

Scale Up from Shake Flask to Orbital Shaken Bioreactors (OSB)

Kühner SHAKER

Hes·SO VALAIS WALLIS
School of Engineering π

Anderlei T.^{1,3}, Bürgin T.¹, Oliviero C.², Gonzalez A.², Hagens G.²

¹ Kühner AG, CH ² University of Applied Sciences, Institute of Life Technologies, Sion, CH
³ Corresponding author

Introduction / Abstract

The aim of this study was to initiate a manufacturing process development for a recombinant CHO-K1 cell line expressing a biosimilar monoclonal antibody (Alemtuzumab) and to evaluate whether certain supplements (galactose, uridine, manganese chloride) can modify the glycosylation pattern of the monoclonal antibody without affecting cell viability or product titres. Best supplement concentrations in terms of product quantity and quality were first determined in shake flask cultures (200ml working volume) before applying to an 8L-culture, run in an OrbShake bioreactor (SB10-X). This poster focuses on the cultivation data.

We demonstrate that the culture conditions optimised in shake flask cultures could be seamlessly applied to the scaled up cell culture, run in an OrbShake Bioreactor (OSB) with a working volume of 8 litres. Also, viable cell density and product titre almost doubled in the bioreactor run compared to the shake flask cultures. Most importantly, the improved glycosylation pattern of the monoclonal antibody obtained in shake flask cultures did not differ significantly from the pattern obtained in the bioreactor run.

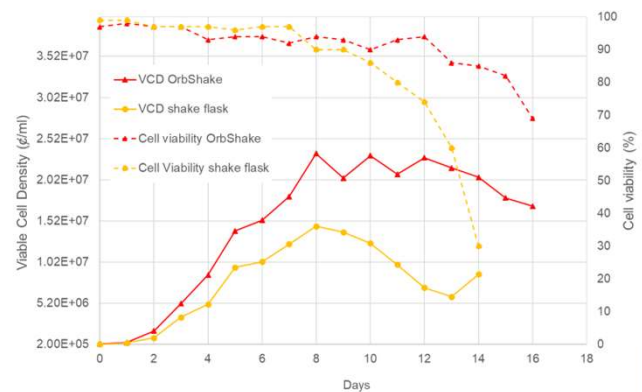
Materials and Methods

parameter	unit	shake flask (1000mL)	orbital bioreactor SB10-X
shaking speed	rpm	120	90
shaking diameter	mm	50	50
temperature	°C	37	37
humidity	%	85	-
pH	-	not controlled 5% CO ₂ (continuously)	7.0
DO	%	not controlled	40
filling volume	L	0.2	8

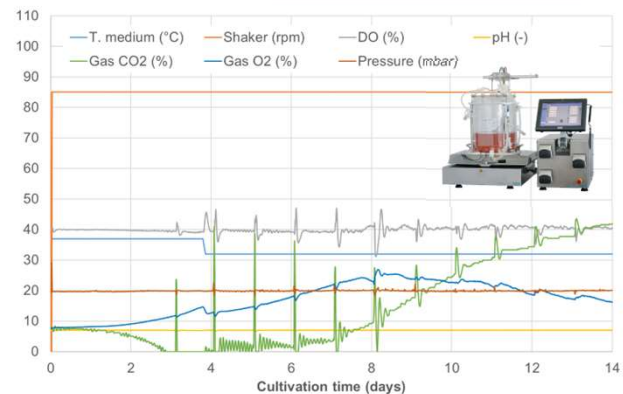
type	name of product	reference	supplier
cell type	recombinant CHO-K1 expressing Alemtuzumab	-	industrial partner
basal medium	BalanCD® CHO Growth A medium – liquid 1L	91128	Irvine Scientific®
	L-glutamine 200mM	25030081	Gibco® by Life Tech.
	Pluronic F-68	24040032	Thermo Fisher
feeds	Acti-CHO feedA CD	U21-072	GE Healthcare
	Acti-CHO feedB CD	U21-054	GE Healthcare
	D-(+)-glucose	G7021-1KG	Sigma-Aldrich®



Results and Discussion



Differences between shake flask and SB10-X bioreactor cultivation (picture above) can be explained by the lacking of control (pH, DO) in the shake flask.



As can be seen in figure below, glucose was consumed by the cell culture and needed to be added to the culture as soon as concentration dropped to 2g/L to reach 3g/L. Lactate concentration increased over time and started to be consumed from day 7 onward. Galactose, one of the supplements added daily, accumulated during the cultivation period. A very similar metabolite profile was observed in shake flask cultures (data not shown).

