Evidence of Excretion of Chlorinated Hydrocarbon Pesticides by the Human Liver*

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Physiologic mechanisms for disposition of dieldrin stored in body tissues apparently exist in man and in laboratory mammals. These mechanisms are much more efficient in rats (1) than in man (2). Even so, metabolites of dieldrin have been detected in the urine of applicators handling dieldrin (3), as well as in the feces and urine of rats fed dieldrin (4). If the human disposition of dieldrin parallels that of rats, one expects to find the pesticide excreted by the liver as well as the kidney.

On February 21, 1973, a pest control worker who has cooperated with our project for 6 years underwent cholecystectomy. He had engaged in pest control work since the summer of 1965, spending most of these years in regular contact with a special dieldrin formulation, which, when applied to indoor surfaces, exerts a long term insecticidal effect. Substantial personal absorption of the chemical had been indicated by serum concentrations from 100 to 250 parts per billion consistently over the past 5 years. Availability of this man's bile, gall stone, and adipose fat offered an opportunity to determine whether dieldrin and/or its metabolites are excreted by the liver when body stores of the chemical are over 100 times those seen in the general population.

In addition to this study, we examined bile from the common duct T-tube drainage of five hospitalized patients (who had not been associated with pesticide-using industries) following cholecystectomies.

Methods:

The gas-liquid chromatogram (GLC) of a standard mixture of pesticides used for identification and quantitation of pesticides is shown in figure 1. In addition to the purified chlorinated hydrocarbon materials often found in tissues, it includes the hexane-extractable products resulting from treatment of HEOD (1,2,3,4,10,10-hexachlor-6,7 epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4,5,8-endo-exo-dimethanonaphthalene) in ethyl alcohol with chromous

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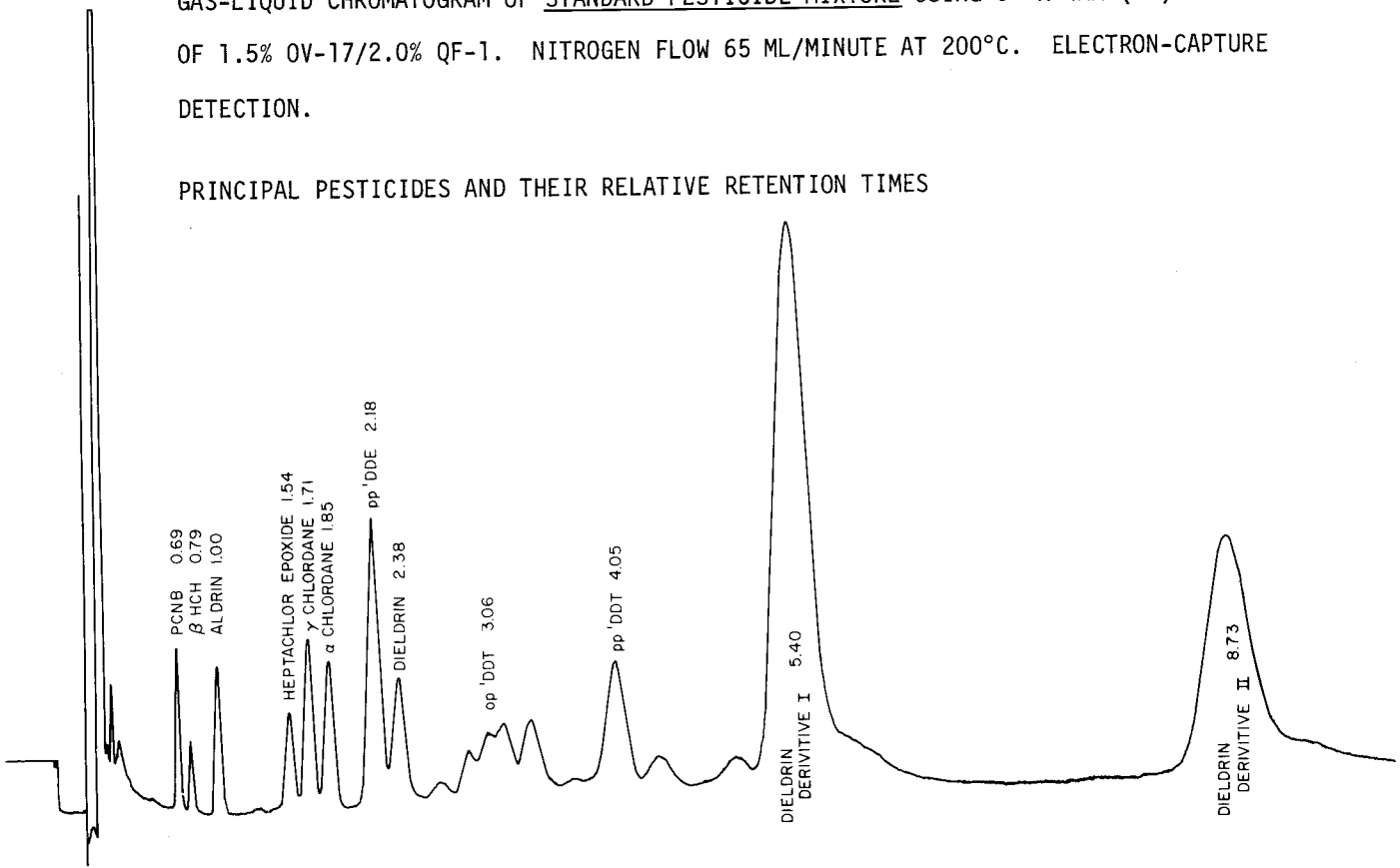
FIGURE I

GAS-LIQUID CHROMATOGRAM OF STANDARD PESTICIDE MIXTURE USING 6' x 4MM (ID) COLUMNS OF 1.5% OV-17/2.0% QF-1. NITROGEN FLOW 65 ML/MINUTE AT 200°C. ELECTRON-CAPTURE DETECTION.

PRINCIPAL PESTICIDES AND THEIR RELATIVE RETENTION TIMES



chloride, hydrochloric acid, and heat. Derivatization by similar methods has been described by Chau and Cochrane (5) and by Wiencke and Burke (6). The object of adding these materials was to establish the relative retention times (RRT) of particular dieldrin degradation products resulting from such treatment, so that tissue metabolites of similar nature would be recognized if present. It appears likely that the "dieldrin derivative I" in figure 1 (RRT= 5.40) is the aldehyde of HEOD, while the later peak, "dieldrin derivative II" (RRT=8.73) is the ketone, as demonstrated by Chau and Cochrane (5). We learned that the aldehyde product is retained on the florisil column. For this reason, extracts of specimens were examined without cleanup. We have employed the Microtek-220, having 6' x 4 mm ID columns of 1.5% OV-17/2% QF-1 coating on Chromasorb support, operated at 200°, carrying nitrogen at 65 ml/ minute and using electron capture detection.

Adipose fat was ground in a Kontes tissue homogenizer containing several ml of 1:1 mixture of ethanol-ethyl ether. The extract was transferred quantitatively to a 250 ml separatory funnel containing 10 ml hexane. This mixture was washed gently 3 times with distilled water to remove the alcohol. Extract was then concentrated in a stream of clean dry air, and a part was analyzed by GLC (figure 2). An aliquot of the extract was cleaned up by the method of Mills (7), and was similarly examined by GLC to quantitate accurately the DDT and dieldrin present.

Bile was extracted with twice its volume of acetonitrile in a 250 ml separatory funnel. Transferred to a 1 liter separatory funnel, the entire mixture was then shaken vigorously with 100 ml of n-hexane and 500 ml of distilled water. The hexane layer was washed three times with distilled water to remove the acetonitrile, and was then concentrated to a convenient volume, for GLC analysis (figure 3).

The hard gall stone, weighing about 1 gm, was ground in a Kontes tissue homogenizer, in the presence of 10 ml n-hexane. The hexane extract was washed three times with distilled water, concentrated to a convenient volume, and analyzed by GLC (figure 4).

Results:

Figures 2,3 and 4, are chromatograms of the extracted adipose fat, bile, and gall stone, respectively, from R.W. All demonstrate strong peaks for dieldrin and DDE at their respective relative retention times. Certain lesser peaks correspond to other commonly found chlorinated hydrocarbons. The adipose fat, bile, and gall stone all appear to contain a material corresponding in RRT to the aldehyde product of dieldrin, while no similar evidence could be found for the presence of the ketone, which has been identified in the urine of dieldrin-fed rats (4). A few unidentified peaks appear in the specimen chromotograms which correspond to unidenti-

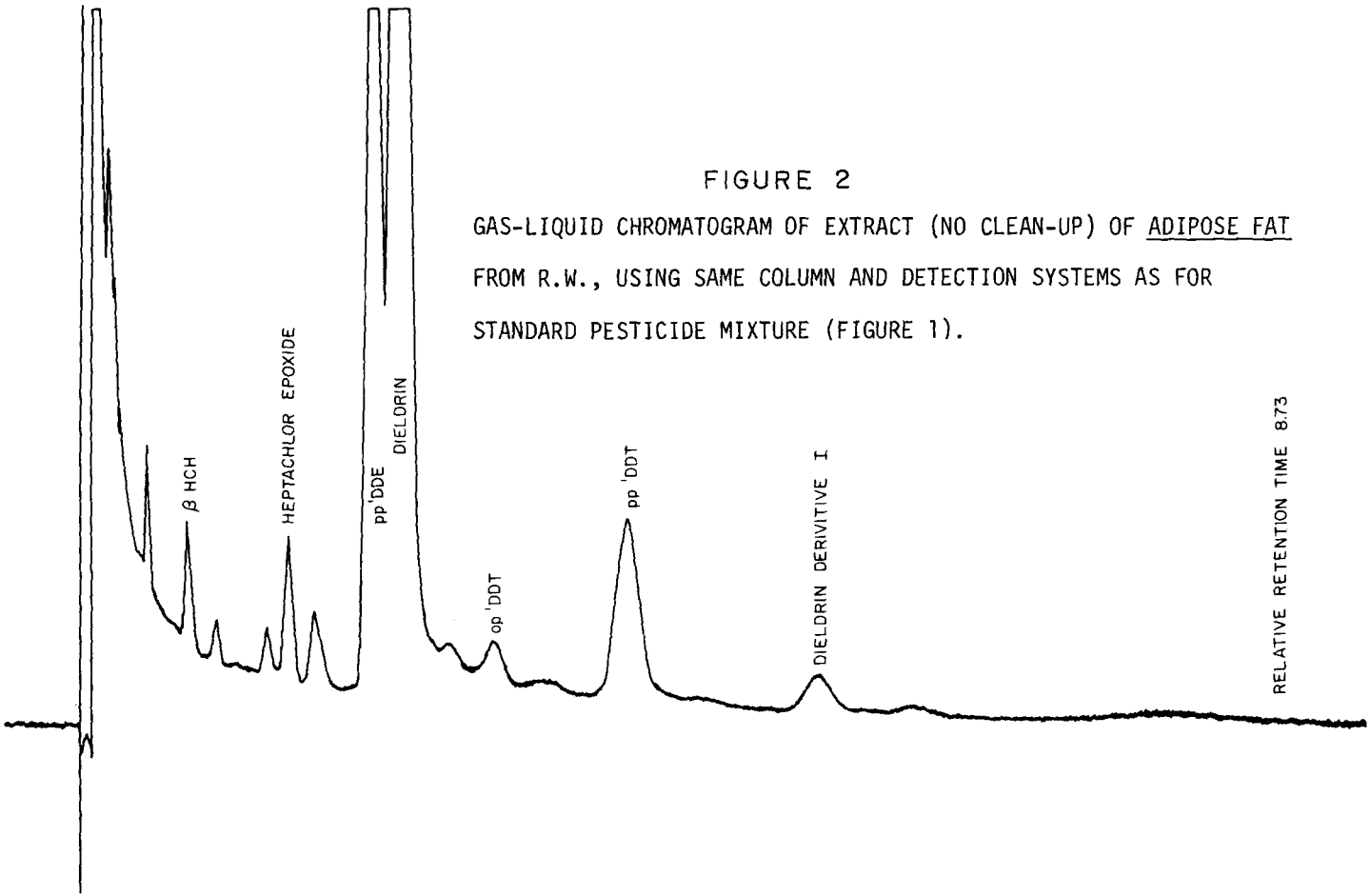


FIGURE 2

GAS-LIQUID CHROMATOGRAM OF EXTRACT (NO CLEAN-UP) OF ADIPOSE FAT FROM R.W., USING SAME COLUMN AND DETECTION SYSTEMS AS FOR STANDARD PESTICIDE MIXTURE (FIGURE 1).

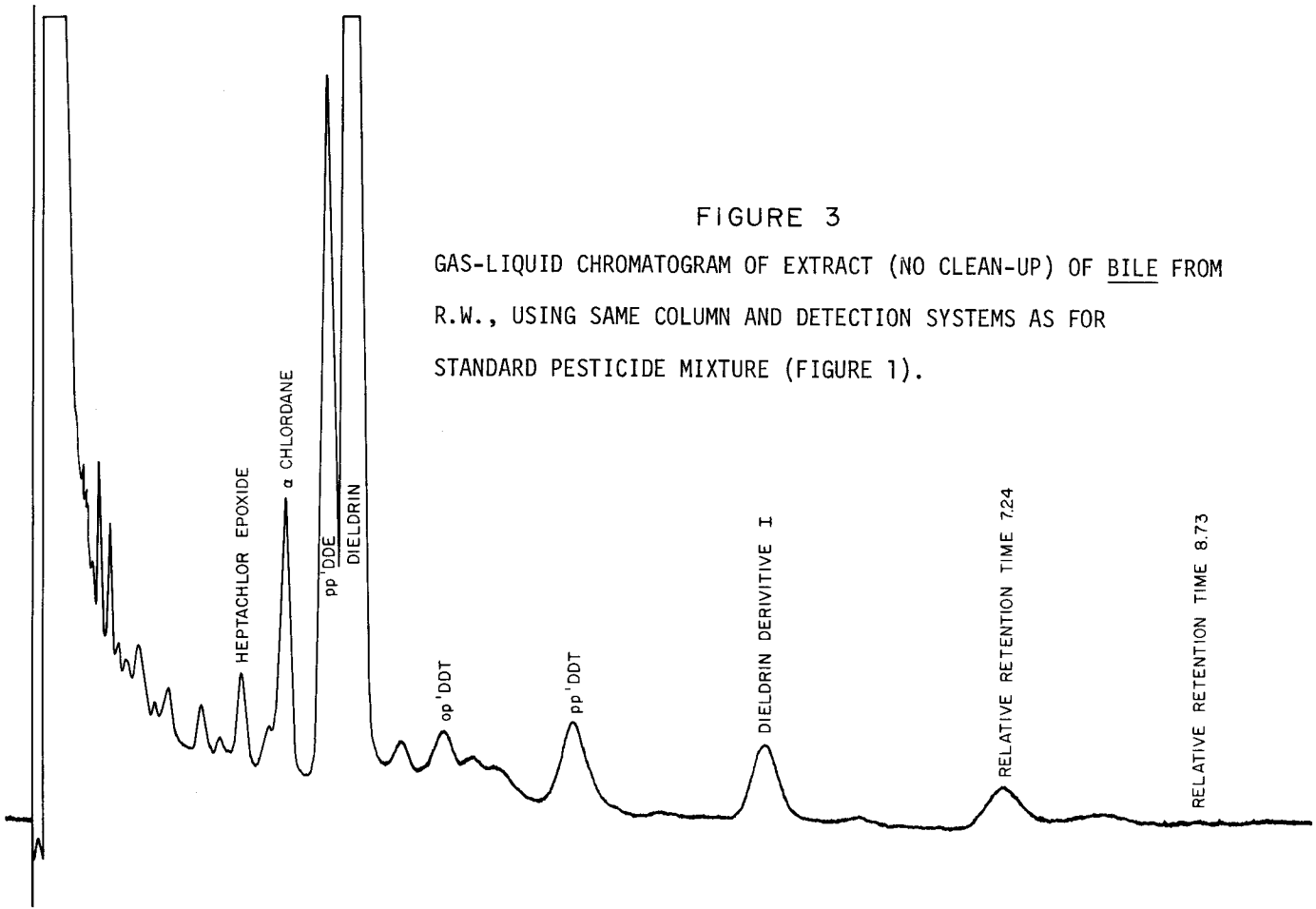


FIGURE 3

GAS-LIQUID CHROMATOGRAM OF EXTRACT (NO CLEAN-UP) OF BILE FROM R.W., USING SAME COLUMN AND DETECTION SYSTEMS AS FOR STANDARD PESTICIDE MIXTURE (FIGURE 1).

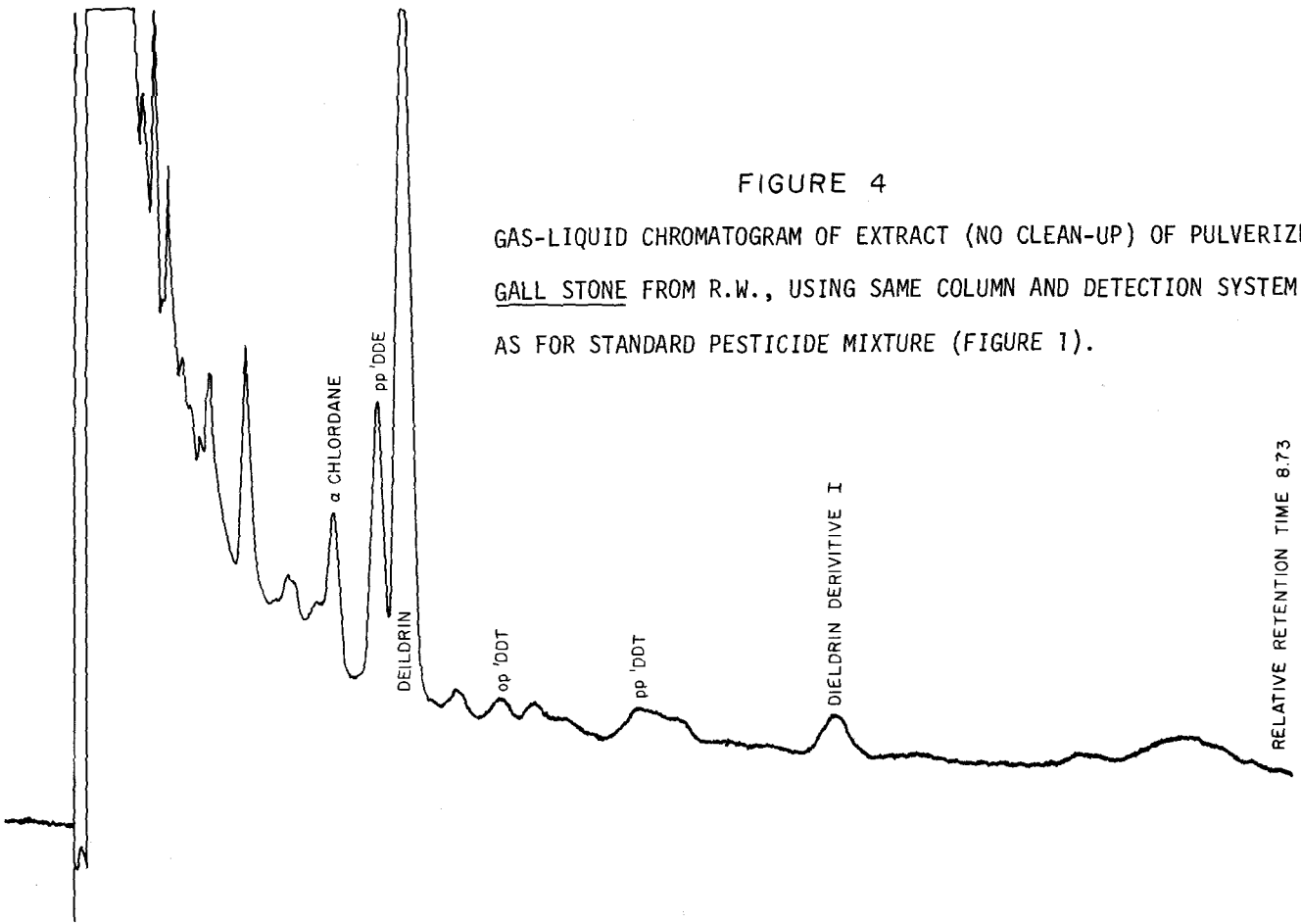


FIGURE 4

GAS-LIQUID CHROMATOGRAM OF EXTRACT (NO CLEAN-UP) OF PULVERIZED GALL STONE FROM R.W., USING SAME COLUMN AND DETECTION SYSTEM AS FOR STANDARD PESTICIDE MIXTURE (FIGURE 1).

fied peaks in the standard mixture. These could well represent other dieldrin degradation products. The identity of the substance appearing at RRT 7.24 in bile, but not in other specimens, or in the standard mixture, is not known.

The following concentrations of pesticides were found in the specimens from R.W.:

TABLE 1

Concentrations of Pesticidal Chemicals in Serum, Fat, Bile, and Gall Stone of R.W., Professional Pest Control Operator

Concentrations in Parts Per Billion

	pp' DDT	op' DDT	pp' DDE	β HCH	Dieldrin	Heptachlor Epoxide
Serum	11	2	60	3	165	3
Adipose Lipid	2,200	300	11,300	400	24,600	400
Bile	3	1	19	0	59	1
Gall Stone	11	2	35	0	92	1

The striking result here, of course, is a concentration of dieldrin in fat and serum well over 100 times that found in the tissues of persons not occupationally exposed. This is no doubt responsible for the high levels in bile and stone.

Pesticide in human bile from choledochostomy T-tubes.

T-tube drainage specimens from 5 elderly male patients were extracted and examined for pesticide content without cleanup:

TABLE 2

Chlorinated Hydrocarbon Pesticides in Choledochostomy T-Tube Drainage from Five Men Who Had Not Been Exposed Occupationally to Pesticides

Concentrations in Parts Per Billion

Patient	Age	pp' DDT	op' DDT	pp' DDE	Dieldrin
M.F.	73	0.4	0.0	1.2	0.5
R.S.	74	0.7	0.2	5.1	0.1
W.S.	74	0.4	0.1	1.3	0.1
H.C.	77	0.1	0.0	0.5	0.0
J.W.	52	0.0	0.0	5.6	0.0

The amount of pesticide found in these specimens is extremely small. However, identification in bile from these persons with no occupational exposure confirms the role of hepatic excretion even at the very low levels of pesticide intake derived from diet. It is possible, if not probable, that substantial amounts of pesticide are excreted as metabolites or conjugates which our present methods fail to detect. With regard to the possibility of conjugates, it should be recorded that, in our hands, treatment of the bile with strong acid or alkali prior to analysis has failed to generate larger concentrations of pesticide.

Conclusions:

1. The liver excretes DDT and dieldrin into the bile.

2. The dieldrin content of bile from a worker having very high tissue stores is much greater than it is in persons with no occupational exposure. This suggests the existence of substrate-responsive excretory mechanisms.

3. We have tentatively identified the aldehyde degradation product of dieldrin in adipose fat, bile,and gall stone. The ketone product has not been found in fat, bile, or gall stone.

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