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Antibiotics in the Environment as one of the Barriers to Sustainable Development

Antybiotyki w środowisku jako jedna z barier dla zrównoważonego rozwoju

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Abstract

The paper has analyzed the presence of antibiotics in crude (hospital, medicine production and municipal) waste water, treated waste water, surface water and drinking water across the world. The concentrations of antibiotics in medicine production waste water reached a level of up to 900 μ/dm^3; in hospital waste water, up to 124 μ/dm^3; and in municipal waste water, up to 64 μ/dm^3. Antibiotic concentrations in treated waste water approached 260 ng/dm^3. The presence of antibiotics in surface water has also been covered. The most often identified medicines were: Ciprofloxacin, Erythromycin, Norfloxacin, Sulfamethoxazole and Trimethoprim. The maximum antibiotic concentrations in surface water are as high as up to 2 μg/dm^3. In the majority of cases, identified antibiotics occurred in concentrations from several to several dozen ng/dm^3, and less often in several hundred ng/dm^3. The presence of antibiotics in drinking water, similarly as for waste water, was identified worldwide, e.g. in China, USA, Germany, Canada, France. Very high antibiotic concentrations were noted in Guangzhou, China, which reached a level of up to 679.7 ng/dm^3 (Ciprofloxacin), but also in the USA (Triclosan) – 734 ng/dm^3). In the majority of instances, antibiotics are present in water in much lower concentrations. The consequence of environmental contamination with antibiotics is the drug resistance of many bacterial strains with the resultant deaths of 25 000 people in the European Union and 700 000 people across the globe. The other effects of the presence of antibiotics in the natural environment are not fully understood yet. For example, carcinogenic, teratogenic or mutagenic effects are attributed to these contaminants.

Key words: antibiotics, water pollution, drug resistance

Streszczenie

W pracy przeanalizowano obecność antybiotyków w ściekach surowych (szpitalnych, z produkcji leków, komunalnych), oczyszczonych, wodach powierzchniowych i wodzie pitnej na świecie. Stężenia antybiotyków analizowane w ściekach z produkcji leków dochodziły do 900 μ/dm^3, w ściekach szpitalnych do 124 μ/dm^3 i komunalnych do 64 μ/dm^3. Stężenia antybiotyków w ściekach oczyszczonych dochodziły do 260 ng/dm^3. Przedstawiono również obecność antybiotyków w wodach powierzchniowych. Najczęściej identyfikowanymi lekami były: ciprofloxacin, erytromycyna, norfloxacin, sulfamethoxazole i trimethoprim. Maksymalne stężenia antybiotyków w wodach powierzchniowych dochodzą nawet do 2 μg/dm^3. W większości przypadkach identyfikowane antybiotyki występowały w ilości od kilku do kilkudziesięciu ng/dm^3, rzadziej w ilości kilkuset ng/dm^3. Obecność antybiotyków w wodzie pitnej jest identyfikowana, podobnie jak w przypadku ścieków na całym świecie np. w Chinach, USA, Niemczech, Kanadzie, Francji. Odnotowano bardzo wysokie stężenia antybiotyków Chinach w Guangzhou dochodzące do 679,7 ng/dm^3 (ciprofloxacin), ale również w USA (triclosan – 734 ng/dm^3). W większości przypadków antybiotyki w wodach są w znacznie niższych stężeniach. Konsekwencją zanieczyszczenia środowiska antybiotykami jest lekooporność wielu szczepów bakterii i w konsekwencji coroczna śmierć 25 000 osób w Unii

Europejskiej i około 700000 na całej kuli ziemskiej. Nie do końca poznane są inne skutki obecności antybiotyków w środowisku. Przypisuje się temu zanieczyszczeniu właściwości rakotwórcze, teratogenne lub mutagenne.

Słowa kluczowe: antybiotyki, zanieczyszczenie wody, lekooporność

Introduction

One of the problems of sustainable development is the rapid increase in the resistance of many bacterial strains to antibiotics used in heath care. The significance of this issue can be indicated by the fact that, in the USA, as many as 70% of bacteria involved in hospital infections are resistant to at least one antibiotic, which was previously effective in the treatment of a specific bacterium **(**Bruton et al., 2007). It is estimated that about 25 000 people in Europe die each year due to infections caused by bacterial strains resistant to all antibiotics possible to be used in a given therapeutic recommendation. A constantly increasing percentage of bacteria resistant to many antibiotics simultaneously is being observed, for both Gram-negative and Gram-positive bacteria **(**Żabicka et al., 2012**)**. The invention of penicillin by Alexander Fleming in 1928 gave hope for the effective treatment of many diseases and significantly extended the life expectancy of people. This invention won him the Nobel Prize in 1945. It seemed a breakthrough invention that would solve the problem of bacterial diseases. An it is still considered one of the greatest inventions of the 20th century. At present, in spite of synthesizing ever newer antibiotics, we are increasingly often helpless in combating antibiotic-resistant bacterial strains. So, the main principle of sustainable development, which is to use the environment in such a manner that does not reduce the potential of future generations for development, has not been met for antibiotics. The antibiotic-resistance problem was highlighted, e.g., by the establishment of the European Antibiotic Awareness Day in 2008 by the European Commission upon a motion by the European Centre for Disease Prevention and Control. The aim of this action has been to provide information on antibiotics, their effect and risks that may arise from their improper use. One of the major threats is the constantly aggravating phenomenon of the antibiotic resistance of microorganisms (WHO, 2014). Also the presence of antibiotics in various elements of the environment and food arises concern due to its not fully understood consequences.

One of the problems of concern is the presence of antibiotics in the aquatic environment, because water is among the factors that determine the existence of life. The protection of this element of the natural environment is a prerequisite for eco-development. Antibiotics present in the water environment are toxic to many aquatic organisms, including animals (Wollenberger et al., 2000; Yu et al. 2016). They may reduce the human immunity and exhibit carcinogenic, teratogenic or mutagenic effects. Acting as hormones, part of antibiotics may disrupt human physiological functions (Jones et al., 2005). An inevitable consequence of the presence of antibiotics in the environment, including water, is the emergence of super-bacteria resistant to all antibiotics (Martínez, 2009).

An important issue is to identify the sources of antibiotics in water and to assess their concentrations in surface, ground and potable waters. The presence of antibiotics in surface and ground waters, and even in drinking water, is identified worldwide, e.g. in the UK (Mompelat et al., 2009), Italy (Grenni et al., 2017), China **(**Zhao et al. 2016), Australia (Watkinson et al. 2009), and the USA (Loraine and Pettigrove, 2006).

The purpose of the study is to analyze the problem of environmental contamination with antibiotics and the assess the effectiveness of their removal in conventional waste treatment plants based on the literature review.

The sources of antibiotics in water

The identification of drugs in the environment is a relatively new problem. It was not until 1998 that Thomasa Ternesa carried out the first trials to analyze drugs in the environment (Thomasa, 1998). As a result monitoring the state of rivers, streams and waste waters in the area of Germany, the presence of analgesic, anti-inflammatory, psychotropic and antiepileptic drugs, beta-blockers, hormones and the regulators of fats and their simpler structures, so-called metabolites, was found. Further, extended examinations found antibiotics present in treated waste water and surface water in Germany (Thomasa, 2001**)**.

Antibiotics are used in the treatment of people and animals, in agriculture as growth promoters, in aquaculture and in animal husbandry (poultry and pig farming). The quantity of antibiotics used by people is large. In 2012, in 26 UE countries and in Iceland and Norway, approx. 3400 tons of antibiotics were sold to treat people and 7982 tons in slaughter animal farming (per active substances). Per biomass, the antibiotic dose averaged out at 116.4 mg/kg for people and 144.0 mg/kg for slaughter animals (ECDC/EFSA/EMA, 2015; Osek and Wieczorek, 2015). Part of the antibiotics, either in the unchanged form or as metabolites, find their way to the environment. This leads also to the contamination of meat with antibiotics. For example, the presence of tetracyclines in the amount of up to 100 mg/kg in the muscles, 300 mg/kg in the liver, 600 mg/kg in the kidneys, and streptomycin in the amount of 500 mg/kg in the meat, fat and the liver, and as much as 1000 mg/kg in the kidneys was found (Stec, 2015).

Especially controversial is administering antibiotics to animals to accelerate their growth and increase their meat mass, or dosing them onto the fields with the aim of increasing the crop, thus reducing the costs (Liewska et al., 2006). In animal husbandry, antibiotics are used for both therapeutic and metaphylactic purposes (the treatment of the whole herd when isolated animals fall ill). Due to significant side effects, among which antibiotic resistance was predominant, using antibiotics prophylactically with feed was banned in the entire European Union in 2006 (Biernasiak et al., 2010).

Veterinary antibiotics and their metabolites may be leached from the farmland replenished with animal fertilizers to water reservoirs, or get there as a result of the direct application of medicinal products, e.g. in pisciculture (Stec, 2015).

So, other drug sources in the environment can include waste water from medicine production and veterinary clinics, natural fertilizers, and surface run-offs **(**Kemper, 2008; Li, 2014). In the case of antibiotics used therapeutically by humans, a substantial load of these contaminants occurs in waste water. They are excreted from the body either in the unchanged form or as metabolites. Also, part of pharmaceuticals past their sell-by date, in spite of organizing their collection in pharmacies, find their way to the sewerage or onto landfill sites. Even in the case of a well operating conventional waste treatment plant, the effectiveness of removal of many pharmaceuticals, including antibiotics, is low **(**Golovko et al., 2014; Wu et al., 2016). So, antibiotics get to the water environment with treated waste water, which are directly discharged to surface water or used, e.g., for the irrigation of fields or the replenishment of ground water, or even underground water (MED-EUWI, 2007). Depending on their structure and properties, part of hard decomposable pharmaceuticals and their metabolites are retained in sewage sludge which, in turn, may be used for land reclamation or for soil fertilization in agriculture. As indicated by literature data, antibiotics from the groups of tetracyclines, macrolides and fluoroquinolones are most often identified in sewage sludges (Kümmerer, 2009**)**. Another source of antibiotics can be landfills, liquid manure reservoirs, sewage sludge lagoons, or domestic no-outflow sewage tanks.

A large load of antibiotics and their metabolites is discharged to the environment together with hospital waste water. In Hanoi (Vietnam), waste waters originating from the six biggest hospitals in that region were examined for their content of the most commonly used antibiotics of the fluoroquinolone group. The presence of ciprofloxacin in a concentration ranging from 1.1 do 44 μg/l and norfloxacin from 0.9 to 17 μg/l was found. The concentrations were comparable to the results of studies carried out, e.g., in Germany, Switzerland and Sweden (Bielińska and Nałęcz-Jawecki, 2009; Duong et al., 2008).

There is a very high contamination of soils and ground water with veterinary antibiotics. It is estimated that the load of antibiotics introduced to the soil with fertilizers reaches a level of several kilograms per hectare. The concentrations of assayed antibiotics often exceed 500 mg/kg of soil, with tetracycline-group antibiotics and sulphonamides, which are commonly used in pig and poultry farming, making up the largest share (Kemper, 2008**)**.

Waste water as the main source of antibiotics in water

Domestic sewage, hospital and antibiotic production waste waters constitute a major source of antibiotics in the water environment. In spite of the fact that waste treatment plants receive the majority of waste waters (treated waste water makes up 95% (GUS 2016), they are not prepared to remove such peculiar contaminants, as antibiotics. In conventional waste treatment plants, antibiotics may either undergo either total or partial mineralization as a result of biodegradation, or be retained on the sewage sludge (Fig. 1) (Adamek et al., 2015). Nevertheless, the effectiveness of removal of these contaminants is often low (Golovko et al., 2014; Wu et. Al., 2016). Conventional waste treatment technologies rely most often on degradation processes (either aerobic or anaerobic), that is they utilize microorganisms. These are fairly cheap and relatively simple technologies, which are characterized by a high effectiveness of organic matter decomposition. The presence of antibiotics in waste water may adversely affect the operation of the biological section of a waste treatment plant (Michael et al., 2013; Guerra et al., 2014).

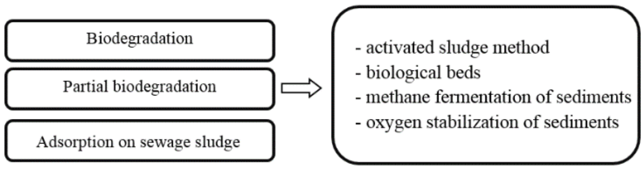

Figure 1. Municipal sewage treatment processes influencing the antibiotic concentrations

Particularly high antibiotic concentrations occur in hospital and antibiotic production waste waters (Table 1). In hospital waste water, e.g., Ciprofloxacin concentrations approached a level of up to 124.5 μg/dm^3, and Ofloxacin concentrations, up to 39.1 μg/dm^3 (Ahmad et al., 2012**)**. Even higher concentrations were noted in drug production waste water (Table 2). In this case, the examined concentrations approached the following levels, respectively: for Enrofloxacin – 900 μg/dm^3; for Norfloxacin – 420 μg/dm^3, for Ofloxacin – 160; for

Table 1. Antibiotic concentrations in hospital waste water and antibiotic production waste water

Antibiotic	Wastewater μg/dm^3	Country	Reference
Cipro-floxacin	3-87	USA/hospital wastewater	Carmosini and Lee, 2009
	15-26	Italy/ hospital wastewater	Verlicchi et al., 2012
	28-31	India/ drug production facilities	Larsson et al., 2007
	0.7-124.5	Germany/ hospital wastewater	Ahmad et al., 2012
	3,6-101	Sweden/ hospi-tal wastewater	Lindberg et al., 2004
	3-87	Switzerland/ hospital wastewater	Ashfaq et al., 2016
	2,5-15	Australia/ hospital wastewater	Watkinson et al., 2009
Enoxacin	150–300	India/ drug production facilities	Larsson et al., 2007
Enrofloxa-cin	780–900	India/ drug production facilities	Larsson et al., 2007
Lomeflox-acin	150–300	India/ drug production facilities	Larsson et al., 2007
Norfloxa-cin	390–420	India/ drug Production facilities	Larsson et al. 2007
Ofloxacin	150–160	India/ drug production facilities	Larsson et al., 2007
	7.9-39.1	Pakistan/ hospi-tal wastewater	Ahmad et al., 2012
	1,66-4,2	China/ hospital wastewater	Chang et al., 2010
	3.7-31	Italy/ hospital wastewater	Verlicchi et al., 2012

Lomefloxacin and Enoxacin – 300 μg/dm^3 and for Ciprofloxacin – 31 μg/dm^3 (Larsson et al., 2007). Lower antibiotic concentrations were observed in municipal sewage. These occur in nanogram concentrations. The concentrations of the following antibiotics were found in waste water in concentrations of up to, respectively: Ciprofloxacin 860 ng/dm^3 – Czech Republic (Golovko et al., 2014); Cephalexin 175 ng/dm^3 – China (Wu et al., 2016); Norfloxacin 1330 ng/dm^3 – Czech Republic (Golovko et al., 2014); Moxifloxacin 180 ng/dm^3- Spain (Gracia-Lor et al., 2012); Trimethoprim 4300 ng/dm^3 – Australia (Watkinson et al., 2009). Nevertheless, even such concentrations are often too high and are not completely removed in the waste water treatment processes (Table 2). In the majority of waste treatment plants, a partial removal of antibiotics took place. The efficiency of those processes was varying, being dependent both on the waste water treatment method and conditions and on the antibiotic being removed.

Table 2. Concentrations of selected antibiotics in crude and treated waste waters, respectively

Antibio-tic	Wastewater before treatment μg/dm^3	Waste-water cleaned μg/dm^3	Country	Refe-rence
Cipro-floxacin	0.278	0.120	WWTP of Lede, Belgium	Ver-geynst et al., 2015
	0.86	0.19	WWTP, Czech Republic	Golovko et al., 2014
	1.1	-	WWTP Australia Queensland	Watkin-son et al., 2009
Cepha-lexin	0.175	0.064	WWTP Shanghai, China	Wu et al, 2016
	64	0.26	WWTP Australia Queensland	Watkin-son et al., 2009
Enroflox-acin	23.93 3.67	2.47 2.35	WWTP Shanghai, China	Wu et. al 2016
	0.04	0.002	WWTP Australia Queensland	Watkin-son et al., 2009
Erythro-mycin	28.6 22.4	11.7 20.8	WWTP Shanghai, China	Wu et al., 2016
	0.3	0.35	WWTP, Czech Republic	Golovko et al., 2014
Moxi-floxacin	0.149	0.062	WWTP of Lede, Belgium	Ver-geynst et al., 2015
	0.072	-	WWTP China	Jia et al., 2012
	0.18	-	WWTP Spain	Gracia-Lor et al., 2012
Sparflox-acin	0.004	-	WWTP China	Jia et al., 2012
	0.022	-	WWTP India	Ashfaq et al., 2016
Oxyter-acycline	0.126 0.012	nd 0.011	WWTP Shanghai, China	Wu et al., 2016
	0.35	0.07	WWTP Australia Queensland	Watkin-son et al., 2009
Penicillin V	13.8	2	WWTP Australia Queensland	Watkin-son et al., 2009
Roxithro-mycin	0.077 0.028	0.023 0.012	WWTP Shanghai, China	Wu et al., 2016
	0.5	0.5	WWTP Australia Queensland	Watkin-son et al., 2009
Sulfa-methoxa-zole	245	133	WWTP of Lede, Belgium	Ver-geynst et al. 2015
	55.6 138.5	39.5 70.6	WWTP Shanghai, China	Wu et al., 2016
	3	0.2	WWTP Australia Queensland	Watkin-son et al., 2009
	0.49	0.26	WWTP, Czech Republic	Golovko et al., 2014

Antibiotic	Wastewater before treatment µg/dm³	Wastewater cleaned µg/dm³	Country	Reference
Sulfadiazine	0.544 0.009	0.010 nd	WWTP Shanghai, China	Wu et al., 2016
Sulfamethazine	0.010	0.006	WWTP Shanghai, China	Wu et al., 2016
Trimethoprim	0.158	-	WWTP of Lede, Belgium	Vergeynst et al., 2015
	4.3	0.25	WWTP Australia Queensland	Watkinson et al., 2009
	0.53	0.44	WWTP, Czech Republic	Golovko et al. 2014
	0.04	0.05	WWTP Australia Queensland	Watkinson et al., 2009
	0.22	0.25	WWTP Australia Queensland	Watkinson et al., 2009
	1.33	0.25	WWTP, Czech Republic	Golovko et al., 2014
Ofloxacin	2.937	0.196	WWTP Shanghai, China	Wu et al., 2016

WWTP – Wastewater treatment plant

The majority of antibiotics are removed in 50-70% by means of biodegradation, hydrolysis of photolysis. Another mechanism is adsorption on the active sludge, which eliminates Erythromycin in 25%, Clarithromycin in 54%, Trimethoprim even in 69%, and Sulphamethoxazole in a maximum of 55% (Kasprzyk-Hordern, 2009; Sukul and Spiteller, 2006; Monteiro and Boxall, 2010). The antibiotic removal efficiencies given by the authors are much higher than those in operating waste treatment plants, e.g. in China (Wu et al., 2016). It should be emphasized that it is low antibiotic concentrations that favour the formation of immunity mechanisms and resultant drug-resistance.

The occurrence of antibiotics in surface water

In surface water, almost all antibiotics used in medicine and veterinary are identified. The occurrence of antibiotics in the natural environment is closely related to their structure. In terms of their chemical structure, antibiotics can be divided into: β-lactam antibiotics, peptide and glycopeptide antibiotics, aminoglycosides, tetracyclines, macrolides, lincosamides, amphenicols, fusidic acid, rifamycines, ketolides, fluoroquinolones, streptogramins and chemotherapeutics of a different chemical structure (Janiec et al., 2010).

The assayed concentrations of these substances often come to values of up to 2 µg/dm³ and are detected in surface water, ground water and even underground water (Table 3) (Wu et al., 2016; Grenni et al., 2017; Lucia et al., 2010; Kümmerer, 2009). They are present in waters in all continents and in different countries, both very high developed (the USA, Germany, the UK, Australia), as well as much poorer ones (India or Vietnam). Especially often assayed are: Ciprofloxacin (a maximum concentration of 1300 ng/dm³ – Australia), Erythromycin (max. 450 ng/dm³ – South Korea), Norfloxacin (max. 1150 ng/dm³ – Australia), Sulfamethoxazole (max. 1900 ng/dm³ – USA) and Trimethoprim (150 ng/dm³ – Australia). In the majority of cases, identified antibiotics occurred in concentrations from several to several dozen ng/dm³, and less often in several hundred ng/dm³.

Antibiotics contained in a water environment are subject to the action of both biotic and abiotic factors (sorption, desorption, photodegradation, biodegradation) (Fig. 2). The stability of antibiotics and their metabolites in a water environment depends on many factors, including the concentration of inorganic ions, the presence of organic suspended matter and the intensity of solar radiation (Skół, 2013).

The ability of antibiotics to adsorb on other matter particles depend largely on their diverse chemical constitution, containing groupings both acid and basic in character. For this reason, the distribution of these substances in the water environment largely depends on the pH value. The reaction of the water environment will also determine their solubility, hydrophobicity or sorption coefficient (Reemtsma and Jekel, 2006). One of the elements promoting the degradation of antibiotics in the water environment is photodegradation by UV radiation. Among many groups of antibiotics, quinolones, tetracyclines and sulphonamides are substance sensitive to solar radiation. Photodegradation has a significant importance in the process of surface water self-purification. The effectiveness of photodegradation depends on many factors, including temperature, irradiation intensity and the volumetric flow rate of water (Skół, 2013; Reemtsma and Jekel, 2006; Heberer, 2002).

Responsible for degradation processes in surface and ground waters are chiefly bacteria and fungi contained in them (Ternes, 2001). The biodegradation of antibiotics and their metabolites may lead to their total mineralization or biotransformation, that is the simultaneous formation of intermediate decomposition products that may exhibit much higher stability and higher toxicity compared to the parent substances. Based on the most recent studies it can be stated that antibiotics are substances relatively resistant to degradation processes and, in the majority of instances, undergo transformations resulting in the formation of new, previously unidentified compounds. Residues of antibiotics and their metabolites, together with the treated waste water, are discharged from the waste treatment plant to surface water, or, together with the sludge, migrate into the soil and ground water that is the main source of drinking water (Halling-Sorensen et al., 1998; Watkinson et al., 2007).

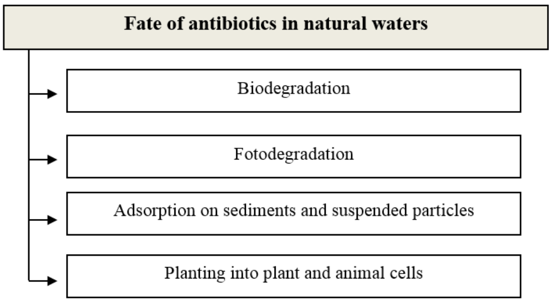

Figure 2. Transformations of antibiotics in natural water

The presence of antibiotics and their metabolites in the water environment has an adverse impact on organisms living in it. The toxicity of these substances to aquatic organisms is high, as they are exposed to them on a continuous basis and through many generations (Fent et al., 2006).

Antibiotics in water intended for drinking

Literature reports on the presence of antibiotic residues in drinking water are scarce. One of the main reasons behind this situation are analytical difficulties due to the determination limits of measuring apparatus used. The progress in analytical chemistry is oriented to the development of methods and the improvement of measuring apparatus to enable the detection of compounds occurring in micro-traces and the determination of new substances (Kümmerer, 2009).

It has been found that the presence of antibiotics in drinking water may have an adverse impact on humans. They may exhibit carcinogenic, teratogenic or mutagenic effects, affect the hormonal regulation and impair the immunity (Jones et al., 2005). An inevitable consequence of the presence of antibiotics in the environment, including water, is the emergence of super-bacteria resistant to all antibiotics (Martínez, 2009). Particularly dangerous is the occurrence of antibiotics in low concentrations, which are non-toxic to bacteria.

A major problem is the identification of antibiotic sources and the assessment of their concentrations in potable water. The presence of antibiotics in drinking water is being identified throughout the world, e.g. in China, USA, Germany, Canada, France (Table 5). Very high antibiotic concentrations were noted in Guangzhou, China ((Lomefloxacin – 197 ng/dm^3, Ciprofloxacin – 679.7 ng/dm^3, Norfloxacin – 82.7 ng/dm^3), but also in the USA (Triclosan – 734 ng/dm^3) (Yiruhan et al., 2010; Loraine and Pettigrove, 2006).). In the majority of cases, antibiotics are present in water in much lower concentrations (Table 4). Due to the analytical difficulties in the identification of those antibiotics, whose concentrations are at a level of ng/dm^3, they are very rarely assayed in drinking water. It is hard

Table 3. Pharmaceuticals most often detected in surface water

Antibiotic	Country/ River	Max. concentration ng/dm^3	Reference
Amoxicillin	UK/ R. Taff	240	Mompelat et al., 2009
	China/ Huangpu R.	53.9	Wu et al., 2016
	Italy/ R. Lambro	16.7	Grenni et al., 2017
	Australia/South–East Queensland	200	Watkinson et al., 2009
Ciprofloxacin	France/ R. Seine	20	Tamtam et al., 2008
	Italy/ R. Lambro	14.4	Zuccato et al., 2006
	Finland/R. Vanta	40	Mompelat et al., 2009
	Streams USA	30	Kolpinet et al., 2002
	China/ Yellow R. Delta	70.3	Wu et. al 2016
	Italy/ R. Po	124	Grenni et al. 2017
	Italy/R. Tiber	19	Grenni et al. 2017
	Australia/South–East Queensland	1300	Watkinson et al. 2009
Chlorotetracycline	Streams USA	670	Kolpin et al., 2002
	Australia/South–East Queensland	600	Watkinson et al., 2009
Erythromycin	China/R. Pearl	423	Zheng et al., 2012
	Vietnam/ R. Mekong	11	Zheng et al., 2012
	Japan/ R.Tamagawa	448	Zheng et al., 2012
	South Korea/R. Youngsan	450	Zheng et al., 2012
	UK/R. Taff	21	Kasprzyk-Hordern et al., 2009
	Italy/ R. Po	15.9	Zuccato et al., 2006
	Italy/R. Lambro	20	Mompelat et al., 2009
	China/ Yellow R. Delta	23.3	Zhao et al., 2016
Enoxacin	France/r. Seine	15	Mompelat et al., 2009
Enrofloxacin	China/ Yellow R. Delta	20.9	Zhao et al., 2016
	China/ Huangpu R.	5.4	Wu et al., 2016
	Australia/South–East Queensland	300	Watkinson et al., 2009
Clarithromycin	Italy/R. Po	4.6	Calza et al., 2013
		128	Grenni et al., 2017
	Italy /R. Lambro	8.3	Zuccato et al., 2006
		149	Grenni et al., 2017
	Japan/R. Tamagawa	1.1	Murata et al., 2011

Antibiotic	Country/ River	Max. concentration ng/dm^3	Reference
Lincomycin	Italy/ R. Po	20	Calza et al., 2013
		248.9	Grenni et al., 2017
	Italy/R. Lambro	24.4	Zuccato et al., 2006
		24.4	Grenni et al., 2017
	Australia/South–East Queensland	50	Watkinson et al., 2009
Norfloxacin	France/R. Seine	40	Tamtam et al., 2008
	Brazil/R. Atibaia	50	Locatelli et al., 2011
	USA streams	150	Kolpin et al., 2002
	Finland/R. Vantaa	140	Mompelat et al., 2009
	Bresil/Rio Grandr	300	Brown et al., 2006
	Australia/South–East Queensland	1150	Watkinson et al., 2009
Ofloxacin	France/R. Seine	70	Vieno et al., 2006
	China/ Huangpu R.	16.4	Wu et al., 2016
	China/Yellow R. Delta	23.4	Zhao et al., 2016
	Italy/R. Po	33.1	Grenni et al., 2017
	Italy/R. Lambro	306.1	Grenni et al., 2017
Oxytetracycline	USA streams	320	Kolpin et al., 2002
	China/Yellow R. Delta	83.5	Zhao et al., 2016
	Italy/ R. Po	8.0	Grenni et al., 2017
	Italy/R. Lambro	14.4	Grenni et al., 2017
Roxithromycin	USA streams	210	Kolpin et al., 2002
	China/Yellow R. Delta	14.1	Zhao et al., 2016
	China/Huangpu R.	2.01	Wu et al., 2016
	Australia/South–East Queensland	350	Watkinson et al., 2009
Spiramycin	Italy/R. Lambro	80	Lucia et al., 2010
		74.2	Grenni et al., 2017
	Italy/R. Po	26.8	Grenni et al., 2017
Sulfamethazine	Vietnam/Makong R.	60	Managaki et al., 2007
	USA streams	260	Kolpin et al., 2002
	China/Huangpu R.	10.8	Wu et al., 2016
Sulfamethoxazole	China/R. Pearl	165	Zheng et al., 2012
	Japan/R. Tamagawa	23	Zheng et al., 2012
	South Korea /R. Youngsan	110	Zheng et al., 2012
	France/R. Seine	75	Tamtam et al., 2008
	Portugal/R. Douro	53.3	Madureira et al., 2010
	UK/R. Taff	8	Kasprzyk-Hordern et al., 2009
	Germany/R. Leine	63	Nödler et al., 2011
	Italy/Lake Maggiore	10	Loos et al., 2007
	Vietnam/R Makong	190	Managaki et al., 2007
	Poland/R. Varta	40	Kasprzyk-Hordern et al., 2009
	USA streams	1900	Kolpin et al., 2002
	China/ Huangpu R.	25.9	Wu et al., 2016
	Italy/ R. Po	2.39	Grenni et al., 2017
	Italy/ R. Tiber	68	Grenni et al., 2017
	Australia/South–East Queensland	2000	Watkinson et al., 2009
Tetracycline	USA streams	130	Kolpin et al., 2002
	China/ Yellow R. Delta	64.8	Zhao et al., 2016
	Australia/South–East Queensland	80	Watkinson et al., 2009
Trimethoprim	Vietnam/ R. Mekong	20	Zheng et al., 2012
	Japan/R. Tamagawa	100	Zheng et al., 2012
	South Korea/R. Youngsan	20	Zheng et al., 2012
	Frnce/R. Seine	20	Tamtam et al., 2008
	Portugal/R. Douro	15.7	Madureira et al., 2010
	UK/ R. Taff	120	Kasprzyk-Hordern et al., 2009
	USA streams	70	Kolpin et al., 2002
	Australia/South–East Queensland	150	Watkinson et al., 2009

to assess the actual exposure of humans to this type of antibiotics.

Antibiotic resistance

At the beginning of 2015, three European institutions, namely the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA), published for the first time a common report concerning the relationship between the consumption of antibiotics and the occurrence of resistance to antibacterial drugs. This problem applies to bacteria causing diseases both in humans and in animals. A consequence of the abuse and misuse of antibiotics both in humans and in animals and the presence of antibiotics in the environment is the rapid increase in the quantity of bacteria and parasites resistant to those antibiotics (Adamek et al., 2015; Bbosa et al., 2014; Barbusiński and Nalewajek, 2011).

Resistance to antibiotics is a genetic adaptive feature that enable bacteria to survive and develop in the

Table 4. Antibiotics in drinking water

Antibiotic	Country	Max. concentration, ng/dm^3	Reference
Ciprofloxacin	China (Macao)	8.2	Yiruhan et al., 2010
	China (Guangzhou)	679,7	Yiruhan et al., 2010
Clarithomycin	China	0.2	Padhye et al. 2014
Erythromycin	Germany	20	Verlicchi et al., 2012
	Canada	12	Kleywegt et al., 2010
	USA	0.3	Bull et al., 2011
	USA	1.3	Deo and Halden, 2013
	Portugal	5	Gaffney et al., 2014
	China	13.8	Padhye et al., 2014
Enrofloxacin	China(Macao)	5.2	Yiruhan et al., 2010
	China (Guangzhou)	8.3	
Lomefloxacin	China(Macao)	37.1	Yiruhan et al., 2010
	China (Guangzhou	197.0	
Norfloxacin	China(Macao)	17.1	Yiruhan et al., 2010
	China (Guangzhou	82.7	
Sulfonamides	Portugal	1.9	Gaffney et al., 2014
Sulfamethoxazole	France	0.8	Bull et al., 2011
	USA	6	Verlicchi et al., 2012
	USA	20	Deo and Halden, 2013
	USA	13.7	Wang et al., 2011
	China	12.7	Padhye et al.. 2014
	USA	3.4	Ye et al., 2007
Sulfathiazole	USA	10	Deo and Halden, 2013
Trimethoprim	France	1.0	Bull et al., 2011
	Germany	2	Verlicchi et al., 2012
	USA	1.7	Wang et al., 2011
	China	19.8	Padhye et al., 2014
Triclosan	USA	734	Loraine and Pettigrove, 2006

One example of antibiotic-resistant bacteria is *Staphylococcus aureus* (mortality without the use of antibiotics is > 80%). At present, only 20% strains are susceptible to Penicillin, Meticillin, Vancomycin and aminoglycosides. Other antibiotic-resistant presence of the drug that is supposed to destroy them. A major problem is multidrug resistance. Some pathogenic bacteria exhibit resistance to many antibiotics, and there are even such strains (superbacteria) that no longer respond to any antibiotics (Davies and Davies, 2010). The antibiotic-resistance problem was foreseen already by Fleming (in his lecture delivered after winning the Nobel Prize in 1946). Nevertheless, it was not until the 21st century that this phenomenon became a global problem. A return to the pre-antibiotic era, when many infectious diseases were incurable, is even expected (Gross, 2013).

infections may cause an increased death risk (up to 2-3 times) (OECD, 2015). The resistance mechanisms have been described for all antibiotics being currently in use in human and veterinarian medicine. It is estimated that the number of deaths cause by antibiotic-resistant bacteria is already large, but the greatest concern is caused by the increasing trend (French, 2010). According to recent estimates, 23 000 people in the USA, 25 000 in the European Union and about 700 000 across the globe die each year due to bacterial antibiotic resistance (Carvalho and Santos, 2016). This problem may become the cause of an annual death rate of 10 million people by around 2050 (O'Neill, 2014). Another adverse side effect is the increased health care cost resulting from the prolonged stay in hospital and the use of many antibiotics, including new-generation and more expensive ones.

Summary

The investigations have confirmed the presence of antibiotics in surface water, ground water and even drinking water. The sources of those contaminants are diverse: human and veterinary medicine, agriculture (animal husbandry, plant growing, aquaculture). Among the most important sources are municipal sewage and hospital, agricultural and industrial (drug production) waste waters. Very high antibiotic concentrations were assayed in drug production waste water (up to 900 μ/dm^3), hospital waste water (up to 124 μ/dm^3) and municipal sewage (up to 64 μ/dm^3). In the majority of cases, the concentrations of various antibiotics in crude waste water are lower. A concern is caused by the presence of antibiotics also in treated waste water (up to 260 ng/dm^3). As a consequence of their penetration into ground water and even underground water, antibiotics are also detected in drinking water. In the majority of instances, the assayed antibiotic concentration in drinking water ranged from several to several dozen ng/l. However, there were cases (China, USA), where these concentrations attained a level of several hundred ng/dm^3. A consequence of the abuse of antibiotics is their presence in the environment. The consequences of the constant exposure of organisms to antibiotics, e.g. in water, are not fully understood yet. Nevertheless, a proven, extremely dangerous phenomenon is the resistance of many bacterial strains to these drugs. It is estimated that this causes the deaths of about 700 000 people in the world, of which 25 000 in Europe. However, a very fast increase in the number of strains resistant to known antibiotics is foreseen. The drug resistance, which may lead to the incurability of many infectious diseases, is the consequence of upsetting the sustainable development conditions. The excessive, often mindless use of antibiotics with the aim of increasing profits, e.g. in agriculture, is contrary to the eco-development principles. Less understood are the carcinogenic, teratogenic or mutagenic effects of environmental contamination with antibiotics. In many cases, though, such adverse effects are confirmed.

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