APPRAISAL OF MICROCARRIER SUSPENSION DYNAMICS IN SHAKEN BIOREACTORS

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The pharmaceutical industry is at the forefront of the production of drug products using mammalian cell-based cultures, some of which rely on adherent-dependant cells. Whilst often adapted to suspension cultures, hybridoma and other cells give increased product yields when cultured attached to a substrate, such as microcarriers, resulting in smaller fermentation runs at higher densities. Microcarriers are also used in tissue engineering and cell for therapy culture. Stem cells are adherent-dependant cells and traditional 2-dimensional static cultures rely on disposable multilayer vessels, which have become the common route for stem cell expansion, although remain labour and handling intensive. Large scale production of stem cells would require the use of 3-dimensional dynamic culture methods by employing microcarrier technology, as demonstrated by Frauenschuh et al. (2007). Microcarriers consist of spherical beads with a size of 100-300 μm, and can be made of a wide variety of materials, some of them biodegradeable.

Whilst most studies have focused on investigating optimal compositions of microcarrier materials, their concentration and cell culture media, little research has been undertaken on the engineering aspects of microcarrier use, such as the just-suspended speed and suspension quality. The aim of the work is to characterize the suspension dynamics of microcarriers in a cylindrical orbitally shaken bioreactor (OSR) with conical bottoms of different heights. The proposed conical bottom geometry has been proven to provide enhanced vorticity when compare to a flat bottom vessel (2). This study builds upon previous works of the research group 3-6) for a flat bottom reactor, where increases in Froude number were found to determine a mean flow transition which was found to be instrumental in determining the just-suspended speed.

The dynamics of solid suspension is studied using commercially available Cytodex-3, stained with trypan for improved visual contrast. Image acquisition and computer image processing is employed to objectively measure suspension. The experimental procedure allows estimating not only the speed required for the solids to lift from the vessel bottom, but also the conditions at which a homogenous distribution of microcarriers is obtained. Preliminary results indicate that the presence of the conical bottom improves solid suspension by requiring lower agitation rates for the microcarriers to lift from the bottom completely. The critical Froude, which determines the flow type controlling the bioreactor, can be used to scale the suspension of microcarriers in OSRs. The suspension results are corroborated by mixing time measurements performed using the Dual Indicator System for Mixing Time (4), which show enhanced global mixing times when a conical bottom geometry is employed.

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