Mini Review

Pharmaceutical BIOPROCESSING

Development of Upstream Bioprocesses Using Vero Cells to Produce Viral Vectors and Vaccines

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Abstract

For the purpose of creating viral vectors and vaccines, the Vero cell line is thought to be the most often employed continuous cell line. It is the first cell line in history to receive WHO approval for use in the creation of human vaccines. The literature contains extensive experimental data on the generation of several viruses utilising the Vero cell line. However, the micro-carrier technology is used in the vast majority of these procedures. Although this technology has been developed for the mass production of viral vaccines, it is still quite labor-intensive and complicated. Additionally, scale-up is still challenging and is constrained by the carriers' provided surface area. It is crucial to continue to expand the Vero cell platform by utilising cutting-edge bioprocess technologies in order to get around these and other issues as well as to establish more effective manufacturing procedures. Advanced and scalable platform technologies could offer more effective and affordable ways to address the worldwide need for vaccines, particularly in situations like the present COVID-19 pandemic. In order to evaluate recent developments in bioprocess development, we analyse the current literature on Vero cell bioprocess development for the creation of viral vectors and vaccines in this article. By utilising recent advancements in the field of cell culture engineering, we critically highlight the necessity for additional research initiatives and outline obstacles to enhance the Vero cell platform [1-5].

Keywords: Bioreactor • Cell culture • Micro-carrier • Optimization • Process development • Suspension culture• Vaccines • Virus production

Introduction

The bioprocess is a specific procedure that uses fully functional living cells or some of their biological components to obtain desired goods. With the help of a biocatalyst, the process is utilised to make food, medications, flavours, energy, and synthetic mixtures. Cells of creatures, plants, or microbes in a bioreactor can act as a catalyst in bioprocessing. Vero cell lines are utilized in biological investigations less frequently than the more well-known HeLa cell line, in part because they are not human. However, Vero cell lines are still often employed for viral, bacterial toxin, and parasite research. Vero cells have the same properties as normal cells, including cell contact inhibition, since they are produced from healthy kidney cells rather than immortal cells like HeLa. Therefore, they must be passaged once they achieve confluence in the cell monolayer because otherwise, they would begin to deteriorate. Additionally, Vero cells have been employed in the creation and approval of methods like super resolution microscopy.

The spread of infectious diseases is thought to be most effectively prevented and controlled via vaccinations. Viruses are one of the primary causes of infectious disorders. The research and improvement of current vaccinations against viral infections, as well as the discovery of new vaccines, are currently of high international priority. Due to the trend of moving away from standard manufacturing tactics, such as production in chicken eggs or main cell lines, the cell culture-based production of viral vectors and vaccines is receiving more and more attention in this sector. The independence from the supply of chicken eggs and the reduction of cross-contamination or allergic responses are benefits of cell culture-based production methods. Additionally, processes can be more consistently carried out when specified and serum-free

cell culture medium are used. Additionally, cell cultures can be used in manufacturing procedures utilising bioreactors that are scalable, take up less space, and allow for the use of process analytical technologies to monitor production, control, and maintain the process within predetermined limits. Additionally, this enables faster manufacture, which is particularly advantageous during pandemics when vaccinations are urgently needed [6-8].

Discussion

Additionally, it covers heredity engineering for the management of microbes, plants, and animals. To remove debasements, mass volume reduction, and concomitant convergence of the ideal item from the bioreactor, downstream handling is necessary. Protein recovery is susceptible to environmental factors because it depends on the integrity of the delicate 3D tertiary structure for its functionality.

Bioprocessing in the upstream

- Upstream bioprocessing is the transformation of raw materials into a state suitable for use in a biologic manufacturing process.
- Examples of this include gathering and purifying natural resources, cultivating cells, and making recombinant proteins.
- The objective of upstream bioprocessing is to produce a superior starting material for downstream bioprocessing.

The upstream and downstream processes are the two main components of the cell culture-based virus manufacturing process. Cells are initially grown in order to produce enough substrate during the cell growth phase. To start the virus replication phase, the cells are next infected. The downstream procedure starts with harvesting the culture once virus production is finished and a virus concentration peak has been reached. This is usually followed by processes for clarity, virus inactivation, virus purification, and formulation of the finished product. From the perspective of upstream bioprocess development, the objective is to design a process with optimised viral productivity in order to lower the overall manufacturing cost. This leads to the guiding notion that more viruses can be created the more cells that are available as substrate. Additionally, maintaining the cells in the optimal physiological state for viral generation is the goal. As a result, the primary objective of upstream process development is to produce the greatest amount of cell material while keeping the cells at their peak virus productivity. This can be accomplished by maximising the period of infection (TOI), and process control is in charge of preserving ideal conditions vital to cell viability and proliferation [9].

The plant-based colchicine may have an impact on serious illnesses like cancer, gout, and cardiovascular problems. Colchicine is often obtained from Gloriosa superba seeds in medicinal preparations. The lack of viable upstream production, which includes all phases of biosynthesis and biomanufacturing before the raw material is suitable for purification, has raised the need for pharmaceutical-grade colchicine. In order to reduce medicine costs, it is crucial to create sustainable upstream industrial colchicine bio-factories. Using specialised bio-rhizomes and via particular enzymes, a new upstream bioprocess has been constructed, which catalyses the creation of biogenic functionalized intermediates that are then transformed into colchicine. The focus of this review is on a unique bio-rhizome method for producing pharmaceutical-grade natural colchicine, as well as the elucidation of a biosynthetic pathway and associated difficulties for synthetic biotechnology [10].

Conclusion

Utilising the Vero cell line, the industrialised micro-carrier technology offers a reliable platform for the production of viruses. To increase virus productivities, this platform must overcome a number of obstacles, though. Vero cell densities are still modest compared to bioprocesses using other animal cell lines and typically do not reach 107 cells/mL. The condition of Vero cells at large cell densities consequently needs to be studied more thoroughly. By creating the ideal environment for Vero cells to grow and produce viruses at high cell densities, new omics technologies like metabolomics, transcriptomics, and proteomics can help. Additionally, advanced feeding techniques are needed. Here, direct control through feeding or perfusion rate change in conjunction with online monitoring of substrate and metabolite concentrations can intensify processes.

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