SAFC®

Protein Quality Supplement

Technical Bulletin

Ex-Cell® Glycosylation Adjust (GAL+)

Catalog No: 14701C

Over the past decade, notable advances in the characterization and control of post translational modifications (PTMs) to enhance therapeutic properties have continued to drive the development of many next-generation biopharmaceuticals. It has been widely reported that the quality of secreted therapeutic proteins is dependent on the consistency of attached glycan moieties. Insufficient glycosylation potentially impairs efficacy and safety.

SAFC's new protein quality supplement, EX-CELL® Glycosylation Adjust (Gal+), provides customers with a novel chemically defined product which targets glycosylation attributes.

EX-CELL® Glycosylation Adjust (Gal+) allows users to easily achieve desired N-linked glycosylation by increasing the galactose site occupancy on the oligosaccharide to a higher level. Although many "trial and error" methods can be implemented to alter the glycoprofile of a protein, these can take months to optimize. EX-CELL® Glycosylation Adjust (Gal+) is the first off-the-shelf protein quality supplement that can achieve functionally relevant shifts in N-linked glycosylation quickly and efficiently.

Product Features Include:

- Ready-to-use, GMP concentrated liquid supplement
- Known start point for titration, 0.2% volume/volume
- Applicable to a broad range of cell lines, including SAFC's CHOZN® Platform

Recommended Use: EX-CELL® Glycosylation Adjust (Gal+) Supplementation

Initiate culture supplementation at 0.2% (v/v) beginning on day 2, and every other day up to day 10 of a two week fed-batch culture. Add in to existing culture strategy for batch and perfusion systems.

Titrate to determine the optimal concentration for the specific process. Begin titration in the 0.5X to 2X range and expand if necessary.

Study Design:

TPP Bioreactor

Fed-batch culture performance was compared with and without EX-CELL® Glycosylation Adjust (Gal+) supplementation across 3 different mAb producing CHO cell lines. Study Conditions: (n=3), 5% CO2, 80-85% relative humidity (RH), 200 rpm agitation (50mM diameter orbit).

1L Bioreactor

Fed-batch culture performance of CHOZN GS cell line compared with and without EX-CELL® Glycosylation Adjust (Gal+) supplementation. The evaluation of scalability was performed in un-optimized bioreactor conditions (n = 3). Parameters were as follows: pH 7.1, DO 40% and temperature 37 °C.

Testing

Samples were removed when appropriate for Vicell counting to monitor growth and viability, NOVA to monitor metabolites, supernatants for Fortebio productivity, spent media analysis, and SEC-MS relative glycan distribution.

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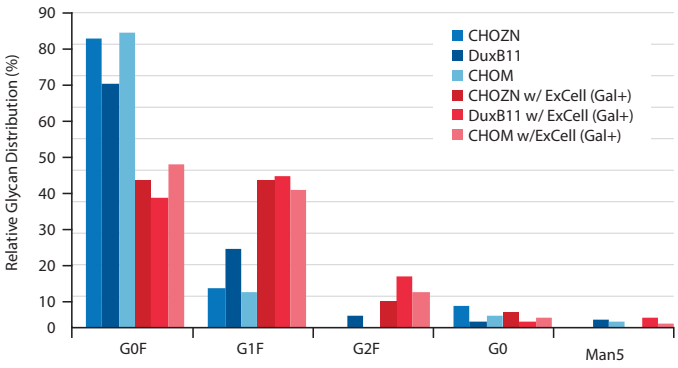
Study Results:

14 Day Fed-Batch Culture Performance

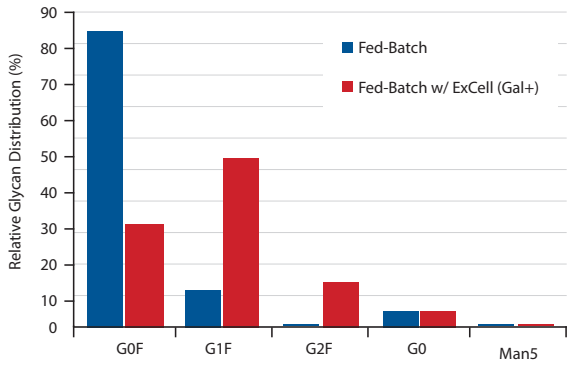
TPP

	Response	Units	Fed-batch	Fed-batch w/ExCELL (Gal+)
CHOZN GS	Vol. Prod	g/L	3.1	3.1
	Peak VCD	vc/ml	1.4E+07	1.5E+07
	Integrated VCD	vc/mL/day	1.4E+08	1.4E+08
DuxB11	Vol. Prod	g/L	2.7	2.7
	Peak VCD	vc/ml	1.1E+07	1.1E+07
	Integrated VCD	vc/mL/day	1.1E+08	1.1E+08
CHOM	Vol. Prod	g/L	1.9	2.5
	Peak VCD	vc/ml	9.9E+06	1.0E+07
	Integrated VCD	vc/mL/day	8.5E+07	9.0E+07



1L Bioreactor

Response	Units	Fed-batch	Fed-batch w/ExCELL (Gal+)
Vol. Prod	g/L	2.6	2.5
Peak VCD	vc/ml	1.3E+07	1.4E+07
Integrated VCD	vc/mL/day	1.1E+08	1.1E+08



Summary

Production processes with EX-CELL® Glycosylation Adjust (Gal+) supplementation demonstrated 2 to 4 fold increases in relative G1F and G2F distributions when compared to processes without the supplement.

EX-CELL® Glycosylation Adjust (Gal+) yields a neutral or better effect on desirable process outputs such as cell densities and volumetric productivities.

Conclusion

Convenient titration of EX-CELL® Glycosylation Adjust (Gal+) into the bioreactor allows the user to directionally adjust their product to match target quality profiles.

The ease of operation and simplicity of the supplementation process enables the rapid development of the biologic and easy transfer into clinical manufacturing.

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