Enzyme Activity of the Cytochrome P-450 Monooxygenase System in the Presence of Single Chain Lipid Molecules

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The influence of single chain lipids on the 7-ethoxycoumarin O-deethyase activity of the reconstituted binary protein complex of isolated cytochrome P450 and NADPH-cytochrome P450 reductase has been examined. The enzyme activity of this binary enzyme complex has been shown to be influenced by (i) altering the complexation process of both proteins, (ii) by altering the catalytic cycle time of the active binary protein complex and (iii) by altering the fraction of substrate molecules at the catalytic center of the enzyme. Competitive inhibition was measured for all single chain molecules. The following dissociation coefficients of substrate and lipids used for the catalytic center of the protein were obtained: 110 μM 7-ethoxycoumarin (substrate), 1.1 μM MOG (1-monooleoyl-*rac*-glycerol), 0.3 μM SPH (D-sphingosine), 1.5 μM OA (oleic acid), 3.0 μM LPC (L-α-lysophosphatidyl-choline), 15.5 μM MSG (1-monostearoyl-*rac*-glycerol), 9.5 μM AA (arachidonic acid), 9.0 μM PaCar (palmitoyl-L-carnitine), 3.5 μM MPG (2-monopalmitoyl-glycerol), 1.5 μM LPI (L-α-lysophosphatidyl-inositol), 50 μM LA (lauric acid), 60 μM MA (myristic acid), 85 μM PA (palmitic acid), >100 μM SA (stearic acid). Only competitive inhibition with the substrate molecule 7-ethoxycoumarin was observed for the single chain lipids LA, MA, PA, SPH, SA, and OA. Non-competitive effects were observed for MPG ($-0.03\ \mu M^{-1}$), PaCar ($-0.02\ \mu M^{-1}$), MSG ($-0.023\ \mu M^{-1}$), LPC ($-0.03\ \mu M^{-1}$), AA ($-0.03\ \mu M^{-1}$), and MOG ($+0.04\ \mu M^{-1}$). The negative sign indicates that the cycle time of the working binary complex is enlarged. The positive sign indicates that the formation of the binary complex is enhanced by MOG.