Effect of hyperosmotic pressure on cell growth, productivity and activity of recombinant human Factor IX in Chinese hamster ovary (CHO) cells

Gue-Wha Lee, Murim Choi, In-hwan Lim, Yeup Yoon, Jung-Seob Kim
Mogam Biotechnology Research Institute, Yongin, South Korea
TEL: +82-31-260-9835, FAX: +82-31-260-9800

The human coagulation factor IX has several post-translational modifications for its proper functions when it is synthesized in human hepatocyte. The recombinant expression of human coagulation factor IX(rhFIX) in Chinese hamster ovary (CHO) cell has been complicated due to the presence of abnormally processed forms, mostly improper post-translational modifications. In CHO cells, the rate of production and intracelllualr processing of rhFIX seems to be influenced by the several factors including the cultivation conditions. Therefore, it has been challenging to maximize the production of rhFIX while minimize the contribution of immature FIX at the same time. In order to increase the productivity of rhFIX, we tested the various hyperosmotic conditions on CHO cell expressing rhFIX (CHO-rhFIX), growing at the serum-free suspension culture. The effect on the total amount of secreted rhFIX was not significant while the cell growth was inhibited at 456 mOsm/kg. Interestingly, the percentage of mature rhFIX was increased in hyperosmotic conditions. When the medium osmolality was increased to 350 mOsm/kg at culture day 3 of mid-log phase, the production of mature rhFIX was increased at 1.7-fold but the maximum cell number was decreased by 20%. In conclusion, CHO-rhFIX cell produce more properly processed mature rhFIX at hyperosmotic conditions suggesting that the controlled process using the precise osmolality control could improved the productivity and quality of rhFIX from CHO cells.

Reference

1. Moon Sue Lee, and Gyun Min Lee, Hyperosmotic pressure enhances immunoglobulin transcription rates and secretion rates of KR12H-2 transfectoma (2000), Biotechnol. Bioeng. 68(3), 260-268.