Impact of CHO Metabolism on Cell Growth and Protein Production: An Overview of Toxic and Inhibiting Metabolites and Nutrients

For over three decades, Chinese hamster ovary (CHO) cells have been the chosen expression platform for the production of therapeutic proteins with complex post-translational modifications. However, the metabolism of these cells is far from perfect and optimized, and requires substantial knowhow and process optimization and monitoring to perform efficiently. One of the main reasons for this is the production and accumulation of toxic and growth-inhibiting metabolites during culture. Lactate and ammonium are the most known, but many more have been identified. In this review, we present an overview of metabolites that deplete and accumulate throughout the course of cultivations with toxic and growth inhibitory effects to the cells. We further provide an overview of the CHO metabolism with emphasis to metabolic pathways of amino acids, glutathione (GSH), and related compounds which have growth-inhibiting and/or toxic effect on the cells. Additionally, we survey relevant publications which describe the applications of metabolomics as a powerful tool for revealing which reactions occur in the cell under certain conditions and identify growth-inhibiting and toxic metabolite. We also present a number of resources that describe the cellular mechanisms of CHO and are available on-line. Finally, we discuss the application of this knowledge for bioprocess and medium development and cell line engineering.

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