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Pharmaceutical pollution of aquatic environment: an emerging and enormous challenge

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Abstract: The global use of pharmaceuticals is on the systematic rise and leads to contamination of surface waters with xenobiotic compounds with a wide range of bioactivity. Waters that receive urban and medical effluents are particularly threatened. The presence of pharmaceuticals in these ecosystems can lead to unpredictable ecological impacts and responses, and may also have an impact on human health. At the same time the identification and quantification of these chemicals, to a large extent remains a subject to scientific investigation than part of a thorough monitoring programme. Their biological effects on aquatic organisms are mainly recognized experimentally and often using concentrations far exceeding environmentally relevant levels. This review paper defines the main sources of pharmaceuticals in the aquatic environment, discusses the fate of these compounds and summarizes the current state-of-the-art of pharmaceutical monitoring in Polish surface waters.

Key words: pharmaceutical pollution, surface waters, effluents, environmental fate

Introduction

Water pollution is a broad environmental issue related to the discharge of various chemical compounds and the dispersion of pathogens from a vast number of human activities. Not only is it responsible for a decrease in the ecological function of aquatic habitats but it can also be a leading cause of disease and mortality in some regions (WHO/UNICEF 2015). Over the years, numerous studies have assessed the contamination of surface waters with various biological agents such as coliforms (Koczura et al. 2015), viruses (Huang et al. 2016), protozoan parasites (Słodkowicz-Kowalska et al. 2015), and chemicals, including fertilizers (O'Neil et al. 2012), toxic metals (Rzymski et al. 2014), arsenic (Yan et al. 2016), pesticides (Rzymski et al. 2013), perchlorate (Kannan et al. 2009), polycyclic aromatic hydrocarbons and polychlorinated biphenyls (Wolska et al. 2014). Recent decades have, however, given rise to a novel issue, namely, the emission of pharmaceuticals and their potential environmental resistance. This so called "drug pollution" or "pharmaceutical pollution" may have distinctive consequences on aquatic biota but estimation of these effects is yet to be fully elucidated (Pal et al. 2014; Obimakinde et al. 2017).

Under no circumstances should pharmaceutical pollution be ignored or regarded as an atypical environmental issue. With the development of medicine, the global use of various pharmaceutical drugs has steadily increased. In 2015, revenue from the worldwide pharmaceutical market reached 1072 billion $ with the greatest share in North America (Statista 2016). A great variety of medications are currently available on the market and include, among many, analgesics (painkillers), antipyretics (fever reducers), antibiotics, antiseptics, hormone replacements, contraceptives, statins, mood stabilizers, antidepressants, and cytostatics. The bioactive compounds of these pharmaceuticals may have a natural origin (derived from microbes, plants or animals), or they may be solely chemically synthesized or derived from genetic engineering. All in all, over 4000 pharmaceuticals are currently in use for medical and veterinary purposes, and in agriculture as part of growth promotion of livestock (Boxall et al. 2012). As forecasted, by 2020 the global use of medicines is estimated to reach 4.5 trillion doses worth a total of 1.4 trillion $ (IMS 2015).

Such an enormous and global use of medication, their varying types and physicochemical properties significantly contribute to the release of active pharmaceu-

tical ingredients (APIs) and their metabolites to the environment, including surface waters. It is important to note that this release is rather unavoidable considering the current and forecasted use of pharmaceutical drugs. The European Union recognizes pharmaceutical residues in the environment as "priority substances", similarly to other micropollutants (EU 2013). Many studies have reported the occurrence of APIs derived from e.g. antibiotics, beta-blockers, anti-depressants, contraceptives, antiepileptic and anti-inflammatory drugs or antibiotics in surface and groundwater in the ppt and ppb concentration range (Herberer 2002; Cardoso et al. 2014; Barra Caracciolo et al. 2015). It is predicted that pharmaceutical pollution of water resources will be a key issue in the future protection of the environment as well as health of humans, unwittingly exposed mostly via contaminated water and food. A great number of chemical compounds used for the production of medications and various processes of transformation which they may undergo, complicate the ability to comprehensively identify APIs and evaluate the total risks arising from their occurrence in the environment. These challenges are yet to be faced.

Sources of pharmaceuticals in the environment

Five general sources of pharmaceuticals in the environment are established:

- raw and treated effluents from manufacturing sites;
- hospital waste;
- excretion by livestock treated with antibiotics, growth promoting agents and other formulations;
- runoff from agricultural fields fertilized with treated sewage sludge;
- excretion by humans and flushing of old and unwanted prescriptions.

Recent evidence has revealed high concentrations of a large number of pharmaceuticals in effluents from pharmaceutical factories and in receiving aquatic ecosystems (Cardoso et al. 2014). Wastewaters generated at such sites may contain APIs in concentrations ranging from several, hundreds to even thousands mg dm^{-3} (Qiting and Xiheng 1988; Larsson et al. 2007; Sim et al. 2011). So far, over 130 different pharmaceuticals have been detected in effluents generated from pharmacological factories (Cardoso et al. 2014). A considerable number of these bioactive compounds survive classical treatment processes so concentrations in receiving freshwaters vary from ng dm^{-3} to µg dm^{-3} (Cui et al. 2006). For example, concentrations of the antibiotic oxytetracyclin in the River Xiao (China) at discharge point and 20 km downstream reached 641 and 250 µg dm^{-3}, respectively (Li et al. 2008). Insufficiently treated wastewaters from pharmaceutical production in one of the world's largest centres for bulk drug production located in India resulted in very high concentrations of ciprofloxacin (up to 6.5 mg dm^{-3}), cetirizine (up to 1.2 mg dm^{-3}), norfloxacin (up to 0.52 mg dm^{-3}), and enoxacin (up to 0.16 mg dm^{-3}) in freshwater lakes (Fick et al. 2009). In Germany, dimethylaminophenazone, an analgesic drug, was detected in groundwater from areas of former drug manufacturing at a mean level of 0.9 µg dm^{-3} despite being banned in 1978 by German authorities due to adverse health effects and its potential to form carcinogenic metabolites (Reddersen et al. 2002). It should be stressed that in Europe effluents from pharmacological manufacturing were generally estimated to account for just 2% of the total pharmaceuticals found in the environment (BIO Intelligence Service 2013) indicating their effective management by selective application of available treatment technologies (Caldwell et al. 2016).

The other route of release of pharmaceuticals to the environment, which is their use in animal breeding and subsequent excretion by livestock, has been less studied but can by no means be neglected due to an extensive list of compounds registered as veterinary drugs. Moreover, some of the medications used currently in the livestock industry had been previously approved for humans but banned due to adverse effects. One should note that as long as pharmaceuticals excreted by humans mostly reach wastewater plants and their concentrations can be decreased to some extent during treatment processes, veterinary drugs are more likely to reach the aquatic environment directly (Khetan and Collins 2009). The manure which is a popular crop fertilizer may contain high concentrations of APIs (e.g. veterinary antimicrobials). Moreover, in many regions use of treated sewage sludge (which may contain pharmaceuticals and transformation products) is approved as a fertilizer in agriculture (Jelic et al. 2011). This leads to their subsequent presence in surface runoff and groundwater, and eventual transport to water bodies and streams near intensive cattle feeding operations (Sura et al. 2015; Łukaszewicz et al. 2016).

Finally, the administration of medicines to humans results in their excretion, primarily with urine, in unaltered form or as an active metabolite. There are two phases of biotransformation of APIs in humans. The first leads to the introduction of a functional group such as hydroxyl, carboxyl, amine or sulfhydryl and increase hydrophilicity. The second phase involves conjugation with polar molecules such as glucuronic acid, acetate esters, carboximides or sulfate. These metabolites are eliminated by renal excretion (Kalgutkar et al. 2002). In fact, administration of a single drug can lead to excretion of its different forms. For example, only 15% of ibuprofen is excreted unaltered or conjugated with

glucuronide, the rest is excreted as carboxy-hydratropic acid, hydroxy-ibuprofen, carboxy-ibuprofen and their respective conjugates (Ternes et al. 2004). The amount of excretion depends on the rate of metabolism which varies between pharmaceuticals but usually falls within the range of 30–70% of an orally ingested dose (Bound and Voulvoulis 2005). For externally applied ointments or gels, washing off with water (e.g. during a bath) may occur. It has been widely reported that domestic sewage contains high concentrations of APIs and that in many cases, they are not effectively removed by wastewater treatment plants (Herberer 2002; Cardoso et al. 2014; Barra Caracciolo et al. 2015). Even greater pharmaceutical concentrations were noted in wastewater generated by hospitals advocating the consideration of specific treatments for such effluents before being discharged into the public sewage system (Mendoza et al. 2015). All in all, insufficient removal of APIs at wastewater treatment plants eventually leads to their discharge into the aquatic environment, mostly rivers and streams which serve as receivers for treated wastewater.

Fate of pharmaceuticals in the freshwater environment

There is no universal fate of APIs released to the aquatic environment (Fig. 1). After being excreted with wastewater they may undergo transformation at wastewater treatment plants. At this stage, transformation of some pharmaceuticals may result in compounds exhibiting greater toxicity and displaying increased persistence (Celiz et al. 2009). Furthermore, the concentrations of transformation products in water may be even higher than the parent compound as proven for carbamazepine, diclofenac and atorvastin (Langford and Thomas 2011). The scenario under which the concentrations of the parent compound are below detection limits but its transformation products are frequently present also needs to be taken into account (Jakimska et al. 2014).

The elimination of APIs and its dynamics in the aquatic environment depend on a number of key factors. The most important are:

- inherent physicochemical properties of the pharmaceutical;
- (sun) light availability;
- temperature;
- pH;
- oxygen availability;
- microbial communities.

The main elimination processes of APIs in the aquatic environment include photodegradation and biodegradation (Fig. 1). The former is possible as various pharmaceuticals contain heteroatoms, aromatic rings and other structures that can absorb light (direct photolysis) or react with photogenerated transient species (indirect photolysis) (Khetan and Collins 2007). The microbial communities which are involved in pharmaceutical degradation in aquatic environments are not well known although it has been suggested that in surface waters biodegradation contributes to the elimination of APIs to a lesser extent than photodegradation (Khetan and Collins 2007). Identification of strains involved in biodegradation is of particular value as they could be potentially applied in the biological treatment of APIs in wastewater.

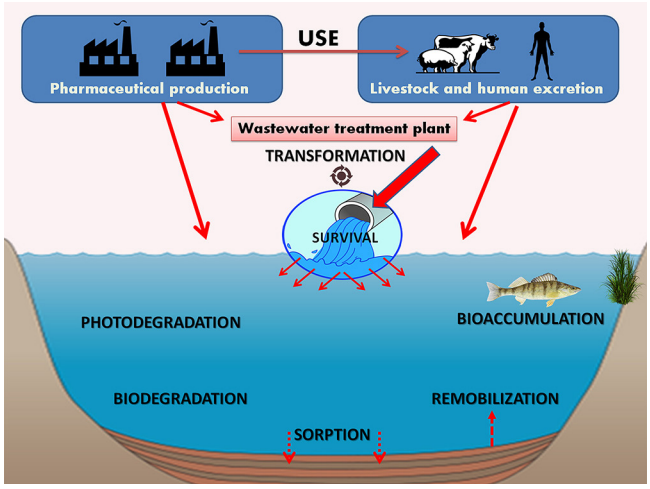

Fig. 1. Main sources and fate of pharmaceuticals in the aquatic environment

The other route for the removal of pharmaceuticals from water is their sorption to sediments – the process depends on pharmaceutical and sediment type (Scheytt et al. 2005). A recent study on five pharmaceuticals reported that their sorption to natural sediments decreases in the following order bendroflumethiazide > oxazepam > carbamazepine > diclofenac > furosemide (Svahn and Björklund 2015). Some of the initially sorbed APIs may potentially undergo desorption, although the exact conditions controlling the re-mobilization of pharmaceuticals in different types of aquatic environment are not fully elucidated (Martínez-Hernández et al. 2015).

The persistence of pharmaceuticals has not yet been completely ascertained (Bu et al. 2016). The United Nations Environmental Programme (UNEP) sets half-life at 60 days to define a chemical as persistent in the aquatic environment. It is obvious that pharmaceutical persistence is a combination of the inherited physicochemical properties of the compound and various environmental conditions. Experimental and in-field studies on the persistence of APIs yield varying and often contradictory results. For example, half-life for carbamazepine during laboratory and in-field research has been reported to vary from 3.5 to 233 days (Yamamoto et al. 2009) and from 63 to 1200 days, respectively (Tixer et al. 2003, Zou

et al. 2015). All studies on diclofenac reported half-life below the threshold of 60 days (Bu et al. 2016) but for ibuprofen half-life in experimental studies was in the range of 19–413 days depending on applied conditions (Yamamoto et al. 2009). It should be noted that pharmaceuticals can be continuously released to aquatic environments from wastewater treatment plants and thus their loading levels may exceed degradation rates, even if they are not very high. Therefore, pharmaceuticals are generally considered as a group of pseudo-persistent contaminants (Daughton et al. 2003).

The presence of APIs in surface waters leads to exposures of aquatic biota. Their effects have been studied predominantly for fish and include alterations in reproductive behaviour, aggression, boldness, activity, sociality and feeding rate (Brodin et al. 2014). The release of antibiotics triggers the development of antibiotic resistance genes and promotes an increase in antibiotic-resistant bacteria not only in hospital wastewaters and animal production wastewaters, but also in domestic wastewater, surface water and groundwater (Zhang et al. 2009).

Some APIs may also bioaccumulate and bioconcentrate in various aquatic organisms (Brodin et al. 2014). For example, the popular non-steroidal anti-inflammatory drugs, diclofenac, naproxen and ibuprofen, were all shown to accumulate in fish (Lahti et al. 2011). The concentration of ibuprofen determined in the fish plasma and bile samples was 100 to 1000-fold higher than in corresponding water samples (Jeffries et al. 2015). Some antibiotics, particularly quinolones, can bioaccumulate at relatively high levels in molluscs (Li et al. 2012). Anti-depressants were also found to bioaccumulate in periphyton, snails (Du et al. 2015), benthic invertebrates (Grabicova et al. 2015), bivalves (Bringolf et al. 2010) and the muscles of fish species used for human consumption (Brooks et al. 2005). It should be noted that some APIs may easily be transferred through the trophic route, although their bioaccumulation in fish may be low due to efficient liver metabolism. Such observations have, for instance been made for propranolol which is a widely used beta-blocker (Ding et al. 2015) and the macrolide antibiotic roxithromycin (Liu et al. 2014). The body of knowledge on accumulation of pharmaceuticals in aquatic biota has extensively increased over the years, yet there remains a need to fully elucidate all transfer routes, estimate environmental and human risks, and screen the content of APIs in waterborne foodstuffs (Puckowski et al. 2016).

The state-of-art for pharmaceutical pollution of water resources in Poland

The monitoring of aquatic pollution with pharmaceutical bioactive components and their metabolites is not regulated in Poland, neither is their occurrence in raw or treated sewage and drinking water. A number of APIs have been detected in the influents and effluents of wastewater treatment plants with the greatest survival rate displayed by carbamazepine (concentrations up to 5128 ng dm^{-3}), diclofenac (up to 5401 ng dm^{-3}), ifosfamide (up to 28 ng dm^{-3}), furosemide (up to 1879 ng dm^{-3}), hydrochlorothiazide (up to 4314 ng dm^{-3}), nafronyl (up to 14 ng dm^{-3}), ramipril (up to 90 ng dm^{-3}), erythromycin (up to 98 ng dm^{-3}), cyclophosphamide (up to 24 ng dm^{-3}), ranitidine (up to 982 ng dm^{-3}), and atenolol (up to 169 ng dm^{-3}) (Kot-Wasik et al. 2016). Wastewaters in Poland were also reported to contain significant concentrations of ibuprofen (up to 74,000 ng dm^{-3}) and naproxen (up to 117,000 ng dm^{-3}) which reflects the popularity of these non-steroidal anti-inflammatory drugs in Poland (Kotowska et al. 2014). All in all, these findings unsurprisingly indicate that treated wastewater is an important route for the introduction of various xenobiotic pharmaceuticals to surface and groundwater. A recent study reported the occurrence of ketoprofen (up to 46 ng ng dm^{-3}), paracetamol (up to 83 ng ng dm^{-3}) and naproxen (up to 21 ng ng dm^{-3}) in groundwater in the vicinity of Gdańsk (Caban et al. 2015). The general status of knowledge on the concentrations of various pharmaceuticals in Polish surface waters is still scarce. In recent years several investigations on both freshwaters (predominantly rivers as receivers of treated sewage) and drinking water have been conducted. The studied compounds, reported concentrations and investigated sites are summarized in Table 1. A number of APIs derived from cardiological (Giebułtowicz et al. 2016), immunosuppressive (Giebułtowicz and Nałęcz-Jawecki 2016), bactericidal (Wagil et al. 2014), non-steroid anti-inflammatory (Migowska et al. 2012) and psychiatric drugs (Giebułtowicz and Nałęcz-Jawecki 2014) have been successfully identified. Although the determined APIs concentrations are in the ppt range, one should note that these compounds are specifically designed to be bioactive at low concentrations. The available data clearly indicate that pharmaceutical pollution is an emerging problem in Poland and that a variety of APIs, at different concentrations, are present in Polish freshwaters. This is not surprising given the fact that Poland is currently the sixth largest pharmaceutical market in Europe, worth over 34 billion PLN (approx. 8 billion EUR) in 2015 and undergoing a systematic increasing trend in recent years (IMS 2015). The greatest concentrations in Polish rivers have so far been reported for the cardiological drugs: valsartan, furosemide, telmisartan, hydrochlorothiazide, metoprolol and sotalol, and non-steroidal anti-inflammatory drugs such as naproxen and diclofenac, analgesic compounds metamizole and

Table 1. List of detected pharmaceuticals in Polish rivers and their maximum determined concentrations

Pharmaceutical group	Active pharmaceutical ingredient	Studied river	Maximum detected concentration [ng dm^{-3}]	References
Cardiovascular drugs: Calcium channel blockers	Amlodipine	Vistula	19	Giebułtowicz et al. 2016
	Diltiazem		24	
	Nifedipine		0.5	
Cardiovascular drugs: Angiotensin-converting enzyme inhibitors	Quinalapril	Vistula	155	
	Ramipril		73	
Cardiovascular drugs: Angiotensin II receptor antagonist	Losartan	Vistula	610	
	Telmisartan		1130	
	Valsartan	Vistula	5260	
		Warta	133	Kasprzyk-Hordern et al. 2007
Cardiovascular drugs: diuretics	Furosemide	Vistula	2670	Giebułtowicz et al. 2016
	Hydrochlorothiazide		1270	
Cardiovascular drugs: beta-blockers	Acebutolol	Vistula	643	Giebułtowicz et al. 2016
	Atenolol		205	
	Bisoprolol		1470	
	Labetalol		3.3	
	Propranolol		69	
	Sotalol		2120	
	Metoprolol		2190	
		Warta	155	Kasprzyk-Hordern et al. 2007
Cardiovascular drugs: antriarrhytmics	Propafenone	Vistula	87	Giebułtowicz et al. 2016
Cardiovascular drug: Lipid-regulating agents	Atorvastatin	Vistula	114	Giebułtowicz et al. 2016
	Bezafibrate	Vistula	4.5	
		Warta	8.0	
	Ciprofibrate	Vistula	60	
	Clofibric acid		130	
	Fenofibrate		0.9	
	Gemfibrozil		3.0	
Immunosuppressive drugs	Mycophenolic acid	Vistula	180	Giebułtowicz and Nałęcz-Jawecki 2016
		Utrata	130	
Non-steroidal anti-inflammatory drugs	Ketoprofen	Wierzyca	25	Migowska et al. 2012
		Warta	47	Kasprzyk-Hordern et al. 2008; Baranowska and Kowalski 2012
	Ibuprofen		76	
	Diclofenac		486	
		Oder	470	
		Vistula	140	
		Kłodnica	70	
	Naproxen	Warta	130	
		Oder	140	
		Vistula	300	
		Kłodnica	850	
		Brda	180	
	Aspirin	Oder	730	Baranowska and Kowalski 2012
		Vistula	400	
Analgesic	Paracetamol	Warta	90	
	Metamizole	Oder	900	
	Tramadol	Warta	2108	Kasprzyk-Hordern et al. 2007
	Codeine		15	
Seizure	Carbamazepine	Warta	794	
	Gabapentin		75	

Pharmaceutical group	Active pharmaceutical ingredient	Studied river	Maximum detected concentration [ng dm^{-3}]	References
Anti-depressants	Citalopram	Vistula	17.0	Giebułtowicz and Nałęcz-Jawecki 2014
		Utrata	4.0	
	Doxepin	Vistula	1.9	
	Fluoxetine	Vistula	3.2	
		Utrata	5.5	
	Mianserin	Vistula	9.0	
		Utrata	7.0	
	Mirtazepin	Vistula	5.0	
		Utrata	2.3	
	Moclobemid	Vistula	28	
		Utrata	45	
	Tianeptin	Vistula	1.8	
	Trazodon		0.9	
	Venlaflaxin	Vistula	250	
		Utrata	140	
Anthelmintic veterinary drugs	Flubendazole	Gościcina	39.2	Wagil et al. 2015a, Wagil et al. 2015b, Wagil et al. 2015c
	Fenbendazole		85.7	
	Metronidazole		136.2	
	Doramectin		1.92	
Synthetic non-steroidal estrogens	Diethylstilbestrol	Wierzyca	8	Migowska et al. 2012
Antibiotics	Ciprofloxacin	Reda	40.7	Wagil et al. 2014
		Gościcina	2745	
	Enrofloxacin	Gościcina	248.7	
	Norfloxacin	Reda	146.5	
		Gościcina	442.8	
	Sulfamethoxazole	Warta	60	Kasprzyk-Hordern et al. 2007
	Sulfapyridine		31	
	Trimethoprim		27	

tramadol, seizure drug carbamazepine and the antibiotic norfloxacin (Table 1). Moreover, some studies have assessed the presence of veterinary drugs, particularly those designed to expel parasitic worms (Wagil et al. 2015a, Wagil et al. 2015b, Wagil et al. 2015c). One study has also detected diethylstilbestrol in river waters, the non-steroidal synthetic estrogen once used as a human drug and transferred to veterinary medicine as a growth promoting agent after its carcinogenic and teratogenic activity was evidenced (Migowska et al. 2012).

At the same time the problem of pharmaceutical pollution appears to be only superficially recognized in Poland as:

- no data on API concentrations are available for Polish lakes;
- no data are available on the potential effects of API occurrence in Polish freshwaters;
- identification of APIs in freshwaters in Poland remains more a subject to scientific investigation than part of a thorough monitoring programme.

The presence and concentrations of APIs in freshwaters can be prone to various effects such as number of generated wastewaters and efficiency of wastewater treatment plants, distance from the point of treated wastewater discharge, seasonality, physicochemical properties of water, and microbial community. The exact effect of these parameters on API concentrations in Poland remains yet to be comprehensively studied. As shown, the concentration of APIs in rivers significantly decreases downstream from the point of wastewater discharge while their concentrations may vary during the year. For example, the greatest concentration of the immunosuppressive agent, mycophenolic acid, in the River Vistula was found during spring (Giebułtowicz and Nałęcz-Jawecki 2016) whereas veterinary drugs from the group of benzimidazoles, designed to treat intestinal parasites, only occurred in river samples (River Gościnna in northern Poland) collected during autumn (Wagil et al. 2015c). Considering that treated wastewater is a significant route through which APIs reach the environment, their concentrations in surface waters are likely to reflect the popularity and seasonal use of certain medications (Kot-Wasik et al. 2016). This strongly advocates monitoring studies to be conducted continuously during the year rather than during a specific season.

Table 2. List of detected pharmaceuticals in drinking water distributed in Poland and their maximum determined concentrations

Pharmaceuticals	Active pharmaceutical ingredient	Maximum detected concentration [ng dm^{-3}]	Detected locations	References
Cardiological	Acebutolol	4.0	Warsaw	Giebułtowicz et al. 2016
	Amlodipine	3.5	Warsaw	
	Atorvastatin	0.3	Warsaw	
	Bisoprolol	17.0	Warsaw	
	Clofibric acid	1.3	Warsaw	
	Diltiazem	1.4	Warsaw	
	Fenofibrate	1.1	Warsaw	
	Furosemide	29	Warsaw	
	Losartan	5.0	Warsaw	
	Metoprolol	14	Warsaw	
	Propafenone	4.0	Warsaw	
	Propranolol	7.0	Warsaw	
	Quinalapril	1.8	Warsaw	
	Sotalol	16	Warsaw	
	Telmisartan	23	Warsaw	
	Valsartan	27	Warsaw	
	Trimetazidine	4.2	Gdańsk	Kot-Wasik et al. 2016
	Nafronyl	3.8		
	Ramipril	2.8	Gdańsk Warsaw	Kot-Wasik et al. 2016; Giebułtowicz et al. 2016
	Hydrochlorothiazide	26	Gdańsk Warsaw	
	Atenolol	1.5	Gdańsk Warsaw	
Anti-depressants	Citalopram	1.5	Warsaw	Giebułtowicz and Nałęcz-Jawecki 2014
	Mianserin	0.9		
	Moclobemid	0.3		
	Venlaflaxin	1.9		
Anti-diabetic	Metformin	8.0	Gdańsk	Kot-Wasik et al. 2016
Gastric	Ranitidine	5.6		
Analgesic	Paracetamol	118.9	Gdańśk	Caban et al. 2015
Antibiotics	Erythromycin	6.0	Gdańsk	Kot-Wasik et al. 2016
	Chloramphenicol	0.9		
Seizure	Carbamazepine	6.0	Gdańsk	
Contraceptives	Levonorgestrel	46.4	Gdańśk	
Hormone replacement	Progesteron	4.8	Gdańśk	
Non-steroidal anti-inflammatory drugs	Ketoprofen	166.9	Gdańśk	
	Ibuprofen	223.6		
	Diclofenac	114.3		

To date, the presence of APIs in sediments or aquatic biota has only been assessed very sporadically in Polish waters. Metronidazol was detected up to 12.0 ng g^{-1} in river sediments and 1.5 ng g^{-1} in the muscle tissue of rainbow trout (Wagil et al. 2015a, Wagil et al. 2015b, Wagil et al. 2015c). Three antibiotics from the group of fluoroquinolones, enrofloxacin, norfloxacin and ciprofloxacin, were determined in muscle tissues of rainbow trout from fish farms at maximum concentrations of 22, 60 and 18.5 ng g^{-1}, respectively (Wagil et al. 2014). The presence of ibuprofen, diclofenac, salicylic acid and 17β-estradiol were reported in sediments collected from fish ponds (Kumirska et al. 2015). Further research on the sedimentary content of pharmaceuticals in different surface waters in Poland as well as in aquatic biota, including that which is harvested for human consumption, is urgently needed.

The occurrence of some of the above-mentioned pharmaceuticals was also screened in samples of tap water. The list of APIs which were quantified with maximum reported concentrations are given in Table 2. The greatest concentrations were determined for non-steroidal anti-inflammatory drugs (ketoprofen, ibuprofen and diclofenac) and paracetamol which again cor-

responds to the popularity of these pharmaceuticals in Poland. To date, the presence of APIs has, however, only been evaluated for tap water from Warsaw and Gdańsk; the presence of pharmaceuticals and their concentrations in drinking water from other Polish locations remains to be studied. The determined concentrations fall within the ppt range (Table 2), thus one could assume they are unlikely to have any adverse effect in humans. Nevertheless, the pharmaceuticals do not appear on their own but as a combination of compounds displaying different bioactive properties. Therefore, their additive and synergistic effects cannot be excluded. Furthermore, human exposure to pharmaceuticals has a life-long character; its effects on health are unknown. Finally, the low concentrations could still be potentially harmful in more vulnerable populations and during early stages of development (e.g. during the fetal period). Although this effect is still to be comprehensively studied, the precautionary principle in this regard must be the guiding one. A further effort is required to screen APIs in water used for human purposes in Poland. These challenges, however, require interdisciplinary and complex efforts, and a great deal of financial and legislative support. The presence of pharmaceuticals in drinking water, even at very low concentrations, should raise reasonable concerns among stakeholders such as drinking-water regulators, governments, water suppliers and the public, with regard to the potential risks to humans. Despite the unavoidable character of pharmaceutical pollution, an effort should be made to maximally decrease the release of APIs to the environment, particularly by the maximum possible increase in the effectiveness of wastewater treatment processes.

Conclusions

Pharmaceutical pollution is a serious and widespread problem which has been recognized globally and given attention by environmental chemists and ecotoxicologists. The increasing occurrence of APIs in aquatic environments can adversely affect living organisms on different organizational levels and lead to alterations in the ecological function of rivers and lakes. Further, contamination of drinking water sources with these compounds may lead to unintended human exposures and potential effects on health. Pharmaceutical pollution will be an increasing challenge for environmental protection, if one considers the forecasted systematic increase in the use of various medications by the human population. Therefore, it is imperative to support systematic research on API detection methods and to monitor the great number of APIs in wastewater, surface and groundwater and tap water.

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