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A critical review of septic tanks as a pathway for active pharmaceutical ingredients to the aquatic environment – existing knowledge and future perspectives on their monitoring and management

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Active pharmaceutical ingredients (APIs) are present in aquatic environments at concentrations that can impact ecosystems. Their major pathway to the environment is in the discharge of wastewater effluents from centralised wastewater treatment works (WWTWs). However, in most rural areas where houses are not connected to a public sewage network, single households or groups of houses rely on onsite wastewater treatment works (OWTWs), mainly septic tanks (STs). Therefore, STs are reviewed as a pathway for APIs to the aquatic environment. Despite STs being extensively used globally, there is a geographical bias in available data with most studies conducted in the USA. Furthermore, studies focus on a few APIs (*e.g.*, carbamazepine, sulfamethoxazole and paracetamol) and the impact of STs to groundwater. Previous reliance on grab sampling and the heterogenous composition of influent wastewater characterised by the small contributing populations makes assessing ST removal efficiency challenging. Available data suggests little or no removal of APIs in the anaerobic environment of STs. Conducting an intensive monitoring approach (*e.g.*, continuous 24 h composite sampling) for durations several times the ST hydraulic retention time will help benchmark their performance for API removal against other processes. Recent studies show surface waters receiving ST discharges have API concentrations exceeding their predicted no effect concentration (PNEC, the concentration below which no adverse effect is expected). Mean concentrations of 17β-estradiol, ampicillin, ibuprofen, memantine, palmitamid, paracetamol and trihexyphenidyl all exceeded their PNEC by up to 50 times. However, there is a lack of data for several APIs identified to be of possible environmental concern in prioritisation watch lists such as those outlined by the EU (*e.g.*, amoxicillin, clarithromycin, desmethylvenlafaxine and clindamycin). Receiving surface waters can be small ecologically important streams, demanding the need for further monitoring and intervention. Other than adopting secondary treatment (*e.g.*, constructed wetlands where possible) or alternative OWTWs which achieve greater API removal, sustainable medicine use is proposed as a viable means of reducing the environmental impact of ST discharges where risks are identified. Utilising environmentally informed prescribing and other 'upstream' interventions such as return schemes for unused pharmaceuticals, have great potential for success where small populations of people can be specifically targeted.

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Environmental significance

Septic tanks (STs) are an important, but often overlooked, pathway for active pharmaceutical ingredients (APIs) entering the environment. API concentrations in aquatic environments impacted by STs can exceed their predicted no-effect concentrations. This highlights the need to consider the influence and management of STs in the protection of aquatic ecosystems.

1 Introduction

Pharmaceuticals are critical for improving public health through the prevention, management, and treatment of various diseases.[1] However, they are also widely recognised for their potential ecotoxicological risk to the environment,[2–5] and are present in water bodies worldwide at ng to μg L^{-1} concentrations.[6–11] Adverse effects have been observed at concentrations relevant to the aquatic environment. For example, long-term exposure to fluoxetine (3×10^{-3} – 0.3 μg L^{-1}) reduces growth and reproductive potential in *Mytilus californianus* mussels.[12] Active pharmaceutical ingredients (APIs)

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can induce their designed effects on non-target organisms. For instance, the swimming activity of *Danio rerio* (zebrafish) embryos is reduced in the presence of β-blockers due to the decreasing heart rate, and thus decreasing swim bladder inflation.[13] They can also induce non-designed effects in the environment. Hormones cause endocrine disrupting effects, such as feminisation, *e.g.*, as observed in *Rutilus rutilus* (roach) after early life exposure to 3×10^{-3} μg L^{-1} of the hormonal contraceptive agent 17α-ethinylestradiol.[14] Furthermore, persistent exposure to antibiotics can promote antimicrobial resistance genes (ARGs).[15] The presence of APIs in complex mixtures in the environment can also result in synergistic or antagonistic effects.[3,16,17] The ecotoxicological risk to the environment of individual APIs can be described using the predicted no effect concentration (PNEC), the concentration below which no adverse effects are expected.[18]

Many countries and continental bodies started addressing the environmental risks of APIs by implementing different prioritisation and monitoring schemes in the last decade.[2,19–24] However, specific regulations, *e.g.*, maximum discharge limits or minimum required removal efficiencies in wastewater treatment works (WWTWs) or maximum concentrations in the receiving environment are rare. Municipal WWTWs in Switzerland, for example, are required to include ozone based advanced treatment to remove 80% of selected organic micropollutants, including ten APIs.[25,26] The recent EU urban wastewater treatment directive also mandates tertiary and quaternary treatment in large WWTWs,[27] improving API removal, and a proposal for priority substances, including eleven APIs, is being revised.[23]

Pharmaceuticals are often not fully metabolised by humans and animals, and thus unchanged APIs are excreted alongside metabolites.[28] The main removal processes for APIs in secondary (aerobic) wastewater treatment are biodegradation and sorption onto sludge that are highly influenced by their individual physicochemical properties.[29] For example, 99% ibuprofen removal compared to 21% propranolol removal was achieved in activated sludge WWTWs.[30] Furthermore, around half of APIs are chiral, existing as mirror images of each other with identical chemical structures but different spatial arrangements (enantiomers).[31] The enantiomeric composition of chiral compounds is typically reported as the enantiomeric fraction (EF), calculated from the enantiomer concentrations.[32] Pairs of enantiomers can demonstrate enantioselectivity in their environmental occurrence, fate, and toxicity.[32–35]

Possible pathways of APIs, including unchanged pharmaceuticals, and wastewater and human metabolites, to the environment include treated effluents from municipal, hospital, and industrial WWTWs, untreated wastewater discharges, *e.g.*, through combined sewage overflows (CSOs), surface water runoff from urban and agricultural areas, aquaculture and landfill leachate.[28,36–40] Due the ubiquitous presence of APIs in municipal influent wastewater, their incomplete removal in conventional wastewater treatment, the continuous discharge of treated effluent, and their use by the majority of the population, they are considered pseudo-persistent in the environment with centralised WWTWs identified as the main pathway of APIs to the environment.[28,36,41,42] Hence, research efforts have been directed toward these centralised WWTWs and their receiving surface waters.[6,36,43–45] One pathway that has received comparatively little attention are onsite WWTWs (OWTWs), *e.g.*, septic tanks (STs), that treat wastewater of single households or small communities in mostly rural areas.[46,47]

2 Septic tanks for wastewater treatment

Wastewater can be treated in centralised WWTWs or close to the source in decentralised OWTWs. OWTWs are especially common in rural areas due to the high costs of building and operating centralised WWTWs and pipe networks in low-density population areas.[46,47] However, historically OWTWs were also used in more urban areas, some of which still remain, *e.g.*, there are 603 STs in Edinburgh, the second largest city in Scotland, of which only some are located in the outskirts of the city.[48] Onsite treatment options include packaged treatment plants and settlement systems, such as STs, possibly followed by further treatment steps.[49] Alternatively, wastewater is stored in a watertight cesspit (cesspool) and regularly removed to be treated at a centralised facility.[50] The principle of STs for wastewater treatment was proposed in 1860, in France, by Mouras and Moigno, and is widely used since their introduction to England in 1895.[51] A ST is a watertight underground tank with an inlet and outlet pipe.[52] Wastewater is treated by the separation of the liquid phase from heavy solids that settle as sludge at the bottom of the tank, and oil, grease and low density solids that build a top layer called scum.[52] The organic matter is partially degraded by anaerobic microorganisms.[49] However, there is a build-up of sludge and scum within the ST which needs removed, typically every few months to years.[51] The removed material is then further treated at centralised WWTWs.[53] STs are designed as a rectangular chamber made of bricks, concrete, or as glass-reinforced plastic (GRP) with one or more compartments in series (Fig. 1a) or as GRP torpedo (onion-shaped) STs (Fig. 1b). Generally, the performance of rectangular STs increases with increasing number of compartments.[51,54] Rectangular STs with multiple compartments are also known as baffled reactors.[55]

The ST effluent may undergo further treatment before being discharged into the ground or a nearby water body, *e.g.*, through infiltration fields or natural systems.[52,55,56] In an infiltration field (also referred to as soil infiltration system, drainfield, drainage field, leach field, soil absorption system or soil treatment unit), ST effluent is distributed into perforated pipes and spread into the soil, often after filtration through stone or gravel.[49,57] Infiltration fields, unlike soakaways where ST effluent is discharged to the ground *via* a single pipe, are considered additional secondary treatment *via* sorption and anaerobic biodegradation.[56] Deep, permeable soils and sufficient space, *e.g.*, to allow sufficient distance from portable water sources, are required for their successful use.[47,51,58] Alternative further treatments are mound filters, constructed wetlands, packaged filters, reed beds and packaged treatment plants.[49,55,56,59] Packaged treatment

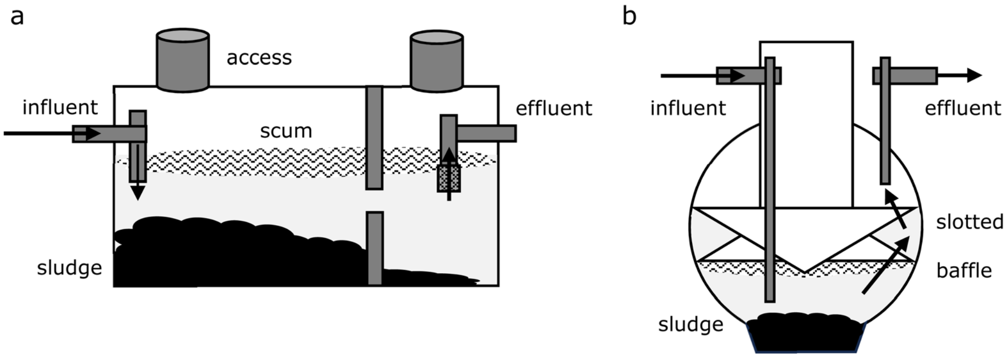

Fig. 1 Outline of different septic tank (ST) designs: rectangular ST with two compartments (a) and torpedo ST (b).

plants, such as activated sludge systems, submerged aerated filters, rotating biological contactors, sequencing batch reactors and biological filters, use aerobic processes and are used as secondary treatment units.[55,56,60–62]

Regulations on STs and how commonly STs are used vary widely between different countries. For instance, it is estimated that 3% of households in Germany, and 33% of households in Ireland use private OWTWs; traditionally a ST.[52,63] Regulatory differences exist even between geographically and politically similar countries, *e.g.*, different regulations on the registration process and discharges apply in the UK for England and Wales, Northern Ireland, and Scotland.[64] STs serve single houses or small communities (sometimes referred to as cluster STs) and can be publicly or privately owned.[65–67] While the majority of STs in the USA discharge to the ground, the direct discharge of ST effluent to rivers, lakes or coastal waters is also possible, and is commonplace in other countries.[68,69]

Regulations depend on the type of treatment, distance from a public sewer, the size of the contributing population and the nature of the receiving environment. Typically, existing STs and those receiving only domestic wastewater, are less strictly regulated than newly installed systems and those receiving other than just domestic inputs.[68,70] For example, trade effluent, such as water used in production, washing, or cooling facilities and businesses, including launderettes and car washes, cannot be treated in STs in Scotland.[68,71] STs have received increasing attention by regulators in recent years, and stricter rules have been introduced. For instance, STs discharging to a watercourse were to be replaced or upgraded to a packaged treatment plant before January 2020 in England unless an exemption is given by the Environment Agency.[64]

Typical problems associated with STs are however often related to systems not working as intended or not being compliant with existing regulations. For example, Yates *et al.*[72] found that in one catchment in England only 15% of STs had the required permit. This could not only lead to significantly underestimating the number of ST discharges, but also increases the risk of performance related issues[72,73] including incorrect maintenance, defective design or malfunctioning, *e.g.*, caused by blockages.[51,52,74] For instance, 45% of participants reported a blockage or overflowing of their ST in a catchment survey in 2012.[75] When STs are not frequently emptied, sludge and scum accumulate in the tank, which reduces the tank volume and thereby the hydraulic retention time (HRT). The HRT is an important factor in the tank performance,[65] as it controls the time for separation of sludge and scum from the wastewater and biodegradation, and thereby the extent and efficiency of the treatment process. STs that were never emptied or last emptied over 15 years ago are still in use.[52,75–78] Existing historic STs, built before current regulations, have increased risk of performance related issues as older STs are associated with out-dated design standards. Examples of out-dated designs include undersized tanks, misconnected pipes, STs made of brick, as they are more likely to leak into the ground, or unsuitable infiltration fields or discharge points.[48,51] When effluent pipes are too short or damaged, ST discharges do not reach the receiving watercourse, particularly during low flow conditions of the watercourse.[48,52] Even for registered STs, further information relevant to determine the possible impact to the environment, *e.g.*, the number of contributing population equivalents (PE), size and age of the ST, treatment type, desludging frequency and discharge point, are often missing.[48,78]

There are four existing literature reviews on organic contaminants in OWTWs.[49,79–81] A recent review on the impact of STs on groundwater contamination also mentions organic contaminants including APIs.[82] Sharma *et al.*[80] reviewed the treatment of hospital effluent for antimicrobial removal in advanced onsite wastewater treatment. However, STs treat wastewater to a lesser degree than secondary and tertiary (advanced) WWTWs as they only rely on the physical separation of sludge and scum from the liquid phase and anaerobic biodegradation.[47] Wardhani *et al.*[81] only included four peer-reviewed studies on seven APIs analysed in ST effluent, a small fraction of the conducted research, to discuss the impact to Indonesia specifically. Both Lusk *et al.*[79] and Schaider *et al.*[49] included the potential impact of STs to groundwater quality but concentrations in receiving surface water were not included, potentially due to the lack of available data in 2017 (Fig. 2). Over the last ten years, OWTWs have received increasing attention as pathways for APIs into the environment, and ground- and surface water has been studied more frequently,[46,83–89] highlighting the need for an up to date review. The aim of this review was therefore to detail the progress made on understanding ST discharges as a pathway of APIs to the aquatic environment. The detection and removal of APIs in STs,

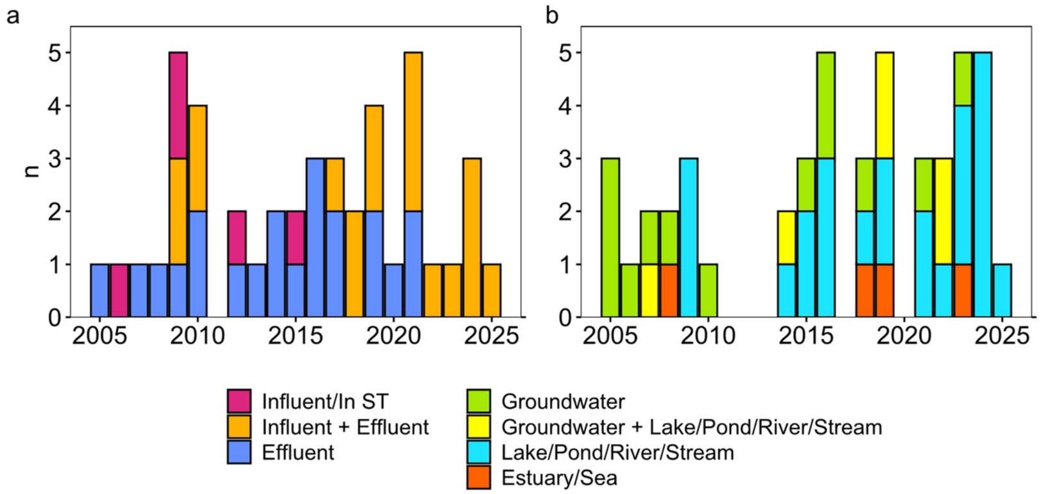

Fig. 2 Number of conducted studies per year (n) on active pharmaceutical ingredients (APIs) in STs (a) and the receiving environment (b).

and the difference to other, alternative, OWTWs and secondary treatment steps, as well as their contribution to the receiving environment, and mitigation strategies are critically discussed.

3 Search strategy and methods

A literature search was conducted on literature available in June 2025 on Scopus and Web of Science using relevant key words: ("pharmaceutical" OR "drug" OR "hormone") AND ("septic tank" OR "septic system" OR "onsite wastewater treatment" OR "on-site wastewater treatment" OR "cluster" OR "decentralised wastewater treatment") and ("emerging contaminant" OR "emerging concern" OR "emerging pollutant" OR "trace organic" OR "micropollutant" OR "organic contaminant") AND ("septic tank" OR "septic system"). Results combining ("emerging contaminant" OR "emerging concern" OR "emerging pollutant" OR "trace organic" OR "micropollutant" OR "organic contaminant") AND ("onsite wastewater treatment" OR "on-site wastewater treatment" OR "cluster" OR "decentralised wastewater treatment") were filtered manually for relevant articles using the title and abstract if appropriate. Research that did not include APIs or hormones was excluded, and studies found through cross-references were added. Caffeine was not included, as its main source is not from pharmaceutical use. One scientific report was included in addition to peer-reviewed scientific articles.[90]

For the purpose of this review, ST refers to a conventional ST (Fig. 1) that can receive wastewater from one or multiple households, a community or from a specialised purpose, *e.g.*, a café, school or office building. When possible, a distinction between the effluent after conventional ST treatment (ST effluent) and after secondary treatment, *e.g.*, an infiltration field or constructed wetland, (final effluent) was made. Alternative treatment systems, such as small packaged treatment plants were also included. For the purpose of this review, an alternative OWTW is anything other than a ST.

To report the concentration of APIs, if it was not given, the arithmetic mean was calculated using only reported concentrations (*i.e.*, not incorporating detection or quantification limits for samples below said limits) as this was the most common approach in studies that reported mean concentrations. When only influent concentrations ($c_{\mathrm{Inf.}}$) and removal efficiencies (eqn (1)) were given, effluent concentrations ($c_{\mathrm{Eff.}}$) were calculated using eqn (2). As a last option, concentrations were estimated from graphs.

$$\text{Removal (\%)} = \frac{c_{\mathrm{Inf.}} - c_{\mathrm{Eff.}}}{c_{\mathrm{Inf}}} \times 100\% \quad (1)$$

$$c_{\mathrm{Eff.}} = c_{\mathrm{Inf.}} - \frac{\text{Removal}(\%) \times c_{\mathrm{Inf.}}}{100\%} \quad (2)$$

When only the median concentration was given, this was used instead.

To determine potential environmental implications, the hazard quotient (HQ) was calculated by dividing the measured environmental concentration of individual APIs by their lowest freshwater PNEC found in the NORMAN Ecotoxicology Database.[69,91]

Data was processed in Microsoft Excel (version 2505) and R92 (version 4.3.1) with RStudio[93] (2023.09.01) using the packages dplyr,[94] openxlsx,[95] readxl,[96] tidyverse[97] and rstatix[98] for data manipulation and statistical analysis. Significant differences ($p < 0.05$) were determined using Wilcoxon tests, due to the nonparametric nature of the data. Graphs were made in R using ggplot2 (ref. 99) and patchwork.[100] The map was produced in QGIS[101] re (version 3.28.3) from open access data (https://www.TechGEO.org (ref. 102)).

4 Occurrence of active pharmaceutical ingredients in onsite wastewater treatment works

4.1 Wastewater concentrations

In total, 77 studies determining APIs in conventional STs, alternative OWTWs or in the receiving environment were

Table 1 Conducted studies on active pharmaceutical ingredients (APIs) in STs and alternative OWTWs with study location, publishing year, the ST design, the wastewater (WW) source, type of receiving environment, types of samples taken, number of septic tanks sampled (STs), number of sampling events, and number of APIs analysed (n). Types of samples taken include influent (inf.) from STs, alternative OWTWs or centralised WWTWs, ST effluent (eff.) or effluent after secondary treatment (final eff.) or from alternative OWTWs

Study location	Year	Design	WW source	Receiving environment	Samples	STs	Sampling events	n	Study
Australia	2010	Alternative	Centralised WWTW (3800 PE[e])	N/A	Inf. + final eff.	1	3	19	116
Belgium	2017	Alternative	Centralised WWTW (450 PE) and hospital	N/A	Inf. + final eff.	1	Lab study	6	114
Brazil[a]	2021	ST + secondary treatment	Residential (student housing, 10 PE)	N/A	Inf. + final eff.	1	16	10	112
Canada	2008	ST + secondary treatment	Households	Ground	ST eff.	2	2	11	104
China	2023	Alternative	N/A	N/A	Inf. + final eff.	3	1	Non-target	83
Denmark	2009	ST + secondary treatment	Households	Ponds, streams	ST eff. + final eff.	13	1	8	139
Germany	2018	Alternative	Households (2500 PE)	N/A	Inf. + final eff.	3	13	27	65
Iran	2018	ST	Hospital (85 beds)	N/A	Inf. + ST eff.	1	3	6	109
Japan	2009	Alternative	Households	N/A	In tank	3	1	5	125
Korea	2019	Alternative	N/A	Streams, creeks	Inf. + final eff.	24	1	8	115
Scotland	2019	ST + sometimes infiltration field	Households: 2–7 people	Streams	Final eff.	15	1	10	87
Scotland	2024	ST	Residential (292 PE)	River	Inf. + ST eff.	1	1	68	111
Scotland	2024	ST	Residential (217–475 PE)	Rivers and stream	Inf. + ST eff.	5	12	68	69
Scotland[b]	2025	ST	Residential (217–475 PE)	Rivers and stream	Inf. + ST eff.	5	12	25	120
South Africa	2021	ST + secondary treatment	Residential (84 households)	N/A	Inf. + ST eff.	1	6	21	110
South Africa[a]	2022	Alternative	Residential (410 PE)	N/A	Inf. + ST eff.	1	1	Non-target	108
Spain	2016	ST + secondary treatment	550–2000 PE	N/A	ST eff. + final eff.	1	2	6	66
Spain	2020	ST + secondary treatment	University campus	N/A	ST eff. + final eff.	1	12	15	138
Spain	2021	ST + secondary treatment	Office (50 people)	N/A	ST eff. + final eff.	1	8	13	103
Spain	2024	Alternative	Offices (3 buildings)	N/A	Inf. + final eff.	1	6	8	88
Sweden[a]	2017	ST + secondary treatment	Residential (1–40 PE)		ST eff. + final eff.	13	2	Non-target	61
Sweden[a]	2019	ST + secondary treatment	Residential (four households)	N/A	ST eff. + final eff.	1	1	Non-target	214
Sweden	2019	Outdoor pond + secondary treatment	Residential (500 and 3000 PE)	Ground	Inf. + final eff.	2	5	56	46
Switzerland[c]	2009	Alternative	Household (3 PE) spiked	Ground	Inf. + final eff.	1	11	23	60
USA	2006	ST + secondary treatment	Residential	Ground	In tank	1	1	2	148
USA	2007	ST + secondary treatment	High school (350 people)	Ground	ST eff.	1	2	18	149
USA[d]	2009	ST	N/A	N/A	Inf.	1	1	6	215
USA	2009	ST + secondary treatment	Residential	Ground	ST eff. + final eff.	15	1	10	140
USA	2009	ST + secondary treatment	Senior centre	Ground	ST eff.	1	1	15	90
USA	2010	ST + secondary treatment	Office + schools: high school (600 students), montessori school (51 students), girls boarding school (40 students)	Surface water and ground	ST eff. + final eff.	5	1 – 6	4	106
USA	2010	ST + secondary treatment	Households (4–5 PE < 65 years and 2 PE > 65)	Ground	Inf. + ST eff.	6	3	8	107
USA	2010	ST + secondary treatment	Households (2–4 PE)	Ground	ST eff.	3	3	13	151
USA	2012	ST/Cluster	Residential (student housing)	N/A	Inf.	2	26	17	119

Table 1 (Contd.)

Study location	Year	Design	WW source	Receiving environment	Samples	STs	Sampling events	n	Study
USA	2012	ST + secondary treatment or alternative	Households (2–6 PE)	N/A	ST eff.	8	1	3	67
USA	2013	Alternative	Centralised WWTWs	N/A	ST eff.	2	7	4	62
USA	2014	ST + secondary treatment	Households (2–4 PE)	Ground	ST eff. + final eff.	4	4	1	150
USA	2014	ST + secondary treatment	Centralised WWTW	N/A	ST eff.	2	2	16	74
USA	2015	ST + secondary treatment	Extended health care facility for the elderly (65 beds)	Ground	In tank	1	1	46	117
USA	2015	ST + secondary treatment	Household	Ground	Final eff.	4	7	8	158
USA	2016	ST + secondary treatment	Residential (graduate student housing, business units)	Ground	ST eff. + final eff.	1	34	7	153
USA	2017	ST + secondary treatment	Residential (graduate student housing, business units)	Ground	ST eff. + final eff.	1	1	8	124
USA	2021	ST + secondary treatment	Centralised WWTWs	Ground	Inf. + final eff.	3	Lab study	5	137
USA	2021	ST + secondary treatment	Centralised WWTW and single households	Ground	ST eff. + final eff.	13	42	21	105

[a] Concentrations could not be calculated from available data. [b] Enantioselective analysis of data available in ref. 69. [c] Wastewater was spiked, all are excluded from Fig. 3. [d] Sampling location not given, author affiliation used instead. [e] PE; population equivalents.

identified, of which 43 included wastewater analysis (Table 1). Most studies used grab sampling only ($n = 40$), taking a specific volume from one location at one point in time. Furthermore, often only effluent samples were taken after ST treatment or/and at the final effluent point (Table 1).[61,66,67,74,87,90,103–106] This could be due to the difficulties associated with accessing the influent, but the expected high variability in household wastewater was also mentioned as a reason.[61] Despite a high number of studies reporting APIs in STs specifically ($n = 32$), only eight studies analysed APIs in both ST influent and ST effluent ($n = 6$)[69,107–111] or ST influent and final effluent ($n = 2$),[66,112] highlighting the challenge of fully assessing the behaviour of APIs in STs. Although additional treatment of ST effluent, *e.g.*, through an infiltration field is common, it is not always required.[113] In recent years, alternative OWTWs have gained increasing attention,[60,62,65,88,108,114] potentially due to the need to improve decentralised wastewater treatment. Influent samples are however usually taken in alternative OWTWs ($n = 9$) or in pilot-scale STs receiving influent from centralised WWTWs (Table 1).[60,65,83,88,114–116]

Generally, API concentrations were higher in ST influent and effluent than in final effluent after secondary treatment and in effluent from alternative OWTWs (Fig. 3 using data from Table 1). However, a high variability of detected concentrations between different STs is observed.[87,107] For instance, Conn *et al.*[107] found naproxen at concentrations <0.1–180 μg L^{-1} in influent and <0.1–150 μg L^{-1} in effluent in composite samples from six different household STs. As STs are used by smaller groups than centralised WWTWs, individuals of the contributing population highly influence API concentrations. Mostly, OWTWs receiving wastewater from a specialised use, such as a school, hospital or café, can show a distinctive pattern in detected API concentrations.[106,117] For example, Stanford and Weinberg[106] reported 17α-ethinylestradiol, an active ingredient in hormonal contraceptives, at up to 0.4 μg L^{-1} in a ST effluent serving a boarding school for girls, higher than typical for centralised WWTWs influents.[118] The temporal variability is also higher in OWTWs as they receive fewer discrete wastewater inputs than centralised WWTWs.[119] In community STs the differences between sampling events were smaller for commonly prescribed pharmaceuticals with chronic use, such as venlafaxine, metformin and propranolol, than for less common pharmaceuticals with chronic use, *e.g.*, metoprolol and sotalol, and for pharmaceuticals with acute use, *e.g.*, antibiotics and antifungals.[69] Differences between STs also demonstrate the impact of localised prescription behaviour. For example, high variability in the enantioselectivity of APIs prescribed in enantiopure and racemic forms, *e.g.*, citalopram and omeprazole, shows the greater use of enantiopure formulations at some locations.[120] While the EF in five centralised WWTWs was 0.29–0.39 for citalopram and 0.39–0.46 for desmethylcitalopram, respectively, EFs > 0.5 were found in STs for both, indicating the prescription of enantiopure escitalopram over the racemate (Fig. 5).[32,120,121]

There are a few APIs that are often analysed using targeted analytical methods, *e.g.*, carbamazepine (56%), sulfamethoxazole (49%) and paracetamol (39%) were included in around half

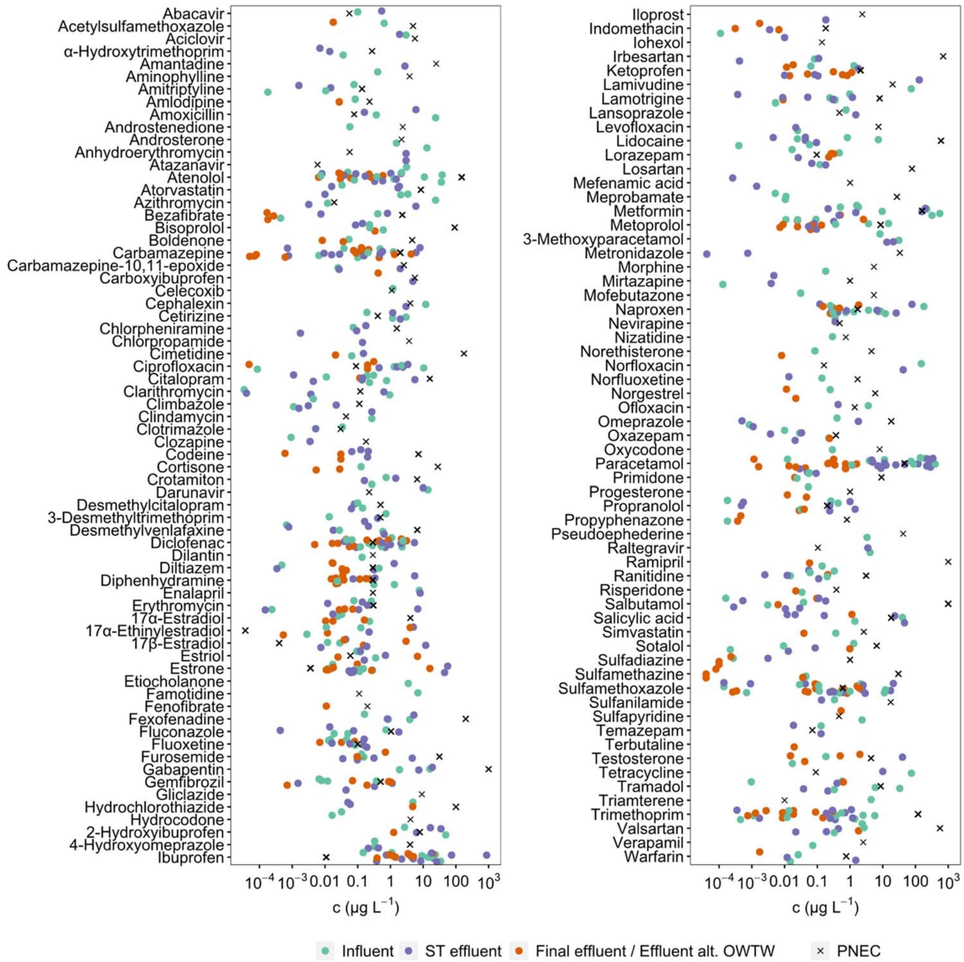

Fig. 3 Mean concentration (one data point for study and treatment type using studies in Table 1) and lowest freshwater PNEC[122] of detected active pharmaceutical ingredients (APIs) in influent, ST effluent, and final effluent (after infiltration field) or effluent from alternative OWTWs (c in μg L^{-1}; logarithmic scale). For systems receiving influent from centralised WWTWs, only effluent values were included.

of the studies. This may be influenced by most studies being conducted in one country (the USA, Fig. 4), and their comparative ease of analysis. However, both carbamazepine and sulfamethoxazole are also recognised as priority substances impacting groundwater quality by the EU.[23] For a number of compounds that are included on EU watch lists as possible APIs of environmental concern,[2,19,20,24] *e.g.* desmethylvenlafaxine,[69,111] tetracycline,[46,109] ofloxacin,[69,111] clindamycin,[110] itraconazole, ketoconazole and oxytetracycline little or no data on their presence in STs is available. Since the performance of wastewater treatment for API removal highly depends on the properties of the individual compound,[29] a large variety of different APIs should be studied to fully assess STs for removal of APIs. Existing prioritisation schemes should be used as guidance to what APIs to include in future studies.[4,19,21,23,25]

Effluent concentrations exceeded the lowest reported PNEC found for freshwater[122] for a number of APIs (Fig. 3), highlighting the need for further treatment or dilution to mitigate environmental risk. The APIs most commonly detected at concentrations above the PNEC (HQ > 1) in ST effluent and final effluent were ibuprofen ($n = 19$), estrone ($n = 15$), diclofenac ($n = 12$) and sulfamethoxazole ($n = 11$), all recognised for their ecotoxicological risk to the environment.[20,123] The highest HQs in effluent samples were found for 17α-ethinylestradiol (140 000),[62] 17β-estradiol (30 000),[62] estrone (16 000)[62] and ibuprofen (79 000)[124] with at least one study determining a mean HQ > 10 000,[62,124] indicating the potential for STs to impact the receiving environment.

4.2 Solid phase concentrations

Most studies solely focus on the liquid phase of wastewater when measuring APIs, potentially due to the additional cost and time associated with including analysis of the solids. So far, ST sludge has only been analysed in one preliminary study for APIs ($n = 57$).[111] Furthermore, one other study analysed hormones in sludge from alternative OWTWs ($n = 5$),[125] and one study investigated degradation and sorption of APIs ($n = 23$) from spiked wastewater in an alternative OWTW.[60]

Sludge can contain a large variety of APIs at a wide concentration range from ng kg^{-1} to few mg per kg dry weight (dw).[126–128] For example, 53% of the analysed APIs ($n = 30$) were found in a sludge sample from a community ST at

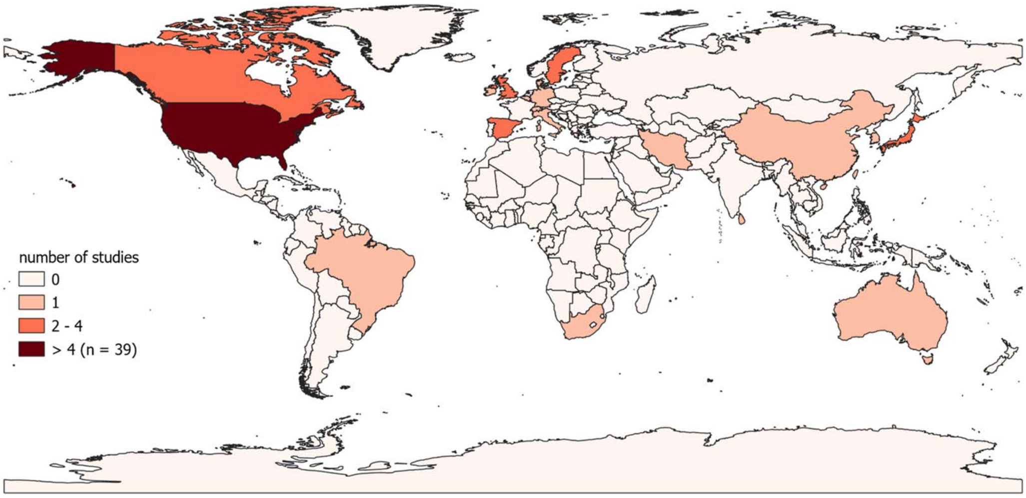

Fig. 4 Number of studies conducted in wastewater, groundwater and surface water (data in Tables 1 and 2).

concentrations from 4 μg per kg dw (bisoprolol) to 3617 μg per kg dw (paracetamol).[111] Similar concentrations are reported in sludge from centralised WWTWs, with concentrations >1 mg per kg dw most frequently reported for antibiotics and anti-inflammatory drugs.[129] Estrone concentrations were similar in activated sludge from single household OWTWs ($n = 3$)[125] and community ST sludge ($n = 1$),[111] but elevated for estriol in one of the single household OWTW, potentially due to pregnancy.[125] ST require regular emptying to remove sludge and scum that were separated from the liquid wastewater phase, and then treated in centralised WWTWs.[51,53] APIs can persist in conventional wastewater treatment and enter the environment when anaerobically digested (treated) sludge is applied in agriculture.[128,130] For example, eight pollutants (sertraline, venlafaxine, *N*-desethylamiodarone, amiodarone, norsertraline, trazodone, amitriptyline and ketoconazole) were found to pose a risk to the environment in digested sludge-amended soils after sludge treatment from centralised wastewater treatment.[126] Although consideration of all possible pathways for APIs entering the environment from STs is required, ST sludge only makes up a small proportion of all sludge treated in a centralised WWTW.

APIs can be excreted in solid matter or sorb to particles present in wastewater influent and effluent. Hence, their total concentration can be underestimated by analysing the liquid phase only,[6,45,111,131] the most common analysis strategy used.[66,88,105,114] Sometimes, samples are not filtered and the total concentration (liquid and solid phase) is reported instead.[119] So far, only two studies analysed suspended solids and liquid phase separately in STs.[69,111] Although contributions of suspended solids to the total concentration of APIs in a sample are generally small, they can be significant for APIs with high sorption tendencies, such as antibiotics and antidepressants.[127,132–134] For instance, contributions of APIs in suspended solids to their total concentration in wastewater (liquid and solid) were found to be >99% for oxytetracycline (1403 μg kg^{-1}), chlortetracycline (1623 μg kg^{-1}) and tetracycline (892 μg kg^{-1}) in final effluent of a centralised WWTW.[134]

A wider range of percentage contribution of APIs in suspended solids to the total concentration was found in STs than centralised WWTWs.[69] For example, the contribution of suspended solids to the total concentration of fluoxetine was 1.2–94% in effluents from five STs ($n = 60$)[69] but 39–74% in effluents from seven WWTWs ($n = 84$),[132] both sampled monthly for one year. Wastewater properties including temperature, pH, ionic strength, organic matter and composition of suspended solids influence the sorption of APIs.[127,135,136] Hence, a range of percentage contribution is typically observed in wastewater, which is higher in STs due to the more variable wastewater composition.[69,119]

Suspended solids can act as a vector for API release into the environment, when particles are not completely removed in wastewater treatment.[6,45] Since, the removal of suspended solids is often lower in STs than centralised WWTWs,[62,69,74] APIs sorbed to particles can have a higher contribution to total concentrations.[69] Hence, the risk of underestimating the possible environmental impact of ST effluent discharges is higher, when the sorbed concentration is not accounted for. For instance, high HQs up to 39 for clotrimazole were found when the total concentration in ST effluent as opposed to the liquid phase only was used, where all HQs were <1.[69]

4.3 Removal

Removal efficiencies are typically calculated by dividing the difference in influent concentrations and effluent concentrations by influent concentrations (eqn (1)),[74] using either mean concentrations or individual detections. While, removal efficiencies were often calculated for advanced treatment ($n = 11$)[65,74,88,103,110,114,115,137–140] and in pilot scale studies or otherwise controlled environments ($n = 8$),[65,74,88,103,110,114,137,138] only two studies report removal efficiencies in full-scale STs.[74,110] The high temporal variability in influent and effluent concentrations, differences between individual STs and often small sample sizes makes the determination of removal efficiencies difficult.[69,107] Alternatively, statistical analysis of influent and effluent concentrations could be a useful tool to determine if there is removal in the STs. Significant differences between API concentrations in influent and effluent concentrations would indicate removal in STs.[139] Effluent concentrations that are significantly higher than in centralised WWTWs also indicate no removal, in particular if the API is easily degraded in secondary wastewater treatment such as metformin and ibuprofen.[69]

The two possible mechanisms discussed for API removal in STs are anaerobic biodegradation and the physical separation of solids from the wastewater when they are bound to sludge or scum particles.[49] Sorption processes have not been studied in STs. In single-house membrane bioreactors, sorption played a significant role in the removal of some APIs, *e.g.*, macrolide antibiotics (azithromycin, clarithromycin, roxithromycin) but was negligible for others, *e.g.*, ibuprofen and sulfonamide antibiotics (sulfamethoxazole, sulfadiazine, sulfamethazine, sulfadimethoxine, sulfapyridine).[60] For instance, due to little biodegradation and high sorption, 40% of clarithromycin remained sorbed to the sludge two weeks after spiking.[60] This is in line with research on sorption of APIs to the sludge in centralised WWTWs.[126–128]

Although, the degradation of APIs is greater under aerobic conditions, anaerobic biodegradation can still be a relevant removal mechanism.[141–143] For example, anaerobic transformation has been reported for sulfamethoxazole, trimethoprim, paracetamol, venlafaxine, atenolol and clarithromycin for iron and sulphate reducing conditions with removal >60% in an anaerobic reactor.[143] Anaerobic biodegradation has not been studied in STs. The comparatively longer solids retention times and HRTs of STs could facilitate the development of different microbial populations that biodegrade APIs. Enantioselective analysis can also be useful to investigate removal processes in STs,[120] as enantiomers are considered to be affected equally by abiotic processes, such as sorption, but biological degradation processes and human metabolism can be stereoselective.[144,145] For instance, the preference of *S*(+)-citalopram over *R*(−)-citalopram in human metabolism and biological wastewater treatment, leads to enrichment of *R*(−)-citalopram in wastewater influent and effluent (EF < 0.5).[8,32] In centralised WWTWs, the EF is reduced during aerobic biological wastewater treatment (Fig. 5, $p = 7.37 \times 10^{-7}$). There are no significant differences between influent and effluent of STs ($p = 0.1583$) and therefore no enantioselective degradation, adding further evidence to the lack of biological degradation processes for APIs in the anaerobic environments of STs. However, a high variability of EFs was found (Fig. 5), introducing uncertainty to identifying small differences in enantioselectivity.

Overall, API removal in STs is expected to be limited,[110] since sorption is generally small for the majority of APIs,[29] and biodegradation is greater under aerobic than anaerobic conditions.[142] Therefore, ST effluent is often further treated, *e.g.*, in infiltration fields, constructed wetlands (mainly anaerobic or aerated), bio- or sand filters or aerobic treatment units[61,103,105,137,139] to increase API removal.[74,105,108] For example, Du *et al.*[74] found 12% removal of atenolol in STs compared to 78% after secondary treatment in a wetland and 48% in a centralised activated sludge WWTW. The removal of APIs can be influenced by the season, *e.g.*, removal efficiencies of diclofenac during warm and cold seasons were 67% and 5% in

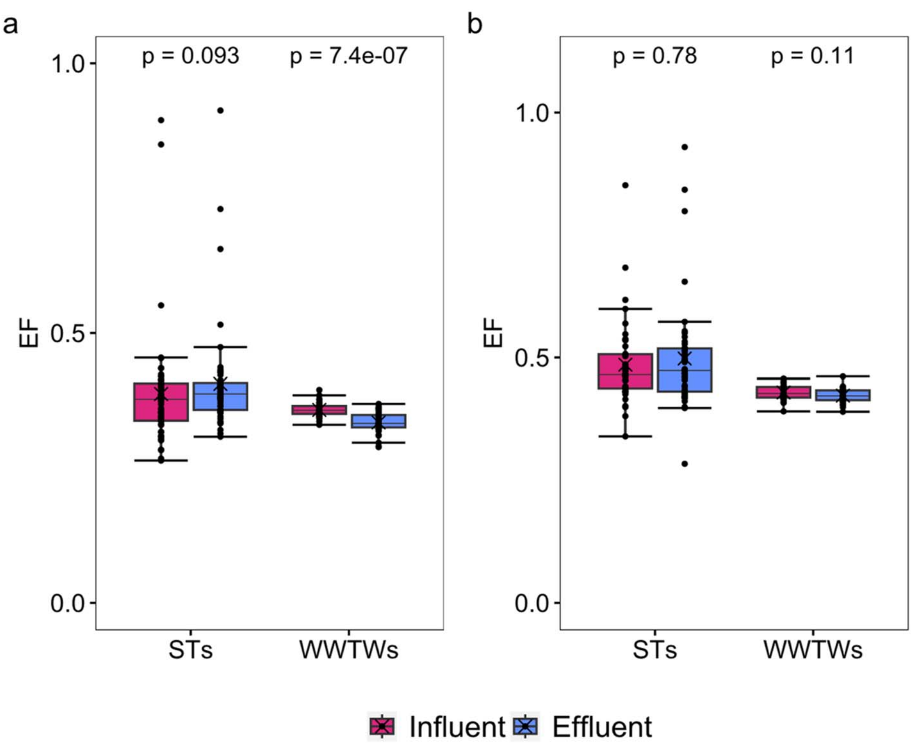

Fig. 5 Enantiomeric fraction (EF) of citalopram (a) and desmethylcitalopram (b) in influent and effluent of five community STs ($n = 60$)[120] and five centralised WWTWs ($n = 35$)[216] with Wilcoxon results (significant difference for $p < 0.05$).

a constructed wetland, and 86% and 42% in an aerated treatment unit, respectively.[66] Removal is particularly high under aerated conditions, such as aerobic treatment systems and aerated wetlands.[66,74,103] For instance, removal of ketoprofen was −30–74% in anaerobic constructed wetlands, 64–100% in continuously aerated wetlands, and 60–97% under intermittent aeration.[103] Hence, the impact of OWTWs to the receiving environment varies depending on the location and treatment technology.

5 Impact of discharges from onsite wastewater treatment works to the aquatic environment

5.1 Groundwater

Discharges from STs and other OWTWs can contribute to API concentrations in ground- and surface water due to comparatively high effluent concentrations despite expected large

Table 2 Conducted studies on active pharmaceutical ingredients (APIs) in the receiving environment impacted by OWTWs with study location, publishing year, environment sampled, number of sampling points, number of sampling events, number of APIs analysed and if any wastewater samples were also taken (WW)

Study location	Year	Environment	Sampling points	Sampling events	APIs	WW	Study
Brazil[a]	2021	River	4	2	10	Yes	112
Canada	2008	Groundwater	11	2	11	Yes	104
Canada	2008	Estuary	11	4–5	10	No	163
Canada[a]	2023	Stream	5	14–17	5	No	84
Canada	2024	River	6	3	5	No	147
China	2023	River	18	1	Non-target	No	83
Denmark	2009	Ponds and streams	13	1	8	Yes	139
Iran	2018	Sea	8	2	6	Yes	109
Ireland	2024	Rivers and streams	22	2	2	No	85
Italy	2021	Groundwater	53	1	1	No	217
Italy	2024	Drainage channels and canal	6	2	6	No	89
Japan	2016	River	30	1	1	No	170
Japan	2018	River	4	17	54	No	162
Korea	2019	Streams and creeks	48	1	8	Yes	115
Scotland	2019	River and streams	14	1	10	Yes	87
Scotland	2024	River	2	1	68	Yes	111
Scotland	2024	Rivers and stream	10	4	68	Yes	69
Scotland[b]	2025	Rivers and stream	10	4	25	Yes	120
Sri Lanka[c]	2022	Canals	11	3	5	No	218
Sweden	2019	Groundwater, lake and streams	9	5	56	Yes	46
USA[c]	1999	Groundwater	18	1	8	No	168
USA	2005	Groundwater	19–25	1	10	No	219
USA	2006	Groundwater	11	4	2	Yes	148
USA	2007	Groundwater	39	2	18	Yes	149
USA	2008	Groundwater and springs	5	2	12	No	156
USA	2008	Pond	6	2	24	No	154
USA	2009	Groundwater	11	1	15	Yes	90
USA	2009	Drainage systems and streams	27	17	15	No	161
USA	2010	Groundwater	3	3	13	Yes	151
USA	2014	Groundwater and streams	12	4	1	Yes	150
USA	2014	Streams	7	5	7	No	220
USA	2015	Groundwater	12	1	46	Yes	117
USA	2015	Lake	28	7	8	Yes	158
USA	2015	Stream	10	15–18	7	No	165
USA	2016	Groundwater	20	1	59	No	157
USA	2016	Groundwater	25	1	103	No	155
USA	2016	Streams and shoreline seeps	20	2	4	No	164
USA	2016	River	4	17	11	No	159
USA	2018	Groundwater	7	3	108	No	152
USA	2019	River, groundwater and springs	27	1	6	No	86
USA	2019	Estuary	12	2	4	No	160
USA	2022	Groundwater and stream	20	4–8	3–6	No	146
USA[c]	2022	Groundwater, canals and sea	18	3	Non-target	No	167
USA	2022	Lake and streams	30	1–4	15–20	No	166
USA	2023	Groundwater	450	1	2	No	169
USA	2023	Streams and springs	47	9	2	No	221
USA	2023	Sea	58	1	52	No	222

[a] Concentrations could not be calculated from available data. [b] Enantioselective analysis of data available in Wilschnack *et al.*[69] [c] APIs are identified but no concentration data is available, both are excluded from Fig. 6.

dilution factors in receiving waters.[46,117,146] Hence, STs and other OWTWs have received increasing attention as pathways for APIs into the environment in recent years (Table 2). Samples were usually taken as grab samples ($n = 46$) but passive samplers were also used ($n = 2$).[112,147] Again, the majority of research (57%) on APIs in ground- or surface water impacted by OWTWs was done in the USA (Fig. 4), mainly at the East coast, potentially driven by the high use of STs there. Approximately 25% of the total population in the USA use OWTWs, mostly being STs that discharge to the ground *via* an infiltration field. This is as high as 85% in some rural and forested areas in the Northeast.[148]

ST discharges have been identified as a pathway for APIs into underlying shallow groundwater and aquifers.[149] Prescription and over-the-counter drugs were detected in groundwater at concentrations from low ng L^{-1} to hundreds of μg L^{-1} (Fig. 6 using data from Table 2). The highest concentrations were found for commonly used nonsteroidal anti-inflammatory drugs (NSAIDs) ibuprofen (20 μg L^{-1}) and the aspirin metabolite, salicylic acid (12 μg L^{-1}).[104] Overall, a high variability in the detection and concentrations of APIs in groundwater is observed (Fig. 6). For example, the two most analysed APIs sulfamethoxazole and carbamazepine were detected at mean concentrations of 6.9×10^{-5} – 0.19 μg L^{-1} and 4.3×10^{-5} – 0.29 μg L^{-1}, respectively (Fig. 6). Groundwater concentrations are impacted by varying household or site specific conditions.[86] Site specific conditions include for instance the type and design of OWTWs and its performance for API removal, the proximity to discharge points, and factors affecting sorption and degradation. Sorption and degradation are for example influenced by the soil type,[150,151] redox conditions,[104,148] pH,[86] organic carbon content,[86,152] water depth,[104,146,152] and travel time from release to sampling point.[46,86,150] Differences between individual APIs depend on their sorption potential, mobility and degradability in soil.[46,104,117,153] Similar to what has been discussed for APIs in ST effluents, groundwater concentrations are also impacted by the small contributing population leading to high temporal variability within OWTWs and spatial variability between different OWTWs.[86]

Generally, concentrations and detection frequencies were lower in groundwater than in STs and infiltration fields[150,151] due to the reduction of many APIs *via* physical, chemical, and biological processes within the vadose "unsaturated" zone

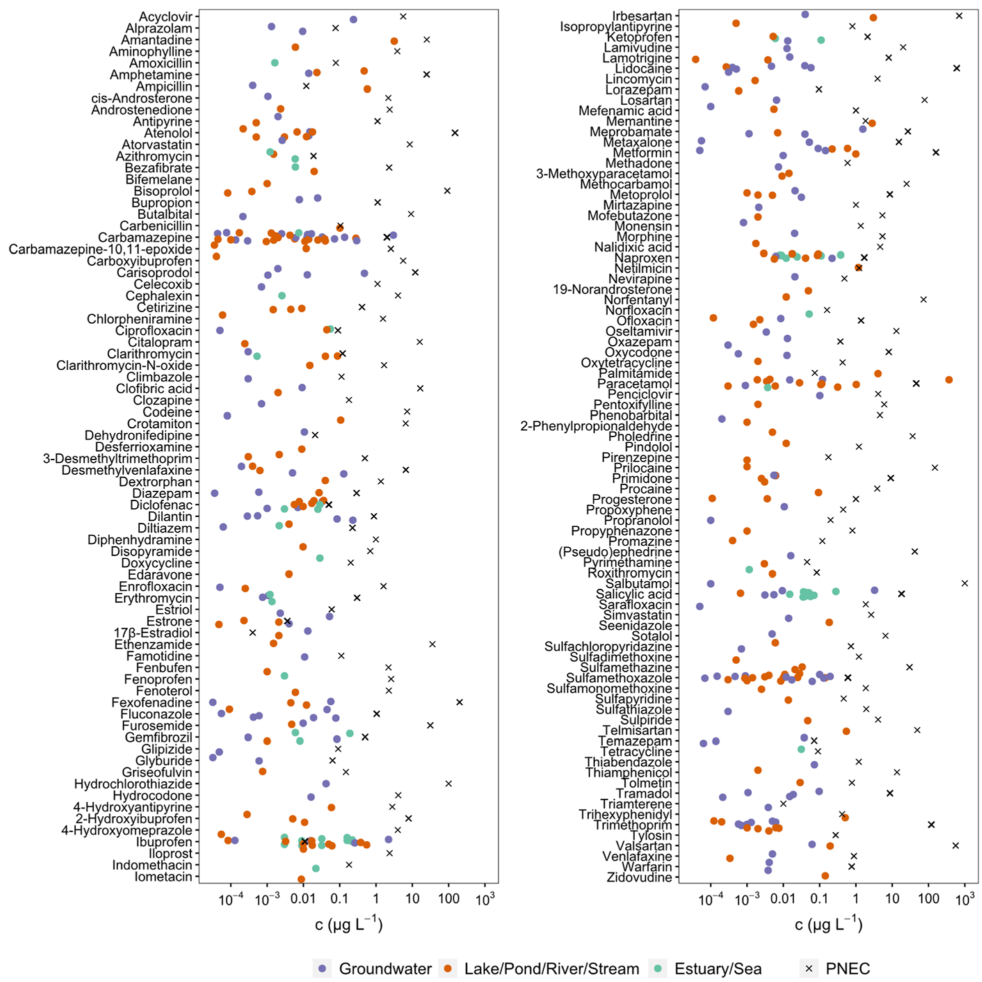

Fig. 6 Mean concentration (data from one study, studies in Table 2) and lowest freshwater PNEC[122] of active pharmaceutical ingredients (APIs) in ground- and surface water, including streams, lakes, ponds, canals and seawater, impacted by OWTWs (c in μg L^{-1}; logarithmic scale). Some locations also receive discharges from centralised WWTWs, but known data points directly downstream of centralised WWTWs were excluded.

between the land surface and the groundwater table.[46,104,117,149,153] For instance, Godfrey *et al.*[149] found a reduction of carbamazepine and sulfamethoxazole concentrations by 1.2–5 times and 15–1200 times, but still detected both compounds in groundwater impacted by STs. However, higher groundwater concentrations similar to WWTW's influent also have been reported.[104] Groundwater concentrations can exceed concentrations found in the corresponding ST effluent.[46,150] This could be due to surface water run-off as a direct pathway for APIs to groundwater, deconjugation of metabolites back to the parent API, accumulation of persistent compounds due to continuous discharges, or desorption when APIs are released from suspended solids in wastewater into groundwater.[29,46,131] Furthermore, groundwater concentrations might appear higher due to the high variability in API concentrations in wastewater which cannot be accounted for by periodic grab sampling. Normally, groundwater concentrations are, as expected, higher at sampling points located on the down-rather than the up-gradient of the ST.[46,149] However, groundwater flow patterns can be difficult to predict[154] and lower or similar concentrations have also been reported down-gradient.[46,150] Del Rosario *et al.*[150] reported higher API concentrations up-gradient, and suggested other STs as the source.

For the majority of APIs and studies, concentrations were below the lowest PNEC found for freshwater,[122] suggesting that they pose a relatively low risk to the environment (Fig. 6). However, PNECs were exceeded for 17β-estradiol, estrone and ibuprofen (Fig. 6) using mean concentrations from individual studies,[46,104,148,150,155] and additionally for individual detections of diclofenac, naproxen and sulfamethoxazole in groundwater.[46,104,152] Since areas with OWTWs, also often rely on groundwater wells as a drinking water source, ST discharges can impact drinking water quality in rural areas.[156–158] Human consumption of the impacted drinking water is the major concern of the detected APIs in groundwater receiving discharges from OWTWs. API concentrations in tap water impacted by OWTWs may exceed those typically found in public drinking water supplies.[157]

5.2 Surface water

Nearby rivers, lakes, ponds or estuaries can be impacted through the transport of APIs from groundwater to surface water or *via* direct discharge of ST effluent or final effluent discharges.[89] Although many STs discharge to the ground through infiltration fields or secondary treatment systems (Table 1), direct effluent discharge to water bodies is possible.[69] For instance, in Scotland 21% of registered private STs discharge directly to an inland water body,[59] which was indicated by high paracetamol concentrations (1100 $\mu g\ L^{-1}$) in one sample by Ramage *et al.*[87] Furthermore, preferential flow paths *via* drainage networks such as storm drains can provide a direct entry pathway of APIs from ground discharge to surface water.[84,89]

In studies where both surface water and ground water were collected from the same geographical area, most API concentrations were lower in surface water than the corresponding groundwater due to degradation and dilution effects.[46,86,146,150] However, similar concentrations for both matrices have also been found. For instance, Brewton *et al.*[146] reported primidone concentrations of 1.1×10^{-3} – 9.6×10^{-3} $\mu g\ L^{-1}$ in groundwater and 6.7×10^{-3} $\mu g\ L^{-1}$ at the nearest surface water sampling point.

Surface water concentrations are often influenced by multiple sources, including point sources, *e.g.*, centralised WWTWs and direct discharge from OWTWs, and diffuse sources, *e.g.*, wastewater impacted groundwater and agricultural runoff.[159–161] Then, centralised WWTWs are generally the main entry source for APIs to the aquatic environment.[89,159,162] However, larger community STs can have significant contributions to river water concentrations for some APIs.[111] For example, concentrations of paracetamol and its metabolite 3-methoxyparacetamol increased by *a* factor of 14 and 10 in river water downstream of a community ST compared to upstream to 0.59 and 0.026 L^{-1}, respectively.[111] Typically, API concentrations are lower in areas impacted by OWTWs only than in areas impacted by centralised WWTWs only, or centralised and decentralised systems.[163] For instance, carbamazepine and paracetamol concentrations were 0.026–0.21 $\mu g\ L^{-1}$ and 2.0×10^{-3} – 0.013 $\mu g\ L^{-1}$ downstream of a centralised WWTWs, and $<1.1 \times 10^{-4}$ – 2.2×10^{-3} $\mu g\ L^{-1}$ and $<5.6 \times 10^{-4}$ – 9.9×10^{-3} $\mu g\ L^{-1}$ upstream of the WWTWs in a river receiving ST discharges only, respectively.[159] While centralised WWTWs have higher removal efficiencies, their greater impact to API concentrations in surface waters can be attributed to lower dilution factors.[62,89,159,164]

STs are still an important pathway for APIs demonstrated by their presence in the impacted environment at ecotoxicologically relevant concentrations.[69,164] For instance, mean concentrations of 17β-estradiol, ampicillin, ibuprofen, memantine, palmitamid, paracetamol and trihexyphenidyl exceeded the PNEC (HQ up to 50) in surface water at 18 detections from a total of nine studies (Fig. 6), representing a small proportion of the analysed samples (≤5%). In particular in surface waters with low effluent dilution factors, *e.g.*, small streams,[69,85,87] or in areas with a high density of OWTWs,[84,154,165] direct ST discharges[87] or malfunctioning STs,[164] concentrations can exceed those typically reported for catchments impacted by centralised WWTWs.[85] Repairing or replacing failing STs can reduce API concentrations in nearby surface waters substantially.[164]

In rural areas with low population densities, other sources than human wastewater such as agriculture, *e.g.* large animal husbandry operations, recreational activities and improper waste disposal, can contribute to API concentrations in surface water.[115,159,161,166] Therefore, effort was made to distinguish between different pathways (STs *vs.* centralised WWTWs and STs *vs.* agriculture) into the environment. Proposed tracers include human consumption products, *e.g.*, sucralose[46,146,167] and caffeine;[85,149,168] human APIs, *e.g.*, paracetamol, carbamazepine[146,149,156] or sulfamethoxazole;[169] traditional water quality parameters, *e.g.*, chloride,[46] or ratios of different compounds or parameters.[85,170] Differences in the enantioselective composition of effluent from centralised WWTWs and STs, *e.g.*, using the EF of naproxen, were also proposed as ST tracers.[120] The simultaneous presence of infrequently used pharmaceuticals, *e.g.*, carbamazepine and sulfamethoxazole, indicates influence of multiple waste streams found in centralised WWTWs or effluent from multiple households over single house STs.[164]

6 Future perspectives

6.1 Monitoring strategy

Previous research, has often focused on the liquid phase of the ST effluent only.[46,61,87,103–105] One challenge of sampling ST influent, particularly for smaller systems, is the accessibility to a suitable sampling point. The majority of STs are used by one or few households over whole communities, where normally the influent pipe directly connects the house to the ST underground. Community STs or STs specifically designed for research purposes are often equipped with suitable sampling points, allowing the collection of influent and effluent samples.[69,109–111,137] However, they are maintained better than smaller systems and their performance therefore may not be representative of such typical ST systems. Furthermore, API concentrations might not be representative of typical single-household STs, as they are used by larger groups of people or people with specific demographics, *e.g.*, university students (Table 1). For full-scale STs, information on maintenance, *e.g.*, the emptying frequency, and design, *e.g.*, torpedo *vs.* rectangular, number of compartments in baffled reactors and tank size are often not discussed, potentially due to limited data availability. However, obtaining this information in future studies is important as it can impact the ST performance for API removal. Future studies should include both private STs (the most commonly used OWTW) and community STs that have highest likely risk due to their smallest dilution factor of discharges in the environment.

Most studies are not extensive in nature, *e.g.*, around half of the studies ($n = 20$; 47%) only sampled once or twice (Table 1) and all except three studies[107,108,112] used grab sampling only ($n = 40$), not allowing to address maintenance related changes in the STs' performance. Owing to the small contributing populations to STs, the temporal variability in influent and effluent concentrations of APIs and the differences between different STs are high,[69,106,119] demanding a composite sampling approach. For instance, Ort *et al.*[171] recommended a flow-weighted sampling process with a sub-sampling frequency of 5 minutes, as time- or flow-weighted samples taken at larger intervals might not be representative of highly dynamic wastewater. This is especially important for STs with highly variable flow conditions and API concentrations. Conn *et al.*[107] took flow-weighted samples from ST influents but time-weighted samples from ST effluent, potentially due to access difficulties at ST effluent points. Mladenov *et al.*[108] collected 24 h time-weighted composite samples from ST influent and effluent points 24 h apart to account for the HRT of 1.4 days. Flow-weighted composite sampling with a high sample number and low sub-sampling frequencies is recommended for future work when investigating API removal in small WWTWs such as STs. Even though this is more expensive and logistically challenging due to the rural location of many STs, benchmarking the removal efficiency of STs accurately for comparison to other WWTWs is essential. This would also allow determining ST performance for API removal at different temperatures and before or after sludge removal. In general, microbial activity and therefore biodegradation increases at higher temperatures, which can impact the efficiency of wastewater treatment.[172–174] Emptying the STs can impact their performance due to an increase in volume and thereby HRT and removal of beneficial microorganisms. Sampling should be conducted over consecutive days equivalent to several times the estimated HRT to account for the temporal variability in wastewater concentrations. Alternatively, passive sampling also allows the determination of time weighted average concentrations over week-long deployment periods,[175,176] and hence the removal efficiencies in STs.[112] Due to changes in ST performance, multiple deployments throughout the year are necessary. Information on short-term variability, only assessable by grab sampling, provide useful information on individual's practices,[120] and it might be beneficial to combine multiple sampling approaches after carefully evaluating the objectives of each study.

Further research on a broad range of APIs in ground- and surface water is needed as their occurrence depends on the physicochemical characteristics of individual APIs that impact their sorption potential, mobility and degradability in soil.[104,117,153] However, 75% of studies ($n = 34$) using targeted methods included 20 or less APIs (Table 2) and often the same APIs, such as carbamazepine ($n = 32$), sulfamethoxazole ($n = 28$), paracetamol ($n = 18$) and ibuprofen ($n = 17$), are analysed (Fig. 6). Alongside ibuprofen (HQ up to 200),[104] high HQ $\geq$ 10 were also found for less frequently analysed APIs palmitamide,[83] ampicillin,[83] 17β-estradiol,[148] and estrone,[148] that are not all recognised as priority substances,[23] highlighting the need for intensive monitoring to further our understanding. There is limited information available on some APIs included on the last EU watch list,[24] *e.g.*, clindamycin ($n = 1$),[161] itraconazole ($n = 0$), ketoconazole ($n = 1$),[155] oxytetracycline ($n = 1$),[162] and guanylurea ($n = 2$). As discussed for ST effluent, the high temporal and spatial variability need to be considered. Both long-term, due to the seasonality of pharmaceutical use and river flow, and short-term variability should be taken into account.[85,159,164] Again, composite or passive samplers would allow to determine average contribution of ST discharges to the receiving environment.[147]

Antimicrobial resistance (AMR) is a significant concern to global human health.[177–179] So far, few studies have been conducted in areas impacted by STs, potentially because discharges from centralised WWTWs and agricultural inputs are usually highlighted as the most important pathways for ARGs into the environment.[177,180–184] Few studies have reported ARGs in effluents from STs, alternative OWTWs and the receiving ground- and surface water.[178,179,185–191] However, all reported a strong abundance of ARGs, *e.g.*, Tan *et al.*[190] found 441 ARGs relating to 26 antibiotic classes in STs, and the contribution to AMR abundance in the environment is highlighted.[185,190,191] For instance, Damashek *et al.*[185] reported samples with the highest abundance of ARGs in a watershed were associated with STs over discharges from centralised WWTWs or agricultural industry, highlighting the need for further research on the contribution of STs to AMR and associated antibiotics.

6.2 Approaches to reduce the impact of septic tank discharges to pharmaceutical concentrations in the environment

The numbers of APIs detected above the PNEC in ST effluent and the receiving environment, highlighted the need for alternative approaches at some locations. Locations with low dilutions, a high density of STs, proximity to bathing waters or environmental protection zones, and where private drinking wells are being used need priority.

A large variety of secondary treatments and alternatives to STs exist that are known to increase API removal and are already in use at full-scale. Existing treatment options include infiltration fields, anaerobic or aerated constructed wetlands or packaged treatment plants.[61,103,105,137,139] Traditionally, ST discharges are treated by infiltration fields, which are easy to construct and can be added to existing STs, but require sufficient space and deep, permeable soils.[47,51,58] Although API concentrations are reduced through sorption and biodegradation in infiltration fields and underlying soil, discharges are still known to contribute to APIs in ground- and surface water.[124,150,151] Furthermore, they are not effective at locations with a high water table or low soil permeability. Here, mound systems, sand filters or constructed wetlands can be used.[49,59] Constructed wetlands combine natural processes such as biodegradation, sorption and plant uptake,[28,138,192] are low in cost and require little maintenance,[138] whilst reducing API concentrations.[103] API removal can be further increased using aeration,[103] *e.g.*, in aerated wetlands or packaged treatment plants. Packaged treatment plants are normally relatively small, but require electricity to operate, can be expensive and challenging to install or/and maintain, have higher operating costs than constructed wetlands, and can produce odour due to ventilation openings.[55,193] The operation costs, maintenance requirements and therefore increased responsibilities for individuals who manage them, increase the risk of these plants not working properly. For example, it was found during inspections that they were not switched on and therefore not operating as intended.[48] Overall, different decentralised wastewater treatment options exist that reduce API concentrations to various degrees and at varying costs.[193] There is no one size fits all approach, but rather the type of wastewater treatment should be decided for each individual site.

Alternatively, the impact of STs to API concentrations in the receiving environment might be reduced by targeting a reduction in their concentrations in influent wastewater, *e.g.*, by improving pharmaceutical design towards more environmentally friendly compounds and optimising their delivery, changing prescribing practices and reducing pharmaceutical waste.[194–198] Environmentally informed "green" prescribing includes changes in medicine selection, use, and dosages.[195,196,199] For instance, diclofenac purchases were reduced in Swedish pharmacies when it was placed behind the counter due to its harmful effects on the environment.[200] For chiral APIs with racemic prescription, switching to enantiopure formulations with the less environmentally toxic enantiomer, when both enantiomers have equal effects on the human body, or by using the enantiomer that has more activity towards the desired therapeutic effect in humans over the racemate can also reduce environmental impact.[120] Furthermore, non-pharmacological interventions, *e.g.*, psychotherapy, exercises or physical therapy, could effectively reduce pharmaceutical use by simultaneously benefitting the patient.[195,199] One of the APIs frequently found above the PNEC was ibuprofen (Fig. 6), hence over-the-counter purchases also need to be considered. Leftover or unwanted pharmaceuticals can enter the environment through landfill leachate[40] and direct down-the-drain disposal.[120,201] Potential direct disposal of antidepressants was previously observed in ST influent.[120] Hence, reducing the need for disposal by decreasing the number of unused pharmaceuticals, preventing waste by controlled reuse or redistribution programs, and encouraging safe disposal, can have a beneficial effect on environmental concentrations.[197] Since those efforts would be targeted towards a small population when considering OWTWs, they are expected to have a greater effect than in more densely populated areas. Deprescribing interventions successfully reduced the numbers of used pharmaceuticals, but are labour intensive,[202,203] and can therefore currently only be directed at small groups. The impact of localised prescription and population behaviour on API concentrations in STs used by smaller populations has previously been shown,[69,88,106] and rural communities have already been targeted in programmes to reduce APIs in the environment *via* upstream solutions.[204] Furthermore, barriers to environmentally informed prescribing, such as lack of knowledge, confidence, time and resources[205] could be more easily addressed at a local level when targeting fewer prescribers. Overall, upstream solutions, such as sustainable medicine use, have great potential of being successful for small populations that can be specifically targeted by interventions. Keeping ethical considerations and the protection of individuals in mind is essential when these interventions are established in small communities.

6.3 Ethical considerations

Considering the ethical implications of any work is important, but essential when working with small groups, or vulnerable individuals or groups. Wastewater data is usually collected without obtaining informed consent from the contributing population as wastewater is considered an environmental matrix and no information on individuals are acquired.[206–210] However, with the COVID-19 pandemic and the increasing use of wastewater based epidemiology for monitoring illicit drug use and pathogens, ethical concerns of wastewater surveillance have received increasing considerations.[207,208,210,211] Wastewater surveillance can generally be justified due its benefits to public health or the environment,[209] and analysing APIs in wastewater or the receiving aquatic environment does not usually raise privacy concerns as individuals cannot be identified when large populations are monitored.[206,208] However, special considerations need to be made when obtaining data related to small groups, *e.g.*, from ST wastewater, or marginalised communities, as results could potentially have negative effects on individuals, *e.g.*, through increased stigmatisation or the creation of adverse policies.[206,208]

Anonymising locations is an essential measure to protect individuals' privacy but might not be sufficient when small populations are monitored. The fewer people that use the ST, the more carefully ethical implications need to be considered. For instance, while anonymising locations for a community ST might be sufficient, informed consent should always be obtained before analysing APIs in household wastewater. The type of APIs selected for a study should also be carefully considered. Even the use of commonly prescribed pharmaceuticals, such as anti-depressants, is still stigmatised.[212,213] Analysing APIs that are taken without the knowledge of other household members or that are illegal in the area, *e.g.*, the abortion medication mifepristone, might put individuals at risk when the use is revealed. Furthermore, study locations should be carefully selected, and implications for marginalised communities considered. For instance, the presence or absence of HIV medications could further increase assumptions around the virus. It is always essential to evaluate the benefits of the study to public health or the environment, against the potential harm to individuals or small groups.

7 Conclusion

This review demonstrates the progress that has been made in understanding OWTWs as a pathway for APIs to the aquatic environment. Investigating APIs in OWTWs and their contribution to the aquatic environment poses several challenges, such as the high variability in API concentrations in wastewater from small communities and the difficulties associated with sampling influent, effluent and groundwater in rural locations. Further research on the detection and removal of a variety of APIs in OWTWs and their impact to ground- and surface water is needed. One priority in future should be to determine removal efficiencies in STs and alternative OWTWs by carefully selecting study design and sampling strategy. The high temporal and spatial variability need to be considered by sampling multiple OWTWs throughout the year. Available data suggests limited removal of APIs in STs, and a potential impact to surface and groundwater, indicated by concentrations exceeding the PNEC. Efforts towards sustainable medicine use and achieving greater API removal in OWTWs should be made.

Author contributions

Kai Wilschnack: writing – original draft, visualization, investigation, formal analysis, data curation, conceptualization. Elise Cartmell: writing – review & editing. Kyari Yates: writing – review & editing, supervision. Bruce Petrie: writing – review & editing, supervision, project administration, funding acquisition, conceptualization.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results have been included, and no new data was generated as part of this review.

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