

# Inhibition of Cytochrome P450 Mediated Enzyme Activity by Alkylphosphocholines

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The inhibitory potency of four alkylphospholipids: rac-1-O-phosphocholine-2-hydroxy-octadecane (rac-2-OH), rac-1-O-phosphocholine-2-O-acetyl-octadecane (rac-2-O-acetyl), rac-1-O-phosphocholine-2-amino-octadecane (rac-2-NH<sub>2</sub>) and rac-1-O-phosphocholine-2-N-acetyl-octadecane (rac-2-N-acetyl), on the cytochrome P450-dependent monooxygenase activity has been evaluated. The IC<sub>50</sub> values of the alkylphosphocholines with 7-ethoxycoumarin as substrate in liver microsomal fractions of PB-treated rats and with a reconstituted CYP2B1: NADPH-P450-reductase system are in the range of 3.2–5.0  $\mu\text{M}$  and 2.8–3.5  $\mu\text{M}$ , respectively. Lineweaver-Burk plots with the inhibitors in concentrations that were found to cause roughly a 50% inhibition and with 7-ethoxycoumarin as substrate revealed for all four alkylphospholipids a competitive inhibition type. The degree of the competitive inhibition is quantified by the  $K_i$  values. With liver microsomal fractions of PB-treated rats, the  $K_i$  values of rac-2-OH ( $K_i = 1.36 \mu\text{M}$ ) and rac-2-O-acetyl ( $K_i = 1.33 \mu\text{M}$ ) differs slightly from those of rac-2-NH<sub>2</sub> ( $K_i = 2.2 \mu\text{M}$ ) and rac-2-N-acetyl ( $K_i = 2.2 \mu\text{M}$ ), but with the reconstituted CYP2B1: NADPH-P450-reductase system all  $K_i$  values are in the small range of 1.8 – 2.6  $\mu\text{M}$ , indicating that the short substituted group at the 2-position (OH; O-acetyl; NH<sub>2</sub>; N-acetyl) of the long chain octadecanol part of the phosphodiester exhibit no essential role on the strong inhibitory potency of these alkylphosphocholines on the 7-ethoxycoumarin-O-deethylase activity.

**Key words:** Alkylphosphocholines, Competitive Inhibitors of Cytochrome P450 Activity, Single Chain Lipids