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IMPROVEMENT OF CHO SPECIFIC PRODUCTIVITY USING AMINO ACID DERIVATIVES

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Industrial fed-batch cultivation of mammalian cells is used for the production of therapeutic proteins such as monoclonal antibodies. Besides medium ensuring initial growth, feeding is necessary to improve growth, viability and antibody production. Amino acids are key elements for the cellular metabolism but also for the quality of the recombinant protein produced. Several studies have already demonstrated the link between amino acid availability and sequence variants [1-3] or specific modifications like trisulfide bonds [4]. To avoid such modifications, the chemical modification of amino acids is an interesting alternative to modulate their overall solubility [5], stability or chemical reactivity.
In this study, we analyzed the beneficial effect of using amino acid derivatives in neutral pH feeds on CHO cell growth and specific productivity in small scale and bioreactor experiments. The mechanisms of extra- or intra-cellular amino acid metabolization were investigated as well as the interaction with other media or cellular components. Additionally, gene expression arrays and western blot analyses were used to decipher the mechanisms of increased productivity. Finally, LC-MS based methods were used to study the impact of the chemical modification on several IgG critical quality attributes.

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