Enhanced Human Prolactin Synthesis by Sodium Butyrate Addition to Serum-Free CHO Cells Cultures

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Prolactin (PRL) is a 23 kD polypeptide hormone with a single chain of 199 aminoacid residues and it is a member of the family of hematopoietic cytokines. In humans, PRL is secreted by pituitary lactotrophs under hypothalamic regulation, and it is best known for its stimulation of lactation and its regulatory roles in the growth and differentiation of mammary gland and in reproduction. The gene of hPRL has been cloned and efficiently expressed in Chinese hamster ovary (CHO) cells in our laboratory, however for increasing its expression, sodium butyrate (NaBu) has been added to the culture medium. NaBu has been shown to alter the structure of chromatin in the nucleus by reducing the activity of histone deacetylase, resulting in enhanced protein expression. CHO cells cultures producing hPRL were thus subjected to treatment with different concentrations of NaBu (0.25 to 4 mM). Only 1 mM NaBu, however, showed a great increase in the expression of hPRL, with a quite small decrease in cell density and viability when compared with the untreated control. Analyses carried out by high performance size-exclusion chromatography and reversed-phase high performance liquid chromatography have thus confirmed a twofold increase in the concentration of hPRL in the presence of NaBu. The biological assay of purified hPRL was carried out using the Nb2 lymphoma cells assay and its activity in the presence of NaBu was found non significantly different when compared to the International Standard of hPRL (WHO 97/714). Our results show that NaBu increases ~ 100% the synthesis of recombinant hPRL, apparently not compromising its structure or function.

Keywords: *CHO, hormone, prolactin, protein, sodium butyrate*.

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