Effective removal of selected active pharmaceutical ingredients in wastewater by conventional and 'nature-based' treatment technologies

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Abstract

Due to recurring expenses like operation costs, which frequently do not justify the investment costs, the economic viability of conventional treatment facilities in areas with large seasonal population turnover or low populations is a big challenge. To successfully decrease the release of toxins into river basins, it has become crucial to consider alternate treatment methods for home and industrial wastewater. 23 active medicinal compounds were examined, and 8 were found in 6 nature-based treatment facilities and 3 in conventional wastewater treatment facilities. It was vital to find out whether the nature-based removal technologies would have comparable removal efficiency to the traditional treatment works while examining the removal efficiencies of the discovered contaminants across the nine locations. This work employed passive Diffusive Gradients in Thin Films (DGT) samplers using XAD Amberlite 18 as the binding gel. Clarithromycin effluent concentrations were higher than influent concentrations at all three conventional treatment facilities, suggesting that CLM may have entered the treatment system in a conjugate form rather than the compounds we looked at. Sui et al. (2015) identified CLM as one of the PPCPs with negative removals in the secondary treatment facility.

Sulfamethoxazole, on the other hand, had clearance rates that ranged from low (1% to 43%) to high (93% in the case of CFX). The total amount of oxidizable chemicals in wastewater are measured by chemical oxygen demand (COD), whereas biological oxygen demand (BOD), which measures the amount of oxygen needed by bacteria and microorganisms in the system to completely oxidise the available organic material, is a

crucial factor in determining the quality of water. The elimination rate is better the greater the BOD: COD ratio (Etchepare & van der Hoek, 2015). The BOD/COD ratio of 0.45, however, made the low removal rate at Olo's conventional treatment facility predictable. influent loads shown to affect removal rates in nature-based technologies; treatment attempts to create and the physicochemical properties of the compounds. The multi-staged pre-treatment system in the nature-based system was shown to have a greater removal rate of CLM, whereas single-bed treatments had lower removal rates. The majority of the chemicals across all nature-based technologies were eliminated compared to the conventional system, with the exception of nature-based Jes treatment technology having removal rates < 1% for SPD, SMX, and CLM. The elimination of certain pharmaceutical compounds may be accomplished using nature-based treatment technologies, which can be regarded as a viable substitute for traditional treatment methods. The amount of land needed for the building, the population to be serviced economically, and the wastewater supply must all be taken into account. The compounds that have removal rates of less than 1% may have entered the treatment facilities in conjugate form, and biological processing changed those compounds into SPD, SMX, and CLM. In other cases, the chemical of interest may be a metabolite of the parent compounds that was not detected in the influent channel. Instead of drawing conclusions about the effectiveness of the treatment systems or processes, more research on a thorough examination of the available PPCPs would provide greater insight and knowledge into the origins of these compounds that are common at the effluent.

Introduction

The improper use and discharge of antibiotics into surface waters has contributed to the widespread appearance of the antibiotic resistance gene. Human use, whether through personal use or veterinary prescriptions, is a significant influence in the rising incidence of antibiotics in the environment (Watkinson et al., 2007; Zheng et al., 2011). Because bacteria have evolved to resist the effects of antibiotics when taken by people, improper antibiotic use has been related to higher death rates. Hospitals (Fischbach & Walsh, 2009; Ling et al., 2015; Hopkins & MullerPebody, 2015) and researchers have noted an upsurge in infections that are resistant to antibiotics. New types of antibiotics may need to be created to treat various bacterial illnesses, according to some publications on antibiotic resistance. In research spanning 76 countries between 2000 and 2015, Klein et al. (2018) reported that daily consumption rates of antibiotics grew by 39%, or 11.3–15.7 DDDs per 1,000 people per day, while antibiotic specified daily doses (DDDs) climbed by 65% (12.1–34.8 billion DDDs). Beyond treating diseases in their cattle, farmers frequently use antibiotics to increase their productivity (Watkinson et al., 2007; Zhou et al., 2011) in intensive food production.

A variety of antibiotics have been created by researchers for the prevention and treatment of infections in humans, animals, and plants, as well as for stimulating and boosting livestock development. Since the discovery of penicillin in 1928, the development of antibiotics has outpaced that of other classes of medications for the betterment of human health (Cabello, 2006; Martinez et al., 2002). However, keeping these advancements in mind, it has been predicted that drug-resistant diseases account for 700,000 yearly deaths, with a prognosis of 10 million deaths annually by 2050. Antimicrobial resistance threatens 100 trillion dollars' worth of economic production (O'Neill, 2016). The main causes of pharmaceutical compounds in the environment are anthropogenic activity (Chen, 2016; Zhang et al., 2012). The overuse of antibiotics should be avoided and restricted, but it is crucial to stress that there will always be a load in wastewater that has to be treated. Some of these toxins have been demonstrated to have negative impacts on aquatic fauna, such as algae, in addition to ties with the spread of antibiotic resistance (Akcha et al., 2010; Wilson, Smith, Denoyelles, & Larive, 2003).

Major classes of Antibiotic

There are seven main categories that may be used to group the therapeutic compounds used in antibiotics, a diverse chemical class obtained from natural sources (Barker, 1998). These classifications, as said, so represent their value for human consumption and agriculture.

β-lactams penicillin, cephalosporins, monobactams, carbapenems, and amoxicillin all have a beta-lactam ring in their molecules. This family of antibiotics is used to treat a variety of bacterial illnesses, such as tonsillitis, throat infections, skin infections, and urinary tract infections. This family of antibiotics is particularly vulnerable to hydrolysis due to the chemical instability of the -lactam ring, whereas penicillin is rapidly removed, having an elimination half-life of roughly 1.4 hours. Penicillin, which has a short half-life and is seldom found in the aquatic environment, as well as amoxicillin, which has a half-life of around 62 minutes (Barker, 1998; Hirsch, Ternes, Haberer, & Kratz, 1999). Records revealed that penicillin and macrolides had the highest prescription rate of 23% before the year 2000 (Vaccheri, Castelvetri, Esaka, Del Favero, & Montanaro, 2000), while prescriptions for penicillin and their consumptions increased from 43% to 52% between 2007 and 2015, despite the lack of comprehensive data on antibiotic consumption rates at the time of this study (Di Martino, Lallo, Kirchmayer, Davoli, & Fusco, 2017)

Tetracyclines have a wide range of antibiotics that are effective in treating numerous illnesses, mostly in impoverished countries. The majority (over 60%) is eliminated in the urine, with an 8–11-hour elimination half-life. This family of antibiotics has the ability to form stable complexes with calcium and other related ions, which have a great attraction for suspended organic materials and sediments (H. Chen, Jing, Teng, & Wang,

2018; Hirsch et al., 1999; R. Zhang et al., 2013). This includes substances like Sumycin, Panmycin, and doxycycline as well as Vibramycin, which are readily identifiable in the freely dissolved condition in the sludge and typically removed between 86.4 and 93.6% of the time (Wang, Ben, Li, Liu, & Qiang, 2018).

***Macrolides*:** This family of antibiotics is used to treat infections brought on by Gram-positive bacteria including Streptococcus, Staphylococcus, Enterococcus, and restricted Gram-negative bacteria such Actinobacillus pleuropneumonia, soft tissue, and respiratory tract infections. Since it has a slightly wider spectrum than common antibiotics and contains erythromycin, roxithromycin, azithromycin, and clarithromycin, which are among the most important antimicrobial agents used for human treatments (Parmar & Rawat, 2012; Piddock, Ricci, Stanley, & Jones, 2000; World Organisation for Animal Health (OIE), 2016), it is a replacement for patients with penicillin allergies. The study also revealed that urine is the primary route of elimination for erythromycin's unconjugated parent molecule, Roxithromycin, 10-20% of Clarithromycin, 6-12% of Azithromycin, and 50–67% of Macrolides (McArdell, Molnar, Suter, & Giger, 2003). During the treatment of wastewater, they are partially eliminated (Giger et al., 2003; Huset et al., 2008; McArdell et al., 2003).

Fluoroquinolones during treatment, have a significant affinity for sewage sludge, and as a result, greater proportions are adsorbed into the sludge. However, this does not preclude the possibility that some of the agents in the group are still present in dissolved form in the treatment water effluents (N. Li, Liu, Xue, Wang, & Dai, 2017; Lindberg et al., 2006). According to Golet, Strehler, Alder, and Giger (2002), the removal rate for this group in wastewater varies from 94.5% to 99.9% biodegradation, whereas soil modified with sewage sludge has a removal rate of 75% to 92%. (Guo et al., 2017) There are two main subcategories of fluoroquinolones (Van Der Heijden et al., 2013). Ciprofloxacin, Norfloxacin, and Ofloxacin are included in the earlier group, whilst Gemifloxacin, Levofloxacin, and Moxifloxacin are included in the more recent category. Some products in this more recent category are even not advised for children (Lipsky & Baker, 1999; Schaad, 2005) because they may result in bacterial resistance and cause arthropathy in young animals. Many of these products are toxic in the body and have been discontinued or used with restriction (Warren, 1997; Zhanel et al., 2002).

Nature-based treatment technology

The biological treatment system of wastewater is used in secondary and/or tertiary stages by nature-based treatment methods, sometimes referred to as reed beds (Sundaravadivel & Vigneswaran, 2017), to eliminate organic contaminants from wastewater. According to Stuart, Gooddy, Bloomfield, and Williams (2011), the development of viable microorganism populations that are in charge of the biodegradation of the waste is crucial for the design of nature-based or artificial treatment wetlands systems. These systems must include vegetation such as cattails,

reeds, and reed canary grass. The wastewater enters the treatment lakes or basins after passing through a filter system to remove the biosolids and gravels in a controlled flow (Rozkosny, Kriska, Salek, Bodik, & Istenic, 2014). Various wastewater types are considered throughout the design process, and suitable treatment systems are available to offer an acceptable level of treatment that satisfies user demands. There may be a vertical or horizontal flow system in some of the designs. Polluted stormwater runoff, municipal wastewater, industrial wastewater, and agricultural runoff are examples of typical wastewaters. A complex interplay of physical, biological, and chemical processes purify wastewater as it moves through a horizontal or vertical permeable filtration system. Figure 1 below shows how these systems may be constructed with sedimentation pre-treatment or without it, which is sometimes referred to as the French System (Rozkosny et al., 2014)

The flow of operations for nature-based treatment methods is regulated by a number of sections or phases. Vertical flow reed bed filters (VRBF) are used in the nature-based technologies under study as the initial step, together with horizontal subsurface flow basins (SFS-h), vertical subsurface flow basins (SFS-v), and free water systems (FWS). The filters separate the organic biosolids and gravels from the wastewater as it passes through them. There are two types of water flow systems: horizontal flow (HF) and vertical flow (VF). In the latter, the water flows vertically while being filtered through a 0.2 to 4 mm gravel-sand bed at a height of 0.9 to 1.5 metres (Nivala et al., 2013). However, the wastewater flow in HF systems, as seen in Figure 1 above, is horizontal across different stages. Another option for VF treatment technology is one without a mechanical pre-treatment chamber (Reeb & Liey, 2011). Wetland macrophytes have been used as a potential replacement for the traditional wastewater treatment system since they were first tested in Germany in 1950 (Vymazal, 2005; Vila, Garf, & Garca, 2013).

Compared to conventional forms of therapy, nature-based technologies, or NBTs, have several advantages. Due to the system's ability to run without power or pumps and its ease of building, operational expenses are extremely cheap. However, the design of the treatment beds, which might be multi-staged or single-stage treatment lakes, could increase the quality of the treated water. NBT has a positive impact on the climate in the area by increasing biodiversity, allowing plants access to biologically rich water, and reducing the need for energy supply. A high treatment performance might be attained with little maintenance costs with suitable design. However, it is an excellent method for the macrophytes to economically remove the bioavailable organic nutrients nitrogen, phosphorus, and potassium on a seasonal basis dependent on climatic circumstances. According to Alvarez, Ruz, and Soto (2008), a well-designed nature-based treatment technique (NBT) may remove COD with an efficiency of 70% to 83%, suspended particles with 48% to 91%, total nitrogen with 27% to 70%, and phosphorus with 26%

to 89%. The elimination of organic matter as measured by biochemical oxygen demand (BOD) was over 80%, total nitrogen (TN) was between 32% and 66%, and total phosphorus (TP) was above 94%, according to separate research of nine NBT that Jenssen et al. (2010) did over the course of three years. This two research concur with one another. Studies have further demonstrated that pre-treatment filters remove the bulk of the nitrogen and BODs.

The main issue with NBT construction is land availability. The size of the site depends on the treatment plan, which may entail primary, secondary, or tertiary stages, and wastewater loads should be considered in proportion to the intended population of the treatment facility. High sorption capacity biofilters have demonstrated efficacy in the removal of phosphorus from the effluent water where 1.0 mg P l1 was discovered from 95.4 to 99.9% where filters in the basic configuration play an essential role. Additionally, the clearance rates for ammonia (NH4) and total nitrogen varied from 32 to 66%. (Jenssen et al., 2010). If the mechanical pretreatment system is poorly built, the filtration material runs the danger of clogging. Despite some worries about the lack of vegetation development, particularly during the harsh winters in Europe, attention should also be paid to the different plant species.

Through the removal of some of the main nutrients through sorption, suitable vegetation in the NBT is essential in the development of a sustainable habitat for microorganisms. These aquatic plants include water hyacinth, duckweed, and green algae (Chlorella Vulgaris). Absorption in the form of plant nutrients improves the efficiency of organic nutrient elimination. The vegetation around the treatment beds consumes these nutrients. It has been demonstrated that plants may reduce nitrogen levels in tested water, improving water quality to a permissible level at which such water may be recycled for irrigation. According to research by Badr El-Din and Abdel-Aziz (2018), over the course of a 21-day trial, duckweeds, green algae, and water hyacinth may all lower the chemical oxygen demand (COD) and biological oxygen demand (BOD5) in wastewater by 43% and 42%, respectively. The study confirmed that duckweeds are a potential plant for wastewater treatment because of their greater N, P, and K pollutants removal effectiveness. Nevertheless, Rozkosny et al. (2014) found that NBT may achieve high COD and BOD treatment performance of 85% BOD5, 75% COD, and 30% NH4-N while filtration and sedimentation (SS) removal efficiency is 80%. With a 35% removal effectiveness, phosphorus is removed through sorption/binding of phosphorus (TP) onto the filter.

Beds made of the substrate, water column, water-tolerant plants, and bacteria that facilitate microbial breakdown are examples of nature-based technology. This substrate stage might consist of soil holding developing wetland plants, gravel, or sand. These treatment methods employ a system of treatment beds or reed beds with wetland plants having hydrophyte and macrophyte leaves (Bouwman et al., 2013; Pinckney, Paerl,

Tester, & Richardson, 2001; Songliu, Hongying, Yingxue, & Jia, 2009). These facilities and the amount of time wastewater spends in the treatment ponds are essential to the process. As an alternative to direct release into receiving rivers or estuaries, these systems can also be utilised to retain and treat excess effluent that has to be treated at conventional wastewater treatment facilities. Daily wastewater loads at the study's chosen locations ranged from 8 to 55,000 m3/day. Small to medium-sized towns and developing nations are best served by nature-based treatment technology, which has been recognised as an effective sustainable wastewater treatment method (Sundaravadivel & Vigneswaran, 2017). They have been observed to be advantageous for the protection of several native species of fauna and flora, amphibians, and invertebrates, as well as for increasing the quality of treated water, in addition to their advantages in terms of operational expenses (Brix, 1994).

Aims and Objectives

This study compared nature-based treatment technology with conventional treatment works to examine the efficacy of removing pharmaceutical active compounds from wastewater. The study also sought to determine whether it was a financially sound and practical alternative to conventional treatment methods. According to its time-weighted integrated sampling capability TWA, portability, which supports its suitability for use in any sampling medium regardless of depth, and its transportability, the Diffusive Gradients in Thin-Film Passive (DGT) Passive Sampler was an appropriate tool in both deep and shallow sampling medium. Removal rates and characteristics of various chemicals in both systems were taken into consideration.

Method and Materials

DGT passive Sampler

About 30 years ago, the first passive water sampler was developed, which has subsequently lowered the operational obstacles associated with water sampling (Kot-Wasik et al., 2007a). Since then, a lot of passive samplers have been created, which has decreased the operational constraints associated with using active samplers, including power supply, downtime due to system failure, field calibrations, and security of the active sampling equipment (Kot-Wasik et al., 2007). Polar Organic Compound Integrative Sampler (POCIS), Membrane Enclosed Sorptive Sampler (MESCO), and Semi-Permeable Membrane Devices are a few of the passive samplers that are readily accessible (SPMD). Grab sampling, which involves removing tiny amounts of fluid from a medium over time to create a representative mixture, was another common sample technique. During the feasibility stage of the study, this method was compared with Diffusive Gradient in Thin-Film (DGT) passive samplers, and DGT was found to be more appropriate and sustainable for this study considering the cost implications of site location and the significant manpower requirements, aside from the fact that it is

unable to consistently monitor chemical activity in the sampled medium. The majority of earlier investigations came to the following conclusions about the dependability of the grab sample method:

Chemical signals exhibit substantial temporal fluctuation, which is taken into account by time integrated sampling techniques like DGT, POCIS, etc.

1. Considering the sample volume to the total flowing, it is not flow proportionate.
2. The "spot check" approach only collects the contaminants in the water column immediately surrounding the sampling horizon.
3. Additionally, samples must be collected throughout time owing to changing factors at the sampled sites in order to obtain representative data averaged across time.
4. Due to biodegradation, long-term storage of these samples may influence the results of the analysis or chemical concentrations.
5. The inability to identify the pollution sources since doing so would involve analyzing extremely many samples over a long period of time and space.

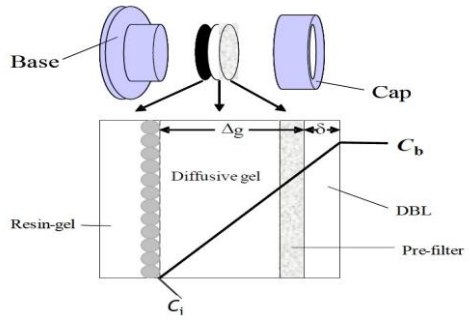

Figure 2. Components of the DGT are shown schematically as follows: DBL, or diffusive boundary layer; Ci, or concentration in the aqueous medium; and Cb, or concentration at the diffusive gel-resin border (Source: Chen 2013)

Preparation of DGT

As described in the procedure part of this work, the standard DGT preparation method was used. However, agarose gel is employed for the diffusive layer, whereas Amberlite XAD-18 with particle sizes of 63 um to 150 um was used for the study's binding gel. The o-other DGT's reagents and elements don't alter. DGTs were created in a single batch of binding and diffusive gels at the Lancaster University lab.

Sampling Preparation

The DGT samplers were made up of Amberlites XAD-18 binding gels to absorb antibiotics. These binding gels were prepared to a thickness of 0.56mm using 0.35mm spacers while they are placed between agarose diffusive gel of 0.80mm and the GHP 0.45um membrane filter. The preparation information for all the various components is contained in chapter 2 of this study.

Chemicals and Reagents

DGT Research Ltd., Skelmorlie, Bay Horse Rd., Quernmore, Lancaster provided the gel solution. UK (LA2 0QJ). This Gel solution can be kept in a refrigerator for at least three months (4oC). On the other hand, ammonium persulphate solution was made every day by mixing 1g of water with 0.1g of dried ammonium persulphate. I bought 99% N,N,N'N'N'Tetramethylethylenediamine (TEMED) from Sigma-Aldrich (UK). From Dow Chemical Company, XAD18 Amberlite was obtained and produced in bead sizes ranging from 65 m to 150 m. Acetonitrile and methanol of HPLC grade were acquired from Fisher Scientific and were the organic solvents employed for this project's work (UK). Other components of the DGT samplers were the 0.22um syringe filter, GH Polypro 0.45um 25mm Hydrophilic Polypropylene membrane filter, and Diffusive gel manufactured from Agarose powder acquired from Bio-Rad Laboratories (UK). The MQ water was created in the Lancaster University Laboratory, along with the assembly and manufacturing of several gels.

Sampling and sampling techniques

Depending on the source of the waste and the influent loads, or population equivalents, that the system has been intended to service, the systems vary from straightforward multi-staged processes to tertiary systems. To evaluate time-integrated removal rates, sampling was done over the course of seven days at each work site using matched influent-effluent samples. Six natural wastewater treatment methods and three conventional WWTPs were sampled. Three conventional treatment facilities with influent loads ranging from 26,173 m3/day to 34,524 m3/day were located in urban/industrial catchments. The daily COD load varies between 6,229 kg and 7,774 kg, whereas the daily BOD load varies between 2,058 kg and 4,050 kg. The wastewater loads for the two bigger sites were 19,500 m3/day and 55,000 m3/day, respectively, whereas the daily loadings for the six built wetlands ranged from 7.5 m3/day to 525 m3/day.

Deployment and Removal

Over the course of seven days, 54 o-DGT samplers were placed in three conventional sewage treatment facilities and six nature-based treatment facilities. At the time of deployment, the average temperature was 18 degrees.

DGT Extraction Process

The DGT mould was opened, and each Amberlite XAD-18 resin gel was taken out and put into a 15ml vial. The samples were spiked with 50 l of a mixed internal standard made up of equal amounts of SMX-d4, CAF-13C3, OFX-d3, and ETM-13C2. 5 ml of methanol was used to extract the samples for 30 minutes in an ultrasonic bath. The procedure was repeated without the addition of an internal standard after the methanol had been decanted into a different vial. The vials were rinsed with 2 more milliliters of MeOH, and the combined 12 milliliter's of extract were dried under a stream of nitrogen

gas at 40 degrees Celsius. In 1 ml of acetonitrile, the extract was reconstituted. Using a 0.22um syringe filter, a 200 l sample was swapped for 20/80 ACN/MQ and then filtered into amber vials for instrumental analysis.

Analysis of Pharmaceuticals ingredients

Table-3 Reagent Information

Acetonitrile	ACN	HPLC	Fisher Scientific (UK)
Agarose	AG	Bio-analysis	Bio-Rad Laboratories (UK)
Ammonium Formate	(AF)	analytical	Fisher Scientific (UK)
Ammonium persulfate	APS	≥ 99%, analytical	Sigma-Aldrich (UK)
Gel solution	-	-	DGT Research Ltd (UK)
Milli-Q water	MQ water	(> 18.2 MΩ cm-1	Waters Corporation (UK)
Methanol	MeOH	HPLC	Fisher Scientific (UK)
N,N,N′,N′-Tetramethylethylenediamine	TEMED	≥ 99%, analytical	Sigma-Aldrich (UK)
Sodium chloride	NaCl	≥ 99%, analytical	Sigma-Aldrich (UK)
XAD-18 Amberlite	XAD-18	-	Dow Chemical

Quantification

For the purpose of quantifying the target analytes in each sample, internal calibration curves for nine concentrations (1, 2.5, 5, 10, 25, 50, 100, 250, and 500ng/ml) were developed. Standard calibration curves demonstrated excellent linearity with a correlation value of 0.999, and for this investigation, a visual detection limit of 0.5 ng/ml was used.

Quality Assurance

Field blanks and laboratory blanks were analysed as part of the study design and execution. The DGT samplers' samples were brought to the field and brought back to the lab without being used.

Results and Discussion

Concentrations of antibiotics in influents of Wastewater treatment works

The cumulative chemical concentrations were measured in terms of ng/ml, which is the same as ng/sampler. Equation 1 below was used to convert concentrations to bulk water concentration; The diffusion coefficient De of the compounds under investigation at the field temperature is necessary to accurately determine the bulk concentration Cb (ngL-1), and this can be calculated based on the measured concentration at 25OC in the laboratory with 0.88mm thickness diffusive agarose gel layer. Zhang, Jones, and C.-E. Chen (2012); C. Chen (2013).

$$\mathbf{C_b} = \frac{\mathbf{M(\Delta g+\delta)}}{\mathbf{D_e A t}} \quad (1)$$

$$\boldsymbol{Log\ D_{e(t)}} = \frac{\mathbf{1.37023(t-25)+8.36\times10^{-4}(t-25)^2}}{\mathbf{109+t}} + \boldsymbol{log}\frac{\boldsymbol{D_{e25}}\mathbf{(273+t)}}{\mathbf{298}} \quad (2)$$

The diffusion coefficient at 25°C is de, and the predicted diffusion coefficient at temperature t is de (t). Temperature is represented at the deployment location as t.

Sulfapyridine (SPD), Lincomycin (LIM), Trimethoprim (TMP), Norfloxacin (NFX), Ofloxacin (OFX), Ciprofloxacin (CFX), Amoxicillin (AMX), Sulamethoxazole (SMX), Clarithromycin (CLM), Erythromycin-H2O (ETM-H2O), Roxithromycin (ROM), and Erythromycin were all (ETM). Sulfamethoxazole (SMX), Clarithromycin (CLM), Lincomycin (LIM), Trimethoprim (TMP), Norfloxacin (NFX), Ofloxacin (OFX), Ciprofloxacin (CFX), and Ofloxacin were all within a detectable and reportable limit.

Table 1. Concentrations of antibiotics in influents and effluents of treatment works

Chemical of Interest	**Influents**		**Effleunts**	
	Nature-Based Treatment Works Range (ngL^{-1})	**Conventional Treatment Works** Range ngL^{-1})	**Nature-Based Treatment Works** Range (ngL^{-1})	**Conventional Treatment Works** Range (ngL^{-1})
Sulfapyridine (SPD)	7-12000	7-79	7-1300	5-85
Lincomycin (LIM)	11-17	6-16	7-14	6-11
Trimethoprim (TMP)	9-45	9-75	5-9	5-24
Norfloxacin (NFX)	7-17	10-11	4-16	nd
Ofloxacin (OFX)	17-880	14-960	15-220	95-410
Ciprofloxacin (CFX)	12-410	12-460	12-113	30-55
Sulfamethoxazole (SMX)	8-69	8-81	8-42	4-46

Clarithromycin (CLM)	11-38	11-17	4-157	15-85

For all the examined channels, chemical uptakes from both influent and effluent channels were utilised to calculate removal rates. In order to compute this, the equation below was used.

$$\frac{\text{Influent mass uptake - Effluent mass uptake}}{\text{Influent mass uptake}} \times 100 \qquad (3)$$

Table 2: Removal rates of antibiotics at the three conventional treatment plants investigated with the removal rates

Conventional Treatment Plant - Olo

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Influents	-	13.00	-	-	-	-	-	11.00
Effluents	-	6.20	4.60	-	95.00	55.00	4.50	15.00
Rem_rate	0%	52%	0%	0%	0%	0%	0%	-36%

Conventional Treatment Plant - Pon

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Influents	78	6	62	11	650	240	47	-
Effluents	85	-	-	-	410	45	42	85
Rem_rate	-9%	100%	100%	100%	37%	81%	11%	0%

Conventional Treatment Plant - Gav

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Influents	22	16	75	-	960	460	81	-
Effluents	5	-	24	-	230	30	46	17
Rem_rate	75%	100%	68%	0%	76%	93%	43%	0%

Calculated removal efficiencies

Antibiotics within each kind of task and between various treatment modalities exhibit obvious variance. Below, the differences between the conventional system and nature-based technology are explained on a case-by-case basis.

Conventional Treatment Plant -Olo,

The removal rates for LIM, TMP, and NFX at the **Conventional Treatment Plant-Pon** were 100%, 37% for OFX, 81% for HFX, and 11% for SMX. With a concentration of 78 ngL-1 at the influent and 85 ngL-1 at the effluent, SPD had a removal rate of 1%, indicating low removal rate. This is a sign that the system was ineffective at getting LIM out. It is also possible to assume that the conjugate of this substance, which was not measured or examined in this work, may have been responsible for regulating the

concentration of LIM in the effluent. CLM, however, was not found in the influent sample, but it was present in the effluent sample at a concentration of 85.2 ngL-1.

Data from the Conventional Treatment Plant – Gav

The removal effectiveness at these works might be inferred to directly correlate with the BOD: COD ratio. According to Zaher and Hammam's (2014) research, untreated municipal wastewater typically has a BOD/COD ratio of 0.3 to 0.6. However, untreated wastewater with a BOD/COD ratio of 0.5 or above is thought to be treatable biologically; wastewater with a ratio of less than 0.3 is not thought to be treatable biologically.

None of the conventional treatment plants, particularly the CLM across the three and OFX, CFX in the case of, had been designed to remove all antibiotics. Therefore, it could be concluded that a variety of parameters, such as the design of the treatment plants (for example, residence duration) and other factors, such as the solubility of antibiotics, BOD/COD ratio, etc., might affect the treatment of wastewater (W. Li, Shi, Gao, Liu, & Cai, 2013; H. Zhang, Liu, Feng, & Yang, 2013; X. Zhang et al., 2017)

Nature-based /Constructed Wetland WWTPs

There are several built-in wetland technologies, from simple secondary systems to complex multi-stage systems whereas the fluxes might occur as either horizontal subsurface flow (HSF), vertical subsurface flow (VSF), or free water surface flow (FWS). All of these play a crucial role in the Constructed Wetland's eradication effectiveness. The influent water in this system travels from the coarse solid removal stage, via the sedimentation tank, and into the free water system, where the filtered water is stored. These wetlands plants provide the nutrients and oxygen needed for the substrate's microbiological development. However, the system's treatment by either aerobic or anaerobic breakdown is the responsibility of the microbial community. Depending on how the system is designed, the filtering step may be horizontal, vertical, or a combination of the two. Constructed wetlands or nature-based treatment methods may be divided into two main categories: free water surface (FWS), which has shallow beds and aquatic vegetation where polluted water is treated by exposed plant. The other kind of wetland is referred to as a subsurface flow (SF) wetland and it is not open to the air.

Table 3: Removal rate for Pharmaceuticals using Nature-Based treatment technologies.

Nature-based treatment plant - Cas

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Inf	115.00	6.60	14.00	-	-	-	-	12.00
Eff	-	14.00	-		-	-	-	-
Rem_rate	100%	-112%	100%	na	na	na	na	100%

Nature-based treatment plant - Dic

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Inf	660.00	-	44.00	7.00	880.00	410.00	69.00	-
Eff	326.00	12.00	-	3.70	17.00	-	42.00	4.70
Rem_rate	51%	0%	100%	47%	98%	100%	39%	0%

Nature-based treatment plant - Mar

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Inf	-	-	7.40	-	710.00	-	-	-
Eff	-	-	-	-	-	-	-	23.00
Rem_rate	na	na	100%	na	100%	na	na	0%

Nature-based treatment plant - Mos

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Inf	11,600.00	17.00	-	-	880.00	-	-	-
Eff	1,295.00	12.00	-	-	-	-	-	31.00
Rem_rate	89%	29%	na	na	100%	na	na	0%

Nature-based treatment plant - Gor

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Inf	-	-	-	-	210.00	49.00	-	17.50
Eff	-	-	-	-	-	-	-	-
Rem_rate	na	na	na	na	100%	100%	na	100%

Nature-based treatment plant - Les

	SPD	LIM	TMP	NFX	OFX	CFX	SMX	CLM
Inf	17.00	-	45.00	-	400.00	190.00	20.00	38.00
Eff	32.00	-	5.00	-	220.00	110.00	27.00	160.00
Rem_rate	-88%	na	89%	na	45%	42%	-35%	-321%

Data from the nature-based treatment plant -Cas

High removal efficiency for TMP, CFX, and OFX were suggested by data from the Nature-based treatment facility - Dic. However, due to the low quantities in the influent, CLM and LIM could not be found there.

This is often a complicated scenario since the anticipated removal rates of these chemicals depend greatly on the wastewater residence duration and dilution rate. However, it is assumed that the supply in the system is constant. There is general agreement that dilution lowers the concentration of hydrophilic compounds in wastewater (Le Corre et al., 2012), but biological degradation of pollutants or conjugates of some antibiotics may also be a factor in why antibiotics ingredients

predominate in the effluent despite having low concentrations in the influents (Joss et al., 2006). Between 40% and 50% were calculated for SPD, NFX, and SMX elimination rates. However, hydraulic retention durations also play a significant role in wastewater treatment due to the chemicals' half-life degradability (Gros, Petrovi, Ginebreda, & Barceló, 2010). The half-life of LIM is 3.99 0.25 hours, that of SPD is 5 to 10 hours, and that of NFX is predicted to be 3 to 4 hours (Sharma, Dumka, Singla, Kaur, & Singh, 2019; Challis, Carlson, Friesen, Hanson, & Wong, 2013; Taggart, McDermott, & Roberts, 1992). (Stein, 1987)

In a similar vein, only OFX, CFX, and CLM were found at Gor's Nature-based Treatment Plant, where removal effectiveness was 100%. For the corresponding population of 2017 this facility processes 55, 296 m3/day of combined sewer overflow. Despite CLM's poor water solubility (0.34 mg/L), biodegradation and sorption as well as the lower population might be to blame for its undetectable quantity at the effluent.

Nature-based treatment plant – Mos is a little urban wastewater pre-treatment facility with a one-stage, one-bed treatment system and a very low daily influents load of 16 m3/day created to serve the 60 people equivalents of the neighbourhood. At this treatment facility, only a small number of chemicals were found, whereas TMP, NFX, CFX, and SMX were completely undetectable. However, the removal rates for SPD were 89%, LIM were 29%, and OFX were 100%, while CLM continued the prior trend with 31 ngL-1 found in the effluent water and no detection at influent wastewater. This system demonstrates that, while the system is in a constant state of wastewater influx, SPD is the most significant compound with 11,500 ngL-1 in the influent and 1,300 ngL-1 in the effluent with logKow 0.35. Even though this substance has been outlawed since 1990, it can still be discovered in people who have taken it occasionally.

For the Nature-based treatment plant – Jes While LIM and NFX were not found in influents or effluents, other chemicals were removed at rates ranging from 1% CLM to 88% TMP. With a 2-stage system and a load of 19,465 m3/day, these 2-tiered treatment facilities are an urban wastewater tertiary pre-treatment site that provides service to an equivalent of 60,000 people. In order to increase removal rates, more phases would be appropriate. The 2000 m3 sedimentation pond, 1 hectare horizontal submerge flow system, and 5 hectares of free water surface system make up this hybrid system. However, the sedimentation pond's accumulated sludge is occasionally pumped into a wetland. Clarithromycin will exist in the cation forms between pH 5 and 9 based on its ability to adsorb to suspended particles and sewage sludge, and its pKa of 8.99 shows this. DGT measures ions that are readily dissolved, whereas CLM's poor removal effectiveness by the treatment system is caused by its low solubility (0.33 mg/L), strong sorption to suspended particles, huge population serviced by high daily influent loads, and low solubility (0.33 mg/L).

Chemical Concentrations in the Nature-Based Treatment Technologies

The treatment system uses techniques such volatilization, ion exchange, chemical reaction, adsorption, and biodegradation to lower the quantities of contaminants in NBT. Climate has an impact on biological activity and volatilization. In the free water system (FWS), the higher bed layer insulates the microbial population from cooler temperatures; this effect is less pronounced in the subsurface flow system (SFS). Enzyme activity declines and protein macromolecules get disordered at lower temperatures (Strambini & Gonnelli, 2007). Except for the Nature-based treatment plant-Jes, where the removal rate of Sulfapyridine, SPD was 1% in this investigation, all systems where it was detected had removal rates of 51% to 100%. The treatment facility in Mos is a small rural facility with just 1 bed that serves a population of roughly 60. It was a daily inflow.

Lincomycin is a common antibiotic used in the pig and poultry industries that is polar and has a high-water solubility (927 mg/L at 25 °C). It was found in greater concentrations in the effluent of the nature-based treatment plants Cas and Dic, which resulted in removal rates of 1% and 0% (12 ngL1), respectively, but the removal rate at treatment plant Mos was 29%. The treatment facility was built to take the place of an activated sludge system that the community no longer deemed suitable. However, the layout of the factory also contributed significantly to this process. The biosolids build up on the surface of the vertical flow reed bed filters (RBF) at the first stage, and these solids are removed and utilized after every 15-20 years. Two vertical subsurface flow basins (VF) in the second tier, however, offer habitat for wetland plants. It may be inferred that the design of this system, which is a multistage system SFS-h + SFS-v + SFS-h + FWS, plays a key role in the treatment of lincomycin. Overall, a multi-stage treatment system aids in the treatment process where more stages may be helpful during an influx of extra wastewater in addition to improving overall performance through a longer residence period.

Trimethoprim In research, the lowest solubility was 0.28 g/L at pH 3.22, 25 oC, while the highest solubility was 1 g/L at 24 oC. (Dahlan, Mcdonald, & Sunderland, 1987). The elimination of this chemical was determined to be successful using the natural systems chosen for this investigation. According to studies, the amount of TMP removed by sorption to activated sludge may be quite low (Göbel, Thomsen, McArdell, Joss, & Giger, 2005), while another research indicated that the amount of TMP in raw sewage and effluent water was roughly equal (Lindberg et al., 2006). However, using a certain type of sand filter, a trimethoprim clearance rate of 74 14% was discovered (Göbel, McArdell, Joss, Siegrist, & Giger, 2007), indicating that they were removed in a crystalline form. This study corroborated our observations across the NBTs that were investigated.

Norfloxacin was found in the treatment facility Dic at low quantities, with an average daily wastewater inflow of 525 m3/day. Strong absorption of this antibiotic rises quickly between pH 5 and pH 10. Nevertheless, just 47% of this hardly water-soluble molecule was removed. A secondary treatment facility, NBT-Dic, provides services to 3500 residents. The four-stage system was created to create a high biodiversity area for 16 Tuscany's autoctone or native species of vegetation. It consists of a horizontal subsurface flow system (SFS-h) linking a vertical subsurface flow system (SFS-v), a horizontal subsurface flow system (SFS-h), and supplying into free water surface (FWS) (Person & Typology, 2003). This design would have been extremely efficient at removing Norfloxacin by sorption, but because DGT only analyses dissolved compounds, the undissolved portion of the drug may have been absorbed into organic matter. This study did not look at organic materials or sewage sludge, which would have given us a greater understanding of the chemical partitioning.

Ofloxacin is an antibiotic that dissolves in water. Except for Cas, it was found in every treatment facility. With daily influent loads of 75 m3 and a landmass of 2014 m2, this treatment plant serves a large variety of individuals, from a few dozen in the winter to as many as 1000 in the summer. As a result, the system is vulnerable to wide changes in the component concentrations that can be found in effluent. This explains why several of the chemicals that were looked at, such as Norfloxacin, Sulfamethoxazole, and Ciprofloxacin, were not discovered in this plant.

Ciprofloxacin This substance has a low LogKow of 0.4, indicating that it is quite insoluble in water. At 20 °C, it is 30,000 mg/L in water. High LogKow compounds become more hydrophobic, and low LogKow compounds become hydrophilic. All treatment plants where this substance was present effectively removed it, with the exception of Jes, which had a 42% removal rate, suggesting that sorption may have played a major role in its removal. Ciprofloxacin concentrations in dry weight biosolids have been observed to reach as high as 2.27 to 2.42 mg kg-1 in studies (Petrie et al., 2014), indicating that the presence of organic materials must have affected the drug's clearance.

The 60,000 people it serves use the treatment facility, which was built to also handle rainfall. As a result, it typically gets 19,465 m3/day of wastewater. It has been noted that the 60,000m2 treatment plant, which has the typology Sedimentation basin + SFS-h + FWS, is less effective than other plants in treating most of the chemicals. Ciprofloxacin, on the other hand, is frequently used to treat clinical bacterial infections, including cancer.

Sulfamethoxazole is eliminated via adsorption into organic materials, where it has a 610 mg/L water solubility (at 37 °C) (Ryan et al., 2011; Rioja et al., 2014). This supports the findings of the inquiry, according to which DGT exclusively measures dissolved substances in water. Only the treatment plants in Dic and Jes were able to

identify this substance, and clearance rates ranged from 0% to 39%. The multi-stage treatment plant design in Dic must have favoured the removal of this chemical, whereas the sedimentation design in the Jes plant may have been to blame for the subpar removal rate. However, the breakdown of 5-methyl-isobutyl-3-carboxamide results in sulfamethoxazole, whose quantities in effluent may grow.

Clarithromycin. According to studies (Calamari, Zuccato, Castiglioni, Bagnati, & Fanelli, 2003; Göbel et al., 2005; Rioja et al., 2014), 25% of clarithromycin is excreted in an unaltered form. The levels of clarithromycin in the areas under investigation are comparable to those reported by McArdell et al., 2003 and other research' data (Golet, Alder, & Giger, 2002; Yamashita et al., 2006). This investigation demonstrated that Clarithromycin concentrations at the effluent are greater than at the influent in all treatment facilities with urban wastewater sources, which indicates inadequate removal by sorption or degradation. Treatment facilities Gor and Cas, however, had a 100% eradication rate. 60,000 people are served by treatment plant Jes, which has a removal rate of less than 1% and daily influent loads of 19,465 m3/day.

Conclusion

Using DGT passive samplers, the occurrence, concentration, and removal efficiency of 23 pharmaceuticals in 3 conventional WWTPs and 6 nature-based treatment systems in the vicinity of Florence, Italy, were examined. Eight different antibiotics were consistently examined, with some amounts falling below the method's detection limits. Concentrations ranged from 6 ngL-1 to 960 ngL-1 in influents and 4.5 ngL-1 to 410 ngL-1 in effluents of typical WWTPs. The influent antibiotic concentrations varied from 6.6 ngL-1 to 11,600 ngL-1, while the effluents from the nature-based plants ranged from 3.7 ngL-1 to 1,295 ngL-1. The study found that partitioning behaviour, pH of the wastewater, and NBT designs, such as multi-stage/single bed, all had an impact on removal rates. Some of the components of antibiotics were found in larger amounts in the effluent than in the influent, which may have been caused by the conjugated forms' breakdown during treatment, where the system had turned into a source of the chemical through desorption. The role of parent chemical degradation in the treatment process, as well as other metabolic events that may have raised the amounts of interest compounds, has not been examined in this work. It indicates that even if the treatment plant may have strong removal efficiency, it is not always certain that the chemicals that are reported at the effluents were the signals that were detected at the influents. Future research might examine the contributions of the parent or conjugate forms utilising a comprehensive chemical spectrum scan as opposed to the focused chemicals used in this investigation.

While a removal rate of 1% to 100% was reported in the nature-based system, certain unusual removal rates were noted in the conventional treatment works, ranging from 1%

(CLM (Conventional treatment-Olo)) to 100%. According to prior study by other researchers, the elevated concentrations at the effluent channels may have been caused by the molecule of interest being created throughout the process as a metabolite of parent compounds that were not found at the influent channels (Ni & Zeng, 2015). This is not an indication of how well the medication is working; rather, it is a possible sign of systemic biochemical activity. It suggests that the best way to explore these compounds with negative removals is to conduct a thorough chemical spectrum scan of the parents' forms and some other group metabolites. A toxicity examination of certain antibiotic compounds would also be beneficial because they may only slightly endanger human health. This supports the findings of Vymazal & Kröpfelová (2009), who found that designed treatment wetlands are particularly successful at removing suspended and organic materials. The study's conclusion that both removal systems and efficiency are chemically dependent. The long-term study done by Vymazal and Kröpfelová supports the conclusion that nature-based treatment methods are successful in the removal of organic compounds and suspended particles (2009). It can also be recommended as a good replacement for the traditional treatment system, particularly in areas with a relatively small population that cannot support the cost of the conventional system. This implies that while choosing the best design for a nature-based removal technology, factors such as land availability, daily influent loads, population, and wastewater kinds must be considered.

Notes and references

Akcha, F., Arzul, G., Rousseau, S., Bardouil, M., Antia, N, J., Berland, B. R., … Yang, Y. (2010). Effects of three pharmaceutical and personal care products on natural freshwater algal assemblages. *Limnology and Oceanography*, *15*(2), 1713–1719. https://doi.org/10.1021/es0259741

Álvarez, J. A., Ruíz, I., & Soto, M. (2008). Anaerobic digesters as a pretreatment for constructed wetlands. *Ecological Engineering*. https://doi.org/10.1016/j.ecoleng.2008.02.001

Ávila, C., Garfí, M., & García, J. (2013). Three-stage hybrid constructed wetland system for wastewater treatment and reuse in warm climate regions. *Ecological Engineering*. https://doi.org/10.1016/j.ecoleng.2013.09.048

Badr El-Din, S. M., & Abdel-Aziz, R. A. (2018). *Potential uses of aquatic plants for wastewater treatment*. *2*(3), 47–48.

Barker, S. A. (1998). Antibiotics. In *Journal of Chromatography Library* (Vol. 60, pp. 737–
777). https://doi.org/10.1016/S0301-4770(08)60315-2

Bouwman, A. F., Bierkens, M. F. P., Griffioen, J., Hefting, M. M., Middelburg, J. J., Middelkoop, H., & Slomp, C. P. (2013). Nutrient dynamics, transfer and retention

along the aquatic continuum from land to ocean: Towards integration of ecological and biogeochemical models. *Biogeosciences*, *10*(1), 1–23. https://doi.org/10.5194/bg-10-1-2013

Brix, H. (1994). Use of constructed wetlands in water pollution control: historical development, present status, and future perspectives. *Water Science and Technology*, *30*(8), 209–223.

Cabello, F. C. (2006). Heavy use of prophylactic antibiotics in aquaculture: A growing problem for human and animal health and for the environment. *Environmental Microbiology*, Vol. 8, pp. 1137–1144. https://doi.org/10.1111/j.1462-2920.2006.01054.x

Calamari, D., Zuccato, E., Castiglioni, S., Bagnati, R., & Fanelli, R. (2003). Strategic survey of therapeutic drugs in the rivers Po and lambro in Northern Italy. *Environmental Science and Technology*. https://doi.org/10.1021/es020158e

Challis, J. K., Carlson, J. C., Friesen, K. J., Hanson, M. L., & Wong, C. S. (2013). Aquatic photochemistry of the sulfonamide antibiotic sulfapyridine. *Journal of Photochemistry and Photobiology A: Chemistry*. https://doi.org/10.1016/j.jphotochem.2013.04.009

Chen, C.-E., Zhang, H., & Jones, K. C. (2012). A novel passive water sampler for in situ sampling of antibiotics. *Journal of Environmental Monitoring*, *14*(6), 1523. https://doi.org/10.1039/c2em30091e

Chen, C. (2013). *Development and Applications of a Novel Passive Water Sampler for Polar Organic Contaminants-Antibiotics*. (December).

Chen, H., Jing, L., Teng, Y., & Wang, J. (2018). Characterization of antibiotics in a large-scale river system of China: Occurrence pattern, spatiotemporal distribution and environmental risks. *Science of the Total Environment*, *618*, 409–418. https://doi.org/10.1016/j.scitotenv.2017.11.054

Chen, W. (2016). Fate of Emerging Organic Contaminants in Chinese Wastewater Treatment Plants. In *Unpublished work*.

Dahlan, R., Mcdonald, C., & Sunderland, V. B. (1987). Solubilities and intrinsic dissolution rates of sulphamethoxazole and trimethoprim. *Journal of Pharmacy and Pharmacology*. https://doi.org/10.1111/j.2042-7158.1987.tb06261.x

de Jesus Gaffney, V., Almeida, C. M. M., Rodrigues, A., Ferreira, E., Benoliel, M. J., & Cardoso, V. V. (2015). Occurrence of pharmaceuticals in a water supply system and related human health risk assessment. *Water Research*, *72*, 199–208. https://doi.org/10.1016/j.watres.2014.10.027

Di Martino, M., Lallo, A., Kirchmayer, U., Davoli, M., & Fusco, D. (2017). Prevalence of antibiotic prescription in pediatric outpatients in Italy: The role of local health districts and primary care physicians in determining variation. A multilevel design

for healthcare decision support. *BMC Public Health*. https://doi.org/10.1186/s12889-017-4905-4

Etchepare, R., & van der Hoek, J. P. (2015). Health risk assessment of organic micropollutants in greywater for potable reuse. *Water Research*, *72*, 186–198. https://doi.org/10.1016/j.watres.2014.10.048

Fischbach, M. A., & Walsh, C. T. (2009). Antibiotics for emerging pathogens. *Science*, Vol. 325, pp. 1089–1093. https://doi.org/10.1126/science.1176667

Gagnon, E. (2010). Release of pharmaceuticals into the environment by consumers: A Canadian perspective. *Journal of Population Therapeutics and Clinical Pharmacology*, *17 (1)*, e117–e118.

Giger, W., Alder, A. C., Golet, E. M., Kohler, H.-P. E., McArdell, C. S., Molnar, E., … Suter, M. J.-F. (2003). Occurrence and Fate of Antibiotics as Trace Contaminants in Wastewaters, Sewage Sludges, and Surface Waters. *CHIMIA International Journal for Chemistry*, *57*(9), 485–491. https://doi.org/10.2533/000942903777679064

Göbel, A., McArdell, C. S., Joss, A., Siegrist, H., & Giger, W. (2007). Fate of sulfonamides, macrolides, and trimethoprim in different wastewater treatment technologies. *Science of the Total Environment*. https://doi.org/10.1016/j.scitotenv.2006.07.039

Göbel, A., Thomsen, A., McArdell, C. S., Joss, A., & Giger, W. (2005). Occurrence and sorption behavior of sulfonamides, macrolides, and trimethoprim in activated sludge treatment. *Environmental Science and Technology*. https://doi.org/10.1021/es048550a

Golet, E. M., Alder, A. C., & Giger, W. (2002). Environmental exposure and risk assessment of fluoroquinolone antibacterial agents in wastewater and river water of the Glatt Valley watershed, Switzerland. *Environmental Science and Technology*. https://doi.org/10.1021/es0256212

Golet, E. M., Strehler, A., Alder, A. C., & Giger, W. (2002). Determination of fluoroquinolone antibacterial agents in sewage sludge and sludge-treated soil using accelerated solvent extraction followed by solid-phase extraction. *Analytical Chemistry*. https://doi.org/10.1021/ac025762m

Gong, X., Li, K., Wu, C., Wang, L., & Sun, H. (2018). Passive sampling for monitoring polar organic pollutants in water by three typical samplers. *Trends in Environmental Analytical Chemistry*, *17*, 23–33. https://doi.org/10.1016/j.teac.2018.01.002

Gong, Y., Wang, N., Li, Y. C., Zong, N., Luo, J., & Xie, H. (2015). Forms and bioavailability of phosphorus in water and sediments of Lake Caohu. *Journal of Ecology and Rural Environment*. https://doi.org/10.11934/j.issn.1673-4831.2015.03.014

Gros, M., Petrović, M., Ginebreda, A., & Barceló, D. (2010). Removal of pharmaceuticals during wastewater treatment and environmental risk assessment using hazard indexes. *Environment International*. https://doi.org/10.1016/j.envint.2009.09.002

Guo, X., Yan, Z., Zhang, Y., Kong, X., Kong, D., Shan, Z., & Wang, N. (2017). Removal mechanisms for extremely high-level fluoroquinolone antibiotics in pharmaceutical wastewater treatment plants. *Environmental Science and Pollution Research*. https://doi.org/10.1007/s11356-017-8587-3

Hirsch, R., Ternes, T., Haberer, K., & Kratz, K. L. (1999). Occurrence of antibiotics in the aquatic environment. *Science of the Total Environment*, *225*(1–2), 109–118. https://doi.org/10.1016/S0048-9697(98)00337-4

Hopkins, S., & Muller-Pebody, B. (2015). *UK One Health Report: Joint report on human and animal antibiotic use, sales, and resistance, 2013*. 64. Retrieved from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/447319/O ne_Health_Report_July2015.pdf