

A big cheese in biotherapeutics: Lactoyl leucine and isoleucine are bioavailable alternatives for canonical amino acids in cell culture media

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Abstract

Increasing demands for protein-based therapeutics such as monoclonal antibodies, fusion proteins, bispecific molecules and antibody fragments require researchers to constantly find innovative solutions. To increase yields and decrease costs of next generation bioprocesses, highly concentrated cell culture media formulations are developed but often limited by the low solubility of amino acids such as tyrosine, cystine, leucine and isoleucine, in particular at physiological pH. This work sought to investigate highly soluble and bioavailable derivatives of leucine and isoleucine that are applicable for fed-batch processes. N-lactoyl-leucine and N-lactoyl-isoleucine sodium salts were tested in cell culture media and proved to be beneficial to increase the overall solubility of cell culture media formulations. These modified amino acids proved to be bioavailable for various Chinese hamster ovary (CHO) cells and were suitable for replacement of canonical amino acids in cell culture feeds. The quality of the final recombinant protein was studied in bioprocesses using the derivatives, and the mechanism of cleavage was investigated in CHO cells. Altogether, both N-lactoyl amino acids represent an advantageous alternative to canonical amino acids to develop highly concentrated cell culture media formulations to support next generation bioprocesses.

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