Antibiotica

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Lindane.

The second world war stimulated experimental work on different chemicals to act as substitutes for unavailable materials. One of the important discoveries during that period was based upon the early work of *van der Linden,* who in 1912 isolated and described physical and chemical properties of the isomers gamma and delta benzene hexachloride, the isomers alpha and beta being described long before by other authors. This work was reviewed again by British and American chemists about 1943 and examinations for insecticidal possibilities indicated the potency of formulations based upon the different isomers and in particular the gamma isomer.

Early work indicated that the most toxic agent in benzene hexachloride was the gamma isomer and with *van der Linden*'s early work as a guide, researchers endeavored to produce the gamma isomer itself by an economic commercial process. They were succesful in doing this early in 1949 and were able to isolate a material which contains a minimum of 99 % gamma isomer with only traces of other isomers. This highly refined material is practically free of the objectionable musty odor of benzene hexachloride technical grade 6—36 % gamma. In honor of the chemist who did the early work on this material and in conjunction with the different technical societies of the United States and he Federal Government this material was named lindane. The pure substance forms white crystals mp. 112° C.

Soon after discovering the disadvantages associated with the use of the unrefined technical grade benzene hexachloride as an insecticide, research work was started in this country to investigate and further develop the pure gamma isomer. This work has progressed to a point where pure gamma isomer is now in large-scale commercial production and is being marketed in suitable formulations as an insecticide by many companies. It is not dominated by patents, and is available to the public as a wettable or dispersible power, solutions and emulsifiable liquid. U.S. government and state research and large-scale commercial usage by pest control operators, dairy farmers and the producers of agricultural crops have established the fact that pure gamma isomer has a wide field of specific uses in the insect control field.

Essentially benzene hexachloride is produced by a chlorination of benzene in the presence of actinic light (ultra-violet). The production can take place either as a continuous process or as a batch-wise process. The usual technical grade of benzene hexachloride contains 12 to 14 % gamma isomer. The chlorination takes place at atmospheric pressure anywhere in the temperature range of 15° to 80° C. The reaction is carried out in glass lined chlorination vessels or kettles.

There are many variations for producing the pure gamma isomer but they are essentially an extraction of the gamma isomer from the crude benzene hexachloride by the use of methyl alcohol or other solvents. This is followed by crystallization of the gamma isomer from the extracting solvent.

During the past 2 years crude benzene hexachloride having an objectionable odor and flavor which prevented its use on certain agricultural crops has come into wide use. In 1949 40 million lbs. based on 12 % gamma product was produced.

The importance of lindane has become more evident during the last 12 months with the development of certain insects, namely flies and mosquitoes that have a resistance to DDT and certain chlorinated insecticides. Lindane has proven effective in controlling flies, mosquitoes, gnats, roaches, silverfish, spiders, ants, clothesmoths, bedmugs and appears to be one of the most effective and best insecticides that have ever been developed. Lindane has a quick knockdown (KD) plus a good residual kill as may be noted from the chart listed below.

Lindane is one of the few insecticides which kills as a stomach poison, by contact action, as well as by fumigation. It acts as a stomach poison against leaf-feeding insects, such as cucumber beetles, leaf miners, army worms, cutworms, grasshoppers and caterpillars; as a contact poison against a wide range of insects including roaches, flies, mosquitoes and ants, aphids, lice, ticks, fleas, etc., as a fumigant against soil infesting insects, such as wireworms, white grubs, cutworms and Diabrotica larvae.

In the April 1950 issue of the Journal of Economic Entomology an article by *R. A. Fulton* et-al entitled, „The Toxicity of lindane vapor to insects" is quoted:

> The vapors from lindane show fumigating action when applied in an aerosol or as a spray containing a water-dispersible powder. The house fly and the banded greenhouse thrips are susceptible to concentrations above 0.001 mg per

Treatment	Fly strain. Bellflower	San Jose	Laboratory
		minutes.	
A. DDT 100 mg/sq.ft.			
KD 50 %	720	420	91
KD 100 %	—	KD never reaches 100 %	—
B. Methoxychloor 100 mg/sq.ft			
KD 50 %	255	56	37
KD 100 %	360	108	67
C. Lindane 100 mg/sq.ft			
KD 50 %	11	16	13
KD 100 %	15	20	20

liter. High mortalities were found for all these insects subsequent to the application of lindane in aerosol form at the rate of 0.1 gram per 1000 cubic feet.

The following statement was made by Dr. *Arnold J. Lehman,* Division of Pharmacology, Food and Drug Administration, Federal Security Agency of the U.S. Government regarding the toxicity of lindane:

We have just completed a two-year feeding study on lindane, the gamma isomer of benzene hexachloride, and on commercial benzene hexachloride. When we compare these results with similar studies conducted on DDT, we find that commercial benzene hexachloride required a moderately higher, and lindane a considerably higher dietary level to produce liver changes than does DDT. If we rate the toxidity of DDT as 1 then the commercial benzene hexachloride has a toxicity of ½ and lindane a toxicity of ¼, or they are respectively ½ and ¼ as toxic as DDT. Lindane is rapidly metabolized and does not accumulate in body fat, and on this basis we can see no objection to its use as a dairy barn spray. The spraying of lindane directly into dairy cows causes the appearance of small amounts of the insecticide in the milk for the first 48 hours, and as "the purity of milk must be safeguarded in every way possible" there would be objections to such use. Government recommendations are that lindane be applied on walls and certain surfaces in dairy barns where its residue is of value. Lindane has been suggested as a household spray. The formulations we have seen call for 0.1% lindane. In our opinion this concentration would be safe for household use.

Because of the low toxicity of lindane and the fact that it is not stored in human fatty tissue it has found widespread use in the cattle industry and particularly in use in dairy barns, dairy plants and food processing plants. Lindane is outstanding in the chlorinated compound field for all purpose use because of its quick knockdown and good residual kill. Based upon extensive tests by entomologists and scientific workers throughout the United States lindane in the future will be widely used in the agricultural field where it has proven to be effective in the control of aphids, leaf-hoppers, and other insects encountered in agricultural production. Excellent control of wireworms in the soil has already been obtained. All indications point to the fact that in the not too distant future lindane will have become as important if not more so than DDT.

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