Short Communication Rapports De Pharmacie Vol.2 (2), 2016, 268-269
ISSN: 2455-0507

A SHORT COMMUNICATION ON THE AGITATION REQUIREMENTS FOR MAMMALIAN CELL CULTURES IN BIOREACTORS

P. Vasanth Raj
Faculty of Pharmacy, AIMST University, Semeling, Kedah, Malaysia 08100

The function of the fermentor or bioreactor is to provide a suitable environment in which an organism or cells can efficiently produce a target product [1]. The target product can be cell biomass, metabolite or a bioconversion product. The bioreactor should be designed in such a way that it is able to provide the optimum environmental conditions for supporting the growth of the microorganisms or cells [1,2]. Some of the essential parameters to be considered before designing the bioreactor are the agitation speed, the aeration rate, the heating intensity or cooling rate, the nutrients feeding rate, acid or base valve [3, 4]. Precise environmental control is of considerable interest in fermentations [5]. This short communication is focused towards giving some insight about agitation and aeration requirements for mammalian cell cultures using fermentor.

Agitators are one of the important components in the design of bioreactor. The main objective of using agitators is to achieve fluid-gas phase mixing, air dispersion, oxygen and heat transfer, maintain uniformity of suspended particles and enhancement of mass transfer between dispersed phases[3]. Disc turbines, vaned discs, open turbines are some of the most commonly used agitators in the design of bioreactors [6]. Disc turbine is most suitable in a fermentor since it can break up a fast air stream without itself becoming flooded in air bubbles. Air from the sparger hits the base of the disc and is displaced towards the vanes where the air bubbles are broken up into smaller bubbles [1]. While successful for microbial cultures, one of major drawback of the above mentioned agitators are that they are not suitable for sensitive cultures like animal cell culture [7]. Agitation and aeration requirements for mammalian cell cultures are very different from those for microbial culture. Oxygen transfer rate requirements are very much lower, but the cells are much more easily damaged by fluid mechanical forces generated by impellers or collapsing gas bubbles [8]. In most cases, the impeller must provide enough mixing to keep the cells or micro carriers suspended homogenously while creating as little fluid force as possible. A few, including marine propellers, have worked well under specific conditions up to several thousand liters, but most simply are not suitable for viable application. The impeller, termed as elephant ear is satisfactorily used in tissue culture vessels up to 500 L, provides sufficient mixing and oxygen transfer rate, with little or no cell damage [9]. Magnetic drives can also be used in animal cell culture vessels but are quite expensive. Added, baffles can also cause shear damage. Baffles can be substituted with bottom drive axial impellers when using mammalian cell cultures [10].

The agitation of cell cultures is difficult because the large mechanically sensitive eukaryotic cells can be damaged by the cutting edges of any stirrer. New softest agitation methods have been developed exclusively for bioreactors using cell cultures. A special ‘fish-tail’ stirring disc based on the principle of the tail of a fish has been developed. The up and down movement of one or more ‘fish-tail’ stirring discs provides gentle mixing both in horizontal and vertical way. At the same time this type of stirring is more efficient and it reduces cutting edges and micro-eddies formation on all common impellers used in bioreactors [11]. As an outcome, the cell viability is improved. In similarity to a fish tail, this form of the stirring disc creates a long range movement of the liquid (culture medium). No other stirrer type provides a similar positive blend of advantages for the agitation in cell cultures. Thus, with the ‘Fish-Tail’ stirring disks cell cultures with sensitive cells can be well aerated without damaging the cells. Thus the appropriate choice of agitation devices will make sure not to damage the cells and to have better product yield.

REFERENCES

[1] PF Stanbury, A Whitaker and SJ Hall. Principles of fermentation technology, 2005. Second edition, PP 167-209. Elsevier India Pvt Ltd, New Delhi.

[2] J Wu, MR Rostami, DP Cadavid Olaya, ES Tzanakakis. Oxygen transport and stem cell aggregation in stirred-suspension bioreactor cultures. *PLoS One*, 9(7):e102486 (2014).

[3] C Fenge, C Klein, C Heuer, U Siegel, E Fraune. Agitation, aeration and perfusion modules for cell culture bioreactors. *Cytotechnology*, 11(3): 233-44 (1993).

[4] FR Schmidt. Optimization and scale up of industrial fermentation processes. *Appl Microbiol Biotechnol*, 68 (4): 425-35 (2005).

[5] S Zhang, X Cao, J Chu, J Qian, Y Zhuang. Bioreactors bioseparation. *Adv Biochem Eng Biotechnol*, 122: 105-50 (2010).

[6] H Zhang, W Wang, C Quan, S Fan. Engineering considerations for process development in mammalian cell cultivation. *Curr Pharma Biotechnol*, 11(1): 102-12 (2010).

[7] Z Xing, BM Kenty, ZJ Li, SS Lee. Scale-up analysis for a CHO cell culture process in large-scale bioreactors. *Biotechnol Bioeng*,103(4): 733-46 (2009).

[8] A Koynov, G Tryggvason, JG Khinast. Characterization of the localized hydrodynamic shear forces and dissolved oxygen distribution in sparged bioreactors. *Biotechnol Bioeng*, 97(2): 317-31(2007).

[9] D Wang, W Liu, B Han, R Xu. The bioreactor: a powerful tool for large-scale culture of animal cells. *Curr Pharma Biotechnol*, 69(5): 397-403 (2005).

[10] CA Rodrigues, TG Fernandes, MM Diogo, CL da Silva, JM Cabral. Stem cell cultivation in bioreactor. *Biotechnol Adv*, 29(6): 815-29 (2011).

[11] MR Rostami, J Wu, ES Tzankakis. Inverse problem analysis of pluripotent stem cell aggregation dynamics in stirred-suspension cultures. *J Biotechnol*, 208:70 -9 (2015).