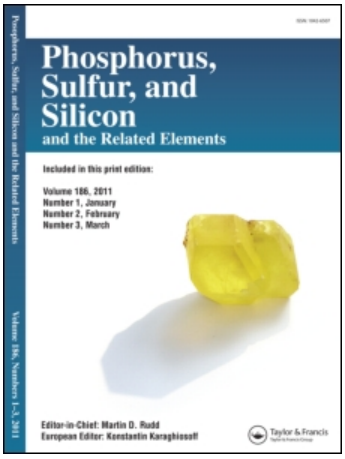

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INTERACTION OF DIALKYL(α-CARBOMETHOXY-β,β,β-TRIFLUOROETHYL) AND DIALKYL-S-CARBOETHOXYCHLOROMETHYLTHIOL PHOSPHATES WITH MAMMALIAN ESTERASES. ROLE OF ESTERASES IN TOXICITY MECHANISMS

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The interaction of insecticides $(RO)_2P(O)OCH(CF_3)COOCH_3$ (I) and $(RO)_2P(O)SCH(X)COOC_2H_5$ (X=Cl(II), Br(III); R=Me, Et, Pr, i-Pr, Bu, i-Bu, Am, Hex) with acetylcholinesterase (AChE), butyrylcholinesterase (BChE) and carboxylesterase (CE) was studied in connection with their role in organophosphate toxicity mechsnisms. Toxicity of I-III to mice was determined. I-III were not hydrolysed by CE and irreversibly inhibited all the enzymes, II, III had a greater inhibitory potency compared to I: lgk^{II}_{AChE} = 2-4 (I), 6 (II, III); lgk^{II}_{BChE} = 3-6 (I), 5-8 (II, III); lgk^{II}_{CE} = 3-7 (I), more than 8 (II, III). With multiple regression analysis the dependence of antienzymatic activity on hydrophobicity and steric properties of alkyl substituents was investigated. The contribution of the hydrophobic interactions to BChE and CE (enzymes-"sites of loss") inhibition was the same and more significant than that to AChE (target enzyme) inhibition. Steric effects are more important in AChE inhibition. The dependences $lg(1/LD_{50}) = f(\Sigma\Pi)$ for I-III were in great extent determined by binding with nonspecific esterases that rises with increasing hydrophobicity. These results indicate that nonspecific esterases CE and BChE play a buffer role in toxic action of I and especially II and III.