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JOURNAL ARTICLE

Inhibition of 5 alpha-reductase activity and alteration of nuclear testosterone. Dihydrotestosterone ratio in human genital skin fibroblasts

G. D. Berkovitz, T. R. Brown and C. J. Migeon

17 beta-N, N-diethyl carbamoyl -4-methyl -4-aza-5 alpha-androstan-3-one (4-MA) inhibits 5 alpha-reductase activity in cultured human genital skin fibroblasts. Enzyme kinetic studies analyzed by Eadie-Hofstee plots demonstrated that 4-MA is a competitive inhibitor, with an apparent K_i of 15 nM. 4-MA had a very low binding affinity for the androgen receptor. When fibroblasts were incubated in the presence of testosterone (T) and 4-MA, nuclear uptake of 5 alpha-dihydrotestosterone (DHT) decreased in parallel with the inhibition of 5 alpha-reductase activity. While the overall sum for the nuclear uptake of T and DHT diminished, the nuclear uptake of T increased. Biological androgen inactivity cannot be precluded on the basis of nuclear T plus DHT uptake.

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