NOVEL AMINO ACID FEEDING STRATEGY IN PERFUSION CULTURES TO ENHANCE MONOCLONAL ANTIBODY PRODUCTION

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Amino acids represent an essential source of nutrients in all the cell culture media. The concentration of each individual amino acid in the media has a huge impact on the performance of the cell culture. Traditionally, their concentrations in commercially available basal media have been determined in laborious studies using batch and fed-batch experiments. Hence, the resulting amino acid composition in the culture media is optimized based on the metabolic requirements of a specific cell line in a batch process. These requirements are likely to be different when the cell line is changed and the medium is used in perfusion processes. In order to optimize the performance of a perfusion culture by means of increasing cell specific productivity, decreasing byproduct formation and minimizing the cell specific perfusion rate, we developed a screening procedure for different media with distinct amino acid compositions in pseudo-perfused spin tubes. The results obtained from a monoclonal antibody expressing CHO-K1 (GS) cell line in these media revealed significant differences in amino acid uptake rates, and led to diverse metabolic behaviors. Cell specific productivities varied in a range of 35 % and ammonium production was even completely ceased under certain conditions. The lactate production rates differed widely and was mostly influenced by the seed cell density. From the results of an initial screening we designed a modified medium to target the amino acid consumption to a desired metabolic state with maximized antibody productivity and minimized byproduct formation. The performance of the medium was assessed with a perfusion culture in an ATF bioreactor system, where the amino acid consumption was precisely controlled to the targeted value by the appropriate feeding of amino acids. This strategy can be potentially widely applied across various cell lines to define the optimum concentration of amino acids or other components in perfusion media.