

tion on the β position of pyridine it is evident that the presence of the carboxyl group decreases the toxicity of the molecule. Conversion of this group to the simple amide markedly increases toxicity; the presence of a substituted amide on this position increases the toxicity so that it exceeds that of the unsubstituted pyridine. The high toxicity of coramine suggests the necessity for caution in its administration.

Summary. The relative toxicity of subcutaneous injections of nicotinic acid, nico-

tinamide, coramine, pyridine and their respective methyl derivatives has been determined. Methylation decreases the toxicity of coramine and nicotinamide, increases the toxicity of pyridine and has little or no apparent influence on the toxicity of nicotinic acid. The toxicity of the non-methylated compounds appears to be due directly to the structure of the compounds rather than to the depletion of the body stores of methyl donors in the process of detoxication.

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Distribution of 2,2 (p-Chlorophenyl) 1,1,1 Trichlorethane (DDT) in Tissues of Rats after Its Ingestion.*

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The data for the distribution of DDT in tissues of experimental animals fed DDT are limited. Smith and Stohlmann^{1,2} analyzed blood, kidney, liver, central nervous-system and bile after acute and chronic poisoning in rabbits and cats by determining organic chloride. The highest DDT concentration was observed in the bile. Laug³ determined the DDT concentration in tissues of rats fed on diets containing small amounts of DDT for periods varying from 6 months to 2 years. By far, the greatest amount of DDT was found in perirenal fat. In spleen, liver and kidney, the amount of DDT stored appeared to be roughly proportionate to the amount of total ether extractable-material in these organs. Woodward⁴ studied the DDT concentrations in tissues of a chronically poisoned dog, monkey, pig and turkey. The highest concentration of DDT was found in fat; the

adrenals of the dog and the monkey contained appreciably larger amounts of DDT than the liver, kidney and brain.

The distribution of DDT in the brain, liver, kidney and adrenals of rats fed diets containing 0.1 and 0.2% DDT was determined at frequent intervals.

Methods. Inbred male rats of Wistar stock, 60 to 70 days old, and weighing 150-200 g were used as experimental animals. They were maintained on a stock diet until the experimental diet was fed. The diet contained 20% casein (Labco), 8% crisco, 4% inorganic salt,⁵ 65% sucrose, 2% agar, vitamin supplements and 0.1 or 0.2% DDT (M.P. 108.6-109.5°). The animals were fed *ad libitum* and were sacrificed at frequent intervals. After nembutal injection, the animals were exsanguinated and the tissues immediately removed for the DDT determination.

The tissues were prepared for analysis according to Ofner's⁶ recommendation and the

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¹ Smith, M. I., and Stohlmann, E. F., *Pub. Health Rep.*, 1944, **59**, 984.

² Smith, M. I., and Stohlmann, E. F., *Pub. Health Rep.*, 1945, **60**, 289.

³ Laug, E. P., personal communication.

⁴ Woodward, G., personal communication.

⁵ Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, 1913, **15**, 317.

⁶ OSRD Insect Control Committee, Report No. 65.

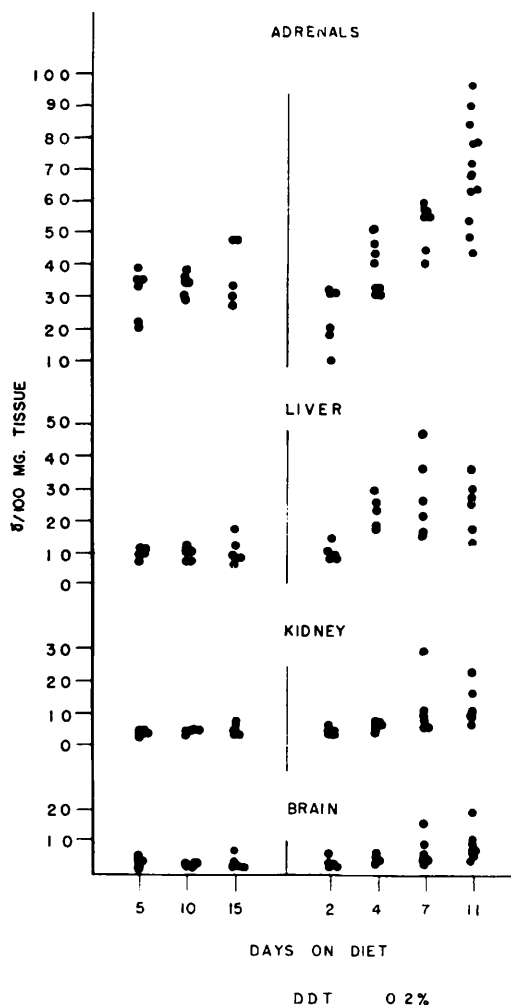


Fig. 1.

Distribution of DDT in brain, kidney, liver and adrenals of rats after ingesting diets containing 0.1 and 0.2% DDT.

DDT was determined by the Schechter-Haller⁷ colorimetric method. Both adrenals and aliquots of kidney, liver and brain extracts were used for analyses. The Evelyn

⁷ Schechter, M. S., Soloway, S. B., Hayes, R. A., and Haller, H. L., *Ind. and Eng. Chem., Analyt. Ed.*, 1945, **17**, 704.

photometer with filter No. 600 was used. Standard solutions of DDT were analyzed with each set of determinations to serve as checks for accuracy of the analysis.

Results. The results of the analyses are shown in Fig. 1. The tissues of animals fed the diet containing 0.1% DDT store small amounts of the agent and the concentrations of DDT remain constant during the 5-15-day period of observation. The animals gained weight despite the characteristic tremors while on this experimental diet and no deaths occurred during the period of observation.

The DDT concentrations of the brain and kidney of rats on the diet containing 0.2% DDT increase slightly on the 7th and 11th days. It is surprising that the brain, which is rich in total lipids, stores only a small amount of DDT. The concentration in the liver appears to reach a maximum on the 4th day. There is a marked and significant increase in the DDT concentration in the adrenals which reaches its maximum on the 11th day. The adrenals are comparatively rich in lipids, but no data concerning the changes in the amount and character of these lipids are available. All animals lost weight and approximately half died during the first 9 days.

Summary. The DDT contents of the liver, kidney, brain and adrenals of rats fed diets containing 0.1% and 0.2% DDT were determined at various intervals.

The amounts of this agent stored in the respective tissues reaches a maximum within a few days and remains at a constant level in animals fed 0.1% DDT. The greatest concentration was noted in the adrenals.

The concentrations of DDT in the brain, liver and kidney of rats fed 0.2% DDT increase slightly and progressively with time. The concentration of this material is markedly increased in the adrenal at the time when the animals are severely intoxicated.