EXPOSURE TO DEFINED MIXTURES OF PERSISTENT ORGANIC POLLUTANTS (POPs) LEADS TO MITOCHONDRIAL INJURY IN THE RAT DR-4HIE HEPATOCYTES

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INTRODUCTION

Persistent organic pollutants (POPs) are defined as organic chemicals
• resistant to degradation in the environment
• bioaccumulate and biomagnify in living organisms
• have potential harms on humans and wildlife

Humans are exposed to POPs as mixtures and not as a single compound
• Few available scientific research on the effect in mixture of POPs
• Rat liver transgenic lines (DR)-4HIE (Biodetector system, Netherlands) are widely applied for screening the Aryl hydrocarbon receptor transactivitivity of POPs
• High Content Analysis (HCA): a high-throughput, quantitative fluorescence technique to study subcellular and subcellular cytotoxicity

Aims to determine the overall health effects regarding several cellular responses of seven complex mixtures in the rat DR-4HIE using HCA

MATERIALS AND METHODS

29 POPs prevalent in Scandinavian human blood (Stockholm Convention 2001)

POPs mixture = Mixture of 29 tested POPs and 6 Sub-mixtures at concentration found in Scandinavian human blood (Berntsen et al, 2017)

6 PFAA, Perfluorinated Compounds 7 Br- Brominated Compounds 13 Cl: 7 PCBs + 9 Organochlorine Compounds

POFHS  BDE 47  PCB 28  HCB
POFOS  BDE 99  PCB 52  α-chlordane
POFDA  BDE 100  PCB 101  β-chlordane
PFNA  BDE 153  PCB 118  t-nonachlor
PFDA  BDE 154  PCB 138  a-HCH
PFUnDA  BDE 209  PCB 153  β-HCH
HBCD  BDE 209  PCB 180  γ-HCH

POFSA- Sub mixture  Cl Sub mixture  Br Sub mixture

POFSA  Cl + Br Sub mixture  Cl + PFAA Sub mixture  Br + PFAA Sub mixture

Methods

Detect subcellular and nuclear mitochondrial cytotoxicity in DR-4HIE (Biodetector system, Netherlands) exposed to POP (sub-)mixtures by applying High Content Analysis (HCA)

Cell number (CN) and mitochondrial intensity (MI): good markers for sublethal cytotoxicity of the rat DR-4HIE exposed to the POP (sub-)mixtures

Only Cl containing mixtures (the total POP mixture, Cl+Br+CI and PFAA+CI) were significantly decreasing in CN and MI at 1000 folds the blood levels, except the Br+Cl at already 100 blood folds

PFAA and Br or their combination PFAA+Br sub-mixtures alone did not exhibited significant cytotoxicity effects.

REMARKS AND CONCLUSIONS

POPs and early Menopause in U.S. Women http://jnci.oxfordjournals.org/content/102/4/234.full

REFERENCES


Figures

Figure 1: Use images of (A) apoptotic control (OMRI), (B) protective control (OMRI Valomycin). (C) example of DR-4HIE exposed to total POP mixture at 1000 label blood levels after 24h exposure. The image was acquired by 10× objective/specimen using blinded eye (blue nuclear staining) and MitoTracker dye (orange mitochondrial staining).

Figure 2: Cell viability, small number (NC, Figure A1), and mitochondrial intensity (MI, Figure B1) of the total POP mixture groups, total PFAA (blue), total PFOA (green), total PFOA (green), total PFOA (blue), total PFOA (blue), total PFOA (blue), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP (orange), total POP 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