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## THE OXYGEN BINDING PROTEIN, HEMOXCell®, INCREASES CHO CELL GROWTH AND EXTENDS VIABILITY BY ENHANCING OXYGEN DELIVERY

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Most biopharmaceuticals are currently produced in animal cell cultures (e.g. CHO) due to their distinct capacity to perform the necessary post-translational modifications needed for glycoproteins such as antibodies. In the last decade the demand for these biopharmaceuticals has drastically increased to meet the demand of unmet medical needs. Hence various efforts have been made to increase the specific and volumetric productivity of cell cultures. One parameter that has shown an impact on cell growth and viability is the dissolved oxygen content in a culture. At high or low oxygen content the cell health can be affected. Hence an approach to continuously provide the right amount of oxygen to the cell would be favorable. This could be done by adding to the culture, a naturally polymerized biomaterial able to mimic the function of red blood cells in human - hemoglobin. HEMOXCell® produced by HEMARINA (Morlaix-France) is an oxygen carrier (molecule with high oxygen affinity) able to distribute oxygen according to the oxygen demand of the cells based on a PO<sub>2</sub> gradient. The HEMOXCell® molecule can load and unload oxygen and release it to the cells even in a low dO<sub>2</sub> environment (hypoxic conditions). In addition, the molecule has an intrinsic superoxide dismutase activity favorable for cell culture. In batch culture shake flask experiments using CHO cells the addition of 0.0025 g/L of HEMOXCell® resulted in a 1.3 – 1.9-fold increase in the maximum viable cell density in a variety of cell culture media. Furthermore, the addition of HEMOXCell® maintained the cultures at a higher viability compared to the control cultures. The resulting improvement in cell growth and production with the media additive could present in a change in the overall CHO cell metabolism. Any potential changes in the metabolism between these cultures are currently under investigation. Also, while an increase in volumetric productivity is desirable in biopharmaceutical production, it is also important to maintain the quality attributes (i.e. glycan profile) of the biopharmaceutical produced to maintain current production standards. Therefore, the glycan analysis for these cultures over time will be performed and glycosylation profiles will be compared. Overall, HEMOXCell® presents an excellent candidate in bubbling-free batch cultures or possibly in high cell density cell cultures (as e.g. perfusion mode) to compensate the lack of oxygen and increase cell density in a bioprocess while also extending viability.

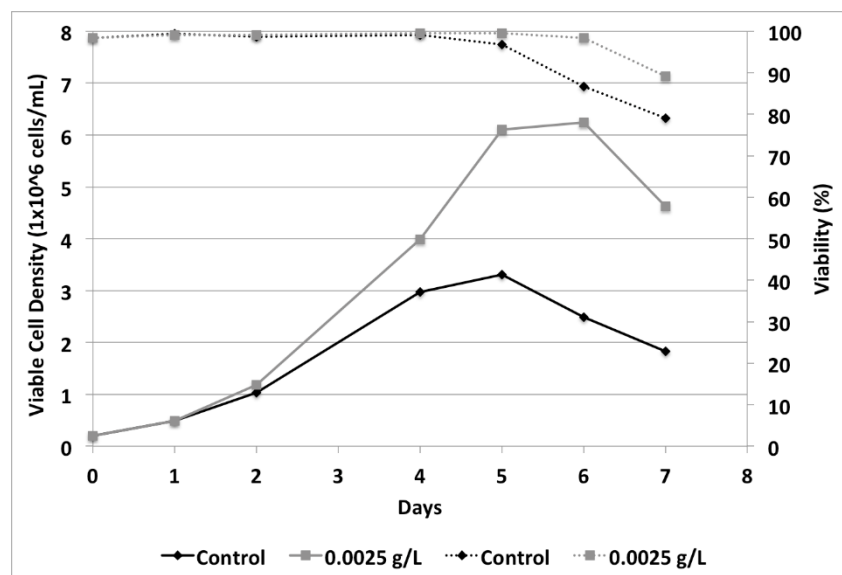


Figure 1 – Impact of the addition of HEMOXCell® at 0.0025 g/L on the viable cell density and viability in a shaker flask CHO culture.