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Perfluoroalkylated substances (PFAS) are used in a wide range of industrial applications including coatings for cookware, food contact papers, waterproofed clothing and fire-fighting fluids. PFOA (perfluorooctanoic acid) has raised major public health concerns over the last few years. Although its industrial use is decreasing, consumers are still exposed to this extremely persistent and bioaccumulative substance. Dietary intake is reported as the main source of human exposure to PFOA, with seafood and freshwater fishes being the highest contributors. Epidemiological surveys and results from *in vivo* studies in rodents suggest that PFAS can induce hepatotoxicity and exert metabolic effects, including effects on lipid metabolism. However, the mechanisms underlying these effects remain largely unexplored.

In this study, we assessed the effects of low doses of PFOA on mice hepatic xenobiotic metabolizing enzyme (XME) activities. XMEs are involved in the biotransformation of xenobiotics, playing an essential role in the protection of organisms, and are also involved in a number of endogenous anabolic and catabolic processes.

Adult C57BL/6 male mice were exposed *via* drinking water to 0, 1.5, 150 or 15,000 ng/kg body weight/day (n=10 per group) for 90 days. Livers were collected, perfused and subcellular fractions (microsomal and cytosolic fractions) were prepared. Following protein content assessment, *in vitro* incubations with specific probe substrates and cofactors were carried out to measure key phase I and II activities. Specific cytochrome P450 (CYP450) isoform activities were assessed in microsomal fractions, including CYP2C37 (probe substrate: diclofenac; monitoring of 4'-hydroxydiclofenac formation by HPLC-UV); CYP4A10 ([^{14}C]-lauric acid; formation of [^{14}C]-12-hydroxylauric acid; Radio-HPLC); CYP3A11 ([^{14}C]-testosterone; formation of [^{14}C]-6β-OH-testosterone; Radio-HPLC). Phase II enzyme activities such as glutathione S-transferases (GST) were also investigated using microsomal and cytosolic fractions, by measuring 1-chloro-2,4-dinitrobenzene conjugation by spectrophotometry.

A significant impact of PFOA exposure on hepatic CYP2C37 activity, an isoform involved in liver fatty acid and eicosanoids metabolism (endogenous substrates), was demonstrated. CYP2C37 activity was inhibited by PFOA at the highest dose. Conversely, PFOA exposure had no significant effect on CYP4A10 activities, involved in ω-oxidation of medium-chain fatty acids and eicosanoid metabolism. Phase II cytosolic and microsomal GST activities were not significantly modulated by PFOA exposure, whatever the exposure level.

In conclusion, our study has demonstrated that *in vivo* exposure to PFOA impacted liver phase I XME activities. This research is ongoing and further experiments will be performed to gain a broader overview of the modulation of these enzymes, consecutive to low-dose *in vivo* exposure to this PFAS, with the aim to improve the understanding of its mode(s) of action.