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Metabolism of 32-Hydroxylated 24,25-Dihydrolanosterols by Partially Purified Cytochrome P-450$_{14DM}$ from Rat Liver Microsome*

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Metabolism of 32-hydroxylated 24,25-dihydrolanosterols, including the intermediate of lanosterol and 24,25-dihydrolanosterol (DHL) demethylation, were 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 lanost-8-ene-3β,32-diol (Δ^8-32-OH) to 4,4-dimethyl-5α-cholesta-8,14-dien-3β-ol, the 14-dehydroxymethylated product, in the same way as DHL. Lanost-7-ene-3β,32-diol and lanost-6-ene-3β,32-diol, the isomers of Δ^8-32-OH, were not converted to the corresponding 14-dehydroxymethylated products. The apparent K_m value of P-450$_{14DM}$ for Δ^8-32-OH was about 1/6 of that for DHL. The metabolism of DHL was inhibited by 7-oxo-24,25-dihydrolanosterol (7-oxo-DHL), which is a potent inhibitor of cholesterol biosynthesis from lanosterol or DHL. However, the metabolism of Δ^8-32-OH was less inhibited by 7-oxo-DHL than that of DHL.

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