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FISH AND CHEMICALS: THE PROCESS OF ACCUMULATION[1]

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INTRODUCTION

After three decades (1, 2) of intensive research, the environmental behavior of DDT is still almost incomprehensible. Consider for a moment that fish can easily accumulate a million times the concentration of DDT found in the water they inhabit. Yet, incredible as it may seem, fish are doing that every day with DDT and several other interesting compounds. At the same time, there are numerous other chemicals they cannot bioaccumulate with such efficiency. These associations constitute the subject for this review. Fish and chemicals—how does the one accumulate the other?

The effects of pollutants on fish have been comprehensively reviewed annually since 1968 (3a–h) in the *Journal of the Water Pollution Control Federation.* Johnson has published two critical reviews (4, 5) dealing with pesticides and fish that are

[1]Symbols and identities of compounds mentioned in the text (in order of appearance): DDT (p,p'-DDT), 2,2-bis (*p*-chlorophenyl)-1,1,1-trichloroethane; DDT-R, sum of all isomers and alteration products of DDT detected in sample; Dieldrin, 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-*endo,exo*-5,8-dimethanonaphthalene; Aroclor® 1254, registered trademark of the Monsanto Co., St. Louis, Mo., for a mixture of PCBs; DDD (p,p'-DDD), 2,2-bis(*p*-chlorophenyl)-1,1-dichloroethane; DDE (p,p'-DDE), 2,2-bis (*p*-chlorophenyl)-1,1-dichloroethylene; PCBs, polychlorobiphenyls (mixtures of chlorinated biphenyl compounds); 2,2',4,4'-tetrachlorobiphenyl, a single isomer of PCB; Endrin, 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-*endo-endo*-5,8-dimethanonaphthalene; Chlorpyrifos, O,O-Diethyl O-(3,5,6-trichloro-2-phyridyl) phosphorothioate (Dursban); 3,5,6-trichloropyridinol, 3,5,6-trichloro-2-pyridinol (a metabolite of chlorpyrifos); Hexachlorobenze, hexachlorobenzene; Trifluralin, α,α,α-trifluro-2,6-dinitro,N,N-dipropyl-*p*-toluidine; Methyl mercury, methyl mercury.

particularly useful because they summarize the state of the art at two distinct stages of development. In his first review (4), acute toxic effects of various chemicals on many different kinds of fish were emphasized. But he recognized that "major gaps obviously exist in understanding the modes and temporal relationships of pesticide uptake by fishes. . . . " Although considerable progress was made in the next five years (5), many questions and apparent contradictions remained unresolved before chemical residue accumulation by fish could be quantified.

UNIQUE ASPECTS OF THE PROBLEM

Predicting when, where, and to what degree a fish will accumulate a particular chemical has ecologic and economic importance. This need for predictability has many unique aspects foreign to mammalian toxicology. The fish themselves display a vast diversity of anatomical design, represented by over 20,000 species spanning 400 million years of evolution (6). Because they live in a world virtually devoid of oxygen by terrestrial standards, fish are required to satisfy their oxygen demands by extracting volumes of water weighing thousands of times their body weight each day. Osmoregulation is a continuous battle. Freshwater fish must actively absorb salts and excrete copious volumes of dilute urine. Conversely, marine fish drink sea water and actively excrete salts to maintain ionic homeostasis. Water itself undergoes an extremely rapid flux (i.e. the half-life of water in a whole fish is only 0.5–1.5 hr) (7). Furthermore, contrary to the conclusions drawn from some early investigations, certain metabolic detoxication processes, such as conjugation, are important in fish (8, 9). Finally, fish are poikilothermous, so rates of metabolism and chemical uptake are inexorably linked to the temperature of their environment. Thus, we find that the uptake of DDT directly from water by fish increases with temperature in proportion to their oxygen consumption (10, 11).

The residue problem is further complicated by the tremendous size range and indeterminate growth patterns within a single species of fish. For example, adult carp (*Cyprinus carpio*) may weigh a million times more than their newly hatched larvae (12). In addition, the size differences between species are equally great. Yet, for practical reasons, essentially all experimental research on pesticide accumulation has been done on small fish (13), making extrapolations to natural populations difficult. Consequently, while unique aspects such as these have impeded the direct adoption of predictive models designed for mammalian systems, they have fostered many innovative interchanges between a variety of disciplines that may ultimately benefit mammalian studies.

HOW FISH ACQUIRE CHEMICAL RESIDUES

Laboratory Studies

The accumulation of chemical residues by fish was originally attributed to a process defined as biological magnification through the "food-chain" (2, 14–16). The basic assumption underlying this hypothesis is that for each step in the food-chain proportionately more chemical residues are retained than energy (in the form of body

weight gain). This process was illustrated by Woodwell (16) who shaded each segment of an ecological pyramid with colored dots to represent DDT. The dots were widely spaced within the broad base of primary producers, more closely spaced in the consumer levels, and crowded in the narrow pinnacle of top carnivores. Accompanied by an illustration of DDT levels in an estuarine food web, it made an artistic and convincing portrayal of the accumulation process. But, direct experimental studies were later to reveal that the factors controlling uptake and retention of chemicals by fish were more complex than originally envisioned.

The growth efficiency (i.e. body weight gained per weight of food consumed) of fish is about 8% (17). Hence, any dietary uptake efficiency of contaminants which is greater than 8% will result in an accumulation of residues. The dietary uptake efficiencies reported for various chlorinated hydrocarbons range from 9 to 68% (18–26). As might be expected, this variability appears to be largely attributable to the length of exposure, dosage level, and the type of food employed. For example, Grezenda et al fed individual goldfish (*Carassius auratus*) artificial diets contaminated with DDT (19) or dieldrin (20). They found that the dietary uptake efficiency of DDT declined as the residue concentrations of DDT-R increased with time (19). Also, the proportion of dieldrin retained was less in fish receiving the higher of two treatment levels (20). Furthermore, dieldrin residue concentrations rose throughout the trial while DDT-R levels reached a steady state. Reinert et al (26) observed that the uptake efficiency for DDT dissolved in corn oil and then mixed into an artificial diet was only about 20%. This is substantially less than the 68% retention of Aroclor® 1254 observed by Lieb et al (21) under similar experimental conditions. However, Lieb et al incorporated the Aroclor with salmon oil, which may improve availibility. Because dietary factors compromise availability, the utility of laboratory data to predict dynamics under natural conditions may be highly arbitrary.

Fish can rapidly take up high concentrations of DDT and other chemicals directly from the water (27–29). Atempting to assess the importance of this source relative to uptake from food by means of laboratory studies is confusing. For example, Macek & Korn (24) demonstrated that brook trout (*Salvelinus fontinalis*) obtained only 10 times more residues from food contaminated with 3 ppm DDT than from water containing 3 pptr DDT. It must be noted that the dose levels were selected to approximate concentrations present in forage organisms and water of Lake Michigan, not to bias the results.

Reinert et al (26) obtained somewhat different results with lake trout (*S. namaycush*) dosed with 6 to 9 pptr of both DDT and dieldrin in the water and/or 2.3 ppm DDT and 1.7 ppm dieldrin in food. After 152 days of exposure the fish obtained progressively higher concentrations of DDT from water alone ($\bar{x}$ = 352 ppb), food alone ($\bar{x}$ = 648 ppb), and food and water combined ($\bar{x}$ = 776 ppb). On the other hand, there was no significant difference between dieldrin levels obtained from water ($\bar{x}$ = 478 ppb) or from food ($\bar{x}$ = 470 ppb) even though water and food combined still appeared to be additive ($\bar{x}$ = 670 ppb). Hence, the actual differences in the concentration of each chemical taken up were relatively slight regardless of the source. Furthermore, they estimated that the efficiency of uptake directly from the

water ranged somewhere between 12 and 59% for DDT and 20 to 102% for dieldrin, while dietary uptake efficiencies were only 20 and 17%, respectively. Contrary to these observations, Chadwick & Brocksen (18) and other investigators (22, 25) demonstrated that natural food and water sources did not appear to be additive for dieldrin uptake by various species of small-sized fish under a variety of laboratory conditions. Therefore, we must conclude that uptake from *both* water and food can be substantial depending on the conditions of exposure, duration, dose level, and individual fish involved in the process.

Field Studies

Synthetic pollutants do not behave in the same manner as essential nutrients, notably phosphorus, in aquatic environments. If a single dose of radioactive phosphorus is added to a lake, the concentration in each trophic level rises and falls in an orderly succession, following the tranfer of the element through the food-chain (30). By comparison, a single dose of DDT produces a very rapid and simultaneous concentration increase in all organisms from all trophic levels, yet substantial differences in concentrations between trophic levels still develop (31). Furthermore, virtually the same concentration differences result whether a complete food-chain or an artificially interrupted food-chain is used. To explain these results, Hamelink et al (31) proposed that the processes of absorption onto body surfaces and partition into lipids control the accumulation of chlorinated hydrocarbons by the various members of a lake biota. Thus, under this hypothesis, the physical characteristics of the organisms, such as size and lipid content, become more important factors than their ecological interactions.

The influence of age, body weight, and lipid content on chemical residue levels in natural fish populations has been evaluated by many authors (13, 32–39). In fact, residue concentrations are commonly reported on both a lipid basis and a whole body basis in fish, which frequently helps reduce variability among samples (32–37). However, no consistent pattern has emerged, as illustrated by the data for landlocked salmon (*Salmo salar*) from Sebago Lake, Maine (33, 35). DDD and DDE increased with age and lipid content, dieldrin only increased with lipid content, while age and lipid content were interdependent on DDT levels found in the salmon (35). However, one should recognize that residue-lipid content correlations do not necessarily prove a cause and effect relationship. That is, the presence of more lipids may not cause greater quantities of residues to be accumulated; rather the factors that result in lipid deposition may also promote residue storage.

Fish must obviously expend energy in order to acquire and store energy. Because lipids have a greater caloric content than muscle, a "fat" fish must do more eating, swimming, and respiring than a "lean" fish of the same weight and age. As a result, the "fat" salmon from Sebago Lake presumably had more opportunities to take up residues than "lean" fish. That the "fat" fish did in fact retain greater concentrations of residues probably just relates to the lipophilic nature of the chemicals. There just happened to be a convenient place to store the chemicals, but the presence of the lipids did not cause the compounds to be taken up and stored.

The factors of age and weight cannot be separated because they normally co-vary in fish populations. Residues of DDT-R and PCBs in lake trout (38, 39) show exponential increases with age of fish under uniform conditions of exposure. Since weight also increases exponentially, the data give good correlations between residue concentration and weight as well. For this reason, Eberhardt (13) has recommended that the log of residue concentration be expressed as a function of log body weight to reduce variability among samples. Such correlations in field data again suggest that the mechanism of residue uptake is ultimately linked to the metabolic activities of the fish. Given these realizations, the use of various kinetic and bioenergetic growth models becomes a more plausible means for solving the prediction problem.

PARTITION AND KINETIC MODELS

The exchange-equilibria hypothesis (31), coupled with some uptake and clearance data (19, 23, 28, 29), presumably helped foster interest in using pharmacokinetic models to predict bioaccumulation in fish. Branson et al (40) applied a two-compartment kinetic model to the uptake and clearance of 2,2',4,4'-tetra-chlorobiphenyl by rainbow trout (*Salmo gairdneri*) in the laboratory. The validity of this approach was demonstrated when the projected steady state residue levels based on five days of exposure compared favorably to experimental results obtained during 42 days of exposure. Neely, Branson & Blau used this same technique to develop a regression equation for projected steady state residue concentrations in trout muscle versus calculated *n*-octanol-water partition coefficients (P) for a variety of synthetic compounds (41). Over a log P range of 2.64 to 7.62 they obtained the regression: log (bioconcentration factor) $= 0.542$ (log P) $+ 0.124$. This regression was verified by using the P values for endrin (log $P = 5.6$), chlorpyrifos (log $P = 4.82$), and 3,5,6-trichloropyrindinol (log $P = 1.35$) to predict the bioconcentration factors reported for whole mosquito fish (*Gambusia affinis*). Except for the more water-soluble pyridinol, which is a metabolite of chlorpyrifos, very close agreement was obtained between the predicted and observed bioconcentration factors. The predicted values for endrin and chlorpyrifos were log 3.47 ± 0.989 and 2.87 ± 0.963 compared to experimentally observed factors of log 3.17 and 2.67, respectively. The predicted value for the pyridinol on the other hand was 0.88 ± 1.139 verus an observed value of 0.49.

Metcalf and associates (42, 43) derived similar uptake-partition regressions for other organic chemicals and mosquito fish as evaluated in model ecosystems. However, they based their regression on experimentally determined *n*-octanol-water partition coefficients which were substantially lower than the calculated values used by Neely et al (41). For example, the log P value measured by Lu (43) for hexachlorobenzene was 4.13 compared to a calculated value of 6.18 reported by Neely et al (41). Hence, the upper range log P values reported by Metcalf et al (42) appear to be low, and as a result their equation (log BCF $= 1.1587$ log $P - 0.7504$) has a much steeper slope than Neely et al (41) since comparable bioconcentration factors were observed by both groups.

The Neely et al (41) regression also provided a reasonable estimate for the bioconcentration of trifluralin (calculated log $P = 5.33$) measured in several species of large fish from the Wabash River (44). The equation yielded a log value of 3.01 compared to observed mean values of 3.22 in golden redhorse (*Moxostoma erythrurum*), 3.45 in shorthead redhorse (*M.macrolepidotum*), and 3.73 in sauger (*Stizostedion canadense*). Thus, the partition coefficient of a lipophilic compound can often provide a good measure of its bioaccumulation potential in fish and presumably other aquatic organisms.

In reality, predicting bioaccumulation based on partition values alone is risky. Satisfactory results usually can be derived for an analogue series within a family of chemicals for which confirmatory experiments have been conducted on a few representative compounds. Many pitfalls and exceptions exist. For example, compounds with low P values, being more polar, may be more susceptible to biodegradation or excretion (8, 45) such that accumulation may be overestimated. Likewise, the uptake of acidic or basic compounds is strongly affected by the degree of ionization as regulated by the pH (46). Conversely, direct application of a partition coefficient regression appears to underestimate bioaccumulation of compounds having P values something greater than log 6 (41, 47, 48). Compounds in this class often display bioconcentration factors greater than log 5 in whole fish from natural environments (49). Because the amount of time required to reach a steady state is extremely long (40), growth and fat deposition have to be considered in the analysis (48). Consequently, the bioaccumulation of a few "super pollutants" such as DDT and some PCBs require more complex models that incorporate the bioenergetics of the fish (47).

FISH GROWTH AND BIOMASS DYNAMICS

Models for growth have been based either on the biomass (50) or on the energy content (51) of fish as the primary unit of measure. Both methods are complex and require detailed knowledge of the biology of each species, as well as the community they inhabit (52). As a consequence we do not dwell on the specifics involved, but encourage our readers to carefully review the literature we have cited before attempting to employ these more advanced techniques for predicting chemical residue accumulation.

Norstrom et al (53) reasoned that the uptake rate of pollutants by fish should fall within limits set by those factors that control metabolism and growth, as modified by environmental factors such as temperature and food availability. To evaluate this concept, they developed a pollutant accumulation model based on fish bioenergetics (51, 54) combined with some data on pollutant biokinetics. In essence, they devised an equation that stated that pollutant body burden changes with respect to time were equal to the uptake from the water plus uptake from the food minus the depuration rate, wherein each rate was modified by complex body weight–dependent functions. The obvious disadvantage of this approach is the difficulty one encounters in measuring all of the various metabolic rate constants needed for the model. Nevertheless, their detailed analysis did serve to support the log-log transformation,

mentioned previously (13), and further demonstrated that for PCBs and mercury in yellow perch (*Perca flavesens*) the entire model could be approximated by

$$dP/dt \doteq AW^{0.7} - k_{cl} PW^{-0.58}, \quad 1.$$

where A is a constant which combines all the coefficients in the uptake parts of the model, W the body weight, and P the pollutant body burden. Since this is essentially the equation for a simple compartment model, one might expect an equilibrium state to be reached. However, the exponents operating on the changes in body weight prevent an equilibrium from actually being achieved. That is, if the relative value of the exponent terms on body weight are correct, then the uptake factors for methyl mercury and PCBs have increasing "power" over the depuration factors ($0.7 > 0.58$) as the weight of the aquatic animal increases with time. Thus, it follows that if a compound is persistent, has a high bioconcentration potential, and the animal gains appreciable weight with time, there is more opportunity to "capitalize" on these seemingly small differences and steady state conditions cannot be reached.

Accepting an assumption that a fish's "fill" works faster than its "flush" relative to body weight, is certainly tempting. In fact, an adjustment factor of this sort would undoubtedly account for some of the anomalies observed in residue studies with natural fish populations. However, a physiological reason for this disproportionality still needs to be elucidated.

The equation implies that the surface area or metabolic rate of uptake tissues (e.g. gills and gut) decreases less relative to body weight than that of the excretory tissues (e.g. gills, kidney, and ovaries) as fish gain weight while growing older. How this sort of differentiation would be physiologically possible is a mystery. Alternatively, it may arise as a result of a difference between adsorption and desorption or some other physical-chemical phenomena unique to these "super pollutants." Regardless of the cause, the absolute value of these exponents must vary between species and between various life-stage stanzas for each species.

Thus, one can envision that the kinetic rates and relative importance of body weight would change as the fish grows, matures, spawns, and finally reaches senescence. Furthermore, overlying these physiological changes, their food habits change and seasonal factors (such as temperature), alter food consumption, habitat selection, etc. Each of these factors contributes to the bioenergetics of the fish and its subsequent bioaccumulation of various trace contaminants. Therefore, to be absolutely precise would require a combined biomass-bioenergetics model which incorporated seasonal changes from year to year in the pollutant levels of the environment, plus various subroutines for individual fish stocks that might be further subdivided on the basis of sex and year class.

Achieving this level of refinement would be a truly monumental task! Consider for example that Kitchell et al (50) estimated that over 100 man-years of effort were required just to compile the relatively simple set of data needed to formulate a growth model for bluegills (*Lepomis macrochirus*) in a small lake. Expanding this model to include pollutant kinetics both within a lake and the fish would be staggering, although not impossible. So, we have to ask ourselves: Is this level of refinement really needed? In truth, we have to conclude it would be informative but probably

is not necessary at this time. There are just too many other questions pertinent to the environmental behavior of pollutants which need to be resolved before we, as fisheries scientists, need this degree of sophistication.

CONCLUSION

The environmental behavior of pollutants appears to depend more on their chemical-physical properties than on the biological-ecological features of the receiving body. By this statement we do not intend to imply that biology and ecology are not important. They are! It is just that greater insight can probably be achieved more quickly by applying the structure-activity concepts developed by Hansch (55) and others (56) before we try to develop totally comprehensive models for pollutants in aquatic environments.

The environmental fate and effects of chemicals have to relate, ultimately, to the unique properties of each compound. We have discussed how one biological event, that of accumulation, can frequently be related to the parameter of partition. Perhaps then photo-decomposition can be related to metabolism (47) and environmental distribution to surface area and mass ratios via adsorption (57). Thus, what is needed now are more simple, universal approximations which can serve to guide future studies intended to resolve particular issues and unique situations, not more complex solutions to the peculiar problem posed by a few chlorinated hydrocarbons.

We have briefly discussed the concepts of exchange equilibria (31), kinetics (40), and bioenergetics (53). Taken together, these may form the basis for a simpler approach to the problem of quantifying residue accumulation by fish in natural environments. Bioenergetics can define the range of food consumption and respiration that might be expected for a given species under reasonably narrow environmental conditions. Kinetic studies should be able to define quickly the various rate constants for both direct and dietary sources. The concept of exchange equilibria can then be used to delineate the residue concentrations expected for both the water and food sources, provided that total inputs can be quantified. Given this framework it should be relatively easy to derive approximations for residue accumulation which are accurate within an order of magnitude. Considering the latitude associated with most dose-effect relationships, we should then be able to judge whether some definable effect threshold is likely to be exceeded. Thus, by following a rationale of this nature we should be able to streamline our research activities, yet maximize our opportunity for identifying potentially hazardous substances in the environment.

Overall, we are encouraged by the progress made in this field during the past few years. Furthermore, we expect to see even more dramatic results in future years. However, in contrast to the eye-catching headlines generated by studies on fish and chemicals over the past decade, these results will be dramatic for their simplicity and sobriety. As such, they will not be very newsworthy, but for those of us who have muddled through the myriad of environmental toxicology, they will be most welcome.

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