

Metabolism of Gamma-Benzene Hexachloride in the Animal Body

IN order to gain a better insight into the means of defence against benzene hexachloride (BHC) intoxication, which the animal organism has at its disposal, the metabolism of this insecticide has been the object of investigations in our laboratory.

For the quantitative assay of the toxicant in animal tissues we used a method¹ which combines the simplicity of the method described by Reith² for qualitative purposes with the accuracy of the method published by Schechter and Hornstein³. The principle of this method consists of dechlorination of BHC to benzene by means of zinc dust in acetic acid, nitration of benzene to dinitrobenzene and colorimetric determination of the intensely violet-red reaction product formed by the latter compound with methyl ethyl ketone and alkali.

A series of related substances has been tested by this method. Only the four principal isomers of BHC and benzene gave a positive reaction. No colour at all was obtained with phenol, meso-inositol, hexamethoxy cyclohexane, trichloro benzene and monochloro cyclohexane. Moreover, scarcely any colour was obtained after running control analyses on the tissues of untreated animals. We are inclined to consider the method rather specific. Nevertheless it is possible that a positive colour reaction will be shown by metabolites of BHC.

After subcutaneous, intraperitoneal or intravenous injection of gamma-BHC into albino mice a rather rapid breakdown of the toxicant could be observed. A subcutaneously injected dose of 1 mgm. gamma-BHC was eliminated in the course of four days by a mouse of about 15 gm. weight. When 200 μ gm. of gamma-BHC was injected intravenously (in peanut oil-Ringer emulsion) all the toxicant had disappeared within twenty-four hours. The excreta contained no BHC, or only negligible amounts; the amounts in brain, liver, kidney and muscle tissue after subcutaneous, intravenous and oral administration turned out to be rather low. Mostly only 20 μ gm. or less per gram of tissue were found. Accumulation of the toxicant in these tissues could not be demonstrated. There are some indications that gamma-BHC may be accumulated in the fat depots of the body. However, it should be kept in mind that BHC was injected in oily solution.

A rather rapid breakdown of gamma-BHC was also observed in resistant houseflies; twenty-four hours

after injection of 22 μgm . per gram of animals, only negligible amounts could be recovered. Here, too, none was found in the excreta. One of us (F. J. O.) deals with this subject in the following communication.

As to the nature of the metabolites of gamma-BHC we are entirely ignorant. It should be emphasized that breakdown in the above sense and detoxication (conversion into a non-toxic compound) need not parallel each other.

Investigations concerning the metabolism of other isomers of BHC are in progress now. Moreover, a closer study of the correlations between the symptoms of intoxication and the course of the metabolic changes after administration of different isomers of BHC is to be made.

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¹ Asperen, K. van, and Oppenoorth, F. J., *Chemisch Weekblad* (in the press, 1954) (Dutch text only; publication in English will follow in due course).

² Reith, J. F., *Chemisch Weekblad*, 49, 691 (1953) (Dutch text only).

³ Schechter, M. S., and Hornstein, I., *Anal. Chem.*, 24, 544 (1952).
