CULTIVATION OF INSECT CELLS IN AIRLIFT REACTORS: INFLUENCE OF REACTOR CONFIGURATION AND SUPERFICIAL GAS VELOCITY

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Abstract - Large-scale cultivation is an essential step towards the feasible production of baculovirus in insect cell cultures. Airlift reactors appear to offer considerable advantages over other insect cell culture systems. In order to evaluate the impact of reactor design on the behavior of insect cell cultures, the IPLB-Sf-21 cell line was cultivated in three different concentric tube airlift reactors that differ in their geometrical parameters. The ratio of downcomer to riser cross sectional areas, the shape of the bottom and the ratio of height to diameter of the reactor proved to be important since they produce significant differences on cell growth behavior. Modifying the reactor design the cellular growth rate could be improved from 0.016/h to 0.031/h, while the maximum viable cell density could be elevated from \(9 \times 10^5\) to \(2.4 \times 10^6\) cells/ml. Once selected a reactor configuration, the influence of gas flow rate was determined, finding an optimal value of superficial gas velocity that renders sufficient oxygenation without any significant effect on the cellular viability. In addition, the influence of the reactor design on fluid circulation in the reactor was tested.

Keywords: Insect cell culture, Airlift reactor, Geometrical parameters, Gas flow rate, Liquid velocity.

I. INTRODUCTION

Cultivation of insect cells on a large-scale is an important step towards the in vitro feasible production of entomopathogenic baculovirus used as bioinsecticides. Airlift reactors (ALR) appear to offer considerable advantages over other culture systems for the scale-up of insect cells propagation in suspension cultures (Maiorella et al, 1988; Merchuk, 1990; Shah et al, 1992).

The main aim in the engineering design of a bioreactor for this type of process is to maintain the shear generated in the equipment within the range permitted by the biological process, while reducing at the same time mass transfer limitations. This is possible in small size reactors, but is extremely difficult for large scale cultures. Airlift reactors present an advantage in this aspect. Since the driving force for liquid circulation is not provided by a focal input of energy, but by differences in local fluid density, the shear field is much more homogeneous and easier to set within the range required by the bioprocess.

Concentric tube ALRs can be designed to satisfy simultaneously the oxygen demand and the mildness of flow required for minimal cell damage. Published work on this subject has generally focused on the effect of both the ratio of cross-sectional area of riser to the downcomer (Bello, 1981; Chisti and Moo-Young, 1987), the height of the reactor (Merchuk et al, 1992), the gas-separation section at the top of the reactor (Siegel and Merchuk, 1987), and the design of the bottom section (Blenke, 1979). The evidences stress the importance of geometry in the performance of airlift reactors, since geometrical configuration has a direct effect on the fluid dynamics of the system (Merchuk et al, 1994a). Although the design of an ALR had been pointed out as an important factor to be taken into account (Shuler et al, 1990; Merchuk, 1994a; Merchuk, 1994b; Merchuk and Gluz, 1999), few specific papers are found in the literature that systematically consider the influence of the reactor geometry on the behavior of animal cell cultures in general, and insect cell cultures in particular. A major problem encountered in scaling up insect cell culture systems is the shear sensitivity of these cells (Tramper and Vlak, 1988). Gas flow rate is, in airlift reactors, a parameter closely related to shear, because fluid dynamics depends mainly on the gas flow rate (Merchuk and Berzin, 1995). In addition to the shear in the bulk of the liquid, the bursting of bubbles at the liquid-gas interface at the top of the ALR has been recognized as important cause of cellular death (Murhammer and Goochee, 1988; Tramper and Vlak, 1988; Wu, 1995). On the other hand, if the gas flow rate is too low, cells may fail to be in full suspension. Therefore, the gas flow rate becomes a critical parameter in order to optimize the culture of insect cells in ALRs.

In the present work we report a set of experiments that were carried out in ALRs of different geometry in order to study the influence of ALR design on the