Absorption, Distribution and Elimination of all 2,3,7,8-substituted PCDD/PCDFs Resulting from Chronic Exposure of Chickens to ppt Level Contaminated Soil

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INTRODUCTION

Polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/PCDFs) released in the environment can result in deposition onto soils, plant surfaces, bodies of water and sediments. Through any of these matrices PCDD/PCDFs can enter the food chain and, given their lipophilic properties, may bioconcentrate through trophic levels. Although root uptake from soil and translocation in plants is negligible, deposition on above ground portions of plants is an important route for herbivore animals. Earlier studies from this laboratory showed that PCDD/PCDFs in grazing chickens and cows were related to local soil contamination[1,2]. The hypothesized mechanism of uptake of PCDD/PCDFs by grazing animals is the ingestion of contaminated soils while feeding. To test this mechanism, a study was undertaken by this laboratory to expose food producing animals to known amounts of contaminated soils in their food supply. Specifically, we used chickens as a model to determine the bioavailability and the rate of PCDD/PCDF uptake from soils, the congener-specific, tissue-specific bioconcentration factors (BCFs), and the effect of soil PCDD/PCDF concentration on BCFs. Data were generated by congener specific PCDD/PCDF analysis of soils, feed, tissues, eggs, and feces over the period of the study[3]. Although the primary objective was to elucidate the relationship between soil PCDD/PCDFs and human foods and to provide a basis for setting regulatory limits on allowable concentrations in soil used in agriculture, the data allowed observations on absorption, distribution and elimination rates. These will be the focus of this presentation.

MATERIALS AND METHODS

The experimental design has been described in detail earlier[4]. In summary, White Leghorn chickens were randomly assigned to three exposure groups. The control group was fed a formulated laying-bird diet containing 10% uncontaminated soil (less than 0.5 ppt I-TEQ). The low exposure group was fed the same formulated diet containing 10% soil with a PCDD/PCDF concentration of 42 ppt I-TEQ and a profile consistent with

pentachlorophenol (PCP) contamination. The high exposure group was fed the same diet containing the same soil as the Low exposure group, but with some congeners fortified (one per homologue group), to a PCDD/PCDF concentration of 460 ppt I-TEQ[4]. The three soils used in the study represent three possible environmental situations. The soil used in the control group, at less than 0.5 ppt I-TEQ is representative of uncontaminated background soil[5,6,7]. The low level soil at 42 ppt I-TEQ represents what might be a low level contamination with a congener profile indicative of pentachlorophenol. At a 100 fold higher PCDD/PCDF concentration, this low level soil is clearly distinguishable from the control soil, while at the same time, 42 ppt I-TEQ is significantly below most action levels for contaminated soil. The high level soil at 460 ppt I-TEQ is believed to be representative of more significant contamination. However, even this level is still below the commonly utilized standard of 1 ppb for residential soils.

All chickens had unlimited access to feed and water and average per capita feed intake was calculated from the amounts of feed prepared and consumed over a period of time. Baseline eggs and tissues were collected at day 0. Exposure lasted for 178 days and was followed by a depuration period of 100 days. Eggs, tissues and feces were collected over the duration of the study.

RESULTS AND DISCUSSION

The average daily dose was estimated from the PCDD/PCDF concentration in the feed, the average amount of feed ingested daily and the average body weight of the chickens. For the high exposure group the daily dose was 2.5 ng/kg-day (I-TEQ), while for the low exposure group it was 0.3 ng/kg-day[3].

Following ingestion of PCDD/PCDFs, any toxic response would be a function of the absorption of these chemicals in the gut, with only the fraction that is bioavailable reaching the target organ to trigger an effect. Although a number of studies have estimated bioavailability of 2,3,7,8-TCDD following single dosing at μg/kg levels of guinea pigs[8,9,10] and rats[9,11], few have attempted to estimate bioavailability following chronic exposure (42 days[12]; 19 days[13]; 32 to 94 days[14]) and no study has reported on chronic exposure to all seventeen 2,3,7,8-substituted congeners at low ng/kg-day levels.

Bioavailability was estimated through a mass balance calculation using estimates of the total intake and the total body burden of each of the PCDD/PCDF congeners at day 80 and 164 of the study. The total body burden was determined from the measured concentration of the congeners in each of the tissues and either a measured or an estimated size of the tissue compartments. The data showed that bioaccumulation was tissue dependent and congener dependent, with the lower chlorinated compounds showing the highest degree of bioaccumulation. Availability of the tetrachlorinated congeners was in the 70-80% range and this availability dropped to approximately 10% for the octachlorinated congeners, with the penta through hepta congeners showing bioavailability between these extremes[3]. Previous chronic feeding studies[10,11,13,14,15] using various matrices place the bioavailability of TCDD at 10-50%. The bioavailability of TCDD administered by gavage in a corn oil/acetone vehicle to rats was estimated at 85%[16]. Data reported in this paper suggest that the bioavailability of TCDD to chickens from the soils in the study compares closely with that of direct administration by gavage

in a solvent vehicle. The difference in exposure level between the study reported in this paper (0.3-2.5 ng/kg) and that of earlier studies (10-50 μg/kg range) should be noted.

Contrary to earlier reports,[10,15,17] no significant difference was found in the bioavailability of the congeners in recontaminated soils (fortified in the laboratory) and those in the original soils. In conclusion, the results of this study represent a conservative model for ambient soils and they suggest that the bioavailability of at least the toxic congeners of PCDD/PCDFs is greater than previously reported.

A number of studies have reported on the tissue distribution of 2,3,7,8-TCDD. Based on a study of two humans, TCDD concentrations were similar in liver and adipose[18] when expressed on a lipid basis, while another study estimated that about 90% of TCDD was contained in the adipose[19]. Little is reported on the relative tissue distribution of all seventeen toxic congeners.

Figures 1 and 2 show concentration profiles over the duration of the study for OCDD and PeCDD measured in liver and adipose in the high and low exposure groups. Qualitatively, it can be seen that, in the low exposure group, an apparent equilibrium concentration is reached in the adipose and liver after 80 days. This apparent equilibrium is observed again in the high exposure group adipose but not in the liver whose concentrations continue to increase beyond the 80th day of exposure, with OCDD exhibiting the sharpest increase. The liver also showed different behavior during the depuration phase of the study, exhibiting a higher rate of loss of the accumulated PCDD/PCDFs than did the adipose and the eggs. OCDD in the liver showed the sharpest decrease.

The mass balance calculation showed that, after 80 days in the high exposure group, between 5 and 30% of any congener ingested over that period was excreted in the eggs, 7-54% was deposited in the adipose tissue, with less than 0.5% measured in the liver. On a fat weight basis, however, the liver showed the highest concentrations of the measured congeners of all tissues for both the low and high exposure groups. The relatively small size of the liver in the chicken and the low fat content accounted for the low total accumulation. Within each tissue type, the fraction unaccounted for (not absorbed, excreted in the feces, metabolized, or stored in some other tissue) increased with the degree of chlorination.

Within the limits of the number of data produced by this study, model calculations were carried out to elucidate the kinetics of the depuration phase. As a first approach, a monophasic first order elimination process was examined. Based on the linear regression coefficients (R^2), tetra- to hexa- congeners fit this model quite well (R^2s of 0.77 to 0.99) with half-lives in the range of 25 to 40 days in the adipose and eggs. The liver in the low exposure group demonstrated similar fit (R^2s of 0.70 to 0.99) and half-lives ranging from 21 to 78 days but, in the high exposure group the linear fit diminished (R^2s of 0.33 to 0.89) with half-lives ranging from 21 to 64. A biphasic first order elimination model was attempted for the hepta- and octa- congeners in the eggs. The method of residuals, or "feathering"[20], was applied and the results showed half-lives of 2 or 3 days for the first phase and 30 to 60 days for the second phase with R^2s of 0.71 to 0.99 and 0.85 to 0.97, respectively.

These limited data, point to consistent observations regarding the effect of the degree of chlorination on the uptake and depuration kinetics. They also underline the unique behavior of the liver, a behavior actuated only in the high exposure group. These findings, combined with the observations on the lack of an equilibrium during exposure and the very low levels of PCDD/PCDFs measured in the liver by the mass balance, clearly diverge from the findings in the other tissues and the eggs. This divergence may be an indication of an induction of binding sites in the liver by the higher level of exposure to the PCDD/PCDFs. The hypothesized induction of the liver seems to have a threshold somewhere between the low and high exposure levels (0.3 to 2.5 ng/kg/day). These results suggest that the rate of absorption of all seventeen congeners into adipose and eggs is independent of concentration, but in the liver, absorption shows a strong concentration dependence for all congeners. As a result of this behavior, tissue distribution of the congeners will be different at different exposure levels. Additionally, as the kinetics of absorption into the liver appears to be concentration dependent, tissue distribution will change as a function of length of exposure. This time and concentration dependent absorption and distribution of the seventeen toxic congeners needs to be considered in the use of pharmacokinetic models, as well as in the assessment of the effects of soil contamination on foraging animals.

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FIGURE1. LOW EXPOSURE

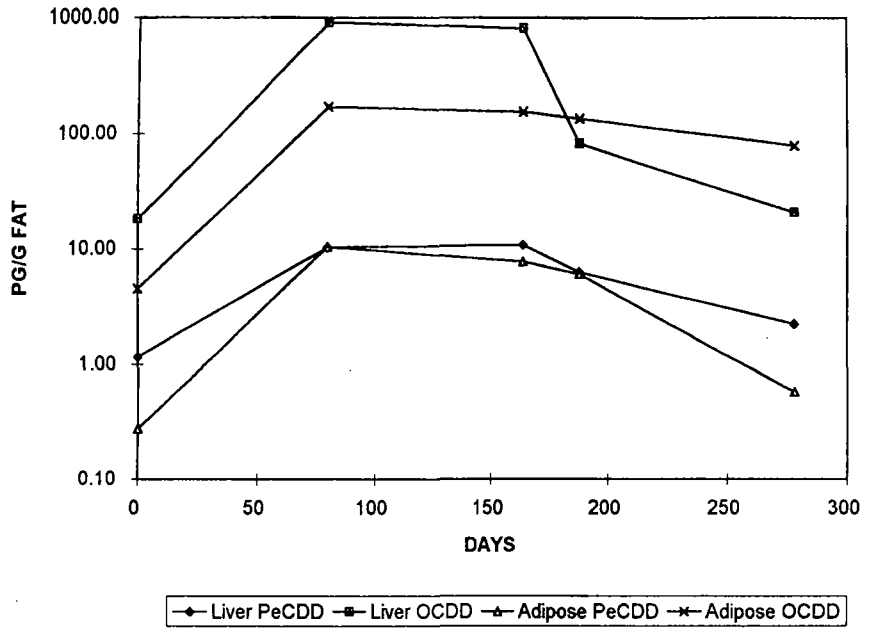

FIGURE 2. HIGH EXPOSURE