Optimization and Development of Recombinant Human Coagulation Factor VII Expression Level in Baby Hamster Kidney (BHK) Cell Culture

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Abstract

Recombinant factor VII (rFVII) was originally developed for the treatment of hemophilic patients. Lately, it has been used in non-hemophilic bleedings such as congenital FVII deficiency or in the case of trauma and surgery. Production of rFVII in sufficient quantity is a pre-requisite for treatment of patients with long life recurrent bleeding episodes. This study was conducted to evaluate recombinant human coagulation factor VII (rFVII) expression level by using adherent BHK cell culture in roller bottles. Perfusion cell culture process was performed. The impacts of different factors such as cell culture osmolality and protein hydrolysates and lipid supplementations were evaluated. Optimized harvest intervals were studied within 24, 48 and 72 hours. Moreover, according to cells' metabolic profile different feeding strategies were conducted by changing the volume and concentration of cell culture media. Protein titers were measured at constant osmolality of 450 mOsm/kg with different concentrations and volumes of cell culture media. The osmolality of the medium was changed by addition of ionized NaCl solution. Impact of various concentration of commercial ProCHO5 media on protein expression level was studied. The results demonstrated that the total protein content was the highest at 450mOsm/kg osmolality and protein expression in the medium showed a 37% increase through supplementation by hydrolysates and lipid due to maintaining cells' metabolic activity and an appropriate nutritional environment. Approximately attainment of 2-fold increase in rFVII titer in the medium with 450 mOsm/kg was observed, which was a drastic increase in comparison to the control group. The optimum harvesting schedule was found to be every 24 hours producing the highest total protein. Optimum concentrations and volumes were determined basically by consideration of economical requirements for large-scale productions for the goal of maximum protein production.