing CHO cell line was used in this study. Cells were grown in 1.5 L suspension cultures in CDM4CHO medium

using a 3 L stirred-tank bioreactor (Applicon). Culture temperature was controlled at 37°C, dissolved oxygen was controlled at 50% air saturation, and culture pH at 7.0.

The culture was pulse-fed at 40 mL/L with Cell Boost 2 supplement (hydrated at 149 g/L in injection-grade water and pH adjusted to ≥ 9.5) on day 4 to 8.

Results

Viable cell density reached a maximum of 6.9×10^6 cells/mL within the culture span of 13.5 days (Fig 1). The rMAb yield for the process was 0.86 g/L. Glucose was added to the culture as needed when fed with Cell Boost 2 supplement. Glucose and lactate profiles are shown in Figure 2. As shown, cells started to metabolize lactic acid after day 5. Using the described fed-batch process, productivity was improved 2–4-fold compared with initial production levels (0.1796 g/L) in batch mode (Fig 3).

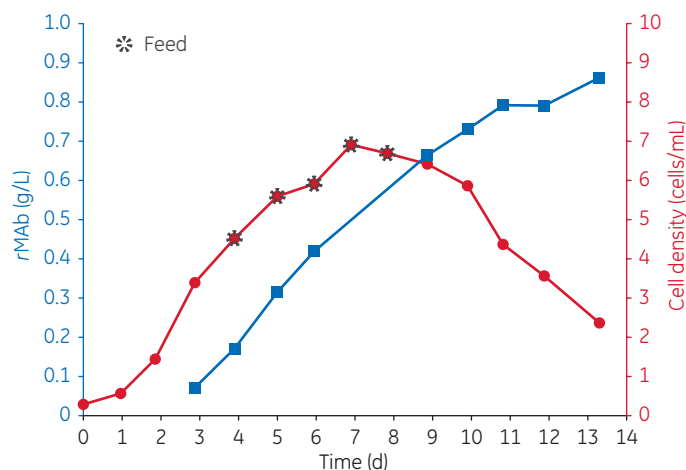


Fig 1. Cell density and rMAb production in fed-batch CHO cell culture using CDM4CHO base medium and Cell Boost 2 feed supplement.

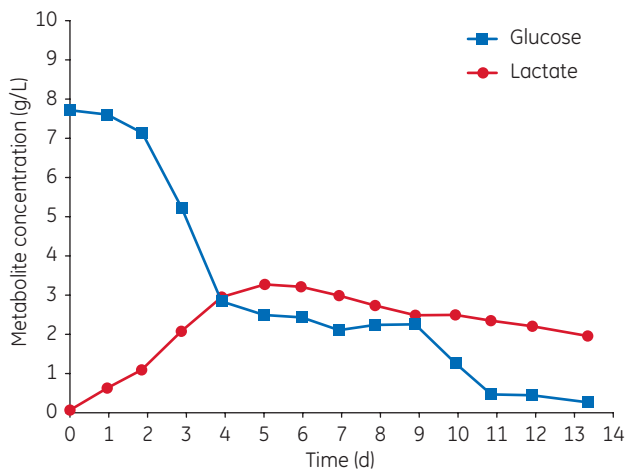


Fig 2. Glucose and lactate profiles of CHO cells in fed-batch cultures using CDM4CHO base medium and Cell Boost 2 feed supplement.

Conclusion

CHO cells were successfully grown in fed-batch suspension culture utilizing CDM4CHO medium supplemented with Cell Boost 2. Compared with initial production levels in batch mode, a significant productivity improvement could be achieved with the described fed-batch process.

Ordering information

Product	Product code
CDM4CHO	SH30556
Cell Boost 2	SH30596

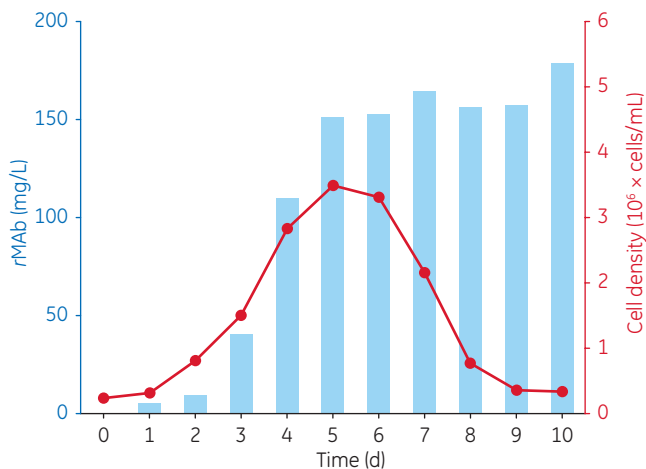


Fig 3. Cell density and rMAb production in batch CHO cell culture using CDM4CHO base medium.

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