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Supplemented Cell Culture Media: An Effective Approach for Enhanced Monoclonal Antibody Production

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EDITORIAL

Monoclonal antibodies (mAbs) are broadly used in medical research, therapeutics and diagnostics (Jorgensen *et al.,* 2007). mAbs are among the best-selling class of biopharmaceutics (Ho *et al.,* 2013). The in vitro hybridoma culture is an appropriate method for monoclonal antibody production using the culture supernatant (Falkenberg *et al.,* 1995; Sen and Roychoudhury, 2013). The production of recombinant therapeutic biologics in cell culture is a rapidly growing industry, creating many opportunities for bioprocess engineering research and development. To meet this increasing demand for therapeutic biologics, the primary goal of increasing the yield of bioprocesses, either by increasing maximum cell densities of cultures, or improving hybridoma cell culture that requires optimizing the nutrient medium in order to support cell growth, reduce cell death, and enhance mAb production (Kelley, 2009). Supplemental feeding of amino acids has proven effective for improving cell viability (Duval *et al.,* 1991) and protecting cells from apoptosis-induced death and nutrient deprivation (Ducommun *et al.,* 2001).

The cell line and its recombinant DNA construct, culture media, and process conditions are known to have a significant effect on the expression and stability of therapeutic products. Perhaps, the most important and crucial step in cell culture, however, is the selection of appropriate growth medium for *in vitro* cultivation (Zarei *et al.,* 2014). The cell culture medium provides an artificial environment conducive to survival and proliferation of cultured cells and maintains the desired pH and osmolality. The choice of cell culture media has been known to significantly affect the physiochemical characteristics of mAbs. The selection of the media depends on the type of cells to be cultured and also the purpose of the culture and resources. The complexity of composition of cell-culture media offers many challenges towards optimization of the individual media components. Synthetic or chemically defined media are prepared by adding defined concentration of nutrients (both organic and inorganic) such as vitamins, salts, traces elements, carbohydrates, and cofactors.

CHO are supplied largely in the form of glucose as a carbon source for the hybridoma cells. Besides glucose is the energy source and supplementation with glucose supports viable cells in extended stationary phase. In some cases, glucose is substituted with other sugars to improve cell growth, viability and protein production (Wilkens *et al.,* 2011). Many previous studies focused on glucose and glutamine feeding to progress a strategy for procuring improved cell performance (Glacken *et al.,* 1986). In numerous researches, glutamine supplementation did not stimulate cell proliferation (Geaugey *et al.,* 1989) or show a reasonable growth supportive effect (Franek, 1995).

In our study, four test media containing RPMI-1640, 10% FBS, and penicillin/streptomycin, supplemented with glucose (control), fructose, galactose and maltose at concentration of 15 mg/mL each as carbon sources were used for cell culture. Cells were cultured in a humidified atmosphere of 5% CO_2 at 37°C to optimize media components. Spleen cells were isolated from the immunized mice and mixed with Sp2/0 murine myeloma cells at ratio of 1:10 in presence of 1mL 50% PEG. Cell fusion and hybridoma culture procedures were carried out essentially following previous reports by limiting dilution (Ling *et al.,* 2014; Ling *et al.,* 2018; Ling *et al.,* 2015). The most effective culture medium for hybridoma clones was supplemented with maltose that achieved best titer as determined by icELISA. Viable hybridoma cell densities were increased when supplemented with maltose as compared to the control. The monoclonal antibody produced by using supplemented culture media was specific. Another study evaluated the use of maltose supplementation in the production of a recombinant monoclonal antibody, demonstrating improvements in recombinant monoclonal antibody titer (Leong *et al.,* 2018). Therefore, the use of supplemented cell culture media is an effective approach for enhanced production of monospecific-antibody, better hybridoma growth and viability.

CONFLICT OF INTEREST

All the authors have declared that no conflict of interest exists.

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