재조합 *Saccharomyces cerevisiae*를 이용한 enterokinase의 발효배양 최적화 및 scale-up 공정개발

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Abstract

Optimization and scale-up of recombinant enterokinase (rEK_L) fermentation process were performed with a recombinant *Saccharomyces cerevisiae* containing a bovine enterokinase gene. Firstly, media optimization for carbon and nitrogen sources was conducted with flask cultures. As a result, an enzyme yield of about 1.0 mg/L was obtained, which corresponds to about 100 times compared to that before optimization. We carried out batch fermentations in 5 L jar vessels. A maximum productivity was attained when the specific growth rate was 0.067 h^{-1}. The specific substrate consumption rate was 0.0086 g-galactose/g-cell · h. Continuous chemo-stats were performed in order to find major factors such as μ, q_p and q_s. The optimum feeding rate of galactose as an inducer was determined. When the dissolved oxygen tension was below 50%, ethyl alcohol was produced up to 2 g/L. Under these conditions the ratio of plasmid bearing cells was decreased to 20% whereas the production yield of rEK_L was seriously decreased to 1.5 mg/L. However the rEK_L production was dramatically increased up to 3.0 mg/L when the DOT was maintained at higher than 70% by control of aeration rate and agitation speed. Based on constant impeller tip speed, fermentation scale-ups were carried out in a 5 L jar to a 300 L pilot. A yield of 2.9 mg/L was attained in a 300 L pilot.

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