Scientific Paper:

Bioprocess and Biosystems Engineering (2022) 45, 1033-1045

A comprehensive comparison of mixing and mass transfer in shake flasks and their relationship with Mab productivity of CHO cells

Saumel Pérez-Rodriguez, Greta I. Reynoso-Cereceda, Norma A. Valdez-Cruz, Mauricio A. Trujillo-Roldán
Unidad de Bioprocesos, Departamento de Biologiá Molecular y Biotecnologiá, Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, México

Abstract:

The selection of highly recombinant protein (RP)-productive Chinese hamster ovary (CHO) cell lines is widely carried out in shake flasks. It is assumed that increases in the operating parameters in shake flasks lead to impairments in cell growth and RP production. These effects in cells metabolism are widely associated with high mass transfers and hydrodynamic stress. This study examined the impact of commonly used operational parameters on growth and specific productivity (*qP*) of two CHO cell lines differentially secreting a humanized anti-hIL8 monoclonal antibody (mAb) and cultured in 250 ml flasks. The evaluated parameters are filling volume (10, 15, and 20%), shaking frequency (60 and 120 revolutions per minute -rpm-), and orbital diameter (25.4 and 19 mm). The analysis of the oxygen transfer was done in terms of the measured volumetric mass transfer coefficient (*kLa*) and of the hydrodynamics in terms of power input per unit volume of liquid (P/V), the turbulent eddy length scale measured by the Kolmogorov's microscale of turbulence, the energy dissipation rate, the average shear stress, and the shear rate. Though almost all measured kinetic and stoichiometric parameters remained unchanged, mAb titer included, significant differences were found in maximum cell concentration, 10–45% higher in conditions with lower values of *kLa* and P/V. Changes in glucose metabolism contributing to *qP* were only shown in the higher producer cell line. Non-lethal responses to elevated oxygen transfer and shear stress might be present and must be considered when evaluating CHO cell cultures in shake flasks.

Keywords: CHO cells, specific productivity, metabolism, mass transfer, power input, shake flasks