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## Phosphorus, Sulfur, and Silicon and the Related Elements

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# INTERACTION OF DIALKYL( $\alpha$ -CARBOMETHOXY- $\beta$ , $\beta$ , $\beta$ -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 mechanisms. 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:  $lgk_{AChE}^{II} = 2-4$  (I), 6 (II, III);  $lgk_{BChE}^{II} = 3-6$  (I), 5-8 (II, III);  $lgk_{CE}^{II} = 3-7$  (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.