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Metabolism of 32-Oxo-24,25-dihydrolanosterols by Partially Purified Cytochrome P-450_{14DM} from Rat Liver Microsomes

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Metabolism of 32-oxo-24,25-dihydrolanosterols (3 β -hydroxylanost-8-en-32-al (4, Δ^8 -CHO) and 3 β -hydroxylanost-7-en-32-al (5, Δ^7 -CHO)) was studied in a reconstituted system consisting of rat liver partially purified cytochrome P-450, which catalyzes lanosterol 14-demethylation (P-450_{14DM}), and NADPH-cytochrome P-450 reductase. The reconstituted system converted Δ^8 -CHO (4) to 4,4-dimethyl-5 α -cholesta-8,14-dien-3 β -ol (2, 8,14-Diene), which corresponds to the 14-deformylated product. Δ^7 -CHO (5), the isomer of Δ^8 -CHO (4), was not converted to the corresponding 14-deformylated product. The apparent K_m value of cytochrome P-450_{14DM} for Δ^8 -CHO (4) was about 1/20 of that for 24,25-dihydrolanosterol (1, DHL). The metabolism of Δ^8 -CHO (4) was inhibited by 7-oxo-24,25-dihydrolanosterol (6, 7-oxo-DHL), which is a potent inhibitor of cholesterol biosynthesis from lanosterol or DHL (1). However, the metabolism of Δ^8 -CHO (4) was less inhibited by 7-oxo-DHL (6) than that of DHL (1).

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