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Internal and Maternal Distribution of Persistent Organic Pollutants in Sea Turtle Tissues: A Meta-Analysis

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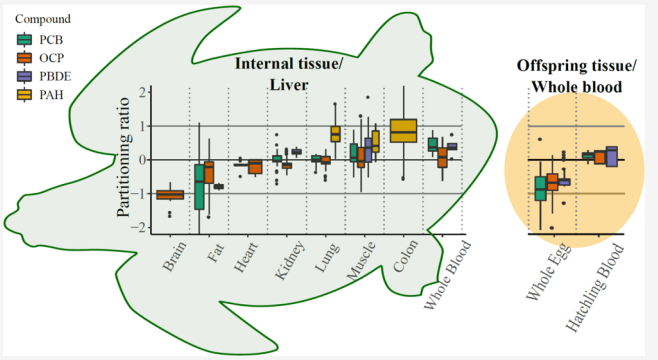
ABSTRACT: We aimed to identify patterns in the internal distribution of persistent organic pollutants (POPs) and assess contributing factors using sea turtles and their offspring as a case study of a long-lived wildlife species. We systematically synthesized 40 years of data and developed a lipid database to test whether lipid-normalized POP concentrations are equal among tissues as expected under steady state for lipophilic compounds. Results supported equal partitioning among tissues with high blood flow or perfusion including the heart, kidney, muscle, and lung. Observed differences in the brain, fat, and blood plasma, however, suggest the physiological influence of the blood−brain barrier, limited perfusion, and protein content, respectively. Polybrominated diphenyl ethers partitioned comparably to legacy POPs. Polycyclic aromatic hydrocarbons, meanwhile, partitioned more into the lung, colon, and muscle compared to the liver under chronic and acute field exposure. Partitioning ratios of individual POPs among tissues were significantly related to the lipophilicity of compounds (as estimated by K_{ow}) in half of the observed cases, and significant differences between juveniles and adults underscore physiological differences across life stages. The comprehensive tissue partitioning patterns presented here provide a quantitative basis to support comparative assessments of POP pollution derived from biomonitoring among multiple tissues.



KEYWORDS: *fugacity capacity, tissue affinity, diffusion limitation, maternal transfer, tissue physiology, lipophilicity, chemical partitioning, pollution biomonitoring, tissue residue*

1. INTRODUCTION

Persistent organic pollutants (POPs) pose a threat to wildlife due to their global distribution, high persistence in the environment, and their tendency to accumulate in the tissues of organisms.[1,2] POPs originate from a wide range of sources, including industrial, domestic, and agricultural activities, leading to a complex mixture of pollutants being present in the environment.[3] Polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) have long been recognized as POPs, and their release to the environment is regulated in global conventions.[4,5] New or continuously sourced chemicals, such as polybrominated diphenyl ethers (PBDEs), perfluorinated compounds (PFCs), and polycyclic aromatic hydrocarbons (PAHs) are now also recognized in a broader context as POPs, for example, by the European Union Chemical Agency,[6] and some of them have been included in the Stockholm Convention.[5]

Several internal processes, including absorption, distribution, metabolism, and excretion, influence the distribution of legacy and emerging POPs among tissues (also referred to as tissue partitioning or biodistribution). Consequently, a pollutant can reach different concentrations in different tissues. For pollutants with specific target sites, the concentration in the target tissue is most relevant in determining its toxic effect.[7,8] However, internal concentrations are often deduced from concentrations within the external medium or food items, which might not represent tissue-specific concentrations.[8,9] Furthermore, when internal concentrations are measured for wildlife species, this is often conducted on easy-to-sample tissues for which the relation to concentrations in other tissues is generally unknown. Hence, biomonitoring results obtained across different tissues might not be directly comparable. There is thus a critical need to better understand the distribution of POPs in internal and offspring tissues, so that data from different studies can be combined and assessments of toxicity refined.

Under stable conditions, the distribution of POPs in an organism will reach a dynamic equilibrium with its external environment and among internal tissues (steady state). The

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equilibrium distribution of a POP among tissues is determined by the fugacity capacities of the tissues.[10,11] The fugacity capacity of a tissue for hydrophobic organic contaminants, such as the major POPs, is largely dependent on the lipophilicity of the POP, which can be estimated by the octanol−water partitioning coefficient (K_{ow}). Consequently, the equilibrium distribution of POPs can often be approximated by differences in lipid contents between the tissues.[10,12] However, individual POPs can differ in their affinity for specific lipid fractions or nonlipid compartments, such as proteins, within specific tissues which can influence their distribution among tissues.[10,13−15] Moreover, physiological changes such as growth, fasting, migration, and reproduction bring the organism out of a steady state by changing the lipid dynamics.[13,14,16] Maternal transfer is a similar change in the steady state that can vary POP concentrations among sexes.[14,17] Data on POP concentrations, measured jointly across different tissues, are therefore valuable to gain baseline knowledge regarding the lipid-based fugacity capacities of different tissues and the subsequent distribution of POPs in wildlife.

Sea turtles might be highly susceptible to POPs due to their long life span[18] and the less developed POP detoxification mechanisms among reptiles compared to other vertebrates.[19−21] Moreover, given the late sexual maturity of sea turtles, POPs can accumulate over many years before being transferred from the mother to offspring where they can interfere with sensitive early life development processes.[17] POPs have been demonstrated to negatively impact sea turtle health and survival.[22−25] The long-term accumulation of POPs, large migrations, and fidelity to specific foraging and nesting locations make sea turtles suitable sentinels for POPs in oceanic locations that might be hard to monitor otherwise.[26,27] For example, eggs and dead hatchlings have been used to monitor POP pollution in sea turtle populations.[26,28] Nonetheless, internal and offspring tissue distribution patterns are not well established for sea turtles,[17] limiting comparative assessments of POP pollution levels derived from biomonitoring data collected among multiple tissues.

We aimed to identify patterns in the internal and offspring distribution of POPs and assess factors contributing to it using sea turtles as a case study of a long-lived wildlife species chronically exposed to POPs. Specifically, we compared the observed distribution patterns against those expected under steady state considering the lipid-based fugacity capacity of tissues. Additionally, we assessed the influence of biological characteristics (sex, life stage, and species) and the lipophilicity (estimated as the K_{ow}) of individual compounds in explaining deviations from the expected tissue partitioning. To achieve these aims, we synthesized and harmonized current data reported in scientific publications regarding POPs measured jointly across different sea turtle tissues.

2. METHODS

2.1. Data Extraction. A systematic search for data on POP concentrations within tissues of sea turtles reported in peer-reviewed publications was conducted following the guidelines on transparent reporting of systematic reviews and meta-analyses[29] (Tables S1 and S2). To identify potential publications, the Scopus and Web of Science databases were systematically searched in July and October 2020. The article title, abstract, and keyword fields were searched across all available dates covered within the databases. The search terms "sea turtles" and "tissues" were combined with any of the following: "contaminants", "persistent organic pollutants", "POPs", "organochlorine pesticides", "OCPs", "pesticides", "DDT", "polychlorinated biphenyls", "PCBs", "polybrominated diphenyl ethers", "PDBEs", "polycyclic aromatic hydrocarbons", "PAHs", "perfluorinated acids", "PFCAs", "perfluorooctane sulfonate" or "PFOS". Including the search terms "organs" or "marine turtles" in the search did not lead to additional results. Only studies published in international peer-reviewed journals in English were considered. Title and abstracts of all identified publications (including reviews) were screened and selected when they reported new data on POP concentrations within sea turtles. The full texts of selected publications were then screened and publications that measured POP concentrations with a minimum of two tissues within the same (group of) individual(s) were retained. Reference lists of retained publications were checked for additional papers matching the above criteria.

To avoid duplication during the extraction of data on POP concentrations, sums of compounds were only included when they incorporated compounds that were not reported individually. Priority was given to data reported for individuals, rather than groups of individuals. When data were only reported across groups, the geometric mean (or if this was lacking, the arithmetic mean) was used. The number of replicate individuals creating the mean was also recorded per tissue (Table S2). Together with data on POP concentrations, data on lipid content in the analyzed tissues were extracted (Table S1), and biometric details regarding sex (classified as female, male, or unknown) and life stages (classified as adult, juvenile, hatchling, egg, or unknown) were recorded (Table S2). All data were extracted from the full published text and supplements. When data were lacking or unclear, contact with the authors was sought (18 cases, Table S1). Preference was given to data presented in tables. Data that were only presented in figures were digitized using ImageJ[30] (Supporting Information, S3).

Data on the lipophilicity of POPs, expressed as the octanol−water partition coefficient (K_{ow}), were estimated for each compound using the software KOWWIN of the Estimation Programs Interface (EPI) Suite that covers compounds with molecular weights of 18−720 and correlates closely with experimentally observed K_{ow} values (r^2 = 0.98, S4).[31] In the case of coelutions reported during the analytical detection of compounds, a log K_{ow} value was only assigned when each individual compound yielded the same estimated log K_{ow}. For the coelution of PCB 82 with PCB 151, the log K_{ow} value was experimentally derived following ref 32.

2.2. Data Treatment. All extracted tissue concentrations were converted to the unit of nanogram per gram on a lipid basis. To enable conversion to lipid basis, tissue- and species-specific lipid contents reported in each publication were used when available. The lipid contents reported in the selected publications were gathered into a lipid content database (Supporting Information, S5). This database was then used to convert POP concentrations for publications that did not report lipid contents (Table S1). Specifically, the average lipid content for a specific tissue was taken for the same species or the nearest phylogenetically related species (Supporting Information, S5). The terms "blood" and "whole blood"; "muscle" and "pectoral muscle"; and "fat", "subcutaneous fat", "yellow or brown fat", and "adipose tissue" were considered synonyms (Supporting Information, S6). Among sea turtles,

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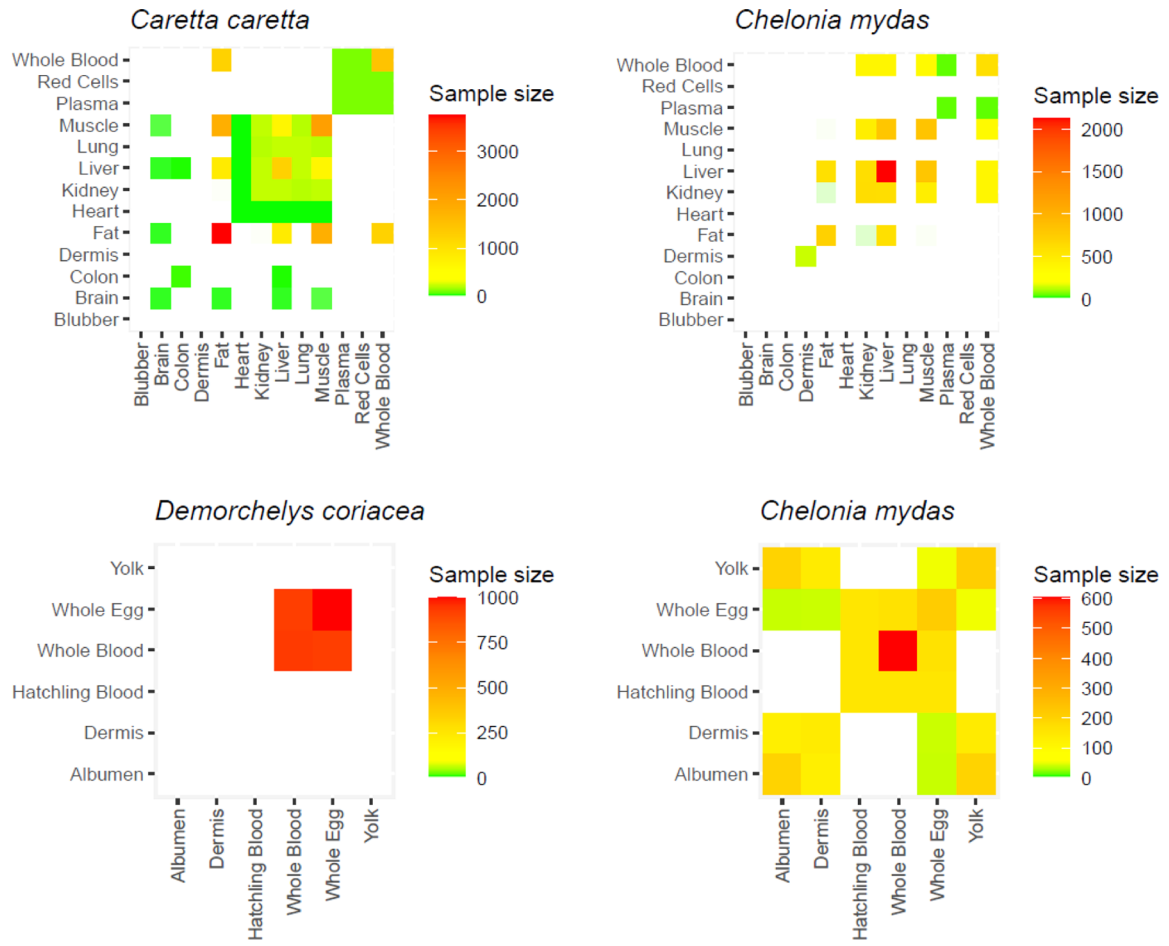

Figure 1. Sample size of data on POPs (weighted by sample replication) among sea turtle tissue combinations. Top panel: internal tissues. Lower panel: offspring (albumen, whole egg, yolk, and hatchling blood) and related maternal (dermis, whole blood) tissues. Combinations that have not been studied are indicated in blank. Plotted here are the species with the most available data, and plots for all species are in Figures S2 and S3.

"blubber" occurs only in leatherback turtles, and it was therefore considered separate from "fat".[33] Data extraction and conversion were conducted twice, each time by an independent researcher, to minimize errors in data entry. Four publications, although matching our search criteria and containing potentially relevant data, were excluded because (1) uncertainties involved in converting concentrations on a dry weight basis to lipid basis were considered too high;[34] (2) sampled tissues could not be related to specific individuals;[35] or (3) all compounds analyzed occurred in concentrations below detection limits.[36,37]

While some data points represented concentrations within individual turtles, others represented averages across a group of turtles. To account for this varying sampling effort, all subsequent analyses were weighted based on the number of replicate turtles sampled for a specific tissue combination. When POP concentrations reported were all below the detection or quantification limit, they were removed to avoid bias and uncertainty in the data set and subsequent analyses. This solution was chosen because detection and quantification limits are frequently not reported. Moreover, when reported, the true concentration of that data point can, at best, only be estimated or, otherwise, substituted by an arbitrary, often biased, value. Such measures could strongly influence data analysis as they interact selectively with the lower end of the range in POP concentrations. POP concentrations reported as zero were considered to be points below the detection or quantification limit and treated as such.

2.3. Data Analysis. The distribution of POPs in turtles was quantified by calculating the partitioning ratio in lipid-normalized concentrations ($\log_{10}$ transformed) between two tissues. Partitioning ratios for internal tissues were standardized against liver concentrations (tissue/liver). Liver and muscle were most often sampled in combination with other tissues (Figures 1 and S2). We standardized against the liver rather than the muscle because of the higher lipid content in the liver and therefore more reliable quantification of POP concentrations in this tissue. To complement comparisons with the liver, partitioning ratios between fat versus blubber (important in energy storage and mobilization of POPs[13]) and between blood compartments (whole blood, plasma, and red cells) were also calculated. For offspring tissues, we standardized against the maternal whole blood concentration as this was most available (Figures 1 and S3).

The influence of biological characteristics on partitioning ratios was analyzed using one-way ANOVAs with Tukey post hoc analysis when significant differences were found. Specifically, a comparison was made among nine classes composed of sex (male, female, or unknown) in combination with the life stage (adult, juvenile, or unknown). The analysis among sex−life stage classes was only conducted when at least

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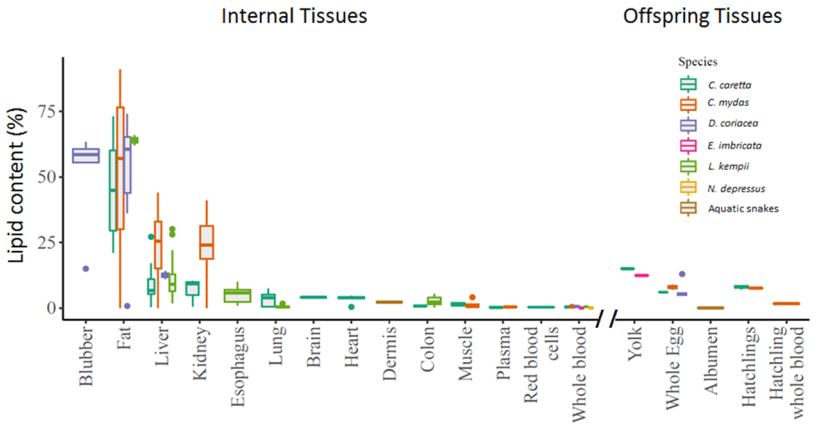

Figure 2. Lipid contents of sea turtle tissues (values in S5). Boxes include the 25−75th percentiles and median. Whiskers extend 1.5× the interquartile range, with outliers beyond this as individual points. Data derived from the systematic review (Table S1).

two classes were available, each represented with at least four unique data points.

The influence of lipophilicity of POPs (estimated as the log K_{ow}) on partitioning ratios was assessed as the significance of log K_{ow} as a parameter in linear regression, accounting for sex−life stage classes, and log K_{ow} as a categorical and continuous explanatory variable, respectively.

For each of these analyses, the factor "reference" was included in initial analyses to identify systematic biases related to a specific study (e.g., because of using borrowed lipid contents to normalize a specific study or due to varying methodological, analytical, and quality control procedures used in a specific study).

3. RESULTS

3.1. Overview of Current Studies. Our systematic search identified 26 studies investigating POP distribution between internal and offspring tissues (Tables S1 and S2). A variety of internal tissue combinations have been studied, mostly relating to either the liver or muscle (Figure 1 for *Caretta caretta* and *Chelonia mydas*, Figure S2 for all species). The link between maternal and offspring tissues was investigated as combinations of various offspring tissues with either dermis or maternal blood (Figure 1 for *C. mydas* and *Dermochelys coriacea*, Figure S3 for all species). Most studies focused on *C. caretta* (60%) and *C. mydas* (48%). Most data, after weighting for sample replication, were available for juveniles of unknown sex (39%), individuals of unknown sex−life stage (24%), and female adults (15%), with few data on males (juvenile 2.5%, unknown sex 2.5%, and adult 1%). Most studies focused on the North Atlantic Ocean (50%) and Mediterranean Sea (27%) and have been published after 2000 (85%, Table S1).

Legacy POPs, such as OCPs (76%) and PCBs (73%), were most often studied, while data on PBDEs (30%), PAHs (10%), and toxaphenes (5%) were less prevalent (Table S1). Concentrations were generally reported on a wet mass basis in either nanogram per gram or picogram per gram as units (Table S2). Data were often reported in a condensed manner as sums of compounds, yet without explicitly specifying which individual compounds were included. About half of the studies report lipid contents (Table S1), allowing conversion to a lipid basis using data from the studied individuals.

3.2. Lipid Contents. Fourteen of the 26 publications reported lipid contents (Table S1), mostly in tissues of *C. caretta*, followed by *C. mydas*, *D. coriacea*, and *Lepidochelys kempii* (Figures 2 and S5). Blubber and fat were the most lipid-rich tissues, followed by liver and kidney, and tissues from hatchlings, whole eggs, and yolk. *C. mydas* had higher lipid contents in fat, liver, kidney, and whole egg than *C. caretta*. The lipid content of the whole blood was reported across six sea turtle species (Figure 2), with lipid contents differing little among the species. By contrast, fat lipid contents often showed a wide variability (mean ± SD: *C. caretta* 45.51 ± 20.54%, *C. mydas* 52.94 ± 25.91%, *D. coriacea* 51.18 ± 22.45%, and *L. kempii* 63.9 ± 2.69%). Lipid content data on the albumen and skin of sea turtles were lacking and therefore borrowed from the closest related species (aquatic snakes) for which such data were reported.[38,39]

3.3. Tissue Distribution. *C. caretta* provided the most complete record regarding the distribution of legacy pollutants (PCBs and OCPs) relative to the liver (Figure 3A). In this species, lipid-normalized concentrations of PCBs and OCPs in the lung and muscle were close to those in the liver, while those in the heart and kidney were slightly lower than the liver. Partitioning in fat, although variable, was on average about 7.4 and 6.1 times lower than in liver for PCBs and OCPs, respectively. The partitioning into the brain was 10 times lower than into the liver. These patterns can be complemented with insights derived from *C. mydas*. Specifically, concentrations in whole blood were around equilibrium with the liver for OCPs, while PCBs partitioned more into whole blood than the liver. Additionally, maternal transfer of PCBs and OCPs resulted in comparable lipid-normalized concentrations between hatchling blood and maternal whole blood in *C. mydas*, although lipid-normalized concentrations in hatchling blood were up to an order of magnitude higher than those in whole egg (Figure 3B).

Among emerging POPs, PBDEs showed generally comparable patterns to the PCBs and OCPs within *C. mydas* and *D. coriacea* (the two species for which the available data allowed a comparison among compound groups), except in whole egg and fat (Figure 3A,B). Specifically, PBDEs partitioned more into whole blood than in whole egg; however, they partitioned less so than for PCBs and OCPs. PBDEs accumulated more into the liver than in fat of *C. mydas*. PAHs, meanwhile, partitioned relatively more in the lung and colon than in the liver in *C. caretta* and *L. kempii* and slightly more in muscle than in the liver in *C. mydas*.

Of special interest is the distribution among storage tissues (blubber/fat), due to their capacity to buffer short-term

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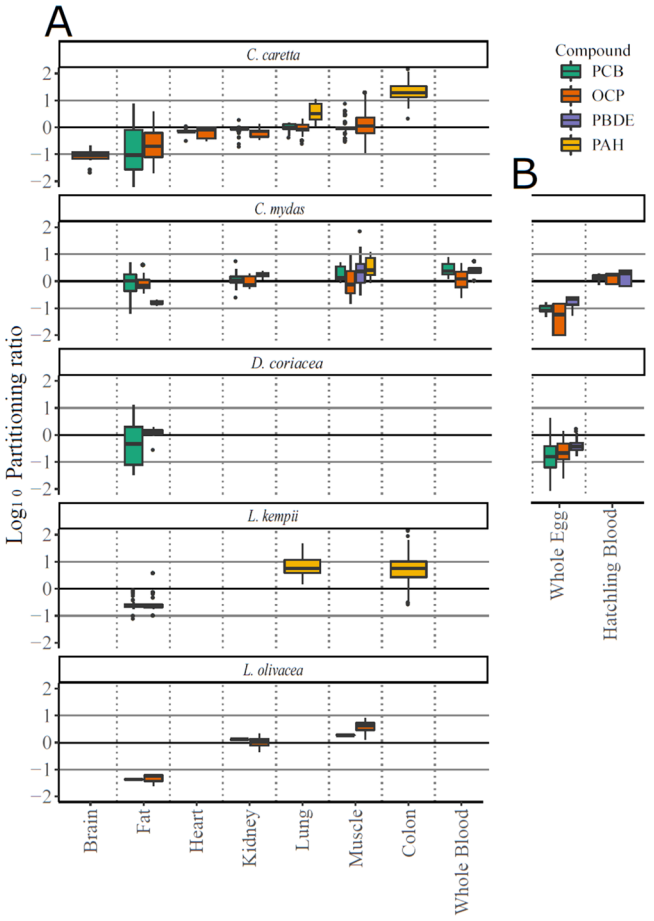

Figure 3. Partitioning of POPs among the following: (A) internal tissues (tissue/liver) and (B) offspring tissues (tissue/maternal whole blood). The 0-line indicates the expected equilibrium for lipid-normalized POP concentrations, and gray lines at 1 and −1 indicate 10 times higher or lower partitioning. Boxes include the 25−75th percentiles and median. Whiskers extend 1.5× the interquartile range, with outliers beyond this as individual points. Data derived from the systematic review (Tables S1 and S2).

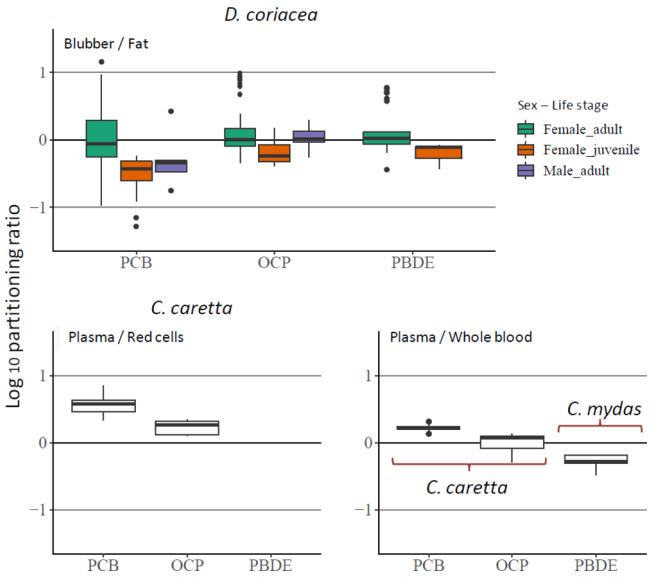

Figure 4. Partitioning of POPs between storage and blood tissues, with the former split across sex−life stage classes. The 0-line indicates the expected equilibrium for lipid-normalized POP concentrations, and gray lines at 1 and −1 indicate 10 times higher or lower partitioning. Boxes include the 25−75th percentiles and median. Whiskers extend 1.5× the interquartile range, with outliers beyond this as individual points. Data from refs 33, 40, and 41.

fluctuations in POP concentrations,[13] and the distribution among blood compartments (plasma/red blood cells; plasma/whole blood), due to their role in the transport and distribution of POPs among tissues (Figure 4). Among storage tissues, PBDEs, OCPs, and PCBs partitioned equally between fat and blubber in adult female *D. coriacea*, although patterns in PCBs were more variable. Juvenile female *D. coriacea*, meanwhile, showed partitioning ratios more toward fat than blubber for these three compound groups (with significant differences among sex−life stages for PCBs, S8). Few data were available for male adult *D. coriacea*. Regarding blood compartments, PCBs and OCPs partitioned more toward plasma than red cells in *C. caretta*, which was most pronounced for PCBs. Likewise, the distribution of PCBs and OCPs between plasma and whole blood for the same turtle species followed a similar order, with PCBs partitioning more toward plasma than whole blood, while OCPs were near equilibrium. Meanwhile, PBDEs (recorded for *C. mydas*) showed more affinity for whole blood than plasma, opposite to PCBs.

3.4. Biological Characteristics. Although distribution patterns (relative to the liver) were similar between *C. caretta* and *C. mydas* (two species for which most data were available) for some tissues such as kidney and muscle, tissue partitioning differed among species for other tissues (Figure 3A). For example, PCBs and OCPs partitioned equally between fat and liver in *C. mydas* for both compound classes and in *D. coriacea* for OCPs, while PCBs and OCPs partitioned more into fat in *C. caretta*, *L. kempii*, and *Lepidochelys olivacea*, although the latter two species had low quantities of data. PCBs, OCPs, and PBDEs partitioned more into whole blood than whole egg in both *C. mydas* and *D. coriacea*, with the difference in the partitioning most pronounced for *C. mydas* (Figure 3B).

Life stage, and only to a limited extend sex, influenced tissue partitioning of OCPs and PCBs. For example, between juvenile and adult *C. caretta*, significant differences in tissue partitioning were observed for OCPs between fat and liver and muscle and liver (with insufficient data available regarding juveniles for heart, kidney, and lung, Figures 5 and S8). Similarly, adult and juvenile *C. caretta* differed in their partitioning of PCBs between fat and liver (with no data on other tissues for PCBs, Figures 5 and S8). Meanwhile, males and females did not differ significantly in tissue partitioning (relative to the liver) of OCPs among heart, kidney, lung, and muscle in adult *C. caretta* (Figures 5 and S8). Males and females also did not differ in tissue partitioning between fat and liver for both OCPs and PCBs in this species. A significant difference in the distribution of PCBs between liver and fat, however, was observed between adult male and female *D. coriacea*, although few data were available. Moreover, the distribution of PAHs displayed a sex-specific pattern, where PAH compounds reaching higher concentrations accumulated more in the colon of female than male *L. kempii* with a wide range of carapace sizes including both juveniles and adults[42] (Figure 6).

3.5. Lipophilicity. Partitioning ratios of individual POPs among tissues were significantly related to the lipophilicity of compounds (as estimated by the K_{ow}) in half of the cases (19 out of 34 cases, S9), with 11 cases where the rate of change exceeded a slope of 0.10 on a $\log_{10}$ scale (Figure 7).

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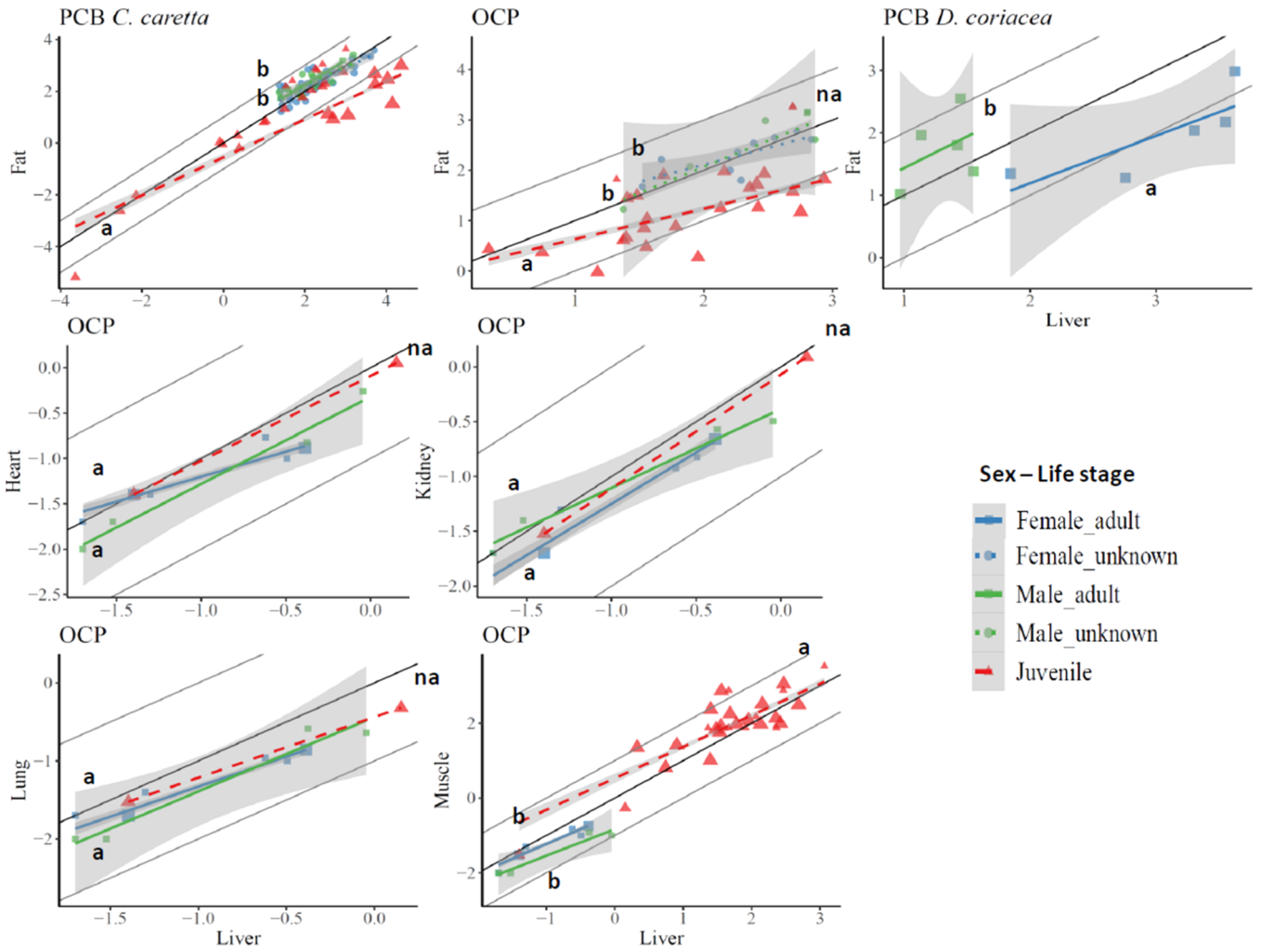

Figure 5. Lipid-normalized OCP and PCB concentrations (log_{10} transformed) among tissues of *C. caretta* and *D. coriacea*. Data points (sized relative to each other in each graph based on the weighted number of replicate samples), letters (results of ANOVA with the Tukey test between sex-life stages, Supporting Information, S8), linear regressions by sex (females: blue, males: green, juveniles: red), and life stage classes (adults: full lines with squares, juveniles: dashed lines with triangles, and unknown: dotted lines with circles) including 95% confidence interval as a gray-shaded area, 1:1 line black and 10-fold difference (gray lines). Data from refs 43−50.

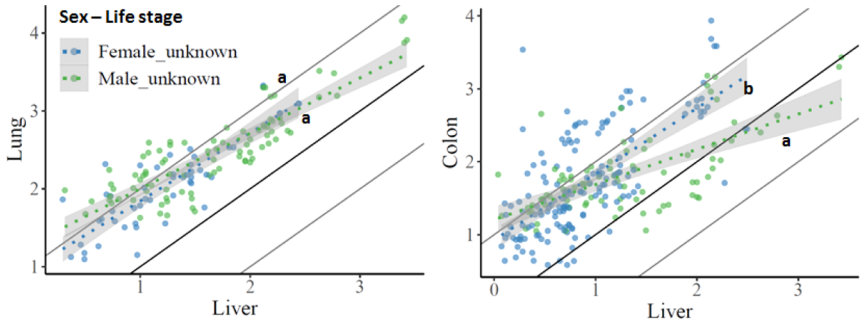

Figure 6. Lipid-normalized PAH concentrations (log_{10} transformed) among tissues of *L. kempii*. Data points (dots), linear regressions (lines colored by sex−life stage class with 95% confidence interval as a gray-shaded area), letters (results of ANOVA between sexes, S8), 1:1 line black, and 10-fold difference (gray lines). Data from[42] as provided by NOAA (National Marine Fisheries Services Northwest Fisheries Science Center) as part of the Deepwater Horizon NRDA conducted cooperatively among NOAA, other Federal and State Trustees, and BP.

Specifically, the partitioning ratio of OCPs between muscle and liver decreased with higher log K_{ow} values in both *C. caretta* and *C. mydas*, as well as for PCBs in *C. caretta*. Similar decreasing partitioning ratios were also observed between whole blood and liver for OCPs in *C. mydas*, between fat and liver for PCB and OCPs in *C. caretta*, between lung and liver for PAHs in *L. kempii*, and for the maternal transfer between whole egg and maternal whole blood for PCBs and PBDEs in *D. coriacea*. An increasing partitioning ratio was only detected in 2 of the 11 cases, namely, between whole blood and liver for PBDEs in *C. mydas* and between fat and liver for OCPs in *C. mydas*.

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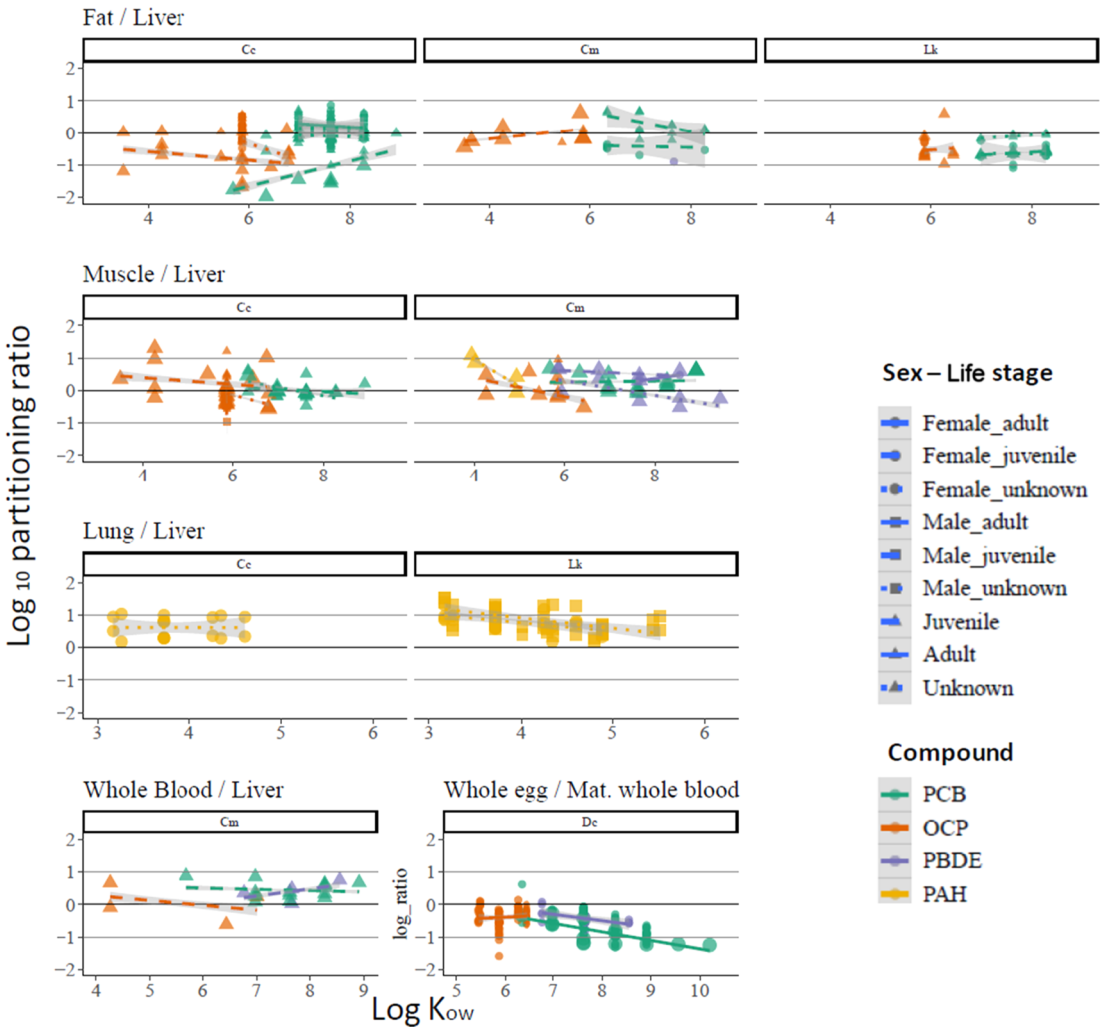

Figure 7. Partitioning of POPs among tissues relative to the log K_{ow}, considering sex (female: circle, male: square, unknown: triangle) and life stages (adults: full line, juveniles: dashed line, and unknown: dotted line) for different species [*C. caretta* (Cc), *C. mydas* (Cm), *L. kempii* (Lk), and *D. coriacea* (Dc)] and compounds. Data points are sized relative to each other in each graph based on the weighted number of replicate samples. Linear regressions (Supporting Information, S9), including 95% confidence intervals, are plotted to illustrate the general trend. Data from refs 33 and 41−60.

4. DISCUSSION

4.1. Internal Tissue Distribution. The current study presents, for the first time, a comprehensive, quantitative overview of POP distribution among multiple sea turtle tissues by synthesizing and harmonizing scattered data across publications spanning 40 years of research. POP concentrations recorded within individual tissues were normalized against the lipid content of these tissues under the assumption that the fugacity capacities of tissues for lipophilic contaminants, including the major POPs, are largely driven by tissue lipid contents.[61] Under equilibrium conditions, lipid-normalized POP concentrations would then be equal among tissues. In agreement with this assumption, OCPs and PCBs in *C. caretta* (the species for which most data, and thus information, was available) reached comparable lipid-normalized concentrations (standardized against liver concentrations) in tissues that are characterized by high blood flow rates in turtles such as heart, kidney, and lung (Figure 3A).[62,63]

In deviation of our assumption, lipid-normalized concentrations of PCBs and OCPs were on average 7.4 and 6.1 times lower in fat than the liver tissue of *C. caretta*. In part, the lower partitioning into fat could be attributed to the poor blood perfusion of fat tissue in turtles, leading to a diffusion limitation for compounds being transported into fat tissues. This diffusion limitation might delay the time to reach steady-state conditions.[62] In fact, the partitioning of PCBs and OCPs between fat and liver differed significantly among life stages in *C. caretta* (Supporting Information, S8), with higher partitioning into liver for juveniles (Figure 5). Juvenile sea turtles direct a large part of their energy toward growth;[64] consequently, their fat reserves might not reach the steady state. By contrast, adults might invest relatively more in building up energy reserves into fat tissues, allowing these fat tissues sufficient time to equilibrate their pollution burdens and thus overcoming the restraint posed by diffusion limitation. Matching this concept, partitioning of PCBs, OCPs, and PBDEs in *D. coriacea*, the only sea turtle species to build up blubber reserves,[33] also displayed differences among life stages, where these compounds partition more into fat than blubber for juvenile females, while they reach equal partitioning between fat and blubber in adult females (Figure 4).

OCPs and PCBs in muscle tissue, which has a comparable blood flow rate to fat in turtles,[62] reached comparable lipid-

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normalized concentrations to those in the liver in *C. caretta* and *C. mydas* (Figure 3A) and were thus much higher than those in the fat tissue of *C. caretta*. The shorter distance between capillaries and muscle tissue cells compared to fat tissue cells, and consequently, the shorter distance that POPs have to diffuse over to reach muscle tissue cells compared to fat tissue cells after leaving the blood circulatory system could be at the basis of this difference.[61] Specifically, diffusion limitation might be less influential in the distribution dynamics of POPs into muscle as compared to fat tissue. Nevertheless, the partitioning of individual OCPs between muscle and liver was significantly influenced by log K_{ow} (Supporting Information, S9), with OCPs with lower log K_{ow} partitioning relatively more into the muscle than liver compared to OCPs with higher K_{ow} in both species (Figure 7), with a similar pattern for PCBs in *C. caretta*. The results obtained for both fat and muscle support the importance of accounting for the diffusion limitation in addition to blood flow limitation when predicting the distribution of POPs among tissues of organisms.[61]

Lipid-normalized concentrations of OCPs and PCBs in the brain, despite having one of the highest blood flow rates in turtles,[62] were an order of magnitude lower than those in the liver of *C. caretta* (Figure 3A). The blood−brain barrier (BBB) restricts the transfer of xenobiotics toward the brain via the interlocking of endothelium cells at the BBB with tight ligands.[65] As lipophilic compounds, POPs might diffuse through endothelium cells and thus bypass the barrier posed by the tight ligands. However, active transporters present in the endothelium cells can efflux xenobiotics back to the blood.[65] The expression of such transport proteins increases in the presence of POPs such as PCBs and dioxins in endothelium cells.[66] In a counter mechanism, the presence of PCBs can also increase the permeability of the tight ligands between endothelium cells in the BBB.[67] The rate at which the BBB restricts the transport of POPs toward the brain as a result of interactions between these mechanisms has to the best of our knowledge not been quantified for reptiles. Data regarding sea turtles were only available for three brain samples in *C. caretta*, with 12 OCP compounds analyzed (Table S2).[45] Nonetheless, OCPs and PCBs have been detected in the brain of other reptiles.[68] These results suggest that the BBB, although not eliminating, can buffer the brain at least to some extent against POPs and associated neurotoxic effects by lowering the exposure of the reptile brain tissue to POPs.

While the distribution of OCPs and PCBs matched with the expected lipid-based equilibrium partitioning in the lung and muscle relative to the liver, lipid-normalized concentrations of PAHs were higher than in the liver for those two tissues (Figure 3A). POPs can to a certain extent be metabolized or immobilized by binding to proteins,[14,20,69] increasing the affinity of the POP for that tissue. This is particularly the case for PAH compounds which can be metabolized by marine organisms[42,70] and might explain their different distribution patterns compared to the more persistent PCBs and OCPs.[71] Specifically, metabolization in the liver, the main tissue involved in detoxification processes, would lower concentrations in this tissue compared to the lung and colon. In addition to dietary exposure, the main uptake route for PAHs is via the air. The binding of PAHs to proteins upon the first contact with the lungs could then result in higher concentrations in the lungs compared to the liver. Likewise, the binding of PAHs to proteins associated with excretion into the colon could explain the higher concentrations in this tissue in comparison to the liver tissue. On the other hand, data on PAHs synthesized in the current study for the lung and colon of *C. caretta* and *L. kempii* were derived from research[42] on turtles exposed to the Deepwater Horizon (DWH) oil spill and thus reflect a recent, acute exposure that might have brought the PAH distribution in these turtles temporarily out of the steady state. Nonetheless, observations of muscle tissue in *C. mydas*, derived from turtles chronically exposed to PAH pollution in the Gulf of Oman,[57] also demonstrated greater differences in distribution between the muscle and liver for PAHs than for OCPs and PCBs (Figure 3A). Considering the potentially different distribution mechanisms, including the influence of metabolization, of more recently recognized POPs such as PAHs and PBDEs, complementing the currently relatively limited data set on these compounds is a critical research direction.

4.2. Offspring Tissue Distribution. The lower lipid-normalized concentrations of PCBs, OCPs, and PBDEs in whole eggs relative to maternal whole blood in both *C. mydas* and *D. coriacea* (Figure 3B) likely reflect a slow compound-specific transfer of POPs during egg formation. The uptake of POPs into yolk is most influential in determining whole egg POP content given the higher lipid content (Figure 2) and thus higher relative contribution to lipid-normalized substance concentrations of yolk compared to albumen and other egg compartments. Uptake of POPs by yolk might only be partially complete before vitellogenesis finishes.[17] Highly lipophilic POPs in particular can be slow to mobilize from existing tissues, preferentially be reabsorbed by maternal tissues, and have slower diffusion speeds.[17] Such compound-specific maternal transfer of POPs into egg yolk is reflected in the progressively higher partitioning of PCBs and PBDEs in whole blood compared to whole eggs with increasing lipophilicity (estimated by a higher log K_{ow}) in *D. coriacea* (Figure 7). Similarly, lower chlorinated PCBs have been observed to be relatively more prevalent than higher chlorinated PCBs in eggs compared to the liver and fat tissues of freshwater turtles.[72] The latter authors suggested that the higher prevalence of lower chlorinated PCBs could also be a reflection of the use of dietary rather than stored lipid reserves during egg development.[72] In sea turtles, the relative importance of income versus capital breeding as a strategy for egg production is still debated.[17] Sea turtles generally do not feed during their nesting migrations. Hence, the values in maternal whole blood at the time of sampling on the nesting beach might not be representative of the maternal POP composition during vitellogenesis in the foraging grounds. Nonetheless, the evidence of a relation between log K_{ow} and distribution for both PCBs and PBDEs between whole egg and maternal whole blood in *D. coriacea* and the relatively smaller difference in the partitioning between these two tissues for PBDEs compared to PCBs (Figure 7) underscore the importance of chemical characteristics in determining their maternal transfer rates. Moreover, the selective representation of individual POP compounds in eggs should be considered when using eggs (either whole eggs or yolk) to monitor POPs in sea turtle populations.[26−28]

Despite the lower relative distribution toward whole eggs compared to maternal whole blood, lipid-normalized concentrations of OCPs, PCBs, and PBDEs in hatchling whole blood were at the same level as maternal whole blood in *C. mydas* (Figure 3B). Less lipophilic PCBs were observed to be more prevalent in hatchling whole blood compared to whole eggs in

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the study of ref 73. The authors suggested this pattern to relate to a selectively higher uptake of highly lipophilic PCBs by hatchling fatty tissue, faster metabolization of highly lipophilic PCBs by hatchlings, or lower transfer rates of highly lipophilic PCBs from eggs to hatchlings.[73] The latter argument corresponds with the selectively higher uptake of less lipophilic PCBs and PBDEs into eggs from maternal blood observed for *D. coriacea* in the current synthesis (Figure 7). To explain the relatively higher distribution (compared to maternal blood) in hatchling blood than in whole egg, we hypothesize two additional mechanisms. First, since lipids present in the yolk are being converted into energy to support the embryonic development, the resulting embryo will have fewer lipids, leading to higher lipid-normalized concentrations of POPs. Second, whole blood, including hatchling whole blood, might accumulate POPs relatively more than other tissues, as a result of proteins that bind to POPs. In the current research synthesis, we observed that adult *C. mydas* obtained higher POP concentrations in whole blood than in the liver (Figure 3A). Moreover, while lipid-normalized concentrations of OCPs were comparable across the plasma, red cells, and whole blood in *C. caretta*, PCB concentrations were relatively higher in plasma than in red cells in this species (Figure 4). The relatively higher lipid-normalized concentrations of PCBs in plasma could be due to the higher protein content of plasma and the specific binding of PCBs to plasma proteins.[13−15,74] Consequently, proteins present in hatchling blood might increase POP concentrations in this tissue relative to other hatchling tissues. Nonetheless, interactions of POPs with blood proteins and the biochemical profile of sea turtle blood across life stages are still poorly determined. Only 11 pooled hatchling blood samples were available (Table S2).[73] Early life stages such as embryo and hatchling stages, where major development processes take place, are generally considered to be highly susceptible to environmental pollution,[75] with demonstrated negative effects of embryonic POP exposure on health and survival.[73] Nonetheless, processes of distribution among different hatchling tissues and uptake mechanisms of POPs during the embryonic development of sea turtles,[28] and reptiles in general, remain a critical research direction.

4.3. Biological Characteristics. The pattern of distribution of POPs in kidney and muscle relative to the liver and in whole egg relative to maternal whole blood was comparable between *C. mydas*, *C. caretta*, and *D. coriacea* (species with most data available), while for other tissues, most notably the fat relative to the liver, the pattern differed among all investigated species (Figure 3A,B). Some of the distribution patterns observed here for sea turtles correspond with tissue distribution patterns observed in freshwater turtles. For instance, similar to the observed lower partitioning among whole eggs than maternal whole blood in the current study (Figure 3B), lower lipid-normalized concentrations were also observed in whole eggs of freshwater turtles relative to maternal liver concentrations.[72,76] Comparable lipid-normalized concentrations between fat and liver, observed here for *C. mydas* (Figure 3A), were likewise observed in freshwater turtles.[72,76] By contrast, *C. caretta* and *D. coriacea* displayed lower partitioning ratios in fat versus liver (Figure 3A). These interspecific differences might indicate species-specific partitioning processes. In part, these species-specific differences could be attributed to different energetics and the related use of fat reserves during the life cycle of these species.[64,77] *C. caretta* and *D. coriacea*, for example, have biogeographic distributions which cover relatively colder climates compared to *C. mydas*.[78] Additionally, *D. coriacea* is known to undertake the most extensive migrations among the sea turtle species.[79] Thermoregulation and migration are both processes that require energy. Alternatively, as discussed above, partitioning ratios also differed between juvenile and adult life stages (Supporting Information, S8). Information regarding life stages, however, was often lacking, preventing quantification of the relative influence of species versus life stages in the interspecific differences in fat to liver partitioning. Therefore, these interspecific patterns should be considered with caution as different amounts of data were available across the different species and for the different sex and life-stage characteristics.

Physiological changes such as growth, fasting, migration, and reproduction bring an organism out of the steady state by changing the lipid dynamics, leading to mobilization and subsequent redistribution of POPs among tissues.[13,14,16] This has important implications for toxicity assessments as the release of POPs built up in lipids can expose sea turtles to levels of POPs that are elevated above normal background contamination levels.[13] Tissue partitioning of OCPs and PCBs between fat and liver or muscle and liver in *C. caretta* and between fat and blubber in *D. coriacea* showed significant differences between juvenile and adult stages (Figures 4, 5, and S4), potentially because juveniles, due to their growth, are not in the steady state.

Overall, sex had little influence on tissue partitioning, with male and female *C. caretta* not differing significantly in their distribution among tissues (Figures 5 and S8). Nonetheless, most sea turtle species undertake extensive migration, thereby utilizing their lipid reserves.[80,81] Differences in migration behavior among sexes could relate to the observed significant difference in PCB distribution between fat and liver for male and female *D. coriacea* (Figure 5 and S8). Mobilization of lipids for yolk formation (and subsequent maternal transfer of POPs to offspring) is a similar change in the steady state, which can explain some differences among sexes.[14,17] Differences in POP levels have also been related to higher metabolic rates and energy expenditures among males, leading to higher feeding and thus POP uptake rates, differences in growth rates among sexes leading to different growth dilutions, or different habitat use behaviors.[2,82] Additionally, the distribution of PAHs in the colon relative to the liver with female *L. kempii* having relatively higher lipid-normalized concentrations in the colon compared to the liver, particularly for PAH compounds occurring at high concentrations, than males (Figure 6), suggest potentially different elimination or metabolization capacities between sexes.

4.4. Research Directions. Synthesizing and harmonizing data on POPs in sea turtle tissues presented challenges corresponding with key issues identified previously in synthesizing studies on POPs in sea turtle eggs,[17] specifically data Access, Transferability, and Transparency, and wise use of Conservation-sensitive materials (ATTAC). To best convert these ATTAC issues toward opportunities for future research, we follow and add to the best practice guidelines proposed by these authors[17] (Supporting Information, S10). Specifically, we highlight three main challenges. First, knowledge is lagging behind, with often long times, up to a decade, between sampling, analysis, and publication (Table S1). This delay in knowledge generation limits the inclusion of pollution threats in vulnerability assessments and their uptake into management actions for these red-listed species.[83] Second, our analysis

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identified significant differences in tissue partitioning among life stages and in some cases among sexes. Nonetheless, comparisons between sexes and life stages were restricted because details on sex or life stage were not described, concentrations were reported among mixed sex−life stage groups, or data were only presented within one sex−life stage class in our compiled data set. Specifically, the number of data points for males and information on the sex of juveniles were often low or absent, which likely reflects the difficulty in establishing these parameters in the wild.[84] If data on biological characteristics become more available, the relative importance of these biological characteristics on tissue partitioning among different tissue combinations can be better quantified. Finally, the development of a lipid content database (Figure 2 and S5) allowed us to homogenize data across studies even when lipid contents were not reported and to compare the resulting patterns to those expected under the assumption that the fugacity capacity of tissues for lipophilic contaminants such as the major POPs is largely driven by tissue lipid contents. Our results support this assumption for tissues with a high blood flow or perfusion in turtles such as heart, kidney, muscle, and lung (Figure 3A). Nonetheless, deviation from this assumption for tissues such as brain, fat, and blood plasma underscores the importance of physiological features such as the BBB, poor blood perfusion, and protein contents in tissue partitioning. Further physiological research and development of associated databases, such as lipid and protein content databases, would improve our mechanistic knowledge of factors driving tissue partitioning and ultimately allow for better predictions regarding POP tissue distributions, a critical component in toxicity assessments.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.est.1c02845.

Overview of pollutants in the systematic search, sample details from the systematic search, extraction of data from figures, K_{ow} derivation, lipid content database, tissue synonyms, available tissue combinations per species, influence of sex−life stage classes, influence of lipophilicity, future improvements and ATTAC issues, and literature cited in the Supporting Information (PDF)

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Notes

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