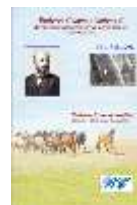




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## **Perfusion cultivation technology “Bevacizumab”**

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**Keywords:** cells, culture fluid, perfusion, column, bioreactor, seed material.

### **Abstract**

The article presents a comparative analysis of the main methods of industrial production of therapeutic proteins using the CHO cell expression system. Two well-studied cultivation technologies, Fed-batch and Perfusion, are compared to determine the feasibility of using the latter. The methods discussed in this paper are effective only when using disposable, sterile systems. The mechanism of action of the drug on the body is given, the sequence of all stages of cultivation, growth curves, types of bioreactors and a brief description of the technological process, the formula for calculating the seed material, the ATF perfusion column, through which the process is carried out, is described.

The article presents data on the viability of cells and their concentration at different stages, and indicates the critical points (DO-35%, temperature 37 °C, pH 7.00±0.2) that allow optimal cell growth. It is concluded that the use of perfusion technology intensifies the cultivation process, since the resulting concentration of cells at the stage of a 250-liter reactor accelerates further operating time in a 1000-liter bioreactor, due to the fact that re-sowing takes place at a higher concentration of cells, due to less dilution of the seed material. This fact will allow large-scale industries to use this type of equipment more often and meet the needs of the market. Perfusion significantly accelerates the cultivation process and, in principle, allows you to increase the seed material to a concentration of 108, unlike Fed-Batch technology, because there is no constant updating of the medium. Among the disadvantages of Perfusion technology, it should be noted that its implementation requires five times more nutrient medium than in Fed-Batch technology.

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## References

- [1] J. Liu. The History of Monoclonal Antibody Development - Progress, Remaining Challenges and Future Innovations. *Annals of Medicine and Surgery*. **2014**. 116p.
- [2] M. Campoli, R. Ferris, S. Ferrone, X. Wang. Immunotherapy of malignant disease with tumor antigen-specific monoclonal antibodies. *Clin Cancer Res*. **2010**. Vol.16. P.11-20.
- [3] S.S. Farid. Process economics of industrial monoclonal antibody manufacture. *B Analyt. Technol. Biomed. Life Sci*. **2007**. No.848. P.8-18.
- [4] J. Kim, G. Lee. CHO cells in biotechnology for production of recombinant proteins: current state and further potential. *Appl Microbiol Biotechnol*. **2012**. Vol.93. P.917-930.
- [5] D. Voisard, F. Meuwly, P.A. Ruffieux, G. Baer, A. Kadouri. Potential of cell retention techniques for large-scale high-density perfusion culture of suspended mammalian cells. *Biotechnol Bioeng*. **2003**. Vol.82. P.751-765.
- [6] K. Han, M. Sha. High-Density Vero Cell Perfusion Culture in BioBLU® 5p Single-Use Vessels. *Eppendorf Application Note*. **2017**. P.359.
- [7] F. Tapia, D. Vázquez-Ramírez, Y. Genzel, U. Reichl. Bioreactors for high cell density and continuous multi-stage cultivations: options for process intensification in cell culture-based viral vaccine production. *Appl. Microbiol. Biotechnol*. **2016**. Vol.100(5). P.2121-2132.
- [8] M.F. Clincke, et al. Very high density of CHO cells in perfusion by ATF or TFF in WAVE Bioreactor. Part I: Effect of the cell density on the process. *Biotechnol. Prog*. **2013**. Vol.29. P.754-767.
- [9] M.F. Clincke, et al. Very high density of Chinese Hamster ovary cells in perfusion by alternating tangential flow or tangential flow filtration in WAVE Bioreactor. Part II: Applications for antibody production and cryopreservation. *Biotechnol*. **2013**. Prog.29. P.768-777.
- [10] S. Xu, et al. Impact of Pluronic™ F68 on hollow fiber filter-based perfusion culture performance. *Bioprocess Biosyst. Eng*. **2017**. Vol.40. P.1317-1326.
- [11] Arseny M. Lyagin, Larisa M. Popova. Perfusion cultivation technology “Bevacizumab”. *Butlerov Communications*. **2021**. Vol.66. No.5. P.89-94. DOI: 10.37952/ROI-jbc-01/21-66-5-89 (Russian)