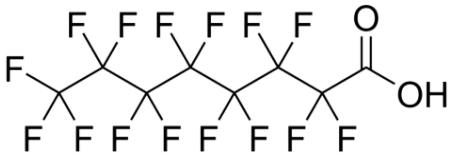
Marija Opacic

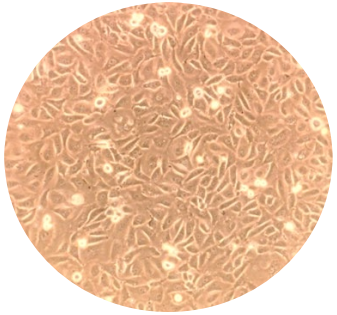
Benchmark Concentration Modeling of Apical Endpoints In Human Vascular Endothelial Cells Following Acute and Chronic *In Vitro* Exposure to Perfluorooctanoic Acid

6th December 2024

Materials and methods



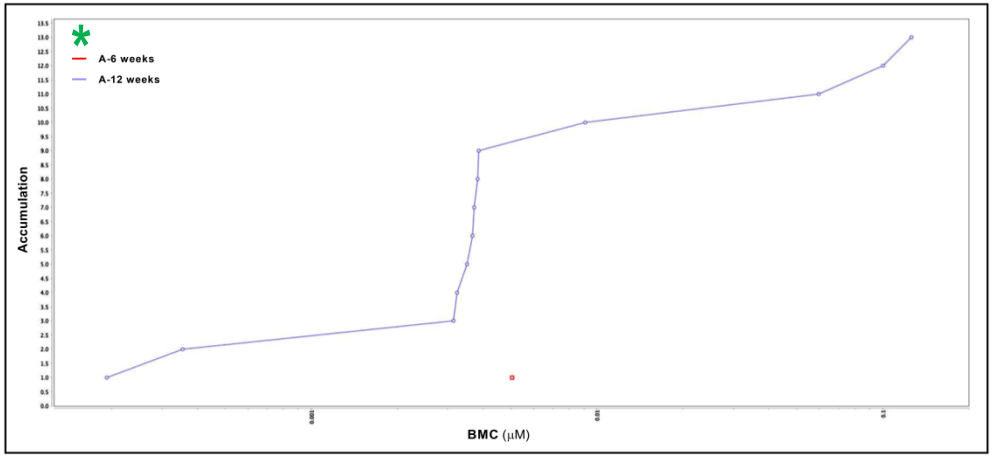
Perfluorooctanoic acid **(PFOA)**



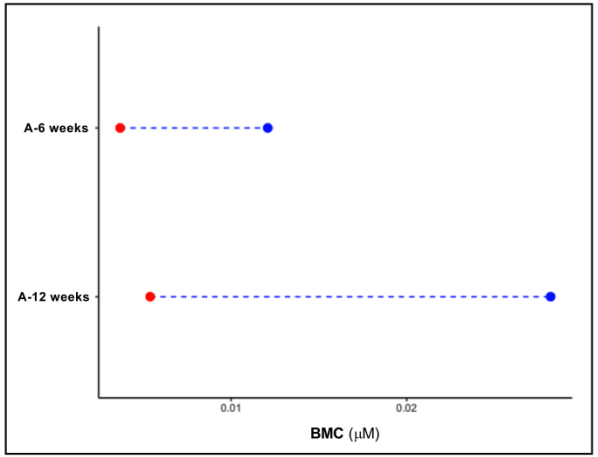
Human macrovascular endothelial cell line **EA.hy926**

- **Acute exposure (48 h): 1, 10, and 100 μM PFOA**
- **Chronic exposure (6 and 12 weeks): 1, 10, and 100 nM PFOA**
- **Benchmark concentration (BMC) modeling: BMDExpress v3.20.0106**
  - Derive and compare points of departure **(POD)** for apical changes **(A-POD)** in EA.hy926 cells
- **Apical endpoints: metabolic activity** (alamarBlue assay), **apoptosis and necrosis** (Annexin V-FITC and PI with flow cytometry), **cell cycle progression** (PI with flow cytometry), **endothelial permeability** (FITC-dextran in a 0.4 μm-pore size Transwell system), **monocyte adhesion** (calcein AM-labeled U937 human monocytes), **cell adhesion to the extracellular matrix** (fibronectin-coated plates), **cell migration** (8 μm-pore size Transwell system), **endothelial tube formation** (Cultrex 3D matrix), **and the production of reactive oxygen species** (H_2DCFDA assay).

Results of the research



Accumulation plot of BMC values for apical (A) data following acute (48 h) and chronic (6 and 12 weeks) exposure of EA.hy926 cells to PFOA



Range plot of the BMC-lower confidence limit (BMCL; red dot) and BMC-upper confidence limit (BMCU; blue dot) values for apical (A) data following acute (48 h) and chronic (6 and 12 weeks) exposure of EA.hy926 cells to PFOA

* A-48 h – no data

Discussion

- A-POD (BMCL) could not be calculated for the 48-h exposure, as none of the apical endpoints showed a concentration-dependent response.
- Average BMC values for the 6-week and 12-week exposures were determined to be 5 nM and 8.6 nM, respectively.
- Average BMCL (A-POD) and BMCU values were the following: 3.7 nM and 12.1 nM for the 6-week exposure, and 5.4 nM and 28.2 nM for the 12-week exposure.
- These findings support the idea that chronic *in vitro* exposure may offer a more sensitive approach for assessing the risks of PFOA in human endothelial cells.
- Our study provides novel insights into the effects of PFOA on human vascular endothelial cells and highlights the potential of employing different *in vitro* approaches in chemical risk assessment.

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