SCALABILITY OF CO_2 STRIPPING EFFICIENCY FROM BENCH (3 L) TO PILOT SCALE (200 L) FOR SUPPORTING INTENSIFIED BIOPROCESSES

Samantha Whitney, Merck
samantha.whitney@milliporesigma.com
Marisa Maher, Merck
Amy Wood, Merck

Key Words: CO_2 stripping, scalability, bioreactor intensification

Intensified bioprocesses are being developed to increase productivity and product yield while reducing facility footprint, production costs and timelines for biologics manufacturing. The higher cell densities generated by intensification result in increased oxygenation requirements and CO_2 generation for a given process. In addition, at larger scales, the increased bubble residence time and lower ratio of volume to liquid-headspace surface area can cause challenges with CO_2 accumulation, making consistent scale-up difficult.[1] Maintaining appropriate CO_2 levels throughout a process is critical for control of pH and can have negative effects on cell growth and product quality if levels deviate from physiological conditions. In one reported study, there was a 40% reduction in specific productivity correlated to increasing levels of CO_2 from scale-up of bench to pilot scale systems.[2] These findings demonstrate the need to appropriately understand and manage sparging activities, for both oxygenation and CO_2 stripping to achieve optimal productivity and product quality during scale-up. The aim of this work was to investigate CO_2 stripping efficiency from bench to 200 L scale systems, in efforts to understand parameters affecting CO_2 stripping capacity and trends for intensified bioprocesses. Influences of buffer, power input and gas flow rate were investigated at bench scale within a Mobius® 3 L Single-use Bioreactor for micro and open pipe spargers. Pilot scale studies were completed in a 200 L bioreactor with drilled hole and open pipe spargers, for comparison to the bench scale results. CO_2 removal rate (%/hr) was calculated within a 5 – 10% CO_2 range to represent typical cell culture limitations for understanding of stripping capabilities. In addition, volumetric mass transfer (kLa) was determined using the static gassing out method for both N_2 and CO_2 saturated solutions to compare with industry reported values. The ratio of N_2 kLa to CO_2 kLa was determined to assess the spargers stripping efficiency for the two gasses and relate the values for oxygenation and CO_2 stripping capacity. With this work, bench and 200 L results for each sparger type provide understanding on CO_2 trends during scale-up.

References:

(1) Sieblist C, Hägeholz O, Aehle M, Jenzsch M, Pohlscheidt M, Lübbert A. Insights into large-scale cell-culture reactors: II. Gas-phase mixing and CO_2 stripping. Biotechnol J. 2011 Dec;6(12):1547-56. doi: 10.1002/biot.201100153. Epub 2011 Sep 13. PMID: 21818861.
(2) Mostafa SS, Gu X. Strategies for improved dCO2 removal in large-scale fed-batch cultures. Biotechnol Prog. 2003 Jan-Feb;19(1):45-51. doi: 10.1021/bp0256263. PMID: 12573005.