Arch Toxicol (1992) 66: 18–22

Archives of
Toxicology

© Springer-Verlag 1992

Dose-related effects of perfluorodecanoic acid on growth, feed intake and hepatic peroxisomal β-oxidation

Tim Borges[1]*, Larry W. Robertson[1], Richard E. Peterson[2], and Howard P. Glauert[1, 3]

[1] Graduate Center for Toxicology and [3] Department of Nutrition and Food Science, University of Kentucky, Lexington, KY 40506–0054, USA
[2] School of Pharmacy, University of Wisconsin, Madison, WI, 53706, USA

Received 8 April 1991/Accepted 5 August 1991

Abstract. The effects of the persistent peroxisome proliferator, perfluorodecanoic acid (PFDA), on growth, feed intake and the enzyme activities associated with peroxisomal β-oxidation were studied in female Sprague Dawley rats. Rats received one of six levels of PFDA (0, 0.3, 1.0, 3.0, 10.0 or 30.0 mg/kg/injection) in four IP doses at 2-week intervals. Rats with cumulative doses of ≤12.0 mg/kg did not differ from control rats in growth or feed intake, while rats receiving cumulative doses of ≥40 mg/kg lost weight and decreased their feed intake. Rats which received cumulative doses between these levels increased their feed intake but did not significantly alter their body weight. Total peroxisomal β-oxidation was decreased in a dose-related manner, whereas the liver to body weight ratio and the activities of individual enzymes comprising the peroxisomal β-oxidation system, namely fatty acyl-CoA oxidase, enoyl-CoA hydratase, 3-hydroxyacyl-CoA dehydrogenase, and thiolase, were increased. This study clearly shows that the inhibition of peroxisomal β-oxidation by PFDA is not reflected in the in vitro measurement of the individual enzyme activities comprising this pathway.

Key words: Perfluorodecanoic acid – Peroxisome – Peroxisomal β-oxidation

Introduction

Numerous and diverse groups of xenobiotic and endogenous substances induce peroxisome proliferation in the rodent liver. These can be divided into distinct categories including hypolipidemic drugs, phthalate ester plasticizers, high dietary fat and vitamin E-deficient nutritional states, and certain halogenated hydrocarbons (Reddy and Lalwani 1983; Hawkins et al. 1987; Lock et al. 1989).

The perfluorocarboxylic acids, including the ten carbon perfluorodecanoic acid (PFDA), are also peroxisome proliferators. These compounds are used in industry as lubricants, plasticizers, wetting agents, corrosion inhibitors and in film-forming fire extinguishers (Guenthner and Vietor 1962; Shinoda and Nomura 1980). Rats treated with doses of PFDA between 40 and 150 mg/kg exhibit delayed lethalities occurring 2–3 weeks after administration of the compound (Olson and Andersen 1983). The target organ of PFDA-induced toxicity is the liver, although thymic atrophy, fatty changes in the proximal tubular epithelium of the kidney and testicular seminiferous tubular degeneration have also been reported (Van Rafelghem et al. 1982; Ikeda et al. 1985; George and Andersen 1986; Harrison et al. 1988). Microscopically, PFDA produces swelling of the hepatocyte with disruption of the endoplasmic reticulum, mitochondrial swelling, the formation and accumulation of lipid droplets within the cytoplasm, and peroxisome proliferation. In conjunction with the increase in peroxisomes, fatty acyl-CoA oxidase activity, used as a measure of peroxisomal proliferation, is increased (Harrison et al. 1988).

In a previous study (Borges et al. 1990), we reported that a single 35 mg/kg IP injection of PFDA increased the activity of fatty acyl-CoA oxidase, the first enzyme in peroxisomal β-oxidation. In contrast, total peroxisomal β-oxidation was decreased. These results suggest that an enzyme in the peroxisomal β-oxidative pathway is inhibited. We also found that PFDA-treated rats gained less weight despite consuming the same caloric content as pair-fed controls.

To further investigate these phenomena, we examined the effect of administering multiple injections of PFDA to female Sprague Dawley rats at 2-week intervals on the activities of all of the peroxisomal β-oxidation enzymes. The effect of multiple PFDA treatments on food intake and weight gain in ad libitum-fed rats was also studied. The effects of PFDA on weight gain and food intake were clearly a function of the administered dose and progressed through several stages. PFDA also produced a dose-dependent decrease in total peroxisomal β-oxidation, even though the activities of each of the individual enzymes involved in β-oxidation were increased.

* *Present Address:* Chemical Hazard Evaluation and Communication Group, Oak Ridge National Laboratory, Oak Ridge, TN, USA

Offprint requests to: H. P. Glauert, Dept of Nutrition and Food Science, 212 Funkhouser Building, University of Kentucky, Lexington, KY 40506–0054, USA

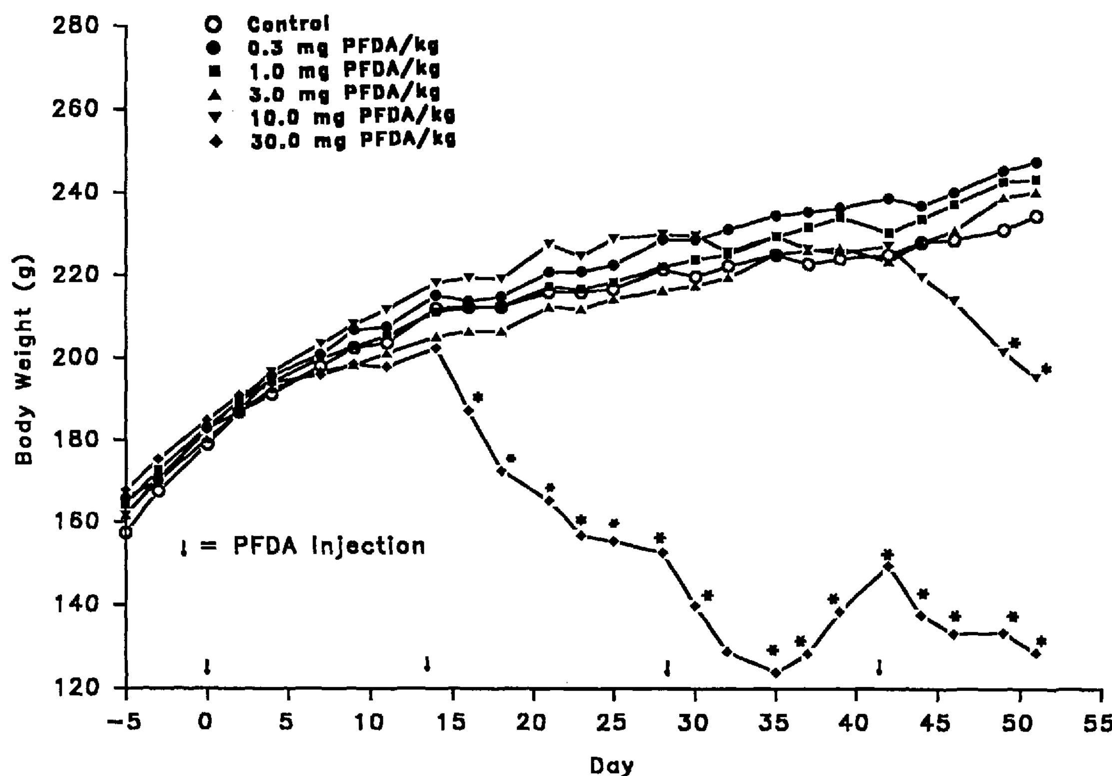

Fig. 1. Effect of four IP PFDA injections at 2-week intervals on the mean body weights of rats. The *arrows* indicate the dates of PFDA injection. Values which are significantly different than control by Dunnett's Multiple Comparison test are indicated with a * (p <0.05) with n = 5

Materials and methods

Reagents and chemicals. Perfluorodecanoic acid (PFDA), obtained from Aldrich Chemical Company (Milwaukee, WI), was treated with refluxing potassium hydroxide solution to remove the mono- and di-protio impurities. The procedure yielded 99% pure PFDA (Reich et al. 1987). TRIS-HCl, NAD, dithiothreitol, bovine serum albumin, Triton X-100, coenzyme A, palmitoyl-CoA, lauroyl-CoA, acetoacetyl-CoA, crotonoyl-CoA, FAD, hydrogen peroxide, sucrose, horseradish peroxidase, 4-hydroxyphenylacetic acid, sodium selenite, potassium phosphate (monobasic), potassium cyanide, sodium phosphate (dibasic), and EDTA were purchased from Sigma Chemical Company (St Louis, MO). Gilford serum cholesterol and triglyceride reagents were purchased from Fisher Scientific (Cincinnati, OH). The components of the purified diets were purchased from Teklad Test Diets (Madison, WI).

Animals. Upon arrival, 30 140–160 g female Sprague Dawley rats (Harlan Sprague Dawley, Indianapolis, IN) were weighed and placed in individual hanging stainless steel cages. Female rats were used in this study in order to compare the effects of PFDA seen in our previous study (Borges et al. 1990). The animals, housed in a controlled environment maintained at 22°C with a 12 h light (0600–1800) dark cycle, were randomly assigned to one of six groups (0.0, 0.3, 1.0, 3.0, 10.0, or 30.0 mg PFDA/kg) of five animals each and fed a modified AIN-76A purified diet (Bieri et al. 1977, 1980) as described previously (Borges et al. 1990). Tap water and the purified diet, fed in screw cap jars fastened to the side of the cage, were provided ad libitum. Feed intake and body weight were recorded three times per week throughout the course of the experiment.

Following a 1-week acclimation period, each rat received an IP injection of PFDA in corn oil and at 2-week intervals thereafter until a total of four injections had been given. One week following the last injection, the rats were fasted 24 h before being killed by decapitation. Trunk blood samples were collected. The liver was perfused in situ with cold 0.25 M sucrose containing 0.1 mM EDTA (pH 7.3) before being removed and weighed. Whole liver homogenates were prepared by mincing and then homogenizing with an Ultra-Turrax homogenizer (Tekmar Co., Cincinnati, OH) in a total volume of 45 ml ice-cold sucrose solution. Aliquots of sera or liver homogenates were placed in appropriately labeled 1.5 ml polypropylene microcentrifuge tubes (Fisher Scientific, Cincinnati, OH), frozen in liquid nitrogen and stored at –70°C until time of assay.

Methods. Enzymatic cholesterol and triglyceride assays were measured on serum samples according to the manufacturer's protocol (Gilford Systems, Oberlin, OH). Optical density was determined with a Shimadzu MPS 2000 spectrophotometer (Shimadzu Scientific Instruments, Inc., Columbia, MD).

Total peroxisomal β-oxidation was determined by the conversion of NAD to NADH at 340 nm according to the method of Lazarow (1981), using palmitoyl CoA as the substrate. Protein determinations on the liver homogenates were estimated according to the method of Lowry et al. (1951) using bovine serum albumin fraction V as the standard. Peroxisomal fatty acyl-CoA oxidase activity (FAO, EC 1.3.99.3) was measured according to the method of Poosch and Yamazaki (1986). Total enoyl-CoA hydratase activity was assessed by following the decrease in absorbance of crotonoyl-CoA at 280 nm (Steinman and Hill 1975; Lalwani et al. 1982). The homogenates were then incubated for 5 min at 57°C to destroy the peroxisomal hydratase activity. The assay was repeated, with the net difference between the total and incubated hydratase activities equated to peroxisomal enoyl-CoA hydratase (HYDRA, E. C. 4.2.1.17) (Osumi and Hashimoto 1979). Total 3-hydroxyacyl-CoA dehydrogenase activity (DEHYDRO, E. C. 1.1.1.35), with acetoacetyl-CoA as the substrate, was measured by following the oxidation of NADH at 340 nm (Nagi et al. 1988). Total thiolase activity (THIO, E. C. 2.3.1.16) was determined as described previously (Middleton 1972; Reddy et al. 1982).

Statistical evaluations were made using analysis of variance and Dunnett's Multiple Comparison Test (Snedecor and Cochran 1982; Gulley 1988). The level of statistical significance for all tests was p = 0.05.

Results

Body weight and feed intake

The effects of multiple doses of PFDA on body weight and feed intake are shown in Figs 1 and 2. Decreased body weight and feed intake were seen only when the total

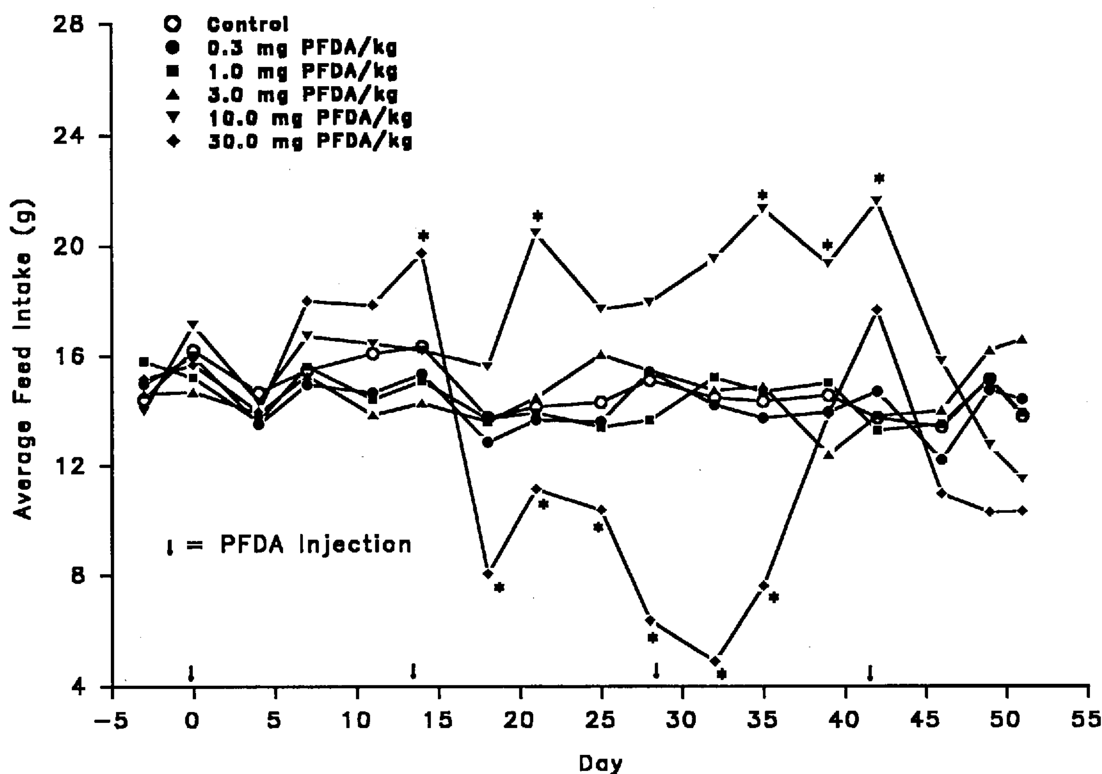

Fig. 2. Effect of four IP PFDA injections at 2-week intervals on the feed intake of rats. The *arrows* indicate the dates of PFDA injection. Values which are significantly different than control values using Dunnett's Multiple Comparison Test (p <0.05) are labeled *

administered PFDA dose exceeded 40 mg/kg. In contrast, when the total administered dose of the rats was 20–40 mg/kg, PFDA had little effect on the rate of body weight gain while food intake was significantly increased (Figs 1 and 2). This was apparent in rats in the 30 mg PFDA/kg/injection group, in which the mean feed intake was significantly increased without appreciably altering the rate of body weight gain following the first dose. Likewise, the mean feed intake of the 10 mg PFDA/kg/injection rats significantly increased following the second PFDA dose without any appreciable change in body weight gain. Both groups, however, lost weight and their feed intakes were decreased when total administered PFDA concentrations exceeded 40 mg/kg. When the total administered PFDA dose was less than 20 mg/kg, neither the mean body weight nor feed intake of the treated animals was appreciably affected.

Tissue parameters

The effects of multiple injections of PFDA on the liver to body weight ratio, total peroxisomal β-oxidation and the individual enzyme activities of peroxisomal β-oxidation

Table 1. Hepatic peroxisomal β-oxidation enzyme activities and liver to body weight ratios

Group mg/kg/injection	Total peroxisomal β-oxidation	FAO[a]	HYDRA[a]	DEHYDRO[a]	THIO[b]	Liver weight (% of body weight)
Control	3.1 ±0.3	4.1 ±0.4	2.4 ±0.3	269 ±21	72 ±8	3.6 ±0.4
0.3	3.4 ±0.2	4.1 ±0.5	2.6 ±0.6	415 ±34	108 ±11	3.7 ±0.4
1.0	2.5 ±0.2	17.5* ±1.2	5.2 ±1.0	838 ±92	188 ±38	4.1 ±0.5
3.0	1.3** ±0.04	49.1** ±1.4	22.5** ±3.6	1248** ±304	299 ±19	5.6 ±0.4
10.0	0.9** ±0.16	95.6** ±2.5	40.0** ±3.2	2612** ±190	1392** ±103	8.1** ±0.5
30.0	0.3** ±0.03	65.2** ±1.8	26.6** ±4.4	1877** ±41	900** ±283	9.8** ±1.2

FAO = fatty acyl-CoA oxidase, HYDRA = peroxisomal enoyl-CoA hydratase, DEHYDRO = total 3-hydroxyacyl-CoA dehydrogenase, THIO = total 3-ketoacyl thiolase
[a] nmol/min/mg protein
[b] μmol/min/mg protein
* Results significantly different than control ($p = 0.05$)
** Results significantly different than control ($p = 0.01$)
Results expressed as mean ± SEM with $n = 5$

Table 2. Effect of multiple injections of PFDA on serum cholesterol and triglyceride

Group (mg/kg/injection)	Cholesterol (mg/dl)	Triglyceride (mg/dl)
Control	108 ± 4.7	57 ± 1.5
0.3	128 ± 6.3	54 ± 3.9
1.0	113 ± 3.1	46 ± 3.6
3.0	91 ± 4.7	59 ± 7.2
10.0	87 ± 9.5	59 ± 8.9
30.0	45 ± 5.1*	34 ± 3.0*

Results expressed as mean ± SEM
* Results significantly different than control ($p < 0.05$), $n = 5$

are shown in Table 1. Following the four injections of PFDA, the liver to body weight ratio increased in a dose-dependent manner, and was significantly increased in the 10 and 30 mg PFDA/kg injection groups.

Total peroxisomal β-oxidation in the liver homogenates was significantly decreased from control in a dose-dependent manner in the 3, 10 and 30 mg PFDA/kg/injection groups. In contrast to decreased total peroxisomal β-oxidation, however, the individual enzyme activities associated with peroxisomal β-oxidation were increased. FAO activity, considered to be a sensitive indicator of peroxisomal proliferation (Poosch and Yamazaki 1986), was significantly increased over control in the 1.0, 3.0, 10.0 and 30.0 mg PFDA/kg/injection groups. Likewise, the activities of the bifunctional protein enzymes HYDRA and DEHYDRO were significantly increased in the 3.0, 10.0 and 30 mg PFDA/kg/injection groups. THIO activity was significantly increased over control in only the upper two treatment groups, 10.0 and 30.0 mg PFDA/kg/injection.

Plasma parameters

In the sera, only the 30 mg PFDA/kg/injection group demonstrated a change from control. Both plasma triglyceride and cholesterol were significantly decreased in this group (Table 2).

Discussion

In this study, we examined the effect of multiple injections of PFDA on peroxisomal enzyme activities and feed efficiency. PFDA is poorly metabolized by rats and is excreted at the rate of 0.5% of the administered dose per day (Vanden Heuvel et al. 1990; Ylinen and Auriola 1991). Because of slow PFDA excretion, many of the effects that we observed in this study were related to PFDA accumulation within the animals.

PFDA had a major effect on food intake and feed efficiency. At cumulative doses between 20 and 40 mg/kg, food intake increased without influencing body weight. The mechanism of this effect is not known. The regulation of food intake is complex, and is influenced by a variety of internal and exogenous factors (Mercer et al. 1990).

Table 1 demonstrates that changes to the liver occurred with cumulative PFDA doses as low as 4 mg/kg, considerably less than those required to produce changes in either feed intake or body weight. Fatty acyl CoA oxidase activity was the most sensitive indicator of PFDA exposure measured. We found dose-related increases of the individual β-oxidative enzyme activities and decreases in total peroxisomal β-oxidation. At the highest dose (30 mg/kg), however, individual enzyme activities were less than those at the 10 mg/kg dose. This decrease may be related to liver toxicity that has been demonstrated at high doses of PFDA (Harrison et al. 1988).

The administration of PFDA to female rats in this study produced large increases in peroxisomal β-oxidation enzyme activities – up to 23-fold higher for FAO. This contrasted with the 7-fold increase we previously observed using male rats, although the experiments cannot be directly compared because of different protocols (Borges et al. 1990). This contrasts with a much higher induction in male rats by the related compound perfluorooctanoic acid (PFOA) (Kawashima et al. 1989). This discrepancy is likely due to different metabolism of the two compounds. PFDA is eliminated twice as fast in males compared to females, whereas PFOA is eliminated 15 times faster in females (Kuslikis et al. 1990; Vanden Heuvel et al. 1991).

In our study, PFDA decreased total peroxisomal β-oxidation of lipids even though the individual enzyme activities involved were increased. This inconsistency could be related to several factors. First, two of the enzyme activities measured, those of DEHYDRO and THIO, were not specific for the peroxisomal enzymes. Therefore, the contribution of their mitochondrial equivalents may have contributed to the results. Second, the progressive inhibition of one of the enzymes of β-oxidation may be reversible and not detectable by the methodology used (for the assay of individual enzyme activities, homogenates required large dilutions). Third, permeability of peroxisomal membranes may have been altered, leading to altered transport of palmitoyl CoA into the peroxisome. Finally, interactions between the enzymes of the β-oxidation pathway may have been affected.

The present study demonstrates PFDA to be an unusual inducer of peroxisome proliferation. Unlike other peroxisome proliferators where hepatic effects return to control values with cessation of treatment (Reddy and Lalwani 1983; Hawkins et al. 1987), PFDA administration resulted in cumulative hepatic effects. However, since the rats were not maintained until all of the PFDA had been excreted, no unequivocal conclusions can be made about the reversibility of PFDA. Second, the ability of PFDA to increase the enzyme activities associated with peroxisomal β-oxidation relative to the administered dose was in contrast to a similarly related decrease in total peroxisomal β-oxidation. The diminished rate of total peroxisomal β-oxidation in PFDA-treated rats may be best explained by a progressive inhibition by PFDA or one of its metabolites on at least one of the enzymes involved with peroxisomal fatty acid β-oxidation. The effect of such an inhibition may be responsible for the increased hepatic lipid content (Olson and Andersen 1983; Van Rafelghem et al. 1988 a).

Van Rafelghem et al. (1988 a, b) have reported a general dose-related shift in hepatic lipid metabolism from oxidation to esterification in PFDA-treated rats occurring with

doses as low as 20 mg/kg. The shift in lipid metabolism increased heptic triglycerides and the body fat content in PFDA-treated rats. This occurred despite the same caloric intake of the treated and untreated rats. Additionally, it has been reported that PFDA-treated rats have higher relative hepatic percentages of oleic acid, suggesting fatty acid mobilization from peripheral stores rather than from dietary sources (Olson and Andersen 1983; George and Andersen 1986). It is possible that the increased body fat and alteration of hepatic lipid composition are related to the decrease in total peroxisomal β-oxidation, but mitochondrial or other hepatic changes are likely to be more important.

In conclusion, we have delineated specific dose-related stages of PFDA-induced toxicity: cumulative doses of PFDA <4 mg/kg (no measured change), 4 mg/kg and above (increases in hepatic activities of enzymes of peroxisomal β-oxidation), 20–40 mg/kg (increases in feed intake with no change in body weight) and >40 mg/kg (decreased feed intake and weight loss).

Acknowledgements. This research was supported by grants from the National Cancer Institute (CA43719) and the National Institute of General Medical Sciences (GM41131); T. B. was supported by a training grant from the National Institute of Environmental Health Sciences (ES07266). Kentucky Agricultural Experiment Station journal article number 91-9-58.

References

Bieri JG (1980) Second report of the ad hoc committee on standards for nutritional studies. J Nutr 110: 1726

Bieri JG, Stoewsand GS, Briggs GM, Phillips RW, Woodard JC, Knapka JJ (1977) Report of the American Institute of Nutrition Ad Hoc Committee on standards for nutritional studies. J Nutr 107: 1340–1348

Borges T, Glauert HP, Chen LC, Chow CK, Robertson LW (1990) Effect of the peroxisome proliferator perfluorodecanoic acid on growth and lipid metabolism in Sprague Dawley rats fed three dietary levels of selenium. Arch Toxicol 64: 26–30

George ME, Andersen ME (1986) Toxic effects of nonadecafluoro-n-decanoic acid in rats. Toxicol Appl Pharmacol 85: 169–180

Guenthner RA, Vietork LM (1962) Surface active materials from perfluorocarboxylic and perfluorosulfonilic acids. I & ED Prod Res Dev 1: 165–169

Gulley DD, Boelter AM, Bergman HL (1988) Toxstat, Release 2.1, University of Wyoming

Harrison EH, Lane JS, Luking S, Van Rafelghem MJ, Andersen ME (1988) Perfluoro-n-decanoic acid: induction of peroxisomal β-oxidation by a fatty acid with dioxin-like toxicity. Lipids 23: 115–119

Hawkins JM, Jones WE, Bonner FW, Gibson GG (1987) The effect of peroxisome proliferators on microsomal, peroxisomal, and mitochondrial enzyme activities in the liver and kidney. Drug Metab Rev 18: 441–515

Ikeda T, Aiba K, Fukuda K, Tanaka M (1985) The induction of peroxisome proliferation in rat liver by perfluorinated fatty acids, metabolically inert derivatives of fatty acids. J Biochem 98: 475–484

Kawashima Y, Uy-Yu N, Kozuka H (1989) Sex-related difference in the inductions by perfluoro-octanoic acid of peroxisomal β-oxidation, microsomal 1-acylglycerophosphocholine acyltransferase and cytosolic long-chain acyl-CoA hydrolase in rat liver. Biochem J 261: 595–600

Kuslikis BI, Vanden Heuvel JP, Van Rafelghem MJ, Peterson RE (1990) Disposition of perfluorooctanoic acid (PFOA) in rats. Toxicologist 10: 50

Lalwani ND, Reddy MK, Mangkornkanok-Mark M, Reddy JK (1981) Induction, immunochemical identity and immunofluorescence localization of an 80000-molecular-weight peroxisome-proliferation-associated polypeptide (polypeptide PPA-80) and peroxisomal enoyl-CoA hydratase of mouse liver and renal cortex. Biochem J 198: 177–186

Lazarow PB (1981) Assay of peroxisomal β-oxidation of fatty acids. Methods Enzymol 72: 315–319

Lock EA, Mitchell AM, Elcombe CR (1989) Biochemical mechanisms of induction of hepatic peroxisome proliferation. Annu Rev Pharmacol Toxicol 29: 145–163

Lowry OH, Rosebrough MJ, Farr AL, Randall RJ (1951). Protein measurement with the folin phenol reagent. J Biol Chem 193: 265–275

Mercer LP, Dodds SJ, Weber MD, Dunn JD (1990) Histidine, histamine, and the neuroregulation of food intake: a review and hypothesis. Nutrition 6: 273–277

Middleton B (1973) 3-Ketoacyl-CoA thiolases of mammalian tissues. Methods Enzymol 30: 128–136

Nagi M, Cook L, Laguna JC, Cinti D (1988) Dual action of 2-decynoyl coenzyme A: inhibitor of hepatic mitochondrial trans-2-enoyl coenzyme A reductase and peroxisomal bifunctional protein and substrate for the mitochondrial β-oxidation system. Arch Biochem Biophys 267: 1–12

Olson CT, Andersen ME (1983) The acute toxicity of perfluorooctanoic and perfluorodecanoic acids in male rats and the effect of tissue fats. Toxicol Appl Pharmacol 70: 362–372

Osumi T, Hashimoto T (1979) Peroxisomal β-oxidation system of rat liver. Copurification of enoyl-CoA hydratase and 3-hydroxyacyl-CoA dehydrogenase. Biochem Biophys Res Commun 89: 580–584

Poosch MS Yamazaki RK (1986) Determination of peroxisomal fatty acyl-CoA oxidase activity using a lauroyl-CoA-based fluorometric assay. Biochim Biophys Acta 884: 585–593

Reddy JK, Lalwani ND (1983) Carcinogenesis by hepatic peroxisome proliferators: evaluation of the risk of hypolipidemic drugs and industrial plasticizers to humans. CRC Crit Rev Toxicol 12: 1–58

Reddy JK, Warren JR, Reddy MK, Lalwani ND (1982) Hepatic and renal effects of peroxisome proliferators: biological implications. Ann NY Acad Sci 386: 81–109

Reich IL, Reich HJ, Menahan LA, Peterson RE (1987) Synthesis of ^{14}C-labeled perfluorooctanoic and perfluorodecanoic acids; purification of perfluorodecanoic acid. J Label Compds Radiopharm 24: 1235–1244

Shinoda K, Nomura T (1980) Miscibility of fluorocarbon and hydrocarbon surfactant in micelles and liquid mixtures: basic studies of oil repellent and fire extinguishing agents. J Phys Chem 8: 365–369

Snedecor GW, Cochran WG (1982) Statistical Methods, 7th edn. The Iowa State University Press, Ames, Iowa

Steinman HM, Hill RL (1975) Bovine liver crotonase (enoyl coenzyme A hydratase). Methods Enzymol 35: 136–151

Vanden Heuvel JP, Kuslikis BI, Van Rafelghem MJ, Peterson RE (1991) Disposition of perfluorodecanoic acid in male and female rats. Toxicol Appl Pharmacol 107: 450–459

Van Rafelghem M, Andersen M, Brunner R (1982) Comparative toxicity of perfluoro-n-decanoic acid (PFDA) in rats and hamsters. Toxicologist 2: 148

Van Rafelghem MJ, Vanden Heuvel JP, Menahan LA, Peterson RE (1988a) Perfluorodecanoic acid and lipid metabolism in the rat. Lipids 23: 671–678

Van Rafelghem MJ, Noren CW, Menahan LA, Peterson RE (1988b) Interrelationships between energy and fat metabolism and hypophagia in rats treated with perfluorodecanoic acid. Toxicol Lett 40: 57–69

Ylinen M, Auriola S (1990) Tissue distribution and elimination of perfluorodecanoic acid in the rat after single intraperitoneal administration. Pharmacol Toxicol 66: 45–48