Boosting CHO Cell Growth and Antibody Yield: Unleashing the Potential of Cell Culture Medium Performance in Shake Flasks and Bioreactors

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Introduction

The production of therapeutic proteins, such as monoclonal antibodies (mAbs), relies heavily on the optimization of cell culture media to maximize yield and maintain cellular health. Chinese hamster ovary (CHO) cells, particularly the CHO-K1 cell line, are widely used in the production of recombinant proteins due to their ability to support high-density cultures and their suitability for large-scale manufacturing[1]. However, optimizing the media to enhance cell growth, productivity, and metabolic efficiency remains a key challenge[1]. In this study, we present an evaluation of OPM Biosciences' chemically defined (CD) cell culture media, including SagiCHO and AltairCHO Basal Medium, as well as OPM Feeds (DenebCHO Feed, SagiCHO Feed, and CDFS36), for their ability to support CHO-K1 cells in fed-batch cultures and improve monoclonal antibody production. Our focus is on assessing cell growth, antibody yield, and metabolic efficiency, providing insights into how these media formulations may contribute to advancing the scalability and efficiency of therapeutic protein production.

Materials & Methods

CHO-K1 Cell Line: CHO-K1 host cells were obtained from ATCC (American Type Culture Collection). The clone utilized in this study was engineered by the OPM Cell Line Development Department for stable expression of the monoclonal antibody mAb1. Cells cultured in OPM or competitors' basal media, passaged at least three times prior to starting fed-batch experiments. For fed-batch shake flask/bioreactor experiments, cells were cultured at an initial density of 1.0 × 10^6 cells/mL of basal medium (Shake Flask total volume=25mL; Bioreactor Vessel total volume=1.2L).

Bioreactors

The following bioreactors platforms were utilized for this study:

- Sartorius (BIOSTAT® B-DCU)
- Applikon (*my*-Control)

Feeding Strategy

- **Fed-batch shake flask experiments**

For OPM basal media in combination with OPM feeds, the following feeding strategy optimized in previous studies, was applied:

Feeding Strategy for Feed# 1 (Every Other Day (EOD))							
D2	D4	D6	D8	D10	D12	Total % of feed# 1	Feed# 2
3%	4%	5%	6%	6%	6%	30%	1/10 of Feed# 1

For competitors' basal media and feeds, the manufacturers' recommended feeding strategies were followed.

- **Fed-batch bioreactor experiments**

For SagiCHO basal medium in combination with DenebCHO feed (run on Sartorius) or SagiCHO feed (run on Applikon), the following daily feeding strategy (D2–D13) was applied:

Feeding Strategy (Daily D2-D13)													
Reactor	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	Total % of Feed# 1
Sartorius	4%	3%	3.5%	4%	4.5%	4%	4%	4%	3.5%	3.5%	3.5%	3%	44.5%
Applikon	4%	3%	3.5%	4%	4.5%	4.5%	4.5%	4.5%	4%	4%	4%	3.5%	48%

Note: The percentage of daily Feed #1 was determined based on glucose consumption and osmolality changes. Feed #2 (CDFS36) was added daily (D2–D13) at a ratio of 1/10 of Feed #1.

Glucose concentration

Throughout the fed-batch process, glucose was supplemented daily to maintain concentrations above 1 g/L.

Analytics: Cell densities and viability were measured with a Vi-CELL BLU Cell Viability Analyzer (Beckman Coulter), glucose and lactate concentrations were measured with an M-100 Biosensor Analyzer (Shenzhen Sieman Technology), and mAb titers were measured using a Cedex Bio Analyzer (Roche CustomBiotech).

Results

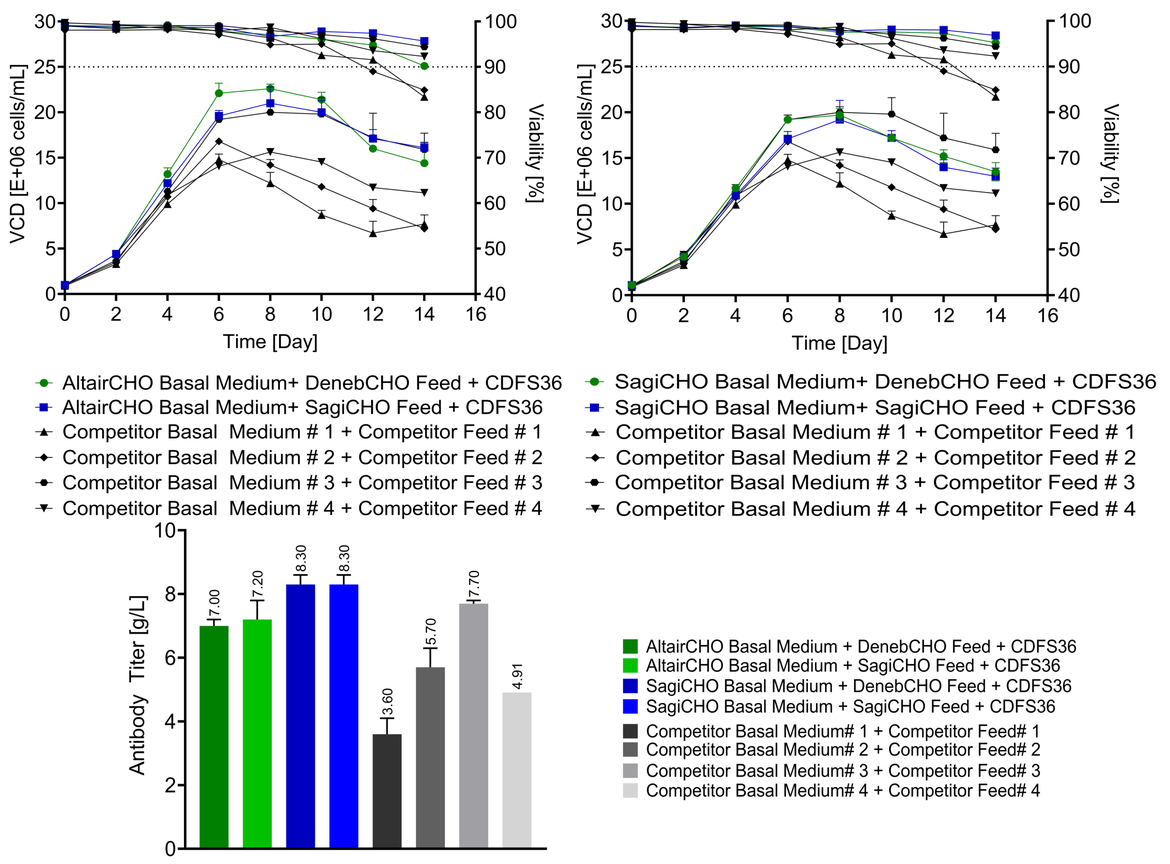

Figure 1. Cells' growth profiles, viabilities and titers during fed-batch shake flask processes. **(A)** OPM AltairCHO basal medium and **(B)** SagiCHO basal medium, in combination with OPM feeds (Feed #1: DenebCHO/SagiCHO Feed and Feed #2: CDFS36), achieved a high peak viable cell density (VCD) on day 8 and maintained viability ≥90% through Day 14. **(C)** The cells demonstrated titers ranging from 7.0 to 8.9 g/L, outperforming most competitors' basal media and feeds.

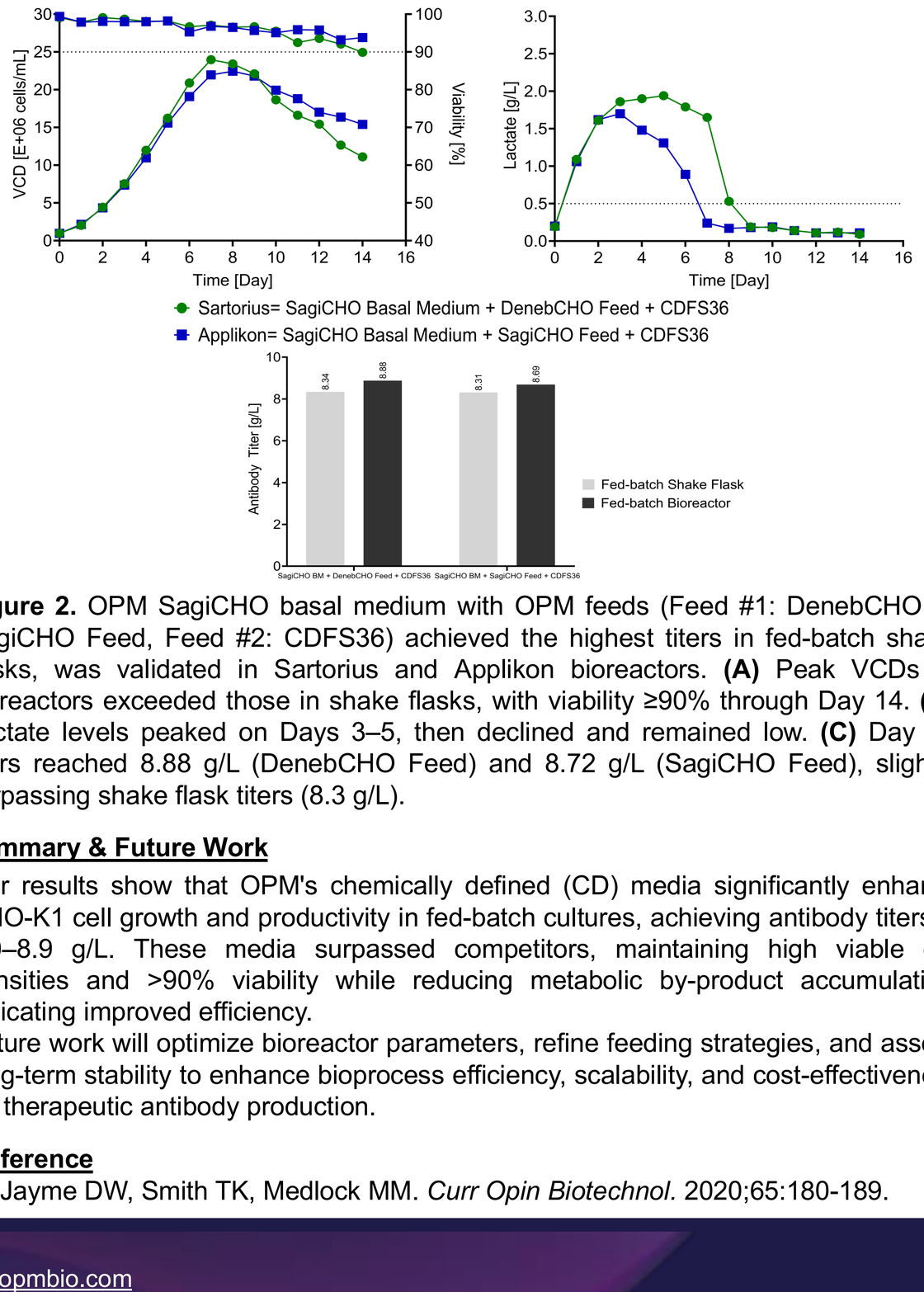

Figure 2. OPM SagiCHO basal medium with OPM feeds (Feed #1: DenebCHO or SagiCHO Feed, Feed #2: CDFS36) achieved the highest titers in fed-batch shake flasks, was validated in Sartorius and Applikon bioreactors. **(A)** Peak VCDs in bioreactors exceeded those in shake flasks, with viability ≥90% through Day 14. **(B)** Lactate levels peaked on Days 3–5, then declined and remained low. **(C)** Day 14 titers reached 8.88 g/L (DenebCHO Feed) and 8.72 g/L (SagiCHO Feed), slightly surpassing shake flask titers (8.3 g/L).

Summary & Future Work

Our results show that OPM's chemically defined (CD) media significantly enhance CHO-K1 cell growth and productivity in fed-batch cultures, achieving antibody titers of 7.0–8.9 g/L. These media surpassed competitors, maintaining high viable cell densities and >90% viability while reducing metabolic by-product accumulation, indicating improved efficiency.

Future work will optimize bioreactor parameters, refine feeding strategies, and assess long-term stability to enhance bioprocess efficiency, scalability, and cost-effectiveness for therapeutic antibody production.

Reference

1. Jayme DW, Smith TK, Medlock MM. *Curr Opin Biotechnol.* 2020;65:180-189.

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