CHARACTERIZATION OF A SINGLE-USE STIRRED-TANK BIOREACTOR VESSEL FOR MICROCARRIER-BASED ADHERENT CELL CULTURE PROCESSES USING EXPERIMENTAL AND COMPUTATIONAL FLUID DYNAMICS STUDIES

Marco C. Rotondi, Aston University, UK
m.rotondi@aston.ac.uk
Alvin W. Nienow, University of Birmingham, Aston University
John Betts, Sartorius Royston UK
Neil Bargh, Sartorius Royston UK
Ned Grace, Sartorius Royston UK
Christopher J. Hewitt, Aston University
Qasim A. Rafiq, Aston University, UK

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Renewed interest in microcarrier-based processes for the large-scale culture of adherent cells for vaccine and cell therapy applications drives the need for effective, high-throughput, single-use, process development tools that can be translated successfully into industrial-scale systems. The automated ambr250® platform is one such technology, operating at a volume between 100 – 250mL and which is both high-throughput and single-use. The ambr250 has demonstrated significant success for suspension-based mammalian cell culture applications. However, no studies have been reported investigating microcarrier-based processes for the culture of adherent cells.

With any cell culture process, the fluid dynamics characteristics of the bioreactor must be sufficiently well understood to enable successful scale-up to larger scale bioreactors. With microcarriers, there is an additional challenge as the fluid dynamics must take into account the presence of the particulate solid phase. A critical aspect for cell cultivation on microcarriers is the minimum agitator speed required to achieve complete microcarrier suspension, N_{JS}. Under these conditions, the surface area of the attached cells is available for transfer of nutrients (including oxygen) to the cells and metabolites from them, whilst higher speeds hardly increase these transport processes and may lead to damaging fluid dynamic stresses being generated[1]. This suspension condition can be studied experimentally if equipment is specially modified to make easy visual observation of the two-phase flow in the bioreactor which during actual culture is very difficult. Therefore, it is extremely beneficial to both measure N_{JS} and then to compare the measured values with predictions based on computational fluid dynamics (CFD) in order to validate the latter. Once validated, CFD modelling is a very useful tool for analysing flow patterns, mixing time, mean and local specific energy dissipation rates and other parameters important for scale up in order to optimise the overall bioreactor geometry.

In addition to the above fluid dynamic aspects, cell culture studies was also performed in parallel to analyse the cell growth at and around the minimum speed for microcarrrier suspension, N_{JS} and the results were compared to the culture performance in well-characterised traditional spinner flask bioreactors[2].The CFD and experimental results with the single-use ambr250 bioreactor will be discussed in detail along with their scale-up implications.

References

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