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The mechanism of the rat liver cytochrome P4502E1 inhibition by the synthetic prostanoids of A-type.

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AIM: The elucidation of mechanism of A-type synthetic prostanoids inhibitory action on microsomal cytochrome P(450)2E1 (CYP2E1) from rat liver activity was carried out. RESULTS: Analogs U-34 and U-26 in a final concentration of 1 x 10(-5)M inhibited CYP2E1 activity by 93% and 46%, respectively; however natural prostaglandins had no effect. These synthetic prostanoids of A-type (5 x 10(-8) to 10(-4)M) inhibited chlorzoxazone hydroxylation in a dose-dependent manner while IC(50)=7.1 x 10(-7)M and 8.0 x 10(-7)M for U-26 and U-34, respectively. The curves of CYP2E1 activity in the presence of different concentrations of chlorzoxazone and varying concentration of prostanoids were hyperbolic. Double-reciprocal plots of these results 1/V=f(1/S) indicated that prostanoids inhibit CYP2E1 through a competitive mechanism with particular effect. CONCLUSION: CYP2E1 is a target for A-type prostanoids, possessing 2-oxo-4-amino-oct-3(E)-enyl in alpha- or omega-chain, which are able to inhibit its action through a competitive mechanism.