1970 #8

DOES DDT INHIBIT CARBONIC ANHYDRASE?

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Birds of prey have been found to lay thin shelled eggs, a phenomenon which has been stated to be due to inhibition of carbonic anhydrase by DDT (Peakall, Science, 168:592, 1970, and Bitman, Cecil, and Fries, Science, 168:594, 1970). Keller (Naturwissenschaften, 39:109, 1952) had observed inhibition of bovine carbonic anhydrase by 50 μg/ml of DDT, in vitro, while Wistrand (cited by Maren, Physiol. Rev., 47:595, 1967) found no inhibition of dog enzyme, in amounts claimed by Keller. Anderson and March (Can. J. Zool. 34:68, 1956) were unable to detect any inhibition by DDT on insect carbonic anhydrase either in vivo or in vitro at concentrations up to 3,550 μg/ml. We examined again, in vitro, the question of whether DDT inhibits this enzyme. The matter is of much theoretical and practical importance, since carbonic anhydrase inhibitors clearly reduce the rate of calcium deposition in shell, both in birds and invertebrates (reviewed by Maren, Physiol. Rev., 47:595, 1967.

Carbonic anhydrase activity was analyzed by the method of Maren, Ash, and Bailey (Johns Hopkins Hosp. Bull., 95:244, 1956) which measures the catalytic hydration rate of CO_2. Master solutions of p,p'-DDT and p,p'-DDE were prepared in absolute ethanol or in N,N-dimethyl formamide (DMF). The final concentration of DDT and DDE in the reaction vessel was 50-85 μg/ml in 16% ethanol or 5% DMF. Concentrations greater than 50 μg/ml in the reaction mixture resulted in some precipitation of drug. Solutions were incubated with drug and enzyme (human red cell) up to three days at room temperature. No inhibition was observed.

The effect of DDT on semi-purified bovine carbonic anhydrase was examined using the method of Maetz (Bull. Soc. Chim. Biol. 38:447, 1956) which had also been used by Keller (see above). This method measures the catalytic dehydration rate of carbonic acid.

A number of solvents were used; DMF (2.5% in final solution) yielded the most reliable data. Inhibition progressed from 37 to 88% when the concentration of DDT increased from 500 to 2000 μg/ml. In these experiments there was also some precipitation of drug in the reaction mixture. However, the degree of inhibition observed at 500 μg/ml is relatively small and suggests that DDT may not inhibit carbonic anhydrase effectively at the usual tissue concentrations following ecological exposure.

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THE FATE OF ^{14}C-2,2-BIS (p-CHLOROPHENYL)-1,1,1-TRICHLOROETHANE (p,p'-DDT) IN *Squalus acanthias*

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We studied the pharmacology of p,p'-DDT in the dogfish, *Squalus acanthias*, with particular