Enhanced production of periplasmic interferon alpha-2b by Escherichia coli using ion-exchange resin for in situ removal of acetate in the culture

Abstract

The possibility of using in situ addition of anion-exchange resin for the removal of acetate in the culture aimed at improving growth of E. coli and expression of periplasmic human interferon-α2b (PrIFN-α2b) was studied in shake flask culture and stirred tank bioreactor. Different types of anion-exchange resin were evaluated and the concentration of anion-exchange resin was optimized using response surface methodology. The addition of anion-exchange resins reduced acetate accumulation in the culture, which in turn, improved growth of E. coli and enhanced PrIFN-α2b expression. The presence of anion-exchange resins did not influence the physiology of the cells. The weak base anion-exchange resins, which have higher affinity towards acetate, yielded higher PrIFN-α2b expression as compared to strong anion-exchange resins. High concentrations of anion-exchange resin showed inhibitory effect towards growth of E. coli as well as the expression of PrIFN-α2b. The maximum yield of PrIFN-α2b in shake flask culture (501.8 μg/L) and stirred tank bioreactor (578.8 μg/L) was obtained at ion exchange resin (WA 30) concentration of 12.2 g/L. The production of PrIFN-α2b in stirred tank bioreactor with the addition of ion exchange resin was about 1.8-fold higher than that obtained in fermentation without ion exchange resin (318.4 μg/L).

Keyword: Acetic acid; Adsorption; Anion-exchange resins; Bioreactors; Fermentation; Periplasmic interferon-alpha2b