Application of cell mass culture technique in biopharmaceuticals

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Abstract: as one of the most important contents in biopharmaceutical, cell culture in vitro is a necessary way. The in vitro culture of animal cells can not only effectively increase the quantity and quality of biological products, but also serve as a tool for testing new drugs. In view of the current development of large-scale cell culture technology, this paper makes an in-depth exploration and analysis of the characteristics of animal cells and the application status of animal cell technology, and makes an extensive study on its application in biopharmaceutical, aiming to put forward a scientific theoretical basis for the future production of biopharmaceutical.

1. Growth and development characteristics of animal cells

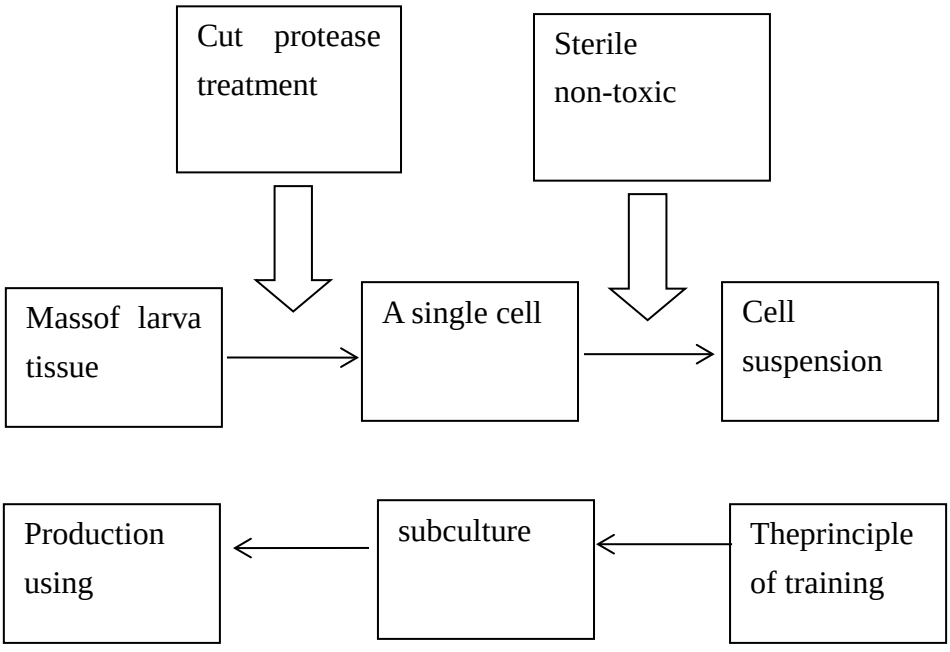

Figure 1 principle of in vitro culture of animal cells

In common with many microbial cells, animal cells can also be cultured on a large scale through artificial control and cultivation in the process of their own growth. However, compared with many microbial cells, animal cells are still different in their culture characteristics and internal structure. Generally speaking, first of all, animal cells occupy more space than microbial cells in terms of shape and volume. Therefore, animal cells are more difficult to operate manually and mechanically, and more sensitive to a series of operations such as cutting during cell culture. Compared with microbial cells, animal cells have less ability to adapt to the environment. Secondly, in the process of cell formation and growth, animal cells have a long growth cycle. In the slow growth process, they are often affected by microorganisms and other bacterial groups. Therefore, certain antibiotics are needed to improve their life cycle. In the end, is the animal cells in the process of cultivating and developing, need to add the right amount of oxygen, not only that, in the process of practical training and breeding, animal cells often way, such as cluster through touching each other for survival, general conditions, the survival of animal cell cycle, after 50 generations will head into

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degradation, and even death. Generally speaking, animal cells have better biological activity and metabolism capacity than other cell bodies. For the biopharmaceutical industry, scientific cultivation can effectively improve the added value of industrial products. In order to show the growth and breeding process of animal cells more clearly and intuitively, the principle of in vitro culture of animal cells is specially designed, as shown in figure 1.

2. Analysis of the development of large-scale cultivation technology

In the early 1960s, when large-scale culture techniques were being developed, researchers used animal cells to make biomolecules. The aim is to tackle a host of hard-to-cure conditions and improve human life by producing vaccines. With the continuous innovation and development of this technology, as well as the continuous maturity of transgenic technology, relevant studies have found that large-scale culture of animal cells can be used for the mass production of large-molecule medicinal proteins, and on the basis of systematic optimization of prokaryotic cells, there are more definite expression forms and advantages. Not only that, through the recombination of animal cells through DNA technology, a series of wiping pairs such as gene transport, processing, folding and assembly can be effectively realized, and then a new bacterial system dominated by inactive inclusion can be generated. Driven by the integration of market economy and business development, the creation of large scale perigenetic cells has led to the unprecedented development of large scale animal cell culture technology, and has gradually become a very important part of biopharmaceuticals.

3. Application research of large-scale cell culture technology

With the development of cell culture technology, many researchers in the industry began to discover its application value and significance. With the progress of science and technology and the development of economy, the industry began to pay more and more attention to the large-scale cell culture. In recent years, a large amount of manpower and material resources have been invested in the research, and on the basis of accelerating the research speed, applied modification molecules with monoclonal antibodies and other glycoproteins have been obtained continuously. However, in the process of extracting and obtaining proteins with drug effects, the operation process and technical requirements are also very complex. Precise processing of glycosylated and folded molecules is required, a seemingly simple process that is difficult to perform in yeast and bacteria. Which is applied to the basic principle of support vector machine, namely

$$(\hbar_1, \lambda_1), (\hbar_2, \lambda_2), \ldots (\hbar_l, \lambda_l)$$

In order to measure the classifiers, Defines the loss function:

$$L\left(\lambda, f(\hbar)\right) = \begin{cases} 0 & \lambda = f(\hbar) \\ 1 & \lambda \neq f(\hbar) \end{cases}$$

Considering the expected value of the loss function, the risk function is defined.

$$R(w) = \int L\left(\lambda, f(\hbar, w)\right) dP(\hbar, \lambda)$$

It can eventually be applied to:

$$R(w) \leq R_{erm}(w) + \frac{\sqrt{h\left(\ln\left(\frac{2l}{h}\right)+1\right) - \ln\left(\frac{\eta}{4}\right)}}{l}$$

In this calculation, RVM simulation model is also used to calculate and measure glucose concentration, lactic acid concentration and cell concentration in cells. Corresponding results are obtained through calculation, as shown in Table 1 RVM soft measurement results analysis

Table 1 Analysis of RVM soft sensing results

Measurement object	Training time (S)	Relevance vector(RVS)	Mean square error (MSE)	Decision coefficient (R^2)
Glucose concentration	0.4566	5	0.036464	0.89875
Lactic acid concentration	0.4256	5	0.036182	0.89183
Cell density	0.4526	5	24.7935	0.87495

Therefore, in order to further simplify the operation, industry researchers have promoted animal cells to effectively secrete a large number of proteins with medicinal value through DNA recombination and hybrida and other related technologies, achieving a major breakthrough in industry research. Moreover, in the applied research process of large-scale cell culture technology, many fields and industries have made unprecedented breakthroughs under the influence of this technological value.

3.1 Research and application of monoclonal antibody

With the support of cell culture technology, monoclonal antibody has gradually become one of the important contents in the industry and medical industry, especially in the medical industry, which has a wide range of applications. Monoclonal antibody can not only provide effective physical treatment for patients through in vitro diagnosis, but also through in vivo imaging, to get to the root of the disease, providing more direct treatment basis for patients. As the demand for monoclonal antibodies continues to increase in the medical industry, industry researchers have begun to increase the magnitude of monoclonal antibodies in a more rational way. Related researchers, through the ascites tumor culture in rats and mice, the diversity of different monoclonal antibody production. For example, through automatic culture, a large number of monoclonal antibody products have been produced abroad and have been well promoted and applied. Subsequently, monoclonal antibody diagnostic reagents were successfully developed in different countries, and the serum-free culture medium was adopted, which greatly improved the application scope of monoclonal antibody. So far, monoclonal approaches have been able to provide effective assays for specific blood types, proteins, and different drugs and pathogens.

3.2 Vaccine research and application

As an important measure affecting human health in the development of society, vaccine has solved many difficult diseases for mankind in the continuous development of vaccine industry. In the early days of vaccine industry research and development, the main experimental research object of animal vaccine production. For example, through the rabbit artificial injection rabies virus way, to extract rabies vaccine, through domestic cream injection smallpox virus way, to extract smallpox vaccine and so on, are through the animal's own immune system resistance, through the way of virus production for vaccine extraction and culture. With the development and application of large-scale animal cell culture technology, as early as the 1950s, relevant researchers could conduct virus production and vaccine research through cell culture. In simple terms, the researchers place cells cultured in the reactor, the density of cells in the reactor to the corresponding demand, to carry on the different types of viruses targeted vaccination, which in turn will carry virus after inoculation of cells to the virus replication and quantitative, and finally, on this basis, work out corresponding virus vaccine.

In the related vaccine research, the data collection and processing should be comprehensive, and the application of environmental parameter measurement method can develop the development and breakthrough of large-scale cell culture technology, greatly reduce the utilization rate of

experimental animals, and increase and improve the production efficiency of vaccine. Finally, bhk-21 suspension culture model is obtained. In order to show the model more intuitively and clearly, the model is shown in the following part, as shown in figure 2 bhk-21 suspension culture model.

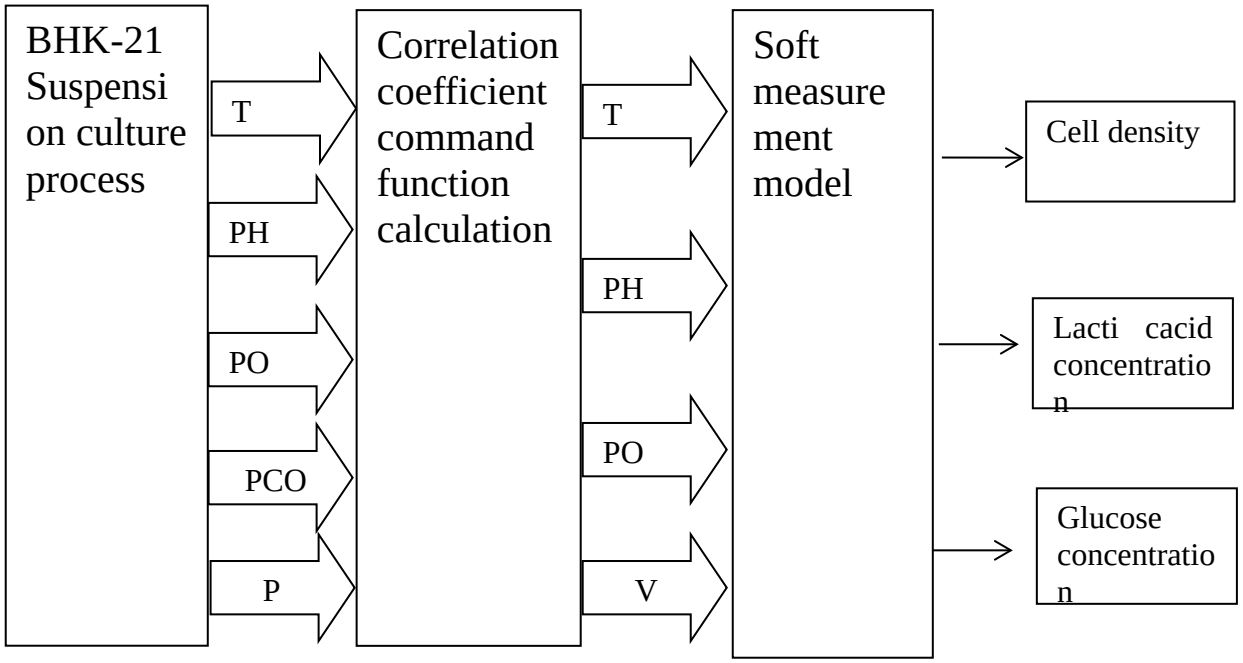

Fig. 2 BHK-21 suspension culture model

The development and breakthrough of large-scale cell culture technology has greatly reduced the utilization rate of experimental animals and increased and improved the production efficiency of vaccines. On the other hand, since animal primary cells have corresponding reproductive capacity, it is necessary to increase the number of cells to improve the ability of cell reproduction and promote the development of vaccine industry. In vaccine research and application in the process, through the mass culture of animal cells, can make effective guarantee for the quality of the vaccine, not only that, through the study of cell of screening and examination, can effectively solve the traditional process of animal research, the existing differences between different individuals, and effectively reduce the pathogen infect animals itself.

In addition, large-scale cell culture technology can effectively secrete necessary target proteins, and develop cytokines, biological products and enzymes by extracting protein cell lines. However, before the emergence, discovery and application of gene technology, the extraction level of protein in cells was very low. However, the application of large-scale cell culture technology can effectively improve the amount of protein extraction and reduce the cost of protein extraction. Therefore, large-scale cell culture technology plays an increasingly important role in the field of vaccines.

4. Conclusion

With the progress and development of science, human beings have more possibilities for development. As a major breakthrough in the human research industry, large-scale cell culture technology not only provides a broader development prospect for the biopharmaceutical industry, but also provides an important guarantee for the promotion of different industries in the whole society. Therefore, in the future development of cell culture technology, industry researchers are still required to make continuous efforts to comprehensively promote the progress and innovation of culture technology. This is also the inevitable development trend and necessary development measures of China's biopharmaceutical industry in the future.

References

[1] Jianguo, Mei Xidong, zhuang ,Ying,zhang et al. Cell culture microcarriers and their applications in the field of biomedicine [J]. Biotechnology, 2017(05):103-108.

[2] TING,ZHANG.Study on the technology of expressing monoclonal antibody in mass culture of CHO cells [J]. Biochemistry, 2018, 4(06):133-134+137. (in Chinese with English Abstract)

[3] Chenrui,Fei Lei, Ma ,Jingxia, gao et al. Vero cell culture A/Shanghai/ cn02/2013 (H7N9)Va influenza virus suiTable conditions study [J]. Biotechnology communications, 2018, 29(06):62-66. (in Chinese with English Abstract)

[4] Alzouguli, Alzouguli,Zilin, Qiao et al. Advances in large-scale culture technology of animal cell bioreactor [J]. Gansu animal husbandry & veterinary science, 2018, 48(11):13-