

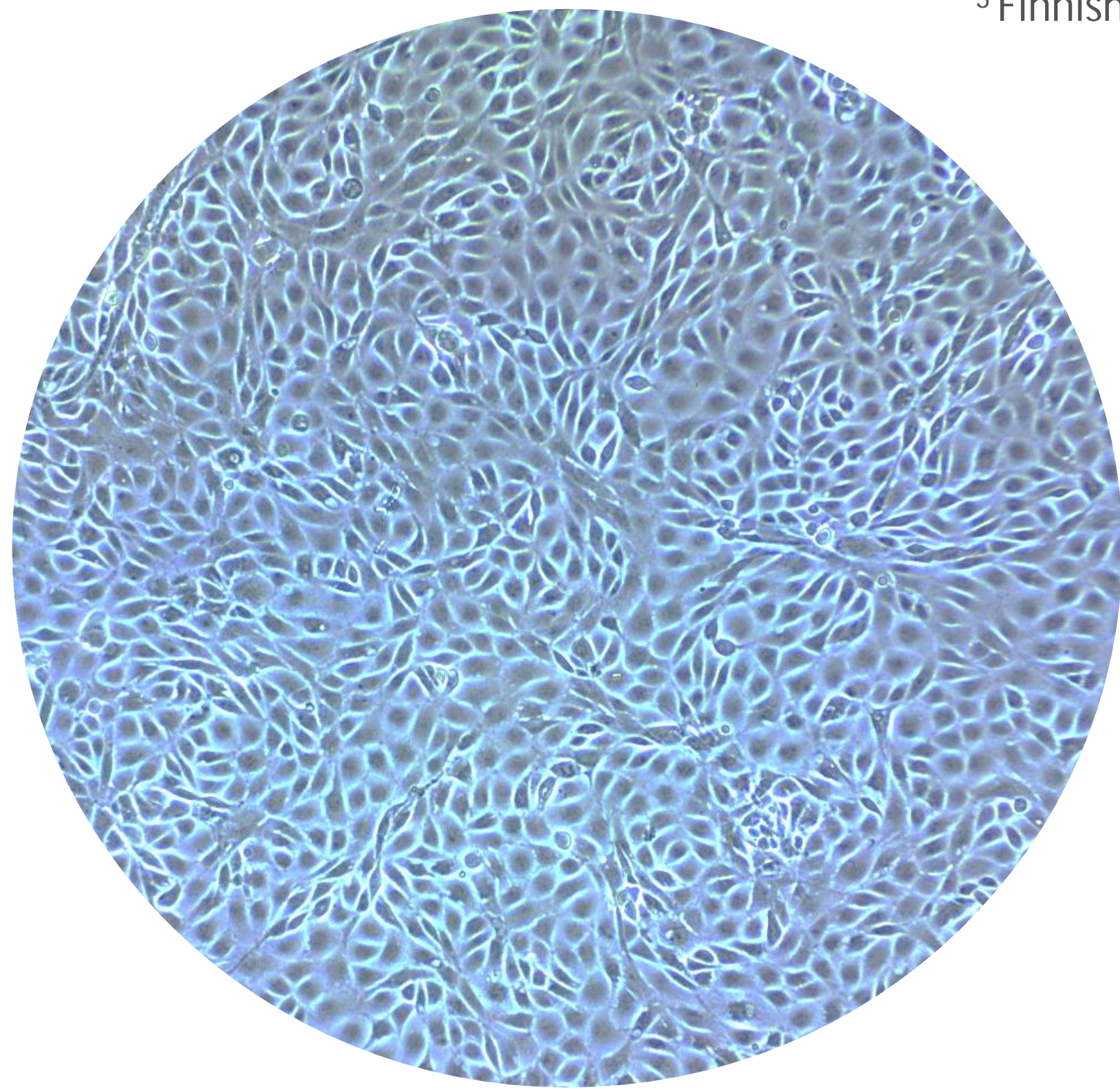
Toxicity of an oxidation product and a metabolite of the chemical warfare agent Clark I/II determined using the rainbow trout liver cell line RTL-W1

Hanna Niemikoski¹, Kari K. Lehtonen², Aino Ahvo², Ilse Heiskanen³, Paula Vanninen¹

¹ Finnish Institute for Verification of the Chemical Weapons Convention (VERIFIN), Department of Chemistry, University of Helsinki

² Finnish Environment Institute, Marine Research Centre

³ Finnish Environment Institute, Laboratory Centre

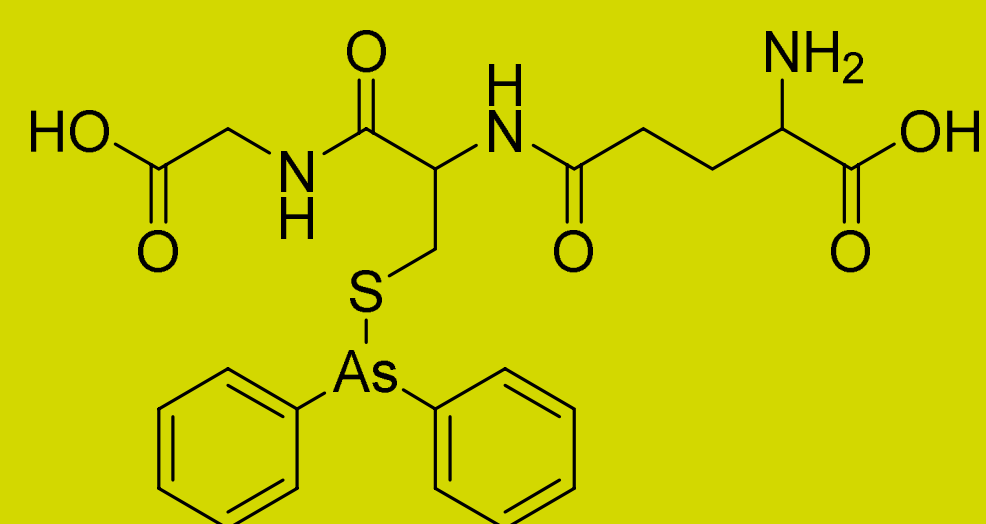


Rainbow trout liver cells

After the first and second world wars, thousands of tons of chemical warfare agents (CWAs) were dumped in the Baltic Sea. Recent studies have shown that diphenylarsenic acid, DPA[ox], an oxidation product of the CWA Clark I/II, is accumulating in fish tissues. The potential effects of dumped chemical munitions in Baltic Sea marine biota are still poorly understood. To link detected chemical in fish to its biological effects, cytotoxicity of DPA[ox], was studied using the rainbow trout liver cell line RTL-W1. Additionally, toxicity of the major metabolite of DPA[ox], diphenylarsine glutathione, DPA-SG, was studied.

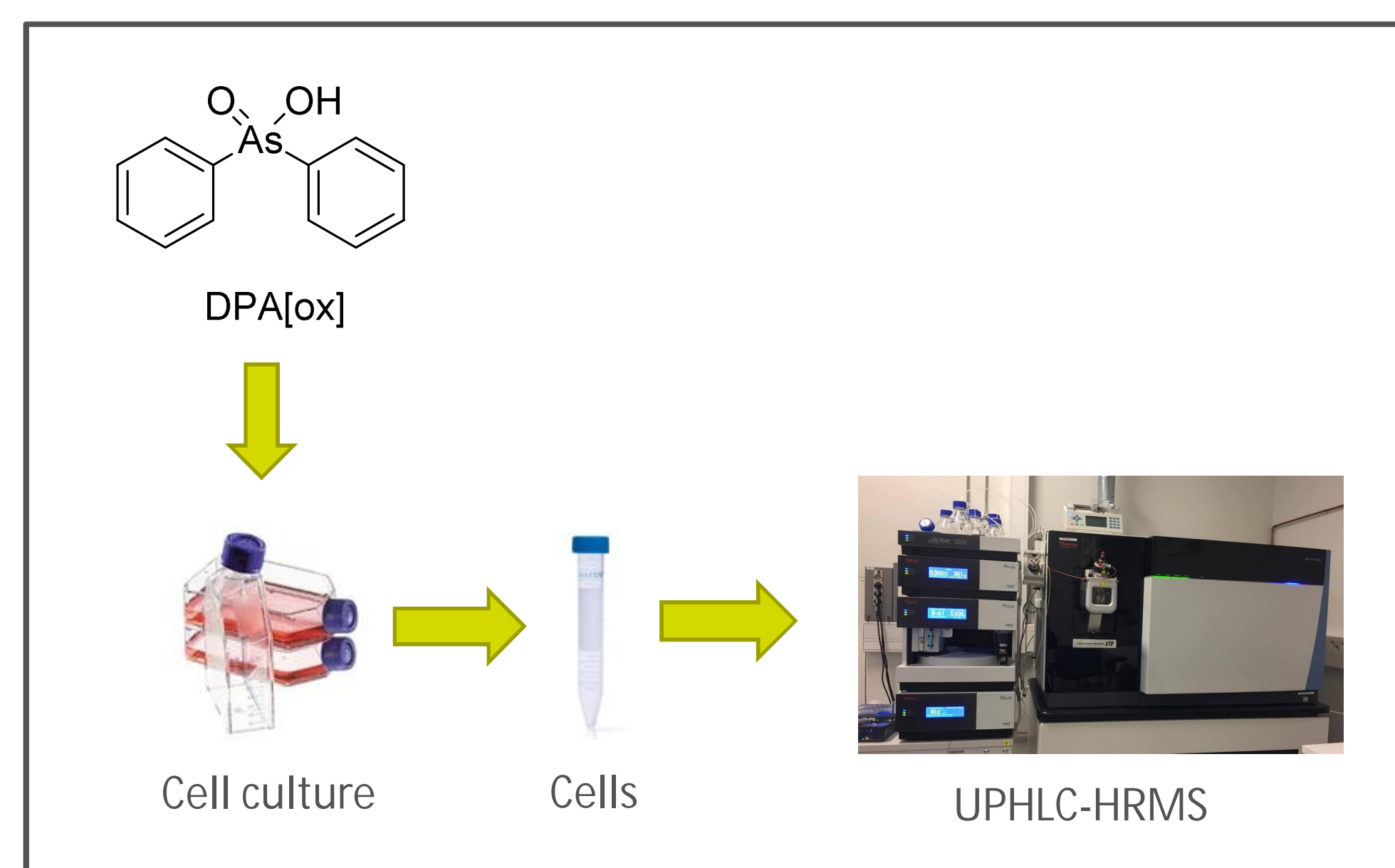
Key observations

- The glutathione conjugate of DPA[ox] is more toxic than the DPA[ox] itself by more than two orders of magnitude.



DPA-SG, glutathione conjugate of DPA[ox]

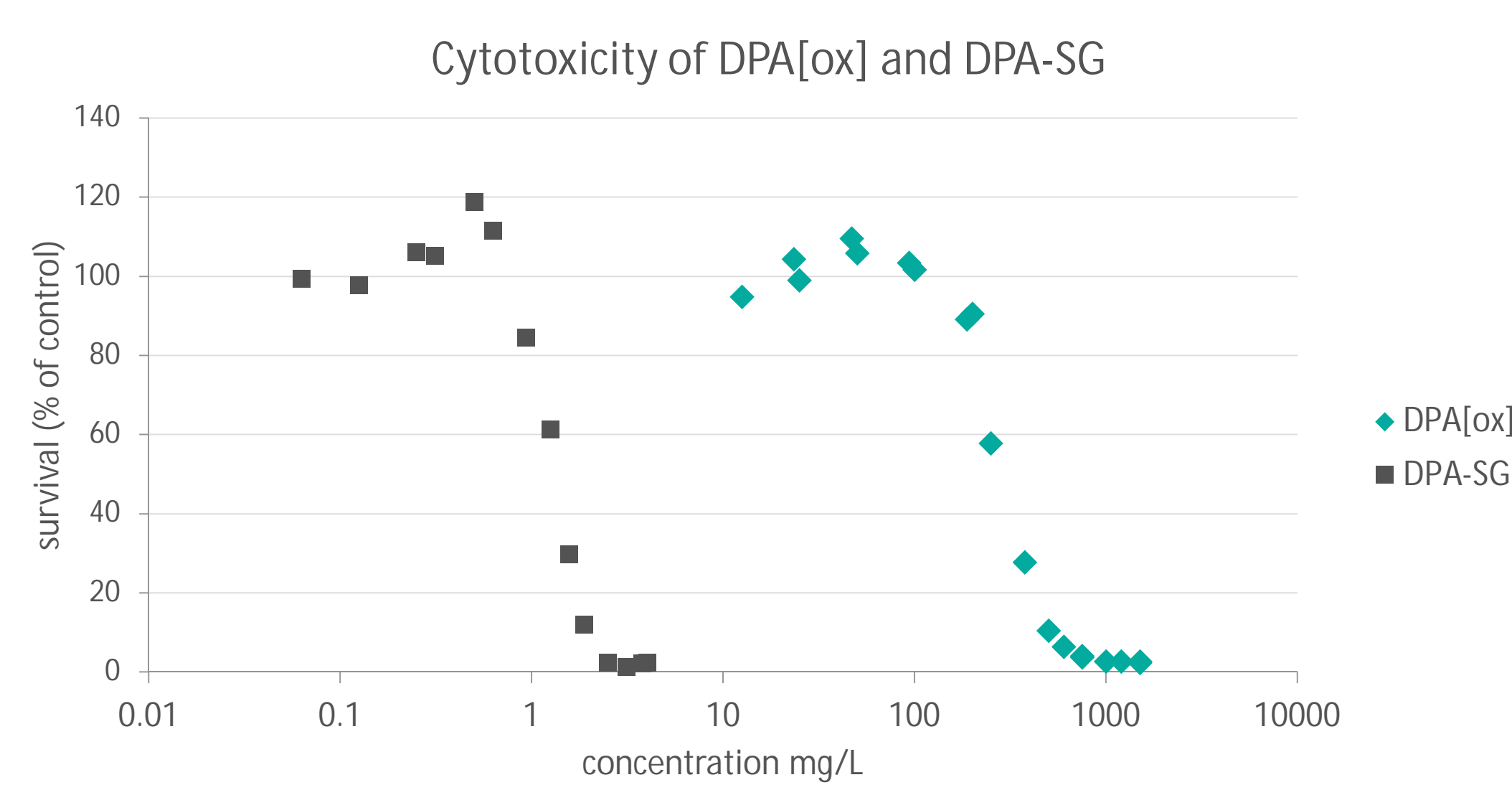
- New intracellular metabolites of DPA[ox] were detected and identified by UPHLC-HRMS
- These studies will elucidate the biological effects of dumped chemical munitions, and help in assessing the environmental and health risks posed by their continued presence and deterioration in the sea bottoms.



Measured toxicity values

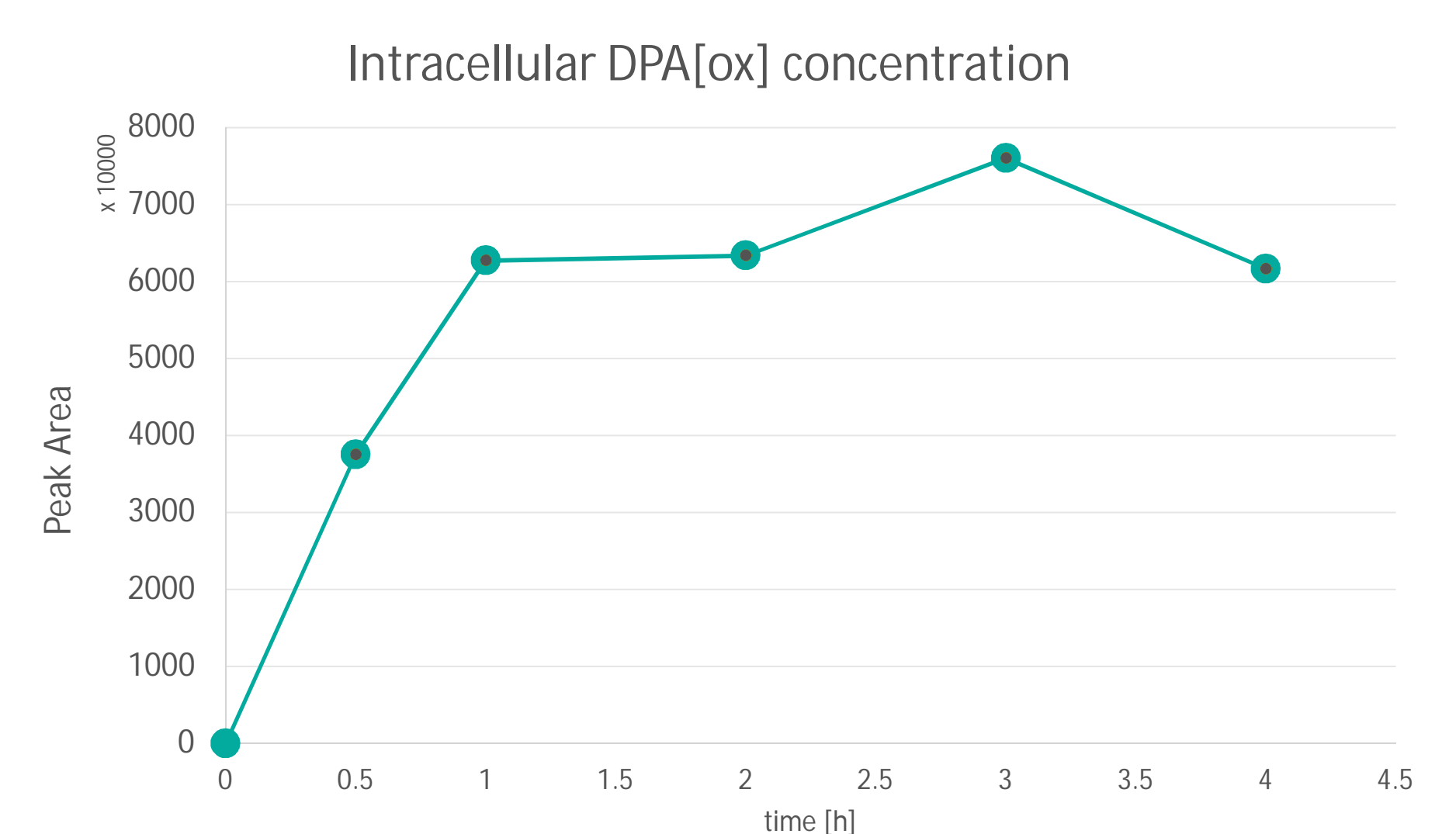
Tested substance	LC50
DPA[ox]	294 mg/L
DPA-SG	1.32 mg/L

Cytotoxicity of DPA[ox] and DPA-SG



- Cytotoxicity of DPA[ox] and DPA-SG was evaluated with the Neutral Red Retention test (96h)

Uptake and metabolism of DPA[ox]



- DPA[ox] uptake and metabolism in the cells was measured after 0.5h, 1h, 2h, 3h and 4h incubation by ultra-high performance liquid chromatography connected to high resolution mass spectrometry (UPHLC-HRMS)

