

DIPEPTIDES IN CELL CULTURE - TOOLS FOR PERFORMANCE INCREASE AND RISK REDUCTION

Christian Kessler, Evonik Nutrition and Care GmbH, Darmstadt, Germany

christian.kessler@evonik.com

Jessica Mueller-Albers, Evonik Nutrition and Care GmbH, Darmstadt, Germany

Key Words: Dipeptides, CHO, Productivity, Solubility, Risk Reduction

Supplying mammalian cells with certain amino acids can be challenging. These challenges range from chemically instable components like L-glutamine to barely soluble ones like L-tyrosine. Scientists in the parenteral nutrition space realized early that coupling the troublesome amino acid to another, forming a dipeptide, can be an elegant solution^{1,2}. In the field of cell culture, only glutamine-containing dipeptides have been established. L-alanyl-L-glutamine is the most common peptide, often sold under a variety of trade names, but there are more products with exciting properties that are not commonly used in the field. The study at hand summarizes screenings with two different CHO cell lines that measured the impact of replacing single amino acids with dipeptides. The dipeptides tackle two types of challenges: glutamine stability and solubility enhancement. For the first challenge, alternative glutamine peptides were investigated and compared to the current benchmark. It was found that while all of them offered chemical stability, the impact on cell growth, titer and metabolites were different. This was shown in both batch and fed-batch experiments. For the second challenge, L-tyrosine as well as other critical amino acids were coupled to solubility-increasing amino acids and tested for their capability to replace the free amino acids in a cell culture medium. Especially for a glycyl-L-tyrosine dipeptide, it could be shown that the peptide is utilized by the cells and overcomes the solubility challenge at neutral pH. This is of significant relevance to an industrial cell culture user, as the current solution to formulate a highly concentrated feed containing L-tyrosine is to use a high pH. That introduces a process risk, as a malfunction in process control can lead to a lost batch. Using a L-tyrosine containing dipeptide is shown to be an elegant solution to the challenge.

¹ Grimble, GK, Annu. Rev. Nutr. 1994; 14:419-47

² Fuerst, P, J Nutr. 2001 Sep;131(9 Suppl):2562S-8S