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Effects of the hypolipidemic drug WY-14643 on stearoyl-CoA and δ6-desaturase in HepG2 human hepatic cell line

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Background and Aims: Synthetic peroxisome proliferator-activated receptor alpha (PPARα) agonists are currently used in the clinic as lipid-lowering and anti-atherogenic drugs. The present study was designed to further explore the effect of PPARα agonist Wy-14643 on fatty acid metabolism of hepatocellular carcinoma cell line HepG2.
Methods: HepG2 cells cultured in RPMI-1640 were exposed to a range of concentrations [from 10-1.30 M (16 mg/L) up to 10-0.5 M (97 mg/L)] of the WY 14643, and investigated with respect to stearoyl-CoA (SCD1) and δ6-desaturase (δ6D) gene expression by RT-PCR and fatty acid composition by gas-liquid chromatography (GLC).
Results: WY 14643 induced both SCD1 and δ6D gene expression in vitro at a concentration as low as 10-1.30 M (16 mg/L; P=0.02). Exposure of cells to the PPARα agonist induced a time and dose-dependent increase in monounsaturated fatty acids (MUFA) and the δ6D index (20:4/18:2). Specifically, 10-0.5 M (97 mg/L) WY-14643 induced a significant increase of oleic acid (+26%; P=0.003) and 20:4/18:2 ratio (4-fold; *P*<0.001) in HepG2 cells.
Conclusions: The present study indicates that WY-14643 treatment of human hepatocytes induces SCD1 and δ6D mRNA, which is accompanied by modified cellular fatty acid composition. These data provide evidence for a lipogenic role of WY-14643 in hepatocytes. We hypothesize that therapeutic and pharmacological effects of PPARα agonists may involve actions on hepatic fatty acid metabolism.

Keywords:PPARα; WY-14643; SCD1; δ6-desaturase