Toxicological assessment of Per- and Poly-fluoroalkyl Substances (PFAS) Mixtures in HepG2 Cells

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Introduction

- PFAS, synthetic chemicals with a wide range of applications have been associated with human health outcomes.
- PFAS exist in humans as complex mixtures, however, the combined effects and toxicological interactions of these compounds remain largely unknown.
- Considering that PFAS mainly accumulate in the liver, it is necessary to investigate how these compounds jointly affect the liver.

Objectives

- To compare the toxicity of PFDA, PFNA, PFOS, PFOA, PFHxS and PFHpA to human liver cell line, HepG2.
- To investigate the toxicological interactions between PFOS and PFOA as well as PFOS and/or PFOA combined with PFDA, PFNA, PFHxS and PFHpA in binary, ternary and multicomponent mixtures using the Combination Index (CI)-isobologram equation method.

Methodology

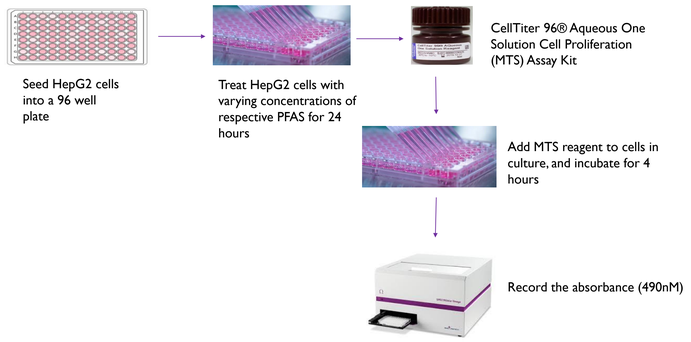

Figure 1. Overview of the experimental procedures for HepG2 cell viability assay.
HepG2 cells were treated with serial dilutions of each compound individually and with a fixed constant ratio (1:1) based on the individual IC_{50} values, in their binary, ternary and multicomponent mixtures for 24 hrs, and cell viability determined using MTS assay

Results

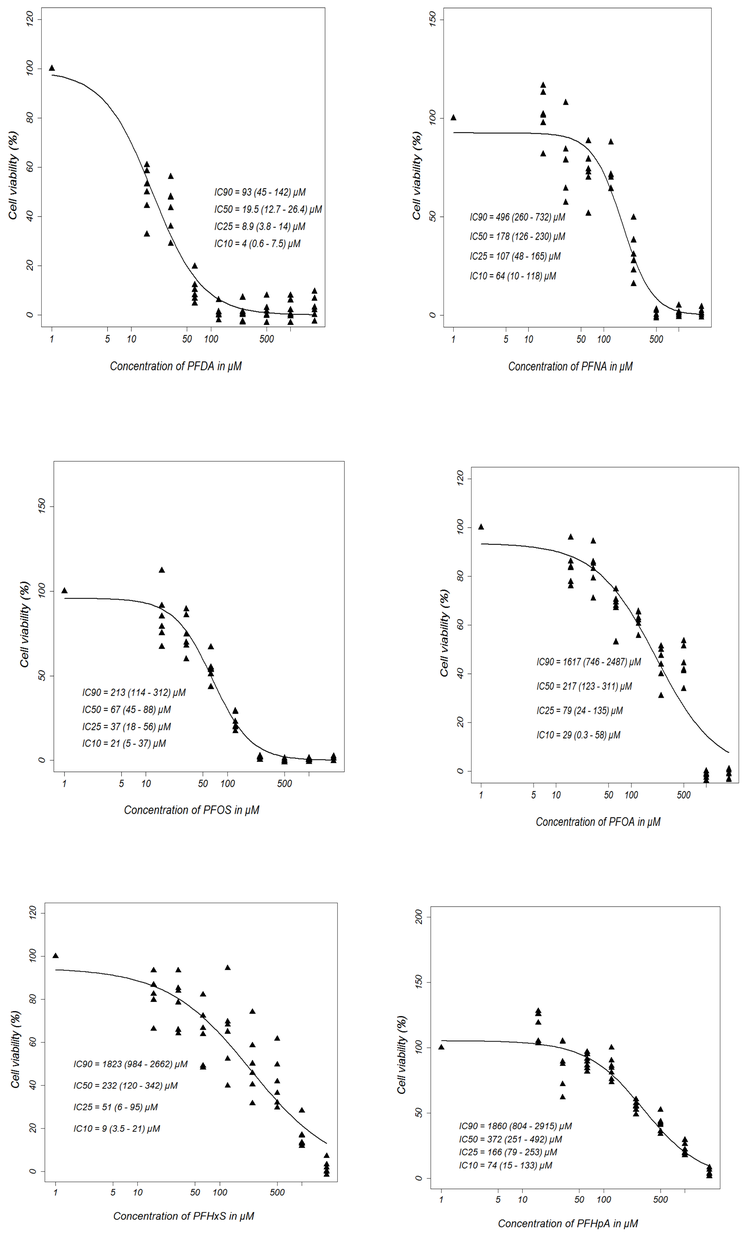

Figure 2. Concentration response curves for the inhibitory effects of PFDA, PFNA, PFOS, PFOA, PFHxS and PFHpA on HepG2 cells after 24 hours exposure

Results Cont.

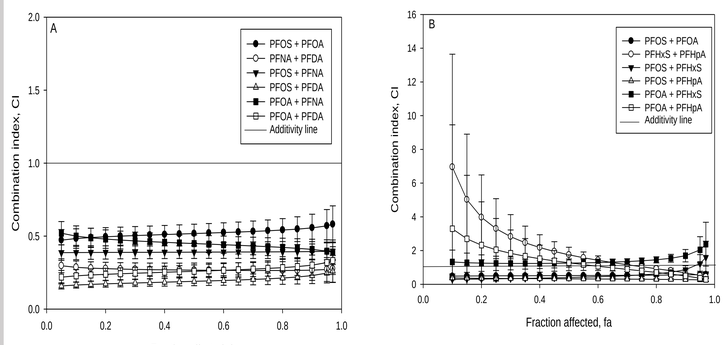

Figure 3. Combination index plot (fa–CI plot) for binary mixtures of PFOS and PFOA with PFDA, PFNA, PFHxS and PFHpA in HepG2 cells

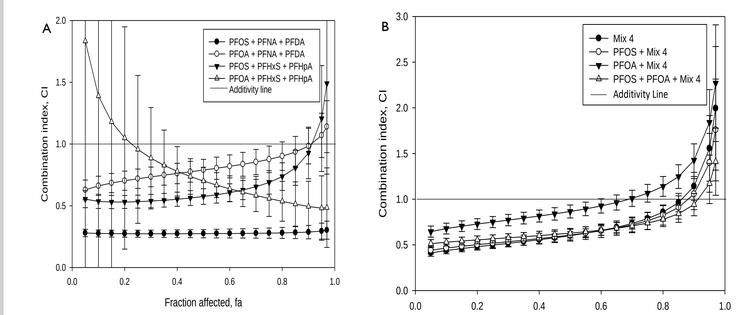

Figure 4. Combination index plot (fa–CI plot) for ternary (A) and multicomponent (B) mixtures of PFOS and PFOA with PFDA, PFNA, PFHxS and PFHpA in HepG2 cells

Conclusions

- The respective cytotoxicity of PFAS is in the order of PFDA > PFOS > PFNA > PFOA > PFHxS > PFHpA.
- The pattern of interactions of PFAS mixtures is dominated by synergism, especially at low to medium effect levels; the exceptions to this were the antagonistic interactions found in the mixtures with PFOA, PFHxS and PFHpA.

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Biography

Name: Atinuke Favour Ojo

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Current Position: PhD Candidate, The University of Queensland, Australia.

I hold a Bachelor of Science degree in Zoology from Obafemi Awolowo University, Nigeria and a Master of Science degree in Contamination, Risk Assessment and Remediation from Lancaster University, United Kingdom. I am currently completing my PhD degree in Clinical Toxicology at the University of Queensland, Australia, and working as a Doctoral research intern with Queensland Department of Health to gain an understanding of the role of Government in response to contamination incidents of public health concern. My PhD research focuses on the toxicity and health risks assessment of per- and polyfluoroalkyl substances (PFAS) mixtures.