Phenotypic and metabolic characterization of A549 lung cancer cells exposed to organophosphorus flame retardants (OPFRs

M. Pramani, A. Pavlidou, J. Jaumot, C. Bedia
Institute of Environmental Assessment and Water Research (IDAEA-CSIC),
Carrer de jordi,18-26,08034, Barcelona, Spain
maryam.pramani@idaea.csic.es

In recent years, organophosphorus flame retardants (OPFRs) have become increasingly prevalent due to their unique properties beneficial for various industries, including plastics, foams, paints, furniture, building materials, electronics, and construction. It is common to find OPFRs in different environmental matrices such as soil, air, water, or sediments. Living organisms and human tissues are extensively exposed to these chemicals through leaking, discarding, abrasion, or volatilization [1]. According to previous studies, OPFRs are frequently detected in indoor environments at high levels, posing health risks to humans. For instance, a recent study in non-small cell lung cancer A549 cells demonstrated that the toxicity of OPFRs depends on dose and time. [2]

The aim of this work was to explore the effects on lung cells of seven OPFRs, namely EHDPP (2-ethylhexyl diphenyl phosphate), TBOEP (tris(2-butoxy ethyl) phosphate), TCEP (tris(2-chloroethyl) phosphate), TCP (Tricresyl phosphate), TDCPP (Tris(1,3-dichloro-2-propyl)phosphate), TEHP (tris (2-ethylhexyl) phosphate), and TPHP (triphenyl phosphate).

The toxic effects were evaluated using the A549 lung cancer cell line in three-dimensional (3D) format to enhance the physiological relevance of the results [3]. Cell cultures were exposed to the seven OPFRs individually with four replicates for 72 hours, and their cytotoxicity, reactive oxygen species (ROS), and interleukin-8 release were assessed. In addition, metabolite and lipid cell extracts were analyzed using LC-HRMS. Data were processed using an untargeted approach through chemometric methods to reveal the most critical metabolite and lipid changes under OPFRs exposure.

The results revealed that TDCPP and TPHP were the most toxic OPFRs and nearly all samples increased ROS production ranging from 100 to 150 %, with respect to the vehicle. Furthermore, EHDDP, TCEP, TDCPP, and TPHP, induced a higher release of interleukin-8 than the vehicle.

Among the seven groups of OPFRs, different trends in metabolites and lipids changes were observed, which were related to the different chemical structures of these organophosphorus compounds. These findings provide valuable insights into the potential health risks associated with OPFR exposure. This is the first study that uses metabolomics and lipidomics to explore the biological impact of OPFRs on lung cells.

References

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