LC-MS-Based Methods for the Characterization and Quantification of Established and New Organophosphate Esters and Metabolism By-Products in Biological Matrices

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Organophosphate esters (OPEs) comprise an expanding suite of synthesized chemicals that have historical and present uses as pesticides, flame retardants (FRs) and plasticizers. Several OPEs have been used as FRs and plasticizers as far back as the 1960s. The phase-out of the FRs such as polybrominated diphenyl ether (PBDEs) has resulted in a substantial increase in the production volumes and usage of an expanding suite of novel OPEs.

An increasing number of OPE triesters and diesters are now ubiquitous in the environment and reported in air, water, wastewater, sewage, soil, sediment and biota samples. The production and use trends of more novel OPEs is toward differing alkyl substitutions such as alkyl-substituted triphenyl phosphates (alkyl-TPHPs) and higher molecular weight and multiple diphenyl phosphate (DPHP) substituted compounds such as resorcinol bis(diphenylphosphate) and bisphenol-A bis(diphenyl phosphate) (BPADP), and even larger oligomeric OPEs. Environmental contamination for newer OPEs remains largely unknown. Studies have shown that OPEs are environmentally unstable and can degrade to complex mixtures of breakdown by-products via atmospheric, photolytic, hydrolytic, metabolic and biotransformation processes. Established OPEs such as (alkyl-)TPHP undergo Phase I metabolism and Phase II conjugation with glucuronide and glutathione as well as protein binding *in vitro*/*in vivo* in biota in mammal, bird and fish model systems. BPADP metabolism may include formation of TPHP, DPHP and the known xenoestrogen bisphenol-A (BPA).

The exposome of OPEs requires better understanding of the toxicokinetics including metabolism and protein binding. However, analytical methods are lacking to characterize, detect and quantify OPEs and degradation products in complex biotic matrices. Citing our recent studies and those reported in the literature, this presentation will give an overview of LC-MS-based methods (e.g. LC-Q-TOF-MS and UHPLC-QQQ-MS/MS) and the characterization and sensitive quantification of OPE triesters/diesters and/or metabolic by-products, metabolites and conjugates in various tissues, body compartments, and/or in field and *in vitro/in vivo* assay samples.