In vitro uptake and transfer of chlorinated hydrocarbons among human lipoproteins

Badri P. Maliwal and Frank E. Guthrie

Toxicology Program, Department of Entomology, North Carolina State University, Raleigh, NC 27650

Abstract The uptake, distribution, and exchange of chlorinated hydrocarbon insecticides (dieldrin and chlordecone) and biphenyls (2,4,5-2′,4′,5′-hexachlorobiphenyl and 3-chlorobiphenyl) among human lipoproteins was examined by fluorescence quenching, gel filtration, and ultrafiltration. The chlorinated hydrocarbons were rapidly taken up from solution or silica particles by lipoproteins. The distribution of chlorinated hydrocarbons among the lipoproteins was independent of the amount taken up by the lipoproteins. The partition coefficient for each lipoprotein and the serum concentration of individual lipoproteins determined the distribution pattern of chlorinated hydrocarbons among lipoproteins. The chlorinated hydrocarbons attached to albumin or one of the lipoproteins were rapidly transferred to all other lipoproteins. The exchange was complete in less than one minute. The role of rapid exchange of chlorinated hydrocarbons among lipoproteins in removal of these chemicals from blood and distribution to other tissues is discussed.—**Maliwal, B. P., and F. E. Guthrie.** In vitro uptake and transfer of chlorinated hydrocarbons among human lipoproteins. *J. Lipid Res.* 1982. **23:** 474–479.

Supplementary key words particle mediated uptake • fluorescence quenching • exchange • distribution

Chlorinated hydrocarbon insecticides and biphenyls have been widely used in agriculture and industry, respectively, for several decades. Only recently it has been recognized that some polychlorinated biphenyls (PCBs) and organochlorine insecticides with very low water solubilities persist in the environment and can accumulate in human adipose tissues (1, 2). The most likely mode of human exposure to these compounds is via contaminated food. Dermal and inhalation exposure can also play an important role at work places and during field operations. In blood, the chlorinated hydrocarbons (CH) with very low water solubilities, such as DDT, dieldrin, chlordecone, PCBs, are associated with lipoproteins (3–8). The number of pharmacokinetic studies of CH are limited and show a very rapid removal from the blood with initial storage, largely in the liver and muscle tissue (8–11). A possible explanation may be rapid exchange of these compounds among various lipoproteins and either selective uptake of a particular lipoprotein by liver (e.g., VLDL has a half life of less than 10 min in the rat (12)) and/or a rapid transfer of these chemicals from lipoproteins to liver and muscle tissue cell membranes, which will be facilitated by heavy blood flow through these tissues. Rapid exchange of DDT among trout lipoproteins (13), between chylomicrons and lipoproteins in rat (10), and transfer of a polynuclear aromatic hydrocarbon, benzo(a)pyrene, among human lipoproteins (14) has been reported. To test the hypothesis of rapid exchange among lipoproteins and its relationship to the rapid removal of CH from blood, we have determined: *a*) the partition coefficients of two CH insecticides (dieldrin and chlordecone), two biphenyls (2,4,5-2′,4′,5′-hexachlorobiphenyl (2,4,5-2′,4′,5′-CB), and 3-chlorobiphenyl (3-CB)) for lipoproteins; *b*) the lipoprotein uptake of CH from silica particles; and *c*) the distribution and transfer of CH among lipoproteins.

MATERIALS AND METHODS

Chemicals

[^{14}C]Dieldrin (85 mCi/mmol) was purchased from Amersham/Searle. [^{14}C]-2,4,5-2′,4′,5′-CB (9.06 mCi/mmol) was purchased from New England Nuclear. [^{14}C]Chlordecone (19.68 mCi/mmol) and [^{14}C]-3-CB (1.02 mCi/mmol) were gifts from Dr. H. B. Matthews of the National Institute of Environmental Health Sciences, Research Triangle Park, NC. The radiochemical purity (greater than 99%) of all the chemicals was confirmed by thin-layer chromatography with appropriate solvent systems.

Non-radioactive dieldrin and chlordecone were purchased from Chem Service and 2,4,5-2′,4′,5′-CB was obtained from Analabs. DADE total lipid reagent and lipid reference sera were purchased from American Scientific Products. Ultrafiltration membranes with molecular

Abbreviations: DDT, 1,1,1,-trichloro-2,2-bis(*p*-chlorophenyl) ethane; 2,4,5-2′,4′,5′-CB, 2,4,5-2′,4′,5′-hexachlorobiphenyl; 3-CB, 3-chlorobiphenyl; VLDL, very low density lipoproteins; LDL, low density lipoproteins; HDL, high density lipoproteins; PCBs, polychlorinated biphenyls; CH, chlorinated hydrocarbons.

weight cutoff points of 300,000 and 1,000,000 (UF type F) were purchased from Nucleopore Corporation. All other chemicals of ACS grade and solvents of spectroscopy grade were purchased from Fisher Scientific Company.

Separation of lipoproteins

Plasma, pooled from several fasting human males, was a gift from Dr. A. C. Chasson, Rex Hospital, Raleigh, NC. Human total lipoproteins were initially isolated by ultracentrifugal flotation (d 1.225 g/ml), then fractionated by agarose gel filtration into three classes: very low density lipoproteins, low density lipoproteins, and high density lipoproteins (15). Purified lipoproteins were analyzed by standard methods for total lipid (16) and total protein (17). The lipoprotein concentration was calculated by summing protein and lipid contents.

Measurement of radioactivity

To measure radioactivity, a 0.6-ml solution containing CH was mixed with 5 ml of Triton X-100 scintillation liquid (18) and counted on a Packard-Tri Carb Scintillation Spectrometer. The radioactivity of all CH was about 10,000 cpm/μg.

Preparation of HDL-protein moiety

The protein moiety was prepared by the extraction of HDL with ether–ethanol (19). After delipidation, the HDL-protein moiety was dialyzed against 0.01 M Tris-HCl–0.15 M NaCl, pH 8.5.

Partition coefficients

The relative solubility of CH in buffer with and without added lipoprotein was used to calculate partition coefficients. The buffer and lipoprotein solutions (0.1 mg/ml for dieldrin, 2,4,5-2′,4′,5′-CB, and 3-CB, and 0.5 mg/ml for chlordecone) were equilibrated with an excess of the compound. The chlorinated hydrocarbons were introduced in small amounts of methanol (0.25% v/v). After 24 hr equilibration, the suspensions were centrifuged for 30 min at 20,000 *g* and the radioactivity in the supernatants was measured. The following equation was used to analyze the partitioning:

$$\underset{\text{(aqueous)}}{\text{chlorinated hydrocarbon}} \underset{\leftarrow}{\overset{k}{\rightleftharpoons}} \underset{\text{(in lipoproteins)}}{\text{chlorinated hydrocarbon}}$$

where k is the partition coefficient and the concentration of the solution is moles of solute per 1000 g of solvent or lipoprotein.

Chlorinated hydrocarbon incorporation and distribution among lipoproteins

The chlorinated hydrocarbons were incorporated into lipoproteins using methanol (10 μl in 3 ml of lipoprotein solution) to achieve final concentrations of 10 μM in all cases except 100 μM in some experiments (as noted in the text). The lipoprotein solutions were equilibrated for 12 hr with the test chemical before use. For distribution experiments, a mixture of lipoproteins (20 to 25 mg in 3-ml concentrations of individual lipoproteins adjusted to simulate plasma levels) was separated on an agarose column (Biogel A-5m, 100 ml bed volume, height 50 cm). The flow rate of buffer was maintained at about 15 to 18 ml per hr. The eluted buffer was collected in small fractions (1.2–1.3 ml) and monitored for protein at 280 nm. Radioactivity in each fraction was also determined. The agarose columns satisfactorily resolved VLDL, LDL, and HDL. The results are expressed as % of total radioactivity recovered in each lipoprotein fraction.

To study the exchange of CH among the lipoproteins, the test chemicals were incorporated into 1 ml of one of the lipoprotein fractions. After 12 hr incubation, equal volumes of the other two lipoprotein fractions, free from the compound, were mixed with this lipoprotein solution. After equilibration for 30 min, the lipoprotein mixture was applied to an agarose column and individual fractions were separated as described earlier. Columns were subjected to lipoprotein mixtures containing 100 μM CH followed by separated lipoproteins containing 10 μM CH. In ultrafiltration studies the same protocol as for the gel filtration experiments was followed except that the equilibration time was 1 min. After equilibrating the lipoprotein mixture for 1 min, pressure (60 psi) was applied to the ultrafiltration unit and 1 ml of ultrafiltrate (from total volume of 3 ml) was recovered in less than 2 min.

Uptake of chlorinated hydrocarbons from silica particles

The rate of uptake was measured by quenching of protein fluorescence when the CH were introduced into 3 ml of lipoprotein solution (1 mg/ml), either as concentrated methanol solutions (10 μl) or as a coating on silica particles (3 mg), containing 75 μg of dieldrin or 3-CB or 2,4,5-2′,4′,5′-CB, or 30 μg of chlordecone. The silica particles were coated with CH by immersing the particles in methanol solution of the chlorinated hydrocarbons and evaporating it under nitrogen. The lipoprotein solutions were excited at 300 nm (3-nm slit width) and emission was measured at 335 nm (5-nm slit width). The fluorescence intensity was recorded 10 sec after incorporation of the methanol solution. In particle-mediated uptake experiments, fluorescence was measured at 20-sec intervals after mixing. The lipoprotein solutions with the same amount of silica, but without any CH coating, served as controls in these experiments. The lipoprotein solutions containing silica particles were constantly mixed during the experiments.

TABLE 1. Partition coefficients of some organo-chlorine insecticides and chlorinated biphenyls for human lipoproteins[a]

	Aqueous Solubility	VLDL M^{-1}	LDL M^{-1}	HDL M^{-1}	HDL[b] Protein M^{-1}
	(μmoles/liter)				
Dieldrin	0.394	6.5×10^4	9.5×10^4	8.0×10^4	3.2×10^4 (37.5)
Chlordecone	3.914	0.2×10^3	0.6×10^3	1.9×10^3	1.8×10^3 (116.1)
3-CB	0.366	3.8×10^4	4.4×10^4	5.0×10^4	N.D.
2,4,5-2′,4′,5′-CB	0.028	1.2×10^6	2.2×10^6	2.0×10^6	5.75×10^5 (61.7)

[a] The partition coefficients were measured from relative solubilities in buffer solution (0.01 M phosphate, pH 7.4, containing 0.15 M NaCl, 25°C) with and without added lipoproteins. After equilibrating the chlorinated hydrocarbons for 24 hr, the buffer and lipoprotein solutions were centrifuged for 30 min at 20,000 *g* to remove the remaining insoluble compound. The lipoprotein concentration was 0.5 mg/ml in the case of chlordecone and 0.1 mg/ml for other compounds. The solubility to calculate the partition coefficient is defined as moles solute per 1000 g solvent or lipoprotein.

[b] The partition coefficients were measured in 0.01 M Tris–HCl buffer containing 0.15 NaCl, pH 8.5. The same results, expressed as percent of partition coefficient of HDL at pH 8.5, are shown in parentheses.

Unless otherwise noted, all studies were carried out at room temperature (25°C) and in 0.01 M phosphate buffer, pH 7.4, containing 0.15 M NaCl. All results are an average of three estimations.

RESULTS

Partition coefficient

The partition coefficients of dieldrin, chlordecone, 3-CB, and 2,4,5-2′,4′,5′-CB for VLDL, LDL, and HDL are given in **Table 1.** The partition coefficients ranged from about 1×10^6 M^{-1} in the case of hexachlorobiphenyl to 0.2×10^3 M^{-1} for chlordecone. With the exception of chlordecone, the partition coefficients for different lipoproteins show little variation for a given CH. In the case of chlordecone, the HDL partition coefficient is several-fold higher than that for VLDL or LDL. The protein moiety in lipoproteins is also involved in the uptake of CH as suggested by significant partition coefficients for lipid-free HDL. The high partition coefficients suggest that CH would tend to accumulate in lipoproteins.

Distribution among lipoproteins

Recovery from the columns in the cases of dieldrin, 3-CB, and 2,4,5-2′,4′,5′-CB was 80–85% initially, indicating some adsorption to agarose. However, all subsequent fractionations with the same column showed more than 95% recovery of the applied radioactivity, suggesting that the sites on agarose were saturated in the first run. Only experiments with more than 95% recovery of radioactivity have been included in the results. Recovery was greater than 95% in all experiments with chlordecone.

The distribution of CH into three lipoproteins is essentially the same at two concentration levels (**Table 2**). In the case of dieldrin and hexachlorobiphenyl, about one-half of the compound is associated with LDL, while the VLDL fraction has less than 20% of the radioactivity. HDL is the main carrier for chlordecone (almost 80% of the radioactivity) while the amount present in VLDL is insignificant (less than 5%).

Transfer among lipoproteins

The exchange of CH among lipoproteins after incubation for 30 min and 1 min is shown in **Tables 3 and 4,** respectively. The distribution of CH among lipoproteins was the same regardless of which lipoprotein was initially labeled. The transfer of CH among lipoproteins was complete in less than 1 min (Table 4). Membranes with a cutoff point of 300,000 will allow only albumin, while ones with a 1,000,000 molecular weight cutoff point will permit passage of only HDL from the lipoprotein mixture. These membranes have some affinity

TABLE 2. Distribution of some chlorinated hydrocarbons among lipoproteins[a]

Chlorinated Hydrocarbon Concentration	Lipoprotein Concentration			% Distribution		
	VLDL	LDL	HDL	VLDL	LDL	HDL
(μM)		*(mg/ml)*				
Dieldrin						
100	2.0	4.0	3.0	19.3	50.8	29.9
10	2.0	4.0	3.0	16.4	52.3	31.3
Chlordecone						
100	1.4	3.1	3.15	4.55	15.7	79.8
10	1.4	3.1	3.15	4.9	15.4	79.8
2,4,5-2′,4′,5′-CB						
100	1.6	4.1	3.05	11.1	60.75	28.1
10	1.6	4.1	3.05	13.5	53.15	33.14

[a] Purified lipoproteins were mixed to simulate original plasma concentrations. About 3 ml of lipoprotein mixture containing the chemical was separated on an agarose column. All the experiments were conducted in 0.01 M phosphate buffer containing 0.15 M NaCl, pH 7.4.

TABLE 3. Exchange of some chlorinated hydrocarbons among lipoproteins[a]

% Distribution					
Before Incubation			After Incubation		
VLDL	LDL	HDL	VLDL	LDL	HDL
Dieldrin					
100	0	0	18.9	50.6	30.6
0	100	0	18.5	50.1	31.4
0	0	100	18.4	51.1	30.5
2,4,5-2′,4′,5′-CB					
100	0	0	12.6	54.6	32.6
0	100	0	13.0	53.5	33.4
0	0	100	13.2	55.5	31.3
Chlordecone					
100	0	0	4.0	15.35	80.6
0	100	0	4.6	14.5	80.9
0	0	100	4.3	14.2	81.5

[a] Concentration of the chemical was 10 μM. Other conditions are the same as in Table 2. The chemicals were incorporated into 1 ml of each lipoprotein fraction in 10 μl methanol. Each labeled fraction was then incubated for 30 min with 1 ml each of the other two lipoprotein fractions not previously exposed to the chemical and subjected to gel filtration.

for halogenated hydrocarbons. Further, the amount of protein that will filter along with the ultrafiltrate will depend on the concentration in the solution inside the ultrafiltration cell. Thus only a fraction of total albumin or HDL will be recovered in 1 ml of the ultrafiltrate. This method is at best a semiquantitative indicator of the exchange of CH among the lipoproteins. However, if there is rapid transfer of CH among lipoproteins, all other conditions being the same, the fraction of radioactivity recovered with either HDL or albumin in the ultrafiltrate will be the same regardless of which protein fraction was initially labeled. The results also suggest a rapid exchange of CH between albumin and lipoproteins.

Uptake from silica particles

There was a decrease in the fluorescence intensity of lipoproteins due to the incorporation of CH added either as methanol solutions or coated on silica particles (**Fig. 1**). The extent of quenching varied among different CH and between LDL and HDL for the same compound. There were small decreases in fluorescence intensity of lipoprotein solutions due to introduction of silica particles (from 5 to 10%). A suitable correction was applied to the results involving uptake of CH from the silica-coated particles. The rate of quenching indicates that the CH are taken up by lipoproteins from the solution in less than 10 sec. The uptake from silica, although not as fast, is also rapid. About 90% of the chemical is adsorbed by lipoprotein in less than 2 min from silica particles. The extent of fluorescence quenching is the same for an equivalent amount of CH added either in 10 μl methanol or as a coating on silica.

DISCUSSION

Because of their very low water solubilities, many CH insecticides are associated with particulate matter in the biosphere. Therefore, the uptake and bioaccumulation in the environment would involve exchange of adsorbed CH from the particulates to the membranes. The observed rapid uptake of CH by lipoproteins indicates that particle-mediated transport of these chemicals into bio-

TABLE 4. Transfer of organochlorine-insecticides and chlorinated biphenyl among lipoproteins in 1 minute[a,b]

Before Incubation % Radioactivity					After Incubation % Radioactivity in 1 ml Ultrafiltrate		
LPs	VLDL	LDL	HDL	Albumin	Dieldrin	Chlordecone	3-CB
100	0	0	0	0	6.0	16.8	6.2
0	100	0	0	0	5.8	16.6	6.1
0	0	100	0	0	6.0	17.8	6.8
0	0	0	100	0	5.6	19.6	5.2
0	0	0	0	100	—	—	5.1

[a] The lipoprotein and albumin concentrations were: VLDL, 2 mg/ml; LDL, 4 mg/ml; HDl, 3 mg/ml; and albumin, 40 mg/ml. The concentration of chemicals was 10 μM. Albumin was used only in experiments with 3-CB.

[b] The chlorinated hydrocarbons were incorporated into each lipoprotein fraction (1 ml) in 10 μl methanol. Each labeled fraction was then incubated with 1 ml each of the other lipoprotein fractions (and albumin in the case of 3-CB) not previously exposed to the chemical. The mixture was subjected to ultrafiltration after incubation for 1 min. About 1 ml of ultrafiltrate (out of a total volume of 3 ml) was collected in less than 2 min and analyzed for radioactivity. A membrane with 10^6 molecular weight cutoff point was used in the experiments with chlordecone and dieldrin, while a membrane with 300,000 molecular weight cutoff point was used in the case of 3-CB. These membranes will allow passage of only HDL and albumin, respectively, from the lipoprotein mixture.

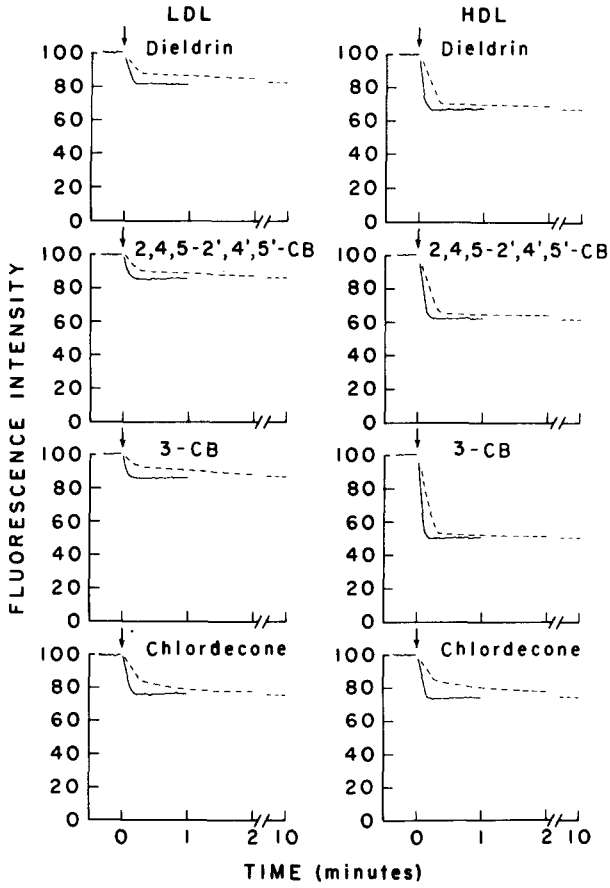

Fig. 1. Uptake of chlorinated hydrocarbons by lipoproteins as observed by quenching of protein fluorescence. At the indicated time (arrow), the chemicals were added either in methanol solution (10 μl, ——) or as a coating on silica particles (3 mg, ---) to lipoprotein solution (3 ml, 1 mg lipoprotein/ml). The solution was excited at 300 nm (slit width, 3 nm) and fluorescence emission was measured at 335 nm (slit width, 5 nm). The fluorescence intensities of the lipoprotein solutions with silica particles without any chlorinated hydrocarbon were taken as controls in the experiments involving coated silica particles.

logical membranes (or any other lipid protein system) is an efficient and rapid process. Similar observations have been made for particle-mediated uptake of chlorinated pesticides and polynuclear aromatic hydrocarbons by phospholipid vesicles (20, 21) and uptake of benzo(a)pyrene by human lipoproteins from glass beads (14).

It is generally assumed that the chlorinated hydrocarbons are dissolved in the lipid phase of lipoproteins. However, the significant partition coefficients for HDL-protein would indicate some role for the protein moiety in the uptake of CH. The actual contribution of the protein moiety in the uptake of CH lipoproteins will be determined by the relative affinities of protein and lipid components for these compounds and the relative concentration of lipids and proteins in the lipoprotein. The partition coefficients for dieldrin in the present study are in agreement with our earlier observations (8). LDL should carry a major portion of CH in plasma because it is the major lipoprotein component of human plasma and because of similar partition coefficients of dieldrin and PCBs for different lipoproteins. Our distribution data in the case of dieldrin and hexachlorobiphenyl, reported plasma distribution patterns of DDT and dieldrin among lipoproteins in exposed human subjects (4, 5) and in vitro distribution of benzo(a)pyrene among lipoproteins (14) substantiated this observation. Unlike other CH, most chlordecone was associated with HDL, which is in agreement with observations made in workers exposed to chlordecone (7). The reason for preferential association of chlordecone with HDl is its several-fold higher affinity for HDL than that for LDL or VLDL (Table 1). The results suggest that the concentration of individual lipoproteins in serum and their relative affinities for CH will determine the distribution patterns of CH in plasma. Further, the amounts of CH required to saturate plasma can be calculated from the partition coefficient, water solubility of the chemical, and serum lipoprotein concentrations. The saturation levels would be quite large for these four CH and considerably higher than the levels likely to occur during exposure.

In general, non-polar chlorinated hydrocarbons that are efficiently metabolized into more polar derivatives are excreted, while those that metabolize slowly are retained in the body (1, 2, 7, 11). Among inefficiently metabolized CH, the more non-polar compounds such as DDT, dieldrin, hexachlorobiphenyls (partition coefficients of the order of 10^5 M^{-1} or more) accumulate in adipose tissue (1, 2). However, because of lower apolarity (the partition coefficients are two to three orders of magnitude smaller than those for other CH), chlordecone will be less likely to accumulate in adipose tissue. This lack of storage in adipose tissue, inefficient metabolism, and an efficient enterohepatic circulatory system (7) would explain the high blood and liver concentrations in the case of chlordecone. The partition coefficients of dieldrin, hexachlorobiphenyl, and 3-chlorobiphenyl for lipoproteins observed in the present study compare favorably with values reported for hexane–water (22) and octanol–water systems (23).

One of the aims in the present investigation was to determine if there is any rapid exchange of CH among lipoproteins. Our observations (Tables 3 and 4) clearly suggest very rapid transfer of these chemicals among lipoproteins which is complete in less than 1 min. Earlier reports of in vivo and in vitro exchange of DDT and benzo(a)pyrene from chylomicron to lipoproteins and among lipoproteins were either based on separation of lipoproteins by ultracentrifugation (10, 13, 14) or by electrophoresis (13). These techniques are time-consuming, especially ultracentrifugation, which takes at least 24 hr to complete and is performed in the presence of

very high ionic strengths. In comparison, ultrafiltration could be carried out at ionic strength similar to that in vivo and was completed in less than 2 min.

VLDL has a half life of less than 10 min in rat plasma and is avidly taken up by the rat liver (12). Also, a rapid exchange of CH between hepatic tissues and lipoproteins, similar to that observed among lipoproteins, can also occur as liver is one of the most highly perfused tissues in the body. Thus, uptake of VLDL and rapid exchange of CH from lipoproteins to liver cell membranes during blood flow could result in rapid removal of an intravenous dose from blood and initial accumulation in the liver (9–11). This exchange will also explain similar rapid clearance of 3-CB from blood, even though it is only partially associated with lipoproteins (6). Chemicals that are bound only to albumin and show no association with lipoproteins should have a different rate of clearance from blood. Depending upon their affinities, many drugs that are bound primarily to albumin in serum have $t_{1/2}$ for plasma clearance ranging from a few hours to several days (24) as compared to less than a few minutes for these CH (9–11).

This research was supported in part by Grant No. PHS ES-00044 from the National Institutes of Health. This is paper no. 7052 of the Journal Series of the North Carolina Agriculture Research Service, Raleigh, North Carolina.

Manuscript received 3 August 1981 and in revised form 3 December 1981.

REFERENCES

1. Brooks, G. T. 1974. Chlorinated Insecticides. CRC Press, Cleveland, Ohio. Part 2, 63–144.
2. Wassermann, A., D. Wassermann, S. Cucos, and H. J. Miller. 1979. World PCBs map: Storage and effects in man and his biological environment in the 1970s. *Ann. N.Y. Acad. Sci.* **320:** 69–124.
3. Moss, J. A., and D. E. Hathway. 1964. Transport of organic compounds in the mammal. Partition of Dieldrin and Telodrin between the cellular components and soluble proteins of blood. *Biochem. J.* **91:** 384–393.
4. Mick, D. L., K. R. Long, J. S. Dretchen, and D. P. Bonderman. 1971. Aldrin and dieldrin in human blood components. *Arch. Environ. Health.* **23:** 177–180.
5. Morgan, D. P., C. C. Roan, and E. H. Paschal. 1972. Transport of DDT, DDE and dieldrin in human blood. *Bull. Environ. Contam. Toxicol.* **8:** 321–326.
6. Matthews, H. B., J. R. Surles, J. G. Carver, and M. W. Anderson. 1977. Polychlorinated biphenyl transport by blood components. *Toxicol. Appl. Pharmacol.* **41:** 201 (Abstract 167).
7. Skalsky, H. L., M. W. Fariss, R. V. Blanke, and P. S. Guzelian. 1979. The role of plasma proteins in the transport and distribution of chlordecone and other polyhalogenated hydrocarbons. *Ann. N.Y. Acad. Sci.* **320:** 231–237.
8. Maliwal, B. P., and F. E. Guthrie. 1981. Interaction of insecticides with human plasma lipoproteins. *Chem. Biol. Interact.* **35:** 177–188.
9. Heath, D. F., and M. Vandekar. 1964. Toxicity and metabolism of dieldrin in rats. *Br. J. Ind. Med.* **21:** 269–279.
10. Pocock, D. M. E., and A. Vost. 1974. DDT absorption and chylomicron transport in rat. *Lipids.* **9:** 374–380.
11. Matthews, H. B., and M. W. Anderson. 1975. Effect of chlorination on the distribution and excretion of polychlorinated biphenyls. *Drug Metab. Dispos.* **3:** 371–380.
12. Eisenberg, S., and R. I. Levy. 1975. Lipoprotein metabolism. *Adv. Lipid Res.* **13:** 1–89.
13. Plack, P. E., E. R. Skinner, A. Rogie, and A. I. Mitchell. 1979. Distribution of DDT between the lipoproteins of trout serum. *Comp. Biochem. Physiol.* **62C:** 119–125.
14. Shu, H. P., and A. V. Nichols. 1979. Benzo(a)pyrene uptake by human plasma lipoproteins in vitro. *Cancer Res.* **39:** 1224–1230.
15. Rudel, L. L., J. A. Lee, M. D. Morris, and J. M. Felts. 1974. Characterization of plasma lipoproteins separated and purified by agarose column chromatography. *Biochem. J.* **139:** 89–95.
16. Knight, J. A., S. Anderson, and J. M. Rawle. 1972. Chemical basis of the sulphophospho-vanillin reaction for estimating total serum lipids. *Clin. Chem.* **18:** 199–202.
17. Lowry, O. H., N. J. Rosebrough, A. L. Farr, and R. J. Randall. 1951. Protein measurement with the Folin phenol reagent. *J. Biol. Chem.* **193:** 265–275.
18. Patterson, M. S., and R. C. Greene. 1965. Measurement of low energy beta-emitters in aqueous solution by liquid scintillation counting of emulsions. *Anal. Chem.* **37:** 854–857.
19. Shore, V., and B. Shore. 1967. Some physical and chemical studies on the protein moiety of a high density (1.126–1.195 g/ml) lipoprotein fraction of human serum. *Biochemistry.* **6:** 1962–1969.
20. Omann, G., and J. R. Lakowicz. 1977. Pesticide uptake into membranes measured by fluorescence quenching. *Science.* **197:** 465–467.
21. Lakowicz, J. R., M. McNamara, and L. Steenson. 1978. Particle-mediated membrane uptake of chemical carcinogens studied by fluorescence spectroscopy. *Science.* **199:** 305–307.
22. Voerman, S. 1969. Distribution ratio of some chlorinated hydrocarbon insecticides between hexane and water. *Bull. Environ. Contam. Toxicol.* **4:** 64–67.
23. Chiou, C. T., V. H. Freed, D. W. Schmedding, and R. L. Kohnert. 1977. Partition coefficient and bioaccumulation of selected organic chemicals. *Environ. Sci. Tech.* **11:** 475–478.
24. Dayton, P. G., Z. H. Israili, and J. M. Perel. 1973. Influence of binding on drug metabolism and distribution. *Ann. N.Y. Acad. Sci.* **226:** 172–194.