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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 *r*MAb-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 *r*MAb-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 *r*MAb 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).

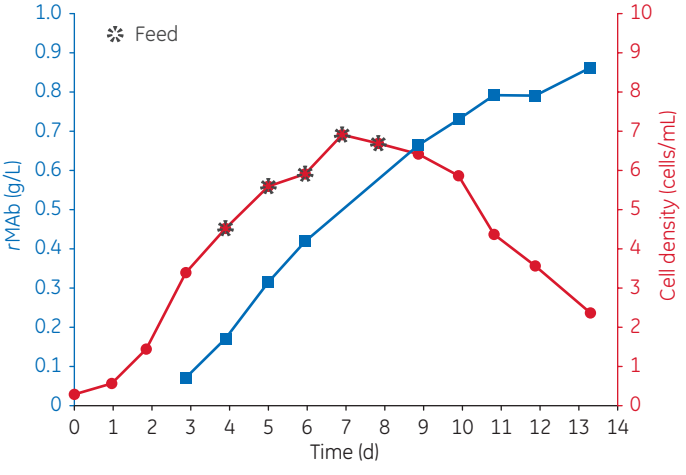

Fig 1. Cell density and *r*MAb production in fed-batch CHO cell culture using CDM4CHO base medium and Cell Boost 2 feed supplement.

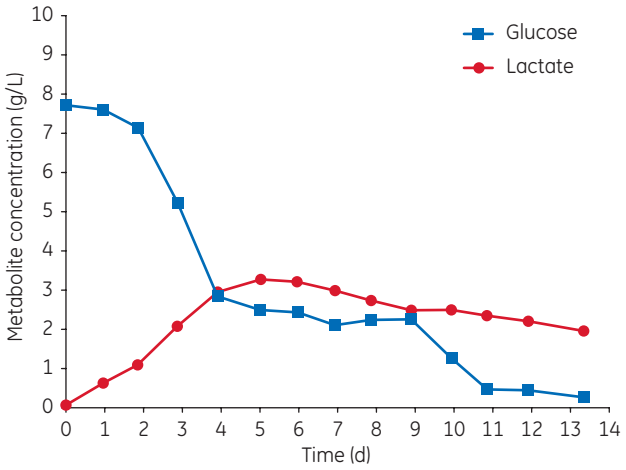

Fig 2. Glucose and lactate profiles of CHO cells in fed-batch cultures using CDM4CHO base medium and Cell Boost 2 feed supplement.

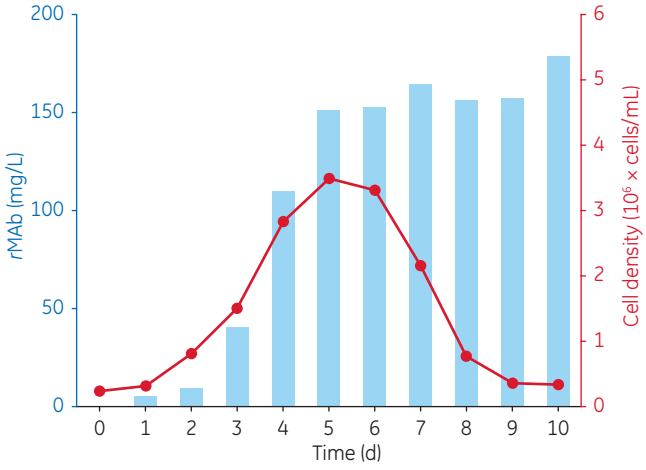

Fig 3. Cell density and *r*MAb production in batch CHO cell culture using CDM4CHO base medium.

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

www.gelifesciences.com/hyclone

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