AROCLOR 1268

DSW 274857

3. CHLORINATED DIPHENYL — COMPOUND #1268 C+25AM

This material was furnished by the Monsanto Chemical Company. It was said to have a chlorine content of 68 per cent, the highest chlorine figure of any compound tested by us during the past three years. It had been our impression that toxicity and chlorine content followed one another closely, but this has not turned out to be the case for #1268. Further discussion of this point will follow the description of the experimental observations and their results.

Experiments. — August 2, 1937. The compound #1268 was administered by inhalation, the technique being that described in the paper entitled The Problem of Possible Systemic Effects from Certain Chlorinated Hydrocarbons, Journal of Industrial Hygiene, 1937, 19, 283. For the first observations 80 adult white rats were used. They were exposed as follows:

Group 1. — 80 animals. Temperature to which the compound was heated to introduce fume into air line 140-190°C. Average concentration in air breathed by rats 0.53 mgm. per cubic meter. Average daily exposure 16 hours. The experiment was continued for 119 days, animals being sacrificed at intervals for pathological examination and for the carbon tetrachloride and alcohol test (see paper previously cited).

The conditions described above caused swelling and increase of granularity of the liver cells. Hyaline inclusions were rare. These changes were quite uniform in all animals examined after the 31st day, but were not certainly progressive. The rats were very healthy throughout the period and there was an almost uniform gain in weight. The carbon tetrachloride-alcohol test was positive after 52 days, which indicates that though liver damages were apparently slight some degree of harm had been done the organ. There was no evidence of damage in any part of the body except the liver. Dr Carl Drinker 15 Sept 38

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At the end of 93 days 10 rats, apparently in excellent condition, were removed from the experiment and set aside for observations upon liver recovery. These recovery animals showed no clinical changes of any sort. When sacrificed 72 and 141 days after removal from exposure it was observed that the swelling of the liver cells had disappeared, but the granular and hyaline material remained in the liver cells and had apparently become permanent. There was absolutely no progression of damage after removal from exposure.

These changes may be compared with those produced in rats by inhalation of chlorinated diphenyl #4465, administered in a similar manner in concentrations of 0.57 to 0.93 mgm. per cubic meter over similar periods of time. In the case of this compound the conspicious difference was the far greater incidence of hyalinization of the liver cells, which in our opinion was the characteristic lesion caused by #4465 and mixtures containing it. One can therefore conclude that #1268 in low concentrations is definitely less toxic than #4465.

Group 2. — After 110 days, the low concentration of #1268 having proved but slightly poisonous, it was decided to increase the concentration in the air breathed by the 54 rats then remaining. Temperature and other conditions were maintained as during the first 119 days, but by the use of 4 vaporizers instead of 1 the average concentration of #1268 in the air was brought to 6.23 mgm. per cubic meter of air. Exposure to this very high concentration was continued for 87 days.

Under these extreme conditions the animals again remained in perfect health. The carbon tetrachloride and alcohol test was positive but there was absolutely no other indication of liver damage and no evidence of disturbance to other organs.

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When examined at autopsy at the end of 87 days — the animals had experienced a total exposure of 206 days — there were no gross evidences of abnormality in any part. On microscopic examination no organ showed changes except the liver. The number of cells containing hyaline and the amount of hyaline in the cells involved increased during this period of exposure to the higher concentration of #1268. The hyaline was most abundant in the portal zone of the lobule with very little in the central area. After 42 days of exposure 10 rats were set aside and were sacrificed 73 days later. They were in excellent condition when removed and did not change. Grossly, at autopsy, they showed nothing abnormal, and on microscopic examination the liver cells had lost their swelling but retained increased granularity and hyaline inclusions.

The experiments on inhalations of high concentrations of #1268 reenforce the conclusion that this compound is of low toxicity as compared with #4465 or with chlorinated naphthalenes above trichlornaphthalene. The question as to why #1268, the most highly chlorinated compound tested, proved but slightly harmful cannot be answered with any definiteness. It has been suggested that the toxicity of all these chlorinated compounds, even though of varied composition, may depend on the ability of the animal to decompose them after lodgment in the tissues, and that this decomposition might be shown by an increase in the chlorine in the urine in suitably conducted feeding experiments. In experiments upon this point we have shown a definite increase in the urinary chlorides when dogs and rats were fed a mixture of penta and hexachlornaphthalenes (#1006) a compound highly injurious to the liver and containing 62.6 per cent of chlorine, but similar observations have not been made with any of the chlorinated diphenyls or allied compounds. It may, however, be that when about 65 per cent chlorination is reached the substances formed are quite stable in the body and so cause a minimum of damage.

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In conclusion, #1268, if handled with ordinary precautions as to ventilation should be entirely harmless to workmen. While it cannot be given an absolutely clean bill as to health, it is preferable to #4465 and #5460.

4. MIXTURE OF CHLORINATED DIPHENYL AND CHLORINATED DIPHENYL BENZENE -- COMPOUND #5460

This substance was furnished by the Monsanto Chemical Company and was said to have a chlorine content of 60 per cent, being in this respect below #4465 and far below #1268.

Experiments -- The inhalation technique was used as in the case of #1268 and #4465.

August 2, 1937. 80 adult white rats were the subjects. Temperature to which the compound was heated to introduce fume into the air line 140-196 196° C. Average concentration in air breathed by rats 0.085 mgm. per cubic meter. Average daily exposure 16 hours. The experiment lasted 119 days. A certain number of animals were sacrificed for pathological examination, others were used for the carbon tetrachloride and alcohol test, and still others set aside for observations as to recovery from possible damage.

In spite of the fact that the concentration in the air breathed by the rats averaged about 1/6 that obtained at comparable temperatures from #1268, a number of these animals became sick and lost weight towards the end of the second month of exposure. When killed, such individuals showed gross mottling of the liver but no changes in other organs. On microscopic examination swelling of the liver cells, increased granularity and hyaline inclusions were noted in animals killed as early as the 16th day of exposure. These changes obviously occurred rapidly. Hyaline deposits were never as numerous as with #1268.

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Animals removed for recovery after 51 and 119 days of exposure did not gain markedly in weight, and one died for no obvious cause. When examined at autopsy the swelling of the liver cells had subsided, but abnormal granularity and hyalinization remained.

Needless to say the carbon tetrachloride and alcohol test was positive whenever used.

In view of the fact that #5460 in such low concentration proved so definitely toxic, no higher concentrations were tested. It seems imperative that whenever this compound is used in industry, great care be taken to keep concentrations in the air at an extremely low level. No liberties can be taken with it, as with #1268.

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