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Comparison Between CHO-derived Thyrotropin Containing α2,6 Sialic Acid Linkages (hlsr-hTSH) and the Conventional Recombinant Product

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In this work two different recombinant thyrotropin (hTSH) preparations were compared for what concerns N-glican structures, biological activity and charge heterogeneity. One of them (hlsr-hTSH) was derived from a CHO cell line with a dual-sialic acid linkage introduction (61% of α2,3 and 39% of α2,6) which had been genetically modified by the introduction of rat α2,6-sialyltransferase cDNA. The other thyrotropin (r-hTSH) was derived from a conventional CHO cell line capable of expressing only α2,3 sialic acid linkages. Concerning the N-glycan structures both preparations presented complex structures (di-, tri- and tetra-antennary), sometimes fucosylated and with variable levels of sialylation. The most remarkable difference was the presence of ~16% more tetra- and ~8% more tri-sialylated structures in hlrs-hTSH than in r-hTSH. These differences, however, did not influence the biological activity. When hlsr-hTSH and r-hTSH were analyzed via an *in vivo* bioassay based on hTSH stimulation of thyroxin (T_4), hlrs-hTSH was shown to be equipotent with r-hTSH ($p < 0.05$). Concerning the distribution of charge isomers, when hlrs-hTSH and r-hTSH were evaluated by isoelectric focusing, no remarkable differences were observed. In both preparations, about six components with pI between 5.20 and 7.35 were found. In conclusion, the genetic modification in the carbohydrate moiety introduced in hlsr-hTSH does not seems to influence significantly the bioactivity and charge isomers distribution of this recombinant glycoprotein, although differences were observed in N-glycan structures and may exist in its pharmacokinetics.

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