Anal Bioanal Chem (2009) 393:847–860
DOI 10.1007/s00216-008-2371-7

REVIEW

Advances in the determination of degradation intermediates of personal care products in environmental matrixes: a review

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Received: 30 May 2008 / Revised: 16 July 2008 / Accepted: 22 August 2008 / Published online: 20 September 2008

Abstract In this review, recent methods developed for the determination of degradation intermediates of personal care products in environmental matrixes focusing on the extraction and determination steps are discussed. The five classes of personal care products evaluated are stimulants, fragrances, sunscreens, antimicrobials, and insect repellents. Methods are critically reviewed in terms of the analytical steps involved in the analysis, sample pretreatment, separation, and detection as well as the different confirmation strategies employed. Preconcentration from aqueous matrixes was performed by solid-phase extraction, liquid–liquid extraction, or solid-phase microextraction, allowing the simultaneous extraction of parent compounds and their degradation intermediates. Following the extraction and cleanup steps, the identification and quantification of degradation intermediates of personal care products at environmental levels (i.e., parts per trillion to parts per billion range) is usually performed by using mass spectrometry techniques such as single quadrupole mass spectrometry and more recently by time-of-flight mass spectrometry or tandem mass spectrometry. The main scope of this review is to critically evaluate the current state of the art of the analytical techniques used and to identify the research needs in the determination of degradation intermediates of personal care products in environmental matrixes.

Keywords Personal care products · Metabolites · Degradation intermediates · Sample preparation

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Introduction

Personal care products (PCPs) constitute a broad class of compounds, some of them belong to the list of high production volume chemicals that are currently used for human and veterinary applications (e.g., food additives, sunscreens, insect repellents, shampoos, and deodorants) [1, 2]. As an example, annual production of PCPs in Germany exceeded 550,000 t [3]. Because these compounds have been applied as skin, hair, and dental care products or soap additives, some of them are directly or indirectly ingested and then frequently transformed in the body, producing the excretion of a combination of nonaltered PCPs and metabolites. Both parent compounds and their metabolites enter the aquatic environment mainly through municipal wastewater treatment plants (WWTPs) in concentrations from parts per billion to low parts per trillion [4–7]. In addition to sewage sludge disposal, these compounds can be directly introduced to surface waters via release from the skin during swimming or bathing; therefore, variable concentrations of these compounds are detected in surface, ground, and coastal waters receiving treated sewage effluents or sewage sludge [8–10]. Additionally, other degradation intermediates can originate from biotic or abiotic processes in WWTPs or surface waters, as reported for galaxolide and triclosan [6, 11].

Regarding the possible ecotoxicological impact of PCPs and their degradation products, several effects in

aquatic organisms have been reported. These include the inhibition of multixenobiotic resistance in polycyclic musks [12], estrogenic behavior of several parabens [13], direct toxicity of triclosan on benthic invertebrates [14], and coral bleaching by sunscreen compounds [15]. Although there is no information related to degradation intermediates of PCPs, increasing toxicity of pharmaceutical oxidation products has been reported [16, 17]; hence, it is expected that degradation intermediates of PCPs might produce effects on biota that have not yet been evaluated.

Recent advances in hyphenation of chromatography with mass spectrometry (MS) techniques allowed the detection and identification of numerous PCPs [18] but limited information related to their degradation intermediates is currently available.

This review summarizes the analytical methods employed for the determination of degradation intermediates of PCPs from biotic or abiotic processes. These compounds are reported in terms of their chemical structures and degradation pathways. The groups of PCPs studied are stimulants, fragrances, sunscreens, antimicrobials, and insect repellents. Analytical methods are discussed in three steps: (1) sample pretreatment, (2) separation and detection, and (3) confirmation of degradation products. Finally, future methodological developments are discussed.

Summary of degradation products analyzed

Table 1 summarizes the reported PCPs and their major degradation intermediates as well as the degradation processes that cause their release into the aquatic environment (i.e., human or microbial metabolism, photodegradation, and advanced oxidation treatment). Generally, degradation intermediates increase the degree of oxidation of the parent compounds as is usually done in biological detoxification processes. This effect decreases the lipophilicity (e.g., galaxolide log K_{ow}=6 to galaxolide lactone log K_{ow}=4). Advanced oxidation of caffeine, human metabolism of pyrethrum and pyrethroid, or aerobic biodegradation metabolism of Bayrepel produces the release of acidic degradation compounds into the aquatic environment. Therefore, although the carboxylic group is more readily biodegradable, the mobility of acidic compounds in saturated soils is higher than that of neutral compounds. That is consistent with the low interaction manifested by deprotonated carboxylic compounds (low log K_{ow}) as reported in aquifer mobility studies [19]. Hence, these degradation intermediates could be easily remobilized in saturated systems and other aquatic environments.

Analytical techniques

Table 2 summarizes the reported analytical techniques used to identify degradation intermediates of PCPs in different environmental and biological matrixes. In this review, the determination of degradation intermediates of PCPs in human fluids has also been included to provide further information about the compounds formed during human metabolism as they are released into the aquatic environment through wastewaters. It is important to know the structure of the products that can be potentially detected in the aquatic environment.

This section is subdivided according to the analytical steps required for the analysis of selected degradation products (i.e., pretreatment, analytical separation, detection, and the method used for the confirmation of the degradation products) and according to the matrix studied.

Pretreatment

Conjugation cleavage

Because a fraction of the PCPs are excreted in urine, some of them occur in raw wastewater mostly in the conjugated form such as glucuronidates and less frequently sulfates, *N*-acetylates, or amino conjugates. Consequently, they can require a cleavage step of the conjugate form to release the degradation intermediates of the PCP before extraction. Leng and Gries [20] acidified urine samples (Table 2) and kept them at 100 °C for 2 h to hydrolyze conjugates from pyrethroid and pyrethrin metabolites. Alternatively, mild reactions, including enzymatic hydrolysis, are suitable as is done for labile pharmaceutical products [21]. Although in wastewater conjugated forms could be less abundant and only relevant for the compounds that have been ingested or incorporated through skin, in human fluids and biological tissues this cleavage step is compulsory.

Water samples

As the expected concentrations for these compounds in water samples and chiefly in environmental matrixes are very low (parts per trillion to parts per billion range), a preconcentration step is compulsory prior to their determination.

Several preconcentration techniques have been employed for the extraction of degradation intermediates of PCPs from water samples. The most widely used techniques are solid-phase extraction (SPE), liquid–liquid extraction (LLE), and solid-phase microextraction (SPME) (Table 2). While LLE has been extensively used for the determination of the most hydrophobic compounds in wastewater, SPE and SPME have been employed to expand the range of polarities of

Table 1 Personal care products and their respective degradation products obtained through biotic or abiotic pathways

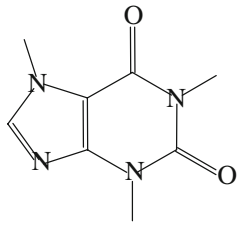
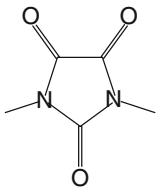
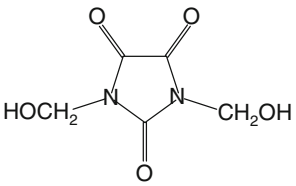
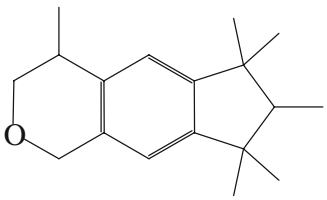
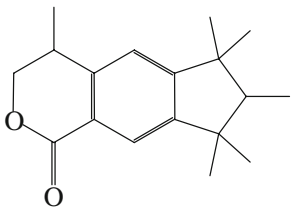
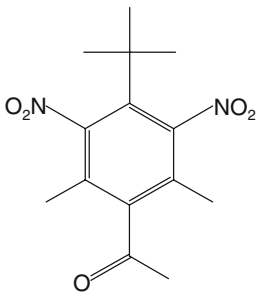
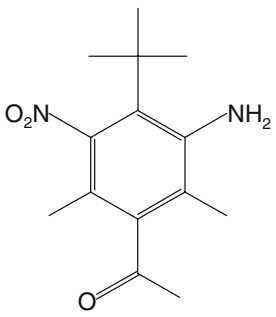
Parental compound (class)	Degradation Intermediates	Source	References
 Caffeine (stimulant)	 *N*-Dimethylparabanic acid	Advanced oxidation reactions	[37]
	 Di(*N*-hydroxymethyl)parabanic acid		
	14 metabolites (methyl xanthines)	Human metabolism	[44]
 Galaxolide (fragrance)	 Galaxolide lactone	Biodegradation (wastewater)	[27]
 Musk ketone (fragrance)	 2-Amino musk ketone	Biodegradation (water samples)	[43]
		Metabolism (biota)	[31]

Table 1 (continued)

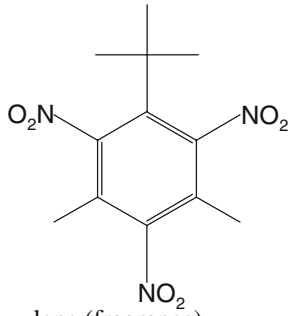
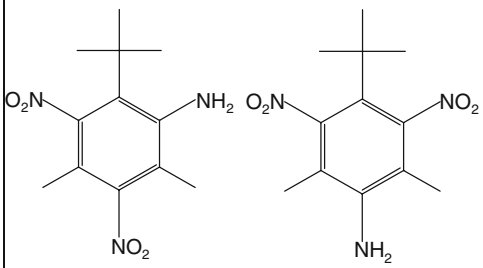
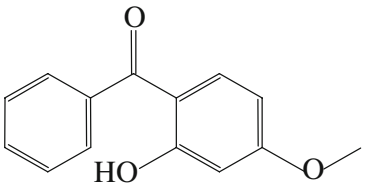
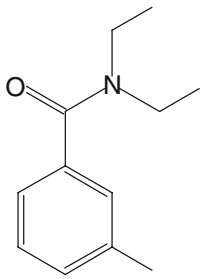
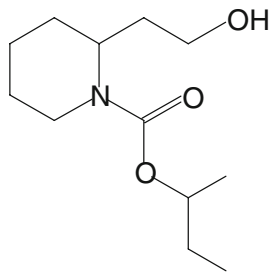
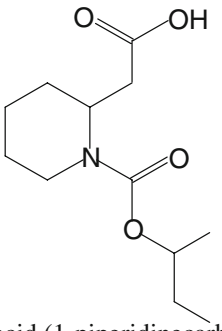
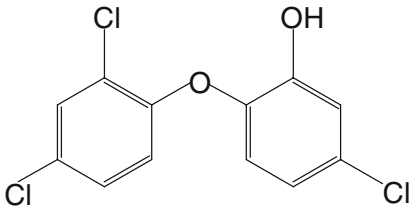
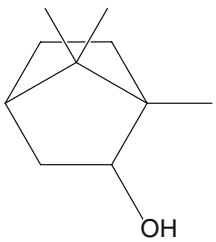
 Musk xylene (fragrance)	 2-Amino musk xylene 4-amino-musk xylene	Biodegradation (water samples)	[43]
		Metabolism (biota)	[31]
 Oxybenzone (fragrance)	2,4-Dihydroxybenzophenone 2,2′-Dihydroxy-4-methoxybenzophenone 2,3,4-Trihydroxybenzophenone	Human metabolism	[45]
 *N*,*N*-Diethyl-*m*-toluamide (DEET) (insect repellent)	*N*,*N*-Diethyl-*m*-hydroxymethylbenzamide *N*,*N*-Dipropyl-*m*-toluamide *N*-Ethyl-*m*-toluamide	Human metabolism	[45]
	N,*N*-Diethyl-*m*-toluamide-*N*-oxide *N*-Ethyl-*m*-toluamide-*N*-oxide *N*-Ethyl-*m*-toluamide	Biodegradation	[46]
Allethrin, phenothrin, pyrethrum, resmethrin, tetramethrin (insect repellent)	*trans*-Chrysanthemumdicarboxylic acid (*trans*-CDCA)	Human metabolism	[20]
Cypermethrin,deltamethrin permethrin (insect repellent)	*cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid		
Deltamethrin (insect repellent)	*cis*-3-(2,2-Dibromovinyl)-2,2-dimethylcyclopropane carboxylic acid		
Cyfluthrin, cypermethrin, deltamethrin, permethrin (insect repellent)	3-Phenoxybenzoic acid		
Cyfluthrin (insect repellent)	4-Fluoro-3-phenoxybenzoic acid		

Table 1 (continued)

 Bayrepel [1-piperidinecarboxylic acid, 2-(2-hydroxyethyl), 1-methylpropyl ester; KBR 3023] (insect repellent)	 Bayrepel acid (1-piperidinecarboxylic acid, 1-methylpropyl ester, 2-acetic acid)	Aerobic biodegradation	[36]
 Triclosan (antimicrobial)	Dichlorohydroxydiphenyl ether, monochlorohydroxydiphenyl ether 2,4-Dichlorophenol Monochlorophenol 2,8-Dichlorodibenzo-*p*-dioxin	Photodegradation	[26, 47]
	Methyl triclosan, 2,4-dichlorophenol, 2,3,4-trichlorophenol	Biodegradation (wastewater)	[22, 35]
 Camphor (insect repellent)	5-Hydroxycamphor 5-Ketocamphor 9-Hydroxycamphor 8-Hydroxycamphor 3-Hydroxycamphor 8-Camphor carbonic acid trimethylsilylester or 9-camphor carbonic acid trimethylsilylester Isoborneole	Human metabolism	[48]

the extracted analytes and to reduce or eliminate the use of solvents in the extraction.

SPE of degradation intermediates from water samples was accomplished by using different stationary phases, from hydrophobic phases (C-18) to polymeric or copolymeric phases (i.e., hydrophilic–lipophilic balance, e.g., divinylbenzene–*N*-divinylbenzenepyrrolidone copolymer). Hence, owing to the increased polarity of degradation intermediates of PCPs, polymeric hydrophilic–lipophilic balance phases are recommended because they allow the coextraction of both the parent and degradation intermediates.

Canosa et al. [22] reported a suitable preconcentration technique for triclosan metabolites from Milli-Q water, river water, and influent and effluent wastewater by SPME on-fiber derivatization with *N*-methyl-*N*-(*tert*-butyldimethylsilyl)trifluoroacetamide. The use of polyacrylate fibers was preferred to that of polydimethylsiloxane–divinylbenzene since better repeatability was obtained.

In addition, Felix et al. [23] reported the preconcentration of benzophenone metabolites in water and human urine by SPME. Carbowax–divinylbenzene fiber exhibited the highest extraction efficiency in a wide linear range (10–1,000 ng mL^{-1}) and with a precision averaging 7% relative standard deviation.

Furthermore, photo-SPME, developed by Llompart and coworkers [24, 25], is a recent and very elegant tool to carry out photochemical studies of organic lipophilic pollutants, including PCPs. The main advantage of that technique in comparison with conventional methods relies on the fact that the preconcentrated pollutants in a polydimethylsiloxane fiber are directly photodegraded on it. Then, the photooxidation products following the photooxidation step can be easily analyzed after the photooxidation by thermal desorption into the gas chromatograph injector port without any additional step. By using this approach, Sanchez-Prado et al. [26] reported a detailed

Table 2 Analytical methods for the identification and quantification of degradation intermediates of personal care products

Parent compound	Intermediates	Matrix	Extraction and sample preparation	Analytical method	Mass ions (*m/z*)	Confirmation	References
Caffeine	*N*-Dimethylparabanic acid	Aqueous solution	1. Derivatization with $Si(Me)_3Cl$	GC-HRMS	142/114/70/**58**	–	[37]
	Di(*N*-hydroxymethyl) arabanic acid		–	(ESI+)-HRMS/MS	**175**/143		
	N-Dimethylparabanic acid				**143**/128/58		
	14 metabolites (methyl xanthines)	Urine	1. LLE, acetic acid (0.05%, v/v) and methanol (10%, v/v)	LC-(ESI+/-)-MS/MS	–	Authentic standards	[44]
Galaxolide	Galaxolide lactone	Wastewater	1. Unfiltered samples 2. LLE with toluene 3. Frozen to remove water	GC-MS	**272**/257	Authentic standards	[27]
		Sediment	1. Soxhlet extraction with ethyl acetate 2. Silica SPE eluted with ethyl acetate 3.GPC with cyclohexane-ethyl acetate	GC-MS	**272**/257	Authentic standard	[27]
		Biota	1. LLE, 2-propanol/hexane 2. Dried with sodium sulfate 3. GPC 4. Silica gel column	GC-MS	**272**/257	Authentic standards	[32]
Musk ketone	2-Amino musk ketone	Wastewater	1. Unfiltered samples 2. LLE with hexane 3. Frozen to remove water 4. Cleanup step using alumina column	GC-MS	**264**/215/191	Authentic standards	[43]
		Biota	1. Homogenized with sodium sulfate 2. Soxhlet extraction with hexane/acetone (9:1, v/v) 3. GPC 4. Silica gel column	GC-MS	**264**/215/191	Authentic standards	[31]
Musk xylene	4-Amino musk xylene 2-Amino musk xylene	Wastewater	1. Unfiltered samples 2. LLE with hexane 3. Frozen to remove water 4. Cleanup step using alumina column	GC-MS	267/**252**/218	Authentic standards	[43]
		Biota	1. Homogenized with sodium sulfate 2. Soxhlet extraction with hexane /acetone (9:1, v/v) 3. GPC 4. Silica gel column	GPC-GC-MS	267/**252**/218	Authentic standards	[31]
Oxybenzone	2,4-Dihydroxybenzophenone	Biological samples	1. LLE with methanol/acetonitrile (1:2, v/v)	LC-UV	-	Authentic standards	[45]
		Wastewater samples	1. HS-SPME, Carbowax–divinylbenzene fiber 2. 10-min extraction with 25% saturated salt solution	GC-MS	**213**/137/105	Authentic standards	[23]

	2,2'-Dihydroxy-4-methoxybenzophenone	Wastewater	1. SPE (C-18) 2. Elution with methyl chloride	GC-MS	244/227/121	Authentic standards	[23]
	2,3,4-Trihydroxybenzophenone	Biological samples	1. LLE with methanol/acetonitrile (1:2, v/v)	LC-UV	–	Authentic standards	[45]
N,*N*-Diethyl-*m*-toluamide (DEET)	N,N-Dipropyl-m-toluamide N-Ethyl-m-toluamide N,N-Diethyl-m-hydroxymethylbenzamide	Biological samples	1. LLE with methanol/acetonitrile (1:2, v/v)	LC-UV	–	Authentic standards	[45]
	N,N-Diethyl-m-toluamide-N-oxide	Fungal culture	1. LLE with ethyl acetate 2. Evaporated 3. dissolved in methanol	LC-(ESI+)-MS	249/**208**/135	Authentic standards	[46]
	N-Ethyl-*m*-toluamide-*N*-oxide			LC-(ESI+)-MS	221/**180**/135	Authentic standards	[46]
	N-Ethyl-m-toluamide			LC-(ESI+)-MS	205/**164**/119	Authentic standards	[46]
Allethrin, phenothrin, pyrethrum, resmethrin, tetramethrin		Urine	1. Acidic hydrolysis (HCl)				
Cypermethrin, deltamethrin permethrin	*trans*-Chrysanthemumdicarboxylic acid (*trans*-CDCA)		2. LLE with *tert*-butyl methyl ether	GC-(EI+)-HRMS	331.007	Authentic standards	[20]
			3. Evaporated and dissolved with acetonitrile	GC-NCI-HRMS	330.069		
Deltamethrin	*cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid		4. Derivatization with 1,1,1,3,3,3-hexafluoro-2-propanol and *N*,*N*-diisopropylcarbodiimide	GC-(EI+)-HRMS	323.027		
			5. Elimination of derivatization reagent with sodium hydrogencarbonate solution (1 M)	GC-NCI-HRMS	322.020		
Cyfluthrin, cypermethrin, deltamethrin, permethrin	*cis*-3-(2,2-Dibromovinyl)-2,2-dimethylcyclopropane carboxylic acid			GC-(EI+)-HRMS	368.975		
				GC-NCI-HRMS	365.969		
Cyfluthrin	3-Phenoxybenzoic acid			GC-(EI+)-HRMS	364.053		
				GC-NCI-HRMS	213.055		
Allethrin, phenothrin, pyrethrum, resmethrin, tetramethrin	4-Fluoro-3-phenoxybenzoic acid			GC-(EI+)-HRMS	384.044		

Table 2 (continued)

Parent compound	Intermediates	Matrix	Extraction and sample preparation	Analytical method	Mass ions (*m/z*)	Confirmation	References
				GC-NCI-HRMS	231.046		
Bayrepel	Bayrepel acid (1-piperidinecarboxylic acid, 1-methylpropyl ester, 2-acetic acid)	Wastewater	1. Sample filtration and acidification (pH 2)	GC-MS	184/**156**/128	Synthesized standard	[36]
			2. SPE, glass cartridges filled with 0.1 g LiChrolute EN (Merck) and 0.25 g Isolute C_{18}ec (end-capped C_{18}, IST)	LC-(ESI-)-MS	**242**/198/168	Synthesized standard	[36]
			3. Elution with methanol	LC-ESI-ToF-MS	244.20085	Synthesized standard	[36]
			4. Derivatization for GC-MS with diazomethane				
Triclosan	Dichlorohydroxydiphenyl ether	Wastewater (photodegradation)	1. HS-SPME, polydimethylsiloxane fiber	GC-MS	256/**254**/112	NIST library	[26]
			2. 30-min magnetic stirring				
	Monochlorohydroxydiphenyl ether			GC-MS	222/**220**/185	NIST library	[26]
	2,4-Dichlorophenol			GC-MS	164/**162**/63	NIST library	[26]
	Monochlorophenol			GC-MS	130/**128**/65	NIST library	[26]
	2,8-Dichlorodibenzo-*p*-dioxin	Wastewater	1. Filtration	GC-MS	**254**/252/189	Authentic standard	[47]
			2. SPE, Oasis™ HLB (divinylbenzene–*N*-vinylpyrrolidone copolymer)				
			3. Elution with methanol				
			4. Concentrated to dryness and recomposed in ethyl acetatea				
	Methyl triclosan	Biota	1. LLE, cyclohexane/dichloromethane (35:65, v/v) 1. Accelerated solvent extraction, extracted with cyclohexane/dichloromethane (1:1, v/v)	GC-MS	**254**/252/189	Authentic standard	[33]
			2. GPC				
			3. Cleanup on silica minicolumn				
		Wastewater	1. Unfiltered samples	GC-MS	**304**/302/252	Prepared by authors	[35]
			2. LLE with toluene				
			3. Frozen to remove water				
	2,4-Dichlorophenol		1. Unfiltered samples adjusted to pH 4.5	GC-MS	**304**/302	Authentic standard	[22]
			2. HS-SPME, polyacrylate fiber, 30 min	GC-MS	**221**/219/183	Authentic standards	[22]
			3.On-fiber derivatization with *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluoroacetamide				

		1. SPE, SPE, Oasis™ HLB					
	2,3,4-trichlorophenol	2. Elution with ethyl acetate	GC-MS	**255**/253	Authentic standards	[22]	
		3. Derivatization with *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluoroacetamide					
Camphor	5-Hydroxycamphor	Urine/serum	1. LLE, hexane	GC-MS	168/125/**111**	Spectra library MSD 3.1	[48]
	5-Ketocamphor				166/109/**69**		
	9-Hydroxycamphor				153/**108**/107		
	8-Hydroxycamphor				168/108/**95**		
	3-Hydroxycamphor				153/108/**107**		
	8-Camphor carbonic acid trimethylsilylester or 9-camphor carbonic acid trimethylsilylester				254/108/**73**		
	Isoborneole				139/110/**95**		

The base peak is indicated in *bold*.
EI electron impact, *ESI* electrospray ionization, *GC* gas chromatography, *GPC* gel permeation chromatography, *HRMS* high-resolution mass spectrometry, *HS-SPME* headspace solid-phase microextraction, *LC* liquid chromatography, *LLE* liquid–liquid extraction, *MS* mass spectrometry, *MS/MS* tandem mass spectrometry, *NCI* negative chemical ionization, *SPE* solid-phase extraction, *ToF-MS* time-of-flight mass spectrometry

photodegradation pathway of triclosan by photo-SPME and additionally it has been validated by the identification of key intermediates in irradiated wastewater (Table 2). Figure 1 shows the postulated photodegradation pathway for triclosan by using photo-SPME. Therefore, photo-SPME could be a suitable method for identifying new photodegradation intermediates of PCPs. Additionally, similar methods might be used for the identification of biodegradation metabolites.

Sediment and sewage sludge

The determination of degradation intermediates of PCPs in sediment and sewage sludge needs at least a cleanup step owing to the matrix complexity prior to the determination of the target analytes. Extraction of degradation intermediates of PCPs such as methyl triclosan and galaxolide lactone from sediments has already been accomplished by using solid–liquid extraction or leaching techniques. Galaxolide lactone has been extracted from sludge using a Soxhlet apparatus with ethyl acetate, then the extracts were cleaned on silica SPE cartridges and the target analytes were eluted with ethyl acetate. A further cleanup step included gel permeation chromatography (GPC; Bio-Rad SX-3) where metabolites were purified with a cyclohexane/ethyl acetate mixture. Under these chromatographic conditions, analyte enrichment is based on the molecular volume (exclusion) and dispersive interactions (adsorption). The final determination was performed by gas chromatography (GC)–MS in the electron impact mode [27]. On the other hand, methyl triclosan was extracted from river sediments by sequential dispersion extraction with acetone and hexane. Then, the recovered leachates were fractionated by liquid chromatography (LC) by using a semipreparative silica gel column and by increasing the polarity of the binary mixtures from that of pentane to that of dichloromethane and methanol as the mobile phase. Finally, samples were analyzed by GC-MS and a recovery in spiked samples of about 37% was obtained [28]. The low recoveries obtained are attributable to the losses in the solvent evaporation steps owing to the high volatility of the methylated derivative.

Biota

Solvent extraction of biota samples leads to the coextraction of a lipid fraction that needs to be removed before the determination of degradation intermediates of PCPs. In this regard, amino musk xylene and ketone metabolites were extracted from fish and zebra mussel samples with a mixture of water/acetone/petroleum ether [29, 30] or *n*-hexane/acetone (9:1) with a Soxhlet apparatus [31]. Then, the recovered extracts were purified by GPC (SX3

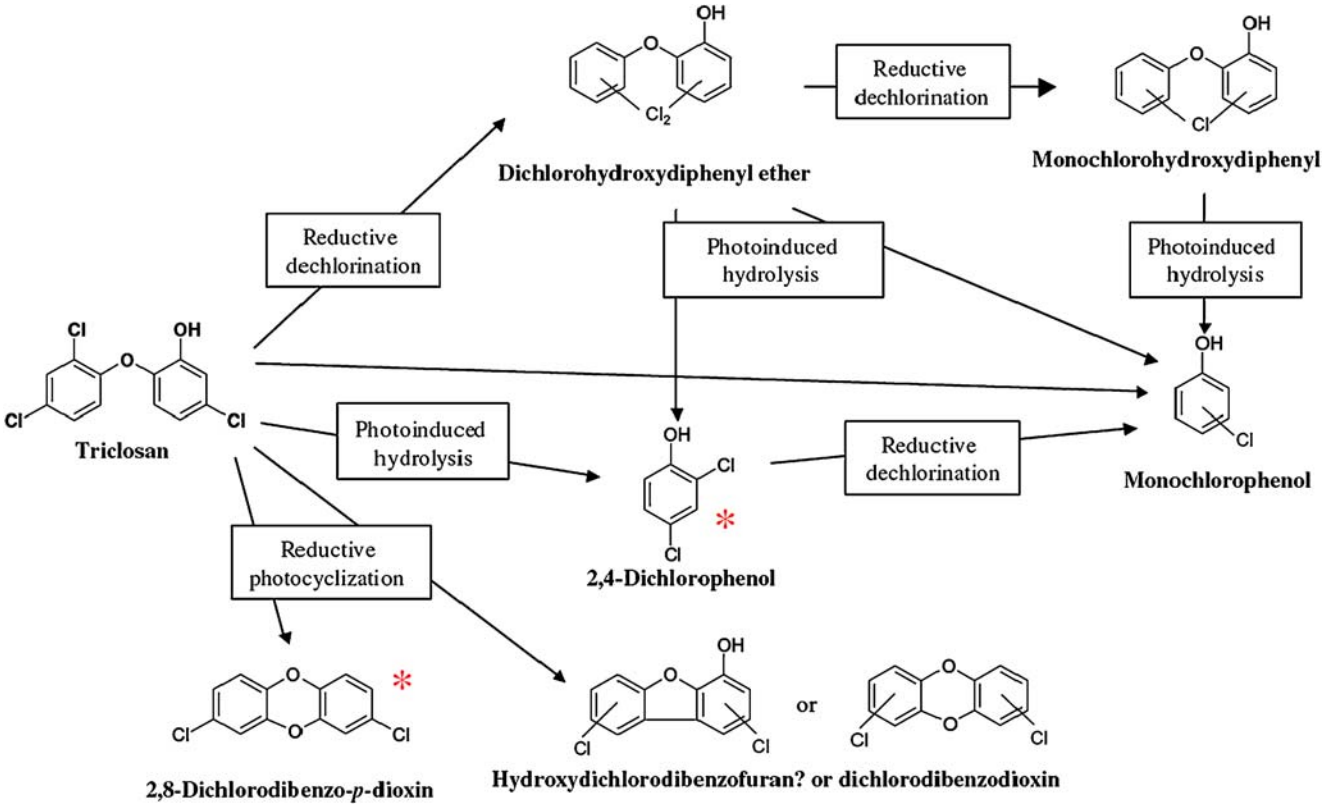


Fig. 1 Postulated photochemical degradation mechanisms of triclosan. *Asterisks* compounds found in aquatic environmental samples. (Reprinted with permission from [26])

Biobeads) to remove fatty components, followed by silica gel adsorption chromatography. Gaterman et al. [31] obtained recoveries of amino xylene and ketone metabolites in spiked biota samples of 66–75% and limits of quantification between 4 and 5 ng L^{-1}. Galaxolide lactone was extracted from fish with 2-propanol and hexane and then the extracts were dried with sodium sulfate and purified by GPC and silica fractionation [32].

Balmer et al. [33] extracted methyl triclosan from fish samples. Dried and homogenized samples were extracted by cyclohexane/dichloromethane, and then the recovered extracts were subjected to GPC (SX3 Biobeads) cleanup to remove lipids. For some samples, an alternative procedure using accelerated solvent extraction was applied: homogenized fish samples were mixed with Hydromatrix and extracted with cyclohexane/dichloromethane (1:1) at room temperature and at a pressure of 1,500 psi, for 9 min (three cycles). Both methods showed acceptable recoveries (46–108%) and limits of detection lower than 1 ng g^{-1}.

Separation and detection

Degradation intermediates have been separated either by LC or by GC depending on their polarity. Chromatographic columns frequently reported are the conventional C-18 and DB-5 (5% diphenyl polydimethylsiloxane) for LC and GC, respectively. Nevertheless, because of the high polarity of degradation intermediates of PCPs, more polar GC columns are needed. In this regard, Leng and Gries [20] used a 65% diphenyl polydimethylsiloxane column for the separation of pyrethroid and pyrethrin metabolites. The polarizable phenyl group allowed increased selectivity for the determination of polar analytes.

However, as degradation products from biological or oxidation processes show, in general, increased polarity, LC is usually the preferred separation technique. Alternatively, degradation intermediates of PCPs can be analyzed by GC prior to a derivatization step usually to block polar functional groups, leading to an increase in volatility and a reduction in polarity. As an example, Bayrepel acid and the acidic metabolites from pyrethrum and pyrethroid were analyzed by GC prior to an esterification step with diazomethane (methyl ester) and hexafluoro-2-propanol (hexafluoro-2-propanol ester), respectively (Table 2). The main advantage of GC versus LC is the large libraries currently available for electron impact ionization mode exceeding 190,000 spectra of 160,000 different chemical compounds, which facilitate the identification of unknowns.

The most predominant detection system is MS, which permits the identification and characterization of degrada-

tion products generated from different degradation mechanisms. MS techniques have increased their importance in elucidating the structure of transformation products [34]. Single-quadrupole MS instruments were initially used for the identification of degradation products in environmental samples as shown for galaxolide lactone or methyl triclosan [27, 35]. Nevertheless, the low concentration of the target analytes in environmental samples required more sensitive and selective spectrometry instruments. Therefore, high-resolution MS (HRMS) or tandem MS (MS/MS) was preferred for the identification of minor degradation intermediates. Leng and Gries [20] proposed a GC-HRMS method which enables for the first time a very sensitive and reliable determination of synthetic pyrethroid metabolites occurring in urine in a single analytical run.

More recently, time-of-flight MS (ToF-MS) permitted an increase in full-scan sensitivity, high mass resolution, and mass accuracy compared with quadrupoles, being specially suited to the identification of new degradation intermediates. In this regard, when fragmentation is weak or absent, high-resolution ToF-MS permitted the identification of the compound from calculation of its molecular formula. Knepper [36] reported the identification of Bayrepel acid, a degradation product of Bayrepel, with a low mass error (0.002–0.64 ppm). Similarly, Dalmazio et al. [37] reported caffeine oxidation intermediates with mass errors from 5 to 38 ppm depending on the compound. Moreover, the fast scanning of ToF-MS allows its coupling with GC×GC, which has a remarkably high chromatographic resolution capability [38], allowing the identification of minor components in complex mixtures [39, 40]. That technique reduces the sample pretreatment steps (e.g., elimination of GPC fractionation step for biota samples), increasing the sample throughput. Figure 2 shows a contour plot of a raw wastewater analyzed using GC×GC-ToF-MS, where degradation products from galaxolide and oxybenzone have been identified (V. Matamoros, E. Jover, and J.M Bayona, unpublished results). According to authors' findings, whereas parent compounds (galaxolide and oxybenzone) are able to be identified by using a one-dimensional GC system, their degradation products cannot be detected because they occur at lower concentrations and are often coeluted with other matrix components. In this case, high-resolution systems, such as GC×GC-ToF-MS, are particularly useful.

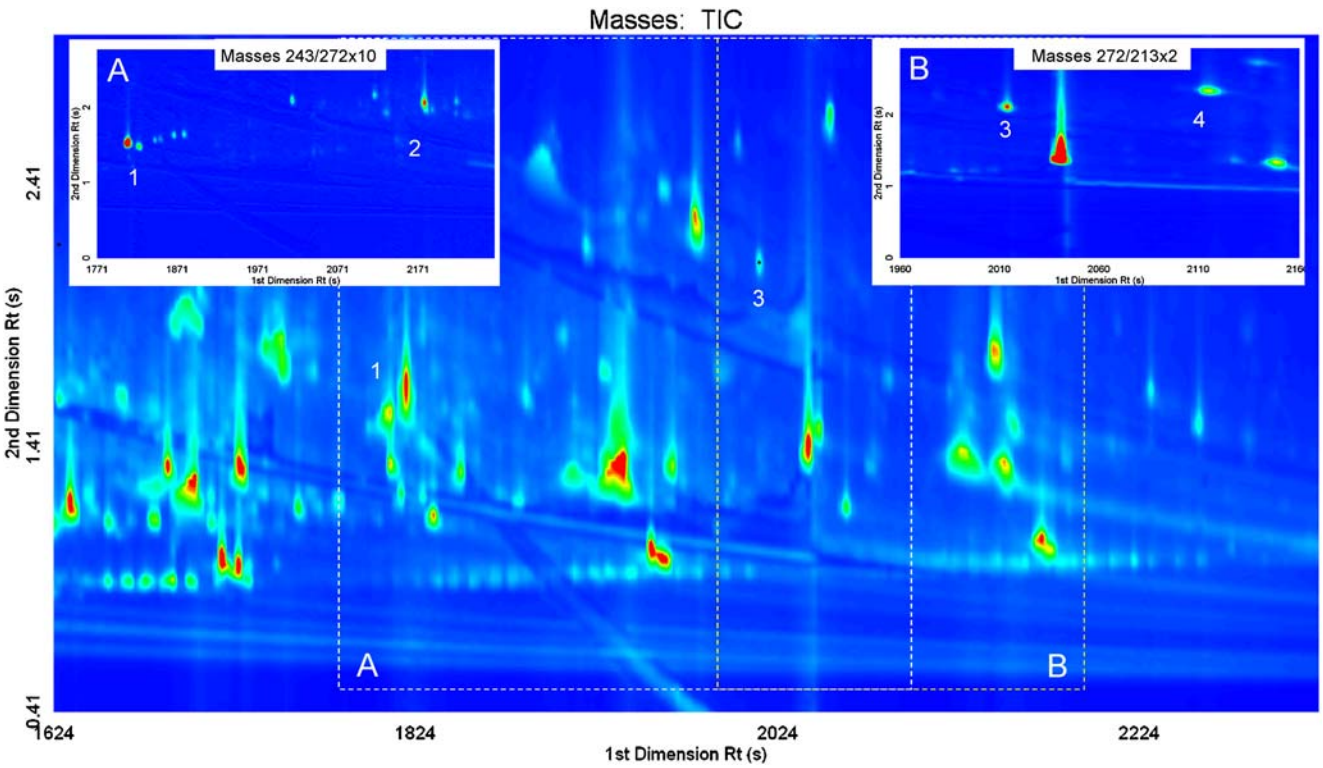


Fig. 2 Contour plot of a raw wastewater sample by using comprehensive two-dimensional gas chromatography time-of-flight mass spectrometry. The first-dimension column was TRB5-MS (30 m× 0.25-mm inner diameter and 0.25-μm film thickness) and the second-dimension column was TRB50-HT (1 m×0.1-mm inner diameter and 0.1-μm film thickness), both from Teknokroma (Sant Cugat del Vallès, Spain). Identification of galaxolide lactone (*2*), a metabolite of galaxolide (*1*), and 2,4-dihydroxybenzophenone (*4*), a metabolite of oxybenzone (*3*) (V. Matamoros, E. Jover, and J.M. Bayona, unpublished results). The library hit similarity index was higher than 900 for identified degradation intermediates of personal care products using NIST Mass Spectral Library version 2.0 (mass ions are shown in Table 2). *TIC* total ion chromatogram, *Rt* retention time

Dalmazio et al. [37] described the identification of oxidation by-products formed during advanced oxidation of caffeine by using continuous on-line and real-time monitoring in electrospray ionization (ESI) MS and ESI-MS/MS experiments allowing the identification of two caffeine by-products [di(*N*-hydroxymethyl)parabanic acid and *N*-dimethylparabanic acid] compared with only one (*N*-dimethylparabanic acid) when working with off-line GC-MS. In this case, the use of LC for the separation of high-polarity compounds such as di(*N*-hydroxymethyl)parabanic acid is recommended.

Nevertheless, classical GC-MS has been extensively used for that purpose, elucidating a variety of intermediate products as described in Table 2. The suitability of LC in particular for the analysis of polar degradation intermediates of PCPs should be pointed out. In addition, the use of MS/MS or ToF-MS rather than single-quadrupole MS is especially relevant when it is coupled with LC owing to the lower chromatographic resolution of this technique and to the often low fragmentation pattern obtained. One of the common drawbacks of ESI-LC-MS in the determination of complex mixtures is ion suppression when complex samples are analyzed, leading to biased quantitative results [41]. In this regard, sample purification or dilution is highly recommended.

Degradation product confirmation

Although some degradation intermediates have been confirmed by authentic standard comparison, usually they are not commercially available and need to be elucidated by using alternative approaches (Table 2). The first approach is related to the chemical synthesis in the laboratory of degradation products of personal care products. Knepper [36] synthesized Bayrepel acid by an oxidation process with $KMnO_4$ from the parent compound. Methyl triclosan was synthesized from triclosan by methylation with trimethylsulfoniumhydroxide solution [35]. Amino musk xylene and ketone metabolites were also chemically synthesized from parent compounds [42, 43]. The second approach is based on the elucidation of solely MS data, leading to a tentative structure. It can be done on the basis of the direct interpretation of the mass fragmentation pattern of molecules or using an already existing spectral library (e.g. NIST library) or on the basis of exact mass measurements obtained from HRMS instruments. In this regard, sample preconcentration and analyte isolation (e.g., GPC, semiprep-LC) and nuclear magnetic resonance are highly recommended for accurate compound identification. Finally, the third approach is based on the use of isotopically labeled reference compounds subjected to degradation experiments from which the resultant labeled degradation intermediates of PCPs can be more easily identified.

Environmental relevance

Table 3 shows the concentration of degradation intermediates of PCPs in different aquatic environments; however, because of the lack of authentic standards, in many cases the calibration in the quantitative analysis is usually

Table 3 Concentration and limit of quantification (*LOQ*) of degradation intermediates of personal care products in different aquatic environments and organisms

Intermediates	Concentration	LOQ	Matrix	References
Galaxolide lactone	231±42 ng g^{-1}	5 ng g^{-1}	WWTP influent	[27]
	367±34 ng g^{-1}		WWTP effluent	
2-Amino musk ketone	ND–250 ng L^{-1}	0.5 ng L^{-1}	WWTP effluent	[30, 43]
	0.04–4.7 ng g^{-1}(WW)	–	Exposed biota	
4-Amino musk xylene	ND–34 ng L^{-1}	0.5 ng L^{-1}	WWTP effluent	
2-Amino musk xylene	2–30 ng g^{-1}(WW)	–	Exposed biota	
	ND–10 ng L^{-1}	0.5 ng L^{-1}	WWTP effluent	
	0.2–1.6 ng g^{-1}(WW)	–	Exposed biota	
Bayrepel acid	0.14–1.5 μg L^{-1}	0.10 μg L^{-1}	WWTP influent	[49]
2,8-Dichlorodibenzo-*p*-dioxin	3.2 μg L^{-1}	–	WWTP influent	[47]
	0.2 μg L^{-1}	–	WWTP effluent	
Methyl triclosan	0.3–5 ng L^{-1}	0.3 ng L^{-1}	River	[35]
	20 ng L^{-1}	0.3 ng L^{-1}	WWTP effluent	
	1–365 ng g^{-1} lipid	1 ng g^{-1} lipid[a]	Biota	[33]
2,4-Dichlorophenol	183±18 ng L^{-1}	4–7 ng L^{-1}	WWTP influent	[22]
2,3,4-Trichlorophenol	ND	2 ng L^{-1}	WWTP influent	

WW wet weight, *WWTP* wastewater treatment plant, *ND* not detected
[a] Limit of detection

performed using the parent compounds, leading to a bias in the concentrations reported. An additional problem in the quantitative analysis of degradation intermediates of PCPs is that their recovery is assumed to be similar to those of the parent compounds, which obviously is not always true. Then, in most of the cases, the reported quantitative data can be considered, in fact, as semiquantitative.

As expected, concentrations were compound- and matrix-dependent, ranging from nanograms per liter to micrograms per liter in water samples, with limits of quantification from 0.3 to 100 ng L^{-1}. Balmer et al. [33] observed a high bioaccumulation factor of methyl triclosan in fish, which is consistent with the lipophilic properties of this compound (log K_{ow}=5.0). Coogan et al. [11] pointed out an increase of methyl triclosan concentration at higher trophic levels. In addition, the galaxolide lactone concentration increases through WWTPs owing to the degradation of galaxolide. Consequently, not only the issue of the reduction of PCP discharge into the aquatic environment should be tackled, but also much work is needed to characterize the behavior of the degradation intermediates. Finally, it is of high importance to follow the formation of degradation intermediates of PCPs in all environmental compartments. Therefore, although hydrophobic PCPs are mostly associated with sediment, their degradation intermediates, in general more polar, are present predominantly in the aquatic compartment.

Conclusions and future research trends

Despite the effort focused on the identification of degradation intermediates of PCPs, there is still a large variety of intermediates that remain unknown.

In summary, degradation intermediates of PCPs can be analyzed in environmental matrixes by the different approaches presented in this review. Different pretreatment methods have been reviewed; such as LLE, SPE, and SPME. Copolymeric phases are particularly effective in SPE; single-component polar absorbent (polyacrylate) or multiple-component bipolar sorbent coating fibers have been selected in SPME owing to the wide polarity range of the analytes. Furthermore, it should be pointed out that the use of LLE is expected to decrease owing to the trend of reducing solvent use in analytical chemistry.

Extraction of degradation intermediates of PCPs from sediment and biota requires an additional purification step to eliminate lipids and interfering matrix constituents. GPC has been selected for that purpose in the majority of methods. Target analytes were analyzed by direct injection into a LC system or into a GC system after a derivatization step for the most polar compounds. Although MS has always been employed for detection, the identification confirmation has been accomplished by using authentic standards that are not always commercially available.

Additionally, the use of higher-resolution LC analytical columns such as in UltraPerformance LC will improve the identification and quantification of polar degradation intermediates of PCPs in environmental samples, reducing more easily the matrix interferences.

Moreover, further research is needed to establish the chemical stability of the parent compounds during the sample handling and extraction steps since some of the degradation intermediates could also be produced as artifacts during the extraction steps. That could be of high relevance in solid samples where additional sources of energy are used. In this regard, isotopically labeled surrogates could be used to follow the possible degradation pathways during the extraction by spiking them into the sample and in this way confirm that the origin is not associated with an extraction artifact. Nevertheless, some artifacts could not be taken into account by this approach because they might have originated from other compounds or might even have formed when samples were transported to the laboratory. Therefore, because the reported methods summarized in this review include both parental PCPs and their degradation intermediates, these new identified compounds could be easily implemented in current monitoring programs. Nonetheless, a lot of work is still required in the study of degradation pathways of the single PCP compounds to assign the stability of their degradation intermediates (less stable intermediates would be only relevant when they are toxic and formed in large amounts).

Acknowledgements This work was funded by the Spanish Ministry of Science and Education through the CONTWET (CTM2005–06457-CO5–04/TECNO) project. E.J. kindly acknowledges a postdoctoral Juan de la Cierva contract from the Spanish Ministry of Science and Innovation.

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