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Continuous optical in-line glucose monitoring and control in CHO cultures contributes to enhanced metabolic efficiency while maintaining darbepoetin alfa production quality

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Abstract:

Great efforts are directed towards improving productivity, consistency and quality of biopharmaceutical processes and products. One particular area is the development of new sensors for continuous monitoring of critical bioprocess parameters by using online or in-line monitoring systems. Recently, we developed a glucose biosensor applicable in single-use, in-line and long-term glucose monitoring in mammalian cell bioreactors. Now, we integrated this sensor in an automated glucose monitoring and feeding system capable of maintaining stable glucose levels, even at very low concentrations. We compared this fed-batch feedback system at both low (< 1 mM) and high (40 mM) glucose levels with traditional batch culture methods, focusing on glycosylation and glycation of the recombinant protein darbepoetin alfa (DPO) produced by a CHO cell line. We evaluated cell growth, metabolite and product concentration under different glucose feeding strategies and show that continuous feeding, even at low glucose levels, has no harmful effects on DPO quantity and quality. We conclude that our system is capable of tight glucose level control throughout extended bioprocesses and has the potential to improve performance where constant maintenance of glucose levels is critical.

Keywords: bioprocess monitoring, biosensors, cell culture, CHO cells, recombinant proteins