

Growth of BHK-21 Cells

Objective

BHK 21 cells and Vero cells are the most commonly used cell for vaccine production. When used for this application, usually a cell strain adapted to grow in suspension is used. Cultured at 3 000 l volume cell yields of $2 \cdot 10^6$ cells/ml are achieved. Elimination of microcarriers decreases the cost for this large-scale operation. By using a strictly adherent culture system based on porous microcarriers several advantages can be gained. The most important is that perfusion systems easily can be used, that permits cell densities to be increased up to 10 times.

Culture conditions

Vessels: 50 ml spinners(Techne).

Microcarrier: 2 g/l CultiSpher-G prepared according to instructions.

Cell line: BHK 21(Syrian hamster kidney fibroblast, PHLS).

Agitation speed: 45 RPM.

Media: DME supplemented with 10% FBS, penicillin G(100 U/ml) and streptomycin(100 µg/ml). pH was controlled through CO₂ atmosphere for both media.

Results

BHK cells attached and grew efficiently on CultiSpher-G. At maximum growth rate the doubling time was 10 hours. After 8 days of growth the cell concentration was $6.1 \cdot 10^6$ cells/ml which corresponds to an a yield of $30 \cdot 10^8$ cells/g dry CultiSpher-G. The growth span was 40 times.

Discussion

BHK 21 cells are one of the few cell lines that can be grown both in suspension as well as anchorage dependent. Both culture systems offers distinct advantages. Suspension cultures are very easy to scale-up and there is no need to dislodge the cells for subculture. The main difficulty is media exchange and adaption to perfusion systems. Cell metabolism is also affected by the cell morphology. Recombinant CHO cells have been reported to have a 10 times lower specific productivity. These differences make microcarrier culture an attractive alternative. CultiSpher-G eliminates the major difficulties associated with microcarrier culture, scale-up difficulties and low harvest yields. The large growth span obtained through macroporosity makes it possible to use scale-up steps of more than 50 times. As CultiSpher-G is based on highly purified gelatin, enzymes that are very specific can be used for harvesting. This results in high cell yield with almost 100% viability.

