SCREENING CHEMICALS IN COMMERCE TO IDENTIFY POSSIBLE PERSISTENT AND BIOACCUMULATIVE ORGANOHALOGEN CHEMICALS: NEW RESULTS

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Abstract
Although environmental analytical chemists have had great success over the past 40 years in identifying and quantifying persistent (P) and bioaccumulative (B) organohalogen compounds in environmental media only a small fraction of the organic substances in wide commercial usehave been thoroughly assessed for P and B characteristics and/or measured in environmental media. Of particular concern are those substances that are P, B and toxic and that have characteristics of persistent organic pollutants (POPs). Recently we published a review of the ongoing screening and categorization of existing chemicals for P and B and long range transport characteristics (Muir and Howard ES&T 40, 7157-7166, 2006). In this presentation we have updated our list by combining the Canadian Domestic Substances List with the US EPA Toxic Substances Control Action Inventory Update Rule list and other data on high production volume (HPV) chemicals yielding 22,043 chemicals for screening using quantitative structure property relationships and expert judgment. We have identified about 400 chemicals which may have P and B characteristics. Of these, 70% were halogenated and 10% were siloxanes. Because a high proportion are halogenated, semi-volatile and hydrophobic they are likely extractable by conventional methodology for POPs and amenable to gas chromatographic analysis.

Introduction
Although environmental analytical chemists have had great success over the past 40 years in identifying and quantifying persistent (P) and bioaccumulative (B) organohalogen compounds in environmental media, the fact remains that only a small fraction of the organic substances in wide commercial use (>~1 t/y) have been thoroughly assessed for P and B characteristics and/or measured in environmental media[1]. Of particular concern are those substances that are persistent, bioaccumulative and toxic (PB&T) and that have characteristics of persistent organic pollutants (POPs) as defined by UNEP [2] and other agencies [3-5]. These characteristics include log Kow>5, bioconcentration factor (BCF) >5000, atmospheric oxidation half-life (AOt1/2)>2 days, and predicted persistence in soil and sediment of >180 days.

As software for Quantitative Structure Property Relationships (QSPRs) has improved over the past 10-15 years, it has become possible to screen large lists of chemicals in commerce (discrete substances, i.e. not uncharacterized mixtures or polymers) for P&B and POPs criteria. For example, Walker and Carlsen[6] screened 8511 chemicals, from the US EPA 1998 Toxic Substances Control Act Inventory Update Rule (IUR) listing (http://www.epa.gov/oppt/iur/) for persistence and bioaccumulation potential. They developed a list of 56 chemicals with medium bioaccumulation (BCFs >1000) and high predicted persistence. Öberg[7] applied QSPRs for baseline toxicity to fish (acute toxicity to fathead minnows), and for atmospheric oxidation by hydroxyl (OH) radical reaction, to 98,000 compounds on the SMILESCAS Database (SRC, North Syracuse, NY). A total of 50,074 compounds were judged to be within the domain of applicability for both models. In all, 1653 compounds were predicted to meet criteria of persistence (AO t½>2 days) and toxicity (fish acute toxicity LC50<10 mg/L) and 88% of these were halogenated. Wiandt and Poremski[8] selected 400 substances from the Nordic Substance Database (about 18 000 substances), the Danish Miljøstyrelsen QSPR database (more than 166,000 substances) and the database of the Netherlands' BKH/Haskoning report (about 180,000 substances) with potential PB&T characteristics. However, only 203 out of 400 substances could be ranked because production volumes and use characteristics were not available for most chemicals. Lerche et al.[9] drew upon some of the same large chemical databases as Öberg[7] and Wiandt and Poremski [8], to identify compounds with long range atmospheric transport (LRAT) potential, as well as P&B characteristics. They identified 42 chemicals with P & B characteristics and 12 compounds, all halogenated, that were predicted to meet all POP screening criteria. Several of the compounds in their top 12 (dicofol, PCNs, and hexachlorobutadiene) are now being considered for the United Nations Economic Commission for Europe (UNECE) POPs list[10].

Possibly the most extensive screening and categorization of existing industrial chemicals has been conducted in Canada on the Canadian Domestic Substances List (DSL)[11]. About half of the 23,000 substances on the DSL (11,713) were assigned log Kow values (16% were measured values). The other half were of "unknown or variable composition and biologicals" (UVCBs), or were polymers, metals and inorganics, organo-metallics or organometal salts and could not be assigned physical properties using QSPRs. About 21% (2320) of the 11,317 individual organic chemicals had predicted log Kow>=5, and 3.2% had predicted BCFs > 5,000. The categorization concluded that about 700 substances were predicted to be P and B and requiring more thorough exposure and risk assessment (http://www.ec.gc.ca/ CEPARegistry/subs_list/dsl/dslsearch.cfm).

Recently we published a review of the ongoing screening and categorization of existing chemicals for persistence, bioaccumulation and long range transport[1]. Using data from the Environment Canada DSL categorization we identified 30 chemicals with high predicted bioconcentration and low rate of biodegradation and 28 with long range atmospheric transport potential based on predicted atmospheric oxidation half-lives > 2 days and log air-water partition coefficients (log Kaw) >-5 and <-1. These chemicals were a diverse group including halogenated organics, cyclic siloxanes and substituted aromatics. Some of these chemicals and their transformation products may be candidates for future environmental monitoring. In this presentation we have updated our list by combining the DSL with the USEPA TSCA IUR and other data on high production volume (HPV) chemicals to more fully address the issue of whether there are additional chemicals, produced or imported into the US and Canada in significant quantities, with P, B and POPs characteristics. We also examine the question of whether selected chemicals can be analysed by existing methods or will require new isolation and quantification procedures for the analysis in environmental media.

Methods

The Canadian DSL list totaling 11,317 compounds was combined with the US EPA high production volume (HPV) list available at http://www.epa.gov/HPV/hpvchmlt.htm. After removing duplicates, the HPV list contained 3549 unique Chemical Abstracts Service (CAS) numbers. From previous work (Howard and Meylan, unpublished data), we had derived discrete, representative Simplified Molecular Line Entry System (SMILES) notations for 3059 substances of "Unknown or Variable composition Complex reaction products and Biological materials" (UVCBs). These 3059 substances were added to the DSL list to yield a combined list of 14,376 compounds. The list was combined with the IUR database which contains production ranges for the following five years: 1986, 1990, 1994, 1998, and 2002 for 13,958 CAS numbers. Finally we added 500 chemicals from the EPA's Enhanced HPV (EHPV) program, which covered substances that were not in the HPV program, but were produced in over 1 million pounds during 2002. The CAS numbers were cross-compared to remove duplicates yielding a total of 22,043 chemicals.

Selected physical and chemical property values estimated with the EPI Suite software[12] included log Kow (Kowwin), BCF (Bcfwin), Henry's law constant (Henrywin), various biodegradation probabilities (Biowin), log Koa (octanol-air), vapor pressure (Mpbpwin), and atmospheric oxidation (Aopwin).

Results and Discussion

The combined dataset is summarized in Table 1. Quantitative structure property relationships (QSPRs) were used in screening of the thousands of chemicals and for the identification of chemicals of high priority for further assessment.

Table 1. Development of a combined the Canadian and US database of chemicals in commerce

Source	# substances	Reporting threshold	Reporting date
US EPA High production volume (HPV) and EHPV program	4049	10^6 lbs/yr (454 t/yr)	IUR reporting years; 1990, 1994, and 2002
US EPA TSCA Inventory update rule (IUR)	13,958	$>10^4$ lbs/yr (4540 kg/yr)	IUR reporting years; 1986 to 2002
Canadian DSL categorization	11,317 organics	>100 kg	Mid-1980s
UVCBs	3059 organics	>100 kg	Mid-1980s
Total (after duplicates removed)	22,043		

The results of the screening of the 22,043 chemicals are summarized in Table 2. A significant proportion of the chemicals had predicted log Kow >5 (19%), AOt1/2 >2 days (10%) and log Kaw >-5 and <-1 (32%) when sorted by individual criteria. However, when these criteria were combined, and broadened to capture additional compounds, only 105 substances had all 3 characteristics based on log Kow >1000, AOt1/2 >1 day and log Kaw >-5 and <-1 . Of these 65 were halogenated.

On further evaluation some of these chemicals are not of concern as P& B chemicals and some of the traditional criteria for selection may not be inclusive enough[1]. A recent example is Dechlorane-Plus, a decachlorinated flame retardant HPV chemical, which has been detected in Great Lakes air, fish, and sediments[13]. Dechlorane-Plus did not make it into the list of 105 P & B substances estimated by QSPRs because it has a predicted low BCF of 0.5 due to a very high predicted log Kow (11.3). However, it appears to be a widespread

Table 2. Persistence and Bioaccumulation Characteristics of the 22,043 Chemicals

Characteristics*	#	%	Notes
log Kow > 5	4239	19	Indicates tendency to adsorb to sediments and to bioaccumulate
BCF > 2000	924	4.6	BCF is an estimate of bioaccumulation potential
BCF > 5000	566	2.8	
BCF > 50000	19	0.1	
AO t1/2 > 2 day	1973	10	AO half-life indicates stability to atmospheric oxidation
AO t1/2 > 10 day	840	4	
log Kaw > -5 and log Kaw < -1	6515	32	Kaw describes air-water partitioning. Compounds with log Kaw >-5 & <-1 have long range transport potential
Combined BCF > 2000, AO t1/2 >1 d and log Kaw > -5 and <-1	105	0.5	The number of substances with all 3 characteristics combined is much smaller
Combined BCF > 2000, AO t1/2 >1 d and log Kaw > -5 and <-1	79	0.4	

contaminant in the sediments in the Great Lakes region and may deserve further exposure and risk assessment. This illustrates the potential for some false negatives in the screening process. Of course, the combined database can also be used to identify P chemicals that have high log Kow values that may bioaccumulate like Dechlorane-Plus, but have low predicted BCF estimates.

To further refine the screening process, chemicals with high production volume were individually screened using expert judgement for persistence, persistence of potential metabolites, and bioconcentration/bioaccumulation factors (BCF/BAF) of the parent and potential metabolites. These four endpoints (P, P-Metabolite, B, B-Metabolite) were evaluated separately. Chemicals that had high log Kow values (above 8) were considered to be potential BCF/BAF chemicals unless that had very high molecular weights. This second selection process added another 295 chemicals. Of the 400, 70% were halogenated and 10% were siloxanes, reflecting the generally higher P and B characteristics of these classes of compounds.

Table 3 lists selected brominated and chlorinated chemicals with high predicted persistence and AOt1/2. All chemicals have been reported to be manufactured or imported into the USA at >4.5t/y between 1986 and 2002 although not all may be in current use. They were selected from the list of 400 substances because they are likely easily isolated and quantified by current analytical methodology for PCBs, PBDEs and organochlorine pesticides. Indeed many are analogs of known P and B compounds such as hexachlorocyclohexane and chlorobenzenes. Not all are predicted to bioaccumulate, mainly because of high molecular weight and very high log Kow. This is particularly the case for the brominated flame retardant octabromo-1,1,3-trimethyl-3-phenyl indane, which is listed on the TSCA IUR with production/import of 4.5t-227t/yr in 2002, and is predicted to be recalcitrant by EPI suite QSPRs. With estimated Log Kow of 11.8 Bcfwin predicts a low BCF for this compound. Given that octabromodiphenyl ethers are also generally not detected or present only at low concentrations in biota [14] this may be also be the case for this brominated indan. To the best of our knowledge, none of the 10 compounds on the list in Table 3 have been reported in environmental media. However, in our

previous study using just the Canadian DSL chemical list, we also identified several bromo-chloro cyclohexanes as possible candidates for further assessment and we are aware of several groups now planning to analyse for those compounds.

Table 3. Selected persistent brominated and chlorinated compounds identified by QSPR screening and expert judgment. AOt1/2 and partition coefficients are predicted with EPI suite software

Common name	CAS #	AO t1/2	LogKaw	logKow	Log Koa	BCF
1,3,6,8 tetrabromopyrene	128632	6.6	-5.1	8.5	13.6	2424
1,2-dibromo-4-(1,2-dibromoethyl)cyclohexane	3322938	2.2	-2.8	5.2	8.0	2153
Octabromo-1,1,3-trimethyl-3-phenyl indan	155613937	6.2	-6.9	11.8	18.7	1
pentabromo-6-chloro-cyclohexane	87843	15.7	-4.4	4.7	9.1	860
dichlorotetrabromocyclohexane	30554724	16.4	-3.9	4.6	8.5	716
Pentachloro-benzene-thiol	133493	76.7	-2.3	5.9	8.2	7066
Heptachlorocyclo-pentane	68258902	93.5	-2.6	4.0	6.6	253
1,2-dichloro-4-(trifluoromethyl)-benzene	328847	133	0.02	4.2	4.2	370
1,3-dichloro-5-(tetrachloro-1-methylpropyl)-benzene	73588428	4.6	-3.3	6.8	10.1	34420
pentachloronitrobenzene	82688	1479	-3.7	5.0	8.7	746

Conclusions

Our screening of 22043 organic substances in commerce has yielded some interesting probable P&B substances Most of the 400 we identified are not currently analysed in environmental media. Because the QSPR selection process favors compounds with high log Kow and long AOt1/2, a high proportion are halogenated and hydrophobic and thus would likely be extractable by conventional methodology for POPs. Most are also likely amenable to gas chromatography and thus could be analysed in environmental media although suitable analytical standards would need to be available. Nevertheless there are major uncertainties in this type of screening including the possibility of false positives (e.g. readily degradable chemicals such as anhydrides and esters are screened in). False negatives are also a concern; high molecular weight compounds have low estimated BCF but may still be a concern if persistent in sediments. Lack of information on uses and actual emissions of the chemicals also presents a problem for designing measurement programs for these chemicals. Some of the 400 are chemical intermediates and may be entirely consumed in manufacturing process or present as residuals in products, while others may yield recalcitrant degradation products.

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