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REVIEW PAPER

Biodegradation and removal of pharmaceuticals and personal care products in treatment systems: a review

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Abstract Pharmaceuticals and personal care products (PPCPs) have been the focus of much recent research as concerns rise about their occurrence in bodies of water worldwide. In an effort to characterize the risk and determine the prevalence of these micropollutants in lakes and rivers, many researchers are examining PPCP removal from impaired water during wastewater treatment and water recycling (soil passage) processes. Biodegradation studies and projects considering combinations of biodegradation and other removal processes have been conducted over a wide range of compound categories and therapeutic classes, as well as across different systems and scales of study. This review summarizes the extent of PPCP removal observed in these various systems.

Keywords Biodegradation · Personal care products · Pharmaceuticals · Wastewater treatment

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Abbreviations

HRT	Hydraulic retention time
MBR	Membrane bioreactor
NSAID	Non-steroidal anti-inflammatory drug
PPCP	Pharmaceutical and personal care product
SBR	Sequencing batch reactor
SRT	Solids retention time
WWTP	Wastewater treatment plant

Introduction

Pharmaceuticals and personal care products (PPCPs) have become the center of much current environmental research. These "emerging contaminants" have been known to be present in the environment for decades, from sources such as wastewater treatment plant (WWTP) effluent and confined animal feeding operation run-off (Daughton and Ternes 1999). Yet it has only been within the past 10–15 years that analytical methods have been developed to detect emerging contaminants at environmentally-relevant trace concentrations (Ternes and Joss 2006). The increased analytical sensitivity has allowed PPCP occurrence studies to be undertaken (Kolpin et al. 2002; Tixier et al. 2003; Ashton et al. 2004). Scientific and public awareness were raised when PPCPs were found in the environment by these projects, such as one study that showed that organic wastewater contaminants, including PPCPs, were present in 80% of 139 U.S. streams (Kolpin et al. 2002).

Because the effects of these compounds on human health and the environment have not been fully characterized, the presence of PPCPs in the environment is cause for concern. Though PPCPs are present usually only at trace concentrations in the environment, questions are raised regarding chemical persistence, microbial resistance, and synergistic effects of the numerous PPCPs present (Daughton and Ternes 1999). Researchers examining the toxicological implications of PPCPs in the environment have found that these low concentrations can elicit adverse effects on aquatic life (Choong et al. 2006; Crane et al. 2006). These findings have engendered public concerns as to the possible effects the compounds may exert on both human health and waterway ecology (Ankley et al. 2007).

Since it is known that PPCPs are present in the environment and could be causing adverse ecological and health impacts, ways to remove these micropollutants from water are being examined. Researchers have examined PPCP removal by biodegradation in many different systems, including WWTPs, membrane bioreactors (MBRs), sequencing batch reactors (SBRs), sand columns, and constructed wetlands. Some of these studies focus solely on biodegradation as a removal process, whereas others examine overall removal due to a combination of processes, including biodegradation. These experiments have been carried out at varying scales, ranging from lab scale bench experiments to full scale field studies. The results of these research projects have been compiled in this article to provide the reader with the current knowledge regarding the range of removal efficiencies possible for PPCP removal processes.

Mechanics of this literature review

The literature was searched for journal articles pertaining to PPCP biodegradation. The information from those articles was organized into two tabular summaries (Tables 1, 2). Table 1 focuses on studies in which the removal mechanism for the PPCP was identified as biodegradation. Most of the studies included in Table 1 were batch experiments and other lab scale studies. Table 2 includes projects in which the PPCP removal reported is attributed to biodegradation in combination with other removal mechanisms, such as sorption.

In both tables, the PPCPs are grouped by compound class, and then organized alphabetically within that section. The numbers presented in the second column of the table are removal efficiencies, and the third column describes the system in which the removal was assessed. PPCPs studied in more than one system (e.g., in a full scale WWTP and in a lab scale batch study) have the results of each presented in separate rows within the table. Multiple studies of one PPCP in the same type of system are presented in a single row, with different studies identified by superscripts to the right of the removal efficiency number. Each of these superscript notations corresponds to an entry in Table 3, so that the reported removal may be linked to its corresponding citation and additional experimental details. Any parenthetical numbers or letters appearing in the superscript codes of Tables 1 or 2 correspond to additional information provided with that reference in Table 3. For the details of any study, the reader should refer to the original paper referenced. Only articles that reported removal efficiencies or data that could be used to calculate removal efficiencies were included in this review.

Discussion

The studies of PPCP biodegradation and removal found in the literature have contributed greatly to our knowledge regarding the fate of these compounds in various treatment systems. Generalizing compound behavior in these systems would allow further characterization of the fate and risk associated with PPCPs in the environment, yet this description of trends is impeded by the wide variation in removal efficiencies across therapeutic classes, treatment processes, and even among separate studies for the same individual compounds. As shown in Tables 1 and 2, it can rarely be said that any compound included in this review is always entirely removed or poorly eliminated. In part, these differences in reported removals may stem from the different definitions of removal that researchers are employing when studying the removal of PPCPs. The majority of studies summarized used “removal” to describe the elimination of parent PPCP compounds and did not consider the extent of biodegradation. The mere disappearance of the parent compound cannot be

Table 1 PPCP removal efficiencies specifically attributed to biodegradation

Compound	Removal efficiency (%)	System studied
Analgesic		
Acetaminophen	$>99^{cg}$	Batch
Antibiotic		
Azithromycin	$0.4^{x(1)}$, $0.5^{x(2)}$	Batch
Benzylpenicillin	$\sim 25^{aj}$	WWTP, lab scale
Ceftriaxone	$<1^{aj}$	WWTP, lab scale
Roxithromycin	$85 \pm 15^{i(M)}$, $95 \pm 5^{i(T)}$	Anaerobic digester, pilot scale
Sulfamethoxazole	$99 \pm 1^{i(M)}$, $99 \pm 1^{i(T)}$	Anaerobic digester, pilot scale
Tetracycline	ND^{al}	Batch
Trimethoprim	$<1^{aj}$	WWTP, lab scale
	$\sim 70^{b(1)}$, $\sim 25^{b(2)}$	Batch
Anticancer		
5-Fluorouracil	$ND^{ap(1)}$, $2^{ap(2)}$, 50^{cg}	Batch
Cytarabine	$80^{ap(1)}$, $>95^{ap(2)}$	Batch
Exemestane	$19.2^{x(1)}$, $8.6^{x(2)}$	Batch
Gemcitabine	$45^{ap(1)}$, $50^{ap(2)}$	Batch
Ifosfamide	$<3^{aq}$	WWTP, lab scale
	ND^{aq}	Batch
Anticonvulsant		
Carbamazepine	$0^{i(M)}$, $0^{i(T)}$	Anaerobic digester, pilot scale
Gabapentin	90^{cg}	Batch
Phenytoin	50^{cg}	Batch
Valproic acid	$>99^{cg}$	Batch
Antidepressant		
Diazepam	$ND^{bh(1)}$	Batch
	$60 \pm 18^{i(M)}$, $38 \pm 21^{i(T)}$	Anaerobic digester, pilot scale
Fluoxetine	ND^{as}, $ND^{bh(1)}$, $ND^{bh(2)}$	Batch
Antiseptic		
4-Chloro-m-cresol	$>99^{cg}$	Batch
Biosol	80^{cg}	Batch
Biphenylol	$>99^{cg}$	Batch
Chlorophene	$>99^{cg}$	Batch
p-Chloro-m-xylenol	80^{cg}	Batch
Triclocarban	$97 \pm 1^{af(1)}$, $21 \pm 30^{af(2)}$	WWTP, full scale
	$41^{cf(1c)}$, $ND^{cf(2)}$	Soil batch
Triclosan	$95 \pm 2^{bn(1)}$, $98 \pm 2^{bn(2)}$, $93 \pm 4^{bn(3)}$	Continuous flow aerobic reactors, lab scale
	$>99^{cg}$, 74^{bn}	Batch
	$38^{cf(1a)}$, $83^{cf(1b)}$, $92^{cf(1c)}$, $ND^{cf(2)}$	Soil batch
Barbituate		
Phenobarbital	80^{cg}	Batch
Secobarbital	70^{cg}	Batch
Calcium channel antagonist		
Verapamil	$ND^{bx(1)}$, $100^{bx(2)}$	Batch

Table 1 continued

Compound	Removal efficiency (%)	System studied
Fragrance ingredient		
Galaxolide	$65 \pm 15^{i(M)}$, $67 \pm 16^{i(T)}$	Anaerobic digester, pilot scale
Tonalide	$60 \pm 8^{i(M)}$, $67 \pm 15^{i(T)}$	Anaerobic digester, pilot scale
H_2 blocker (anti-ulcer)		
Ranitidine	$22.4^{n(1)}$, $<0^{n(2)}$	Batch
Hormone (synthetic)		
17α-Ethinylestradiol (EE2)	$<1^{q}$	MBR, lab scale
	$85 \pm 5^{i(M)}$, $75 \pm 15^{i(T)}$	Anaerobic digester, pilot scale
	$\sim 100^{by}$, 20.2 ± 11^{at}	Batch
Lipid regulator and statin		
Bezafibrate	$ND^{bf(1)}$, $100^{bf(2)}$	Batch
Clofibric acid	$26–30^{ci(2)}$	Lab columns
Gemfibrozil	$>99^{cg}$	Batch
Non-steroidal anti-inflammatory drug (NSAID)		
Diclofenac	$60 \pm 18^{i(M)}$, $73 \pm 9^{i(T)}$	Anaerobic digester, pilot scale
	ND^{aa}, $93–94^{ab}$, $1–4^{ci(1)}$, $34–38^{ci(2)}$	Lab columns
	$ND^{bf(1)}$, $ND^{bf(2)}$, 30^{cg}	Batch
Ibuprofen	$40 \pm 15^{i(M)}$, $47 \pm 10^{i(T)}$	Anaerobic digester, pilot scale
	$64–70^{ci(1)}$, $17–21^{ci(2)}$	Lab columns
	$97– >99^{h}$, $ND^{bf(1)}$, $100^{bf(2)}$, $>99^{cg}$	Batch
Ketoprofen	$ND^{bf(2)}$, $>99^{cg}$	Batch
Naproxen	$87 \pm 5^{i(M)}$, $91 \pm 5^{i(T)}$	Anaerobic digester, pilot scale
	$ND^{bf(1)}$, $60^{bf(2)}$, 80^{cg}	Batch
Smoking deterrant		
Cotinine	$100^{e(O)}$	Batch
Varenicline	$0.3^{x(1)}$, $0.45^{x(2)}$	Batch
Stimulant		
Caffeine	$>95^{e(O)}$, $68 \pm 10 – 100^{e(A)}$, $100^{e(1)}$, $3 \pm 2^{e(2)}$, $ND^{e(3)}$	Batch
Surfactant component		
Disodium cocamphodiacetate	$\sim 100^{bj(1)}$, $\sim 100^{bj(2)}$	Batch
Surfactant metabolite		
Nonylphenol	42^{p}	MBR, lab scale
X-ray contrast media		
Diatrizoate	ND^{ad}	WWTP, lab scale
	$\sim 100^{ad}$, $ND^{ak(2)}$, $ND^{ak(3)}$	Batch
Iopromide	$23 \pm 15^{i(M)}$, $23 \pm 11^{i(T)}$	Anaerobic digester, pilot scale
	$\sim 97^{b(1)}$, $\sim 86^{b(2)}$, $85^{ak(2)}$, $ND^{ak(1)}$	Batch

PPCPs are sorted by compound class and system studied as described in the "Mechanics of this literature review" section. Superscript notation is explained in Table 3

ND indicates that no significant degradation was reported

Table 2 PPCP removal efficiencies attributed to biodegradation in addition to other removal mechanisms

Compound	Removal efficiency (%)	System studied
Analgesic, Antipyretic		
Acetaminophen	99 ± 4^{z}, 91.93^{ah}, 98.4^{bg}, $>99^{cg}$	WWTP, full scale
	$>99^{am(1)}$, $>99^{am(2)}$, 99.6^{bg}	MBR, pilot and lab scale
	98.9^{bm}	Batch
Angiotensin converting enzyme inhibitor		
Enalapril	$18^{o(1)}$, $100^{o(2)}$	WWTP, full scale
Antibiotic		
Amoxycillin	$75^{o(1)}$, $100^{o(2)}$	WWTP, full scale
Ampicillin	$16.4^{ch(1)}$, $42.1^{ch(2)}$	Anaerobic baffled reactor, pilot scale
	$8.9^{ch(1)}$, $9.5^{ch(2)}$	Biofilm airlift suspension reactor, pilot scale
	$67.8^{ch(1)}$, $ND^{ch(2)}$	Batch
Aureomycin	$25.9^{ch(1)}$, $31.3^{ch(2)}$	Anaerobic baffled reactor, pilot scale
	$6.2^{ch(1)}$, $8.7^{ch(2)}$	Biofilm airlift suspension reactor, pilot scale
	$51.5^{ch(1)}$, $ND^{ch(2)}$	Batch
Azithromycin	$-26 \pm 8^{y(1b)}$, $-18 \pm 7^{y(1c)}$, $55 \pm 4^{y(2a)}$, $22 \pm 11^{y(2b)}$, $30 \pm 6^{y(FBRa)}$, $-13 \pm 10^{y(FBRb)}$, $ND^{y(SF1)}$, $ND^{y(SF2)}$	WWTP, full scale
Chloramphenicol	$>93^{be}$, 45^{ce}	WWTP, full scale
Ciprofloxacin	$60^{o(1)}$, $63^{o(2)}$, $84^{cb(all)}$, $86^{cb(1)}$, $79^{cb(2)}$, $96^{cb(3)}$	WWTP, full scale
Clarithromycin	$0^{o(1)}$, $0^{o(2)}$, $9 \pm 4^{y(1a)}$, $-45 \pm 7^{y(1b)}$, $-7 \pm 5^{y(1c)}$, $4 \pm 7^{y(2a)}$, $20 \pm 6^{y(2b)}$, $5.6 \pm 6^{y(FBRa)}$, $14 \pm 6^{y(FBRb)}$, 54^{bs}	WWTP, full scale
	$>88^{bs}$	Subsurface flow
Erythromycin	$0^{o(1)}$, $0^{o(2)}$, $6 \pm 4^{y(1a)}$, $-14 \pm 4^{y(1b)}$, $-22 \pm 4^{y(1c)}$, $-6 \pm 8^{y(2a)}$, $-9 \pm 8^{y(2b)}$, $7 \pm 7^{y(FBRa)}$, $-13 \pm 8^{y(FBRb)}$, 23.8^{bg}, 25^{bs}, 26^{ce}	WWTP, full scale
	$9.1^{am(1)}$, $4.5^{am(2)}$, 67.3^{bg}	MBR, pilot scale
	$>95^{bs}$	Subsurface flow
	78.9^{bm}	Batch
Lincomycin	$0^{o(1)}$, $0^{o(2)}$	WWTP, full scale
	$69.4^{n(1)}$	Batch
Norfloxacin	66^{ce}	WWTP, full scale
Ofloxacin	$43^{o(1)}$, $57^{o(2)}$, $>84^{be}$, 23.8^{bg}, $82^{cb(all)}$, $83^{cb(1)}$, $88^{cb(2)}$, $75^{cb(3)}$, 57^{ce}	WWTP, full scale
	94.0^{bg}	MBR, lab scale
Roxithromycin	$-58^{t(1)}$, $27^{t(2)}$, $-80^{t(3)}$, $18 \pm 4^{y(1a)}$, $38 \pm 3^{y(1b)}$, $-18 \pm 6^{y(1c)}$, $38 \pm 5^{y(2a)}$, $5 \pm 8^{y(2b)}$, $35 \pm 6^{y(FBRa)}$, $4 \pm 8^{y(FBRb)}$, $-8^{ao(4a)}$, $27^{ao(2)}$, $-4^{ao(4b)}$, $58^{ao(1a)}$, $61^{ao(1c)}$, 33^{bs}, 48^{ce}	WWTP, full scale
	$9^{ao(1)}$, $62^{ao(2)}$, $66^{ao(3)}$, $39^{ao(4)}$	WWTP, lab scale
	$>99^{t}$, $75^{ao(1b)}$	MBR, pilot and lab scale
	94 ± 9^{m}	Anaerobic digester, lab scale
	$>95^{bs}$	Subsurface flow
Spiramycin	$0^{o(1)}$, $0^{o(2)}$	WWTP, full scale
Sulfadiazine	$>97^{be}$, 50^{ce}	WWTP, full scale
Sulfadimidine	50^{ce}	WWTP, full scale

Table 2 continued

Compound	Removal efficiency (%)	System studied
Sulfamethoxazole	-250^{c}, 57^{j}, 57^{k}, $50^{l(2)}$, $17^{o(1)}$, $71^{o(2)}$, $66^{t(1)}$, $-280^{t(2)}$, $32^{t(3)}$, $-107 \pm 8^{y(1a)}$, $9 \pm 3^{y(1b)}$, $-79 \pm 7^{y(1c)}$, $-138 \pm 15^{y(2a)}$, $60 \pm 3^{y(2b)}$, $-61 \pm 10^{y(FBRa)}$, $29 \pm 4^{y(FBRb)}$, $ND^{y(SF1)}$, $ND^{y(SF2)}$, $33^{ao(3)}$, $62^{ao(1b)}$, $>98^{be}$, 55.6^{bg}, 24^{bs}, 0–64^{ce}	WWTP, full scale
	$68^{ao(1)}$, $66^{ao(2)}$, $91^{ao(3)}$, $72^{ao(4)}$	WWTP, lab scale
	61^{t}, $64^{am(1)}$, $70^{am(2)}$, $57^{ao(1a)}$, 60.5^{bg}	MBR, pilot and lab scale
	99 ± 1^{m}	Anaerobic digester, lab scale
	$\sim 100^{w}$	SBR, lab scale
	82^{bs}, $95^{ac(1)}$, $53^{ac(2)}$	Subsurface flow
	77.3^{bm}	Batch
Sulfapyridine	$-74 \pm 66^{y(1a)}$, $-16 \pm 45^{y(1b)}$, $-107 \pm 8^{y(1c)}$, $49 \pm 5^{y(2a)}$, $72 \pm 5^{y(2b)}$, $52 \pm 5^{y(FBRa)}$, $41 \pm 9^{y(FBRb)}$, $-28^{y(SF1,SF2)}$	WWTP, full scale
Tetracycline	$86.4 \pm 8.7^{al(1)}$, $85.1 \pm 5.4^{al(2)}$, $78.4 \pm 7.1^{al(3)}$	SBR, lab scale
Trimethoprim	$<1^{b(1)}$, $\sim 50^{b(2)}$, 49^{c}, $3 \pm 5^{y(1a)}$, $-1 \pm 6^{y(1b)}$, $14 \pm 5^{y(1c)}$, $20 \pm 11^{y(2a)}$, $-40 \pm 20^{y(2b)}$, $17 \pm 11^{y(FBRa)}$, $12 \pm 11^{y(FBRb)}$, $15^{y(SF1)}$, $74^{y(SF2)}$, <10–40^{bd}, 69^{bs}	WWTP, full scale
	$-48^{am(1)}$, $-33^{am(2)}$	MBR, pilot scale
	$>92^{bs}$	Subsurface flow
	23.8^{bm}	Batch
Anticancer		
Ifosfamide	ND^{aq}	WWTP, full scale
Anticonvulsant		
Carbamazepine	30^{c}, 7^{d}, $0^{o(1)}$, $0^{o(2)}$, $ND^{r(M,J,D)}$, $<20^{s(1)}$, $<20^{s(2a)}$, 20–$40^{s(2b)}$, $<20^{s(3)}$, $<20^{s(4a)}$, $<20^{s(4b)}$, $<20^{s(4c)}$, $14^{t(1)}$, $-3^{t(2)}$, $-43^{t(3)}$, 20 ± 15^{z}, $0^{ao(4a)}$, $-3^{ao(2)}$, $35^{ao(4b)}$, $14^{ao(1b)}$, $10^{ao(1c)}$, -122–24^{bc}, <10–53^{bd}, $<10^{bg}$, 7^{br}, 0^{bs}, $-121^{cb(all)}$, $-44^{cb(1)}$, $-193^{cb(2)}$, $-32^{cb(3)}$	WWTP, full scale
	$<20^{s(1)}$, $<20^{s(2)}$, $<20^{s(3)}$	WWTP, pilot scale
	$<20^{s(2)}$, $<20^{s(3)}$, $<20^{s(4)}$, $-9^{ao(1)}$, $6^{ao(2)}$, $-11^{ao(3)}$, $1^{ao(4)}$, $<10^{bp}$	WWTP, lab scale
	13^{d}, 12^{t}, $-9.5^{am(1)}$, $-4.8^{am(2)}$, $ND^{r(M,J,D)}$, $11^{ao(1a)}$, $-8^{ao(1b)}$, $9^{ao(1c)}$, $<10^{bg}$	MBR, pilot and lab scale
	0^{m}	Anaerobic digester, lab scale
	$<20^{s}$	SBR, lab scale
	$30 \pm 10^{ay(1)}$, $47 \pm 6^{ay(2)}$	Constructed wetland
	$<-4450^{v}$, ND^{av}, 73^{bs}	Subsurface flow, field scale
	$5 \pm 4^{ax(1)}$, $5 \pm 5^{ax(2)}$	Subsurface flow, lab scale
	53.5^{bm}	Batch
Gabapentin	$>99^{cg}$	WWTP, full scale
Phenytoin (Dilantin)	44^{cg}	WWTP, full scale
	76.8^{bm}	Batch
Primidone	$<-5^{v}$	Subsurface flow, full scale
Valproic acid	$>99^{cg}$	WWTP, full scale
Antidepressant		
Citalopram	29^{bz}	WWTP, full scale
Fluoxetine	$>70^{bz}$	WWTP, full scale
	98.7^{bm}	Batch

Table 2 continued

Compound	Removal efficiency (%)	System studied
Fluvoxamine	>63[bz]	WWTP, full scale
Paroxetine	90.6[bg], 94[bz]	WWTP, full scale
	89.7[bg]	MBR, lab scale
Sertraline	11[bz]	WWTP, full scale
Antiseptic		
4-Chloro-m-cresol	>99[cg]	WWTP, full scale
Biosol	>99[cg]	WWTP, full scale
Biphenylol	80[cg]	WWTP, full scale
Chlorophene	73[cg]	WWTP, full scale
p-Chloro-m-xylenol	80[cg]	WWTP, full scale
Thymol	98.1–99.8[bc]	WWTP, full scale
Triclosan	58[c], 88 ± 5[z], 48 ± 19[ae], 95.4[bb(1)], 96.2[bb(2)], 58.0[bb(3)], 86.1[bb(4)], 82.5[bb(5)], 58.2–86.2[bc], 55–94[bd], 58–96[bw(1)], 86–97[bw(2)], 95–98[bw(3)], 98.4[cc], 69[cg]	WWTP, full scale
	66[am(1)], 73[am(2)]	MBR, pilot scale
	67.9[cc]	Constructed wetlands, pilot scale
	98.8[bm]	Batch
	38[cf(1a)], 83[cf(1b)], 92[cf(1c)], ND[cf(2)]	Soil batch
Barbituate		
Phenobarbital	>99[cg]	WWTP, full scale
Biocide		
Permethrin	88 ± 9[z], 90[ar]	WWTP, full scale
Bronchodilator		
Salbutamol	0[o(1)], 0[o(2)], 94.60[ah]	WWTP, full scale
Diuretic		
Furosemide	8[o(1)], 54[o(2)]	WWTP, full scale
Hydrochlorothiazide	24[o(1)], 44[o(2)], 76.3[bg]	WWTP, full scale
	66.3[bg]	MBR, lab scale
Flame retardant		
Tris (2-chloroethyl) phosphate	−6.7[am(1)], 0.4[am(2)]	MBR, pilot scale
Tris (2-chloro-isopropyl) phosphate	19[c]	WWTP, full scale
Fragrance ingredient		
Acetyl cedrene	98.5[bk(1)], 95.1 ± 4.4[bk(2)], 97.7[bk(3)], 98.0[bk(4)], 71.3 ± 40.5[bk(5)], 87.7[bk(6)]	WWTP, full scale
Benzyl acetate	99.9[bk(1)], 95.2 ± 7.1[bk(2)], 98.9[bk(3)], 95.5[bk(4)], 86.4 ± 7.4[bk(5)], 98.3[bk(6)]	WWTP, full scale
Benzyl salicylate	99.9[bk(1)], 99.5 ± 0.5[bk(2)], 91.1[bk(3)], 99.7[bk(4)], 94.9 ± 4.6[bk(5)], 98.6[bk(6)]	WWTP, full scale
Galaxolide	−37[c], 85[j], 46.6[l(1)], 76.9[l(2)], ~80[r(M,J,D)], 85[t(1)], 38[t(2)], 36[t(3)], 2[ao(4a)], 27[ao(2)], 56[ao(4b)], 44[ao(3)], 85[t], 85[ao(1a)], 86[ao(1b)], 89[ao(1c)], 78[ar], 99.7[bk(1)], 87.8 ± 7.9[bk(2)], 73.5[bk(3)], 89.6[bk(4)], 78.1 ± 8.7[bk(5)], 80.8[bk(6)], 44[bs]	WWTP, full scale
	~80[r(M,J,D)], 85[t], 85[ao(1a)], 90[ao(1b)], 92[ao(1c)]	MBR, pilot scale

Table 2 continued

Compound	Removal efficiency (%)	System studied
	69 ± 9^{m}	Anaerobic digester, lab scale
	$85 \pm 2^{ay(1)}$, $88 \pm 1^{ay(2)}$	Constructed wetland
	$45 \pm 1^{aw(1a)}$, $50 \pm 7^{aw(1b)}$, $61 \pm 10^{aw(1c)}$, $31 \pm 11^{aw(2a)}$, $44 \pm 6^{aw(2b)}$, $>96^{bs}$	Subsurface flow
g-Methyl ionine	$99.3^{bk(1)}$, $96.5 \pm 4.4^{bk(2)}$, $87.1^{bk(3)}$, $98.7^{bk(4)}$, $87.7 \pm 16.8^{bk(5)}$, $98.4^{bk(6)}$	WWTP, full scale
Hexyl salicylate	$99.7^{bk(1)}$, $99.8 \pm 0.1^{bk(2)}$, $97.3^{bk(3)}$, $99.8^{bk(4)}$, $96.4 \pm 4.0^{bk(5)}$, $99.9^{bk(6)}$	WWTP, full scale
Hexylcinnamaldehyde	$99.9^{bk(1)}$, $99.8 \pm 0.1^{bk(2)}$, $96.3^{bk(3)}$, $99.9^{bk(4)}$, $98.6 \pm 1.7^{bk(5)}$, $99.8^{bk(6)}$	WWTP, full scale
Isobornyl acetate	$99.9^{bk(1)}$, $99.6 \pm 0.4^{bk(2)}$, $99.8^{bk(3)}$, $92.0^{bk(4)}$, $96.8 \pm 2.0^{bk(5)}$, $98.7^{bk(6)}$	WWTP, full scale
Methyl dihydrojasmonate	$99.0^{bk(1)}$, $98.2 \pm 0.8^{bk(2)}$, $82.5^{bk(3)}$, $97.9^{bk(4)}$, $93.1 \pm 3.7^{bk(5)}$, $99.9^{bk(6)}$	WWTP, full scale
	$99 \pm 1^{aw(1a)}$, $99 \pm 1^{aw(1b)}$, $99 \pm 1^{aw(1c)}$, $94 \pm 2^{aw(2a)}$, $61 \pm 8^{aw(2b)}$	Subsurface flow
Methyl salicylate	$99.5^{bk(1)}$, $99.6 \pm 0.3^{bk(2)}$, $98.7^{bk(3)}$, $99.3^{bk(4)}$, $92.0 \pm 5.1^{bk(5)}$, $95.7^{bk(6)}$	WWTP, full scale
Musk ketone	$96.7^{bk(1)}$, $91.0 \pm 5.2^{bk(2)}$, $93.1^{bk(4)}$, $87.8 \pm 4.6^{bk(5)}$, $85.2^{bk(6)}$	WWTP, full scale
Musk xylene	$99.5^{bk(1)}$, $97.8 \pm 1.0^{bk(2)}$, $89.3^{bk(3)}$, $97.3^{bk(4)}$, $87.6 \pm 14.2^{bk(5)}$, $89.1^{bk(6)}$	WWTP, full scale
OTNE	$99.2^{bk(1)}$, $91.7 \pm 10.0^{bk(2)}$, $66.0^{bk(3)}$, $96.6^{bk(4)}$, $80.0 \pm 16.3^{bk(5)}$, $90.7^{bk(6)}$	WWTP, full scale
p-t-bucinal	$98.3^{bk(1)}$, $96.1 \pm 3.5^{bk(2)}$, $85.9^{bk(3)}$, $96.2^{bk(4)}$, $94.8 \pm 2.9^{bk(5)}$, $94.8^{bk(6)}$	WWTP, full scale
Phantolide	$>40^{ar}$	WWTP, full scale
Terpineol	$99.9^{bk(1)}$, $99.9 \pm 0.1^{bk(2)}$, $99.6^{bk(3)}$, $99.9^{bk(4)}$, $95.4 \pm 5.6^{bk(5)}$, $99.9^{bk(6)}$	WWTP, full scale
Tonalide	90^{j}, $72.2^{l(1)}$, $74.0^{l(2)}$, $\sim 80^{r(M,J,D)}$, $87^{t(1)}$, $64^{t(2)}$, $19^{t(3)}$, 71^{ar}, $90^{ao(1a)}$, $87^{ao(1b)}$, $86^{ao(1c)}$, $6^{ao(2)}$, $68^{ao(3)}$, $-2^{ao(4a)}$, $67^{ao(4b)}$, $99.3^{bk(1)}$, $88.8 \pm 6.3^{bk(2)}$, $58.6^{bk(3)}$, $88.9^{bk(4)}$, $81.0 \pm 5.7^{bk(5)}$, $81.7^{bk(6)}$, 70^{bs}	WWTP, full scale
	$\sim 80^{r(M,J,D)}$, 85^{t}, $85^{ao(1a)}$, $92^{ao(1b)}$, $91^{ao(1c)}$	MBR, pilot scale
	63 ± 14^{m}	Anaerobic digester, pilot and lab scale
	$88 \pm 2^{ay(1)}$, $90 \pm 1^{ay(2)}$	Constructed wetland
	$44 \pm 9^{aw(1a)}$, $65 \pm 3^{aw(1b)}$, $64 \pm 4^{aw(1c)}$, $32 \pm 10^{aw(2a)}$, $53 \pm 6^{aw(2b)}$, $>75^{bs}$	Subsurface flow
Traseolide	$>30^{ar}$	WWTP, full scale
H_2 blocker (anti-ulcer)		
Ranitidine	$39^{o(1)}$, $84^{o(2)}$, 42.2^{bg}	WWTP, full scale
	95.0^{bg}	MBR, lab scale
Hemorrheologic agent		
Pentoxifylline	98.6^{bm}	Batch
Hormone (synthetic)		
17α-ethinylestradiol (EE2)	90^{a}, 85 ± 14^{f}, $60–70^{r(M,J)}$, $60^{r(D)}$, $40–60^{s(1)}$, $<20^{s(2a)}$, $<20^{s(2b)}$, $80–100^{s(3)}$, $60–80^{s(4a)}$, $80–100^{s(4b)}$, $60–80^{s(4c)}$, $94 \pm 2^{ai(1a)}$, $\geq 75^{ai(1b)}$, $71 \pm 9^{ai(2a)}$, $69 \pm 9^{ai(2b)}$, $70^{ao(1a)}$, $81^{ao(1b)}$, $69^{ao(1c)}$, $51^{ao(2)}$, $-11^{ao(4a)}$, $70^{ao(4b)}$, 67^{bs}, $ND^{bv(1)}$, $78^{bv(2a)}$, $64^{bv(2b)}$	WWTP, full scale

Table 2 continued

Compound	Removal efficiency (%)	System studied
	80–100[s(1)], 20–40[s(2)], 60–80[s(3)],	WWTP, pilot scale
	60–80[s(2)], 60–80[s(3)], 60–80[s(4)], 59[ao(2)], 58[ao(3)], 37[ao(4)]	WWTP, lab scale
	60–70[r(M,J)], ND[r(D)], 80[ao(1a)], 25[ao(1b)], 66[ao(1c)]	MBR, pilot scale
	86 ± 9[m]	Anaerobic digester, lab scale
	<20[s]	SBR, lab scale
	ND[bu(1)], ND[bu(2)], 78.9[bm]	Batch
Mestranol	80[bu(1)]	Batch
Hypoglycaemic agent		
Glibenclamide	44.5[bg]	WWTP, full scale
	47.3[bg]	MBR, lab scale
Insect repellant ingredient		
Diethyltoluamide (DEET)	19.2–46.2[bc]	WWTP, full scale
	−5.6[am(1)], 0[am(2)]	MBR, pilot scale
Lipid regulator and statin		
Bezafibrate	15[o(1)], 87[o(2)], >95[r(M,J)], 90[r(D)], 20–40[s(1)], <20[s(2a)], 20–40[s(2b)], 40–60[s(3)], 80–100[s(4a)], 80–100[s(4b)], 80–100[s(4c)], >99[t(1)], 37[t(2)], 54[t(3)], 51[ag], 91[ao(1a)], 99[ao(1b)], 99[ao(1c)], 37[ao(2)], 54[ao(3)], −5[ao(4a)], 36[ao(4b)], −11–100[au], 91 ± 4[bf(MBR)], 48.4[bg], 27[bo(1)], 50[bo(2)], 83[br], 97[bs], 94[ca]	WWTP, full scale
	80–100[s(1)], 60–80[s(2)], 80–100[s(3)]	WWTP, pilot scale
	80–100[s(2)], 80–100[s(3)], 80–100[s(4)], −11[ao(1)], 94[ao(2)], 99[ao(3)], 96[ao(4)]	WWTP, lab scale
	>95[r(M,J)], 76[r(D)], 95[t], 94[ao(1a)], 76[ao(1b)], 97[ao(1c)], 95.8[bg]	MBR, pilot and lab scale
	>80[bs]	Subsurface flow
	<20[s]	SBR, lab scale
	88.5[ag(1)], 77.0[ag(2)]	Lab columns
Clofibric acid	26[d], 30[o(1)], <0.36[o(2)], 0[ag], 27.7[bg], 15[bo(1)], 34[bo(2)], ND[bq(2, 3)], 51[br], 52[bs]	WWTP, full scale
	29[an(1,2)], 1–6[ci]	WWTP, pilot scale
	54[d], 71.8[bg]	MBR, lab scale
	ND[cd]	Rotating annular bioreactor
	36 ± 3[ay(1)], 32 ± 8[ay(2)]	Constructed wetland
	ND[az], >79[bs]	Subsurface flow, field scale
	ND[ax(1)], ND[ax(2)]	Subsurface flow, lab scale
	16.7[ag(1)], 48.3[ag(2)], 1–4[ci(1)]	Lab columns
Fenofibric acid	6[bo(1)], 45[bo(2)], 64[br]	WWTP, full scale
	>80[bs]	Subsurface flow
Gemfibrozil	75[c], <10–75[bd], 38.8[bg], 16[bo(1)], 46[bo(2)], 69[br], 68[cg]	WWTP, full scale
	89.6[bg]	MBR, lab scale
	>99[v]	Subsurface flow
	98.9[bm]	Batch
Pravastatin	61.8[bg]	WWTP, full scale
	90.8[bg]	MBR, lab scale
Narcotic analgesic		
Codeine	46 ± 19[z]	WWTP, full scale

Table 2 continued

Compound	Removal efficiency (%)	System studied
Hydrocodone	$\leq -40^{am(1)}$, $\leq -50^{am(2)}$	MBR, pilot scale
	47.0^{bm}	Batch
Non-steroidal anti-inflammatory drug (NSAID)		
Diclofenac	22^{c}, 24^{d}, 40–$60^{r(M,J,D)}$, $<20^{s(1)}$, $<20^{s(2a)}$, 20–$40^{s(2b)}$, $<20^{s(3)}$, 60–$80^{s(4a)}$, 60–$80^{s(4b)}$, 60–$80^{s(4c)}$, $53^{t(1)}$, $7^{t(2)}$, $14^{t(3)}$, 59 ± 17^{z}, 21^{ag}, $52^{ao(1a)}$, $46^{ao(1b)}$, $69^{ao(1c)}$, $7.9^{ao(2)}$, $13^{ao(3)}$, $9^{ao(4b)}$, 9–60^{au}, <10–80^{bd}, $23 \pm 30^{bf(MBR)}$, 50.1^{bg}, $9^{bo(1)}$, $75^{bo(2)}$, $ND^{bq(all)}$, 69^{br}, 33^{bs}, 13^{ca}, 18^{cg}	WWTP, full scale
	$<20^{s(1)}$, 40–$60^{s(2)}$, 40–$60^{s(3)}$, $59.3 \pm 25^{an(1)}$, $49.0 \pm 32^{an(2)}$, 1–6^{ci}	WWTP, pilot scale
	20–$40^{s(2)}$, $<20^{s(3)}$, $<20^{s(4)}$, $0^{ao(1)}$, $36^{ao(2)}$, $13^{ao(3)}$, $3^{ao(4)}$, $<20^{bp}$	WWTP, lab scale
	58^{d}, -7^{t}, 44–85^{aa}, $-150^{am(1)}$, $-120^{am(2)}$, $-8^{ao(1a)}$, $39^{ao(1b)}$, $51^{ao(1c)}$, 87.4^{bg}	MBR, pilot and lab scale
	69 ± 10^{m}	Anaerobic digester, lab scale
	$<20^{s}$	SBR, lab scale
	$96 \pm 1^{ay(1)}$, $73 \pm 7^{ay(2)}$	Constructed wetland
	$>87^{v}$, $45 \pm 17^{aw(1a)}$, $0 \pm 5^{aw(1b)}$, $0 \pm 10^{(1c)}$, $11 \pm 42^{aw(2a)}$, $0 \pm 12^{aw(2b)}$, $>98^{bs}$	Subsurface flow
	$71.0^{ag(1)}$, $64.5^{ag(2)}$	Lab columns
	73.5^{bm}	Batch
Dimethylamino-phenazone	38^{br}	WWTP, full scale
Dipyrone	71 ± 15^{z}	WWTP, full scale
Fenoprofen	91.8–97.5^{bc}	WWTP, full scale
	$>71^{v}$	Subsurface flow
Flunixin	$ND^{ay(1)}$, $64 \pm 3^{ay(2)}$	Constructed wetland
Ibuprofen	96^{c}, 97^{d}, 96–99.9^{h}, 63^{j}, $68.7^{l(1)}$, $69.0^{l(2)}$, $38^{o(1)}$, $93^{o(2)}$, $>95^{r(M,J,D)}$, $<20^{s(1)}$, $<20^{s(2a)}$, 80–$100^{s(2b)}$, 80–$100^{s(3)}$, 80–$100^{s(4a)}$, 80–$100^{s(4b)}$, 80–$100^{s(4c)}$, $>99^{t(1)}$, $-4^{t(2)}$, $98^{t(3)}$, 95 ± 7^{z}, 67^{ag}, 86.03^{ah}, $-1^{ao(4a)}$, $-4^{ao(2)}$, $92^{ao(4b)}$, $98^{ao(3)}$, $99^{ao(1a)}$, $99^{ao(1b)}$, $99^{ao(1c)}$, 78–100^{au}, 96.1–99.2^{bc}, 52–99^{bd}, $97 \pm 4^{bf(MBR)}$, 82.5^{bg}, 65^{bi}, $>95^{bl}$, $22^{bo(1)}$, $75^{bo(2)}$, $79^{bq(1)}$, $53^{bq(2a)}$, $72^{bq(2b)}$, $ND^{bq(2c)}$, $20^{bq(3)}$, 90^{br}, 96^{bs}, $>99^{ca}$, 87^{cg}	WWTP, full scale
	80–$100^{s(1)}$, 80–$100^{s(2)}$, 80–$100^{s(3)}$, $90.8 \pm 13^{an(1)}$, $91.5 \pm 6^{an(2)}$, $\sim 60^{bl(1)}$, 81–$82^{bl(2)}$, 57–60^{ci}	WWTP, pilot scale
	80–$100^{s(2)}$, 80–$100^{s(3)}$, 80–$100^{s(4)}$, $9^{ao(1)}$, $96^{ao(2)}$, $99^{ao(3)}$, $99^{ao(4)}$, 82^{bp}	WWTP, lab scale
	99^{d}, 99^{t}, $>99^{am(1)}$, $98^{am(2)}$, $99^{ao(1a)}$, $97^{ao(1b)}$, $99^{ao(1c)}$, 99.8^{bg}, $>99^{bl}$	MBR, pilot and lab scale
	41 ± 15^{m}	Anaerobic digester
	$<20^{s}$	SBR, lab scale
	$>90^{cd}$	Rotating annular bioreactor
	$96 \pm 2^{ay(1)}$, $95 \pm 1^{ay(2)}$	Constructed wetland
	$>99^{v}$, $80 \pm 2^{aw(1a)}$, $71 \pm 8^{aw(1b)}$, $62 \pm 2^{aw(1c)}$, $52 \pm 1^{aw(2a)}$, $17 \pm 11^{aw(2b)}$, $>80^{bs}$	Subsurface flow, field scale
	$52 \pm 3^{ax(1)}$, $51 \pm 2^{ax(2)}$	Subsurface flow, lab scale

Table 2 continued

Compound	Removal efficiency (%)	System studied
	96.3[ag(1)], 100[ag(2)]	Lab columns
	98.9[bm]	Batch
Indomethacin	23.4[bg], 71[bo(1)], 83[bo(2)], 75[br]	WWTP, full scale
	46.6[bg]	MBR, lab scale
Ketoprofen	65[c], 51–100[au], 51.1–68.4[bc], 62 ± 21[bf(MBR)], 51.5[bg], 48[bo(1)], 69[bo(2)], 52[bq(1)], 43[bq(2a)], 53[bq(2b)], 8[bq(2c)], 8[bq(3)], 92[ca], 77[cg]	WWTP, full scale
	91.1 ± 10[an(1)], 89.6 ± 7[an(2)]	WWTP, pilot scale
	91.9[bg]	MBR, lab scale
	99 ± 1[ay(1)], 97 ± 1[ay(2)]	Constructed wetland
	>77[v], 69 ± 5[aw(1a)], 0 ± 8[aw(1b)], 45 ± 5[aw(1c)], 0 ± 14[aw(2a)], 0 ± 29[aw(2b)]	Subsurface flow
Mefenamic acid	91.54[ah], 29.4[bg], 50[bq(1)], 2[bq(2a)], 49[bq(2b)], 43[bq(2c)], 41[bq(3)]	WWTP, full scale
	74.8[bg]	MBR, lab scale
Naproxen	93[c], 55[j], 56.2[l(2)], 0[ag], 55–98[au], 64.9–82.9[bc], 42–93[bd], 71 ± 18[bf(MBR)], 85.1[bg], 45[bi], 15[bo(1)], 78[bo(2)], 66[br], 95[ca], 88[cg]	WWTP, full scale
	93.6 ± 8[an(1)], 86.6 ± 11[an(2)]	WWTP, pilot scale
	68[bp]	WWTP, lab scale
	36[am(1)], 41[am(2)], 99.3[bg]	MBR, pilot and lab scale
	88 ± 4[m]	Anaerobic digester, lab scale
	92 ± 1[ay(1)], 52 ± 9[ay(2)]	Constructed wetlands
	>99[v], 90 ± 3[aw(1a)], 85 ± 4[aw(1b)], 80 ± 9[aw(1c)], 0 ± 10[aw(2a)], 47 ± 22[aw(2b)]	Subsurface flow
	ND[g], 75.9[ag(1)], 100[ag(2)]	Lab columns
	97.8[bm]	Batch
Phenazone	33[br]	WWTP, full scale
	91[av]	Subsurface flow
Propyphenazone	−282–36[bc], 42.7[bg]	WWTP, full scale
	64.6[bg]	MBR, lab scale
	25[v], 100[av]	Subsurface flow
Salicylate		
Aspirin	99.3–99.6[bc], 81[br]	WWTP, full scale
Scabicide		
Crotamiton	−5–24[bc]	WWTP, full scale
Lindane	>99[az]	Subsurface flow constructed wetlands
Skin care ingredient		
Salicylic acid	98 ± 1[aw(1a)], 92 ± 2[aw(1b)], 97 ± 1[aw(1c)], 97 ± 1[aw(2a)], 77 ± 5[aw(2b)]	Subsurface flow
Stimulant		
Caffeine	94[c], 85 ± 4[z], 99.7[bs]	WWTP, full scale
	>98[am(1)], 99[am(2)]	MBR, pilot scale
	98 ± 1[aw(1a)], 94 ± 1[aw(1b)], 99 ± 1[aw(1c)], 94 ± 1[aw(2a)], 85 ± 2[aw(2b)], >88[bs]	Subsurface flow
	92.2[bm]	Batch

Table 2 continued

Compound	Removal efficiency (%)	System studied
Sunscreen agent		
3-(4-methylbenzyl-idene) camphor	90[ar]	WWTP, full scale
Octyl-methoxy cinnamate	~100[ar]	WWTP, full scale
Octyl-triazone	74[ar]	WWTP, full scale
Oxybenzone	50[am(1)], 41[am(2)]	MBR, pilot scale
	98.9[bm]	Batch
Surfactant component		
Hexadecanoic acid	98[c]	WWTP, full scale
Octadecanoic acid	98[c]	WWTP, full scale
Tranquilizer		
Diazepam	25[ao(1a)], 20[ao(1b)], 23[ao(1c)], 0[ao(2)]	WWTP, full scale
	−5[ao(1)], 7[ao(2)], −5[ao(3)], 2[ao(4)], <10[bp]	WWTP, lab scale
	50 ± 16[m]	Anaerobic digester, lab scale
	82.2[bm]	Batch
Meprobamate	47.6[bm]	Batch
X-ray contrast media		
Adsorbable organic iodine (surrogate)	37[u]	Constructed wetlands
	50[u(1)], ~60[u(2)], 0[u(3)], ~60[ac(1)], ~30[ac(2)]	Subsurface flow
	ND[u(1)], 20[u(2)], 57.3[u(3)]	Lab columns
Amidotrizoic acid	0[ag]	WWTP, full scale
	8.0[ag(1)], 28.0[ag(2)]	Lab columns
Diatrizoate	0[bs], ND[bt]	WWTP, full scale
	−73[bs]	Subsurface flow
Iohexol	0[ag], 89[bs]	WWTP, full scale
	>97[bs]	Subsurface flow
	94.3[ag(1)], 54.5[ag(2)]	Lab columns
Iomeprol	0[ag], 89[bs], ND[bt]	WWTP, full scale
	>97[bs]	Subsurface flow
	87.1[ag(1)], 33.3[ag(2)]	Lab columns
Iopamidol	17[bs], ND[bt]	WWTP, full scale
	>99[bs]	Subsurface flow
Iopromide	ND[b(1)], ~61[b(2)], −41[j], −32[t(2)], −862[t(3)], 0[ag], 83[bs], ND[bt], 25[ao(1a)], 0[ao(2)], −8[ao(4a)], 50[ao(4b)]	WWTP, full scale
	−12[ao(1)], 49[ao(2)], 42[ao(3)], 40[ao(4)]	WWTP, lab scale
	22 ± 11[m]	Anaerobic digester, lab scale
	>97[ac(1)], >97[ac(2)], >99[bs]	Subsurface flow
	100[ag(1)], 48.8[ag(2)]	Lab columns
	33.0[bm]	Batch
Iotalamic acid	0[ag], ND[bt]	WWTP, full scale
	0[ag(1)], 16.7[ag(2)]	Lab columns
Ioxithalamic acid	ND[bt]	WWTP, full scale

Table 2 continued

Compound	Removal efficiency (%)	System studied
β-blocker		
Acebutolol	$47^{cb(all)}$, $60^{cb(1)}$, $38^{cb(2)}$, $50^{cb(3)}$	WWTP, full scale
Atenolol	-433^{c}, $10^{o(1)}$, $55^{o(2)}$, $79 \pm 17^{ba(1)}$, $73 \pm 9^{ba(2)}$, $<10^{bd}$, $<10^{bg}$, 84^{bs}, $58^{cb(all)}$, $63^{cb(1)}$, $37^{cb(2)}$, $77^{cb(3)}$	WWTP, full scale
	65.5^{bg}	MBR, lab scale
	$33.5^{n(1)}$, $36^{n(2)}$	SBR, lab scale
	$>93^{bs}$	Subsurface flow
	$28.7^{n(1)}$, $45.3^{n(2)}$	Batch
Celiprolol	36^{bs}	WWTP, full scale
	$>91^{bs}$	Subsurface flow
Metoprolol	-19^{c}, $31 \pm 11^{ba(1)}$, $29 \pm 5^{ba(2)}$, <10–10^{bd}, $<10^{bg}$, 83^{br}, 65^{bs}, $17^{cb(all)}$, $34^{cb(1)}$, $2^{cb(2)}$, $34^{cb(3)}$	WWTP, full scale
	58.7^{bg}	MBR, lab scale
	$>98^{bs}$	Subsurface flow
Propranolol	32^{c}, $28 \pm 2^{ba(1)}$, $35 \pm 3^{ba(2)}$, 96^{br}, 65^{bs}	WWTP, full scale
	$>86^{bs}$	Subsurface flow
Sotalol	$26 \pm 7^{ba(1)}$, $27 \pm 2^{ba(2)}$, 48^{bs}, $66^{cb(all)}$, $54^{cb(1)}$, $71^{cb(2)}$, $67^{cb(3)}$	WWTP, full scale
	$>98^{bs}$	Subsurface flow

Removal efficiency is not limited to biological mechanisms, but may also include physical and chemical processes such as sorption and volatilization in addition to biotransformation. PPCPs are sorted by compound class and system studied as described in the "Mechanics of this literature review" section. Superscript notation is explained in Table 3

ND indicates that no significant removal was reported

considered synonymous with complete biodegradation. If adequate controls for physical and chemical removal mechanisms are in place, the loss of the parent compound indicates biotransformation of an unknown degree, and not necessarily mineralization. Only monitoring for metabolites or end products of mineralization can provide information about the degree of biotransformation. In order to determine the actual biodegradability of PPCPs, detailed biodegradation studies, such as mineralization experiments and biodegradation pathway studies, are necessary.

In this review, we discuss 4 methods for determining the biotransformation-influenced removal of PPCPs, which are studies focusing on: (1) biotransformation, (2) multiple removal mechanisms, (3) laboratory-based simulations, (4) and computer-based prediction tools.

Biotransformation studies

As shown in Table 1, the literature suggests that the biodegradability of PPCPs often eludes generalizations at the levels of an individual compound or PPCP class. This is, in part, due to only a small number of studies focusing on certain PPCPs and contradictory removals reported in the literature for compounds so that a consensus cannot be reached among many studies. PPCP categories whose underrepresentation in Table 1 prevents meaningful generalizations include anticonvulsants, barbituates, calcium channel antagonists, H_2 blockers, lipid regulators, smoking deterrents, surfactant components, and X-ray contrast agents. Generalizations can also be difficult for well-represented categories due to the disparity of reported removal efficiencies for PPCPs within the class. For instance, antibiotics exhibit biotransformation-based removals ranging from no removal for tetracycline in a batch study (Kim et al. 2005) to $99 \pm 1\%$ for sulfamethoxazole in a pilot scale anaerobic digester (Carballa et al. 2006). Anticancer drugs studied do not exhibit any removal trend either. Ifosfamide was reported to have negligible removal in batch and lab scale WWTP studies (Kümmerer et al. 1997), whereas cytarabine

Table 3 The superscript notations included in Tables 1 and 2 are explained with pertinent experimental details provided

	Reference	System details and abbreviations
a	Andersen et al. (2003)	*WWTP*: 24 h flow proportional, composite samples; system includes denitrification and nitrification tanks
b	Batt et al. (2006)	*WWTP*: 24 h flow proportional, composite samples, $^{(1)}$activated sludge, $^{(2)}$nitrifying activated sludge *Batch*: 96 h incubation, 250 mg l^{-1} of PPCP, $^{(1)}$nitrifying sludge inoculum, $^{(2)}$inhibited nitrifying sludge inoculum
c	Bendz et al. (2005)	*WWTP*: 24 h flow proportional, composite samples
d	Bernhard et al. (2006)	*WWTP*: 24 h time proportional, composite samples *MBR*: Lab scale, operated in parallel to WWTP activated sludge process, 24 h time proportional, composite samples
e	Bradley et al. (2007)	*Batch*: Sediments taken upstream of WWTP served as inocula: $^{(O)}$oxic sediment inoculum, 3 river sediments, incubation time for caffeine was 32 d, for cotinine 72 d; $^{(A)}$anoxic sediment inoculum, 3 river sediments, incubation time for caffeine was 52 d Rivers water oxic inoculum: $^{(1)}$South Platte River $^{(2)}$Fourmile Creek, $^{(3)}$Boulder Creek; incubation time for caffeine was 46 d
f	Baronti et al. (2000)	*WWTP*: 24 h flow proportional, composite samples, 5-month averages of overall removal from six WWTPs
g	Boyd et al. (2005)	*Lab column*: Storm water inoculum, 5 mg l^{-1} naproxen solution, unacclimated reactor of 30.5 ft of tubing
h	Buser et al. (1999)	*WWTP*: 24 h flow proportional samples, influent to biological stage and treated effluent sampled *Batch*: WWTP influent inoculum and activated sludge, incubated for 8 h
i	Carballa et al. (2006)	*Anaerobic digester:* Pilot scale, mesophilic (M) and thermophilic (T) conditions, 4–400 μg l^{-1} PPCP
j	Carballa et al. (2004)	*WWTP*: 24 h composite samples, removals from entire WWTP calculated
k	Carballa et al. (2005)	*WWTP*: 24 h samples, overall removal
l	Carballa et al. (2007a)	*WWTP*: 24 h liquid samples, grab samples for sludge $^{(1)}$degradation in a WWTP calculated from actual concentration measurements in sludge and liquid phases, $^{(2)}$calculated from K_d in combination with liquid phase measurements
m	Carballa et al. (2007b)	*Anaerobic digester*: Lab scale, continuously stirred, 4–400 μg l^{-1} PPCP in influent, average removals from thermophilic and mesophilic digesters
n	Carucci et al. (2006)	*Batch*: Inocula from $^{(1)}$WWTP and $^{(2)}$SBR activated sludge, aerobic, 4 h incubation, 2 mg l^{-1} drugs *SBR*: Lab scale, inoculum from WWTP activated sludge, influent 2 mg l^{-1} drugs, $^{(1)}$aerobic and $^{(2)}$anoxic/aerobic modes
o	Castiglioni et al. (2006)	*WWTP*: 24 h time proportional, composite samples $^{(1)}$winter sampling of four WWTPs, $^{(2)}$summer sampling of three WWTPs
p	Cirja et al. (2006)	*MBR*: Lab scale, ^{14}C-labeled nonylphenol isomer (4-[1-ethyl-1,3-dimethylpentyl]phenol); percent recovered as degradation products reported
q	Cirja et al. (2007)	*MBR*: Lab scale, % mineralization reported, 100 μg l^{-1} PPCP
r	Clara et al. (2004)	*WWTP*: 24 h composite samples *MBR*: Pilot scale, with ultrafiltration membrane, 24 h composite samples $^{(M)}$May, $^{(J)}$July, $^{(D)}$December sampling campaigns for both systems
s	Clara et al. (2005a)	*WWTP*: 24 h composite samples, four separate WWTPs with different SRTs: SRT = $^{(1)}$2 d, $^{(2a)}$0.6 d, $^{(2b)}$19 d, $^{(3)}$48 d, $^{(4a)}$42 d, $^{(4b)}$182 d, $^{(4c)}$550 d; *WWTP*: pilot scale, SRT = $^{(1)}$22 d, $^{(2)}$40 d, $^{(3)}$82 d; *WWTP*: lab scale, SRT = $^{(2)}$10 d, $^{(3)}$34 d, $^{(4)}$68 d; *SBR*: lab scale, SRT = 2 d
t	Clara et al. (2005b)	*WWTP*: 24 h composite, time proportional samples; $^{(1)}$WWTP 1 (first sampling reported), $^{(2)}$WWTP 2, $^{(3)}$WWTP 3 *MBR*: Pilot scale, first sampling reported; Removals calculated from mean influent and effluent values

Table 3 continued

	Reference	System details and abbreviations
u	Drewes et al. (2001)	*Constructed wetlands*: Anaerobic, travel time less than 10 d; *Subsurface flow*: Groundwater recharge field studies, water travel times $^{(1)}$6–12 months and $^{(2)}$6–10 years in saturated, anoxic flow; $^{(3)}$aerobic conditions in vadose zone; *Lab columns*: Three columns, $^{(1)}$aerobic (water travel time = 3 d), $^{(2)}$anoxic (16 d), and $^{(3)}$anaerobic (14 d)
v	Drewes et al. (2002)	*Subsurface flow*: Groundwater recharge, 2 h composite secondary effluent samples compared with hydraulically corresponding groundwater samples
w	Drillia et al. (2005)	*SBR*: Lab scale, aerobic, PPCP concentration from 20–320 mg l^{-1}, activated sludge inoculum
x	Ericson (2007)	*Batch*: Water/sediment studies, 100 d incubation, % detected as CO_2, volatiles, and methane; $^{(1)}$aerobic, $^{(2)}$anaerobic
y	Göbel et al. (2007)	*WWTP*: 24 h flow proportional, composite samples, two WWTPs with different temperatures (°C) and SRTs (d): $^{(1a)}$T = 14, SRT = 12, $^{(1b)}$T = 12, SRT = 12, $^{(1c)}$T = 16, SRT = 10, $^{(2a)}$T = 19, SRT = 25, $^{(2b)}$T = 12, SRT = 21; fixed-bed reactor $^{(FBRa)}$T = 19, $^{(FBRb)}$T = 12; sand filters $^{(SF1)}$at WWTP1, $^{(SF2)}$ at WWTP2
z	Gómez et al. (2007)	*WWTP*: 24 h composite samples
aa	González et al. (2006)	*MBR*: Pilot scale, 24 h composite samples of effluent, grab samples of influent *Lab column*: River water inoculum
ab	Gröning et al. (2007)	*Lab column*: River sediment and river water, 3.5–3.7 μM PPCP
ac	Grunheid et al. (2005)	*Subsurface flow*: $^{(1)}$Bank filtration, short aerobic zone, then mostly anoxic and anaerobic, 4–5 month recharge; $^{(2)}$artificial recharge, aerobic, 50 d travel
ad	Haiß and Kümmerer (2006)	*Batch*: Modified Zahn-Wellens test, 30 d incubation, 1.86 g l^{-1} PPCP, sludge inoculum *WWTP*: Lab scale, 0.14–1.44 mg l^{-1} PPCP
ae	Heidler and Halden (2007)	*WWTP*: Hourly and 24 h composite samples, digested sludge composite samples
af	Heidler et al. (2006)	*WWTP*: 24 h composite samples, grab samples of dewatered, digested sludge for mass balance; $^{(1)}$removal from aqueous phase, $^{(2)}$PPCP lost, likely by biotransformation
ag	Hua et al. (2003)	*WWTP*: Sampled every 2 weeks *Lab columns*: Sieved sewage trickled through anoxic columns; $^{(1)}$segmented, 5–25 cm columns, $^{(2)}$125 cm column
ah	Jones et al. (2007)	*WWTP*: Grab samples from every 6 h averaged for daily concentration
ai	Joss et al. (2004)	*WWTP*: 24 h flow proportional, composite samples, two WWTPs; $^{(1a)}$ activated sludge removal at WWTP1, $^{(1b)}$MBR removal at WWTP1, $^{(2a)}$activated sludge removal of WWTP2, $^{(2b)}$fixed bed reactor removal at WWTP2
aj	Junker et al. (2006)	*WWTP*: Lab scale, 28 μg l^{-1} benzylpenicllin, 14 μg l^{-1} ceftriaxone, and 30 μg l^{-1} trimethoprim; percent mineralization presented
ak	Kalsch (1999)	*Batch*: Aerobic primary sludge inoculum, 1.5 nmol l^{-1} diatrizoate or 1.85 nmol l^{-1} iopromide; $^{(1)}$54 h incubation, % mineralized, aerobic, $^{(2)}$54 h incubation, % transformed, $^{(3)}$2 week incubation, % transformed, anaerobic
al	Kim et al. (2005)	*SBR*: Lab scale, 250 μg l^{-1}; 3 operating phases with varying HRT and SRT (d) $^{(1)}$HRT = 24, SRT = 10, $^{(2)}$HRT = 7.4, SRT = 10, $^{(3)}$HRT = 7.4, SRT = 3 *Batch*: 200 μg l^{-1} PPCP, diluted sludge inoculum, ~20 d incubation, aerobic
am	Kim et al. (2007)	*MBR*: Pilot scale, two types of modules; $^{(1)}$plate and frame type module, $^{(2)}$hollow-fiber type module
an	Kosjek et al. (2007)	*WWTP*: Pilot scale, two separate reactors, ± reported standard deviation; $^{(1)}$reactor 1, 0.05 mg l^{-1} PPCPs, $^{(2)}$reactor 2, 0.005 mg l^{-1} PPCPs
ao	Kreuzinger et al. (2004)	24 h composite samples, removal based on mass balance, SRT normalized to 20°C: *WWTP*: 4 lab scale, $^{(1)}$1 d, operated as SBR $^{(2)}$5 d, $^{(3)}$17 d, $^{(4)}$35 d; *MBR*: 1 pilot scale, $^{(1a)}$11 d, $^{(1b)}$20 d, $^{(1c)}$41 d; *WWTP*: 4 full scale, $^{(1a)}$24 d, $^{(1b)}$96, $^{(1c)}$275 d, $^{(2)}$0.7 d, $^{(3)}$23.6 d, $^{(4a)}$0.3 d, $^{(4b)}$9.6 d

Table 3 continued

	Reference	System details and abbreviations
ap	Kümmerer and Al-Ahmad (1997)	*Batch*: Inoculum from WWTP [(1)]closed bottle test, 40 d incubation, 4.5–9.02 mg l^{-1} PPCP; [(2)]Modified Zahn-Wellens test, 175–1,660 mg l^{-1} PPCP
aq	Kümmerer et al. (1997)	*WWTP*: 1–2 h samples; *WWTP*: Lab scale, 11.4 μg l^{-1} drug, 56 d operation; *Batch*: Modified Zahn-Wellens test, 42 d incubation, activated sludge inoculum, 4.3–160 mg l^{-1} PPCP
ar	Kupper et al. (2006)	*WWTP*: 24 h flow proportional, composite samples, removals calculated from mean concentrations from primary and secondary effluents
as	Kwon and Armbrust (2006)	*Batch*: Activated sludge supernatant inoculum, 1 mg l^{-1} PPCP, 28 d incubation
at	Layton et al. (2000)	*Batch*: 72 μg l^{-1} PPCP, 24 h incubation, WWTP biosolids inoculum; % mineralization presented
au	Lindqvist et al. (2005)	*WWTP*: 24 h composite samples, range of removals from 7 WWTPs
av	Massmann et al. (2006)	*Subsurface flow*: Artificial recharge, travel time was from hours to <3 d, representing first few meters of flow
aw	Matamoros and Bayona (2006)	*Subsurface flow*: Horizontal flow pilot constructed wetlands, daily grab samples, 1–25 μg l^{-1} PPCPs; [(1a)] 0.27 m bed depth, May 2004, [(1b)]0.27 m water depth, May 2005, [(1c)]0.27 m water depth, July 2005, [(2a)]0.5 m water depth, May 2004, [(2b)]bed with 0.5 m water depth, May 2005
ax	Matamoros et al. (2008a)	*Subsurface flow*: Lab scale, horizontal subsurface flow constructed wetlands microcosms, 25 μg l^{-1} PPCP; [(1)]glucose added as carbon source, [(2)]starch added as carbon source
ay	Matamoros et al. (2008b)	*Constructed wetlands*: Full scale, surface flow constructed wetland; WWTP secondary effluent was wetland influent, HRT = ~1 month, [(1)]June sampling, [(2)]February sampling
az	Matamoros et al. (2007)	*Subsurface flow*: Horizontal subsurface flow constructed wetlands, 2.5 mg l^{-1} PPCP
ba	Maurer et al. (2007)	*WWTP*: 24 h flow proportional, composite samples over 3 d, [(1)]WWTP 1, [(2)]WWTP 2
bb	McAvoy et al. (2002)	*WWTP*: Overall removal from 5 WWTPs; [(1),(2)]activated sludge, [(3),(4),(5)]trickling filters
bc	Nakada et al. (2006)	*WWTP*: 24 h composite samples of influent and secondary effluent; May 2002 samplings of 4 WWTPs; ranges across plants presented
bd	Paxéus (2004)	*WWTP*: Average flow proportional samples from 5 WWTPs and grab samples from 1 WWTP, range of means across WWTPs presented
be	Peng et al. (2006)	*WWTP*: Grab samples from 2 WWTPs; removals during activated sludge treatment calculated, combined values for both WWTPs presented
bf	Quintana et al. (2005)	*WWTP*: 24 h composite samples from WWTP MBR, mean removals reported; *Batch*: sludge inoculum, mean removals by transformation reported, 28 d incubation; [(1)]20 mg l^{-1} PPCP as sole carbon source, [(2)]5 mg l^{-1} PPCP and 50 mg l^{-1} milk
bg	Radjenovic et al. (2007)	*WWTP*: 24 h time proportional composite samples, mean removals presented; *MBR*: Lab scale, installed at WWTP, mean removals presented
bh	Redshaw et al. (2008)	*Batch*: [(1)]liquid culture, 60 d incubation, agricultural biosolid-amended soil inoculum, ~192 mg l^{-1} PPCP; [(2)]soil culture, >200 d incubation, 1.5 μg PPCP spiked into 15 g soil
bi	Rodríguez et al. (2003)	*WWTP*: 24 h composite samples
bj	Sharvelle et al. (2008)	*Batch*: Acclimated activated sludge inoculum, 93 h incubation, aerobic, 216 mg l^{-1} PPCP in [(1)]mineral salts medium, [(2)]tryptic soy broth
bk	Simonich et al. (2002)	*WWTP*: Composite samples of entire sampling period, averages for 17 WWTPs; [(1)]lagoon, [(2)]primary treatment and activated sludge, [(3)]primary treatment and carousel, [(4)]oxidation ditch, [(5)]primary treatment and trickling filter, [(6)]primary treatment and rotating biological contactor
bl	Smook et al. (2008)	*WWTP*: Aeration tank, time-proportional grab samples *WWTP*: Pilot scale, grab samples, [(1)]anaerobic tank, [(2)]aerobic tank *MBR*: Pilot scale, time-proportional grab samples

Table 3 continued

	Reference	System details and abbreviations
bm	Snyder et al. (2004)	*Batch*: 10–100 ng l^{-1} PPCP, river water with biologically active sand, 5 d incubation
bn	Stasinakis et al. (2007)	*Batch*: Aerobic, activated sludge inoculum, 1 mg l^{-1} PPCP, 10 h incubation
		Continuous flow aerobic reactors: [(1)]acclimated sludge, 0.5 mg l^{-1} PPCP, 24 d incubation, [(2)]acclimated sludge, 2 mg l^{-1} PPCP, 48 d incubation, [(3)]unacclimated sludge, 1 mg l^{-1} PPCP, 10 d incubation
bo	Stumpf et al. (1999)	*WWTP*: 24 h composite samples, [(1)]trickling filter, [(2)]activated sludge
bp	Suárez et al. (2005)	*WWTP*: Lab scale, nitrifying-denitrifying plant
bq	Tauxe-Wuersch et al. (2005)	*WWTP*: 3 WWTPs, 24 h flow proportional, composite samples for [(1)]WWTP 1 and [(2)]WWTP 2; samples every 15 min for [(3)]WWTP 3; [(2a)]winter 2003 sample, [(2b)]summer 2003 sample, [(2c)]winter 2004
br	Ternes (1998)	*WWTP*: Flow proportional composite samples taken over 5 periods of 6 d, mean removals reported
bs	Ternes et al. (2007)	*WWTP*: 24 h flow proportional, composite samples; mean removals from 4 samplings reported;
		Subsurface flow: Soil-aquifer passage, WWTP effluent and sludge irrigated onto soil, well water sampled, data calculated from Well 1 presented, 12–15 m well depth
bt	Ternes and Hirsch (2000)	*WWTP*: Flow propotional composite influent and effluent samples
bu	Ternes et al. (1999a)	*Batch*: Aerobic, activated sludge inoculum; [(1)]1 μg ml^{-1}, incubation is 48 h for EE2, 24 h for mestranol, [(2)]1 ng ml^{-1} EE2, 24 h
bv	Ternes et al. (1999b)	*WWTP*: Composite influent and effluent samples; [(1)]German WWTP, [(2a)]Brazilian WWTP aerator tank, [(2b)]Brazilian WWTP biological filter
bw	Thompson et al. (2005)	*WWTPs*: Grab samples from 3 WWTPs with three different biological processes, [(1)]rotating biological contactors, [(2)]trickling filters, [(3)]activated sludge
bx	Trautwein et al. (2008)	*Batch*: [(1)]Zahn-Wellens test, sludge inoculum, 76.75 mg l^{-1} PPCP, 30 d incubation, [(2)]Closed Bottle test, 28 d incubation, 2.33 mg l^{-1} PPCP, WWTP effluent inoculum
by	Vader et al. (2000)	*Batch*: Nitrifying activated sludge inoculum, 6 d incubation, 50 μg l^{-1} PPCP
bz	Vasskog et al. (2006)	*WWTP*: 24 h flow proportional influent and effluent samples
ca	Vieno et al. (2005)	*WWTP*: 24 h composite samples, removals calculated from means with all samples considered
cb	Vieno et al. (2007)	*WWTP*: 24 h composite samples from 12 WWTPs; mean removals presented, 12 WWTPs[(all)] sorted by process: [(1)]activated sludge process, [(2)]denitrifying processes, [(3)]ditch oxidation processes
cc	Waltman et al. (2006)	*WWTP*: 24 h cycle of 8 h composite grab samples from influent and effluent
		Constructed wetlands: Pilot scale, same sampling as for WWTP
cd	Winkler et al. (2001)	*Rotating annular bioreactors*: Lab scale, river water inoculum, 10–100 μg l^{-1} PPCP
ce	Xu et al. (2007)	*WWTP*: Average overall removals for 4 WWTPs, 2 WWTPs sampled as time proportional grab samples, 2 WWTPs sampled as 24 h composites
cf	Ying et al. (2007)	*Batch*: Agricultural soil, 1 mg kg^{-1} PPCP, [(1a)]aerobic, 7 d incubation, [(1b)]aerobic, 28 d incubation, [(1c)]aerobic, 70 d incubation, [(2)]anaerobic, 70 d incubation
cg	Yu et al. (2006)	*WWTP*: 24 h composite influent and effluent samples
		Batch: Activated sludge inoculum, 50 d incubation, 1, 10, and 50 μg l^{-1} PPCP
ch	Zhou et al. (2006)	*Anaerobic baffled reactor*: pilot scale, 1.0–3.2 mg l^{-1} PPCP, HRT of [(1)]1.25 d and [(2)]2.50 d;
		Biofilm airlift suspension reactor: Pilot scale, 1.0–3.2 mg l^{-1} PPCP, followed anaerobic baffled reactor treatment, HRT = 12.5 d, previous anaerobic treatment time = [(1)]1.25 d and [(2)]2.5 d;
		Batch: 3.5–4.6 mg l^{-1} PPCP, inoculum from ditch near sewer, [(1)]anaerobic, 8 d incubation and [(2)]aerobic, 10 h incubation
ci	Zwiener and Frimmel (2003)	*WWTP*: Pilot scale, activated sludge inoculum, 10 μg l^{-1} PPCP + 30 mg l^{-1} acetone;
		Lab column: Activated sludge inoculum, 10 μg l^{-1} + 35 mg l^{-1} acetone, [(1)]oxic, [(2)]anoxic

had 80% and greater than 95% removal for two batch conditions (Kümmerer and Al-Ahmad 1997). In the non-steroidal anti-inflammatory (NSAID) therapeutic class, diclofenac showed no greater than 30% removal while ibuprofen and ketoprofen both showed greater than 99% removal in the same batch study (Yu et al. 2006).

These widely varying removals within a therapeutic class suggest that accurately predicting biodegradability based on a PPCP's intended function may not be possible. This is not surprising as compounds within the same PPCP class can have vastly different chemical structures. For example, anticonvulsant drugs have chemical structures as diverse as branched chain carboxylic acids and complex azepines. Kümmerer and Al-Ahmad (1997) considered that inherent differences in biodegradability are due to chemical structures, pointing out that the presence of sugar moieties on the compounds or fluorination could make parent compounds more or less biodegradable, respectively. Since biodegradation involves enzymatic reactions specific to chemical structures, the biodegradability of PPCPs with different structures grouped in the same therapeutic class is expected to vary, thwarting efforts to observe general trends. In spite of these difficulties, there is a noteworthy exception in the antiseptic category. Antiseptic removals of greater than 70% in the majority of studies found in Table 1 are surprising due to the compounds' intended function of harming bacteria.

Describing biotransformation trends even just at the compound level is further complicated by vastly different reported removals for a single PPCP. One of the potential explanations for the diversity of reported values is that removal can denote different degrees of biodegradation in two separate studies. This complication is demonstrated by the X-ray contrast agent iopromide. A batch biodegradation study was monitored for both loss and mineralization of the parent compound. Biotransformation of 85% of the iopromide was observed, whereas no mineralization was detected (Kalsch 1999).

Reasons other than monitoring endpoint differences for discrepancies in removals of specific compounds include differences in initial PPCP concentrations, primary substrate concentrations, incubation times, and microbial inoculum sources. Initial concentrations of PPCPs in these biotransformation studies can vary greatly from one study to another. For example, a biodegradation study with an initial concentration of more than 800 mg l^{-1} of anticancer drug 5-fluorouracil yielded a removal of 2% (Kümmerer and Al-Ahmad 1997), whereas a study starting with 50 μg l^{-1} or less of 5-fluorouracil reported a removal of 50% (Yu et al. 2006). Commonly used Organization for Economic Co-operation and Development (OECD) test guidelines tend to require a high substrate concentration, while other environmental experiments maintain a more oligotrophic level of usable substrates. These differences in experimental design may dictate how the microorganisms are transforming the PPCPs. Studies using PPCPs in high concentrations are supplying the compound as the carbon and energy source for microbes. Even when an alternative primary substrate is added in low concentrations, PPCPs could potentially serve as primary substrates for microorganisms. Studies providing trace PPCP concentrations along with higher concentrations of non-PPCP substrates enable observation of how microbes use these compounds through cometabolism. With lack of data suggesting otherwise, the current assumption is that at low environmentally relevant concentrations of PPCPs, these micropollutants are degraded by microbial enzymes through cometabolism (Ternes and Joss 2006). The difference in the utilization of PPCPs as either a primary substrate or as a secondary substrate degraded through cometabolism likely contributes to the removal discrepancies observed between different biodegradation studies. Another concern regarding differences in concentrations is that increased PPCP levels could inhibit biotransformation, perhaps through toxicity to the microorganisms.

In addition to PPCP concentrations, the incubation period of laboratory studies is also a potential reason for removal differences. These times can be arbitrary, and therefore the biotransformation results may be experiment specific. In fact, the incubation time varied widely in different studies shown in Table 1, ranging from 4 h (Carucci et al. 2006) to 100 d (Ericson 2007). A batch study examining the fate of triclosan over time in soil showed biotransformation-based removal increasing from 38%, to 83%, to 92% as the incubation time increased from 7 d, to 28 d, to 70 d under aerobic conditions (Ying et al. 2007).

Biotransformation results could also depend on the source and concentration of the inoculum. Prior

exposure and adaptation of the microorganisms to the PPCPs of interest could also affect removal efficiencies and lag times. Wastewaters from residential, industrial, and medical sources will have vastly different compositions, as will different environmental sources of inocula. For example, when studying the biodegradation of the smoking deterrent cotinine, three different river waters were used as the inocula for batch studies. It was found that cotinine was not removed with the first river's water, yet was removed approximately 100% by the second river's water and 24% by the third river's water (Bradley et al. 2007). Batt et al. (2006) also demonstrated this phenomenon when they found that the antibiotic trimethoprim was biotransformed about 70% by conventional activated sludge inoculum, but only about 25% by a nitrifying sludge inoculum.

Overall, these biodegradation and biotransformation studies provide a good first step in understanding the potential for biodegradation in the environment, but one must proceed with caution in extrapolating these results to understand the biodegradability of these compounds outside of the laboratory, in natural or engineered systems. The results shown in Table 1 provide a good overview of the potential biotransformation of the studied PPCPs, but the results may not be directly applicable to understanding PPCP fate in full scale treatment systems or in the environment.

Studies with multiple removal mechanisms

Trends for therapeutic classes are no easier to identify with biotransformation occurring in conjunction with other removal mechanisms than they are with biotransformation as the sole removal mechanism. Vastly different removals were found within classes and for individual compounds, as shown in Table 2. Differences at the field scale level can be seen from inspection of the entries for the antibiotic therapeutic class. Within the class, lincomycin and spiramycin showed no removal from WWTPs (Castiglioni et al. 2006), whereas sulfadiazine was shown to have greater than 97% removal from a WWTP (Peng et al. 2006). In addition to such wide variation of removal efficiencies within a class, individual compounds showed great disparity in eliminations as well. The removal efficiency for the antibiotic sulfamethoxazole during wastewater treatment in full scale plants ranged from no removal (Bendz et al. 2005) to greater than 98% removal (Peng et al. 2006).

There were some individual PPCPs that had remarkably similar removals even in studies of different systems. The analgesic acetaminophen had a removal of greater than 95% as reported in 6 studies examining full scale WWTPs, pilot and lab scale MBRs, and a batch system. Caffeine, a stimulant, exhibited removals greater than 80% in 6 studies that examined full scale WWTP, pilot scale MBR, subsurface flow, and a batch system. Conversely, the anticonvulsant carbamazepine, notorious for its poor elimination, never showed removal levels higher than 30% across 20 studies examining lab and full scale subsurface flow, lab scale SBR, lab scale anaerobic digester, pilot and lab scale MBR, and full, pilot, and lab scale WWTP systems. It should be noted that there were 3 studies that reported slightly higher removals for batch, field scale subsurface flow, and constructed wetlands.

Aside from these three compounds behaving similarly in various systems, many of the other PPCPs do not. Several factors have been considered to explain why removals vary within the same types of systems. In field scale studies, the solids residence time (SRT) and hydraulic residence time (HRT) have been proposed as significant factors affecting PPCP removal. Maurer et al. (2007) found that HRT and reactor design were responsible for the variation they observed in removal efficiencies from one WWTP to another. Even though Göbel et al. (2007) found comparable removals in a fixed bed reactor and an activated sludge process that had vastly different HRTs (<1 h and up to 31 h, respectively), they suggested that this occurred because the lower HRT of the fixed bed reactor was balanced by a higher concentration of microbes. Another study taking HRT into account assessed the effect of dilution of WWTP influent by rain on PPCP elimination. A decrease in removal efficiency of β-blockers was found when the WWTP HRT was decreased to accommodate the increased amount of water that needed to be treated following a rainfall event (Vieno et al. 2007). The SRT has also been proposed as a significant factor in PPCP removal. One study examined the effect of SRT on the removal of 20 PPCPs from full scale treatment systems in the United States. Critical SRT values, or the SRTs necessary for removal efficiencies of 80% or greater, were determined for the compounds. Caffeine and

oxybenzone, two compounds classified as consistently exhibiting excellent removal, had critical SRTs less than 5 d. On the other hand, PPCPs classified as having poor removal, such as galaxolide and tris(2-chloroethyl)phosphate, had critical SRTs greater than 15 d (Oppenheimer et al. 2007). Another study found that in activated sludge systems, trimethoprim and several macrolide antimicrobials showed removals up to 50% when SRTs were 16 ± 2 and 33 ± 3 d, but when the SRT was increased to 60–80 d, up to 90% removal was observed (Göbel et al. 2007).

Another often-cited explanation for variability in same-system studies is operating temperature. Though some researchers found no difference in compound removal based on incubation temperature (Göbel et al. 2007), others did find that temperature was responsible for differences in eliminations (Vieno et al. 2005; Castiglioni et al. 2006). Castiglioni et al. (2006) examined seasonal temperature variations and found that removal rates for total loads of target compounds in the summer were 31%, versus 0% in the winter, even though individual compounds could be classified into three categories of greater removal in summer than in winter, comparable removal in summer and winter, and negligible removal regardless of season. The difference between the winter temperature of 9.7°C and the summer temperature of 18.6°C was considered responsible because of its effect on microbial activity. These findings are in agreement with observations at a WWTP in Finland, in which the pharmaceuticals had winter effluent concentrations that were 3–5 times higher than concentrations found any other time of year (Vieno et al. 2005).

In several studies, the concentrations of PPCPs appear to increase during the treatment process, in which case the values in the table are presented as negative numbers. It is possible that systems operating in arid regions could experience an increase in the concentration of PPCPs during treatment due to water evaporation or that a sampling interval may not accurately reflect the temporal variations in influent and effluent concentrations. It has also been proposed that influent PPCPs can be encased in fecal particles, leading to an apparent increase in concentration during treatment as the fecal particles are degraded (Göbel et al. 2007). Another reason that has been suggested is that PPCPs are entering the WWTP as conjugates and are then cleaved during treatment, leading to an apparent increase in concentration of the PPCP of interest when influent and effluent concentrations are compared (Lindqvist et al. 2005; Ternes 1998). These conjugates are formed during the biotransformations involved in drug metabolism in the body. If the parent compound is not polar enough to be excreted by the body, its functional groups can combine with substrates, such as amino acid, acetic acid, sulfuric acid, or glucuronic acid. The newly formed conjugate is more polar and readily eliminated (Correia 2007). For example, fenofibric acid and clofibric acid are excreted from humans mostly in the form of glucuronides of their metabolites. Throughout the compounds' travel through a water treatment system, the glucuronides may be cleaved, resulting in an apparent increase in the concentration of the PPCPs (Ternes 1998).

Field scale studies have provided valuable data on the behavior of these compounds during biological treatment, but the actual contribution from biotransformation in these processes is seldom documented. Thus, low removals in these systems signal the low biodegradability of these compounds, while high removal efficiencies cannot be definitively attributed to biotransformation alone. Results from Table 2 serve as an indicator for the PPCP biotransformation behavior, but it is important to consider the contribution of other competing removal mechanisms. For example, Heidler and Halden (2007) considered the roles of volatilization, photodegradation, abiotic hydrolysis, and other chemical transformations in addition to biotransformation in the removal of triclosan from a WWTP. After taking into account the properties specific to triclosan, they determined that biological transformation was the dominant process responsible for loss of the antiseptic in their mass balance, but they also found that 50 ± 19% of the influent triclosan mass accumulated in the WWTP sludge. Kim et al. (2005) found that sorption was responsible for removal of tetracycline during batch and SBR studies and found no evidence of biodegradation. They raised concerns about a sorbed drug desorbing if environmental conditions change and sorption had been the compound's main removal mechanism. A change in environmental conditions did affect removal processes in a study by Thompson et al. (2005) in which they observed that biodegradation was responsible for the majority of triclosan removal in WWTP processes when there were high

dissolved oxygen levels. Yet in processes with lower oxygen levels, sorption became the dominant removal mechanism. The changing relative importance of competing removal mechanisms can complicate reporting the role of biodegradation.

Laboratory-based simulations

To attempt to bridge the gap between the PPCP removals shown to be due to biotransformation in Table 1 and the removals reported in natural and engineered treatment systems due to a combination of processes in Table 2, researchers have conducted laboratory studies involving laboratory scale treatment simulations. For instance, laboratory columns have been used to simulate soil passage (Drewes et al. 2001; Hua et al. 2003), and lab scale WWTPs have been used to examine the processes occurring in their full-scale counterparts (Kreuzinger et al. 2004; Clara et al. 2005a; Suárez et al. 2005; Junker et al. 2006). Laboratory scale simulated treatment studies are included in both Tables 1 and 2, reporting biotransformation removals and a combination of biotransformation and other mechanisms, respectively. By conducting these studies in the laboratory and closely controlling experimental conditions, researchers are able to use these simulated treatment studies to gain insight into the behavior of PPCPs in full scale treatment systems. These laboratory simulated studies often determine parameter guidelines for enhancement of PPCP removal through changes in operational or environmental conditions. It has been suggested that a prolonged SRT increases removal efficiencies of PPCPs, as was demonstrated by Clara et al. (2004), who reported SRT-dependent removal of the NSAID diclofenac in a conventional activated sludge WWTP and a laboratory scale MBR. The effect of HRT on the antibiotic ampicillin's removal was studied in a pilot scale anaerobic baffled reactor at steady state. Removal increased from 16.4% to 42.1% when HRT was increased from 1.25 to 2.50 d. With the same HRT increase, the antibiotic aureomycin had a removal increase from 25.9% to 31.3% (Zhou et al. 2006). Redox conditions were also found to be important for PPCP removal by Drewes et al. (2001), who studied the removal of adsorbable organo-iodine (AOI) in laboratory soil columns under different redox conditions. They found that unsaturated aerobic conditions did not lead to significant biotransformation of AOI, saturated anoxic conditions yielded removals of about 20%, and saturated anaerobic conditions caused removals of 57.3% (Drewes et al. 2001). Another laboratory scale study provided insight into the actual biological removal of sulfamethoxazole. In a lab scale SBR, cometabolism of sulfamethoxazole with acetate was observed and it was found that microorganisms may use the degraded antibiotic as a nitrogen source (Drillia et al. 2005).

There are several reasons why laboratory scale studies do not exactly match removals reported from their full scale counterparts. Many of the reasons cited in the above discussion for biotransformation studies and multiple mechanisms apply to laboratory scale treatment studies as well, such as the use of arbitrarily chosen PPCP concentrations that can be much higher than those encountered in treatment systems and in the environment. These higher concentrations facilitate analytical detection and quantification, but they also have the potential to induce toxic effects in the microbes present. Laboratory and field scale studies can also vary markedly in their incubation times for biodegradation. Batch studies following OECD guidelines can have incubations of 28 d, whereas full scale studies of a conventional plug flow reactor in a WWTP, for example, consider HRTs of 4–8 h and SRTs of 3–15 d (Metcalf and Eddy, Inc. 2003). If the microorganisms have a longer time during which they can degrade the PPCPs, it is likely that differences in removals will arise. In spite of the differences between the two, lab scale studies provide valuable insight into critical parameters for PPCP removal in full scale systems.

Computer-based prediction tools

Though their predictions are not included in either table, computer-based predictive tools are also used to determine the potential biodegradability of PPCPs. There are three general approaches to biodegradation prediction modeling, which are regression analysis, expert opinions, and artificial intelligence (AI) (Baker et al. 2004). The regression models have been shown to possess the highest utility and are currently being adapted by the U.S. Environmental Protection Agency as EPA BIOWIN predictive models, but AI approaches have recently gained attention for their potential to greatly improve prediction accuracy

(Klopman and Tu 1997; Rorije et al. 1999; Baker et al. 2004). The majority of current regression models rely mainly on structure activity relationships, in which statistical models (mostly regressions or Bayesian statistics) are applied based on expert knowledge regarding the biodegradability of organic compounds according to their structures (Boethling et al. 2004). Advances in the understanding of structure-biodegradability relationships have provided valuable information regarding the biodegradability of PPCPs. Tunkel et al. (2000) used results from biodegradation tests of 884 organic chemicals to develop structure-biodegradability relationships. They found that certain compounds, including esters, nitriles, and aromatic alcohols, have functional groups that usually increase a compound's biodegradability, whereas aromatic amines, iodide, nitro, and azo groups tend to render a compound more recalcitrant (Tunkel et al. 2000). Boethling et al. (2004) have demonstrated the utility of the computational model by predicting the readily biodegradable nature of 63 pharmaceuticals with reasonable accuracy (83% and 87%) using BIOWIN 5 and 6 models. However, though current prediction models have proven useful, inconsistencies between different models and inaccuracies have been observed. For example, Yu et al. (2006) have shown that the BIOWIN 5 (MITI) models tend to underpredict the likelihood of a PPCP being readily biodegradable, predicting that only 4 of 18 compounds would fit this designation. Conversely, the BIOWIN 1 and 2 (BIODEG) models tend to overpredict the likelihood of being readily biodegradable, predicting 15 of 18 compounds would be in this category. Advances in the understanding of structure-biodegradability relationships have provided valuable information regarding the biodegradability of PPCPs. However, the predictions made by such relationships are not always fully accurate when model outputs are compared to batch study results (Tunkel et al. 2000; Yu et al. 2006).

Research needs

Though the knowledge regarding the occurrence and fate of PPCPs in the environment has increased greatly in recent years, there are still gaps worthy of further research. As seen in Tables 1 and 2, biodegradability cannot often be generalized or predicted for therapeutic classes, individual PPCPs, or the systems studied. Research in the following areas will likely help elucidate further reasons why variations in PPCP biodegradation exist.

Biodegradation pathways need to be further developed to understand which byproducts are forming and their potential for ecological and human health impacts compared to the parent PPCPs. In a study where only 4 of 52 compounds could be detected after soil-aquifer treatment, Ternes et al. (2007) cautioned that even though the parent compounds were not detected, transformation products may still be of concern due to their potential stability or toxicity. Discrepancies between removals in studies measuring mineralization and those measuring disappearance of parent compounds also emphasize the need for metabolic pathways and breakdown products to be examined. For example, <1% of trimethoprim was mineralized in a lab scale WWTP (Junker et al. 2006), yet in full scale studies looking for the disappearance of the parent compound, removal was found to be 69% (Ternes et al. 2007).

The microbial communities degrading PPCPs also merit further research. Whether biodegradation of a compound is carried out by one specific microbial species or whether the process depends on the interactions of an entire microbial community could prove useful in removing PPCPs efficiently. Also of interest would be investigating if a community needs to adapt to the presence of a PPCP or if it is already producing the enzymes needed to degrade the micropollutants.

As discussed earlier, biodegradation is usually only one of many removal processes possible. The other mechanisms need to be further explored so that a clearer understanding of the processes controlling PPCP removal and the interactions of the various mechanisms can be developed. For instance, sorption has been designated a removal mechanism for many compounds, but the degree to which sorption limits PPCP bioavailability is poorly understood.

Synergistic interaction among multiple chemicals is also an important issue that needs to be addressed. PPCPs are not occurring individually in treatment systems, but rather in mixtures whose known numbers of constituent PPCPs seem to be limited currently only by what scientists are aiming to detect. Synergism has great potential for impeding

biodegradation through microbial toxicity. Kümmerer and Al-Ahmad (1997) suggested that degradation of compounds in hospital effluent was hindered due to the synergistic effects of 5-fluorouracil and antibiotics. Synergistic interactions are also a concern for human and environmental health.

Research in the above areas will help increase the understanding of PPCP behavior in the environment. This knowledge of PPCP fate will provide a better indication of how much of a threat, if any, exists from PPCPs in the environment and how biodegradation can be better utilized to prevent or reduce PPCP contamination of the environment.

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References

Andersen H, Siegrist H, Halling-Sorensen B, Ternes TA (2003) Fate of estrogens in a municipal sewage treatment plant. Environ Sci Technol 37:4021–4026. doi:10.1021/es026192a

Ankley GT, Brooks BW, Huggett DB, Sumpter JP (2007) Repeating history: pharmaceuticals in the environment. Environ Sci Technol 41:8211–8217

Ashton D, Hilton M, Thomas KV (2004) Investigating the environmental transport of human pharmaceuticals to streams in the United Kingdom. Sci Total Environ 333:167–184. doi:10.1016/j.scitotenv.2004.04.062

Baker JR, Gamberger D, Mihelcic JR, Sabljic A (2004) Evaluation of artificial intelligence based models for chemical biodegradability prediction. Molecules 9:989–1003. doi:10.3390/91200989

Baronti C, Curini R, D'Ascenzo G, Di Corcia A, Gentili A, Samperi R (2000) Monitoring natural and synthetic estrogens at activated sludge sewage treatment plants and in a receiving river water. Environ Sci Technol 34:5059–5066. doi:10.1021/es001359q

Batt AL, Kim S, Aga DS (2006) Enhanced biodegradation of iopromide and trimethoprim in nitrifying activated sludge. Environ Sci Technol 40:7367–7373. doi:10.1021/es060835v

Bendz D, Paxéus NA, Ginn TR, Loge FJ (2005) Occurrence and fate of pharmaceutically active compounds in the environment, a case study: Höje River in Sweden. J Hazard Mater 122:195–204. doi:10.1016/j.jhazmat.2005.03.012

Bernhard M, Müller J, Knepper TP (2006) Biodegradation of persistent polar pollutants in wastewater: comparison of an optimised lab-scale membrane bioreactor and activated sludge treatment. Water Res 40:3419–3428. doi:10.1016/j.watres.2006.07.011

Boethling RS, Lynch DG, Jaworska JS, Tunkel JL, Thom GC, Webb S (2004) Using Biowin (TM), Bayes, and batteries to predict ready biodegradability. Environ Toxicol Chem 23:911–920. doi:10.1897/03-280

Boyd GR, Zhang S, Grimm DA (2005) Naproxen removal from water by chlorination and biofilm processes. Water Res 39:668–676. doi:10.1016/j.watres.2004.11.013

Bradley PM, Barber LB, Kolpin DW, McMahon PB, Chapelle FH (2007) Biotransformation of caffeine, cotinine, and nicotine in stream sediments: implications for use as wastewater indicators. Environ Toxicol Chem 26:1116–1121. doi:10.1897/06-483R.1

Buser HR, Poiger T, Muller MD (1999) Occurrence and environmental behavior of the chiral pharmaceutical drug ibuprofen in surface waters and in wastewater. Environ Sci Technol 33:2529–2535. doi:10.1021/es981014w

Carballa M, Omil F, Lema JM, Llompart M, Garcia-Jares C, Rodriguez I, Gomez M, Ternes T (2004) Behavior of pharmaceuticals, cosmetics and hormones in a sewage treatment plant. Water Res 38:2918–2926. doi:10.1016/j.watres.2004.03.029

Carballa M, Omil F, Lema JM, Llompart M, Garcia C, Rodriguez I, Gomez M, Ternes T (2005) Behaviour of pharmaceuticals and personal care products in a sewage treatment plant of northwest Spain. Water Sci Technol 52:29–35. doi:10.1007/1-4020-3297-8_3

Carballa M, Omil F, Alder AC, Lema JM (2006) Comparison between the conventional anaerobic digestion of sewage sludge and its combination with a chemical or thermal pre-treatment concerning the removal of pharmaceuticals and personal care products. Water Sci Technol 53:109–117. doi:10.2166/wst.2006.241

Carballa M, Omil F, Lema JM (2007a) Calculation methods to perform mass balances of micropollutants in sewage treatment plants. Application to pharmaceutical and personal care products (PPCPs). Environ Sci Technol 41:884–890. doi:10.1021/es061581g

Carballa M, Omil F, Ternes T, Lema JM (2007b) Fate of pharmaceutical and personal care products (PPCPs) during anaerobic digestion of sewage sludge. Water Res 41:2139–2150. doi:10.1016/j.watres.2007.02.012

Carucci A, Cappai G, Piredda M (2006) Biodegradability and toxicity of pharmaceuticals in biological wastewater treatment plants. J Environ Sci Health Part A 41:1831–1842

Castiglioni S, Bagnati R, Fanelli R, Pomati F, Calamari D, Zuccato E (2006) Removal of pharmaceuticals in sewage treatment plants in Italy. Environ Sci Technol 40:357–363. doi:10.1021/es050991m

Choong AMF, Teo SL-M, Leow JL, Koh HL, Ho PCL (2006) A preliminary ecotoxicity study of pharmaceuticals in the marine environment. J Toxicol Environ Health Part A 69:1959–1970. doi:10.1080/15287390600751371

Cirja M, Zühlke S, Ivashechkin P, Schäffer A, Corvini PFX (2006) Fate of a ^{14}C-labeled nonylphenol isomer in a laboratory-scale membrane bioreactor. Environ Sci Technol 40:6131–6136. doi:10.1021/es060668z

Cirja M, Zuehlke S, Ivashechkin P, Hollender J, Schäffer A, Corvini PFX (2007) Behavior of two differently

radiolabelled 17[alpha]-ethinylestradiols continuously applied to a laboratory-scale membrane bioreactor with adapted industrial activated sludge. Water Res 41:4403–4412. doi:10.1016/j.watres.2007.06.022

Clara M, Strenn B, Ausserleitner M, Kreuzinger N (2004) Comparison of the behaviour of selected micropollutants in a membrane bioreactor and a conventional wastewater treatment plant. Water Sci Technol 50:29–36

Clara M, Kreuzinger N, Strenn B, Gans O, Kroiss H (2005a) The solids retention time—a suitable design parameter to evaluate the capacity of wastewater treatment plants to remove micropollutants. Water Res 39:97–106. doi:10.1016/j.watres.2004.08.036

Clara M, Strenn B, Gans O, Martinez E, Kreuzinger N, Kroiss H (2005b) Removal of selected pharmaceuticals, fragrances and endocrine disrupting compounds in a membrane bioreactor and conventional wastewater treatment plants. Water Res 39:4797–4807. doi:10.1016/j.watres.2005.09.015

Correia MA (2007) Drug biotransformation. In: Katzung BG (ed) Basic and clinical pharmacology, 10th edn. McGraw-Hill Companies, Inc, New York

Crane M, Watts C, Boucard T (2006) Chronic aquatic environmental risks from exposure to human pharmaceuticals. Sci Total Environ 367:23–41. doi:10.1016/j.scitotenv.2006.04.010

Daughton CG, Ternes TA (1999) Pharmaceuticals and personal care products in the environment: agents of subtle change? Environ Health Perspect 107:907–938. doi:10.2307/3434573

Drewes JE, Fox P, Jekel M (2001) Occurrence of iodinated X-ray contrast media in domestic effluents and their fate during indirect potable reuse. J Environ Sci Health A 36:1633–1645. doi:10.1081/ESE-100106248

Drewes JE, Heberer T, Reddersen K (2002) Fate of pharmaceuticals during indirect potable reuse. Water Sci Technol 46:73–80

Drillia P, Dokianakis SN, Fountoulakis MS, Kornaros M, Stamatelatou K, Lyberatos G (2005) On the occasional biodegradation of pharmaceuticals in the activated sludge process: the example of the antibiotic sulfamethoxazole. J Hazard Mater 122:259–265. doi:10.1016/j.jhazmat.2005.03.009

Ericson JF (2007) An evaluation of the OECD 308 water/sediment systems for investigating the biodegradation of pharmaceuticals. Environ Sci Technol 41:5803–5811. doi:10.1021/es063043+

Göbel A, McArdell CS, Joss A, Siegrist H, Giger W (2007) Fate of sulfonamides, macrolides, and trimethoprim in different wastewater treatment technologies. Sci Total Environ 372:361–371. doi:10.1016/j.scitotenv.2006.07.039

Gómez MJ, Martínez Bueno MJ, Lacorte S, Fernández-Alba AR, Agüera A (2007) Pilot survey monitoring pharmaceuticals and related compounds in a sewage treatment plant located on the Mediterranean coast. Chemosphere 66:993–1002. doi:10.1016/j.chemosphere.2006.07.051

González S, Muller J, Petrovic M, Barcelo D, Knepper T (2006) Biodegradation studies of selected priority acidic pesticides and diclofenac in different bioreactors. Environ Pollut 144:926–932. doi:10.1016/j.envpol.2006.02.021

Gröning J, Held C, Garten C, Claußnitzer U, Kaschabek S, Schlömann M (2007) Transformation of diclofenac by the indigenous microflora of river sediments and identification of a major intermediate. Chemosphere 69:509–516. doi:10.1016/j.chemosphere.2007.03.037

Grunheid S, Amy G, Jekel M (2005) Removal of bulk dissolved organic carbon (DOC) and trace organic compounds by bank filtration and artificial recharge. Water Res 39:3219–3228. doi:10.1016/j.watres.2005.05.030

Haiß A, Kümmerer K (2006) Biodegradability of the X-ray contrast compound diatrizoic acid, identification of aerobic degradation products and effects against sewage sludge micro-organisms. Chemosphere 62:294–302. doi:10.1016/j.chemosphere.2005.05.007

Heidler J, Halden RU (2007) Mass balance assessment of triclosan removal during conventional sewage treatment. Chemosphere 66:362–369. doi:10.1016/j.chemosphere.2006.04.066

Heidler J, Sapkota A, Halden RU (2006) Partitioning, persistence, and accumulation in digested sludge of the topical antiseptic triclocarban during wastewater treatment. Environ Sci Technol 40:3634–3639. doi:10.1021/es052245n

Hua J, An P, Winter J, Gallert C (2003) Elimination of COD, microorganisms and pharmaceuticals from sewage by trickling through sandy soil below leaking sewers. Water Res 37:4395–4404. doi:10.1016/S0043-1354(03)00334-8

Jones OAH, Voulvoulis N, Lester JN (2007) The occurrence and removal of selected pharmaceutical compounds in a sewage treatment works utilising activated sludge treatment. Environ Pollut 145:738–744. doi:10.1016/j.envpol.2005.08.077

Joss A, Andersen H, Ternes T, Richle PR, Siegrist H (2004) Removal of estrogens in municipal wastewater treatment under aerobic and anaerobic conditions: consequences for plant optimization. Environ Sci Technol 38:3047–3055. doi:10.1021/es0351488

Junker T, Alexy R, Knacker T, Kümmerer K (2006) Biodegradability of ^{14}C-labeled antibiotics in a modified laboratory scale sewage treatment plant at environmentally relevant concentrations. Environ Sci Technol 40:318–324. doi:10.1021/es051321j

Kalsch W (1999) Biodegradation of the iodinated X-ray contrast media diatrizoate and iopromide. Sci Total Environ 225:143–153. doi:10.1016/S0048-9697(98)00340-4

Kim S, Eichhorn P, Jensen JN, Weber AS, Aga DS (2005) Removal of antibiotics in wastewater: effect of hydraulic and solid retention times on the fate of tetracycline in the activated sludge process. Environ Sci Technol 39:5816–5823. doi:10.1021/es050006u

Kim SD, Cho J, Kim IS, Vanderford BJ, Snyder SA (2007) Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters. Water Res 41:1013–1021. doi:10.1016/j.watres.2006.06.034

Klopman G, Tu MH (1997) Structure-biodegradability study and computer-automated prediction of aerobic biodegradation of chemicals. Environ Toxicol Chem 16:1829–1835. doi:10.1897/1551-5028(1997)016<1829:SBSACA>2.3.CO;2

Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT (2002) Pharmaceuticals, hormones,

and other organic wastewater contaminants in U.S. streams, 1999–2000: a national reconnaissance. Environ Sci Technol 36:1202–1211. doi:10.1021/es011055j

Kosjek T, Heath E, Kompare B (2007) Removal of pharmaceutical residues in a pilot wastewater treatment plant. Anal Bioanal Chem 387:1379–1387. doi:10.1007/s00216-006-0969-1

Kreuzinger N, Clara M, Strenn B, Kroiss H (2004) Relevance of the sludge retention time (SRT) as design criteria for wastewater treatment plants for the removal of endocrine disruptors and pharmaceuticals from wastewater. Water Sci Technol 50:149–156

Kümmerer K, Al-Ahmad A (1997) Biodegradability of the anti-tumour agents 5-fluorouracil, cytarabine, and gemcitabine: impact of the chemical structure and synergistic toxicity with hospital effluent. Acta Hydrochim Hydrobiol 25:166–172. doi:10.1002/aheh.19970250402

Kümmerer K, Steger-Hartmann T, Meyer M (1997) Biodegradability of the anti-tumor agent ifosfamide and its occurrence in hospital effluents and communal sewage. Water Res 31:2705–2710. doi:10.1016/S0043-1354(97)00121-8

Kupper T, Plagellat C, Brändli RC, de Alencastro LF, Grandjean D, Tarradellas J (2006) Fate and removal of polycyclic musks, UV filters and biocides during wastewater treatment. Water Res 40:2603–2612. doi:10.1016/j.watres.2006.04.012

Kwon JW, Armbrust KL (2006) Laboratory persistence and fate of fluoxetine in aquatic environments. Environ Toxicol Chem 25:2561–2568. doi:10.1897/05-613R.1

Layton AC, Gregory BW, Seward JR, Schultz TW, Sayler GS (2000) Mineralization of steroidal hormones by biosolids in wastewater treatment systems in Tennessee USA. Environ Sci Technol 34:3925–3931. doi:10.1021/es9914487

Lindqvist N, Tuhkanen T, Kronberg L (2005) Occurrence of acidic pharmaceuticals in raw and treated sewages and in receiving waters. Water Res 39:2219–2228. doi:10.1016/j.watres.2005.04.003

Massmann G, Greskowiak J, Dunnbier U, Zuehlke S, Knappe A, Pekdeger A (2006) The impact of variable temperatures on the redox conditions and the behaviour of pharmaceutical residues during artificial recharge. J Hydrol (Amst) 328:141–156. doi:10.1016/j.jhydrol.2005.12.009

Matamoros V, Bayona JM (2006) Elimination of pharmaceuticals and personal care products in subsurface flow constructed wetlands. Environ Sci Technol 40:5811–5816. doi:10.1021/es0607741

Matamoros V, Puigagut J, Garcia J, Bayona JM (2007) Behavior of selected priority organic pollutants in horizontal subsurface flow constructed wetlands: a preliminary screening. Chemosphere 69:1374–1380. doi:10.1016/j.chemosphere.2007.05.012

Matamoros V, Caselles-Osorio A, García J, Bayona JM (2008a) Behavior of pharmaceutical products and biodegradation intermediates in horizontal subsurface flow constructed wetland. A microcosm experiment. Sci Total Environ 394:171–176. doi:10.1016/j.scitotenv.2008.01.029

Matamoros V, García J, Bayona JM (2008b) Organic micropollutant removal in a full-scale surface flow constructed wetland fed with secondary effluent. Water Res 42:653–660. doi:10.1016/j.watres.2007.08.016

Maurer M, Escher BI, Richle P, Schaffner C, Alder AC (2007) Elimination of β-blockers in sewage treatment plants. Water Res 41:1614–1622. doi:10.1016/j.watres.2007.01.004

McAvoy DC, Schatowitz B, Jacob M, Hauk A, Eckhoff WS (2002) Measurement of triclosan in wastewater treatment systems. Environ Toxicol Chem 21:1323–1329. doi:10.1897/1551-5028(2002)021<1323:MOTIWT>2.0.CO;2

Metcalf & Eddy Inc. (2003) Wastewater engineering: treatment and reuse. McGraw-Hill Companies, Inc, New York

Nakada N, Tanishima T, Shinohara H, Kiri K, Takada H (2006) Pharmaceutical chemicals and endocrine disrupters in municipal wastewater in Tokyo and their removal during activated sludge treatment. Water Res 40:3297–3303. doi:10.1016/j.watres.2006.06.039

Oppenheimer J, Stephenson R, Burbano A (2007) Characterizing the passage of personal care products through wastewater treatment processes. Water Environ Res 79:2564–2577. doi:10.2175/106143007X184573

Paxéus N (2004) Removal of selected non-steroidal anti-inflammatory drugs (NSAIDs), gemfibrozil, carbamazepine, beta-blockers, trimethoprim and triclosan in conventional wastewater treatment plants in five EU countries and their discharge to the aquatic environment. Water Sci Technol 50:253–260

Peng X, Wang Z, Kuang W, Tan J, Li K (2006) A preliminary study on the occurrence and behavior of sulfonamides, ofloxacin and chloramphenicol antimicrobials in wastewaters of two sewage treatment plants in Guangzhou, China. Sci Total Environ 371:314–322. doi:10.1016/j.scitotenv.2006.07.001

Quintana JB, Weiss S, Reemtsma T (2005) Pathways and metabolites of microbial degradation of selected acidic pharmaceutical and their occurrence in municipal wastewater treated by a membrane bioreactor. Water Res 39:2654–2664. doi:10.1016/j.watres.2005.04.068

Radjenovic J, Petrovic M, Barceló D (2007) Analysis of pharmaceuticals in wastewater and removal using a membrane bioreactor. Anal Bioanal Chem 387:1365–1377. doi:10.1007/s00216-006-0883-6

Redshaw CH, Cooke MP, Talbot HM, McGrath S, Rowland SJ (2008) Low biodegradability of fluoxetine HCl, diazepam and their human metabolites in sewage sludge-amended soil. J Soils Sediments 8:217–230. doi:10.1007/s11368-008-0024-2

Rodríguez I, Quintana JB, Carpinteiro J, Carro AM, Lorenzo RA, Cela R (2003) Determination of acidic drugs in sewage water by gas chromatography-mass spectrometry as tert.-butyldimethylsilyl derivatives. J Chromatogr A 985:265–274. doi:10.1016/S0021-9673(02)01528-5

Rorije E, Loonen H, Muller M, Klopman G, Peijnenburg W (1999) Evaluation and application of models for the prediction of ready biodegradability in the MITI-I test. Chemosphere 38:1409–1417. doi:10.1016/S0045-6535(98)00543-8

Sharvelle S, Skvarenina E, Banks MK (2008) Biodegradation of disodium cocoamphodiacetate by a wastewater microbial consortium. Water Environ Res 80:276–281. doi:10.2175/106143008X268489

Simonich SL, Federle TW, Eckhoff WS, Rottiers A, Webb S, Sabaliunas D, De Wolf W (2002) Removal of fragrance materials during US and European wastewater treatment.

Environ Sci Technol 36:2839–2847. doi:10.1021/es025503e

Smook TM, Zho H, Zytner RG (2008) Removal of ibuprofen from wastewater: comparing biodegradation in conventional, membrane bioreactor, and biological nutrient removal treatment systems. Water Sci Technol 57:1–8. doi:10.2166/wst.2008.658

Snyder SA, Leising J, Westerhoff P, Yoon Y, Mash H, Vanderford B (2004) Biological and physical attenuation of endocrine pisruptors and pharmaceuticals: Implications for water reuse. Ground Water Monit Remediat 24:108–118. doi:10.1111/j.1745-6592.2004.tb00719.x

Stasinakis AS, Petalas AV, Mamais D, Thomaidis NS, Gatidou G, Lekkas TD (2007) Investigation of triclosan fate and toxicity in continuous-flow activated sludge systems. Chemosphere 68:375–381. doi:10.1016/j.chemosphere.2007.01.047

Stumpf M, Ternes TA, Wilken RD, Rodrigues SV, Baumann W (1999) Polar drug residues in sewage and natural waters in the state of Rio de Janeiro, Brazil. Sci Total Environ 225:135–141. doi:10.1016/S0048-9697(98)00339-8

Suárez S, Ramill M, Omil F, Lema JM (2005) Removal of pharmaceutically active compounds in nitrifying-denitrifying plants. Water Sci Technol 52:9–14

Tauxe-Wuersch A, De Alencastro LF, Grandjean D, Tarradellas J (2005) Occurrence of several acidic drugs in sewage treatment plants in Switzerland and risk assessment. Water Res 39:1761–1772. doi:10.1016/j.watres.2005.03.003

Ternes TA (1998) Occurrence of drugs in German sewage treatment plants and rivers. Water Res 32:3245–3260. doi:10.1016/S0043-1354(98)00099-2

Ternes TA, Hirsch R (2000) Occurrence and behavior of X-ray contrast media in sewage facilities and the aquatic environment. Environ Sci Technol 34:2741–2748. doi:10.1021/es991118m

Ternes TA, Joss A (2006) Human pharmaceuticals, hormones and fragrances. IWA Publishing, New York

Ternes TA, Kreckel P, Mueller J (1999a) Behaviour and occurrence of estrogens in municipal sewage treatment plants–II. Aerobic batch experiments with activated sludge. Sci Total Environ 225:91–99. doi:10.1016/S0048-9697(98)00335-0

Ternes TA, Stumpf M, Mueller J, Haberer K, Wilken RD, Servos M (1999b) Behavior and occurrence of estrogens in municipal sewage treatment plants—I. Investigations in Germany, Canada and Brazil. Sci Total Environ 225:81–90. doi:10.1016/S0048-9697(98)00334-9

Ternes TA, Bonerz M, Herrmann N, Teiser B, Andersen HR (2007) Irrigation of treated wastewater in Braunschweig, Germany: an option to remove pharmaceuticals and musk fragrances. Chemosphere 66:894–904. doi:10.1016/j.chemosphere.2006.06.035

Thompson A, Griffin P, Stuetz R, Cartmell E (2005) The fate and removal of triclosan during wastewater treatment. Water Environ Res 77:63–67. doi:10.2175/106143005X41636

Tixier C, Singer HP, Oellers S, Muller SR (2003) Occurrence and fate of carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, and naproxen in surface waters. Environ Sci Technol 37:1061–1068. doi:10.1021/es025834r

Trautwein C, Kümmerer K, Metzger JW (2008) Aerobic biodegradability of the calcium channel antagonist verapamil and identification of a microbial dead-end transformation product studied by LC-MS/MS. Chemosphere 72:442–450. doi:10.1016/j.chemosphere.2008.02.022

Tunkel J, Howard PH, Boethling RS, Stiteler W, Loonen H (2000) Predicting ready biodegradability in the Japanese Ministry of International Trade and Industry test. Environ Toxicol Chem 19:2478–2485. doi:10.1897/1551-5028(2000)019<2478:PRBITJ>2.3.CO;2

Vader JS, van Ginkel CG, Sperling F, de Jong J, de Boer W, de Graaf JS, van der Most M, Stokman PGW (2000) Degradation of ethinyl estradiol by nitrifying activated sludge. Chemosphere 41:1239–1243. doi:10.1016/S0045-6535(99)00556-1

Vasskog T, Berger U, Samuelsen PJ, Kallenborn R, Jensen E (2006) Selective serotonin reuptake inhibitors in sewage influents and effluents from Tromso, Norway. J Chromatogr A 1115:187–195. doi:10.1016/j.chroma.2006.02.091

Vieno NM, Tuhkanen T, Kronberg L (2005) Seasonal variation in the occurrence of pharmaceuticals in effluents from a sewage treatment plant and in the recipient water. Environ Sci Technol 39:8220–8226. doi:10.1021/es051124k

Vieno N, Tuhkanen T, Kronberg L (2007) Elimination of pharmaceuticals in sewage treatment plants in Finland. Water Res 41:1001–1012. doi:10.1016/j.watres.2006.12.017

Waltman EL, Venables BJ, Waller WZ (2006) Triclosan in a North Texas wastewater treatment plant and the influent and effluent of an experimental constructed wetland. Environ Toxicol Chem 25:367–372. doi:10.1897/05-112R.1

Winkler M, Lawrence JR, Neu TR (2001) Selective degradation of ibuprofen and clofibric acid in two model river biofilm systems. Water Res 35:3197–3205. doi:10.1016/S0043-1354(01)00026-4

Xu WH, Zhang G, Li XD, Zou SC, Li P, Hu ZH, Li J (2007) Occurrence and elimination of antibiotics at four sewage treatment plants in the Pearl River Delta (PRD), South China. Water Res 41:4526–4534. doi:10.1016/j.watres.2007.06.023

Ying GG, Yu XY, Kookana RS (2007) Biological degradation of triclocarban and triclosan in a soil under aerobic and anaerobic conditions and comparison with environmental fate modelling. Environ Pollut 150:300–305. doi:10.1016/j.envpol.2007.02.013

Yu JT, Bouwer EJ, Coelhan M (2006) Occurrence and biodegradability studies of selected pharmaceuticals and personal care products in sewage effluent. Agric Water Manag 86:72–80. doi:10.1016/j.agwat.2006.06.015

Zhou P, Su CY, Li BW, Yi Q (2006) Treatment of high-strength pharmaceutical wastewater and removal of antibiotics in anaerobic and aerobic biological treatment processes. J Environ Eng 132:129–136. doi:10.1061/(ASCE)0733-9372(2006)132:1(129)

Zwiener C, Frimmel FH (2003) Short-term tests with a pilot sewage plant and biofilm reactors for the biological degradation of the pharmaceutical compounds clofibric acid, ibuprofen, and diclofenac. Sci Total Environ 309:201–211. doi:10.1016/S0048-9697(03)00002-0