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Inhibitory Effect of 15-Oxygenated Sterols on Cholesterol Synthesis from 24, 25-Dihydrolanosterol*

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Several 15-oxygenated sterols were examined as to their inhibitory activity toward cholesterol synthesis from [24,25-³H]-24,25-dihydrolanosterol in the 10,000×g supernatant fraction of a rat liver homogenate (Table 1). At 40 μM, three 15α-hydroxylated compounds, 14α-ethylcholest-7-ene-3β,15α-diol, 14α-methylcholest-7-ene-3β,15α-diol, and lanost-7-ene-3β,15α-diol, were found to be extremely potent inhibitors (more than 90% inhibition) of dihydrolanosterol metabolism. The inhibitory effect of the C-15 substituents appears to be in the order of : 15α-hydroxyl > 15-ketone > 15β-hydroxyl.

Table I. Cholesterol biosynthesis during incubation of the S-10 fraction of a rat liver homogenate with [24,25-³H]-24,25-dihydrolanosterol in the presence of oxygenated sterols.

Compound	Distribution of radioactivity in		Inhibition (%)
	Dihydrolanosterol fr. (%)	Cholesterol fr. (%)	
None (Control)	32.0	31.2	—
Cholest-8(14)-ene-3β,15β-diol	32.1	29.7	5
Cholest-(14)-en-3β-ol-15-one	49.3	18.1	42
14α-Methylcholest-7-en-3β-ol-15-one	51.8	16.2	48
14α-Methylcholest-7-ene-3β,15α-diol	89.9	1.3	96
14α-Ethylcholest-7-en-3β-ol-15-one	66.3	8.8	72
14α-Ethylcholest-7-ene-3β,15α-diol	88.5	2.3	93
14α-Ethylcholest-7-ene-3β,15β-diol	63.1	10.0	68
Lanost-7-en-3β-ol-15-one	85.6	4.2	87
Lanost-7-ene-3β,15α-diol	88.5	1.2	96
Lanost-7-ene-3β,15β-diol	55.9	15.3	51
15ξ-Fluorolanost-7-en-3β-ol	59.4	12.3	61
Lanost-7-en-3β-ol	39.6	25.6	18

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