Screening for Component Diversity in CHO Cell Culture Media – Fast At-line Media Analysis with the REBEL

Background

Cell culture media (CCM) and feeding strategy optimization for bioprocess development is crucial, but time-consuming. Regardless of bioreactor type and scale, it is important to understand the starting materials (by fresh media analysis), as well as establish metabolite consumption and accumulation (by spent media analysis). Media can greatly influence product quality, such as glycosylation and protein charge variants[1]. However, when using commercially-sourced CCM, not knowing the medium composition hinders the correlation of process parameters to product quality. Screening a diverse set of CCM can expedite media selection for a specific cell line. At-line amino acid analysis can speed up the upfront media selection significantly.

Furthermore, performing rapid measurements of fresh basal and feed media for every lot or batch in storage ensures consistency in the cell culture process.

The Experiment

Amino acid components in nine commercially available chemically defined CCM optimized for Chinese Hamster Ovarian (CHO) cells were measured (Figure 1). None of the media tested contained glutamine. Samples were taken from freshly delivered media and diluted 100X prior to analysis. The concentrations reported by the REBEL™ were averaged across 20 replicates for each formulation. The error bars represent the standard deviation between the replicates.

Discussion

In this panel of CHO CCM, essential amino acids histidine, methionine, isoleucine, leucine, tryptophan and non-essential tyrosine, were present at very similar levels. Other amino acids like alanine were not present, or below the limit of detection, in certain formulations. The dipeptide cystine had a six-fold difference in concentration between formulations, whereas, for asparagine, the difference between the lowest and highest detected concentration was more than 80x. There was a 20x difference between the highest and lowest concentration for serine and more than 10x for arginine.

These large differences demonstrate the versatility of commercially available CHO CCM, which can be leveraged to find the best medium for a specific cell line. However, some amino acids may need to be supplemented with a specific feeding strategy for cells that require more than included in any basal media. This upfront information about a critical raw material enables well-informed decisions on medium selection and further correlation during optimization.

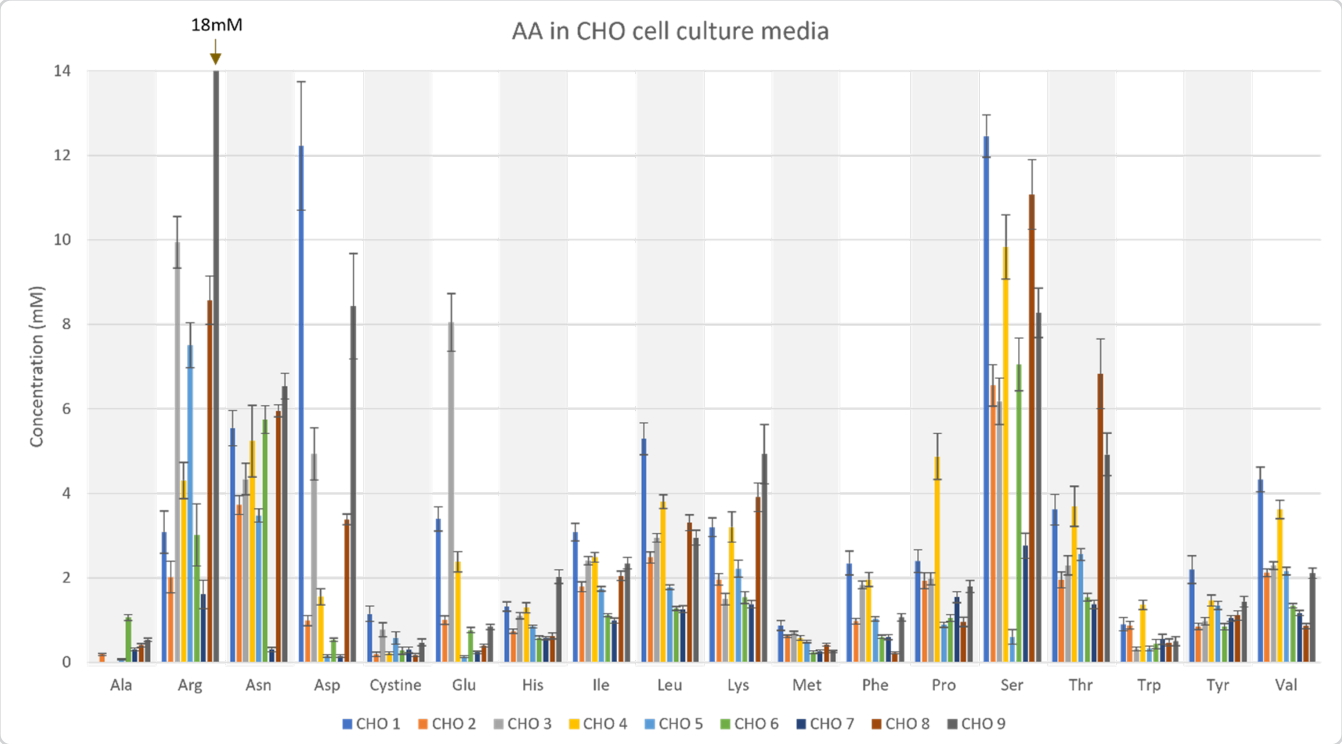

Figure 1. Nine chemically defined CHO- cell culture media were analyzed (20 replicates) with the REBEL at-line media analyzer. Asp, Ser and Arg showed the greatest concentration differences in this media panel.

Reference:

1. Ritacco FV, Wu Y, Khetan A. Cell culture media for recombinant protein expression in Chinese hamster ovary (CHO) cells: History, key components, and optimization strategies. *Biotechnol Prog.* 2018 Nov;34(6):1407-1426.