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Widening knowledge horizons on legacy POPs: Chlorinated Paraffins and Polychlorinated Naphthalenes

Chlorinated paraffins (CPs) remain one of the enduring analytical chemistry challenges of our times. Tens of thousands of individual CP congeners, sterically hindered in commercially produced mixtures, contrive to defy characterisation of the residual burdens that occur ubiquitously in the environment and biota. However, recent advances in our knowledge on behaviour and occurrence, supported by high resolution mass spectrometric and nuclear magnetic resonance (NMR) techniques are providing new insights into the nature and fate of these contaminants in the biotic and abiotic environment.

Contrastingly, the polychlorinated naphthalenes (PCNs) are a well- defined group of 75 diaromatic planar chlorinated compounds, many of which show potent binding affinities for the aryl hydrocarbon receptor (AhR), eliciting a range of pleiotropic responses, including pre-carcinogenesis. Other biological effects are also being investigated which is timely as they are known contaminants in all environmental media and occur in food as well as human tissues. Some CPs (SCCPs), as well as the PCNs are classified as persistent organic pollutants (POPs) and have recently been listed in Annex A (and Annex C for PCNs) of the Stockholm Convention – which calls for elimination of future production. This special issue is devoted to the dissemination of the latest findings covering analytical aspects, synthesis of new standards, transformation, occurrence in the environment and food, and the toxicological effects of these chemicals.

1. Chlorinated Paraffins

The challenge with characterising CPs is multi-faceted. Commercial CP mixtures contain chlorinated alkane chains that nominally range from C10 to at least C30. The convention of classifying these as short-, medium- and long-chain CPs allows a convenient although superficial description; in reality, the composition of commercial mixtures does not necessarily follow this convention and products are identified based on the degree of chlorination and/or the requirements of particular applications. Estimating the number of individual CP congeners (estimates range from 10s to 100s of thousands) in these mixtures based on carbon number, degree of chlorination, number of chlorines per carbon and stereogenicity is only important as a demonstration of the numerical complexity (Vetter et al., 2022), and the resulting challenge to characterisation – the real numbers remain unknown as stearic interactions make the congeners inseparable. More importantly, the composition of the mixtures can change from the moment they are used (e.g. selective evaporation and thermal degradation from the high temperatures used in machining/drilling applications), followed by environmental modification – through evaporation, atmospheric photoionisation, microbial degradation, etc., followed by metabolic changes in animals and humans. The final composition of the CP mixtures that humans are exposed to and which should form the basis of risk assessment is likely to be very different to individual commercial products.
The commercial CP mixtures are also known to contain by-products – some, such as chlorinated alkenes (olefins), can interfere with the mass spectrometric measurement processes whilst the presence of other minor, but more toxic by-products such as chlorinated benzenes, polychlorinated biphenyls and polychlorinated naphthalenes raise questions about the toxicity that has been associated with the commercial CP mixtures. There is also relatively little

information on the toxicological effects of the longer chain CPs. Any risk assessment is thus faced with at least two important unknowns – the extent/nature of the exposure and the toxicity that can be attributed to CPs. Thus both, occurrence data on CPs in the environment, food (as a potentially major route to exposure) and humans, and an updating of the toxicology, are required. Despite these challenges, steady progress has been made on the analytical chemistry of CPs over the last decade. The wider use of high resolution mass spectrometric techniques has resulted in more of the recent studies reporting data on specific CP chain lengths and homologue groups (Meziere et al., 2021; Fernandes et al., 2022; Wang et al., 2021; Sprengel et al., 2022), which was identified as a first step to the characterisation of the CP profiles observed in biota and foods (Fernandes et al., 2020). In conjunction with a database that is currently being compiled on CP homologue occurrence in food and human tissues, this refinement would allow better characterisation of the occurrences. The occurrence patterns in commonly consumed foods that emerge from these studies should in turn, allow more targeted toxicological studies and ultimately, better tools for risk assessment, particularly through dietary intake. New NMR techniques such as two dimensional heteronuclear spectral quantum coherence (HSQC, 1H–13C) are also providing insights into the structural configurations of CP molecules (Yuan et al., 2020; Sprengel and Vetter, 2020; Sprengel et al., 2022) and the link between higher degrees of chlorination and multiple chlorine substitution (Fernandes et al., 2022). This information provides an indication of the nature of the CPs that are formed during production and together with studies on microbial degradation (Knobloch et al., 2021), should allow further characterisation of the occurrences, by indicating which chain lengths and configurations are likely to be more persistent. These studies using microbial dehalogenase (Knobloch et al., 2021, 2022a, 2022a) together with chemical dehalogenation methods (Fujimori et al., 2021) also provide indications of the strategies that could be used for decontamination, by detoxifying stockpiles or remediating contaminated sites.

Achieving a meaningful risk assessment of CP exposure still poses a number of challenges, both, analytical as well as toxicological:

- Toxicological studies should be extended to cover some of the longer (and shorter, C6-9) chain length congeners that have been shown to occur in food and in animal tissues. Emerging occurrence data on food and human tissues should provide qualitative guidance for these studies. They should also confirm that the end-points reported earlier, were not influenced by the presence of the reported by- products, most of which are highly potent toxicants.
- More occurrence data on CPs is required, and the reliability of this information will potentially benefit from a wider range and better quality of reference standards (Fernandes et al., 2022; Knobloch et al., 2022a, 2022b; Sprengel et al., 2022) that will also allow characterisation to be extended to the longer chain length CPs (very few or in some cases, no standards are currently available for longer chain length CPs).
- Analytical methods should be developed or improved in order to quantify those CP configurations (e.g. congeners with less than 4 chlorines) that are currently not included in the occurrence estimates due to poor detectability. The use of higher resolution mass spectrometry should help to exclude closely related interferants such as the chlorinated olefins, if these survive environmental weathering, metabolism and the analytical purification techniques.

The advances made in characterising CP occurrences are encouraging as are the studies on physical parameters such as homologue specific vapour pressure (Hammer et al., 2021), decontamination and inventorying CP occurrence (Guida et al., 2022). Further advances will require the support of new and better standards, more information on characterised occurrence and an improvement in the reliability and comparability of CP determination. Currently, interlaboratory studies show better agreement between participant's results when test materials are fortified with standards or when the same standards are used (Hanari and Nakano, 2022), in comparison to when naturally contaminated test materials are used (Fernandes et al., 2022).

2 Polychlorinated naphthalenes

The 75 congener group of PCNs presents a considerably better defined set of analytes for those researchers engaged in characterising environmental (biotic and abiotic) and human exposure. A few decades have passed since widescale production ceased, and although anthropogenic combustion sources such as waste incineration continue to add to global PCN levels, the legacy of the earlier use of commercial PCN products continues to dominate the occurrence profiles in environmental media and many common foods such as fish, eggs, poultry, shellfish, etc. (Fernandes et al., 2017; Zacs et al., 2021)

AhR mediated (dioxin-like) toxicity is recognised as one of the potent effects of PCN exposure and although the chlorinated planar aromatic structure bestows this property to potentially the whole group, some of the higher chlorinated congeners show considerably higher potency. There have been very few recent studies (Suzuki et al., 2020) to re-evaluate individual potencies and further investigation would allow confirmation of these findings and prioritisation of congeners for monitoring studies. The contribution of PCN toxicity should also be considered cumulatively with that of PCDD/Fs, PCBs and PBDD/Fs, in order to provide more holistic risk assessment for this mode of toxicity.

Over the last decade, other toxic responses such as disruption of endocrine systems, embryotoxicity, immunotoxicity, hepatotoxicity, effects on steroidogenesis etc. have been increasingly studied. Most recently, the neurotoxicity of a mixture of higher chlorinated PCN congeners has also been investigated in vitro. The observed effects of diminished dopamine content and release, and the expression of antioxidant enzymes noted in the study (Boczek et al., 2022), may potentially be related to the anorectic behaviours observed earlier in humans following occupational exposure to PCNs. Earlier animal studies have shown other effects – reduced fetus length and weight, renal pelvis extension, as well as indications of delayed ossification and retarded development of internal organs. Unlike the AhR mediated effects which are generally associated with the higher chlorinated congeners, some of these studies show that lower chlorinated PCN congeners can also induce or mediate effects, albeit at higher concentrations. These effects should be reviewed alongside the relatively more studied AhR mediated effects so that they can be considered holistically for risk assessment.

However, this effort requires more and current occurrence data. Much of the reported PCN data on occurrence in environmental media, food and humans is derived from individual isolated studies which confirm the ubiquity of these contaminants but do not allow the trend to be followed. More understanding is also required on the contribution of combustion sources to the overall burden of PCN bioaccumulation in biota, food webs and human exposure.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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