

Sodium butyrate greatly enhances human thyrotropin (hTSH) synthesis by serum-free
CHO cell culture, with alterations of the carbohydrate moiety

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The influence of sodium butyrate (NaBu) on the synthesis of recombinant human thyrotropin (r-hTSH) by CHO cells was investigated for the first time. A volumetric productivity of ~10 µg hTSH/mL, over a control culture with ~3 µg/mL was obtained, corresponding to a ~3-fold increase. Considering the growth arresting properties of NaBu, the difference in specific hTSH expression (µg/10⁶ cells/day) was even more dramatic: ~ 5-fold. It was thus postulated that this enhanced cellular synthesis could probably introduce a significant structural alteration of the carbohydrate moiety, which could influence the biological activity and, consequently, the physiological action of the hormone. Preliminary data have, in fact, shown an approximate 10% increase in total carbohydrate and sialylation. However, *in vivo* biological activity and pharmacokinetic behavior (plasmatic clearance) were found comparable for the two r-hTSH preparations, a matter that must be more deeply studied. Also charge isomers distribution, evaluated by isoelectric focusing (IEF), and hydrophobicity, evaluated by reversed-phase high performance liquid chromatography (RP-HPLC), were found similar for the two hormone preparations. These findings thus may provide a great increase in industrial productivity of this hormone, very utilized for the diagnosis and therapy of thyroid carcinoma, by simple NaBu addition to the culture medium, without any apparent loss of therapeutic efficacy.