

## LETTERS TO THE EDITORS

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## New Synthetic Contact Insecticides

SOME laboratory experiments have been made to estimate the relative toxicity to body lice and to bed bugs of several new synthetic insecticides which have been produced on an industrial scale during recent years in Britain, Germany and the United States. They comprise the following types: (1) D.D.T.; (2) certain analogues of D.D.T.; (3) 'Gammexane'; (4) chlorphenyl chlormethyl sulphone.

The various substances were tested as sprays in mineral oil solution and also (rather less accurately) as dry powders diluted with kaolin. Fuller details of the methods will be published in due course. In the accompanying table, the samples are compared by their median lethal concentrations for the two insects, under the conditions of the experiments. These results call for certain comments.

		Median lethal concentrations (%)			
		Oil spray		Dust	
		Lice	Bugs	Lice	Bugs
1.	D.D.T.	0.3	0.53	0.4	0.5
2a.	'Lauseto' mixture	1.2	—	—	—
2b.	Difluor diphenyl trichlorethane	1.4	5.0	1.2	3.0
2c.	Dichlor diphenyl dichlorethane	0.9	1.2	2.4	1.0
3.	'Gammexane'	0.016	0.051	0.005	0.015
4.	Chlorphenyl chlormethyl sulphone	0.1	0.2	0.2	0.6

(1) D.D.T. There is already a considerable amount of information about this insecticide, so that it may serve as a standard for comparison. The material used was pure *pp*-D.D.T. (m.p. 108° C.) obtained from the Chemical Defence Experimental Station, Porton.

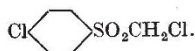
(2) D.D.T. Analogues. (a) 'Lauseto'. In Germany, an insecticide of this name was used during the War to impregnate clothing against body lice, using an emulsion method. A sample of the active principle was tested. This is prepared<sup>1</sup> by the reaction of benzene with chlorobenzene and chloral, so that, as well as D.D.T., it probably contains 2,2-bis-(phenyl)1,1,1-trichlorethane and 2-phenyl, 2-chlorophenyl, 1,1,1-trichlorethane. It was claimed that this mixture, which is a viscous brown liquid containing excess reactants, is easier to emulsify than D.D.T. As can be seen, it is only about a quarter as toxic as pure D.D.T. to lice.

(b) 'Gix'. This is another German insecticide, the active constituent being 2,2-bis-(*p*-fluorophenyl)1,1,1-trichlorethane (m.p. 45° C.), a sample of which was supplied by the Geigy Co., Ltd. It was claimed by workers at the I. G. Plant Protection Laboratory at Höchst that this compound is more effective than D.D.T. to a number of pests, including gypsy moth, brown tail moth, grain weevil, roaches, red scale and houseflies. According to Kilgore<sup>2</sup>, however, their test methods are somewhat suspect. This 'fluorine-D.D.T.' is certainly much less toxic than D.D.T. to lice and bed bugs.

(c) 'D.D.D.' or 'T.D.E.'. The compound 2,2-bis-(*p*-chlorophenyl)1,1,1-dichlorethane (m.p. 111° C.) has been shown to be about as toxic as D.D.T. to mosquito larvae in laboratory tests<sup>3</sup>. It has been produced commercially in the United States with the claim that it is of the order of toxicity of D.D.T. to insects and decidedly less toxic to mammals. Towards lice and bed bugs it appears to be about a third as insecticidal as D.D.T.

(3) 'Gammexane'. Some pure gamma hexachlorocyclohexane (m.p. 112° C.) was obtained from Imperial Chemical Industries, Ltd. The extremely high insecticidal power of this substance, especially towards lice, is noteworthy.

(4) 'Lauseto Neu'. The active principle of this German product represents a new type of insecticidal compound; it is chlorphenyl chlormethyl sulphone:



This compound is a crystalline solid (m.p. 118° C.), odourless and apparently of the same order of permanence as D.D.T. A sample was received from the Public Health Division of the British Control Commission for Germany. It was found to be more toxic to lice and bed bugs than D.D.T., but its use is limited by low solubility in refined mineral oils (about 1 per cent). The Germans used it in the form of a powder and also as dispersions and emulsions; they were in any event so short of oil during the War that kerosene could not be spared for insecticides.

The object of this communication is to direct wider attention to these new insecticides. Considerably more research must be done before sufficient data exist for choosing the most suitable for any particular use.

J. R. BUSVINE

Entomology Department,  
London School of Hygiene and Tropical Medicine.  
June 5.

<sup>1</sup> Kilgore, L. B., *Soap*, 21 (12), 138 (1945).

<sup>2</sup> Kilgore, L. B., *Soap*, 22 (3), 122 (1946).

<sup>3</sup> Deonier, C. L., and Jones, H. A., *Science*, 103, 13 (1946).

## Cause of Physiological Activity of 'Gammexane'

It has been suggested by Slade<sup>1</sup> that the physiological activity of  $\gamma$ -hexachlorocyclohexane, the active constituent of the insecticide 'Gammexane', is due to its antagonism towards the essential metabolite *i*-inositol, which is considered to have the same spatial configuration. Kirkwood and Phillips<sup>2</sup> have recently shown that for the Gebrüder Mayer strain of *Saccharomyces cerevisiae* this is in fact the case, since the  $\gamma$ -isomer has a marked inhibitory effect on the growth of the organism, and the inhibition is overcome by the addition of more *i*-inositol to the medium. The other three isomers of hexachlorocyclohexane are but slightly inhibitory, and excess *i*-inositol is without effect.

We had for some time been working with *Nematospora gossypii*, an ascomycete known to require exogenous *i*-inositol<sup>3</sup>, and had observed a similar effect with the  $\gamma$ -isomer. Our findings, which support those of Kirkwood and Phillips, bear out the original suggestion of Slade. As an example, the results of one experiment are given:

Medium used: Glucose, 2 gm.;  $\text{K}_2\text{HPO}_4$ , 0.5 gm.;  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ , 0.25 gm.; casein hydrolysate ('vitamin free'), to supply 0.25 gm. nitrogen; biotin (Glaxo), 0.1 mgm.; agar, 2 gm.; per 100 ml. medium. Cultures incubated at 30° C. for 7 days.

Wt. of <i>i</i> -inositol per 100 ml. medium	Wt. of mycelium, from pairs of plates, dried at 100° C.	
	without added $\gamma$ -isomer	with $\gamma$ -isomer added to solubility limit
2 mgm.	90 mgm.	20 mgm.
4	122	42
6	154	74
8	178	132
10	190	180

With the  $\beta$ -isomer, no inhibition was found, but a very slight effect was noted with the  $\alpha$ -isomer in a medium with a low *i*-inositol content. In a few tests in which hydrolysed gelatin was used as a source of nitrogen, the inhibitory effect of the  $\gamma$ -isomer was rather more marked.

There is some uncertainty concerning the solubility of  $\gamma$ -hexachlorocyclohexane in aqueous media. The American workers quote a figure of 60  $\mu\text{m}$ . per ml., whereas Slade gives 10  $\mu\text{m}$ . In our experiments, 10 mgm. of the compound, dissolved in 1 ml. ethanol, were added to 100 ml. of the medium. In view of the uncertainty as to the actual amount of the compound dissolving in the medium, and since complete inhibition of growth was not observed, the molecular inhibition ratio (McIlwain<sup>4</sup>) has not been calculated.

We are grateful to Messrs. I.C.I. (General Chemicals), Ltd., for generous gifts of the  $\alpha$ -,  $\beta$ - and  $\gamma$ -isomers of hexachlorocyclohexane.

H. W. BUSTON  
S. E. JACOBS  
A. GOLDSTEIN

Department of Botany,  
Imperial College of Science and Technology,  
South Kensington,  
London, S.W.7.  
May 23.

<sup>1</sup> Slade, Hurter Memorial Lecture, *Chem. and Ind.*, 314 (1945).

<sup>2</sup> Kirkwood and Phillips, *J. Biol. Chem.*, 163, 251 (1946).

<sup>3</sup> Buston and Pramanik, *Biochem. J.*, 25, 1656 (1931).

<sup>4</sup> McIlwain, *Brit. J. Exp. Path.*, 23, 95 (1942).

## Loss of Thiamin During the Baking of Bread

We have just received the published account<sup>1</sup> of a symposium on "Factors Affecting the Nutritive Value of Bread as Human Food". An important issue not touched upon by the various speakers, but raised during discussion, concerned the loss of thiamin during the baking of bread. Two speakers expressed the view that in baking bread the loss of vitamin B<sub>1</sub> is slight. There are published data in support of this statement, but also a great deal of evidence to the contrary (see review by Holman<sup>2</sup>). The idea that little thiamin is lost during baking is surprisingly widespread, but is completely erroneous so far as breads made from very high extraction meals are concerned.

Using a thiochrome assay method<sup>3</sup>, we have investigated the thiamin content of South African wheat-meals and the so-called 'Standard' bread introduced into this country early in the War. The bread is made from 'No. 1 Unsifted meal', originally of 95 per cent extraction but now approaching 100 per cent extraction. The mean values obtained in our survey are given below, together with some published British values for purposes of comparison.

Meal	Extraction (per cent)	Thiamin content ( $\mu\text{m}$ /gm.) <sup>*</sup>		Calculated loss of thiamin during baking (per cent)
		Meal	Bread	
British <sup>4</sup>	85	3.07	1.85	14.8
British <sup>5</sup>	85	3.00	1.83	16.8
British <sup>4,5</sup>	80	2.49	1.50	15.0
South African <sup>6</sup>	95	3.50	1.79	27.8

<sup>\*</sup> Calculated to 11 per cent moisture for flour and 37 per cent moisture for bread.

It will be seen that South African 'Standard' bread, made from 95-100 per cent extraction meal, contains no more thiamin than the British 85 per cent extraction loaf. Yet the original meal is far richer in thiamin. On the assumption that the calculated loss of thiamin is entirely due to baking, and disregarding the other ingredients used in the loaf, it is clear that the destruction of thiamin in 'Standard' bread is almost twice as great as it is in the breads of lower extraction flours.

The greater loss of thiamin from high extraction wheatmeal may be attributed to the longer time required for baking. 'Standard' bread