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Radiolabel Oral Absorption and Intravenous Pharmacokinetic Studies

Absorption: At least 95% of a single oral dose averaging 4.2 mg/kg [^{14}C]PFOS administered to two groups (24 hour and 48 hour sacrifice) of 3 male Charles River CD rats (248-315 g, mean = 285 g) was absorbed within 24 hours (Johnson and Ober, 1979). The radiochemical purity of the [^{14}C]PFOS used in this and the other radiolabel studies listed below was >99% (Johnson and Behr, 1979).

Distribution: By 89 days after a single iv dose of PFOS-^{14}C (mean dose, 4.2 mg/kg) six Charles River CD male rats (initial body weights 262-303 g, mean = 288 g) excreted a mean of 30.2% of the total carbon-14 via urine. Mean cumulative fecal excretion was 12.6%. At 89 days, mean tissue concentration of total carbon-14 expressed as μg PFOS-^{14}C equivalents/g were: liver, 20.6; plasma, 2.2; kidney, 1.1; lung, 1.1; spleen, 0.5; and bone marrow, 0.5. Lower concentrations ($\leq$0.5) were measured in adrenals, skin, testes, muscle, fat and eye. No radioactivity (<0.05) was detected in brain. The carbon-14 in liver and plasma represents 25 and 3 percent of the dose, respectively (Johnson etal, 1979).

Metabolism: Analysis by LC/MS of serum and liver samples from studies where animals have been dosed with perfluorooctanesulfonate have not revealed any evidence of metabolism. There is no known mechanism for the metabolic conversion of perfluorooctanesulfonate.

Excretion: In the previously mentioned study (Johnson etal, 1979) single intravenous doses (mean 4.2 mg/kg) of [^{14}C]PFOS in 0.9% NaCl were administered to male rats. By 89 days after dosing, 30.2% of the administered ^{14}C had been excreted in the urine and 12.6% had been excreted in the feces.

Whole body elimination in the male rat appeared to be biphasic. Initial redistribution from the plasma yielded a plasma elimination half-life of ^{14}C of 7.5 days following single oral administration of [^{14}C]PFOS (mean dose 4.2 mg/kg) to male rats (Johnson and Ober, 1979). In the aforementioned intravenous study, elimination of only 42.8 % of the dose through urine and feces after 89 days indicates that the half-life of elimination from the body is > 89 days in the male rat.

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Fecal and total excretion of ^{14}C were markedly increased in male rats administered cholestyramine (~ 2.7 g/kg/d) in their diet following single intravenous doses of [^{14}C]PFOS. The results suggest that there was significant enterohepatic circulation of PFOS (Johnson and Gibson, 1980, 1984). Cholestyramine administered at 4% by weight in feed to male rats decreased the retention of carbon-14 in liver, plasma, and red blood cells and increased the elimination of carbon-14 via feces after iv dosing with PFOS-^{14}C. Groups of five rats (twelve-week old Charles River CD averaging 320 g) were dosed intravenously with PFOS-^{14}C (mean dose, 3.4 mg/kg). Groups of five control rats were dosed similarly but were not treated with cholestyramine. Rats were sacrificed at 21 days post dose. The mean liver, plasma, and red blood cell concentration as well as fecal and urinary excretion of ^{14}C for cholestyramine-treated rats were compared to mean control rat values. Mean cholestyramine-treated rat ^{14}C concentrations in liver (9.4μg/g), plasma (0.9μg/ml), and red blood cells (0.3 μg/g) represent a decrease from mean control rat concentrations of 3.8, 7.7, and 6.0 fold, respectively. Fecal elimination (75.9% with cholestyramine treatment) was increased 9.5 fold. The extent of urinary ^{14}C elimination, as a result of the relatively high rate of fecal elimination of ^{14}C was lower in cholestyramine-treated rats. The extent of total elimination of ^{14}C (urine plus feces) was higher in the cholestyramine-treated rats. Since cholestyramine is approved for use in humans as a cholesterol lowering agent, these results in rats support the concept of testing cholestyramine in humans to promote excretion of PFOS (Johnson et al, 1980).