Environ. Sci. Technol. **2007**, *41,* 7581−7586

Uptake, Elimination, and Relative Distribution of Perchlorate in Various Tissues of Channel Catfish

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This study was undertaken to determine the kinetics of uptake and elimination of perchlorate in channel catfish, *Ictalurus punctatus*. Perchlorate—an oxidizer used in solid fuel rockets, fireworks, and illuminating munitions—has been shown to effect thyroid function, causing hormone disruption and potential perturbations of metabolic activities. For the uptake study, catfish were exposed to 100 mg/L sodium perchlorate for 12 h to 5 d in the laboratory. Perchlorate in tissues was analyzed using ion chromatography. The highest perchlorate concentrations were found in the head and fillet, indicating that these tissues are the most important tissues to analyze when determining perchlorate uptake into large fish. To calculate uptake and elimination rate constants for fillet, gills, G-I tract, liver, and head, fish were exposed to 100 ppm sodium perchlorate for 5 days, and allowed to depurate in clean water for up to 20 days. The animals rapidly eliminated the perchlorate accumulated showing the highest elimination in fillet (K_e = 1.67 day^{-1}) and lowest elimination in liver (K_e = 0.79 day^{-1}).

Introduction

Perchlorate (ClO_4^-) has been primarily used as an oxidizer in solid rockets and missile propellant systems. Concern over perchlorate contamination has arising due to its stability in water and soils (*1*). In general, perchlorate released into the aquatic environment has been characterized by rapid mobility, stability, and nonreactivity. Because of the development of new methods to detect perchlorate in water at or below the μg/L range, widespread perchlorate contamination has been found in many U.S. states at locations of past or present fireworks or munitions plants and military bases (*2*, *3*).

The main health concern of perchlorate is that it inhibits iodide uptake in the thyroid, due to fact that the hydrated perchlorate anion is similar in size to iodide (*4*, *5*). Recently, perchlorate has been found to affect thyroids of fish and amphibians (*6*−*8*). Although the mechanisms by which perchlorate acts on the thyroid have been well established, there is little information on its toxicokinetics in ecologically relevant species. Uptake and depuration kinetics of perchlorate may provide a better understanding of its effects in fishes, as well as fate in the environment.

Therefore, the purpose of this study was to measure the rates of perchlorate uptake and depuration, and to determine relative tissue distribution, in channel catfish (*Ictalurus punctatus*), following short-term exposure. This species was chosen because (1) it is a widespread species of ecological and economic importance, (2) it often occurs at sites where perchlorate contamination is present (*3*, *9*), and (3) field surveys of contaminated sites have indicated that perchlorate is more often found in this species than many other species of fish (*3*, *9*). Thus, information on uptake and elimination kinetics can contribute to ecological risk assessments, human health risk assessments (because channel catfish are a commonly consumed sportfish), and fate and transport modeling of this salt.

Materials and Methods

Test Chemical. Sodium perchlorate (99%; Sigma Aldrich Chemical Co., St. Louis, MO) was used at a concentration of 100 mg/L. The reconstituted water used during the acclimation period and toxicokinetic tests was reverse-osmosis water supplemented with 60 mg/L Instant Ocean sea salts.

Test Animals. Catfish (46.3 ± 6.0 g, mean ± SD mass, range 38.8−56.4 g; 152.6 ± 7.3 mm, mean ± SD standard length, range 142−172 mm) were purchased from local hatcheries, and acclimated to laboratory condition for at least 5 days in reconstituted water before the start of the experiments. A 14/10 h light/dark-photoperiod was maintained. During the exposure, catfish was fed pelleted food, ad libitum, twice daily. Dissolved oxygen, conductivity, temperature, pH, and salinity were measured with a YSI model 85 meter (YSI, Yellow Springs, OH), and un-ionized ammonia ion in tank water was measured with a Hach spectrophotometer model DR/2000 (HACH, Loveland, CO).

Sodium Perchlorate Exposure and Basic Experimental Design. This experiment was carried out with a static renewal design. One-third of the water in each tank was replaced every other day during the uptake and elimination phase. Water samples were taken from each aquarium for perchlorate analysis during the exposure period. Percent recovery and detection limits were determined from spiked perchlorate tissues (perchlorate solutions injected into fish prior to extraction) and adding known amounts of perchlorate to aqueous tissue extracts, respectively. A 10 g sample of the food used to feed the fish was also analyzed for perchlorate.

Fish Sampling and Analytical Procedures. *Uptake.* One catfish was placed in each of 16 aquaria with 15 L of water. Following exposure, the catfish were euthanized in 1.5 g/L MS-222. The kidney (KY), liver (LV), gill (GL), gonad (GD), gastrointestinal tract (GI), head (HD), and fillet (FL) were dissected out and preserved in liquid nitrogen for determination of perchlorate concentrations in each tissue. The gill tissue included gill filaments and arches, the gastrointestinal tract included the stomach and the intestines (contents removed prior to analysis), and the skin was left attached to the head and fillet. Kidney, liver, and gill tissues from 4 fish were randomly pooled for analysis at each sampling point (n = 4). Gonad tissue from all fish were pooled to make 1 sample (n = 1). The gastrointestinal tract, head, and fillet

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10.1021/es071365n CCC: $37.00
Published on Web 09/22/2007

TABLE 1. Physiochemical Parameters for Channel Catfish Exposed to Sodium Perchlorate

exposure regime[a]	day[b]	ClO_4^- (mg/L)[c]	pH	temperature (°C)	dissolved O_2 (%)	conductivity (μS/cm)	salinity (ppt)	total NH_3 (mg/L)
uptake	1	133.8 (±39.5)	7.1 (±0.2)	20.9 (±0.3)	75.8 (±6.9)	172 (±5.4)	0.1 (±0)	1.9 (±0.2)
	4	133.3 (±16.9)	6.8 (±0.2)	20.5 (±0.3)	81.8 (±1.6)	157.7 (±11.8)	0.1 (±0)	2 (±0.4)
	5	96.4 (±18.5)	7 (±0.2)	20.7 (±0.2)	67.9 (±12.2)	198 (±13.6)	0.1 (±0)	1.3 (±0.3)
elimination, uptake phase	2	86.5 (±2.7)	7 (±0.2)	20.6 (±0.2)	69.5 (±11.2)	219.2 (±19.3)	0.1 (±0)	2 (±0.4)
elimination, depuration phase	1	0.012 (±0.011)	7 (±0.2)	18.4 (±0.5)	84.7 (±1.5)	188.2 (±53.5)	0.1 (±0)	0.2 (±0.1)
	2	0.014 (±0.011)	7.1 (±0.2)	19.2 (±0.5)	92.2 (±1.8)	179.8 (±40.8)	0.1 (±0)	0.7 (±0.2)
	3	0.011 (±0.009)	6.9 (±0.1)	18.4 (±0.7)	91 (±1.4)	199.1 (±27.8)	0.1 (±0)	1.1 (±0.2)
	5	0.007 (±0.006)	6.8 (±0.2)	17.5 (±1)	86.7 (±2.9)	174.7 (±18.9)	0.1 (±0)	1.2 (±0.2)
	7	0.006 (±0.004)	7.1 (±0.2)	18.8 (±0.2)	93.1 (±2.6)	165 (±20.7)	0.1 (±0)	1.6 (±0.2)
	10	0.004 (±0.003)	7.3 (±0.2)	20.4 (±0.2)	76.7 (±6)	237.2 (±19.5)	0.1 (±0)	1.2 (±0.3)
	14	ND	7.2 (±0.2)	20.4 (±0.2)	77.8 (±5.5)	210.8 (±15.4)	0.1 (±0)	1.9 (±0.2)
	18	ND	7 (±0.2)	19.4 (±0.3)	55.8 (±16.8)	195.8 (±65.3)	0.1 (±0)	1.3 (±0.3)

[a] Fish were either sampled after a 5-day exposure to sodium perchlorate or exposed for 5 days and allowed to depurate for up to 20 days. [b] Day of exposure or depuration. [c] Concentration of perchlorate measured in the water, expressed as perchlorate anion.

were large enough to analyze individually ($n = 16$). Based upon the results of this experiment, the exposure was repeated with 5 additional fish and the lower jaw (LJ), upper head (UH), axial muscle (MU), skin (SK; removed from axial musculature), and operculum (OP) were preserved in liquid nitrogen for determination of perchlorate uptake. The lower jaw, upper head, muscle, and skin samples were large enough to analyze individually ($n = 5$), but all of the opercula were pooled into 1 sample ($n = 1$). All tissues and whole body fish were rinsed with deionized water upon completion of exposure and prior to desiccation to ensure determination of perchlorate within the fish tissue. All tissue samples were immediately frozen in liquid nitrogen, and stored at −70 °C until perchlorate analysis. All samples were then weighed, air-dried, and extracted with distilled, deionized water (18.3 MΩ) using an accelerated solvent extractor (ASE 200, Dionex Corp.) (*17*) and analyzed using ion chromatography, as described in Anderson and Wu (*10*).

Depuration. Catfish were exposed to 100 mg/L sodium perchlorate solution for 5 days. Fish were then transferred to pre-cleaned aquaria containing 15 L of clean water and sampled after 12 h and 1, 2, 5, 10, and 20 d ($n = 4$ for each exposure period). One-half of the water was removed and replaced every day. Fish were then removed, rinsed in 3 successive tanks filled with DI water to remove sodium perchlorate on their skin and gills, and anesthetized with MS-222 (1.5 g/L).

Toxicokinetic Parameters and Statistical Analysis. Tissue concentrations of perchlorate in the uptake study were log transformed and then analyzed by 1-way ANOVA. Differences between treatment groups and the control group and differences between individual treatment groups were determined using post-hoc tests within each treatment time period.

When the fish were transferred to clean water, the elimination rate constant (K_e) was determined by fitting a nonlinear regression to the model $C_t = C_o e^{-K_e t}$, where C_o is the whole body concentration of perchlorate in the whole body at the beginning of the experiment, C_t the whole body concentration of perchlorate at time t, and t is time (days). The uptake rate constant (K_u) was calculated by fitting a nonlinear regression to the model

$$C_t = \frac{K_u}{K_e} C_o(1 - e^{-K_e t}) \quad (1)$$

using the value of K_e determined above (*11*). The half-lives ($t_{1/2}$) of perchlorate in tissues were estimated according to the equation $T_{1/2} = -\ln 0.5/K_e$ (*12*, *13*).

Results

During the exposure period, perchlorate concentrations within each aquarium were close to the target concentration (Table 1). The water quality parameters were within acceptable limits (ASTM, 2003) (Table 1). Percent recoveries from tissue extracts ranged from 81 to 101%. The detection limit of perchlorate in water was 1 μg/L, and in aqueous tissue extracts was 2.5 μg/L. For each tissue sample, 4.4−5.6 g of tissue (wet weight) was extracted in a 20 mL volume of water, giving a tissue limit of quantification of 0.009−0.011 μg/g. Perchlorate was not detected in the feed pellets.

Uptake of Perchlorate. The measured concentration of perchlorate, 83.8 ± 4 mg/L (mean ± SD), in aquaria during the exposure periods was close to the nominal concentration of sodium perchlorate, 100 mg/L (Table 1). The trends in tissue concentrations of perchlorate over time are illustrated in Figure 1. Basically, the head, fillet, and liver had "typical" uptake curves, while the gill, GI tract, and kidney displayed unusual kinetics (Figure 1). Because of the unusual shape of the curves in the gill, GI, and kidney, a curve could not be fitted and uptake kinetics were not calculated.

The largest concentrations of perchlorate were found in the head and in the fillet with lower uptake in the gastrointestinal tract, liver, kidney, and gill (Figure 2). Perchlorate was not detected in the gonad tissue. On the basis of the results of this first experiment, the exposure was repeated with 5 catfish to look at sections of the head and the muscle and the skin separately to determine if there is a specific region in which perchlorate accumulates. Figure 3 shows the uptake of perchlorate in the different tissues, and Figure 2 indicates significantly different concentrations of perchlorate among catfish tissues.

The bioconcentration factors (BCFs) for all tissue types indicate that bioconcentration was very low. The highest BCF was in the head of the catfish (0.21), and the 3 head sections had BCFs of about 0.14, indicating that the differences in water concentration may have caused the differences in the head concentration compared to the head sections. The next highest BCF was in the skin (0.14), and the fillet and muscle tissues had BCFs of 0.06 and 0.03, respectively. All other BCFs were less than 0.02 (kidney, liver, gill, gonad, and gastrointestinal tract).

Because of the large variances in the uptake of perchlorate in catfish tissues, data were log transformed and then analyzed by a 1-way ANOVA. Results from the 1-way ANOVA on the log transformed data indicated there was a difference in perchlorate uptake into the various catfish tissues ($p < 0.001$). A comparison of the treatment means showed that

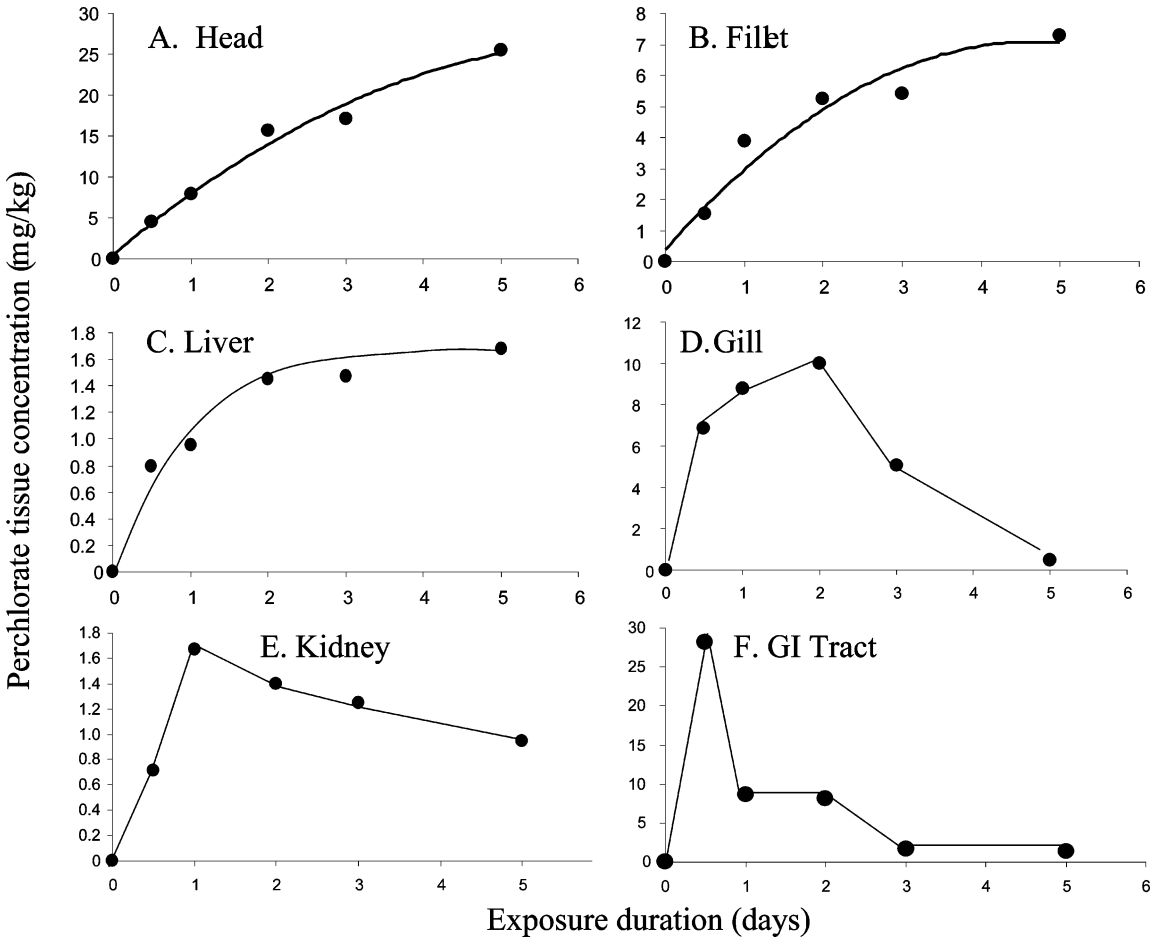

FIGURE 1. Uptake kinetics of perchlorate into various channel catfish tissues. Fish were exposed to 100 mg/L sodium perchlorate for 5 days.

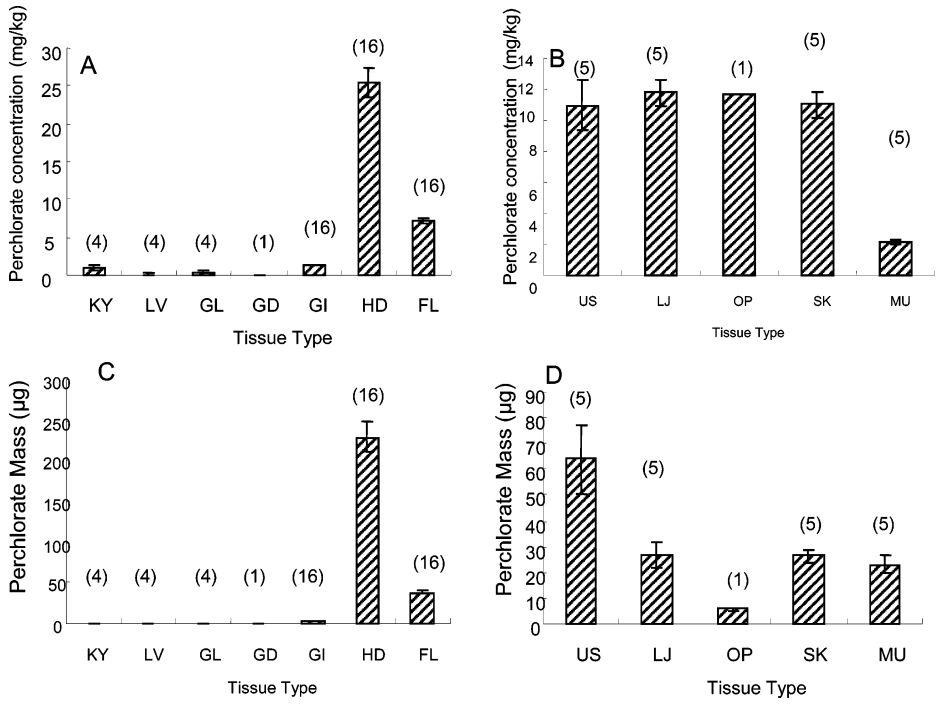

FIGURE 2. Elimination kinetics of perchlorate from various channel catfish tissues. Fish were exposed to 100 mg/L sodium perchlorate for 2 days, and then allowed to depurate for up to 20 days.

most tissues had significantly different uptakes relative to all other tissues examined.

Depuration of Perchlorate. The measured concentrations of perchlorate eliminated by the fish into the aquarium water

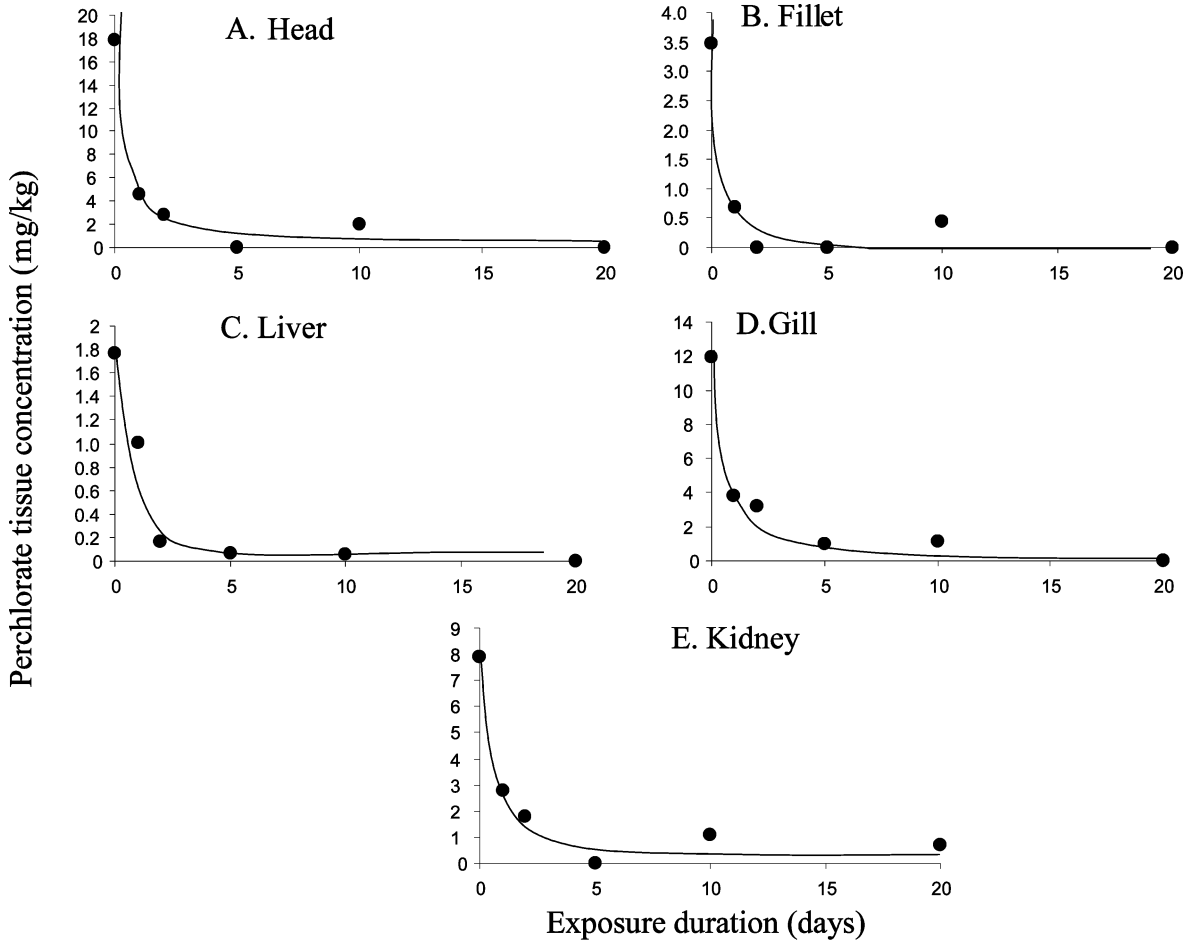

FIGURE 3. Uptake of perchlorate in tissues of channel catfish exposed to 100 mg/L sodium perchlorate for 5 days. Graphs A and C show uptake of perchlorate in intact tissues (KY = kidney; LV = liver; GL = gill; GI = gastrointestinal tract; GD = gonad; HD = head [without gills]; FL = fillet [axial muscle and attached skin]) and graphs B and D show uptake of perchlorate in the head divided into the upper head (UH), lower jaw (LJ), and operculum (OP) and the fillet divided into the skin (SK) and axial muscle (MU). Graphs A and B indicate the concentration of perchlorate in the tissues and graphs C and D indicate the total mass of perchlorate in the tissues. Sample sizes are given in parentheses above each bar. (Bars are the mean of the actual concentrations ± standard error, see Table 1 for sample sizes).

TABLE 2. Perchlorate Toxicokinetic Indices in Tissues of the Channel Catfish (*Ictalurus punctatus*)

tissues	uptake rate constant, K_1 (day^{-1})	elimination rate constant, K_2 (day^{-1})	half-life, $T_{1/2}$ (day)
head	0.22	1.22	0.57
fillet	0.09	1.67	0.41
liver	0.013	0.79	0.88
G−I tract[a]		1.22	0.57
gills		0.88	0.79

[a] GI tract includes stomach and intestines, with contents removed.

in the depuration period are reported in Table 1. Perchorate was detected in the water, presumably due to elimination from the fish. The perchlorate concentration in aquarium water decreased due to the rapid elimination of perchlorate from the fish, and the fact that water was frequently changed. The trends of average perchlorate concentration in water over time are illustrated in Figure 1. The uptake rate constants (K_1) for 2-day exposure calculated in this study showed highest value in head, followed by the liver, GI, and gills, within the fillet showing the lowest value (Table 2). After 1 day of elimination, 80% of the perchlorate was eliminated from the fillet, 75% from head, 74% from G-I tract, 68% from gills, and 43% from liver, respectively (Figure 2). However, perchlorate was still present in all tissues in at least some individuals after 10 days. The uptake (K_1), elimination rate (K_2) and the half-life ($T_{1/2}$) of perchlorate are presented in Table 2. The elimination rate constant was most rapid from fillet and slowest from liver tissue. The elimination of perchlorate residues from fillet was approximately two times faster than liver. In all tissues, perchlorate concentrations significantly varied with time (significance levels were $P < 0.05$), except in liver ($P = 0.14$). After 20 days of depuration, perchlorate was not detected in the fillets, gills, and heads, however there were still detections of perchlorate in liver and G-I tract of catfish at 2 and 0.6 mg/L, respectively.

Discussion

Uptake of Perchlorate. In general, these results indicate that perchlorate is taken up and reaches steady-state relatively rapidly, confirming one of the initial hypotheses. The other hypothesis predicted that perchlorate would be found at the highest concentration in the lower jaw where the thyroid follicles are located. Only minimal differences were seen among the perchlorate concentrations in the 3 head sections (upper head, lower jaw, and operculum), suggesting that there are other sources of contribution for the high concentration in the head of catfish in addition to the thyroid follicles.

The skin had an approximately 5 times higher concentration of perchlorate than the muscles. A possible reason for the high concentration of perchlorate in the skin of the catfish is because of the slime coat that is present in fish, which

could trap contaminants. However, the fish were rinsed 3 times prior to being euthanatized, blotted dry with a towel, skinned, and dissected. The skin was also rinsed 3 more times prior to being analyzed so most likely the slime coat and any perchlorate on the surface of the skin would have been removed before the analysis was conducted.

The unusual uptake kinetics of the gills, kidney, and GI tract were not expected. It appears that perchlorate concentrations initially increase, as expected, but that they then sharply fall. This may be due to altered uptake and/or excretion kinetics, perhaps due to changes in cellular perchlorate elimination or absorption, respectively. It should be noted that both the gills and GI tract are epithelia-rich tissues involved in absorption and excretion of materials into and out of the body, respectively. The organs that are not specialized for this function—head, liver, and muscle fillet—show more normal uptake kinetics. The kidney shows a pattern that is intermediate between the two trends. Bradford et al. (*14*) noted similar trends with whole body perchlorate concentrations in mosquitofish (*Gambusia holbrooki*), in which there seemed to be a "peak" of whole body concentrations at 2 days of exposure, followed by a steady-state concentration at slightly lower levels. Such unusual trends need to be taken into account when modeling uptake and elimination of perchlorate in this species.

Findings from sampling of aquatic species in the field were consistent with findings from the laboratory exposure. Fish that were exposed to perchlorate in the laboratory did not bioaccumulate it, since the tissue concentration of perchlorate was much lower than the exposure concentration of perchlorate. Similarly, aquatic species sampled at LHAAP (Longhorn Army Ammunition Plant) did not seem to bioaccumulate perchlorate since water samples taken at sites where organisms were collected indicated much higher concentrations than was present in the tissues (*3*). Generally, water-soluble chemicals such as perchlorate and metal salts do not bioconcentrate in biota (*12*). Contrary to this study, perchlorate concentrations in wild fish may be greater than those in the water because of uptake of perchlorate via food (*3*).

In addition, the uptake and accumulation of perchlorate in fish may be affected by the concentrations to which they are exposed. This has been found for a wide variety of other contaminants. For example, in aquatic organisms exposed to metals, there is an inverse relationship between the exposure concentration and BCF, with high values occurring with low exposure concentrations and low values occurring with high exposure concentrations (*11*). In mosquitofish, BCF was directly correlated to exposure concentration of perchlorate, with the exception of the highest dose group (*14*). This is an important consideration since BCF is one of the criteria used in determining toxicity in aquatic environments. In this study, relatively high concentrations of perchlorate were used to ensure detection in tissues. However, it is not known if similar kinetics would occur in catfish exposed to concentrations more similar to those found in the field (*9*).

Results from the catfish exposure to perchlorate were consistent with field studies. Under laboratory conditions, the highest perchlorate concentrations were found in the head, with the fillet having the next highest concentration. Perchlorate concentrations in the head were more than 3 times higher than the perchlorate concentrations in the fillets, and other tissues had very small amounts of perchlorate in comparison to the concentrations found in the head. Field studies were conducted to determine the amount of perchlorate present in the heads and fillets of several species of fish. These studies also found that the head had much higher concentrations of perchlorate than did the fillets (*9*).

Depuration of Perchlorate. The study showed that ClO_4^- was absorbed, eliminated, and distributed among fish tissues quickly. Rapid elimination of ClO_4^- in catfish species was observed when the animals were transferred to clean water, with half-lives of ClO_4^- of less than 1 day. Perchlorate was also observed by rapid uptake and depuration in mosquitofish species (*14*). Mosquitofish had a lower elimination rate and higher half-life than any tissue in the catfish. This fact could be considered as the effect of body size on elimination of ClO_4^- between two species because it has been reported that elimination of water-soluble chemicals in fish is affected by allometric (size) relationship (*15*). Alternatively, this could be due to species-specific elimination mechanisms. In channel catfish, the head showed the highest uptake (K_1 = 0.26) of ClO_4^-. This may be due to accumulation in the thyroid follicles, because in teleost fish, thyroid follicles are located mainly in the head part and around the ventral aorta and bulbus arterosus (*16*, *17*).

Many water-soluble xenobiotics are taken into the body by passive diffusion through semipermeable membranes such as gills, lining of the mouth, or gastrointestinal tract. Fish gills are especially vulnerable to foreign chemicals because their design maximizes diffusion (*12*). Due to the high water solubility of ClO_4^-, the respiratory surfaces, gills, of the fish can be the main routes of ClO_4^- uptake (*18*, *19*). Because the body burden of ClO_4^- in gills was relatively high among tissues in this study, the main uptake of ClO_4^- via gills might play an important role in the uptake to the organs through blood system, resulting in high uptake rates in head, liver, and G-I tract. For future studies, it would be important to distinguish among the primary routes of elimination in fish, because the route can be affected differently by temperature, tissue damage, preexposure to toxicants, or the presence of competing chemicals.

The high uptake rate of ClO_4^- in head (K_1 = 0.26 day^{-1}) and GI tract (0.16 day^{-1}) and low uptake rate in fillet (0.07 day^{-1}) are similar to those of Yu et al. (*20*) who investigated the uptake of $^{36}ClO_4^-$ (3.3 mg/kg) over a 48-h time period in rat tissue. These authors reported that uptake of ClO_4^- showed the highest concentration in thyroid and GI tract, while the lowest $^{36}ClO_4^-$ concentration was detected in muscle. Head of catfish had the highest uptake rate together with liver, but perchlorate was more easily eliminated from head (K_2 = 1.22 day^{-1}; $T_{1/2}$ = 0.57 day) than liver (0.79 day^{-1}; 0.88 day). This pattern was also consistent with the findings of Yu et al. (*20*). Although species, concentration, and uptake period of ClO_4^- were different between the two investigations, the trend of elimination was similar, lower half-life in fillet and higher in head, liver, and G-I tract. Compared to rats, the longer half-life in fish is probably the result of lower metabolic rate in fish.

In conclusion, results from the current study indicated that perchlorate is rapidly taken up and eliminated from channel catfish tissue and the elimination rate constants differ between tissues and types, and the head and fillet are the most important tissues to analyze when determining the uptake of perchlorate into fish. Although perchlorate did accumulate in other tissues in the catfish (kidney, liver, gill, and gastrointestinal tract), these tissues had very low concentrations of perchlorate compared to the head and the fillet. This may have important implications for dietary exposure of perchlorate to humans eating contaminated fish, because the muscle tissue usually constitutes the majority of tissue consumed. However, peak, steady-state conditions were not quite reached in the tissues examined in this study. The findings in this study suggest that perchlorate does not bioaccumulate, bioconcentrate, or biomagnify in channel catfish. Perchlorate kinetics in thyroid and different tissues have been well investigated in mammals, to date and to the best of our knowledge, no study has been conducted to determine the uptake and elimination of perchlorate, ClO_4^-, in teleost fish. These results may be critical and used to

develop models of fate, effects, and transport of ClO_4^- in natural water systems, as well as to assess ecological risk in a contaminated ecosystem.

Acknowledgments

We thank Elbia Galo, Stephany Gallegos, and Emilia Cruz-Li for their fish husbandry and technical help. This research was supported in part by the U.S. Department of Defense contract CU1141, through the Strategic Environmental Research and Development Program (SERDP) under a Cooperative Agreement IERA-99-001 with the USAF, Institute for Environment, Safety and Occupational Health, Brooks AFB, TX. The reviews and conclusions contained herein are those of the authors and should not be interpreted as necessarily representing the official policies or endorsements, either expressed or implied, of the 311 HSW/AFIERA or the U.S. Government.

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Received for review June 7, 2007. Revised manuscript received July 31, 2007. Accepted August 14, 2007.

ES071365N