Occurrence and transport of polar pollutants in coastal ecosystems

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Erklärung

Ich versichere hiermit an Eides statt, dass ich die vorliegende Arbeit selbstständig angefertigt und ohne fremde Hilfe verfasst habe, keine außer den von mir angegebenen Hilfsmitteln und Quellen dazu verwendet habe und die den benutzten Werken inhaltlich und wörtlich entnommenen Stellen als solche kenntlich gemacht habe.

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List of Abbreviations

μg/L	micrograms per liter
4-DHB	4,4’-dihydroxybenzophenone
4-MBC	4-methylbenzylidenecamphor
Ac	acetone
approx.	approximately
BP-1	2,4-dihydroxybenzophenone, benzophenone-1
BP-2	2,2’,4,4’-tetrahydroxybenzonphenone, benzophenone-2
BP-3	2-hydroxy-4-methoxy-benzophenone, benozophenone-3
BP-4	5-benzoyl-4-hydroxy-2-methoxybenzenesulfonic acid, benzophenone-4
CTD	conductivity, temperature, depth
DCF	2-(2-((2,6-dichlorophenyl)amino)phenyl)acetic acid, diclofenac
DOC	dissolved organic carbon
e.g.	exempli gratia, for example
EASY	Chromabond Easy
EHMC	2-ethylhexyl-4-methoxycinnamate
etc.	et cetera
Et-PABA	ethyl-4-aminobenzoate
EC	European Commission
EU	European Union
FFB	2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoic acid isopropyl ester, fenofibrate
H_2O	water
HCl	hydrochloric acid
HELCOM	Helsinik Commision
HESI	heated electrospray ionisation
HPLC	high performance liquid chromatography
KPF	2-(3-benzoylphenyl)propionic acid, ketoprofen
LOD	limit of detection
logK_{OW}	n-octanol/water partition coefficient
LOQ	limit of quantification

max.	maximum
MEC	measured environmental concentration
MeOH	methanol
min.	minute
mio.	million
mL	milliliter
MS/MS	tandem mass spectrometer
n.d.	not detected
ng/L	nanogram per liter
NP_1EC	nonylphenoxyacetic acid
NSAIDs	non-steroidal anti-inflammatory drugs
OC	2-ethylhexyl 2-cyano-3,3-diphenyl-2-propenoate, octocrylene
OD-PABA	2-ethylhexyl-4-(dimethylamino)benoate
OECD	Organisation for Economic Co-operation and Development
PBSA	2-phenylbenzimidazole-5-sulfonic acid
PCP	personal care product
pH	potential of hydrogen
Pharm.	pharmaceutical
pK_a	logarithm of acid dissociation constant
PNEC	predicted no effect concentration
POC	particulate organic carbon
PPCPs	pharmaceuticals and personal care products
r	correlation coefficient (PEARSON)
RQ	risk quotient
S	salinity
SA	2-hydroxybenzoic acid, salicylic acid
SDZ	4-amino-N-(2-pyrimidinyl)benzenesulfonamide, sulfadiazine
SMX	4-amino-N-(5-methyl-3-isoxazolyl)benzenesulfonamide, sulfamethoxazole
SMZ	4-amino-N-(4-methyl-2-pyrimidinyl)benzenesulfonamide, sulfamerazine
SPE	solid phase extraction

SPM	suspended particulate matter
T	temperature
$t_{1/2}$	half-life time
TMP	2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine, trimethoprim
UV	ultraviolet
v/v	volume/volume

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1 Introduction

For millennia people have been living in the proximity of the ocean, as coastal regions and their shelves are the most productive regions of the ocean and they provide resources to live and a space for trade. Coasts are the interface between land, ocean and society. Since the early 1960s (approx. 3 billion) the world population has been growing exponentially and is expected to have tripled (9 billion) by 2050 (UN, 2017). These days approximately 60% of the total world population lives within 60 km of coastal regions, which is expected to increase to up to 75% in the next decades. Estimations predict that of the 75% around 1.4 billion people will live in the low elevation coastal zone (10 km), which is exposed to higher risk of natural hazards (Neumann et al., 2015).

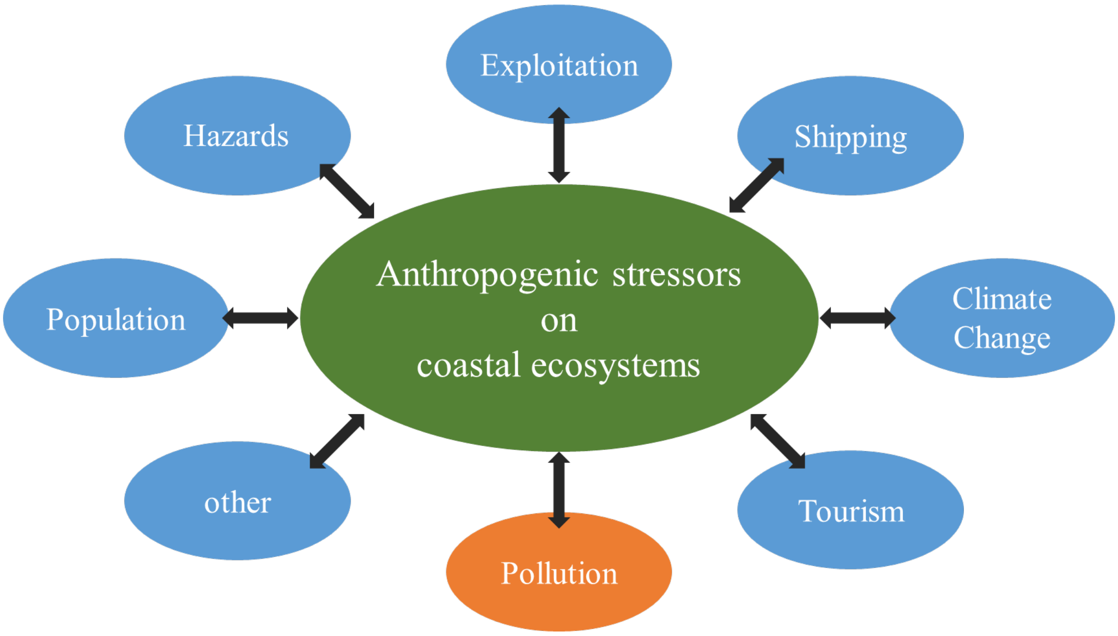

Figure 1.1: Schematic layout of selected anthropogenic stressors on coastal ecosystems.

Oceans and especially their coastal ecosystems are under great anthropogenic pressure due to many different factors (fig. 1.1). As the population in coastal regions grew, the size and number of cities grew with them. Out of today's quickly growing 23 megacities (population $>$ 10 million) 16 are already located in coastal areas of which many are located at large deltas (UN, 2016, UN 2017, Access: 19.12.2017). As the megacities near river deltas keep growing the anthropogenic pressure on the coastal ecosystem increases with them and they become a risk zone to live in. As a consequence of their growth the natural coastal barriers such as mangroves are destroyed (Newton et al., 2012). Furthermore, due to the growth of megacities the land they are build on subsides because of soil compaction and the removal of groundwater, oil or gas. As the land subsides, the sea level rises and the salinization of the soils becomes a problem. In order to satisfy the request of freshwater and energy, large dams are build along the rivers in the back country. As a consequence, the transport of sediments into the deltas is decreased and a stronger erosion of the coast line takes place. Another fact is that monsoon and strong winds reinforce storm events coming from the sea, which often result in the flooding of the delta area. Additionally, the exposure to many natural hazards e.g. tsunamis and hurricanes endanger not only all humans in coastal areas but also the ecosystem itself (Newton et al., 2012; Neumann et al., 2015). As the population has been growing, the consumption of seafood has more than doubled since the 1960s, leading to overfishing of many species (FAO, 2016). Therefore, the exploitation puts further stress on the ocean and its coastal ecosystems (FAO, 2016). Since around 6500 BC mankind has started to explore the sea and discovered it as a means to trade goods with each other. From that time on, the shipping industry has become the most internationally aligned economy sector. Today, approx. 90% of the total world trade occur via sea routes. However, the drawbacks are high emission rates of harmful substances such as sulfur dioxide (SO_2) and nitrogen dioxide (NO_x) and great noise disturbance for marine organisms (UNEP and GRID-Arendal, 2008; IMO, 2015). But not only the industrial shipping routes have expanded, the cruise tourism is on a rise as well. Since the 1950s the number of international travelers has increased forty times and the ocean as an recreational space has gained great popularity in recent years. In 2017, 25.8 million people recovered of their daily routines on cruise ships and one third of the world tourists spend their vacation at the Mediterranean Sea (CLIA, 2018). With the increasing interest in cruise tourism the wish to satisfy more passengers resulted in the construction of larger cruise ships, carrying 3,000-5,000 passengers. The growing cruise industry has led to mass tourism. This and tourism in general puts pressure on the visited ecosystems and on the land, as most of them have reached their ecological capacity (UNWTO, 2016; CLIA, 2018).

Climate change can also be seen as an anthropogenic stressor. Due to global warming the sea level gradually rises, as a result of ice melting and thermal expansion, which poses a risk to many people living in coastal areas as the natural barriers, e.g. mangroves, are destroyed. Furthermore, the warming and acidification of the oceans pose an additional risk to many of its inhabitants e.g. coral bleaching (Wittmann and Pörtner, 2013; UNEP et al., 2014). Coral bleaching can not only originate from the warming of the ocean but to a small percentage also results from pollution. The amount of pollution in the ocean has yet to be determined (Steffen et al., 2011). Pollution of the environment in general can be subdivided into different groups (fig. 1.2), as they all pose risks to the ecosystems and their inhabitants.

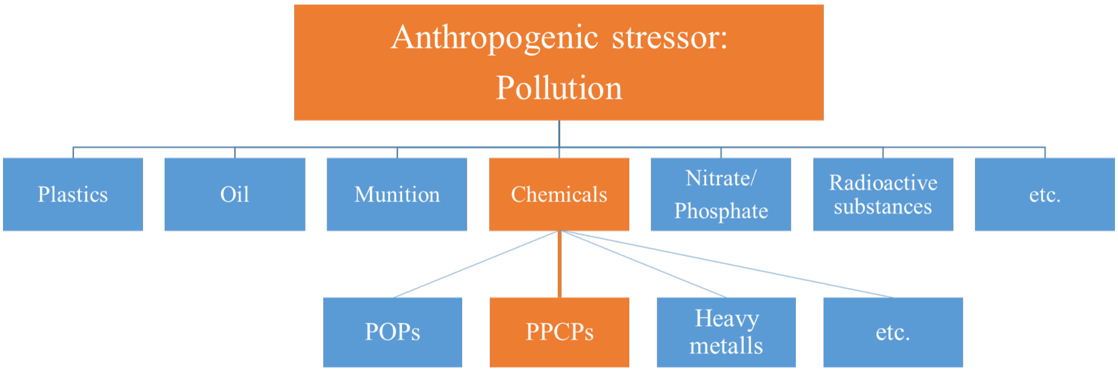

Figure 1.2: Anthropogenic pollution stressors and the classification of pharmaceuticals and personal care products (PPCPs) as chemical stressors.

The pollution of the environment arose with industrialization, the growth of population and the need for energy and food. In the last decades the need for fossil energy e.g. mineral oil, has become an important economic factor for many countries. Yet, the drilling for oil is not without danger to the environment. Even a small leakage of oil bears a risk for marine ecosystems, especially coral reefs or mangroves, as it will take up to twenty years for them to recover from the destruction. Another risk is posed by the munition of former wars, which was disposed at sea and can still be found at the bottom of coastal seas and the ocean. Over the years the salt water has taken its toll on the munition and now their questionable stability complicates recovery. Additionally, they also pose a risk to tourists at the beaches as white phosphorus is often mistaken for amber (Bełdowski et al., 2016). Another risk rises by radioactivity resulting from the usage of nuclear power, which is still greatly discussed around the globe. Since 1994, the discharge of radioactive waste into the aquatic environment is prohibited, as the exposure of humans and wildlife to high amounts of radioactive nuclides can lead to severe health problems and malformations. However, a lot of radioactive waste can still be found at the sea floor, still causing danger to ecosystems (Kennish, 1996; Ringius, 1997). During the time of population growth, the demand for food became more prominent world wide. The soils of areas surrounding large rivers and deltas are of valuable quality and often used for agricultural purposes. As the ongoing demand for food increases the agricultural fields are treated with high amounts of fertilizers to increase and maintain the harvest. Fertilizers are often rich in phosphorus and nitrogen, both necessary nutrients for the plants. Yet, both compounds get leached out of the soil by water and are washed into the marine environment via rivers. The high amounts of discharged phosphorus and nitrogen lead to eutrophication and consequentially to anoxic conditions in the marine ecosystem (Seitzinger et al., 2005; HELCOM, 2009). Not only the discharge of nitrate and phosphorus poses a risk, but so does the increasing discharge of plastics and chemicals. The emergence of plastics, especially microplastics, in the marine environment has attracted a lot of attention and concerns in recent years. The five large garbage patches in the oceans are alarming, but they only reflect a small amount of the existing plastic in the environment. Most of the garbage is washed up at the coasts, where it pollutes the beaches and endangers the coastal and marine wildlife as the plastic enters their metabolism (UNEP and GRID-Arendal, 2005). Unfortunately, plastic poses a secondary risk, as chemicals can be adsorbed, which could later be absorbed by the organism. The Organization for Economic Co-operation and Development (OECD) estimated that up to this time approx. 100,000 different chemicals are globally used (BfR, Access: 20.12.2017). Chemical is a generic term for many industrially produced substances, which are sub-divided into many different classes. The occurrence of some chemicals in the environment has been known for some time. Especially the presence of the so called persistent organic pollutants (POPs) has been of concern for the last decades. These POPs remain in the environment over centuries. They are known for their long half-live times and endocrine disrupting effects on wildlife. This led to the prohibition of their usage, which has been decided in 2001 by the Stockholm Convention (EC, 2004). Nowadays, the emergence of modern pollutants e.g. pharmaceuticals and personal care products (PPCPs) in the environment is of scientific concern, as they potentially have negative effects on the environment and their usage and discharge keeps increasing.

1.1 Environmental concerns of analyzed PPCPs

Until now, most studies have been conducted about the occurrence of PPCPs in waste water influents and effluents of Waste Water Treatment Plants (WWTP) (Fang et al., 2012; Rodil et al., 2012; Tamura et al., 2017), lakes and rivers (Sköld, 2000; Loos et al., 2009; Gothwal and Shashidhar, 2015; Molins-Delgado et al., 2017). Results show that many PPCPs were detected in freshwater systems and as a consequence the focus is now slowly shifting towards marine systems. So far just a few studies about their occurrence in marine ecosystems, have been carried out around the world (fig. 1.3, Annex tab. A1).

PPCPs are composed of two main groups: pharmaceuticals and the group of personal care products. PPCPs include all chemicals used for health care, cosmetics and medical purposes. They are often analyzed together because their entries to the environment are similar. PPCPs reach the environment mainly

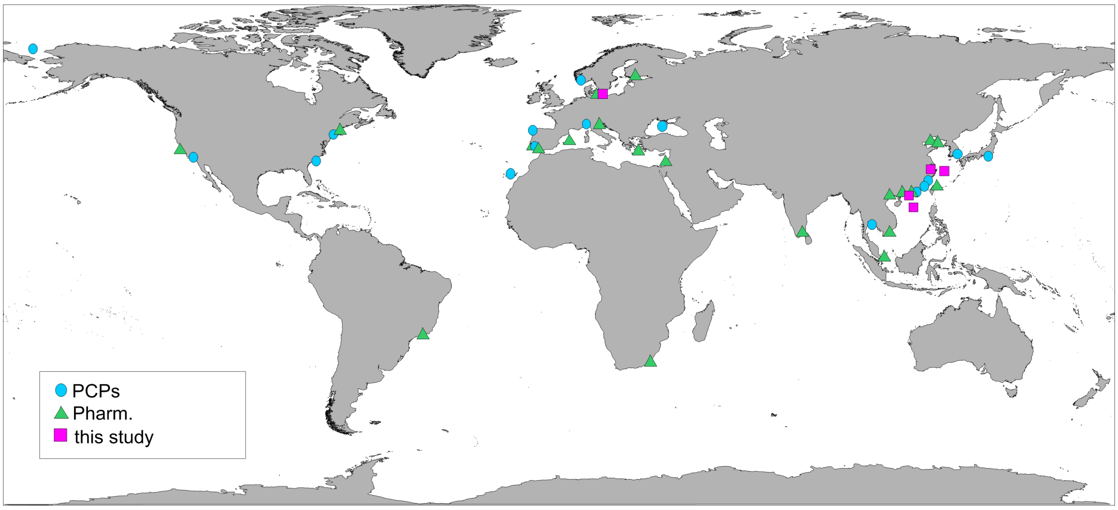

Figure 1.3: Excerpt of studies carried out in the coastal areas around the world. Data source see annex tab. A1. (PCPs - personal care products, Pharm. - pharmaceuticals).

indirectly with waste waters from household or agriculture (livestock farming). As their removal from waste water is not efficient enough and most of the compounds are not degraded, they reach the environment via waste water effluents. Some chemicals, e.g. in lotions or creams, can enter the environment directly due to recreational activities. These compounds are called "pseudo"-persistent as their degradation is slower than the large quantitative input/discharge into the environment (Daughton, 2003). In this study eight pharmaceuticals and eleven personal care products were analyzed (tab. 1.1, 1.2).

1.1.1 Pharmaceuticals

Pharmaceuticals are chemicals used to effectively treat diseases and their residual effects. Pharmaceuticals can be divided into many classes. In 2009, the group of analgetic (2,647 t) and antibiotics (571 t) were number 1 and 3 of the most consumed pharmaceuticals in Germany (lipid regulators (68 t)) (UBA, 2011). In the following years the antibiotic usage increased to $>$ 2,300 t/a (1,619 t veterinary, 500-600 t human (ambulatory), 2012) in Germany (BVL, 2014). The annual usage in China is estimated to be even higher with 180,000 t (human and veterinary) (Zheng et al., 2012). For each class representative compounds were analyzed (tab. 1.1, structure see tab. A2). The group of sulfonamide antibiotics was chosen for the analysis because, sulfonamide antibiotics are not only used in human medicine but are also the group of the 2nd most used antibiotics in veterinary medicine in Germany (UBA, 2011). The antibiotic sulfamethoxazole (SMX) is one of the largely consumed antibiotics in Germany (tab. 1.1). Sulfadiazine (SDZ) and sulfamerazine (SMZ) were chosen for the analysis because they are structurally similar to SMX and also behave similar in the environment. The antibiotic trimethoprim (TMP) was chosen for analysis as it is one of the most used antibiotics in China for human and veterinary treatment (Gulkowska et al., 2007). TMP can be used as a single compound but is more often used in combination with sulfonamide antibiotics. It is mostly used in combination with SMX in a ratio 1:5, as their effects are potentized (Nord et al., 1974). Due to their combined usage, SMX and TMP often occur at the same time in the environment and have been analyzed in combination on numerous occasions (tab. A1). The main usage of sulfonamide antibiotics and TMP is to prevent or treat infectious diseases in human and veterinary medicine, such as red skin disease, bronchitis, bacterial gastroenteritis, as they have a broad bacteriostatic spectrum against gram positive and negative bacteria (Gothwal and Shashidhar, 2015). An additional usage is the application as growth promoters in the livestock industry e.g. poultry and aquaculture (Richardson et al., 2005). Sulfonamide antibiotics and TMP are comparatively persistent in the environment as they are relatively photostable, hydrolysis stable and not easily degradable (Zheng et al., 2012; Straub, 2013). As they are hydrophilic their adsorption to soil or sediment is low (logK_{OW} see tab. 1.1) and they can be transported in the aquatic phase of the environment (Benotti and Brownawell, 2009; Boxall et al., 2002).

The great concern about the occurrence of antibiotics in the environment is the emergence of antibiotic resistant genes/bacteria. The sulfonamide resistant genes sulI and sulII have already been detected in WWTPs, lakes and rivers (Sköld, 2000; Jiang et al., 2011; Gao et al., 2012; Guo et al., 2014). Furthermore, there is a possibility of bioaccumulation, as some sulfonamide antibiotics are bioaccumulative, e.g. sulfadiazine has a bioaccumulation factor of 10,757 L/kg (Na et al., 2013). Additionally, the occurrence of sulfamethoxazole poses a toxic risk to aquatic organisms, e.g. blue-green algae (Ferrari et al., 2004; Na et al., 2013). Some studies have already proven that sulfonamide antibiotics cannot only be found in the aquatic environment (fig. 1.3, tab. A1) but also in aquatic organisms, e.g. shrimp or bivalves *Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri* (Na et al., 2013). These antibiotics where chosen based on their high medical usage and their occurrence in ecosystems world wide (tab. 1.1, A1).

Non-steroidal anti-inflammatory drugs (NSAIDs) belong to the group of analgetic pharmaceuticals. Two NSAIDs and one metabolite (salicylic acid) were analyzed. NSAIDs are widely known and used because of their antipyretic, analgetic and anti-inflammatory effects. Their advantage over other pain medication is that their usage will not lead to addiction, respiratory depression or sedation (Farré et al., 2007). Salicylic acid (SA) is the deacylated and more active metabolite of the globally used acetylsalicylic acid, commonly known as Aspirin® (Wille et al., 2010). Yet, it is also used as an ester or salt for chemical exofoliation of the skin in medicine and in many cosmetic products (Kligman, 2001; CIREP, 2003). SA was chosen for analysis because of its extensive usage as pharmaceutical and in personal care products. Its maximum allowed concentration in personal care products is regulated in the EU cosmetic directive 76/768/EEC/1976 to 2-3% in personal care products (EU, 2009). NSAIDs are generally used to treat fever and as pain medication to relieve symptoms of arthritis and rheumatic disorder (Han et al., 2010). Their main pathway into the environment is the discharge of treated and untreated waste water. Most NSAIDs are organic acids, they have a high water solubility and their removal rate from waste water varies between 3% and 90% depending on the WWTP (Farré et al., 2007; Lindqvist et al., 2005). In contrast to the sulfonamide antibiotics, NSAIDs tend to accumulate in soils and sediment (see logK$_{OW}$ tab. 1.1), are more photolabile and easily degraded by photolysis (Packer et al., 2003; Poirier-Larabie et al., 2016; Carmona et al., 2014). Regardless of being photolabile, their occurrence in the environment is of great danger to its inhabitants. As diclofenac acid (DCF) is one of of the most used NSAIDs with a consumption rate of 84 t/a in Germany (2012), it was chosen for analysis (UBA, 2011). Ketoprofen (KPF) was chosen based on its similar structure and behavior to DCF and it is often used as an alternative for DCF in medicine. Especially, DCF is of emerging environmental concern and has been placed on the watch list by the European Union (EU) under the EU directive 2013/39/EU (EU, 2013; UNESCO and HELCOM, 2017). The EU proposed an annual average environmental quality standard of 10 ng/L for DCF in the aquatic environment (UNESCO and HELCOM, 2017). Many studies have proven the toxicological effects of DCF: It not only causes structural alterations and necrosis in the gills of trout, it also has cytological effects and evokes histological changes in the liver and kidney of trout, e.g. *O. mykiss*, *Salmon trutta*, at low μg/L concentrations (Schwaiger et al., 2004; Triebskorn et al., 2004; Lahti, 2012). It furthermore impairs the osmosis regulatory abilities of the *carcinus maenas*, reduces the lipid peroxidation in zebrafish embryos and has chronic effects on the fern *polystichum setiferum* (Eades and Waring, 2010; HELCOM, 2013). DCF can also be bioconcentrated in the Baltic Sea blue mussels and simultaneously impairs their ability to attach to underlying substrate (HELCOM, 2013). NSAIDs are not only affecting the aquatic but also the terrestrial fauna. For instance, DCF and ketoprofen (KPF) toxicity causes the decline of the *Gyps* vultures in Asia (Naidoo et al., 2010).

The last analyzed pharmaceutical is fenofibrate (FFB), which is used as a lipid-regulator to treat hyperlipoproteinemia, as it reduces the plasma triglyceride concentration (Fent, 2006). It was chosen for analysis based on its consumption rate in Germany in 2012 (tab. 1.1). In the environment it can be counted as persistent as its half-live times ($t_{1/2,water}$ = 60 days, $t_{1/2,sediment}$ = 540 days) exceeds the EU criteria (Hernando et al., 2007). Furthermore, it was proven that FFB poses an acute toxicity and possibly a chronic toxicity to fish (Hernando et al., 2007).

Table 1.1: Characterization of the analyzed pharmaceuticals, their ecological concern and potential for sorption to soils. Based on the octanol/water partition coefficient logK_{OW} compounds can be divided into classes of sorption potential: logK_{OW} < 2.5 low sorption, $2.5 <$ logK_{OW} < 4 medium sorption, logK_{OW} > 4 high sorption (Gothwal and Shashidhar, 2015). (h- human, v- veterinary, NSAID- non-steroidal anti-inflammatory drug)

Name	Commercial Name	Abbr.	Usage	logK_{OW}	Sale* [t/a]	Environmental concern
4-amino-N-(5-methyl-3--isoxazolyl)benzene-sulfonamide	sulfamethoxazole	SMX	antibiotic (h, v)	0.68[1]	26.1	resistant genes (sulI, sulII) in rivers, lakes, wwtp[2, 3, 4, 5] risk to aquatic org. possible toxic[6] mutagenic[7]
2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine	trimethoprim	TMP	antibiotic (h, v)	0.65[1]	5.7	interferes with bacterial dihydrofolate reductase enzyme[8]
4-amino-N-(2-pyrimidinyl)-benzenesulfonamide	sulfadiazine	SDZ	antibiotic (h, v)	-0.34[9]		bioaccumulative[6] resistant genes (sulI, sulII) in rivers, lakes, wwtp[2, 3, 4, 5]
4-amino-N-(4-methyl-2--pyrimidinyl)benzene-sulfonamide	sulfamerazine	SMZ	antibiotic (v)	0.44[9]		resistant genes (sulI, sulII) in rivers, lakes, wwtp[2, 3, 4, 5]
2-(2-((2,6-dichlorophenyl-amino)phenyl)acetic acid	diclofenac acid	DCF	NSAID	4.51[10]	84.4	histological change of kidney and liver in trout[11] structural alteration necrosis in gills of trout[12] impairs osmosis regulatory abilities green shore crab[13, 14] reduces lipid peroxidation in zebrafish embryos[14] chronic effect DNA of fern[14] oxidative stress[15]
2-hydroxybenzoic acid	salicylic acid	SA	NSAID metabolite	2.26[10]		potentially bio-accumulative[1]
2-(3-benzoylphenyl)-propionic acid	ketoprofen	KPF	NSAID	3.12[10]		toxic photoproducts[16] toxic to vulture[17]
2-[4-(4-chlorobenzoyl)-phenoxy]-2-methyl-propanoic acid isopropyl ester	fenofibrate	FFB	lipid regulator	5.19[18]	8.3	toxic for fish, *D. magna*[18]

* Sales data for Germany in 2012 (UBA, 2013)

[1] Wille et al. (2010), [2] Sköld (2000), [3] Jiang et al. (2011), [4] Gao et al. (2012), [5] Guo et al. (2014), [6] Na et al. (2013), [7] Isidori et al. (2005), [8] Straub (2013), [9] Chen and Zhou (2014), [10] Rodil et al. (2009), [11] Schwaiger et al. (2004), [12] Triebskorn et al. (2004), [13] Eades and Waring (2010), [14] HELCOM (2013), [15] Oviedo-Gómez et al. (2010), [16] Hanamoto et al. (2014), [17] Naidoo et al. (2010), [18] Hernando et al. (2007)

1.1.2 Personal care products

Organic ultraviolet filters (UV-filter) belong to the group of personal care products (PCPs), as they are used in many sunscreens, lotions, hair dyes, shampoos, varnishes, soaps, as well as in clothes and all kinds of plastics (Negreira et al., 2009). Their main function is the protection against UV-radiation, e.g. in this case UV-A and UV-B. Furthermore, some UV-filters can additionally be used as stabilizers for other UV-filters or as light stabilizer in polymer-based products and paints (Kameda et al., 2011). In lotions, especially sunscreens, they are used to protect the skin from acute (sunburn) or chronic (skin cancer) exposure to the sun (Grabicova et al., 2013). Up to 28 UV-filters are regulated in the EU cosmetic directive 76/768/EEC/1976 until today. Their maximum allowed concentration in cosmetic products is regulated in annex VI of the regulation (EC) no 1223/2009 (EU, 2009). UV-filters can enter the environment similar to the pharmaceuticals via two different pathways: Indirect via discharge of waste water or directly due to recreational activities. The direct input is expected to be the major pathway into the environment (Balmer et al., 2005).

In this study 11 UV-filters with different chemical properties were analyzed. The UV-filters were chosen based on their maximum allowed concentration in cosmetic products in Europe and China (tab. 1.2) and on their already high detected concentrations in other coastal ecosystems (tab. A1). The most polar UV-filter of this study was benzophenone-4 (BP-4) followed by 2-phenylbenzimidazole-5-sulfonic acid (PBSA) (tab. 1.2, for structure see tab. A2). PBSA strongly absorbs UV-B radiation and prevents erythema. It is not persistent in water and is photolabile even in sunscreen. The direct photolysis is the major loss pathway of PBSA in natural surface waters. Its half-live time in the summer is approx. 3 days (Zhang et al., 2012; Ji et al., 2013), in winter it is expected to be slightly longer. Yet, its high detection frequency in the aquatic environment and its ability to cause toxic stress in fish is of ecological concern (Rodil et al., 2012; Grabicova et al., 2013). The benzophenone's-1,2,3 (BP-1, BP-2, BP-3) and 4-methylbenzylidenecamphor (4-MBC) are medium polar (tab. 1.2). They are more persistent, lipophilic, stable against biodegradation and can possibly be accumulated in the food chain (Díaz-Cruz and Barceló, 2009; Negreira et al., 2009). Benzophenones and 4-MBC have grave effects on marine organisms (tab. 1.2). BP1-4 and 4-MBC exert anti-androgenic and estrogenic actions and possibly interfere with the sex hormone system affecting the reproduction in fish (Negreira et al., 2009; Zucchi et al., 2011; Díaz-Cruz et al., 2012). They not only negatively affect the reproduction but also the fecundity of fish and potentially cause coral bleaching (Kunz and Fent, 2006; Kunz et al., 2006; Coronado et al., 2008; Fent et al., 2008). 4-MBC moreover affects benthic organisms as it decreases the reproduction and increases the mortality rate (Schmitt et al., 2008). The more non-polar UV-filters of this study are octocrylene (OC), padimate-O (OD-PABA) and octinoxat (EHMC) (tab. 1.2). There is reason to assume that these UV-filters might be more persistent in the environment than the others. OC possesses a high lipophilicity and stability in the environment and has a high affinity for the solid phase (Brausch and Rand, 2011). Due to its lipophilicity, OC is possibly bio-accumulative in mussels (*M. galloprovincialis, M. edulis*), fish (*Gadus sp.*) and organisms of higher trophic levels as it was detected in the liver of the *Franciscana dolphin* (Balmer et al., 2005; Bachelot et al., 2012; Gago-Ferrero et al., 2013, 2015; Langford et al., 2015). Besides the bio-accumulation OC also affects the hematopoiesis, blood vessel formation and blood flow in the zebrafish *D. rerio* (Blüthgen et al., 2014).

The compound nonylphenoxyacetic acid (NP_1EC) is an intermediate formed in the aerobic degradation process of nonylphenol polyethoxylate, which is a non-ionic surfactant mostly used in industrial laundry detergents (Marcomini et al., 1988; Montgomery-Brown et al., 2008). NP_1EC can be further degraded to the endocrine disrupting compound nonylphenol. In contrast to nonylphenol, NP_1EC is a more polar compound and more likely to be found in the water phase (tab. 1.2). The usage of nonylphenol polyethoxylate was restricted in the EU (directive 2003/53/EC) and other countries in order to lower the environmental risk of the toxic metabolites (EU, 2003). As NP_1EC also shows endocrine disrupting activities against organisms; it is listed in category 2 of the European endocrine disruptor priority list (Esteban et al., 2014).

Table 1.2: Characterization of the analyzed personal care products, their ecological concern and potential for sorption to soils. Based on the octanol/water partition coefficient logK_{OW} compounds are divided into classes of sorption potential: log$K_{OW} < 2.5$ low sorption, $2.5 <$ log$K_{OW} < 4$ medium sorption, log$K_{OW} > 4$ high sorption (Gothwal and Shashidhar, 2015). The enlarged table can be found in the annex (tab. A3).

Name	Commercial Name	Abbr.	Usage	logK_{OW}	max. Conc* [%]	Environmental concern
4-methylbenzylidene camphor	Enzacamen	4-MBC	cosmetics	4.9[1]	4	estrogenic potential[2] decreases reproduction, increases mortality rates of benthic organisms [3] potential cause of coral bleaching[4] bioaccumulative in fish[5]
2,4-dihydroxybenzophenone	Benzoresorcinol, benzophenone-1	BP-1	cosmetics, plastics	3.2[6]		estrogenic portential[20] potential cause of coral bleaching[4] estrogenic, androgenic and antiandrogenic activity[7]
2,2',4,4'-tetrahydroxybenzonphenone	benzophenone-2	BP-2	cosmetics	3.2[6]		estrogenic potential[2] potential cause of coral bleaching[4] estrogenic, androgenic and antiandrogenic activity[7]
2-hydroxy-4-methoxy-benzophenone	Oxybenzone, benozphenone-3	BP-3	cosmetics	3.79[1]	10	coral bleaching[4] high estrogenic activity[7, 8] estrogenic, antiestrogenic and antiandrogenic activity[7] bio-accumulative[5, 6]
5-benzoyl-4-hydroxy-2--methoxybenzenesulfonic acid	Sulizobenzone, benzophenone-4	BP-4	cosmetics	0.4[1]	5[a]	estrogenic, anti-androgenic action[7] might effect reproduction in fish[7] interferes with sex hormone system of fish[9]
4,4'-dihydroxybenzophenone		4-DHB	UV-stabilizer			estrogenic and antiandrogenic activity[7] metabolite of BP-3
2-ethylhexyl-4-methoxycinnamate	Octinoxat	EHMC	cosmetics	5.8[1]	10	estrogenic potential[2] potential cause of coral bleaching[4]
2-ethylhexyl 2-cyano-3,3-diphenyl-2-propenoate	Octocrylene	OC	UV-filter/stabilizer in cosmetics/plastics	6.9[1]	10	bioaccumulative[10, 11, 12] estrogenic in zebrafish[13] antiestrogenic and antiandrogenic activity[7]
2-ethylhexyl-4-(dimethyl-amino)benzoate	Padimate-O	OD-PABA	cosmetics	6.2[1]	8	antiestrogenic and antiandrogenic activity[7]
ethyl-4-eminobenzoate	Benzocaine	Et-PABA	cosmetics (PCP), anesthetic ointments			estrogenic and antiandrogenic activity[7]
2-phenylbenzimidazole-5-sulfonic acid	Ensulizol	PBSA	cosmetics	1.5[1]	8	cause toxic stress in fish[14]
nonylphenoxyacetic acid		NP_1EC	non-ionic surfactant (metabolite)	2.2[15]		endocrine activity[16]

* max. allowed concentration in EU and China (Sánchez-Quiles and Tovar-Sánchez, 2015), [a] only for China

[1] Rodil et al. (2009), [2] Heneweer et al. (2005), [3] Schmitt et al. (2008), [4] Danovaro et al. (2008), [5] Balmer et al. (2005), [6] Negreira et al. (2009), [7] Díaz-Cruz and Barceló (2009), [8] Díaz-Cruz et al. (2012), [9] Zucchi et al. (2011), [10] Bachelot et al. (2012), [11] Gago-Ferrero et al. (2013), [12] Langford et al. (2015), [13] Blüthgen et al. (2014), [14] Grabicova et al. (2013), [15] Pojana et al. (2007), [16] Esteban et al. (2014)

2 Motivation and hypotheses

Globalization and the rising demand for food has led to the exploitation of the oceans and the destruction of marine ecosystems. The science year 2016-2017 in Germany was placed under the slogan ’Seas and Oceans - Discover, Use, Protect’. As a response to the growing stress of the coastal ecosystem, their protection and sustainment is of great concern to many governments. Therefore, many countries around the world have established programs in order to protect the ocean. MARE:N is a research program embedded in the *Research for Sustainable Development* (FONA - Forschung für Nachhaltige Entwicklung) of the German ministry of education and research, defining the direction for marine research in the upcoming years and focusing on climate change, pollution and sustainability.

The pollution of the ocean and coastal zone is of considerable concern not only for the health of the ocean but for the human population as well, as its degree and impact on the environment still has to be determined (Steffen et al., 2011).

One key aspect in determining the degree of ocean pollution is the investigation of PPCPs in the marine environment. As the knowledge about their occurrence in the coastal ecosystems is even more limited and their possible ecological effects are widely unknown, these substances are in focus of scientific interest and of major scientific concern. The motivation of this thesis was to analyze PPCPs in coastal ecosystems and rivers of extreme differences and to compare them. First it was investigated, if PPCPs occur in marine ecosystems in different climatic zones and if their concentrations are of risk to marine organisms. The comparison was made between a temperate (Baltic Sea), subtropical (East China Sea) and a tropical (South China Sea) ecosystem, based on the detected concentration ranges and the calculated risk assessments. Secondly, rivers of different sizes, with different physical regimes, catchment areas, population densities and degree of anthropogenic influences, were analyzed for PPCPs and the distribution patterns along rivers were examined. Both comparisons were carried out to answer the question, if the occurrence of PPCPs is a regionally restricted or global problem and to quantify the degree of anthropogenic stress on studied ecosystems at the current time.

Before the analysis of environmental samples, a method for solid-phase extraction and liquid chromatography heated electrospray tandem mass spectrometry was developed. This work was done assuming that the PPCPs are transported through the rivers to the marine environment and only the input via the water phase of pre-selected rivers was considered.

3 Methodological approach

In order to analyze pharmaceuticals in marine ecosystems a solid-phase extraction (SPE) and liquid chromatography method was developed. The baseline for it was the previously established method for detecting UV-filters and pesticides published by Orlikowska et al. (2015). At the beginning two different sorbent materials were tested. The Chromabond® EASY (3 mL, 200 mg, Marchery-Nagel GmbH) cartridge with a polystyrene-divinylbenzene co-polymer with an ion exchange was chosen as extraction material. Thereupon the extraction was carried out at different pH-values (pH= 3, 5, 7, 10), as the compounds have different pK$_a$-values and can exist in varying ionic or neutral forms in water. Furthermore, different washing, elution and re-constitution solutions were evaluated allowing the best recovery rates for all pharmaceuticals. The solid-phase extraction of the pharmaceuticals was carried out after the following procedure, which was published in Fisch et al. (2017b): For each sample pre-cleaned amber glass bottles were used. 1 L of sampled water was spiked with an internal standard, consisting of sulfamethoxazole-d4 (20 ng/L) and diclofenac-d4 (10 ng/L), and acidified to pH=5 with 5M HCl. Each SPE cartridge was conditioned with 4 mL acetone (Ac) and 4 mL water. The samples were loaded onto the SPE cartridge via a filtration unit equipped with a GF/F glass-fiber filter (0.7 μm, Whatman). Each SPE cartridge was washed with 4 mL water (pH=5), after the extraction, and gently dried under low-vacuum pressure. The samples were eluted with 10 mL Ac/MeOH (1/1, v/v) and evaporated to total dryness with a Turbo-Vap (LV, Zymark, USA) evaporator. For re-constitution, 1 mL of a mixture of water/MeOH (3/1, v/v) was used. The samples were analyzed with a liquid chromatography heated electrospray ionization tandem mass spectrometer (LC-HESI-MS/MS) from Thermo Fischer Scientific (Germany).

Before the development of a LC-HESI-MS/MS method each compound was tuned for the following parameters: precursor ion, product ion, collision energy, s-lens settings. The LC-HESI-MS/MS method for UV-filters and pesticides by Orlikowska et al. (2015) was used again as a base. For chromatographic separation a reverse-phase Kinetex C-18 column (2.6 μm, 50 x 2.1 mL, 100 Å, Phenomenex, USA), equipped with a pre-connected guard column, was used. Of each 1 mL sample 10 μL were injected unto the column via an Accela Autosampler (Thermo Fischer Scientific, Germany). A gradient program, with a flow rate of 250 μL/min was run with the same mobile phases as used in Orlikowska et al. (2015): mobile phase A (water + 0.1% acetic acid), mobile phase B (MeOH + 0.1% formic acid). The temperatures of the capillary and vaporizer were set to 275°C and 250°C, respectively. All measurements were carried out in the selective reaction monitoring (SRM) mode. For each compound two specific transitions from precursor molecular ion to product ion were monitored (tab. A4). Quantification was performed on the area of the most abundant transition (based on signal-to-noise ratio) and the area of the internal standard. Qualification was done on the area of the second most abundant ion. The area ratios (area standard/area internal standard) were used to calculate the recovery rate for each pharmaceutical (tab. A4). The LC-HESI-MS/MS method was published in Fisch et al. (2017b).

4 Assessment of results

4.1 Occurrence and risk assessment of PPCPs in seawater

The occurrences of PPCPs in three different coastal ecosystems, the Baltic Sea (Fisch et al., 2017b), the East and the South China Sea (Fisch et al., 2017c,a) were under investigation (fig. 1.3). In each analyzed coastal ecosystem PPCPs were detected in different concentration ranges (fig. 4.1). Non-steroidal anti-inflammatory drugs (NSAIDs) were not detected in any marine sample in this study. It is possible that the degradation of NSAIDs due to photolysis (e.g. DCF: $t_{1/2}$ = 0.4 ± 0.05 days), is faster than the transport from the point or diffused source into the marine environment (Poirier-Larabie et al., 2016).

In the Baltic Sea only two pharmaceuticals (SMX, SA) and two UV-filters (OC, PBSA) were detected (fig. 4.1). In comparison to the East and South China Sea a wider concentration range (14.3-54.6 ng/L) with a higher median (28.2 ng/L) concentration was measured (Fisch et al., 2017b). However, the sampling stations were much closer to the shore than in the other two seas. Only the antibiotic SMX was detected in the Baltic Sea and it did not display a strong variation in concentration along the coastline. The detected concentrations in the Baltic Sea were similar to the detected SMX concentration in the river mouths. SMX is not easily degradable and is sufficiently hydrophilic to move in the aquatic environment. With an estimated half-life of 85-100 days in seawater it can be transported over a longer distance and be diluted in the respective basin (Zheng

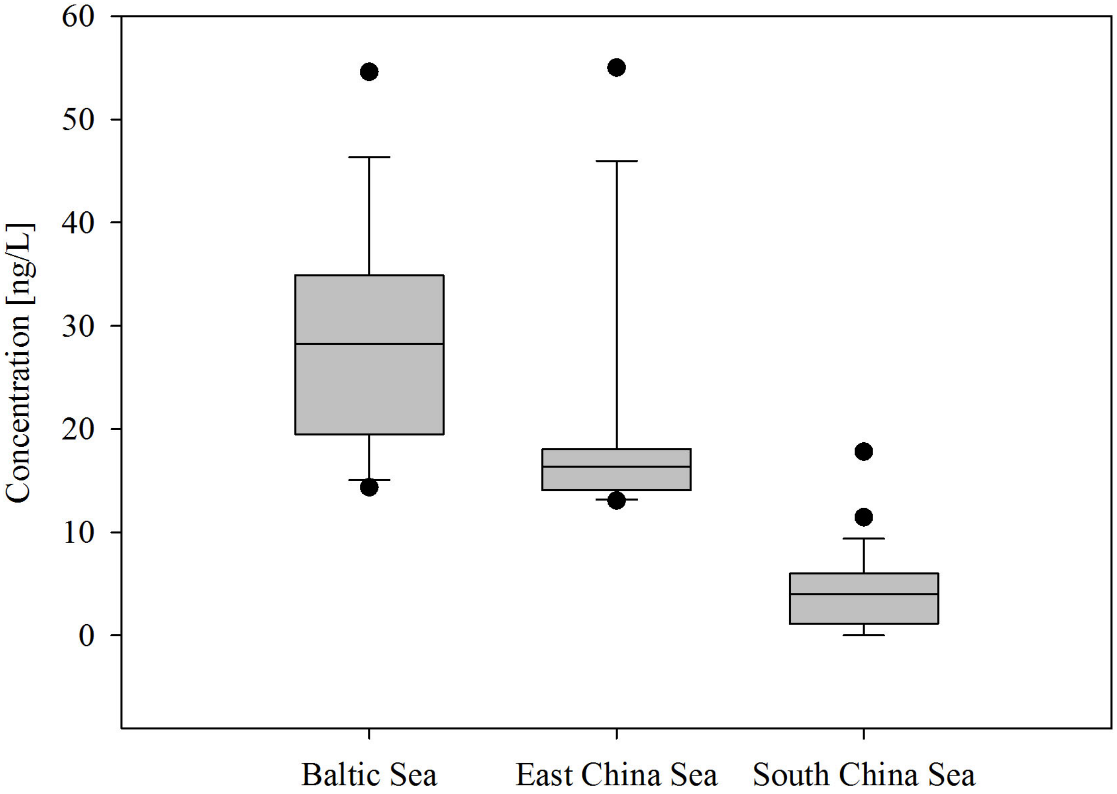

Figure 4.1: Concentration ranges [ng/L] of all detected PPCPs in the Baltic Sea (August 2015, n=14), East (July 2016, n=12) and South China Sea (March 2015, n=29). Each boxplot presents 10-90 % of the data, ⊥ minimum and maximum value, the horizontal lines represent median value.

et al., 2012). The measured concentration of SMX in this study is lower than previously reported median concentration in the Baltic Sea by Nödler et al. (2014) (see also tab. A1 and section 3.1. in Fisch et al. (2017b)). The metabolite SA varies along the coastline. However, more detailed studies focused on the behavior of this compound are needed to better evaluate these variations. Additionally, for both compounds it can be assumed that their low input occurs indirectly via rivers.

The UV-filter PBSA displayed a different occurrence pattern than the pharmaceuticals. The concentration of PBSA slowly increases along the coastline and was only detected from mid-day on. It is relatively photolabile and has a short half-life of approximately 3 days from June-August (Zhang et al., 2012). This would explain its absence during the morning as it is possibly degraded during the late afternoon. Furthermore, elevated concentrations were measured at a time with a high recreational activity rate. The concentration of the other UV-filter OC varied more than PBSA. OC was detected at every station. As for PBSA, an increase and high concentration level were detected during mid-day at the same sampling station. It can be assumed that the direct input of both UV-filters is of importance. Additionally, it was observed that higher concentrations of PBSA than OC were detected in rivers with a reverse situation in the marine environment, as has been reported by other studies (Sánchez-Quiles and Tovar-Sánchez, 2015). However, both compounds were of lower concentration than in other ecosystems mentioned in previously reported studies (tab. A1).

The East China Sea displays the second highest PPCP concentration range (13.5-55.0 ng/L) but it has a lower total median concentration of 16.4 ng/L than the Baltic Sea (fig. 4.1) (Fisch et al., 2017c,a). In contrast to the Baltic Sea, 3 antibiotics (SMX, TMP, SDZ) were detected in the surface waters of the East China Sea. The concentrations decrease from stations near the coast towards stations further off-shore. All sulfonamide antibiotics and TMP are relatively persistent (half-life in seawater: $<$ 100 days) and are not inclined to degrade (Zheng et al., 2012). Furthermore, they have low sorption potential to soils, sediment and suspended particulate matter (SPM), which may explain the presence in the surface water and their absence in the near bottom layer (Yang et al., 2011; Gothwal and Shashidhar, 2015). Results of this study show how far off-shore antibiotics already can be found. However, the comparison with literature data shows that the measured concentrations of this study are lower than concentrations measured in other ecosystems (see tab. A1 and tab. 3 of Fisch et al. (2017c)). Though, most of the studies referred to have been carried out closer to the coast line or in bay areas, which may explain the higher concentrations due to a smaller dilution effect.

OC was the only UV-filter which was found in 33% of the surface water and 50% of the near bottom layer water samples of the East China Sea. Its maximum concentration (30.1 ng/L) was similar to the maximum concentration (30.8 ng/L) in the Baltic Sea. However, it was mostly detected at low ng/L concentrations and close to the limit of detection. OC displays a positive correlation coefficient (PEARSON) with salinity, which indicates that the dilution effect is minor. However, it is still assumed that it was transported with the Changjiang Diluted Water from the Changjiang Estuary into the East China Sea. In contrast to the antibiotics OC was found more often in near bottom layer samples than in the surface water samples and also at slightly higher concentrations. As it is a lipophilic compound, which tends to adsorb to soils (e.g. particulate organic carbon (POC), SPM, sediment), sedimentation may be a possible sink for OC in the environment. A higher detection frequency in the near bottom layer may be partly caused by desorption from re-suspended matter (Tsui et al., 2015). As for the Baltic Sea, the detected concentration of OC in the East China Sea is lower than concentrations reported in literature. This is likely due to a higher dilution effect, because of the longer transport from the coast, as in the case of antibiotics.

Additionally, the polar pollutant NP_1EC was found in all surface waters and in 75% samples of the near bottom layer, in a total range of n.d.-18.2 ng/L (Fisch et al., 2017a). As for the antibiotics the NP_1EC concentration decreases from the near coastal stations towards the off-shore stations and from surface to bottom. A negative correlation coefficient (PEARSON) with salinity, POC and chlorophyll a (Chl a) was detected, indicating that dilution and possibly sorption to particles are major key players shaping the distribution pattern and the decrease of concentration in the water phase.

As only one component (OC) was detected in the South China Sea, the total range of PPCP concentration is smaller than in the other seas (fig. 4.1). OC was detected at low ng/L concentrations in 76% of surface water samples (Fisch et al., 2017a). It was mostly detected on the eastern side of the Pearl River Estuary. The median concentration (4.0 ng/L) is in similar range as median concentration in the Pearl River measured later. The concentration is also in similar range as the detected concentrations in the Baltic Sea and East China Sea of this study. However, it is much lower than the OC concentrations which have been reported for other ecosystems (tab. A1). In this study, higher concentrations of OC were detected near Dongsha Island. A cyclonic eddy exists near the island and it has been reported, that the eastward Pearl River plume is entrained by the eddy's anticlockwise rotation (He et al., 2016). As in the East China Sea a negative correlation coefficient (PEARSON) was calculated between OC and POC and OC and Chl a. It is an indication that the solid phase is a possible sink for OC in the marine environment. However, more detailed studies are needed to determine the significance of it.

In order to evaluate the detected concentrations in all seas, a risk assessment has been carried out. The risk quotient (RQ) has been estimated by dividing the measured environmental concentration (MEC) by the predicted no effect concentration (PNEC) (Fisch et al., 2017b). The RQ is divided into three levels: RQ $<$ 0.1 low risk, 0.1 $\leq$ RQ $\leq$ 1 medium risk, 1 $\leq$ RQ high risk. Results show that the MEC of most components only poses a very low risk to aquatic organisms in the three water systems at this point. Only the antibiotic SMX poses a medium risk to the blue-green algae in the Baltic Sea (RQ=0.2, Fisch et al. (2017b)) and in the East China Sea (RQ=0.2). It has to be noted, that these RQs were calculated for each individual component and not the mixture of detected PPCPs. Firstly, it remains to be investigated, if the RQ of a PPCP mixture is increased as the RQ of mixtures is unknown so far. Secondly, the RQ only considers the acute toxicity and not a possible chronic toxicity, this needs to be investigated as well.

4.2 Distribution pattern along rivers

Pre-selected rivers, which drain into marine ecosystems of Baltic Sea, East and South China Sea, have been analyzed for their contamination with PPCPs. Especially the comparison of three rivers (Mühlenfließ, Huangpu River, Pearl River) demonstrates their different distribution patterns. The most dominant compounds in all rivers were antibiotics, OC and NP_1EC (only analyzed in China). The Mühlenfließ, a small stream draining into the Baltic Sea, displays the largest concentration range of PPCPs (16.6-1403.4 ng/L) (fig. 4.2, concentrations have been divided by factor 2 for graphical reason) (Fisch et al., 2017b). It is the only river in which NSAIDs were detected. Despite its high degree of contamination, its median value (22.9 ng/L) is lower than the median value of the other two rivers. In contrast, the Huangpu River has the lowest concentration range (234.4-681.6 ng/L) but it has the highest median concentration (568.7 ng/L) (Fisch et al., 2017c,a). The Pearl River does display a slightly smaller concentration range (37.7-396.9 ng/L) than the Huangpu River and its median value (346.8 ng/L) is lower as well (Fisch et al., 2017c,a).

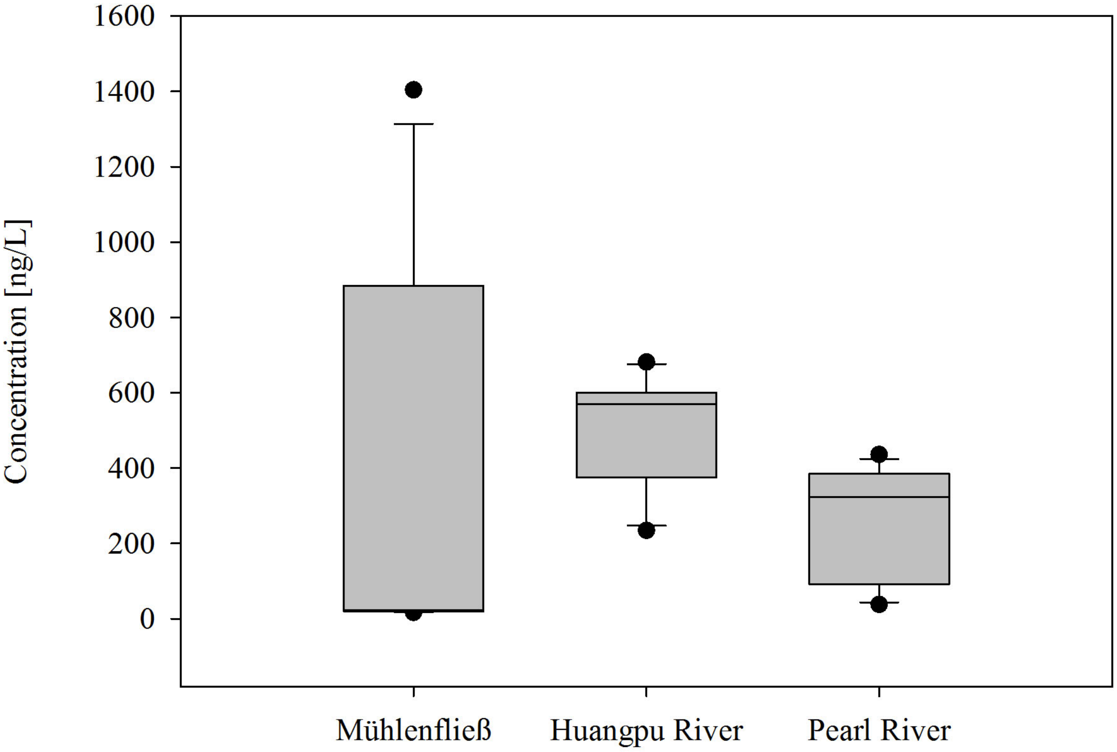

Figure 4.2: Concentration ranges [ng/L] of all detected PPCPs in the Mühlenfließ (August 2015, n=11), Huangpu River (June 2016, n=10) and Pearl River (August 2016 n=12). Each boxplot presents 10-90% of the data, ⊥ minimum and maximum value, the line represents the median value.

The Huangpu and Pearl River are large rivers, flowing through megacities (Shanghai and Guangzhou, respectively), draining large areas with high domestic and industrial activities and are exposed to high amounts of untreated waste water, which explains their higher median values (Lee, 2006; Zhang et al., 2015). The detected concentrations of antibiotics are in similar range as in the literature (tab. A1, fig. 2 and tab. 3 in Fisch et al. (2017c)). In contrast, the Mühlenfließ is a small effluent receiving stream which is mostly exposed to timberland and agriculture, which explains the low median concentrations. The different concentration ranges can be explained by the different distribution pattern which the rivers display (fig. 4.3). As the Mühlenfließ drains an agricultural area, it is only exposed to low doses of PPCPs as the inland stations reflect (stations MF6-11, see Fisch et al. (2017b)). PPCP concentrations are similar at the inland and the last estuary station (fig. 4.3). The high concentration range can be explained by an apparent unknown diffused source near the estuary (see elevated value in fig 4.3). This source exposes the Mühlenfließ to a high amount of additional PPCPs. Yet, the concentration decreases fast towards the Baltic Sea. Excluding the unknown source, the Mühlenfließ represents a small and static freshwater ecosystem.

The Huangpu River represents a large freshwater system, which is exposed to high domestic and industrial activities. During this study the highest concentrations were measured in the Huangpu River (Fisch et al., 2017c,a). The salinity is approx. zero along the river and there is almost no marine impact on the river system. The concentrations along the flow direction show a different distribution pattern than in the Mühlenfließ (fig. 4.3). No obvious input source was found for any component and the river presents a slight static system. The concentrations do not vary as strongly as in the Mühlenfließ, the contribution along the Huangpu River appears to be more uniform. However, a small increase can be seen comparing the inland station with the station in the estuary. This small increase towards the estuary is possibly due to the high rate of cosmetic industries and consequentially a possible higher input of contaminated waste water towards the estuary (Wu et al., 2017).

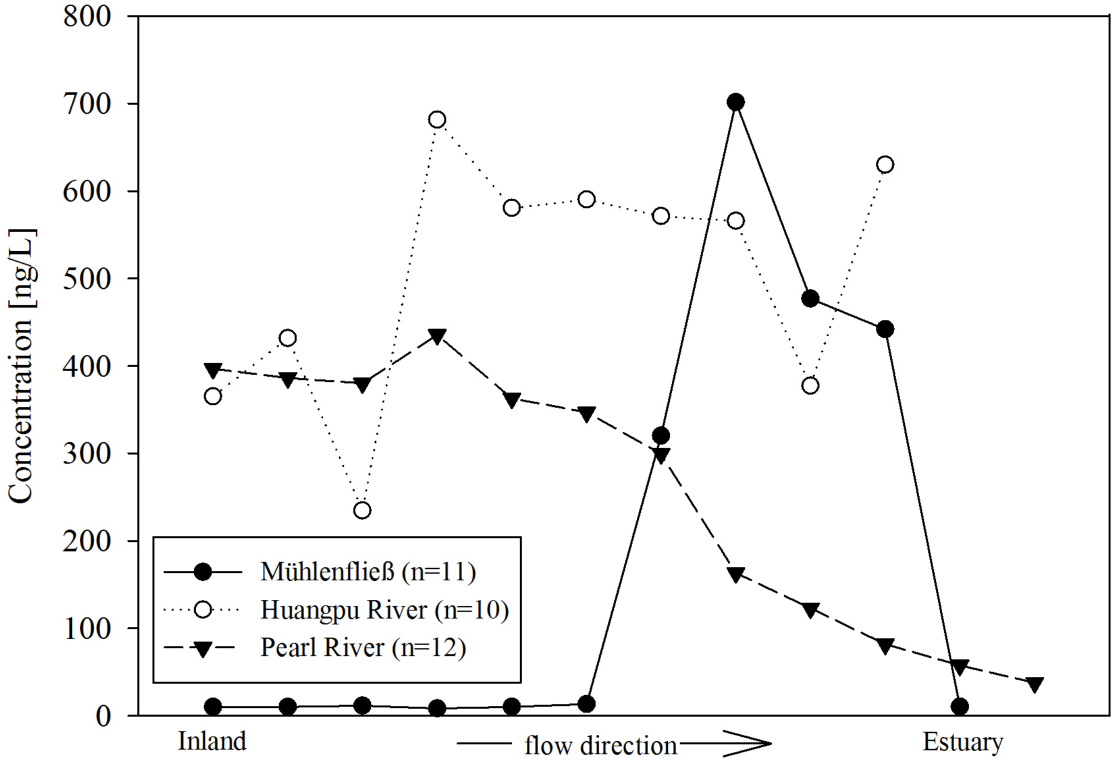

Figure 4.3: Distribution pattern of PPCPs in the Mühlenfließ (August 2015), Huangpu River (June 2016) and Pearl River (August 2016) from inland stations towards the estuaries. Data was obtained from (Fisch et al., 2017b,c,a). The concentrations of the Mühlenfließ have been divided by a factor of 2, only for better graphical comparison.

The Pearl River and its estuary is the largest analyzed river system in this study. It is assumed that due to its larger water volume the concentrations are lower than in the Huangpu River. However, a calculation of the total mass load has shown that the Pearl River carries a higher mass load of PPCPs than the Huangpu River (Fisch et al., 2017c,a). The Pearl River is a dynamic water system influenced by tides. In the Pearl River the dilution effect along a salinity gradient can be seen for the detected PPCPs (fig. 4.3), for more details see fig. 4 in Fisch et al. (2017c) and fig. 7, S1 in Fisch et al. (2017a). The concentration decrease of antibiotics and NP_1EC correlates strongly with the salinity increase (r=-0.9 and r=-0.9, respectively). For the UV-filter the dilution is not as significant as for the other compounds. OC reaches a constant unvarying concentration towards the open South China Sea (Fisch et al., 2017a).

The studies in the Huangpu and Pearl River show that the concentration range of PPCPs and their distribution pattern are a function of many different environmental factors. The physical regimes (e.g. tidal influence) and the morphological properties (e.g. river/estuary width, depth) play an important role when analyzing the temporal and spatial distribution of a compound. For example, lower concentrations in a broader river or estuary do not result in a lower mass load. The mass load depends on the water volume of each river. Lower concentrations of PPCPs were detected in the Pearl River than in the Huangpu River (fig. 4.3). Yet, the mass load in the Pearl River is higher due to a larger water volume (Fisch et al., 2017c,a). The dimension of the catchment areas and their dominant industrial activities are also factors impacting the occurrence of PPCPs in the aquatic environment. The catchment area of the Pearl River is heavily influenced by intensive livestock industry (e.g. pig, poultry, aquaculture) (Richardson et al., 2005). Therefore, the higher concentrations and the much higher mass load of antibiotics in the Pearl River are possibly due to the high agricultural activities in its catchment area (Fisch et al., 2017c). These factors and processes have to be considered, when analyzing a water system, as they influence the observed distribution pattern.

4.3 Regional differences and anthropogenic stress

With this work regional differences in the occurrence of PPCPs in different marine ecosystems (fig. 4.1, tab. 4.1) were detected. The Baltic Sea was found to be the one with the highest median value and concentration range of the three seas. The Baltic Sea is known for being an enclosed sea and is classified as an enrichment basin. The water exchange with the North Sea is very limited and the freshwater input from the Baltic Sea riparian states is dominant. With the freshwater input, the input of contaminants is high, putting the Baltic Sea under great anthropogenic pressure (HELCOM, 2010). The detected PPCP concentrations do not vary much along the coast and it appears to be a steady situation (see fig. 3 in Fisch et al. (2017b)).

Table 4.1: General characteristics of the three seas.

	Baltic Sea[1]	East China Sea[2]	South China Sea[3]
Catchment area [km^2]	1728000	1931100	2500000
Population [mio.]	85	1729	350
Area [km^2]	415120	770000	3685000
Volume [km^3]	21631	398000	3907000
Max. depth [m]	459	2719	5016
Water exchange	restricted	semi-restricted	not restricted
Tides	no	yes	yes
Climate zone	temperate	sub-tropical	tropical
Trophic state	eutrophic	eutrophic (coast)	oligotrophic

[1]HELCOM (2010), [2]UNEP et al. (2005a), [3]UNEP et al. (2005b)

The East China Sea is a less restricted sea than the Baltic Sea and the water exchange between the East China Sea and the Pacific is greater than in the Baltic Sea (UNEP et al., 2005a). PPCPs were still detected but at a lower concentration range (fig. 4.1). The concentrations decreased from near coastal stations toward the more off-shore stations. As all samples were taken from the Changjiang Diluted Water (S $<$ 31), which is the dominant water mass in this region, it can be assumed that the detected PPCPs were transported into the sea with river water from the Chinese coastal area (UNEP et al., 2005a).

The South China Sea is an open system with high water exchange, due to that the Pearl River plume is subjected to strong dilution (UNEP et al., 2005b). Only one component (OC) was detected in this system, at concentrations near the limit of detection. The slightly raised concentrations at two stations were possibly caused by offshore transport of the Pearl River plume and entrainment into an eddy. However, the detection of OC so far off-shore suggests a long half-life time in the marine environment.

It has to be considered, though, that the presented studies were regionally, locally and seasonally strongly limited. This is a first attempt to compare the PPCP pollution in different coastal ecosystems in order to better reveal the anthropogenic influence on each system. It has to be taken into account that each system is influenced by different factors (tab. 4.1). The morphological conditions, e.g. restricted/non-restricted, freshwater input, are important factors. It may be possible that PPCP behave differently in marine ecosystems with different hydrographic (T-gradients, S-gradients, SPM, POC, dissolved organic carbon (DOC), etc.) and climatic (solar, UV-radiation, evaporation, etc.) conditions. For example, if the organic matter content in an ecosystem is very high, it is possible that compounds with a high logK_{OW} value, like OC, are more likely to be found in the solid phase, as they adsorb to particles. Different intensities of solar radiation can influence the degradation process of some compounds. For example, compounds like PBSA and NSAIDs are photolabile and are quickly degraded via direct photolysis in the environment. Whereas, other compounds (e.g. TMP) are photostable and the radiation does not affect their occurrence.

The size of the surrounding catchment area of the ecosystem and its population density are also of importance for the degree of pollution. The population around the Baltic Sea (approx. 85 mio.) is half as large as that around the Pearl River Delta (approx. 168 mio.) half as large, therefore less pollution could be expected. However, due to the enclosed shaping of the Baltic Sea the water exchange is limited, causing elevated concentrations. Furthermore, the different consumption behavior of the human population and the veterinary usage has to be considered, as the usage of PPCPs is different in each country. In Guangdong, the catchment area of the Pearl River, 30% of China's annual pig production, 10% of the poultry production and intensive aquaculture takes place. Antibiotics are greatly used to treat/prevent diseases and as growth promoters in these industries. More than 70% (2004) of the antibiotics prescribed in China were used in the Pearl River Delta/Hong Kong region (Richardson et al., 2005). Due to the high antibiotic usage the input into the environment is also higher. Another reason for larger input amounts are the different regulations and constructions of waste water treatment plants. The waste water treatment rate in China (32%) is lower than in Germany (97%) (OECD, Access: 05.01.2018). The discharge of waste water (treated or untreated) presents the indirect input of PPCPs into the environment. In the end however, the consistent discharge of PPCPs puts anthropogenic stress on the ecosystems and more detailed investigations about their behavior in the environment are essential.

5 Outlook

In this study the occurrence of PPCPs was investigated in ecosystems and rivers differing from each other by physical regimes and catchment areas. As mentioned before, the properties of the ecosystem and their dynamics, especially coastal and wind pattern, need to be considered, in order to gain more insight into the distribution patterns of PPCPs. Also the population density, domestic and industrial activities and federal regulations in the catchment areas are an important factor to estimate the degree of aquatic pollution and anthropogenic stress. These results show that more detailed studies, e.g. on different time scales (seasonality), compartments (air, sediment) are necessary in order to better evaluate those anthropogenic stressors on each ecosystem. Furthermore, their global occurrence and transport into regions with less human influence (polar regions) needs to be investigated as well.

At the same time more information is needed about the behavior of PPCPs in the environment. It is of great importance to evaluate the stability, e.g. half-life time, for many components in the marine environment or in the environment in general. As the results show PPCPs can be transported farther than has been presumed so far, as they were detected in off-shore waters. For some PPCPs degradation pathways have already been studied. Yet, the different degradation processes need to be further studied under environmental conditions and their degradation products need to be evaluated toxicologically as well.

Additionally, more toxicity studies on the effect of PPCPs mixtures and single compounds, which have not been investigated yet, on organisms are required. Most toxicological studies only focus on single compounds and on their acute toxicity, at concentrations higher than in the environment and only over a short time scale. As PPCPs are continuously discharged into the environment at low dosages, chronic toxicity studies of multiple compound mixtures at environmentally relevant concentrations are necessary, to allow for more accurate risk assessments.

As PPCPs with a high logK_{OW} tend to be adsorped onto the solid phase, e.g. POC, Chl a, SPM, particles, future research should also focus on sediments. If solid phase samples are taken at the same time as the water phase, then a more detailed analysis about the partitioning (water/sediment) of PPCPs in the marine environment would be possible. More information could be gained about their possible re-suspension, degradation or persistence as sediments might act as a sink for some of the PPCPs.

The scientific community is globally working on the development of new methods to analyze a greater number of emerging PPCPs. The next important step is to create a method for the analysis of PPCPs in the solid phase, e.g. sediments, particulate matter. A few work groups around the globe already started working on developing methods for the solid phase. However, these methods need to be further optimized and expanded to more PPCPs (Pojana et al., 2007; Kameda et al., 2011; Chen and Zhou, 2014; Tsui et al., 2015).

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The work of Kathrin Fisch to this publication accounts for approximately 85%.

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Contributions: Experiments, sampling, concept and manuscript writing by K. Fisch. Revision of manuscript and organization of sampling strategy in China done by B. Li and M. Zhou. Liang, Q., Ni, Y., and Liang, K. were involved in the organization and sampling in the South China Sea and Pearl River. Wang, Y. researched and determined the population data of the Pearl River Estuary. Revision of manuscript by J. J. Waniek and D.E. Schulz-Bull. Project principal investigator: J. J. Waniek.

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Occurrence of pharmaceuticals and UV-filters in riverine run-offs and waters of the German Baltic Sea

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ABSTRACT

The occurrence of pharmaceuticals and personal care products (PPCPs) in the marine environment is of great concern. This study was done to determine the emergence of eight pharmaceuticals and eleven ultraviolet filters (UV-Filters) in 5 rivers/streams discharging into the Baltic Sea. Furthermore, a focus was put on the influence of wastewater treatment plant as indirect source and the occurrence of the PPCPs in close beach proximity. Two pharmaceuticals (sulfamethoxazole, salicylic acid) and two UV-filters (2-phenylbenzimidazole-5-sulfonic acid, octocrylene) were detected in all analyzed water samples, with concentration ranging from 0.6 ng/L to 836.3 ng/L. In all rivers the PPCP concentration decreases towards the Baltic Sea. Sulfamethoxazole was detected at comparable concentration along the coast, which leads to the assumption of stable concentration in beach proximity. Along the coast UV-filters appeared in varying concentrations, leading to the conclusion that the direct input into the marine environment plays a bigger role than the indirect input.

1. Introduction

Nowadays, the pollution of the marine environment through pharmaceuticals and personal care products (PPCPs) is of growing scientific interest. PPCPs are a diverse group of organic compounds with variable uses and properties. Pharmaceuticals have a defined usage with specific requirements and are used in human or veterinary applications. Ultraviolet-filters (UV-filters) are one group of compounds used in many personal care products (e.g. shampoo, lotion, creams, sunscreen) to protect the skin against UV-radiation of the sun (Sánchez Rodríguez et al., 2015). Furthermore UV-filters are used as light stabilizers in polymer-based products and paints (Kameda et al., 2011). PPCPs can enter the marine environment indirectly through e.g. wastewater or groundwater or directly through recreational activities. Many studies show that PPCPs have a potential negative effect on the marine ecosystem and marine organisms. Some PPCPs can have endocrine disrupting effects (Blüthgen et al., 2014; Han et al., 2010; Schmitt et al., 2008; Zucchi et al., 2011), can cause coral bleaching (Danovaro et al., 2008) or can lead to possible antibiotic resistance (Costanzo et al., 2005; Kümmerer, 2003; Zhang et al., 2009). This study focuses on 8 pharmaceuticals, 4 sulfonamid antibiotics (sulfamethoxazole, sulfadiazine, sulfamerazine and trimethoprim), 3 non-steroidal anti-inflammatory drugs (NSAIDs) (diclofenac, ketoprofen, salicylic acid) and 1 lipid-regulator (fenofibrate) and 11 UV-filters: benzophenone-1 (BP-1), benzophenone-2 (BP-2), benzophenone-3 (BP-3), benzophenone-4 (BP-4), 4,4′-dihydroxybenzophenone (4-DHB), 4-methylbenzylidene-camphor (4-MBC), 2-ethylhexyl-4-(dimethylamino)benoate (OD-PABA), 2-ethylhexyl-4-methoxycinnamate (EHMC), 2-phenylbenzimidazole-5-sulfonic acid (PBSA), octocrylene (OC) and ethyl-4-aminobenzoate (Et-PABA). The occurrence of sulfaonamid resistant genes (sulI, sulII) in waste waster treatment plants, lakes and rivers has been reviewed by several study's (Gao et al., 2012; Guo et al., 2014; Jiang et al., 2011; Sköld, 2000). Additionally sulfonamid antibiotics can be bioaccumulative (Na et al., 2013). It is known that at a low concentration the NSAID diclofenac can have divers negative effects on marine organisms. Diclofenac impairs the osmoseregulatory ability of the green shore crab (*Carcinus maenas*) in the Baltic Sea at less than 100 ng/L (Eades and Waring, 2010; HELCOM, 2013). It can also cause alternations and necrosis in the gill and kidney of trouts (Schwaiger et al., 2004; Triebskorn et al., 2004). Salicylic acid was found in mussels of *Mytilus edulis* in the North Sea (Wille et al., 2011), which indicates a potential bioaccumulation. Most UV-filters tend to have a more lipophilic character than pharmaceuticals ($\log K_{OW} = 3–7$; see Table 1), are stable in the environment and due to their characteristics they tend to concentrate in surface microlayer and are possibly bioaccumulative in soil, particles and adipose tissue (Brausch and Rand, 2011; Gago-Ferrero et al., 2012; Tovar-Sánchez et al., 2013). Study's verified their occurrence in tissues of aquatic organisms such as fishes, crustacean, mussels and marine mammals (Fent et al., 2010; Gago-Ferrero et al., 2013; Sánchez-Quiles and Tovar-Sánchez, 2015). For examples, high

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Table 1
Overview of selected compounds, their detection frequency and range of measured concentration.

Name	Abbreviation	$\log K_{OW}$	Detection frequency [%]	Concentration [ng/L]		
			($N = 42$)	Min.	Max.	Median
UV-filter						
Benzophenone-1	BP-1	$3.17^{(1)}$	11	1.3	2.8	2.2
Benzophenone-2	BP-2	$3.16^{(1)}$	0	< LOD		
Benzophenone-3	BP-3	$3.79^{(2)}$	11	6.7	11.4	8.2
Benzophenone-4	BP-4	$0.37^{(2)}$	0	< LOD		
4,4′-Dihydroxybenzophenone	4-DHB		0	< LOD		
4-Methylbenzylidenecamphor	4-MBC	$4.95^{(2)}$	0	< LOD		
2-Ethylhexyl-4-(dimethylamino)benoate	OD-PABA	$6.15^{(2)}$	0	< LOD		
2-Ethylhexyl-4-methoxycinnamate	EHMC	$5.8^{(2)}$	0	< LOD		
2-Phenylbenzimidazole-5-sulfonic acid	PBSA	$1.5^{(2)}$	77	1.8	836.3	5.5
Octocrylene	OC	$6.88^{(2)}$	79	5.3	30.8	7.9
Ethyl-4-aminobenzoate	Et-PABA		0	< LOD		
Pharmaceuticals						
Sulfadiazine*	SDZ	$-0.34^{(4)}$	20	0.9	7.6	1.4
Sulfamerazine*	SMZ	$0.44^{(4)}$	7	0.7	1.2	0.8
Trimethoprim*	TMP	$0.65^{(3)}$	14	1.6	17.8	7.5
Sulfamethoxazole*	SMX	$0.68^{(3)}$	95	0.6	47.5	4.1
Salicylic acid**	SA	$2.26^{(2)}$	100	2.2	51.0	10.5
Ketoprofen**	KPF	$3.12^{(2)}$	0	< LOD		
Diclofenac**	DCF	$4.51^{(2)}$	52	1.2	486.5	5.9
Fenofibrate***	FFB	$5.19^{(5)}$	0	< LOD		

Detection frequency of each compound in all samples: * antibiotic, ** non-steroidal anti-inflammatory drug, *** lipid-regulator. (1) Negreira et al. (2009), (2) Rodil et al. (2009), (3) Wille et al. (2010), (4) Chen and Zhou (2014), (5) Kujawa-Roeleveld et al. (2008). < LOD — see Supplementary Table 1 or Orlikowska et al. (2015).

concentrations of octocrylene were found in mussels (*M. galloprovincialis* and *M. edulis*) of the Mediterranean French coast (Bachelot et al., 2012; Gago-Ferrero et al., 2012). Some UV-filters have endocrine disrupting properties, e.g. BP-3, 4-MBC, EHMC, or can be toxic to crustacean, marine invertebrates or algae in the rang of μg/L to low mg/L (Blüthgen et al., 2012; Gao et al., 2013; Paredes et al., 2014; Sieratowicz et al., 2011; Zucchi et al., 2011).

The Baltic Sea mostly is under pressure from commercial fishing, anthropogenic input of nitrogen, phosphorus, organic matter and hazardous substances (HELCOM, 2010). The pollution of the Baltic Sea has been of concern for the last generations. In the catchment area (1,728,000 km^2) of the Baltic Sea live about 80 million people, causing a high anthropogenic input. Due to its geological structure (semi-enclosed), high freshwater input and limited water exchange, the Baltic Sea water body is brackish with a turn over time of about 30–50 years. Furthermore, because of its properties and the high anthropogenic pressure the Baltic Sea is one of the most polluted seas (HELCOM, 2010). Germany and Poland are two of the nine countries whose rivers discharge into southern Baltic Sea. Almost 100% of Poland's catchment areas drain into the Baltic Sea. This catchment area is one of the four largest draining areas in the Baltic, which also covers over 50% of the Baltic agricultural land (Kowalkowski et al., 2012). The Oder and Vistula are two major rivers in Poland, which drain approximately 88% of Poland's territory (Buszewski and Kowalkowski, 2003). Germany (catchment area 28,790 km^2) has the smallest percentage of the total catchment area of the Baltic Sea (Mecklenburg-Vorpommern, 2012). About 72% of that area are of agricultural usage (HELCOM, 2010). The largest part of the German catchment area lies in the federal state of Mecklenburg-Vorpommern (16,720 km^2) (Mecklenburg-Vorpommern, 2012). The Warnow is one of the larger rivers in Mecklenburg-Vorpommern draining an area of 3324 km^2 into the Baltic Sea. It is mostly subjected to agricultural pollution and wastewater pollution. In the past a considerable number of studies have been done on the pollution due to pesticides, persistent pollution due to polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs) (Bester and Hühnerfuss, 1993; Pempkowiak et al., 2000; Schulz-Bull et al., 1995; Witt, 2002).

So far, studies focused mostly on occurrence of PPCPs in lakes, rivers and wastewater treatment plants (WWTP) (Blair et al., 2013a,b; Bu et al., 2013; Liu and Wong, 2013; Sacher et al., 2008) and just little research has been done on coastal areas including the Baltic Sea (Borecka et al., 2015; Gulkowska et al., 2007; Sánchez Rodríguez et al., 2015; Siedlewicz et al., 2016; Tovar-Sánchez et al., 2013). The aim of this study was to investigate the occurrence and transport of PPCPs in 5 rivers/streams discharging into the Baltic Sea. Special focus was put on the occurrence of PPCPs in beach proximity of Warnemünde.

2. Experimental

2.1. Chemicals and materials

All reference standards and chemicals were of analytical grade (> 98%). Reference standards of the following pharmaceuticals: diclofenac (DCF), ketoprofen (KPF), sulfadiazine (SDZ), sulfamerazine (SMZ), sulfamethoxazole (SMX), trimethoprim (TMP) and metabolite salicylic acid (SA) were purchased from Dr. Ehrenstorfer GmbH (Germany). Isotope labeled standards of sulfamethoxazole-d4 (SMX-d4) and diclofenac-d4 (DCF-d4) were also obtained from Dr. Ehrenstorfer GmbH (Germany) and used as internal standards. UV-filter reference standards benzophenone-1 (BP-1), benzophenone-2 (BP-2), benzophenone-3 (BP-3), 4,4′-dihydroxybenzophenone (4-DHB), 4-methylbenzylidenecamphor (4-MBC) and 2-ethylhexyl-4-(dimethylamino)benoate (OD-PABA) were obtained from Alfasa Aesar GmbH (Germany) and benzophenone-4 (BP-4) from Sigma-Aldrich (Germany). Reference standards of 2-ethylhexyl-4-methoxycinnamate (EHMC), 2-phenylbenzimidazole-5-sulfonic acid (PBSA), octocrylene (OC) were purchased from Merck (Germany) and ethyl-4-aminobenzoate (Et-PABA) from VWR (Germany). Benzophenone-3-d5 (BP-3-d5) was purchased from CDN Isotopes (Canada) and used as internal standard.

The solvents methanol, acetonitrile and acetone were obtained from Promochem (Germany). From Sigma-Aldrich (Germany) acetic acid and formic acid was purchased. Ammonia (aq.), hydrochloric acid and water (LC-grade) were acquired from VWR (Germany).

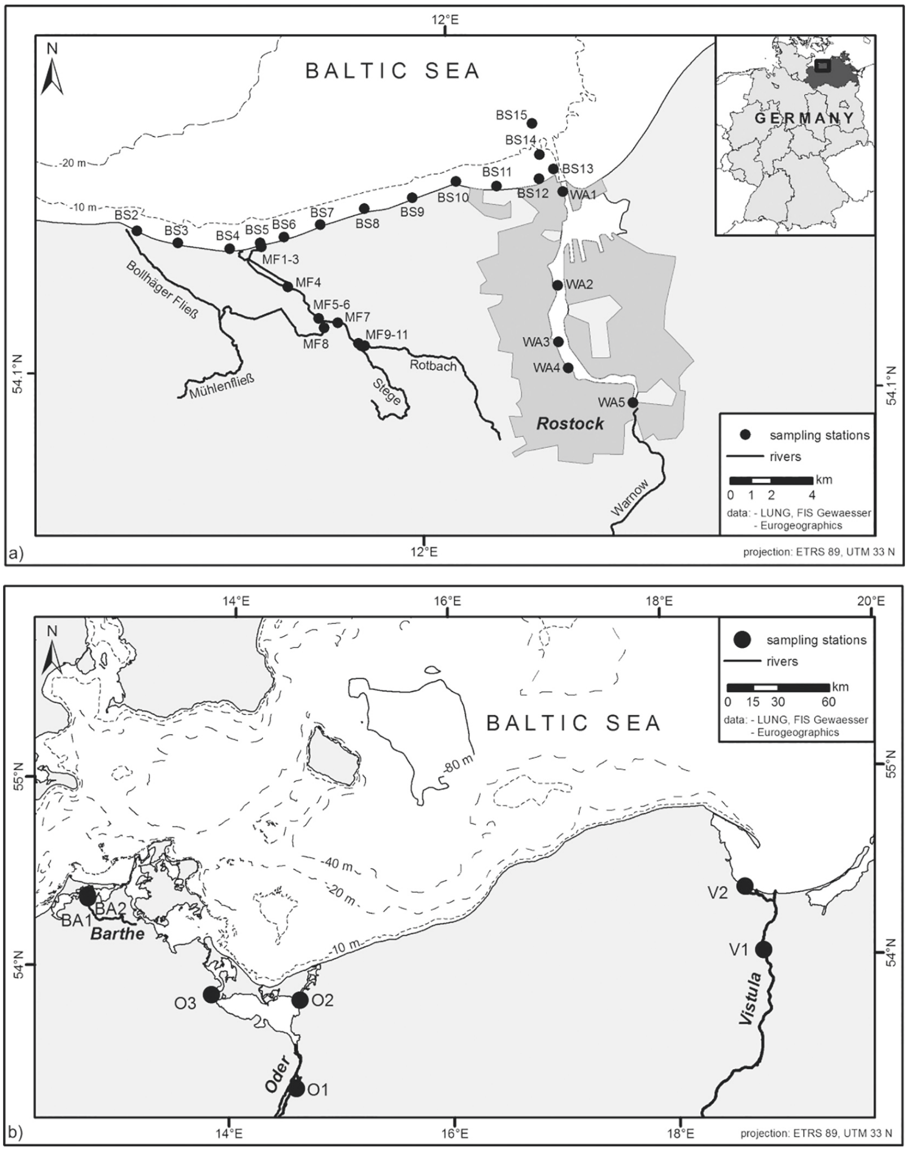

Fig. 1. a) Sampling stations along the Rostock coastline (BS2–15), along the stream Mühlenfließ (MF1–11) and the river Warnow (WA1–5). b) Sampling stations Barthe (BA1–2), Oder (O1–3) and Vistula (V1–2).
Sources: http://www.lung.mv-regierung.de/insite/cms/umwelt/wasser/fis_wasser.htm, http://www.eurogeographics.org/products-and-services/euroboundarymap.

2.2. Sampling sites and sampling strategy

The surface water of the Oder and Vistula was sampled twice in May 2015 (week 1 (W1) and week 2 (W2)) at 5 different stations (O1, O2, O3, V1, V2; Fig. 1b, Table S1). The samples were taken with one week in between. Oder and Vistula are draining the biggest area of this study and are influenced by the cities Szczecin and Gdańsk. Samples were take in flow direction near/before the cities and after the cities in order to see a possible impact and the regional variability of the cities on the aquatic environment. The Warnow and the Mühlenfließ are two rivers in the Rostock region draining into the Baltic Sea as well. The Warnow River is 150 km long, draining an area of 3324 km^2 and discharging into the Baltic Sea near Rostock. It is not only subjected to agricultural and urban run-offs but also to recreational activities. The Warnow was sampled at 5 stations (WA1–5) from the Baltic Sea stream upwards in July 2015 (Fig. 1a). A WWTP is located between the stations WA3 and WA4. The Mühlenfließ is a small stream draining the region around Bad Doberan. It is mostly exposed to agricultural, timberland and urban run-offs and also wastewater treatment plant effluents (Skeff et al., 2015). The Mühlenfließ was sampled stream upwards from the Baltic Sea in July 2015 at 11 different stations (Fig. 1a, MF1–11; Table S1). Station MF1 (Baltic Sea) is located near the river mouth of the Mühlenfließ. Stations MF2 (Mühlenfließ-Estuary) and MF3 (Mühlenfließ) are shortly before the estuary. The sampling station MF7 was near a WWTP-outlet. Station MF6 (pipe) is a street effluent pipe which discharged into the Mühlenfließ. The Mühlenfließ is a combined

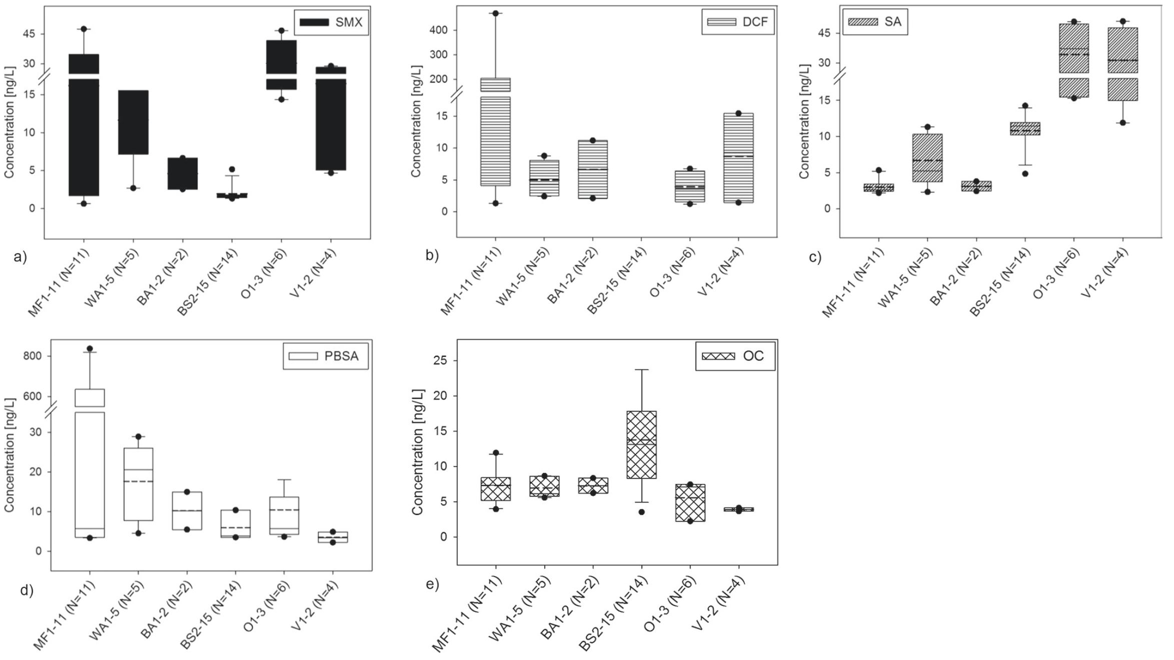

Fig. 2. Concentrations [ng/L] of the most occurring compounds: a) sulfamethoxazole (SMX), b) diclofenac (DCF), c) salicylic acid (SA), d) 2-phenylbenzimidazole-5-sulfonic acid (PBSA), e) octocrylene (OC). Each boxplot presents 10–90% of the data, ⊥ minimum and maximum value, the dashes represent mean value. (MF — Mühlenfließ, WA — Warnow, BA — Barthe, BS — Baltic Sea, O — Oder, V — Vistula).

stream of smaller streams in the area. The streams Rotbach (MF11), Stege (MF10) and Bollhäger Fließ (MF8) drain into the Mühlenfließ. At the same time the Barthe River was sampled at 2 stations (BA1–2) (Fig. 1b). All surface river samples were taken from the approximately 1 m from the river bank. Additional samples were taken in August 2015 near the shore between Kühlungsborn and Warnemünde (BS2–15) to study the effect of tourism in coastal waters (Fig. 1a, Table S1). The distance of the stations to the beach was approximately 200 m, except stations BS14–15, which were not further than 2.8 km from the coastline. All surface samples in the Baltic Sea were taken approximately 1 m from the side of a boat.

2.3. Sample preparation and extraction

At each station 2 L of grab water samples from the surface near layer were taken with a pre-cleaned metal bucket, filled in pre-cleaned amber glass bottles and taken to the laboratory for further analysis. The samples were stored at 4 °C and extracted within 48 h of sampling. The 2 L water samples were divided into two 1 L glass amber bottles and spiked with an internal standard. The internal standard consisted of 10 ng/L isotope labeled DCF-d4, 20 ng/L BP-3-d5, SMX-d4. The extraction and measurement of UV-filters was done according to Orlikowska et al. (2015). In samples for pharmaceutical analysis the pH was adjusted to 5 with 5 M HCl, for the UV-filters the pH was adjusted to 2. Extractions of the samples were done via solid-phase extraction with Chromabond® EASY (3 mL, 200 mg, Marchery-Nagel GmbH) cartridges. Prior extraction the columns were each conditioned with 4 mL acetone and 4 mL LC-H_2O. The samples were brought onto the cartridges via a filtration unit equipped with glass-fiber filters (GF/F, 0.7 µm, Whatman). After extraction the cartridges were cleaned with 4 mL acidified LC-H_2O (pH = 5 for pharmaceuticals, pH = 2 for UV-filters) and gently dried. The cartridges were wrapped in aluminum foil and stored at −20 °C until further analysis. Cartridges for pharmaceutical analysis were eluted with 10 mL acetone/methanol (1/1; v/v) (UV-filter: 4 mL acetone/methanol (1/1; v/v) and 6 mL methanol/13% $NH_{3(aq)}$ (97/3; v/v)). Each eluate was evaporated in a 40 °C water bath and under clean air to complete dryness with a Turbo-Vap (LV, Zymark, USA) evaporator. The pharmaceutical samples were reconstituted with 1 mL water/methanol (3/1; v/v) (UV-filter: 1 mL water/methanol (1/1; v/v) and further analyzed using a liquid chromatography heated electrospray ionization tandem mass spectrometer (LC-HESI-MS/MS) from Thermo Fischer Scientific (Germany), operated in selective reaction monitoring (SRM) mode.

2.4. LC-MS/MS

The determination of UV-filters by LC-HESI-MS/MS was done according to Orlikowska et al. (2015). Separation and detection of pharmaceuticals was done by LC-HESI-MS/MS. A volume of 10 µL was injected via an Accela Autosamplers (Thermo Fischer Scientific, Germany) unto a reverse-phase Kinetex C-18 column (2.6 µm, 50 × 2.1 mL, 100 Å, Phenomenex, USA) equipped with a guard column. Mobile phase A consisted of water (LC-grade) with 0.1% acetic acid and mobile phase B consisted of methanol with 0.1% formic acid. A gradient program was run at a flow rate of 250 µL/min. The capillary and vaporizer temperatures were set to 275 °C and 250 °C, respectively (UV-filters: both temperatures were set to 300 °C). The ionization was achieved in positive and negative mode. In SRM, the transition of two characteristic precursor molecular ion/product ion transitions were monitored (Table S2). For quantification, the most abundant transition (based on signal-to-noise ratio) and the internal standards were used, whereas for qualification the second most abundant ion was used. The average recoveries were calculated from the area ratios (area standard/area internal standard) (Table S2).

Additionally, a risk quotient (RQ) was calculated as the ratio of the maximal measured environmental concentration (MEC) and the predicted no-effect concentration (PNEC) for specific aquatic organisms. The ranking was done by the criterion according to Verlicchi et al.

(2012): RQ < 0.1 low risk, 0.1 ≤ RQ ≤ 1 medium risk, 1 ≤ RQ high risk.

3. Results and discussion

During the three sampling campaigns in the summer season of 2015 4 out of 11 selected UV-filters and 6 out of 8 selected pharmaceuticals were detected (Table 1). The most frequently occurring compounds were PBSA (freq. = 77%), octocrylene (freq. = 79%), sulfamethoxazole (freq. = 95%), salicylic acid (freq. = 100%) and diclofenac (freq. = 52%) (Table 1). The concentration ranges of the detected compounds are displayed in Fig. 2 and Table 1 and are uncorrected. The concentrations of the antibiotics could be corrected by a value of 2 due to the low recovery of the internal standard sulfamethoxazole-d4 (Table S2). In the river sampling campaigns, two rivers (Oder, Vistula), which drain into the Polish coast of the Baltic Sea, two rivers (Warnow, Barthe) were sampled and one small stream (Mühlenfließ), which drain into the German waters of the Baltic Sea. For the German rivers, temperature, salinity, particulate organic carbon (POC) and dissolved organic carbon (DOC) were determined for each sample. POC and DOC can be used to display transport processes in the particular and dissolved phase. A high value for DOC is an indicator for a high anthropogenic pressure on the marine system. No correlation of any occurring PPCP with POC or DOC concentration was found (Figs. 5, S1). Thereby, POC and DOC do not appear to be a source or sink for the analyzed compounds. This can be explained by the properties of the compounds as most of have a low absorption potential to particular matter (logK_{OW}-values: Table 1). The Mühlenfließ was chosen as a sampling site, because of our knowledge about the occurrence of pollutants and possible sources for contamination (Orlikowska et al., 2015; Skeff et al., 2015).

3.1. Coastal sampling

At the beginning of August 2015, we took samples along the coast between Kühlungsborn and Warnemünde. We sampled 12 stations (BS2–13, Fig. 1a) along the beach starting in Kühlungsborn from 9:30 a.m. and also 2 stations further out towards open sea (BS14–15, Fig. 1a, Table S1). Station BS5 is located, where the Mühlenfließ discharges into the Baltic Sea and the locations is nearby station MF1 of our Mühlenfließ sampling campaign (Fig. 1a), allowing us to compare the results between the stations. At station BS13, the Warnow discharges into the Baltic Sea, making this station comparable to station WA1 of the Warnow measurement. The Baltic Sea is known for its strongly stratified basins. The dynamic of the basins is influenced by saltwater inflow events from the North Sea via the Danish Street. The Baltic Sea has a salinity gradient from south-west to north-east and it is not influenced by the tides. The different water bodies of the Baltic Sea can be determined by the salinity. The coastal area is mostly flat and the mixing is driven the combined effect of by wind stress and bottom friction. At the sampling area of this study the salinity did not vary along the coastline, indicating a strongly mixed water body (Table S1). For this reason it can presumed that the same water body was sampled at different locations. The influence of freshwater input via of rivers can only be seen close to the river mouth (Sections 3.2–3.3).

Only two pharmaceuticals, sulfamethoxazole and salicylic acid, were detected along the coast (Fig. 3a, c). Sulfamethoxazole was found at a steady concentration along the coast of 1.5 ng/L. Sulfamethoxazole did not vary with time or location along the coast. Concentrations were also similar to those measured one month before suggesting a stable concentration (estimated half-life in sea water: 85 > 100 days; Zheng et al., 2012) or a steady input of sulfamethoxazole into the Baltic Sea. The concentration at stations BS5 and BS13 (1.4 ng/L and 2.0 ng/L, respectively) are comparable to stations MF1 and WA1 (1.7 ng/L and 2.7 ng/L, respectively). However, our measured concentrations of sulfamethoxazole are lower than the published concentration by Nödler et al. (2014) measured in the Baltic Sea in 2009 (median 21 ng/L, detection frequency 30%). The higher median concentration can possibly be explained by the different sampling time (May 2009) and the larger sampling area. Nödler et al. (2014) took 30 samples along the complete coastline of Mecklenburg-Vorpommern of the Baltic Sea, due to that their samples are influenced by a much larger catchment area than samples presented in this study. In their study, some sampling stations were located in a bay and in the Szczecin Lagoon, where higher concentrations are expected, due to the vicinity to the city of Szczecin in combination to of the limited circulation and water exchange. Despite the higher median value of sulfamethoxazole, trimethoprim was also not found in the Baltic Sea. The lack of other antibiotics can be explained by the results obtained in the rivers, where only very low concentrations of the antibiotics sulfadiazine and trimethoprim were found. At station MF1 and station WA1, these concentrations were below the limit of detection. The concentrations of salicylic acid varied around 11 ng/L along the coast.

Only two UV-filters, PBSA and OC, were found along the coast (Fig. 3b). PBSA was only detected from late morning (station BS10, 11 a.m.) in low concentrations (1.8–10.3 ng/L) along the coast. The highest concentration along the coast was found at station BS12. We detected 3.7 ng/L PBSA at station BS13, which is comparable to the concentration at station WA1 (4.5 ng/L) measured one month before. The concentration of OC varies along the coast more than PBSA and appeared at higher concentrations (8.1–30.8 ng/L) close to Warnemünde. Just as PBSA, the highest OC concentration along the coast was measured at station BS12 (30.8 ng/L). In comparison with the samples at station MF1 (7.0 ng/L) and station WA1 (6.2 ng/L), the samples at station BS5 and station BS13 are slightly higher (8.3 ng/L, 8.1 ng/L, respectively). Stations BS12 and BS13 are popular for bather and water sport activity, ultimately leading to higher concentration of UV-filters. Tovar-Sánchez et al. (2013) indicated for seawater, that the amounts of UV-filters release into seawater is in direct relationship with the bathers affluence. Comparing the results of the river sampling with the Baltic Sea sampling it can be seen, that higher PBSA concentrations were found in the rivers than in the Baltic Sea (Fig. 2d). On the contrary, OC was found in higher concentrations in the Baltic Sea (Fig. 2e). Many studies show a similar result (Sánchez-Quiles and Tovar-Sánchez, 2015). Studies show that PBSA is found in higher concentrations (up to 3240 ng/L) in river water (Wick et al., 2010). A reason might be the short half-life of PBSA (3 days in June–August) and its photolability in water and sunscreen (Zhang et al., 2012). OC on the other hand can be found in higher concentrations in seawater than in river water (Sánchez-Quiles and Tovar-Sánchez, 2015). A study published by Sánchez Rodríguez et al. (2015) demonstrated the occurrence of OC (median 109.7 ng/L) at 5 Gran Canarian beaches between May and October 2011. They assumed that the extensive use of OC in sunscreen (10% EU-regulation, Union, 2009) would be the cause for the high appearance in seawater, despite its affinity to particular matter and its low water solubility (Sánchez Rodríguez et al., 2015). The lower concentrations in the morning can also be explained by the form of the coastline like Sánchez Rodríguez et al. (2015). The coast from Kühlungsborn to Warnemünde is not restricted by any barrier, which allows a high water exchange with the open Baltic Sea. It might be possible that due to the short half-life and higher water solubility of PBSA than OC, PBSA was not found at the stations BS2–BS9 (Fig. 3b) sampled in the morning.

3.2. Pharmaceuticals in rivers

The 5 stations (Oder: O1, O2, O3; Vistula: V1, V2) were sampled twice in May 2015 1 week apart (W1 and W2). During the sampling campaign, 3 antibiotics (sulfamethoxazole, sulfadiazine and trimethoprim) and 2 NSAIDs (diclofenac and salicylic acid (metabolite)) were found in the Oder and Vistula (Fig. 4a, b). The most prominent compound, detected in all samples, was the sulfonamide sulfamethoxazole (SMX). The same is true for the metabolite salicylic acid (SA). Salicylic

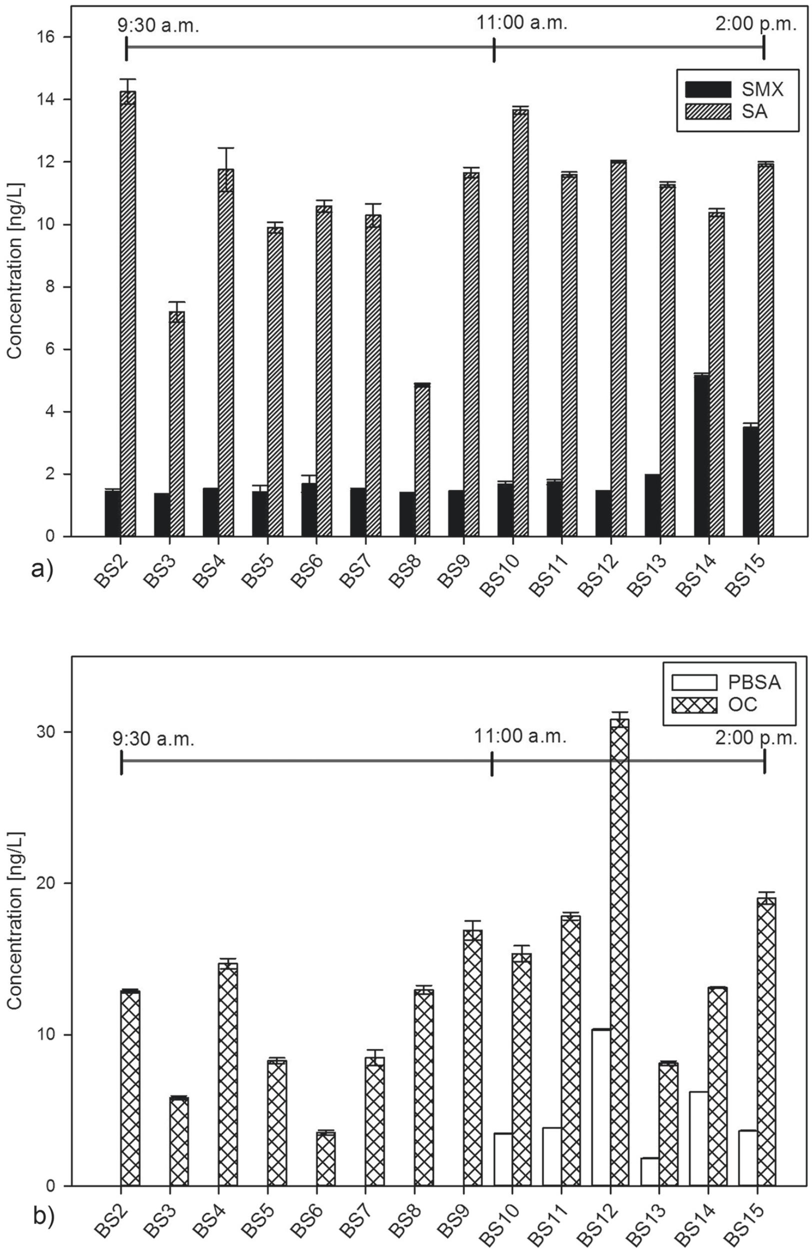

Fig. 3. Detected concentrations [ng/L] along the coast between Kühlungsborn and Warnemünde with time of sampling at sampled positions (BS2–15): a) sulfamethoxazole (SMX) and salicylic acid (SA), b) 2-phenylbenzimidazole-5-sulfonic acid (PBSA) and octocrylene (OC).

acid is the deacylated and more active form of the widely used acetylsalicylic acid (Wille et al., 2010). Additionally, it is used in many personal care products as a salt or ester and in medicine for chemical exfoliation of skin (Kligman, 2001; Panel, 2003). In both, Oder and Vistula, a decrease in concentrations was observed from inland sampling stations towards the Baltic Sea. The decrease in concentration along the Oder river are displayed in Fig. 4c. Stations O1 and O2 are approximately 60 km apart. The highest concentration of sulfamethoxazole was found at station O1 during weeks 1 and 2, with 40.0 ng/L and 46.8 ng/L, respectively. During both weeks the concentration decreased along the river towards the station O2 (32.1 ± 1.3 ng/L) and station O3 (15.2 ± 1.3 ng/L). The concentrations decreased by almost 50% from station O1 to stations O2/O3 (Fig. 4a, c), with the mean value of station O2 slightly higher than station O3, displaying the influence of transport along the river, e.g. distance between stations. Station O3 is located in a narrow river coming from the Szczecin Lagoon, hence it might be less influenced by the Oder discharge itself. Sulfamethoxazole concentrations in the Vistula at stations V1 and V2 are lower than at station O1, 27.5 ng/L, 5.4 ng/L and 43.4 ± 1.3 ng/L, respectively. In both weeks, the concentrations were similar to each other. This could mean that there is a consistent input of sulfamethoxazole and the concentrations are of

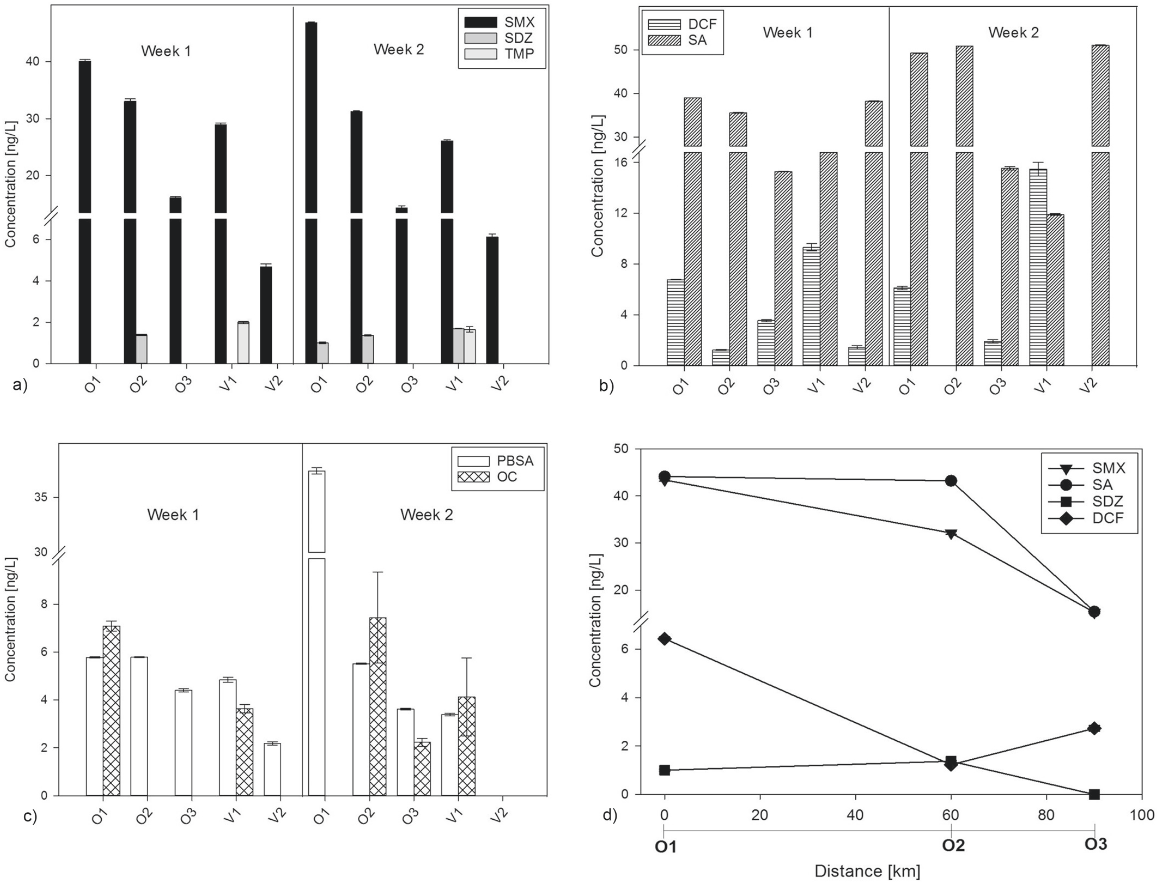

Fig. 4. Detected concentrations [ng/L] in Oder and Vistula in May 2015 during week 1 and week 2 at sampled positions (O1-3, V1-2): a) sulfamethoxazole (SMX), sulfadiazine (SDZ), trimethoprim (TMP), b) diclofenac (DCF), salicylic acid (SA), c) 2-phenylbenzimidazole-5-sulfonic acid (PBSA), octocrylene (OC), d) Concentration development along the Oder from station O1 to O2 and O3, towards the Baltic Sea.

stable occurrence. Again the concentration decreased towards the Baltic Sea, possibly due to dilution. The measured concentrations are in similar range of the sulfamethoxazole concentrations (n.d.–70.1 ng/L) which were found by Borecka et al. (2015) in the southern Baltic Sea in 2012. Higher concentration of sulfamethoxazole are expected in water due to the substance physico-chemical properties, its slight absorption by sediment (Benotti and Brownawell, 2009; Hektoen et al., 1995). The removal rate of sulfamethoxazole by wastewater treatment plan in Gdańsk is estimated to be 47–65% (Luczkiewicz et al., 2013). Several studies reported that the removal efficiency of sulfamethoxazole from wastewater varies between 4.5% to 100% and depends on the system of the wastewater treatment plants e.g. conventional active sludge, fixed-bed reactor or membrane bioreactor (Verlicchi et al., 2012). Göbel et al. (2007) stated that the elimination of sulfamethoxazole is more efficient in an membrane bioreactor than a conventional active sludge reactor, 80% versus 60% respectively. Additionally, a re-transformation of the biological active photo-product N4-acetylate-sulfamethoxazole back into the parent compound during the treatment is possible (Göbel et al., 2007). Su et al. (2016) also studied the reformation of photo-products under river resembling conditions in the lab and assumed that this process might have an influence on the overall persistence and occurrence of sulfamethoxazole in the aquatic environment. The incomplete removal of sulfamethoxazole from wastewater and its reformation could explain the occurrence of sulfamethoxazole in the Oder and Vistula and the other investigated waters. Sulfadiazine (SDZ) was only detected once in the second week at station O3 (1.4 ng/L). During week 1 at station O3 and week 2 at station O1, the concentrations were below limit of detection (LOD) (Table S2). Sulfadiazine was only found at a low concentration of 1.6 ng/L at station V1 during the second week. Trimethoprim (TMP) was not found at the stations O1–O3, but was detected at station V1 at similar concentration of 1.8 ng/L during both weeks.

In difference to Borecka et al. (2015), diclofenac (DCF) was detected in both Oder and Vistula (Fig. 4b). The concentrations of diclofenac at station O1 were similar in both weeks (6.4 ± 0.5 ng/L), pointing towards little or no variability in the concentrations. The concentrations also decreased towards the Baltic Sea like the concentrations of the antibiotics (Fig. 4c). Diclofenac was only found at station O2 during the first sampling (1.2 ng/L). At station O3 diclofenac was found both times, with 3.5 ng/L and 1.9 ng/L, respectively. Due to a longer transportation route from station O1 to O3 the concentration at station O3 is higher during the first week. Diclofenac was also detected in the Vistula at station V1 but not at station V2. The concentration of week 2 was slightly higher then week 1, 15.4 ng/L and 9.3 ng/L, respectively. The measured concentrations are low. Dilution and degradation by photolysis within few days after light exposure might be two possible reasons why diclofenac was not detected at station V2 (Packer et al., 2003; Poirier-Larabie et al., 2016).

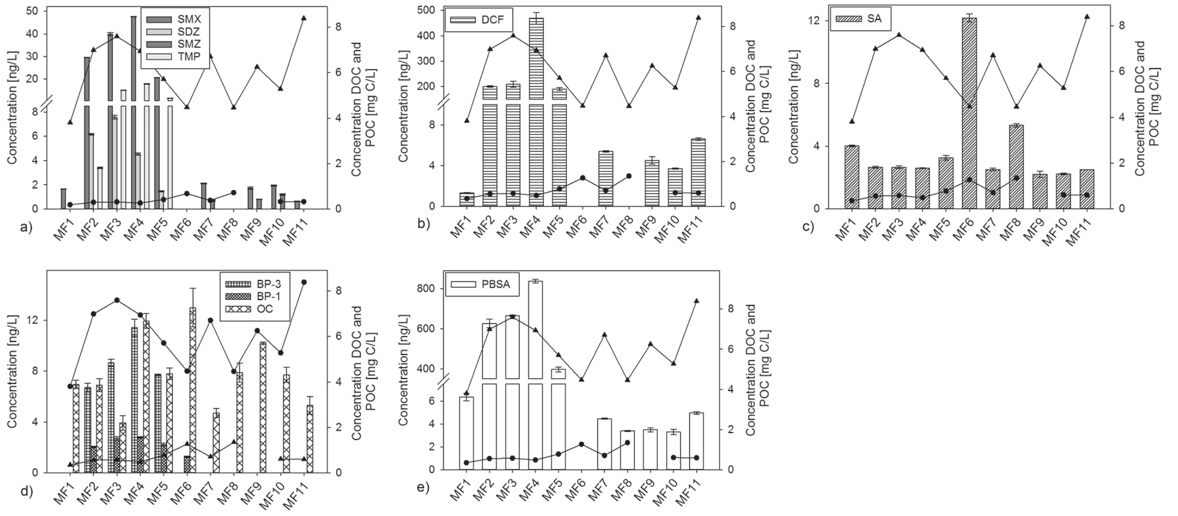

Fig. 5. Detected concentrations [ng/L] in Mühlenfließat sampled positions (MF1–11): a) sulfamethoxazole (SMX), sulfadiazine (SDZ), sulfamerazine (SMZ), trimethoprim (TMP), b) diclofenac (DCF), c) salicylic acid (SA), d) benzophenone-3 (BP-3), benzophenone-1 (BP-1), octocrylene (OC), e) 2-phenylbenzimidazole-5-sulfonic acid (PBSA). Concentrations of DOC (▲) and POC (•) are in mg C/L.

The concentrations of the metabolite salicylic acid (SA) are in similar range to the sulfamethoxazole concentrations (43.4 ± 1.3 ng/L). The highest concentrations of salicylic acid during all our campaigns were measured during first and second week at station O1, 39.0 ng/L and 49.3 ng/L, respectively (Fig. 4b). Again station O3 (W1 and W2 each 15.4 ng/L) showed lower concentrations than station O2 (W1: 35.6 ng/L, W2: 50.9 ng/L). The increase of salicylic acid from W1 to W2 is an unexpected increase, no other component showed similar behavior. Salicylic acid occurrence in Vistula at station V1 (W1: 24.3 ng/L, W2: 11.9 ng/L) and V2 (W1: 38.3 ng/L, W2: 51.0 ng/L) shows different behavior than in the Oder.

In both rivers Warnow and Barthe, we measured lower concentration than in the Oder and Vistula (Fig. 2a–c). The reason might be the greater catchment area of the Oder and Vistula in comparison to the Warnow and Barthe. Warnow River is flowing through Rostock and was sampled at 5 locations (WA1–5) (Fig. 1a). From the Barthe, only two samples were taken (BA1–2) (Fig. 1b). The Barthe was the least polluted river of all sampled rivers. The surrounding area of the Barthe is formed mostly by agriculture and preserved nature and it is not much influenced by big cities. The Mühlenfließ, a small stream in effluent receiving stream, was sampled at 10 locations (MF1–11) (Fig. 1a) and one sample was taken from a pipe discharging into the stream (MF6). A special focus was put on the influence of WWTPs for these rivers. Only sulfamethoxazole and sulfadiazine were found in the Warnow in lower concentrations (Fig. S1a), 2.7–17.8 ng/L and 0.9–1.6 ng/L, respectively. At station WA4, the highest concentrations of pharmaceuticals for the Warnow were measured ($\sum$ pharmaceuticals = 37.5 ng/L), but lower concentrations than the highest concentration in Mühlenfließ (station MF4: $\sum$ pharmaceuticals = 541.0 ng/L). At station WA1, near the Baltic Sea, only sulfamethoxazole (2.2 ng/L) was detected, with values comparable to concentrations at the beach near Warnemünde at Rostock (1.5 ± 0.2 ng/L). Diclofenac was only found in low concentrations (5.0 ± 3.0 ng/L), similar to the ones measured at Mühlenfließ stations MF7–MF10 (5.0 ± 1.2 ng/L) (Fig. S1b). Like for the antibiotics, the highest concentration was measured at station WA4 (8.7 ng/L) for Warnow and BA2 (11.2 ng/L) for Barthe. No diclofenac was found in Warnemünde (WA1), confirming our findings during other samplings. A reason might be the fast degradation of diclofenac or the dilution effect is to high. Salicylic acid again shows a different pattern than other pharmaceuticals (Fig. S1c), with highest concentration at station WA2 (11.3 ng/L) followed by station WA4 (9.3 ng/L). At station WA1, we measured a concentration of 5.1 ng/L which is similar to the concentration measured at station MF1 (Baltic Sea). The WWTPs do not appear to be the main source of pharmaceuticals in theses rivers.

Only 4 antibiotics (sulfamethoxazole, trimethoprim, sulfamerazine, sulfadiazine) were detected in Mühlenfließ (Fig. 5a). No antibiotics were detected at station MF8 and in the water pipe (MF6) by Bad Doberan. Generally low concentrations of 1–2 ng/L were found at stations farther away from the coast (MF10–MF7). At station MF5 an increase in concentrations of each substance was detected. The highest concentration of pharmaceuticals were measured at station MF4 (Mühlenfließ/Conventor See). Sulfamethoxazole was the most prominent one with 47.5 ng/L, followed by trimethoprim with 17.8 ng/L. Sulfamethoxazole and trimethoprim are mostly used together in medical treatments (ratio 5:1), because of their known synergistic effects against bacteria, which would explain their joint occurrence (Chang et al., 2008; Nord et al., 1974; Silveira et al., 2002). The highest concentration of sulfadiazine was found at station MF3. All concentrations of the detected antibiotics decrease towards the Baltic Sea. Sulfamethoxazole was the only antibiotic found in the Baltic Sea at station MF1 (1.7 ng/L). From all analyzed rivers, the highest sulfamethoxazole concentrations were detected in the Mühlenfließ. However, the median concentration for all analyzed rivers is 17.7 ng/L. This median concentration is similar to an EU-wide survey done by Loos et al. (2009). Loos et al. (2009) sampled 122 rivers in Europe and determined a median concentration of 15 ng/L (detection frequency 75%) sulfamethoxazole in European rivers. It is also similar to the median concentration (16 ng/L) in the Danube (2007) stated by Loos et al. (2010).

Furthermore, the only other occurring pharmaceuticals in the Mühlenfließ were diclofenac and metabolite salicylic acid (Fig. 5b, c), respectively. Diclofenac was found in low concentrations at inland stations (3.7–6.6 ng/L) but was not found at stations MF8 and MF6. The highest concentration of diclofenac (468.5 ng/L) was measured at station MF4, where the Mühlenfließ connects to the Conventor See. The concentration also decreased from there towards the Baltic Sea (MF1) (1.3 ng/L). It shows the same pattern as the antibiotics, a major increase from MF5 (189.3 ng/L) to MF4 (468.5 ng/L) and then a decrease towards the Baltic Sea (MF1, 1.3 ng/L). The strong increase of pharmaceuticals from stations MF5 to MF4, points towards existence of an unknown indirect source of those pollutants. In the surrounding area are a few agricultural holdings, which could be a source of the pharmaceuticals. Unfortunately, this cannot be substantiated by any other reference, and results of additional studies at this stage. Contrary to the expectations, stations close to the WWTP did not show higher concentrations. The mean concentration of salicylic acid is around 2.7 ± 0.5 ng/L. Salicylic acid is the only pharmaceutical found at both stations MF8 and MF6, with 5.3 ng/L and 12.2 ng/L, respectively.

3.3. UV-filters in rivers

We were able to detected 4 out of 11 UV-filters from the range of selected substances in the 3 rivers and one stream (Table 1). Only 2 out of 11 analyzed UV-filters were detected in the Polish rivers Oder and Vistula (Fig. 2d, e). Octocrylene (OC) was only detected in 3 samples station O1 week 1 and during week 2 at station O2 and station V1 (7.0 ng/L, 8.5 ng/L, 5.0 ng/L), respectively (Fig. 4d). These concentrations are in a similar range to the measured concentrations of the German sampled rivers (5–8 ng/L) and close to the limit of detection (LOD) of 5 ng/L.

2-Phenylbenzimidazole-5-sulfonic acid (PBSA) was detected in 90% of the samples (Fig. 4d). The concentrations in the Oder region were similar to each other. During second week at station O1 an increased concentration of 37.4 ng/L was detected. The concentration at station O1 (week 1) is insignificantly higher then station O2 and station O3 (W1: 5.8 ng/L, 5.7 ± 0.2 ng/L, 4.0 ± 0.6 ng/L), respectively. Station O3 shows the lowest concentration, which might mirror the reduced influence of the Oder River, but we need to indicate that those values are close/below LOD (1.0 ng/L, Orlikowska et al., 2015). At the Vistula, stations V1 and V2 comparable concentrations were detected as in the Oder region (4.1 ng/L, 2.2 ng/L, respectively). The decrease in concentration of approximately 50% could be due to dilution. Furthermore, PBSA is in the same range as detected at the later measured inland stations of the German rivers (3–4 ng/L). We argue that this might be a general concentrations range of PBSA in rivers, if there is no direct source or a wastewater discharge close by. Similar concentrations of PBSA were found in the Black Sea (1.3–2.3 ng/L) and Baltic Sea (< 1.0–3.4 ng/L) by Orlikowska et al. (2015).

Only PBSA, OC were detected in the Warnow (Fig. S1d–e). Like antibiotics and diclofenac, the highest PBSA concentration was measured at station WA4 (28.9 ng/L). Afterwards, the concentration decreases towards the Baltic Sea, to reach 4.5 ng/L at Warnemünde. The UV-filter OC has apparently different sources from the other contaminants. The highest concentrations were measured at the station WA5 (8.5 ng/L), which is near an outdoor swimming area in the Warnow and the recreational activities of bathers can be a possible source, and at the station WA3 (8.6 ng/L). The concentration of OC does not decrease as much as for the other compounds. At station WA1 a concentration of 6.1 ng/L was measured, which is similar to concentration at station MF1 (7.0 ng/L).

We were able to detect 4 out of 11 analyzed UV-filters (PBSA, OC, BP-3, BP-1) in the Mühlenfließ, (Fig. 5d–e). The Bollhäger Fließ (MF8), which drains into the Mühlenfließ, is the least polluted part and does not contribute to the pollution. As with the pharmaceuticals the highest concentrations of PBSA, BP-3 and BP-1 were measured at the station MF4 (836.3 ng/L, 11.4 ng/L and 2.8 ng/L, respectively). PBSA was not measured in the pipe effluent, but its concentration is also increasing from station MF5 to MF4 (396.5 ng/L, 836.3 ng/L), respectively (Fig. 5e). Before the strong increase, the concentrations are similar to each other (3.9 ± 0.7 ng/L). The PBSA concentration (645.4 ± 27.2 ng/L) at the station MF2/3 is 4-times higher than the concentration measured at the same station in 2014 by Orlikowska et al. (2015). One year earlier BP-3 was not detected. In 2015, it was found at low concentration of 11.4 ng/L at station MF4. From this station towards the Baltic Sea, the concentration decreased. BP-1 was only detected at low concentrations (2.4 ± 0.3 ng/L) in samples from MF5 to MF2 and also in the effluent of the pipe (MF6). The concentrations detected at MF2/3 (2.4 ± 0.4 ng/L) are in similar range to concentration reported by Orlikowska et al. (2015) for the year 2014 (2.5 ng/L). The highest concentration of OC, like salicylic acid, was found at station MF6 in the pipe effluent (12.9 ng/L) (Fig. 5d). At both station MF10 (Stege stream) and station MF11 (Rotbach stream), only low concentrations of OC were detected, with 7.7 ng/L and 5.3 ng/L, respectively. After the streams merge, an insignificant increase in the concentration was measured at station MF9 (10.2 ng/L), close to a WWTP, with an decrease afterwards. The pipe (MF6) appears to be a minor source, but generally the concentration decreases towards the Baltic Sea. This indicates that the direct input of OC via recreational activities into the environment might play a more important role than the indirect input via wastewater.

4. Conclusion

The results of this study show the occurrence of PPCPs in German and Polish rivers and in the beach proximity of the German Baltic Sea. Generally, the concentrations decrease in all rivers towards the Baltic Sea. The Oder shows higher concentration than Warnow, Barthe, Rotbach and Stege, only at Mühlenfließ MF5–MF2 higher concentrations were detected. The pollutants are transported with the riverine water to the Baltic Sea and are diluted and possibly degraded by photolysis or sorption during their residue time. Only low concentrations of PPCPs were found in beach proximity. The Mühlenfließ, especially at station MF4, is the most polluted of the sampled waters. Most of the detected compounds were found in higher concentrations than in the other rivers. Our results show that between stations MF4 and MF5, a source of the contaminates exists causing the strong increase of observed concentration. We assume that an unknown indirect source might be the reason for the higher concentrations. The general pattern of the occurrence of all analyzed PPCPs is the strong increase from MF5 to MF4 and then a decrease towards the Baltic Sea, possibly due to dilution. Sulfamethoxazole occurred at similar concentrations at the mouth of both Mühlenfließ and Warnow. Sulfamethoxazole was found at a steady concentration along the beach. Its occurrence in the Baltic Sea supports the assumption that sulfamethoxazole might always appear at a "stable" concentration of approximately 2 ng/L in the studied region. It is likely that for pharmaceuticals the indirect input via wastewater plays a bigger role than the direct input. The UV-filters showed a different pattern than the pharmaceuticals. For UV-filters the direct input via recreational activities into the environment might be of a more important source as the indirect input as already stated by Poiger et al. (2004). To asses the risk of the detected concentrations a risk quotient (RQ; RQ < 0.1 low risk, 0.1 ≤ RQ ≤ 1 medium risk, 1 ≤ RQ high risk) has been calculated for aquatic organisms (Table 2). Almost all compounds pose a very low risk (< 0.1) to aquatic organisms at the measured concentrations. Only sulfamethoxazole poses a medium risk (RQ = 0.2) to the blue-green algae in the Baltic Sea at the detected concentration. Diclofenac poses a medium risk to in the Oder (RQ = 0.1), Vistula (RQ = 0.3), Warnow (RQ = 0.2) and Barthe (RQ = 0.2). However, it poses a high risk (RQ = 9.4) in the Mühlenfließ to aquatic organisms. Our study clearly shows that there is a need for better evaluation of the prevailing conditions in rivers and the Baltic Sea. Additional studies are especially needed to evaluate the long-term occurrence and their possible long-term effect on aquatic organisms.

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Table 2
Estimated risk quotient (RQ) for detected compounds with known PNEC for representative aquatic organisms with the classification of RQ $<$ 0.1 low risk, 0.1 $\leq$ RQ $\leq$ 1 medium risk, 1 $\leq$ RQ high risk.

	SMX	SDZ	TMP	SA	DCF	BP-1	BP-3	OC
Baltic Sea								
Organism	Blue-green(1) algae			*Vibrio fisheri*(2)				Marine water(3)
PNEC [μg/L]	0.027			43.1				2.3
Max. MEC [ng/L]	5.2			14.3				30.8
RQ	**0.2**			0.0003				0.01
Oder								
Organism	*D. magna*(4)	*M. aeruginosa*(5)		*P. promelas*(4)	*S. trutta* f. *fario*(6)			*L. idus*(7)
PNEC [μg/L]	4.5	0.135		1.28	0.05			0.5
Max. MEC [ng/L]	46.8	1.4		50.9	6.8			7.4
RQ	0.01	0.01		0.04	**0.1**			0.01
Vistula								
Organism	*D. magna*	*M. aeruginosa*	*S. capricornutum*(4)	*P. promelas*	*S. trutta* f. *fario*			*L. idus*
PNEC [μg/L]	4.5	0.135	2.6	1.28	0.05			0.5
Max. MEC [ng/L]	51.0	1.7	2.0	51.0	15.5			4.1
RQ	0.03	0.01	0.0007	0.04	**0.3**			0.008
Mühlenfließ								
Organism	*D. magna*	*M. aeruginosa*	*S. capricornutum*	*P. promelas*	*S. trutta* f. *fario*	*O. mykiss*(8)	*O. latipes*(9)	*L. idus*
PNEC [μg/L]	4.5	0.135	2.6	1.28	0.05	49.2	6	0.5
Max. MEC [ng/L]	47.5	7.6	17.8	12.2	468.5	2.8	11.4	13.0
RQ	0.01	0.05	0.006	0.009	**9.4**	0.00006	0.002	0.03
Warnow								
Organism	*D. magna*	*M. aeruginosa*		*P. promelas*	*S. trutta* f. *fario*			*L. idus*
PNEC [μg/L]	4.5	0.135		1.28	0.05			0.5
Max. MEC [ng/L]	17.8	1.6		11.3	8.8			8.7
RQ	0.004	0.01		0.009	**0.2**			0.02
Barthe								
Organism	*D. magna*			*P. promelas*	*S. trutta* f. *fario*			*L. idus*
PNEC [μg/L]	4.5			1.28	0.05			0.5
Max. MEC [ng/L]	6.6			3.8	11.2			8.3
RQ	0.001			0.003	**0.2**			0.02

(1) Ferrari et al. (2004), (2) Farré et al. (2001), (3) Langford et al. (2015), (4) Sanderson et al. (2003), (5) Halling-Sörensen (2000), (6) Hoeger et al. (2005), (7) Zhang et al. (2015), (8) Fent et al. (2010), (9) Coronado et al. (2008).
The bold data indicates the values of medium and high risk to the organisms.

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Appendix A. Supplementary data

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Antibiotics in Three Chinese Coastal Systems: Huangpu River, East China Sea, Pearl River Estuary

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Abstract

The occurrence of antibiotics in the marine environment over a long time period can lead to development of antibiotic resistant bacteria, which is a major scientific concern. This study was carried out to investigate the occurrence of four antibiotics (sulfadiazine, sulfamerazine, sulfamethoxazole and trimethoprim) in the waters of Huangpu River and Pearl River Estuary and the East China Sea. To our knowledge, our results are the first findings of antibiotics in the East China Sea. The antibiotics were extracted from water and enriched via solid-phase extraction (Chromabond®EASY). The analysis was carried out with a liquid-chromatography tandem mass spectrometer equipped with a heated electrospray ionization source (HPLC-HESI-MS/MS). The selected antibiotics were detected in all three waters at low ng/L concentrations, which are comparable to literature data. In the Huangpu River the antibiotics occurred at a relatively stable concentration, with a slight decrease towards the Changjiang River. In the East China Sea antibiotics were mainly found in the surface water. Only sulfamethoxazole was found at three stations in bottom water. Detected concentrations in the Pearl River Estuary displayed an inverse correlation with salinity, confirming the dominant effect of dilution due to mixing of riverine and oceanic waters.

Keywords: Antibiotics; Huangpu River; Pearl River Estuary; East China Sea; Water

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Introduction

Coastal ecosystems are under threat because of climate change and anthropogenic pressure due to eutrophication and emerging contaminants like antibiotics. Those are ubiquitous contaminants and their occurrence in the ecosystem over a long time period can lead to development of antibiotic resistant bacteria, which is a major scientific concern [1,2]. Countries around the world including China enforce national and international measures to inspect pollution, to control and to improve the water quality and the surrounding environment [3].

Chinese waters are affected by pollutions from industrial, agricultural and domestical activities. Especially in dense metropolitan areas like Shanghai and Guangzhou/Hong Kong at the Pearl River Delta, the aquatic environment is exposed to heavy pollution [4-7]. For recent years a major concern has been the exposure of the aquatic environment to pharmaceuticals, in particular antibiotics. China is the largest producer (248,000 t, 2013) and user (162,000 t, 2013) of antibiotics in the world. In 2013 48% of the total amount was used for human applications and 52% were of veterinary usage. Sulfonamide (SA) antibiotics made up 5% of the total usage [8]. They are used to treat and prevent infections by gram positive and negative bacteria [9]. They are mostly used in combination with trimethoprim (TMP), because of their synergistic effects [10-13]. After application about 15-90% of antibiotics are excreted unchanged [8,14,15]. Based on these rates and the fact that SAs are hydrophilic, hydrologically stable and have low sorption to sediments, SAs can be found in aquatic environments almost everywhere [16-18]. Shanghai and the Pearl River Delta are the metropolitan areas in the east and south China regions, respectively. They are not only the most urbanized cities, but also are of great economical importance due to intensive livestock farming [2,19-21]. Both East and South China regions have a high consumption of SAs, 2270 t and 596 t, respectively. SAs are the second most used antibiotics in Chinese aquacultures [8,22]. As a result of metropolitan areas and high rates of antibiotic usage, the aquatic environments in these areas are under high pressure of pollution by antibiotics.

This study was carried out to determine the occurrences of Sulfonamide and TMP in two Chinese rivers flowing through metropolitan areas (Huangpu River and Pearl River) and to determine how far offshore they are transported via the Changjiang River into the East China Sea.

Materials and Methods

Sampling sites and sample collection

The Huangpu River is approximately 114 km long, originating in Tai Lake and flowing north-east through Shanghai with a discharge rate of 10 billion m^3/a into the Changjiang Estuary [23,24]. The upper river is influenced by suburbs, animal breeding farms and agriculture. The lower river (83 km) flows through an urban area, which is highly subjected to intensive industrial and residential activities [4,6]. The Huangpu River was sampled at 9 stations (HP-1-10, w/o HP-4) in the urban area in July 2016. Station HP-1 is located in the Minhang district and station HP-10 in the Changjiang River. The surface (0.5 m) water samples were taken close to the river bank using a pre-cleaned metal bucket (2 L). In July 2016 samples were taken in the East China Sea with the research vessel ZheHai Ke 1 (Zhejiang Ocean University). The East China Sea is dominantly influenced by the Changjiang River discharge and to a lower degree by the Hangzhou shelf. It is the largest marginal sea of the north western Pacific [25,26]. During the cruise discrete surface and bottom water samples were taken at 12 stations via go-flow bottles. At all stations conductivity, temperature and depth were measured with CTD-sensors (Sea Bird Scientific, Bellevue, WA, USA). The Pearl River is the largest water system discharging into the South China Sea via its 8 major outlets with a discharge rate of 336 billion m^3/a [27]. It is influenced by waste waters from intensive poultry, fish farming and industrial/domestic activities. The Pearl River Estuary was sampled in August 2016 with the research vessel Haiyang 4 (Guangzhou Marine Geological Survey) at 12 stations (PR-1-12) from Dongjiang towards the open South China Sea. The surface and bottom waters were sampled using go-flow bottles at 12 and 9 stations, respectively. At station PR-7-9 and PR-11 water samples were only taken directly from the surface. Conductivity, temperature and depth were measured using a Sea Bird Scientific (Bellevue, WA, USA) CTD-system at station PR-1-6, PR-10 and PR-12 **(Figures 1a and 1b and Table 1)**.

The samples of Huangpu River and Pearl River Estuary were collected in 2 L pre-cleaned amber glass bottles and taken to the laboratory where the solid-phase extraction was carried out. The samples were kept in the dark and cool at 4ºC during transport to the laboratory. Samples from the East China Sea were collected in 1 L pre-cleaned amber glass bottles and extracted on board. All extracted samples were stored at -20°C until further analysis in the laboratory at the Leibniz Institute for Baltic Sea Research in Germany.

Chemicals

All reference standards and chemicals were of analytical grade (>98%). Reference standards of the following pharmaceuticals: Sulfadiazine (SDZ), sulfamerazine (SMZ), sulfamethoxazole (SMX), trimethoprim (TMP) and the internal standard sulfamethoxazole-d4 (SMX-d4) were purchased from Dr. Ehrenstorfe GmbH (Germany). The solvents methanol, acetone and hydrochloric acid (HCl) in China were provided by Shanghai Jiao Tong University and Guangzhou Marine Geological Survey, in Germany methanol was obtained from Promochem (Germany). From Sigma-Aldrich (Germany) acetic acid and formic acid were purchased and water (LC-grade) was acquired from VWR (Germany).

Preparation and analysis of antibiotics

The 2 L water samples were divided into two 1 L glass amber bottles and spiked with an internal standard. The internal standard consisted of 20 ng/mL SMX-d4. The solid-phase extraction with 1 L of sample water was done in China accordingly to the pharmaceutical extraction method published by Fisch et al. [28]. For antibiotic analysis the pH was adjusted to pH=5 with 5 M HCl. Prior to the solid-phase extraction the cartridges (Chromabond® EASY, 3 mL, 200 mg, Marchery-Nagel GmbH) were conditioned

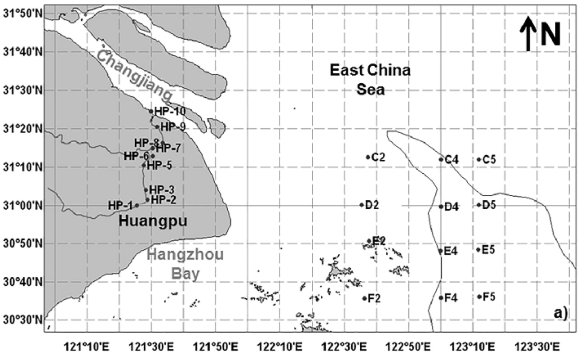

Figure 1a Sampling location: Huangpu River and East China Sea.

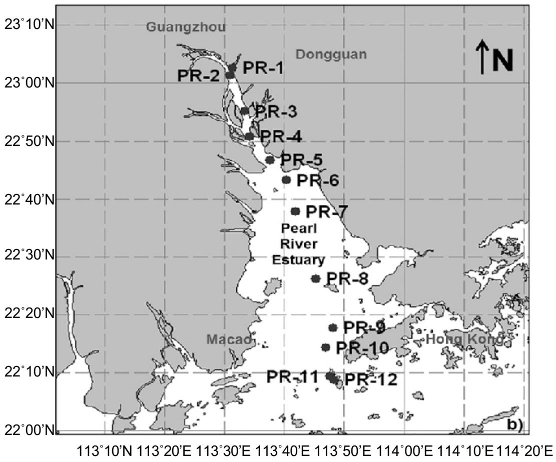

Figure 1b Sampling location: Pearl River Estuary.

Table 1 Station details with measured parameters: Depth, temperature, salinity and the concentrations of sulfadiazine (SDZ, LOD=0.6 ng/L), sulfamerazine (SMZ, LOD=0.6 ng/L), sulfamethoxazole (SMX, LOD=0.5 ng/L), trimethoprim (TMP, LOD=0.9 ng/L).

Station	Coordinates	Depth	Temperature	Salinity	Concentration [ng/L]			
		[m]	[°C]		SDZ	SMZ	SMX	TMP
Huangpu River (25.07.2016)								
HP-1	30.998545°N 121.427541°E	0.5			13.5 ± 0.4	n.d.	9.3 ± 0.1	4.4 ± 0.2
HP-2	31.025168°N 121.483560°E	0.5			14.5 ± 0.1	n.d.	9.6 ± 0.3	4.5 ± 0.1
HP-3	31.067856°N 121.472241°E	0.5			11.2 ± 0.4	n.d.	9.1 ± 0.2	4.1 ± 0.1
HP-5	31.174218°N 121.462442°E	0.5			9.2 ± 0.3	n.d.	7.9 ± 0.1	5.1 ± 0.2
HP-6	31.215413°N 121.508159°E	0.5			10.0 ± 0.1	n.d.	8.1 ± 0.1	5.0 ± 0.2
HP-7	31.249243°N 121.507880°E	0.5			9.8 ± 0.2	n.d.	8.1 ± 0.2	5.7 ± 0.1
HP-8	31.272169°N 121.562656°E	0.5			8.0 ± 0.4	n.d.	7.9 ± 0.2	6.3 ± 0.1
HP-9	31.340310°N 121.533086°E	0.5			10.0 ± 0.3	n.d.	8.3 ± 0.1	4.6 ± 0.1
HP-10	31.408173°N 121.500180°E	0.5			5.3 ± 0.3	n.d.	6.3 ± 0.2	3.0 ± 0.1
East China Sea (12-15.07.2016)								
F2	30.593361°N 122.605972°E	2.0	25.4	20.7	2.0 ± 0.07	n.d.	3.5 ± 0.1	1.3 ± 0.2
		24.8	20.3	33.6	n.d.	n.d.	<LOD	n.d.
F4	30.596722°N 123.002417°E	2.0	25.8	24.0	0.8 ± 0.01	n.d.	2.2 ± 0.02	1.1 ± 0.02
		57.5	19.9	34.4	n.d.	n.d.	n.d.	n.d.
F5	30.599528°N 123.201139°E	2.0	26.9	26.3	n.d.	n.d.	1.4 ± 0.04	1.3 ± 0.01
		51.7	20.2	34.4	n.d.	n.d.	n.d.	n.d.
E2	30.844022°N 122.630761°E	2.0	26.5	9.2	1.6 ± 0.1	n.d.	2.8 ± 0.06	0.9 ± 0.1
		23.9	20.6	32.5	n.d.	n.d.	0.8 ± 0.02	n.d.
E4	30.800833°N 123.001528°E	1.9	23.9	21.7	1.8 ± 0.03	n.d.	3.0 ± 0.02	0.9 ± 0.1
		43.0	20.3	34.2	n.d.	n.d.	<LOD	n.d.
E5	30.807314°N 123.197756°E	2.0	25.7	19.6	1.3 ± 0.05	n.d.	2.8 ± 0.1	1.5 ± 0.3
		54.5	20.3	34.2	n.d.	n.d.	n.d.	n.d.
D2	31.001389°N 122.593611°E	2.0	24.9	13.3	3.0 ± 0.04	n.d.	4.4 ± 0.08	1.1 ± 0.1
		14.9	20.5	31.3	<LOD	n.d.	1.0 ± 0.03	n.d.
D4	30.994981°N 123.004361°E	2.0	24.5	20.4	1.5 ± 0.03	n.d.	3.0 ± 0.04	1.1 ± 0.1
		46.8	20.0	33.9	n.d.	n.d.	<LOD	n.d.
D5	31.001444°N 123.199306°E	1.9	24.7	20.4	1.2 ± 0.03	n.d.	2.6 ± 0.08	<LOD
		51.0	20.6	34.2	n.d.	n.d.	<LOD	n.d.
C2	31.209667°N 122.624361°E	2.0	24.7	18.3	1.5 ± 0.03	n.d.	2.7 ± 0.03	<LOD
		26.8	20.6	33.7	n.d.	n.d.	0.6 ± 0.04	n.d.
C4	31.200417°N 123.003278°E	2.0	26.7	18.3	2.3 ± 0.05	n.d.	3.6 ± 0.2	1.0 ± 0.1
		59.7	20.0	34.1	n.d.	n.d.	<LOD	n.d.
C5	31.200167°N 123.200667°E	2.0	24.0	23.2	1.1 ± 0.01	n.d.	2.4 ± 0.2	0.9 ± 0.1
		51.0	20.6	34.2	n.d.	n.d.	<LOD	n.d.
Pearl River Estuary (29.08.2016)								
PR-1	23.043100°N 113.521020°E	1.5	30.1	0.1	8.3 ± 0.3	11.9 ± 0.2	13.9 ± 0.2	12.0 ± 0.4
		5.9	30.1	0.1	7.7 ± 0.2	11.8 ± 0.2	13.6 ± 0.4	15.2 ± 0.5
PR-2	23.020742°N 113.515870°E	2.0	30.0	0.1	7.5 ± 0.2	11.2 ± 0.2	12.1 ± 0.1	13.5 ± 0.2
		8.8	30.0	0.1	7.9 ± 0.2	11.1 ± 0.2	11.6 ± 0.3	11.4 ± 0.4
PR-3	22.918528ºN 113.557650°E	1.7	30.4	0.1	7.2 ± 0.1	9.3 ± 0.1	11.4 ± 0.4	7.4 ± 0.2
		17.9	30.3	0.1	7.1 ± 0.2	9.7 ± 0.1	11.4 ± 0.3	8.1 ± 0.3
PR-4	22.845817°N 113.570317°E	1.3	30.4	0.8	6.2 ± 0.2	8.0 ± 0.3	11.4 ± 0.2	11.1 ± 0.2
		16.4	30.2	3.9	6.4 ± 0.05	7.4 ± 0.2	11.3 ± 0.4	9.5 ± 0.5
PR-5	22.778505°N 113.628987°E	1.1	30.4	3.1	5.1 ± 0.1	4.5 ± 0.1	10.3 ± 0.1	10.6 ± 0.3
		9.6	30.0	8.8	4.1 ± 0.2	3.2 ± 0.1	9.6 ± 0.2	10.1 ± 0.3
PR-6	22.720088°N 113.672787°E	0.6	30.2	3.2	3.8 ± 0.1	2.9 ± 0.1	9.3 ± 0.3	13.9 ± 0.3
		12.1	29.1	12.6	3.5 ± 0.1	2.8 ± 0.04	9.1 ± 0.1	12.3 ± 0.1
PR-7	22.629917°N 113.697928°E				4.2 ± 0.2	9.2 ± 0.9	9.0 ± 0.7	22.1 ± 1.1
PR-8	22.437782°N 113.754897°E				1.6 ± 0.2	0.9 ± 0.2	5.1 ± 0.3	6.0 ± 0.1
PR-9	22.295800°N 113.802863°E				0.9 ± 0.1	n.d.	3.5 ± 0.1	4.5 ± 0.3
PR-10	22.237382°N 113.783957°E	0.5	27.4	26.3	<LOD	n.d.	2.5 ± 0.02	2.4 ± 0.1

		7.7	27.1	29.1	<LOD	n.d.	2.5 ± 0.05	2.8 ± 0.1
PR-11	22.154925°N 113.793738°E				<LOD	n.d.	1.4 ± 0.1	1.9 ± 0.1
PR-12	22.146218°N 113.804325°E	1.0	27.1	31.0	<LOD	n.d.	1.0 ± 0.1	1.4 ± 0.2
		10.1	26.6	32.3	<LOD	n.d.	0.9 ± 0.04	1.2 ± 0.1

±: Standard Deviation
n.d.: Not Detected
LOD: Limit of Detection

with 4 mL acetone and 4 mL water. Preceding the extraction, the samples were filtered through glass-fiber filters (GF/F, 0.7 µm, Whatman) and directly brought onto the cartridges. Following the extraction cartridges were cleaned with 4 mL pH=5 water and gently dried. All cartridges were stored at -20°C wrapped in aluminum foil and further analyzed in Germany. Samples were eluted with 10 mL acetone/methanol (1/1, v/v), evaporated to dryness at 40°C with a Turbo-Vap (LV, Zymark, USA) evaporator and afterwards reconstituted with 1 mL methanol/water (3/1, v/v). The analysis was carried out using a liquid chromatography heated electrospray ionisation tandem mass spectrometer (LC-HESI-MS/MS) from Thermo Fischer Scientific (Germany). Details of the method and quantification are described in Fisch et al. [28]. For liquid chromatography a reverse-phase Kinetex C-18 (Phenomenex, USA) column was used and 10 µL of sample were injected. Separation was achieved by a gradient program (flow rate: 250 µL/min) of the mobile phases A: water + 0.1% acetic acid and B: methanol + 0.1% formic acid. The temperature for the capillary and vaporizer were set to 275°C and 250°C, respectively. For method quantification the internal standard SMX-d4 and the most abundant transition (based on signal-to-noise ratio) were used, the second most abundant ion was used for qualification. As the antibiotics in this study belong to the group of sulfonamides it is appropriate to use SMX-d4 as an internal standard for all of them. The LODs (0.5-0.9 ng/L), LOQs (0.6-1.0 ng/L) and the recovery rates are displayed in **Table 2**.

Calculation of attenuation coefficient

Calculations of the attenuation coefficient (k) were done according from 3.0 to 14.5 ng/L, assuming a first order attenuation [29,30]. The attenuation of antibiotics involves e.g. dilution, adsorption, photolysis and biodegradation Zhang et al. As stated by the sources of pollution are diffused and the sea currents were not stable [29]. Therefore, the attenuation is the correlation of antibiotic concentration (ci, cl) at the stations (i, l) with distance (L) between the stations:

$$k = \left(\frac{1}{L}\right) ln\left(\frac{c_i}{c_l}\right)$$

Results and Discussion

Huangpu River

The surface water of the Huangpu River was sampled at 9 stations (HP-1-10, w/o HP-4) in July 2016 in the urban area of Shanghai. Only 3 out of 4 analyzed antibiotics were found in concentrations ranging from 3.0 to 14.5 ng/L. All values are uncorrected and could be corrected by a factor of 2, due to the low recovery rate of the internal standard SMX-d4. The antibiotics sulfadiazine (SDZ), sulfamethoxazole (SMX) and trimethoprim (TMP) were all detected with a frequency of 100%. Sulfamerazine (SMZ) was not found at any station. SMZ is only of veterinary usage and in China it is mostly used in aquacultures [22]. This may explain its absence in the urban area of Shanghai, which is an intensive industrial and residential area [19]. The salinity of the Huangpu River does not change significantly along the stream, which means the river is mostly influenced by fresh and waste water inputs [31]. SMX and TMP concentrations are mostly consistent along the river with a slight decrease from station HP-1 to HP-10. The attenuation coefficient for both is k=0.0007 km^{-1}, which indicates that the concentrations are only slightly diluted. SDZ displays a stronger decrease from the urban area towards station HP-10 (k=0.016 km^{-1}). In comparison with literature data by Jiang et al., this study shows that there is a slight increase in concentrations of approximately 10 ng/L [23]. The reason may be an increase in the usage of antibiotics in the last 7 years. Jiang et al. only found SMX at some stations. In this study it was detected at all stations, at a consistent concentration (mean 8.3 ± 1.0 ng/L) along the river [23]. At station HP-10 the concentration of SMX is similar to the concentration measured by Jiang et al. [23]. In this study TMP was detected with concentration of low variability. The increase of TMP (station HP-3-6) detected by Jiang et al. was not confirmed [23]. Like for SMX, TMP was detected at similar concentration at station HP-10 as reported in literature. The domestic waste water effluents are a major source of pollution in the urban area for the Huangpu River [32]. The waste water treatment rate in the urban area was approximately 88% by end of 2010. This corresponds to a direct discharge of approximately 419 million m^3 waste water into the Huangpu River every day [19]. However, the waste water is now supposed to be directly discharged into the East China Sea. Considering that most of the waste water is released to the East China Sea, the small increase of concentrations between 2009 and 2016 in the Huangpu River appears to be realistic. Additionally, all concentrations measured in this study are lower than reported concentrations for winter months and for the upstream area. Studies report, that higher concentrations of antibiotics can be found in winter months due to a higher usage, low flow conditions and lower photo and biodegradation [23,32-36]. An important loss pathway in water is the direct photolysis [37,38]. However, it is known that SA antibiotics are hydrologically stable, water soluble, have a low sorption to particles and soil and are easily transported in water over long distances, explaining the evenly distributed concentrations [17,37,39-41]. Furthermore, SA resistant genes (sulI, sulII) were detected near our sampling stations, which points towards an occurrence of SAs and their extensive usage

Table 2 Overview of selected antibiotics, their recovery rate, limit of detection (LOD) and the limit of quantification (LOQ).

Name	Abbreviation	CAS	Recovery [%]	LOD [ng/L]	LOQ [ng/L]
sulfadiazine	SDZ	68-35-9	85	0.6	0.7
sulfamerazine	SMZ	127-79-7	91	0.6	0.7
sulfamethoxazole	SMX	723-46-6	103	0.5	0.6
trimethoprim	TMP	738-70-5	85	0.9	1.0
sulfamethoxazole-d4	SMX-d4	1020719-86-1	56		

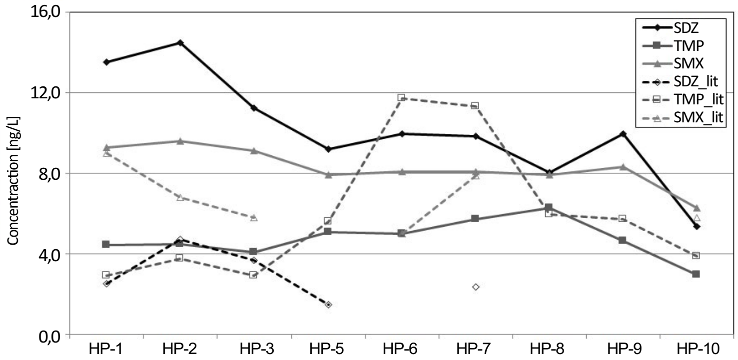

Figure 2 Concentration of sulfadiazine (SDZ), sulfamethoxazole (SMX) and trimethoprim (TMP) measured in Huangpu River with literature data for comparison.

Table 3 Comparison of detected concentration [ng/L] with literature data [ng/L] in surface water for the regions: a) Huangpu River and East China Sea, b) Pearl River estuary. Yang et al. [31,34,47] reported a temperature and salinity range of 10.9-14.8°C and 18.5-30.5, respectively. Liang et al. [32] reported a salinity range for wet and dry season of 0.4-21.7 and 0.3-32.1, respectively.

	Area	Sampling Season	SDZ	SMZ	SMX	TMP	Reference
a)	Huangpu River	June 2009	1.39-17.19 (1.3)$^{(a)}$	n.d. (0.8)	4.86-14.32 (4.5)	2.23-11.73 (2.2)	Jiang et al. [23]
		December 2009	4.19-40.5	n.d.	16.92-55.24	6.75-62.39	
	Huangpu River	July 2012	4.9-112.5	<LOQ	2.2-764.9	-	Chen and Zhou [56]
	(upstream)		(0.03-1.7)	(0.03-1.7)	(0.03-1.7)	(0.03-1.7)	
	Huangpu River	July 2016	5.3-14.5	n.d.	6.3-9.3	3.0-6.3	This study
	(downstream)		(0.7)	(0.7)	(0.6)	(1.0)	
	East China Sea	November 2009	-	-	4.2-40	-	Yang et al. [47]
	(Changjiang Estuary)				(0.08)		
	Changjiang Estuary	July 2011-May 2012	0.3-71.8 (0.41)	n.d. (0.04)	0.3-56.8 (0.3)	-	Yan et al. [35]
	Changjiang Estuary (C16)	Nov-Dec 2012	-	-	11.2	n.d.	Wu et al. [58]
	East China Sea	July 2016	n.d.-3.0	n.d.	1.4-4.4	< LOQ-1.5	This study
b)	Victoria Harbor (HK)	Dec 2004/Feb 2005	n.d. (1.0)	-	n.d. (1.0)	-	Xu et al. [36]
	Pearl River (upstream)	June 2005	max. 141	-	max. 165	-	Xu et al. [36]
	Major Pearl River	Feb/June 2006	<MQL (70)	-	<MQL-510 (80)	<MQL (100)	Peng et al. [21]
	Stonecutters Island (HK)	June-August 2008	-	-	n.d. (0.5)	n.d. (0.4)	Minh et al. [57]
	Pearl River	September 2008	4.9-26.7 (0.2)	-	211-616 (1.0)	81.2-179 (0.3)	Yang et al. [34]
	(upstream, Shijing)						
	Pearl River Estuary	June 2009	10 (1.0)	-	2.3-11.1 (1.0)	-	Xu et al. [2]
	East River (Dongjiang)	July 2009	n.d.-8.2 (1.0)	-	7.9-30.4(1.0)	n.d.-15.5	Zhang et al, [48]
	Pearl River Estuary	August 2011	max. 2.1 (0.5)	-	max. 9.4 (0.6)	-	Jiang et al. [1]
		January 2011	max. 18	-	max. 30.1	-	
	Pearl River Estuary	August 2016	<LOD-8.3	n.d.-11.9	1.0-13.9	1.4-22.9	This study

- not Analyzed
n.d.: not detected
LOQ: Limit of Quantification
LOD: Limit of Detection
Max: Maximum
MQL: Method Quantification Limit
(a) Values in parentheses are quantification limits (ng/L)

[1] **(Figure 2 and Table 3)**.

East China Sea

The surface and bottom water of the East China Sea near the coast was sampled at 12 stations in July 2016. The sampling stations were all located in the Changjiang Diluted Water (CDW), which covers most of the northern East China Sea during flooding and is defined by salinity <31 [42]. The antibiotics SDZ, SMX and TMP were detected in all surface water samples with a detection frequency of 92%, 100% and 83%, respectively. Only SMX was detected in 3 bottom water samples closest to the coast (E2, D2, C2, F2<LOD). To our knowledge, these are the first results of antibiotics in the open East China Sea. SMZ was not detected in any samples. It is an unauthorized antibiotic, but still used in aquacultures. The output of aquatic products for the Shanghai-Zhejiang region is approximately 2.08 mio t per year [22]. It can be assumed that the input of SMZ is too low in order for its detection in the open sea. Only low concentrations of SDZ, SMX and TMP up to 4.4 ng/L were detected, which are lower than the measured concentrations in the Huangpu River. No correlation was found between the occurrence of the antibiotics and particulate organic carbon (POC) and chlorophyll a (ChlA). POC and ChlA data was obtained from satellite images provided by NASA. The concentrations decrease from stations near the coast towards stations in the open sea. An inverse correlation was calculated for SMX (r=-0.7) and SDZ (r=-0.6) with salinity. Only TMP (r=0.4) displayed a positive correlation. Due to the inverse correlation, it can be assumed that the antibiotics are diluted while being transported from the estuary to the open sea [29]. SAs and TMP have a half-life of about 100 days (relatively persistent) in seawater and are not inclined to degrade in surface water, indicating that they can be transported in water for a long distance, which explains their occurrence in the open sea [43-45]. From 1942 to 2002 aquacultures increased by 14% in the Changjiang Delta [46]. SAs are directly added into the water while feeding and are used/applied in larger dosages in order for them to reach the effective inhibition concentration within the animal [22]. The salinity demonstrates that the sampled water originated from the Changjiang River. The CDW and the direct input of the Shanghai waste water are possibly the major sources for these antibiotics in the East China Sea. SAs have a low sorption affinity to soil, sediment and suspended particular matter and are hydrophilic, explaining their occurrence in surface water and their absence in bottom water [16,39-41,47]. In comparison to Changjiang River, lower concentrations were measured during this study. However, the reported higher concentrations in the Changjiang River were detected during the dry season, when the dilution effect is much lower than in the wet season. Additionally, the distance to the coast is much larger than in previous studies, which explains the lower concentrations detected in this study **(Figures 1a and 3 and Table 1)**.

Pearl River Estuary

The surface water of the Pearl River Estuary was sampled at 12 stations and the bottom water at 8 stations. All 4 analysed antibiotics were detected in the surface and bottom water. SMX and TMP were detected at a frequency of 100%. SDZ and SMZ were detected in surface water with a frequency of 75%, 66.6%, respectively and 75% in bottom water. Highest concentrations (∑SA=46.2 ng/L) were measured at station PR-1 which is located in the East River (Dongjiang). The East River is mostly influenced by domestic waste water discharge. It is the most economically developed region in China and has a high livestock production rate [48,49]. The detected concentrations are in similar range as those measured by Zhang et al. [48]. All concentrations decrease with distance from the city center (PR-1) towards the South China Sea (PR-12). Concentrations in surface and bottom water only differ slightly, it can be explained by the mixing between different water bodies [36]. SDZ and SMZ have higher attenuation factors (k=0.028 km^{-1} and k=0.036 km^{-1}, respectively) than SMX and TMP (k=0.024 km^{-1} and k=0.02 km^{-1}, respectively). Only SMZ and TMP have an increased concentration at PR-7 (9.2 ng/L and 22.1

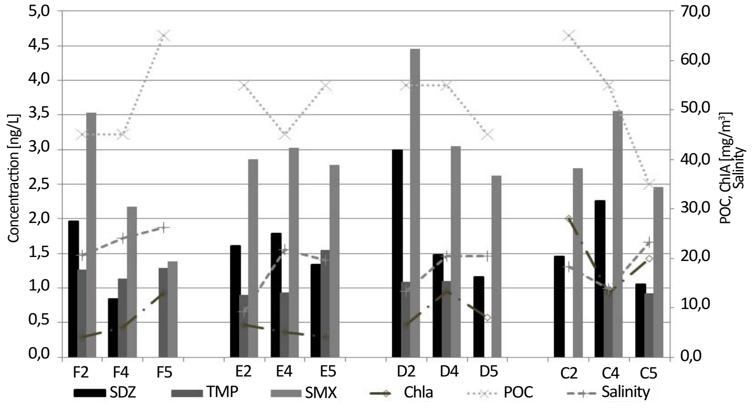

Figure 3 Concentration of sulfadiazine (SDZ), sulfamethoxazole (SMX) and trimethoprim (TMP) measured in East China Sea with particulate organic carbon (POC), chlorophyll a (ChlA) and salinity.

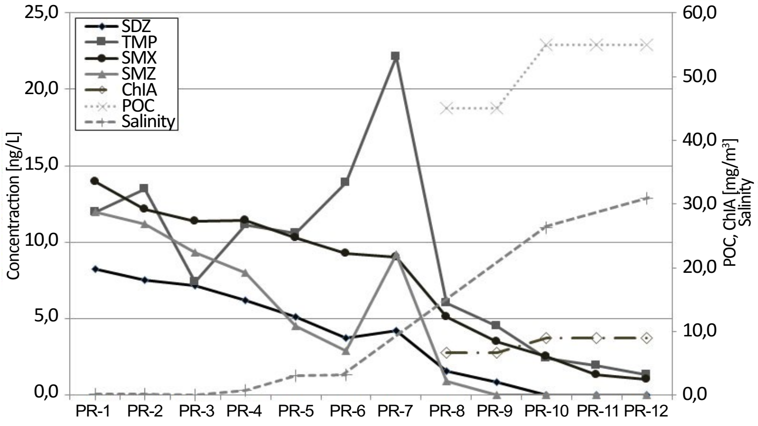

Figure 4 Pearl River estuary surface water concentrations of sulfadiazine (SDZ), sulfamerazine (SMZ), sulfamethoxazole (SMX) and trimethoprim (TMP) with POC, ChlA and salinity.

ng/L, respectively). As mentioned above SMZ is an unauthorized antibiotic and only used in veterinary applications [22,50]. A possible source for SMZ and TMP could be intensive aquacultural activities in the area. SMZ is the only SA which was not detected at every station, possibly reflecting a lower input due to its limited usage. SDZ and SMX in combination with TMP are not only used in veterinary applications but also in human applications to treat bacterial infections [12,51]. Like in the East China Sea, all SAs and TMP display an inverse correlation with salinity (∑r=-0.96). In the Pearl River Estuary the dilution effect is much more dominant than in the Huangpu River. On one hand the dilution is driven by the tidal stage of the river and the riverine input of the other tributaries [32,52]. On the other hand Xu et al. suggested that the occurrence and dilution may more depend on the daily waste water production cycle and its discharge than on the tidal stage [36]. The waste water treatment rate for SAs and TMP in the Pearl River Estuary region varies between 52-85% [8,53]. The region is heavily influenced by urban industry and agricultural activities and has high contribution to China's annual poultry, pig and aquaculture production [54]. Until now China has no requirements for livestock waste treatments, basically meaning it is directly discharged into the river [8]. As a consequence the discharge of treated and untreated waste water increases the concentration of SAs and other antibiotics in general in the aquatic environment [32]. A comparison with former studies shows that, higher concentrations are detected upstream than downstream. Nevertheless the concentrations downstream did not change significantly over time (2005-2016). Due to that it can be assumed that the Pearl River Estuary has been exposed to these antibiotics in low ng/L range for a long time. Leaving it up for discussion which long-term effect they might have on the biota and how significant the occurrence of antibiotic resistant genes (sulI and sulII) [55] **(Figures 1b and 4 and Tables 1 and 3)**.

Mass load into analyzed systems

An approximation of the mass load of SAs and TMP into the rivers was performed using the annual discharge volume (Huangpu River: 10 billion m^3, Pearl River Estuary: 336 billion m^3) and the average measured concentration (Huangpu River: 23.2 ng/L, Pearl River Estuary: 25.1 ng/L) [24,27]. Huangpu River discharges an estimated total amount of 232 kg per year into the Changjiang River. In comparison with the Pearl River Estuary, the Huangpu River is a more static system and mostly influenced by the discharge of the Tai Lake and some additional unidentified waste water. The sampled area is mostly influenced by industrial and urban activities. Due to the waste water policy of Shanghai, it is possible that the influence of the domestic waste water has declined in the urban area. For the Pearl River Estuary a mass load of approximately 8.4 t per year was estimated. The Pearl River Estuary is much more influenced by industrial and agricultural activities and waste water (treated and untreated). Moreover, its annual discharge volume is higher than the Huangpu River, which justifies the higher mass load.

Conclusion

Water samples from three different Chinese water systems (Huangpu River, East China Sea and Pearl River Estuary) were analysed for SAs and TMP. Antibiotics were detected in all three systems in low ng/L range. It is the first study reporting antibiotics in the East China Sea. In the Huangpu River SDZ, SMX and TMP occur at a stable concentration. The same three antibiotics were detected in the East China Sea, at slightly lower concentration than in the Huangpu River. The concentrations slightly decrease from coastal stations towards the open sea. Their occurrence in the open sea points out the long distance they can be transported and their possible stability in the marine environment. All four antibiotics were detected in the Pearl River Estuary. The concentrations of the Pearl River are in similar range as those in the Huangpu River. The mass load, however, is much higher because of the greater water volume. Furthermore, the concentrations in the Pearl River Estuary are stronger diluted than in the Huangpu River. Both cities pursue different water policies and waste water treatment management. However, the widespread co-existence of these antibiotics in the aquatic environment indicates that the common sources are the discharge of treated and untreated water as well as the direct input via aquaculture [48]. Even though SAs are hydrophilic and mostly occur in the water phase, a future research focus should also be put on their occurrence in marine sediments [56-58].

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Occurrence of the Two Endocrine Disruptors Octocrylene and Nonylphenoxyacetic Acid in Four Chinese Aquatic Systems

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Abstract

Worldwide the emergence of endocrine disrupting chemicals in the environment is of growing scientific concern. The aim of the present study was to determine the occurrence and distribution of two endocrine disrupting chemicals, octocrylene (UV-filter) and nonylphenoxyacetic acid (non-ionic surfactant metabolite), in two Chinese rivers (Huangpu and Pearl River). Additionally, a focus was put on their occurrence in the marine ecosystems of the East and South China Sea. Surface and bottom water samples were taken from Pearl River, East and South China Sea using go-flow bottles. From the Huangpu River grab surface water samples were taken at the river bank. All samples were enriched via solid-phase extraction and analyzed with liquid chromatography tandem mass spectrometry. Octocrylene was detected in all four analyzed water systems at a low ng/L range from not detected to 30 ng/L in surface and bottom water samples. Its occurrence at the off-shore stations in the South China Sea indicate that octocrylene can be transported over a long distance. Nonylphenoxyacetic acid was detected at a higher ng/L range (not detected-658.3 ng/L) than octocrylene in three of the four Chinese water systems in surface and bottom water samples. It was not found in the South China Sea. The risk assessment indicates that right now only nonylphenoxyacetic acid poses a medium risk to aquatic organisms in the Huangpu and Pearl River.

Keywords: Octocrylene; Nonylphenoxyacetic acid; Pearl River Estuary; Huangpu River; East China Sea; South China Sea; Aquatic pollution

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Introduction

The world population now exceeds 7 billion people and over 54.9% of the population live in urban areas [1]. Urbanization can be observed worldwide for past-centuries. At present, urbanization can be seen in the emergence of megacities (population: >10 million people) with 8.4% of the world population already living in megacities. Since the 1980s until today China has experienced a population migration from rural to urban areas and approximately 54% (2014) of China's population now live in urban areas [2]. The megacities Shanghai (population: 23.4 million) and Guangzhou (population: 19 million) ranked 7th and 13th place in the list of largest cities in the world in 2016 [1]. Urbanization can be seen by typical foot-prints such as lights at night, from airplane or space. It also leaves its marks in the environment around it e.g. higher waste production and pollution of air and water.

With the growth of the population not only did the urbanization increase but also the request and usage of personal care products (PCPs) and household chemicals increased. PCPs include a wide range of products such as lotions, creams, soaps, cologne and toiletries [3]. There are two major pathways for PCPs to enter the aquatic environment: Either they enter the aquatic environment by an indirect input (e.g. showering, cleaning, washing machine etc.) via the waste water due to an incomplete removal or as is the case for sunscreen, directly via recreational activities. PCPs are counted as ubiquitous contaminants and are defined as 'pseudo'-persistent due to their inefficient removal from waste water and constant input into the environment [4,5]. Their occurrence in the environment is of growing scientific concern, as many of them have endocrine disrupting properties and effects on organisms [6]. One of the investigated compounds is the organic UV-filter octocrylene (OC), which is mainly used in sunscreen products to protect the skin from UV-radiation. In China the total usage of OC was estimated to be 206 t per year, with a total emission of 116 t per year. OC is mostly used in skin care products (63%), which include 80 t sunscreen products and 47 t daily face care products [7]. Additionally, it is also used as a stabilizer for other UV-filters in formulas or in plastics. It is photostable, non-degradable and a lipophilic neutral compound, due to its high logK_{ow} (6.9) [7]. It can be adsorbed to particles or sediments and its neutral form is mostly transported from water to sediment. Most studies about OC have focused on the sediment phase and on biota, as approximately 91% of the discharged OC can be found in freshwater sediment and only 4% in marine sediment [7]. In recent years, studies reported that OC is bio-accumulative and was not only found in mussels (*M. galloprovincialis, M. edulis*), fish, shrimp and squids but also in higher trophic levels such as dolphins and in human breast milk, which suggest that it can possibly be bio-magnified in the food-web [3,8-14]. Blüthgen et al. and Zhang et al. were able to prove that OC is affecting the endocrine system of zebrafish (*D. rerio*) and androgenic, anti-androgenic and anti-estrogenic activities were observed [6,15]. Furthermore, Campos et al. recently published that OC impairs the growth of *C. riparius* larvae and it reduces the weight of imagoes and delays their emergence [16]. Additionally, toxicity against *P. lividus* embryogenesis and the early larval growth has been reported [17]. The other investigated compound is nonylphenoxyacetic acid (NP_1EC). It is an intermediate which is formed e.g. by the aerobic degradation of the non-ionic surfactant nonylphenol polyethoxylate, which is mostly used as an industrial laundry detergent [18,19]. Only few studies have been conducted about NP_1EC so far and not much is known about it. However, NP_1EC is known to have endocrine activities and it is listed in category 2 of the European endocrine disruptor priority list for wild life and human health [20]. In difference to its degradation product nonylphenol, it can mostly be found in the water phase as its logK_{ow}-value is 2.2 [21]. Around the world studies have focused on the occurrence of PCPs and endocrine disrupting chemicals in influents and effluents of waste water treatment plants, in lakes and rivers and also soils and sediments [22-26]. However, only few studies so far have put a focus on the marine environment and the transport of PCPs along salinity gradients [27]. This study is focused on the occurrence of the two endocrine disruption chemicals OC and NP_1EC in two Chinese rivers (Huangpu River, Pearl River), which are influenced by the megacities Shanghai and Guangzhou, respectively. Furthermore, their transport into the open marine environment of East and South China Sea was under investigation.

Materials and Methods

Chemicals

All chemicals and reference standards were of analytical grade (>98%). Reference standards of octocrylene and nonylphenoxyacetic acid were purchased from Dr. Ehrenstorfer GmbH (Germany). The internal standard benzophenone-3-d5 (BP-3-d5) was obtained from CDN Isotopes (Canada). Solvents used in China (acetone, methanol and hydrochloric acid (HCl)) were contributed by Guangzhou Marine Geological Survey and Shanghai Jiao Tong University. Acetone and methanol used in Germany were purchased from Promochem (Germany). Water (LC-grade) was acquired from VWR (Germany) and acetic acid and formic acid were purchased from Sigma-Aldrich (Germany).

Sampling areas and sampling strategy

The Huangpu River (HP) is the largest river (114 km) flowing north-east through Shanghai. It is originating in Tai Lake and discharges north of Shanghai into the Changjiang River (discharge volume: 10 billion m^3/a). Industry and residential areas dominate the lower river (83 km) [28,29]. Samples from Huangpu River (n=10) were collected in July 2016 stream upwards from Minhang district (HP-1) towards the Changjiang River (HP-10). From the Huangpu River 2 L surface water (0.5 m) samples were taken, from the river bank with a pre-cleaned metal bucket. The samples were filled in 2 L pre-cleaned amber bottles, kept cold (4°C) and in the dark for the transport to the laboratory (Shanghai Jiao Tong University), where the solid-phase extraction was carried out within 48 h **(Figure 1a) (Table S1)**.

The East China Sea is the largest marginal sea in the north western Pacific Ocean. It is dominantly influenced by the Changjiang River discharge and slightly by the Hangzhou Bay [30]. The East China Sea receives freshwater from the Changjiang Estuary which forms a strong plume of Changjiang Diluted Water (CDW) on the shelf. It is also influenced by the inshore branch of the Taiwan Warm Water Current (TWCIB) flowing north east during the south west monsoon season. The Changjiang Estuary and the East China Sea shelf are defined by a eutrophic, low-salinity, inshore (CDW, coastal current) current system in the summer. The CDW (S<34) is dominating the upper water column [31]. During a cruise with research vessel ZheHai Ke 1 (Zhejiang Ocean University) in July 2016 discrete surface and bottom (n=12, both) water samples were taken in the East China Sea using a go-flow bottles. At each station conductivity, temperature and pressure were measured with CTD-sensors from Sea Bird Scientific (Bellevue, WA, USA). All samples were collected in 1 L pre-cleaned amber bottles and the extraction was carried out on the ship **(Figure 1a) (Table S1)**.

The Pearl River (PR) is approximately 120 km long and is the largest water system discharging (336 billion m^3/a) into the South China Sea (SCS) [32,33]. It is heavily influenced by the waste waters from industrial and domestic activities but also from intensive agriculture and aquaculture. One of the characteristics is its semi-diurnal tidal cycle [34]. Discrete surface (n=12) and bottom (n=9) water samples were taken from the Pearl River in August 2016 with the research vessel Haiyang 4 (Guangzhou Marine Geological Survey, GMGS) using a go-flow bottle. Samples at station PR-7-9 and PR-11 were taken directly from the surface. Samples were taken from upstream (Dong Jiang River) towards the South China Sea. The conductivity, temperature and pressure were measured at station PR-1-6, PR-10 and PR-12 with a CTD-system (Sea Bird Scientific, Bellevue, WA, USA). The samples were stored in 2 L pre-cleaned amber bottles and kept in the dark at 4°C until extraction in the GMGS-laboratory within 48 h **(Figure 1b)**.

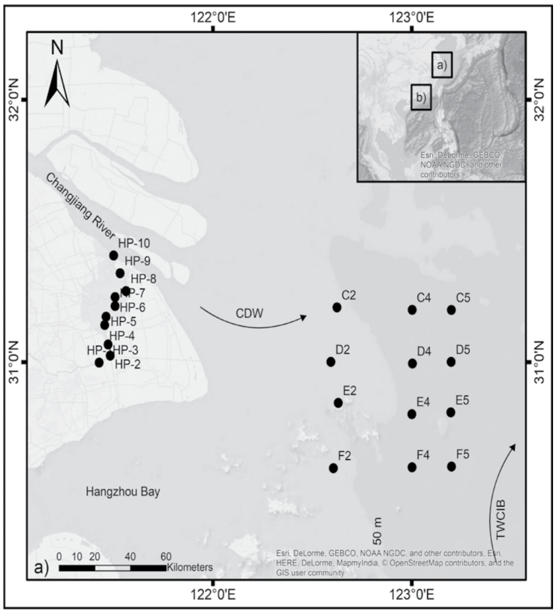

Figure 1a Sampling location: Huangpu River (HP-1-10) and East China Sea (C-F2, 4, 5).

CDW - Changjiang Diluted Water, TWCIB - Taiwan Warm Current Inshore Branch

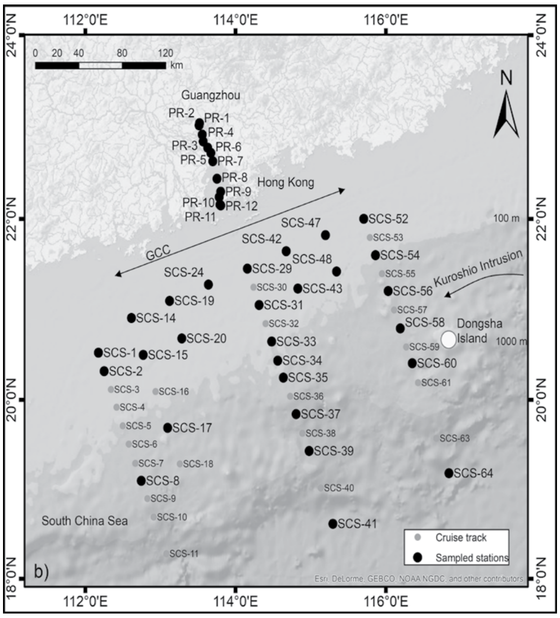

Figure 1b Sampling location: Pearl River Estuary (PR-1-12) and South China Sea (SCS1-64). GCC - Guangdong Coastal Current (He et al., 2016; Jiang et al., 2017)

The South China Sea with a total area of approximately 3.5x10^6 km^2 is the largest semi-enclosed sea in the western tropical Pacific Ocean. The Pearl River Estuary is located midway along the northern boundary of the South China Sea between the Taiwan Shoal and Hainan Island. The coast has ENE-WSW orientation and is connected to a shelf of 150-250 km width [35]. The Pearl River Delta is one of its largest contributor with a drainage area of 453,690 km^2 covering most of south China and Vietnam [36]. The estuary freshwater forms a buoyant plume over the shelf and the winter surface circulation is cyclonic in the South China Sea. During the winter season the north easterly monsoon transports the freshwater plume southwestwards along the coast line [34]. The surface water (n=29) of South China Sea was sampled in March 2015 with the research vessel Haiyang 4. Discrete water samples were taken with go-flow bottles and conductivity, temperature and pressure were measured with the CTD-system (Sea Bird Scientific, Bellevue, WA, USA). All samples were collected in 1 L pre-cleaned amber bottles and extracted on board. **(Figure 1b) (Table S1)**.

The extracted samples were kept in the dark at -20°C and further analyzed in Germany. For the South China Sea, samples for the following parameters were taken during the cruise and measured in Germany: Particulate organic carbon (POC), dissolved organic carbon (DOC), suspended particulate matter (SPM) and chlorophyll a (Chl a). Data of POC and Chl a for the East China Sea was obtained from satellite imagery provided by NASA, in order to estimate transport processes in the particulate phase **(Table S2)** [37].

SPE and LC-MS/MS

The solid phase extraction (SPE) and chromatography analysis have been published by Fisch et al. and Orlikowska et al. [25,38]. The 2 L of sampled water were divided into 1 L amber glass bottles and spiked with 20 ng/L internal standard (BP-3-d5). 1 L of sampled water was extracted and enriched via SPE. Prior to the SPE the pH was adjusted to pH=2 with 5M HCl. Chromabond® EASY (3 mL, 200 mg, Marchery-Nagel GmbH) cartridges were cleaned and preconditioned with 4 mL acetone and 4 mL LC-water. The samples were brought onto the column via a filtration unit equipped with glass-fiber filters (GF/F, 0.7 µm, Whatman), to remove SPM and POC from the water phase. After extraction, the cartridges were cleaned with 4 mL water (pH=2) and gently dried under vacuum. The columns were wrapped in aluminum foil and stored in the dark at -20°C and further analyzed in Germany. In Germany the columns were eluted with 4 mL acetone/methanol (1/1, v/v) and 6 mL methanol/13% $NH_{3\,(aq)}$ (97/3, v/v). The eluate was evaporated to complete dryness in a water bath at 40°C in a Turbo-Vap (LV, Zymark, USA) evaporator. The samples were re-constituted in 1 mL methanol/water (1/1, v/v).

The 1 mL samples were analyzed with liquid chromatography equipped with a heated electrospray ionization source and tandem mass spectrometer (LC-MS/MS) from Thermo Fischer Scientific (Germany). The chromatographic separation was achieved with a reverse-phase Kinetex C-18 column (2.6 µm, 50 x 2.1 mL, 100 Å, Phenomenex, USA), running a gradient program (mobile phase A: water + 0.1% acetic acid, mobile phase B: methanol + 0.1% formic acid, flow rate: 250 µL/min). A sample volume of 10 µL was injected and each sample was measured in triplicate. The temperatures (capillary, vaporizer) were set to 300°C. The measurement was carried out in selected reaction mode (SRM). For each compound two distinctive transitions of the precursor molecular ion/product ion were scanned. The ionization was achieved in positive and negative mode. For quality control the transition of two characteristic precursor molecular ion/product ion transitions were monitored in SRM. Quantification and qualification were conducted on the first and second most abundant transitions, respectively. Both were based on the signal-to-noise ratio and the area ratio of sample to internal standard. Further information can be found in Orlikowska et al. [38].

Calculation of attenuation coefficient and risk quotient

For interpretation of the behavior of OC and NP_1EC in the Huangpu and Pearl River the attenuation coefficient (k) was calculated according to Luo et al. and Zhang et al., assuming a first order attenuation [39,40]. Adsorption, dilution and bio-degradation are often described as factors affecting the attenuation. Additionally, it needs to be considered that currents (direction and strength) may vary within/along the river and that diffused sources are more dominant than point sources.

In addition to the attenuation, a risk quotient (RQ) was calculated to determine the potential risk of the compounds to the environment. RQ is the quotient of measured environmental concentration (MEC) over predicted no-effect concentration (PNEC). It was calculated for all analyzed Chinese water systems. The RQ is classified in three levels: $RQ < 0.1$ low risk, $0.1 \le RQ \le 1$ medium risk, $1 \le RQ$ high risk [41].

Results and Discussion

During the summer 2016 a total of 34 samples of surface and bottom water were collected from Huangpu River, East China Sea and Pearl River. One year prior, 29 surface water samples were taken in South China Sea. Both OC and NP_1EC were detected in Huangpu River, Pearl River and East China Sea and only OC in the South China Sea **(Table 1)**.

Occurrence and distribution of OC in aquatic environment

OC was detected at every station in Huangpu River with a concentration range of 11.9±1.2-23.2±2.3 ng/L. The concentration along the river does not vary much and no significant point sources were detected. The attenuation coefficient of k=0.004 indicates that the dilution of OC is insignificant. The measured concentrations of OC have been correlated with the population density in the area (10 km radius) surrounding the sampling stations as suggested by Wu et al. [42]. There is a slight positive correlation between the population density and the occurrence of OC in the Huangpu River (r=0.2, p=0.5). It can be considered that the consumption in densely populated areas could be of importance. Wu et al. were able to see an increase in UV-filters (benzophenone) from suburban to urban areas and also towards the Changjiang River [42]. The latter increase was explained by the many cosmetic factories and waste water treatment plants (WWTPs) along the Suzhou River and Yunazo Brook, which drain into the Huangpu River near Changjiang River. The same increase could not be confirmed for OC. The connectivity rate of WWTPs in Shanghai is estimated to be around 81%, which exposes the Huangpu River to 419 million m^3 of untreated waste water, pointing towards waste water being a source of OC in the Huangpu River [7,29]. Even though OC is expected to be adsorbed by soil and sediment, due to its lipophilicity ($\log K_{OW}=6.9$) and tendency to bio-accumulate, it can be transported in water as it is highly stable in the environment [4,7,43]. In Shanghai OC has only been detected in indoor dusts by Ao et al. [44]. The median concentration of OC added up to 1170.4 ng/g, which was 5-10 times higher than the other analyzed UV-filters. This result point towards a high consumption rate of OC and explains its presence in the Huangpu River **(Figure 2) (Table 1 and S1)**.

OC was detected in 33% of surface water samples and 50% of bottom water samples in the East China Sea. At the surface it was only detected at the stations closest to the coast (F2, E2 and D2) and station F5, which all were of lower salinity. The maximum concentration (30.1 ± 2.5 ng/L) was measured at station F2, which is higher than in the Huangpu River. OC shows a slight positive correlation with salinity ($r_s=0.1$, p=0.6), indicating that dilution has a minor effect on the distribution pattern of this compound. However, all sampling stations were positioned in the Changjiang Diluted Water (CDW, salinity<31), indicating that OC was transported with the CDW into the East China Sea. An ANOVA analysis displays, that there is a significant statistical difference (p<0.001) between the concentration in the Huangpu River and the East China Sea. Another possible input source can be the waste water of Zhejiang (WWTP connectivity: 71%) or the direct discharge of waste water from Shanghai into the East China Sea [7,28]. OC is photostable and not easily degradable. Higher concentrations in the bottom than surface water can be explained by is tendency to adsorb to particles, resulting in its transport/sinking through the water column or desorption from

Table 1 Measured surface concentrations of octocrylene (OC) and nonylphenoxyacetic acid (NP_1EC) in Huangpu River, Pearl River, East and South China Sea.

Compound	LOD	Huangpu River (n=10)			Pearl River (n=10)			East China Sea (n=12)			South China Sea (n=29)		
		freq.	mean	max.	freq.	mean	max.	freq.	mean	max.	freq.	mean	max.
	[ng/L]	[%]	[ng/L]	[ng/L]	[%]	[ng/L]	[ng/L]	[%]	[ng/L]	[ng/L]	[%]	[ng/L]	[ng/L]
OC	1.7	100	18.1 ± 3.8	23.2	100	3.9 ± 2.1	9.8	33.3	3.6 ± 8.7	30.1	76	4.4 ± 4.0	17.8
NP_1EC	1.0	100	463.9 ± 146.0	658.3	100	226.9 ± 133.9	396.1	100	10.7 ± 3.2	18.2	0	n.d.	n.d.

LOD - limit of detection, freq. - frequency of detection, mean - mean value of samples above LOD, max - maximum concentration, ± - standard deviation re-suspended sediment or particles [43,45]. Due to its lipophilic properties, sedimentation could be a possible sink for OC in the environment. That would explain the occurrence not only in the surface water but in the bottom water as well. The slight negative correlation with POC (r_{POC}=-0.1, p=0.7), is an additional indicator that the sorption of OC to particles can be seen as a sink of OC in the environment. However, it needs to be accounted for that this correlation is based on just few measurements. It is an indicator that there is a possible correlation between the concentration of OC and the particulate organic carbon content. In the East China Sea, OC has only been detected in Tokyo Bay (87-108 ng/L, Tsui et al.) and off-shore near Okinawa (n.d.-8.1 ng/L) [5]. Even though the sampling stations near Okinawa are closer to the coast, they display a slightly lower mean value than the mean concentration (10.7 ng/L) measured in this study **(Figure 3) (Table 1 and S1)**.

In all surface and bottom water samples from Pearl River, OC was detected. No correlation was detected between the occurrence of OC and the population density of the surrounding area (10 km radius) of the sampling stations [47]. The surface and bottom water concentration are in similar range. The highest surface water concentration (9.8 ± 0.3 ng/L) was detected at station PR-1, which is the closest station to the city center of Guangzhou. OC then decreases towards the open South China Sea. Both, surface and bottom water concentration of OC display a negative correlation with salinity (r_s=-0.4, p=0.3, r_s=-0.3, p=0.4, respectively), which is different from the open marine system (see East and South China Sea, positive correlation). The attenuation coefficient adds up to k=0.01. The negative correlation with salinity, together with the attenuation coefficient point towards weak dilution effects as a reason for the declining OC concentration. However, even though OC gets slightly diluted the concentration does not decrease much from station PR-6 to PR-12, being close to a mean concentration of 2.9 ± 0.4 ng/L **(Tables 1 and S1) (Figures 1b, S1 and 4)**.

At 50% of the station OC was found in higher concentration in bottom water. It is possible that OC sinks towards the bottom due to its lipophilicity or is desorpt from sediment as a possible partition to other phases as was suggested by Tsui et al. [45]. The input into the environment occurs either directly (e.g. recreational activities) or indirectly via waste water. The Pearl River drains most of the Guangdong region, which has a WWTP connectivity of 51%, exposing the Pearl River Estuary (PRE) to a large amount of untreated waste water [7]. A few studies have been carried out on the occurrence of OC in the PRE so far. However, all studies were focused on the sediment phase or the biota and not the water phase. OC has been detected in fish, mussels and squid in the estuary [3,14]. OC was found up to >1000 ng/g in sediment of the PRE by Tsui et al. and Pintado-Herrera et al. [45,48]. Another study by Peng et al. detected up to 917 ng/g of OC as a major UV-filter in sediment of the estuary, which were in agreement with other studies carried out in Japan, Hong Kong, France and Germany [26]. Huang et al. reported a mean concentration of 16.0 ± 7.5 ng/g in the sediments of the estuary and a decrease in concentration towards the South China Sea [49]. Additionally, they detected hotspots of OC near the eastern side of the upper Pearl River, which they connected to a high sewage discharge of the large cities on the eastern side of the estuary, this could not be confirmed for the water phase in this study. Only the decrease from the city center of Guangzhou towards the South China Sea could be confirmed **(Figure S1)**.

The Pearl River drains into the South China Sea, which has complex water dynamic. OC was detected in 76% of the surface water samples, mostly at stations on the eastern side of the estuary. The median concentration is 4.0 ng/L, with the maximum being 17.8 ± 0.4 ng/L at station SCS-58, near Dongsha Island. OC has not been measured in the open South China Sea before. The median concentration is slightly higher than in Pearl River (median: 3.2 ng/L), which might be caused by the different sampling

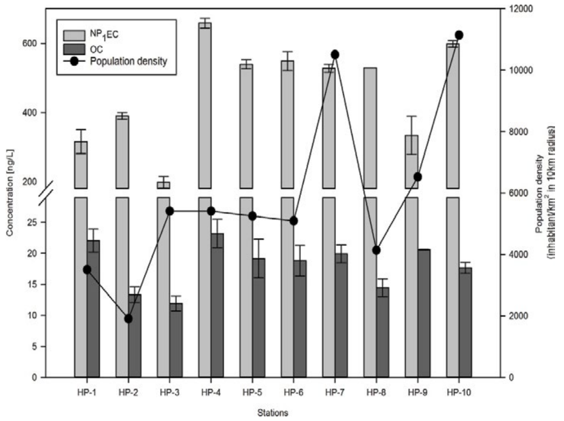

Figure 2 Measured concentration [ng/L] of OC and NP_1EC in the Huangpu River in comparison with the population density surrounding the sampling stations in a 10 km radius. Data regarding population density acquired from Wu et al. (2017) [42].

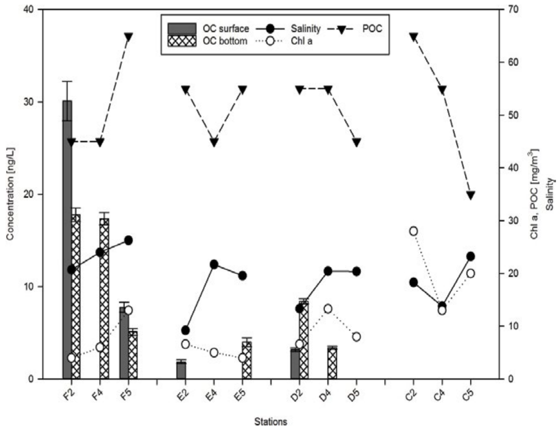

Figure 3 Measured surface (2 m) and bottom (15-60 m) water concentration [ng/L] of OC in the East China Sea collected during a cruise in July 2016.

seasons (March: Wet season, July: Dry season). However, an ANOVA analysis shows that there is no statistical significant difference (p=0.7) between the occurrence of OC in the Pearl River and the South China Sea. At all stations the salinity was slightly above 34, which is an indicator for oceanic conditions. However, a cyclonic eddy exists near Dongsha Island. He et al. reported that when the eastward Pearl River plume is transported towards the Taiwan Bank, it encounters the northern edge of the cyclonic eddy [50]. Its anticlockwise rotation is able to entrain the Pearl River Plume and to force some of the plume water southwestward, which might explain the occurrence and the slightly raised concentrations of OC in this area. The occurrence of OC correlates positively with the salinity (r_S=0.1, p=0.5) as in the East China Sea. Again, this might be an indication that OC can be transported over a longer distance and is not easily degradable in the marine environment. An additional source could be the input of OC through the atmosphere. As has been reported by Ao et al., OC can be found in high amounts in indoor dusts [44]. If OC can be transported through the atmosphere needs to be examined. In agreement to the East China Sea, a slightly negative correlation between POC (r_{POC}=-0.4, p=0.01) and OC could be seen. More data is needed to determine the significance of POC as a sink for OC in the marine environment **(Tables 1 and S1) (Figure 5)**.

In comparison to other seas the measured median (4.0 ng/L) concentration is much lower. OC has been detected at higher concentrations in surface water near beaches in Norway (n.d.-7301 ng/L), Gran Canaria (median: 109.7 ng/L), South Carolina (227 ng/L) and slightly higher in the Baltic Sea (median: 7.9 ng/L) [25,51-53]. However, these measurements were taken much closer to the coast and near beaches with high recreational activities. Furthermore, the mean concentration in the South China Sea is only half of that measured in the East China Sea within this study. A reason could be the different geological surroundings as the waters of the East China Sea are restricted by land, whereas the South China Sea is less restricted and is more openly connected to other seas. Whereas, statistical analysis shows that there is no statistical significant difference (p=0.3, ANOVA) between the East and South China Sea. Yet, it might be of great scientific interest and important for environmental studies to also analyze the sediments of both seas, in order to gain even more information about the behavior of OC and its distribution in the marine environment **(Table 1)**.

Occurrence and distribution of NP_1EC in aquatic environment

NP_1EC is an intermediate in the degradation process from nonylphenol ethoxylate to nonylphenol and is mostly formed during the waste water treatment process (Montgomery-Brown et al., 2008). In the Huangpu River, NP_1EC was detected in all samples with a concentration range from 198.1 ± 16.3 ng/L to 658.3 ± 13.9 ng/L. A negative attenuation coefficient (k=-0.01) was calculated, confirming the increase in concentration along the river towards the Changjiang River. Furthermore, a positive correlation (r=0.4, p=0.3) was found between the occurrence of NP_1EC and the population density surrounding the sampling stations (data acquired from Wu et al.) [42]. As NP_1EC is formed under aerobic conditions in WWTP, it enters the environment via waste water effluents [19]. It is relatively stable and more hydrophilic than nonylphenol, which explains its occurrence in the water phase. The positive correlation indicates a higher input rate of NP_1EC in the densely populated urban area, resulting from a possible higher input of waste water from cosmetic industry and urban area surrounding the Changjiang River, as its parent compound is used in industrial laundry detergents **(Figure 2) (Tables 1 and S1)** [18,42].

In the East China Sea, NP_1EC was detected at all surface water

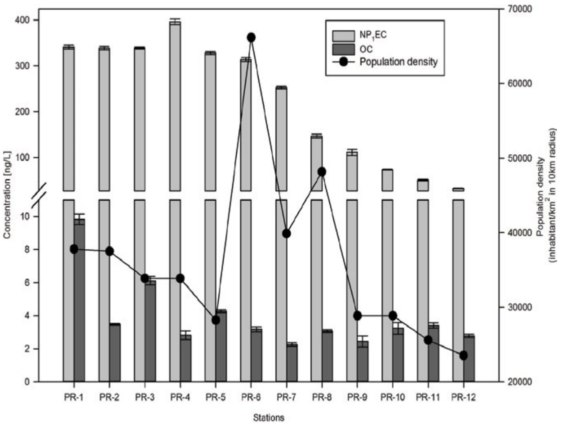

Figure 4 Measured surface (0.5-2 m) water concentration [ng/L] of OC and NP_1EC in the Pearl River in comparison with the population density in a 10 km radius of the sampling stations (NSDG, 2017).

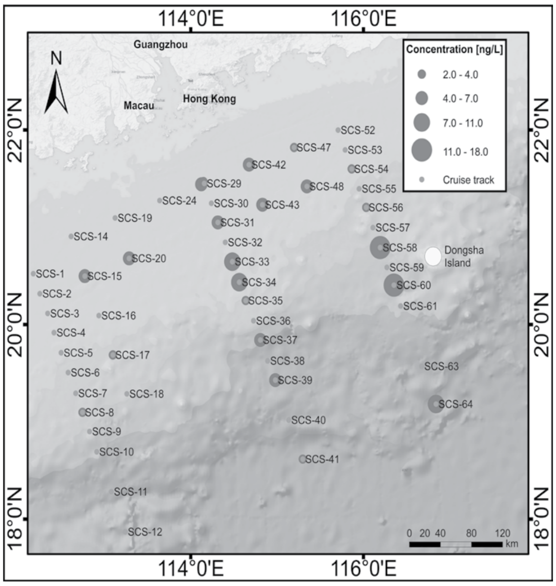

Figure 5 Measured surface water concentration [ng/L] of OC in the South China Sea in March 2015.

stations and in 75% of the bottom water samples. The measured concentrations (n.d. - 18.2 ng/L) are much lower than in the Huangpu River (p<0.001, ANOVA). Additionally, slightly higher concentrations were detected at the stations closest to the coastline (C2, D2, E2, F2) than at the off-shore stations (C5, D5, E5, F5) and in the surface water compared to the bottom water. The inverse correlations with salinity (r_s=-0.3, p=0.3), POC (r_{POC}=-0.3, p=0.3) and Chl a ($r_{Chl\ a}$=-0.4, p=0.2) reconfirm the assumption that dilution is a major key player in the transport process. Furthermore, NP$_1$EC can be degraded in 7-14 days under experimental conditions to nonylphenol, which is more toxic and can dominantly be detected in sediment [19]. The possible degradation to nonylphenol and consequentially the sorption to particular matter might explain the low bottom water concentrations. So far, NP$_1$EC was not detected in marine waters prior to this study **(Figures 6 and S2) (Tables 1 and S1)**.

In the Pearl River, lower concentrations than in the Huangpu River but higher than in the East China Sea of NP$_1$EC were found. In difference to OC, a positive correlation (r=0.4, p=0.2) between NP$_1$EC and the population density of the area surrounding the sampling stations was observed as in Shanghai (NSDG, 2017). NP$_1$EC was not detected in the South China Sea during this study. However, in the Pearl River it was identified in all surface and bottom water samples. Surface and bottom water concentration are similar to each other and they display the same occurrence pattern. The concentrations increase from the city center (PR-1) towards PR-4, at which station the highest concentration was detected. The increase might be due to additional diffuse source e.g. waste water. From the maximum concentration (396.1 ± 6.1 ng/L) at PR-4 it then decreases towards the open South China Sea (PR-12, 32.5 ± 0.5 ng/L). Both, the surface and bottom water concentration display an inverse correlation with the salinity (r_s=-0.9, p<0.01, r_s=-0.9, p<0.01, respectively). This negative correlation is an indicator that the dilution effect is responsible for the decrease in concentration. Additionally, the attenuation coefficient (k=0.021) also provides proof of the transport of NP$_1$EC along the river, with dilution taking place. As in the East China Sea, the NP$_1$EC concentrations display an inverse correlation with POC (r_{POC}=-0.9, p=0.03) and Chl a ($r_{Chl\ a}$=-0.9, p=0.03). A possible explanation might be that NP$_1$EC is degraded to nonylphenol, which then binds to particles and sinks out of the water column **(Tables 1 and S1) (Figures 4 and 7)**.

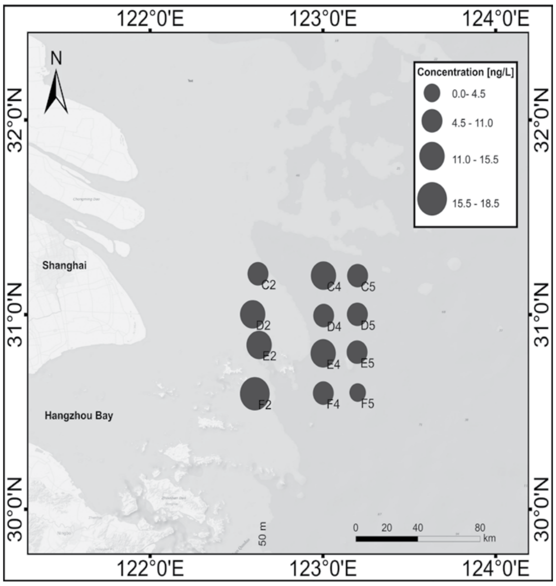

Figure 6 Measured surface (2 m) concentration [ng/L] of NP$_1$EC in the East China Sea in July 2016.

Nonylphenol is a largely analyzed endocrine disruptor in the Pearl River region. As for NP$_1$EC, high amounts of nonylphenol were measured in sediments of the northern part (1906 ng/g) of the river and lower concentrations near Macau (26 ng/g) [48]. In 2011 Xu et al. measured a mean concentration of 45 ng/L of the degradation product nonylphenol in the PRE, which is significantly lower than the mean concentration of NP$_1$EC (226.9 ± 133.9 ng/L) reported during this study [54]. The large difference in reported concentrations of nonylphenol is more likely related to its particle affinity as it can be more often found in the sediment phase due to a higher logK$_{OW}$-value (5.7). In comparison to literature data the median concentration of the Pearl River (283.1 ng/L) is in similar range as the median value of 122 European rivers (233 ng/L) [24]. However, both mean concentrations of the Huangpu and Pearl River are lower than the mean concentration (661 ng/L) measured in the Seine Estuary in France **(Table 1)** [55].

Mass load and risk assessment

The mass load was calculated by multiplying the mean river concentration with the annual discharge volume of the rivers. When comparing the Huangpu and Pearl River, it becomes apparent that in the Huangpu River higher concentrations of both endocrine disruptors were found (mean concentration: 482.0 ng/L, 230.8 ng/L, respectively). In spite of a higher mean total concentration the total mass load in the Huangpu River is much lower than in the Pearl River (total mass load: 4.8 t/a, 77.6 t/a, respectively). This existing difference is due to the large difference in the annual water discharge volumes of the rivers

Table 2 Calculated risk quotient (RQ) of octocrylene (OC) and nonylphenoxyacetic acid (NP$_1$EC) in freshwater systems: Huangpu River and Pearl River and in marine systems: East and South China Sea [57-59].

Compound	PNEC$_{(freshwater)}$	PNEC$_{(marine)}$	Huangpu River	Pearl River	East China Sea	South China Sea
	[µg/L]	[µg/L]	RQ	RQ	RQ	RQ
OC	0.5[1]	2.3[2]	0.04	0.02	0.01	0.007
NP$_1$EC	2.0[3]	2.0[3]	0.3	0.2	0.01	-

RQ<0.1 low risk, 0.1 ≤ RQ ≤ 1 medium risk, 1 ≤ RQ high risk.

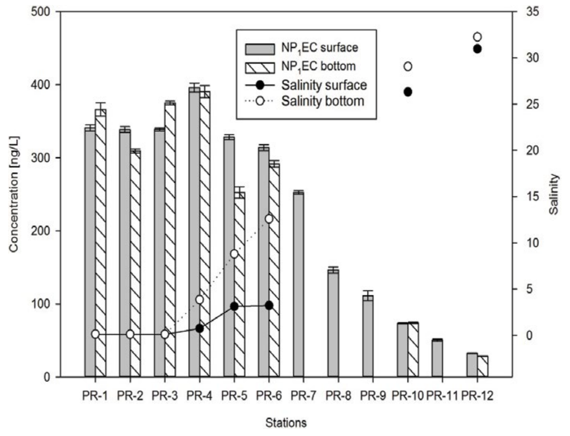

Figure 7 Measured concentration [ng/L] of NP$_1$EC in surface (0.5-2 m) and bottom (6-16 m) water samples of the Pearl River, together with salinity.

(Huangpu River: 10 billion m^3/a, Lee, Pearl River: 336 billion m^3/a, Zhang et al.) [56,57]. The calculated mass load for OC is similar to the estimated emission rate of Zhu et al. [7]. They estimated an OC emission rate of 0.07 - 0.2 t of OC for Shanghai. Our study resulted in a mass load of 0.2 t/a of OC in the Huangpu River, which is within the range of the estimation. The OC mass load (1.3 t/a) of the Pearl River also fits with previous estimates in the range of 0.5-6.6 t for Guangdong [7]. Concentrations and mass load reported in this study mirror the prevailing conditions during the sampling period and are most likely typical for the freshwater discharge season **(Table 1)**.

Furthermore, a risk assessment was carried out to better understand the potential effects of the occurring concentrations. For both endocrine disruptors a risk quotient (RQ) was calculated for each system. So far the measured concentrations of OC are of low risk (RQ<0.1) to aquatic organisms in the evaluated four water systems. For NP$_1$EC no RQ was calculated for the South China Sea as it was not found and only a low risk was calculated for the East China Sea. Yet, it does pose a medium risk to aquatic organisms in both rivers as it was detected in high ng/L range **(Tables 1 and 2)**.

Conclusion

The results obtained in this study validate, that both endocrine disrupting compounds (OC, NP$_1$EC) occur in the Huangpu and Pearl River at concentrations which are comparable to other studies. The occurrence of both compounds in the East China Sea and the occurrence of OC in the South China Sea open up questions about a possible long half-life time and a possible stability in the marine environment. In case of OC, which was mostly found in sediment so far, this study shows that water phase is also of importance. Future studies should focus on the partitioning of OC between the water and sediment phase and a possible re-suspension from the sediment phase. Furthermore, in terms of OC studies are needed to determine, if dust events could be an additional source of these compounds in the open marine environment.

Supporting Information

Supplementary data associated with this article can be found in the online version at: http://www.imedpub.com/supplementary-file/IPJAPT-1s.pdf

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Table A1: References of exemplary studies (shown in fig. 1.3) of pharmaceuticals and personal care products carried out around the world. Listed are only the three most dominant compounds in the environment of each study.

Reference	Area	Compound	Concentration [ng/L]
This study	Baltic Sea	OC	3.5-30.8
		SA	4.8-14.3
		PBSA	n.d.-10.3
	East China Sea	OC	n.d.-30.1
		NP_1EC	4.1-18.2
		SMX	<LOD-4.4
	South China Sea	OC	n.d.-17.8
	Pearl River (China)	NP_1EC	32.5-396.1
		TMP	1.2-15.2
		SMX	0.9-13.9
	Huangpu River (China)	NP_1EC	198.1-658.3
		OC	11.9-23.2
		SDZ	5.3-14.5
	Mühlenflließ (Germany)	PBSA	3.3-836.3
		DCF	1.3-468.5
		SMX	0.6-47.5
Bayen et al. (2013)	Singapore	DCF	3.4
Benotti and Brownawell (2007)	Jamaica Bay (NY, USA)	TMP	n.d.-125
		SMX	n.d.-80.8
Bratkovics et al. (2015)	South Carolina Coast (USA)	OC	n.d.-3730
		BP-3	n.d.-2203
		EHMC	n.d.-438
Bu et al. (2013)	Pearl River (China)	SMX	<LOD-510
		TMP	<LOD-150
		DCF	n.d.-150
	Yangtze Estuary (China)	DCF	n.d.-843
		SMX	4.2-765
Fang et al. (2012)	Danshui Estuary (Taiwan)	DCF	<2.5-53.6
		KPF	<1.7-5.45

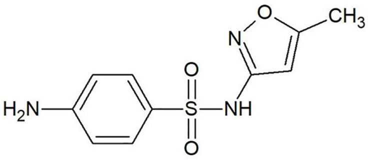
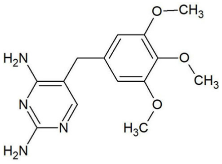
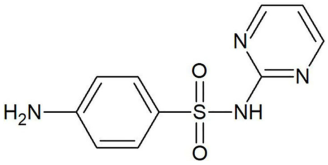
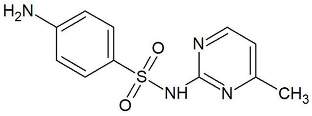
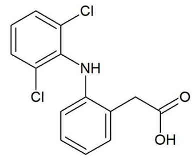
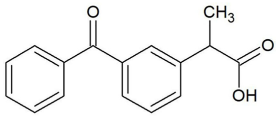
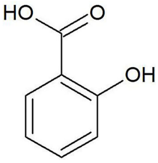
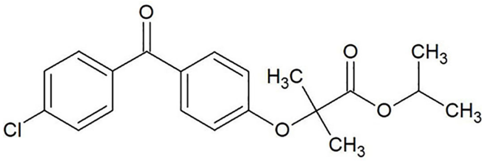
Reference	Area	Compound	Concentration [ng/L]
Liu and Wong (2013)	near Hong Kong (China)	TMP	<LOD-21.8
	Vicoria Harbor (China)	SMX, SDZ	<LOQ
	Pearl River (China)	SDZ	3-336
		SMX	2-193
	Beibu Gulf	SMX	n.d.-10.4
		TMP	n.d.-3.77
		SDZ	n.d.-3.41
	Bo Sea Bay (China)	SMX	n.d.-140
		TMP	n.d.-120
		SDZ	n.d.-41
	Pearl River (China)	SA	24.2-3239
		DCF	8.3-114
	Mekong Delta (Vietnam)	SMX	20-33
		TMP	5 -20
Nödler et al. (2014)	Baltic Sea (Germany)	SMX	n.d.-42
		DCF	n.d.-9.2
	Aegean Sea & Dardanelles (Greece & Turkey)	SMX DCF	n.d.-11 n.d.-9.7
	Northern Adriatic Sea (Italy)	SMX	n.d.-4.1
	San Fransisco Bay (USA)	SMX	<61
	Balearic Sea (Spain)	SMX, DCF	n.d.
	Mediteranean (Israel)	DCF	n.d.-6.1
Orlikowska et al. (2015)	Black Sea	PBSA	n.d.-2.3
	Baltic Sea	PBSA	n.d.-3.4
	Mediteranean Sea	PBSA	n.d.
Rodil et al. (2012)	Galicia (Spain)	BP4	<LOD-603
		PBSA	<LOD-73
		4-MBC	<LOD-16
Sánchez-Quiles and Tovar-Sánchez (2015)	Norwegian coastal zone	OC	n.d.-7301
		4-MBC	n.d.-798.7
		BP-3	n.d.-439.9
	Ria da Coruña (Spain)	OC, PBSA, SA, DCF	< LOD
	Okinawa Island (Japan)	BP-3	n.d.-1258
		EHMC	n.d.-143
		OC	n.d.-798.7
	Genua (Italy)	BP-3	<LOD-118
		EHMC	<LOD-86

Reference	Area	Compound	Concentration [ng/L]
	Bay of Cadiz (Spain)	OC	<100
		BP-3	<70
Shanmugam et al. (2014)	Indian rivers	DCF	n.d.-103
		KPF	n.d.-100
Sousa et al. (2018)	Arade river (Portugal)	DCF	4-31
	Umgeni (South Africa)	DCF	n.d.-10200
		KPF	n.d.-9220
		SA	n.d.-6600
	Busan beaches (South Korea)	PCP (BP-3, 4-MBC, EHMC)	48.5-739
Tsui et al. (2014)	Hong Kong (China)	OC	103-6812
		EHMC	89-4043
		BP-3	39-5429
	Tokyo (Japan)	OC	87-108
		BP-4	71-136
		BP-1	52-95
	New York (USA)	BP-4	89-574
		BP-3	23-178
		EHMC	89-150
	Los Angeles (USA)	BP-3	227-601
		OC	145-377
		EHMC	91-138
	Shantou (China)	BP-3	55-188
		OC	75-107
		EHMC	52-78
	Chaozhou (China)	OC	36-102
		EHMC	<LOD-79
		BP-3	37-49
	Bangkok (Thailand)	OC	153-205
		BP-1	127-166
		BP-3	86-116
	Arctic	EHMC	25-66
		BP-3	17-33
		OC	26-31
	Oslo (Norway)	OC	n.d.-7301
		4-MBC	n.d.-798.7
		BP-3	n.d.-439.9

Reference	Area	Compound	Concentration [ng/L]
Yang et al. (2014)	Rivers Rio de Janeiro State (Brazil)	DCF	20-60
	Vantaa River (Finnland)	DCF	10-55
		KPF	8-28
	Youngsan River (South Korea)	Pharm.	1.1-361
Zhang et al. (2013)	Bohai Sea (China)	TMP	0.1-16.6
		SMX	<LOD-8.3

Pharm.- pharmaceutical, PCP- personal care product
PPCPs- pharmaceuticals and personal care products
n.d.- not detected, LOD- limit of detection, LOQ- limit of quantification

Table A2: Chemical structures of analyzed pharmaceuticals and personal care products with their associate chemical abstract service (CAS) registry number.

Chemical structures of pharmaceuticals		
 SMX (CAS: 723-46-6)	 TMP (CAS: 738-70-5)	 SDZ (CAS: 68-35-9)
 SMZ (CAS: 127-79-7)	 DCF (CAS: 15307-86-5)	 KPF (CAS: 22071-15-4)
 SA (CAS: 69-72-7)	 FFB (CAS:49562-28-9)	

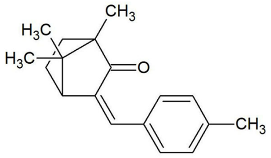
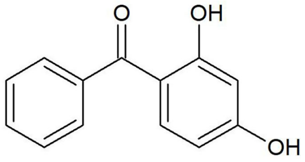
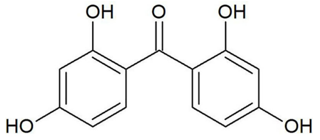
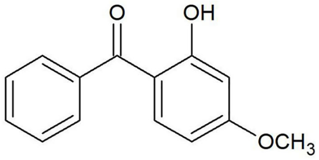
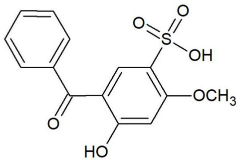
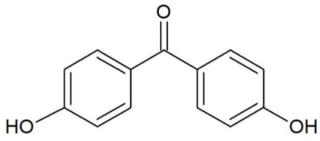
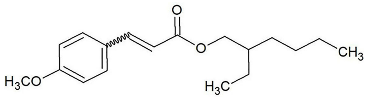
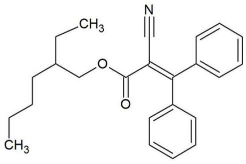
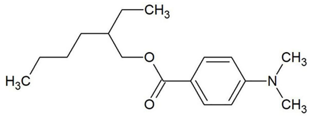
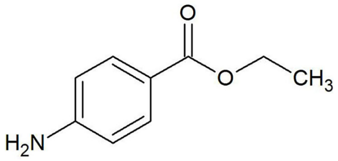
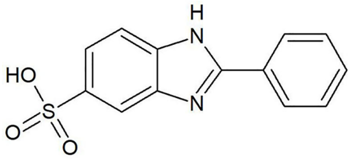
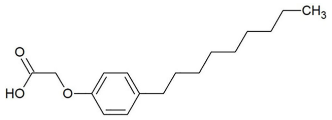
Chemical structures of personal care products		
 4-MBC (CAS: 36861-47-9)	 BP-1 (CAS: 131-56-6)	 BP-2 (CAS: 131-55-5)
 BP-3 (CAS: 131-57-7)	 BP-4 (CAS: 4065-45-6)	 4-DHB (CAS: 611-99-4)
 EHMC (CAS: 5466-77-3)	 OC (CAS: 6197-30-4)	 OD-PABA (CAS: 21245-02-3)
 Et-PABA (CAS: 94-09-7)	 PBSA (CAS: 27503-81-7)	 NP$_1$EC (CAS: 3115-49-9)

Table A3: Characterization of the analyzed personal care products, their ecological concern and potential for sorption to soils. Based on the octanol/water partition coefficient logK$_{OW}$ compounds are divided into classes of sorption potential: logK$_{OW}$ $<$ 2.5 low sorption, 2.5 $<$ logK$_{OW}$ $<$ 4 medium sorption, logK$_{OW}$ $>$ 4 high sorption (Gothwal and Shashidhar, 2015).

Name	Commercial Name	Abbr.	Usage	logK$_{OW}$	max. Conc* [%]	Environmental concern
4-methylbenzylidene camphor	Enzacamen	4-MBC	cosmetics	4.9[1]	4	estrogenic potential[2] decreases reproduction, increases mortality rates of benthic organisms [3] potential cause coral bleaching[4] bioaccumulative in fish[5]
2,4-dihydroxybenzophenone	Benzoresorcinol, benzophenone-1	BP-1	cosmetics, plastics	3.2[6]		estrogenic portential[20] potential cause coral bleaching[4] estrogenic, androgenic and antiandrogenic activity[7]
2,2',4,4'-tetrahydroxybenzonphenone	benzophenone-2	BP-2	cosmetics	3.2[6]		estrogenic potential[2] potential cause coral bleaching[4] estrogenic, androgenic and antiandrogenic activity[7]
2-hydroxy-4-methoxy--benzophenone	Oxybenzone, benozphenone-3	BP-3	cosmetics	3.79[1]	10	coral bleaching[4] high estrogenic activity[7, 8] estrogenic, antiestrogenic and antiandrogenic activity[7] bio-accumulative[5, 6]
5-benzoyl-4-hydroxy-2--methoxybenzenesulfonic acid	Sulizobenzone, benzophenone-4	BP-4	cosmetics	0.4[1]	5[a]	estrogenic, anti-androgenic action[7] might effect reproduction in fish[7] interferes sex hormone system of fish[9]
4,4'-dihydroxybenzophenone		4-DHB	UV-stabilizer			estrogenic and antiandrogenic activity[7] metabolite of BP-3
2-ethylhexyl-4-methoxycinnamate	Octinoxat	EHMC	cosmetics	5.8[1]	10	estrogenic potential[2] potential cause coral bleaching[4]
2-ethylhexyl 2-cyano-3,3-diphenyl-2-propenoate	Octocrylene	OC	UV-filter/stabilizer in cosmetics/plastics	6.9[1]	10	bioaccumulative[10, 11, 12] estrogenic in zebrafish[13] antiestrogenic and antiandrogenic activity[7]
2-ethylhexyl-4-(dimethylamino)benzoate	Padimate-O	OD-PABA	cosmetics	6.2[1]	8	antiestrogenic and antiandrogenic activity[7]

Name	Commercial Name	Abbr.	Usage	logK$_{OW}$	max. Conc* [%]	Environmental concern
ethyl-4-eminobenzoate	Benzocaine	Et-PABA	cosmetics (PCP), anesthetic ointments			estrogenic and antiandrogenic activity[7]
2-phenylbenzimidazole-5-sulfonic acid	Ensulizol	PBSA	cosmetics	1.5[1]	8	cause toxic stress in fish[14]
nonylphenoxyacetic acid		NP$_1$EC	non-ionic surfactant (metabolite)	2.2[15]		endocrine activity[16]

* max. allowed concentration in EU and China (Sánchez-Quiles and Tovar-Sánchez, 2015), [a] only for China

[1] Rodil et al. (2009), [2] Heneweer et al. (2005), [3] Schmitt et al. (2008), [4] Danovaro et al. (2008), [5] Balmer et al. (2005), [6] Negreira et al. (2009), [7] Díaz-Cruz and Barceló (2009), [8] Díaz-Cruz et al. (2012), [9] Zucchi et al. (2011), [10] Bachelot et al. (2012), [11] Gago-Ferrero et al. (2013), [12] Langford et al. (2015), [13] Blüthgen et al. (2014), [14] Grabicova et al. (2013), [15] Pojana et al. (2007), [16] Esteban et al. (2014)

Table A4: Compound specific MS/MS-Parameter for developed method, recovery rate, limit of detection (LOD) and limit of quantification (LOQ) for analyzed pharmaceuticals (Fisch et al., 2017b).

Compound	Classification	Precursor Ion	Product Ions^a	Recovery [%]	LOD [ng/L]	LOQ [ng/L]
sulfadiazine	antibiotic	250	156, 108	85	0.6	0.7
sulfamerazine	antibiotic	264	172, 156	91	0.6	0.7
trimethoprim	antibiotic	290	230, 261	85	0.9	1.0
sulfamethoxazole	antibiotic	253	156, 92	103	0.5	0.6
sulfamethoxazole-d4	internal standard	257	96, 160	56		
salicylic acid (met.)	NSAID	137	93	82	1.0	2.0
ketoprofen	NSAID	254	209, 77	96	0.9	1.0
diclofenac	NSAID	294	250	85	0.9	1.0
		296	252			
diclofenac-d4	internal standard	300	256	83		
		298	254			
fenofibrate	lipid regulator	360	139, 111	76	1.3	1.5

NSAID - non-steroidal anti-inflammatory drug
(a) quantification ion

Scientific C/V

Work experience

since 05.2018	Post-doc, Project: Megapol, Leibniz Institute for Baltic Sea Research Warnemünde
06 - 09.2016	Research stay at Shanghai Jiao Tong University and Guangzhou Marine Geological Survey, Scholarship from German Academic Exchange Service
10.2013 - 04.2018	PhD and master student, Leibniz Institute for Baltic Sea Research Warnemünde, working group: organic trace substances, Prof. Schulz-Bull,
04.2013 - 09.2014	Research assistant, Leibniz Institute for Baltic Sea Research Warnemünde, working group: organic trace substances, Prof. Schulz-Bull
10.2013 - 04.2014	Master student, Leibniz Institute for Baltic Sea Research Warnemünde, working group: organic trace substances, Prof. Schulz-Bull
2008 - 2012	Free University of Berlin, working group of Prof. Rühl, Bachelor thesis

Education

11.2014 - 04.2018	PhD at the Leibniz Institute for Baltic Sea Research Warnemünde, Department: Marine Chemistry, working group: Prof. Schulz-Bull
2012 - 2014	Master of Science (chemistry), University of Rostock
2008 - 2012	Bachelor of Science (chemistry), Free University of Berlin
2004 - 2005	High school year, Octorara High School, Chester County, Pennsylvania, USA
2000 - 2008	High school student at the Marie-Curie-Gymnasium, Ludwigsfelde, Germany