Baicalein reduces oxidative stress in CHO cell cultures and improves recombinant antibody productivity - DTU Orbit (13/10/2019)

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Oxidative stress that naturally accumulates in the endoplasmic reticulum (ER) as a result of mitochondrial energy metabolism and protein synthesis can disturb the ER function. Because ER has a responsibility on the protein synthesis and quality control of the secreted proteins, ER homeostasis has to be well maintained. When H2O2, an oxidative stress inducer, was added to recombinant Chinese hamster ovary (rCHO) cell cultures, it reduced cell growth, monoclonal antibody (mAb) production, and galactosylated form of mAb in a dose-dependent manner. To find an effective antioxidant for rCHO cell cultures, six antioxidants (hydroxyanisole, N-acetylcysteine, baicalein, berberine chloride, kaempferol, and apigenin) with various concentrations were examined individually as chemical additives to rCHO cell cultures producing mAb. Among these antioxidants, baicalein showed the best mAb production performance. Addition of baicalein significantly reduced the expression level of BiP and CHOP along with reduced reactive oxygen species level, suggesting oxidative stress accumulated in the cells can be relieved using baicalein. As a result, addition of baicalein in batch cultures resulted in 1.7 - 1.8-fold increase in the maximum mAb concentration (MMC), while maintaining the galactosylation of mAb. Likewise, addition of baicalein in fed-batch culture resulted in 1.6-fold increase in the MMC while maintaining the galactosylation of mAb. Taken together, the results obtained here demonstrate that baicalein is an effective antioxidant to increase mAb production in rCHO cells.

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