Percell
BIOLYTICA

Effect of Microcarrier Concentration on Cell Yield

Objective

If all other components,like for instance oxygen and nutrients, are provided in excess the final cell yield in a microcarrier culture will be proportional to microcarrier concentration. This application note describes a simple series of experiments to determine the optimum concentration of CultiSpher in a given system.

Culture conditions

Vessel: 50 ml spinner(Techne).
Microcarrier: CultiSpher-G, prepared according to instructions.
Microcarrier concentration: CultiSpher-G was used at concentrations of 0.5, 1.0 and 4 g/l.
Cell line: CHO-K1(PHLS).
Agitation speed: 45 RPM.
Media: DME supplemented with 10% FBS, penicillin G(100 U/ml) and streptomycin(100µg/ml). 80% of the medium was exchanged daily starting from day 3. pH was controlled by CO_2 atmosphere(5%).

Results

When the microcarrier concentration was increased by a factor of 8, the concentration of cells only increased by a factor of 1.6, figure 1. This clearly shows that at higher microcarrier concentrations the culture is limited by other factors. If the number of cells on each microcarrier is calculated for the serie at different times a marked difference is found, figure 2. Number of cells on each microcarrier range from 250 at 4 g/l and almost 2000 at 0.5 g/l of CultiSpher-G.

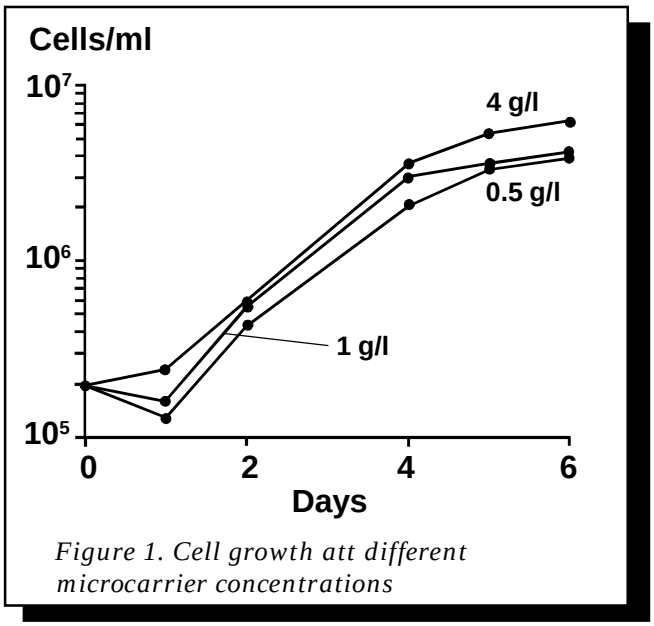

Figure 1. Cell growth att different microcarrier concentrations

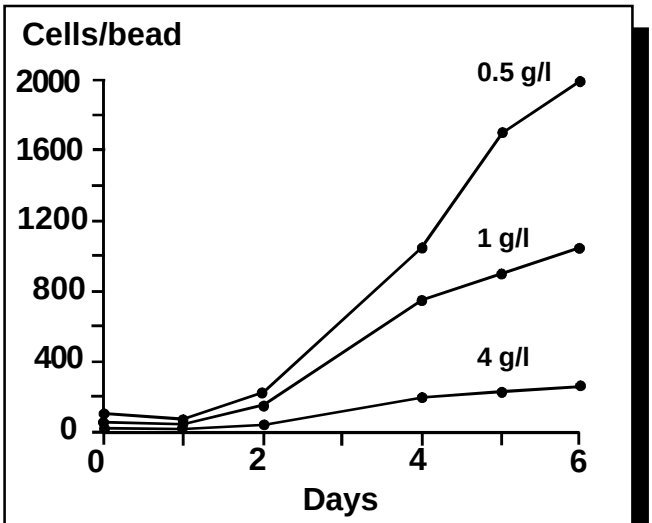

Figure 2. Number of cells on each microcarrier

Discussion

Increasing the concentration of CultiSpher-G results in in a larger available surface area by increasing the number of beads. It is not necessary to supply surface area in excess of that needed for the number of cells the system can supply with nutrients and oxygen. Figure 2 clearly shows that the number of cells on each microcarrier decreases when the concentration of CultiSpher-G increases. The cells will only grow on the outer parts of CultiSpher-G when the culture is limited. This is caused by the naturally formed gradients inside CultiSpher-G under limiting conditions. Our recommendation is to use CultiSpher-G at a concentration of 1 g/l. The available surface area will then under optimized conditions sustain cell concentrations between $5\text{-}10 \cdot 10^6$ cells/ml.
The higher attachment efficiency at 4 g/l as compared to 0.5 g/l is caused by a larger number of beads. The probability that a cell will interact with a bead is directly proportional to the bead concentration. We therefore recommend that cultures be inoculated in a reduced media volume.

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