Occurence of pharmaceuticals in surface waters

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Abstract

This is a short review on the increasing problem of pharmaceutical pollution in surface waters. Non-steroidal anti-inflammatory drugs (NSAIDs) are medicines that are widely used to relieve pain, reduce inflammation, and reduce a high body temperature. The paper presents a literature review on the content of NASIDs in surface waters. Due to the continuous growth of the world's population and the increasing use of pharmaceuticals, the threat to aquatic ecosystems is increasing. Every day, huge loads of pollution are discharged into rivers and seas. Depending on used technology the effectiveness of wastewater treatment varies considerably. The level of removal efficiency by wastewater treatments depends on physicochemical properties of the individual pharmaceutics and on the type of wastewater treatment technology. Therefore, it is recommended to conduct research on removal efficiency of main drug residues in Polish wastewater treatment plants and, if necessary, apply the best available technologies in this area.

Keywords: wastewater, anti-inflammatories, ibuprofen, ketoprofen, naproxen

Introduction

The pharmaceutical industry is one of the fastest growing industries of modern times. Due to technical and medical progress, people live longer and more medications are used to maintain a proper quality of life. The physicochemical properties of drugs are adsorptive, high biological activity, lipophilicity, low volatility and high polarity. Medicinal substances cannot be completely removed in the conventional process of wastewater treatment and water treatment, resulting in their release into the environment [1]. Hospitals consume huge amounts of medications used by patients, therefore their concentration in hospital wastewater is higher than in domestic wastewater. Nevertheless, active pharmaceutical ingredients (APIs) are not completely metabolized by humans and are further excreted into domestic effluents [2]. After administration, drugs in solid (tablets, suppositories) or liquid (e.g. suspensions) form by the oral or rectal route undergo many metabolic changes. Through the sewage system, loads of pollutants from healthcare facilities are discharged to the sewage treatment plant. Pharmaceuticals are widely used for treatment of humans, animals, and livestock, and have the potential to enter the environment, including groundwater. Among them are antibiotics, analgesics, anti-inflammatories, antidepressants, antipyretics, antimicrobials, disinfectants, hormones, stimulants, lipid regulators, psychiatric drugs, endocrine disruptors, beta-blockers and many other pharmaceuticals that are widely used on a daily basis for various purposes [3]. Human misuse of pharmaceuticals contributes to the pollution of surface waters. In non-sewage areas, sewage from households is discharged into tanks that can seep into the soil, and then into groundwater, which also causes soil contamination. On farms, excreted animal excrements are used as a natural fertilizer for soil fertilization, which consequently causes their penetration into groundwater. Animal manure is also used on farms. Pollutants occurring from run off from fertilized farmlands and water exchange in ponds from fish farms get into surface waters [4]. The most commonly detected pharmaceutical compounds in groundwater are anti-inflammatories including diclofenac, paracetamol and ibuprofen because of their large consumption in daily life. A large number of pharmaceuticals and their metabolites were reported at concentrations up to ppb level in groundwater used for drinking water [5]. Wastewater containing persistent pollutants should be treated by biological, physical and chemical methods, like coagulation

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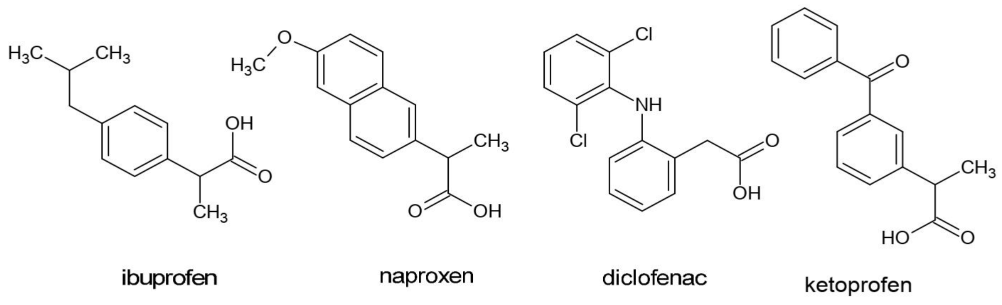
and sedimentation, flotation, activated carbon adsorption, UV irradiation and catalytic photooxidation with TiO_2 as catalyst, advanced oxidation processes, membrane bio-reactor treatment, membrane separation processes [6, 7, 8, 9].

In aquatic ecosystem, mainly in rivers, a phenomenon called self-purification plays an important role, reducing the amount of pollutants and their effects on the environment. However, numerous pharmaceuticals are not easily degraded or the process is very slow and ineffective. Both pharmaceuticals and their metabolites are present in different concentrations in conventional wastewater treatment plants, and their elimination efficacy varies among therapeutic groups [10]. Pharmaceutically active substances during the wastewater treatment process can:

- become mineralized to CO_2 and H_2O by the action of microorganisms in the process of biodegradation;
- be subjected to adsorption processes in sewage sludge;
- enter the aquatic ecosystem with sewage in its original form or in the form of metabolites.

The most abundant non-steroidal anti-inflammatory drugs (NSAIDs) are those readily available in over-the-counter (OTC) medicines containing: ibuprofen, naproxen, diclofenac, ketoprofen (Fig. 1) and salicylic acid [11].



ibuprofen naproxen diclofenac ketoprofen

Figure 1. The most abundant NSAIDs occurring in surface water

Pharmaceuticals present in various components of the environment, especially in surface waters can accumulate in elements of both fauna and flora, posing a real threat with harmful, irreversible effects [12]. Some of the mentioned compounds, e.g. diclofenac, can be used in the form of sodium salts, which increases their solubility in water.

Determination of pharmaceuticals in water

Wastewater contains a large variety of organic and inorganic compounds, and its composition can change significantly over time. A complex matrix of chemical compounds present in the samples can cause analytical errors; therefore, the key step is the appropriate purification of the analytes [4]. Connecting the sample preparation step of solid-phase extraction, which extracts and purifies water or wastewater samples, with chromatography makes the used analytical method highly sensitive. Therefore, the selection of the type of SPE cartridge, the amount of adsorbent, the elution solvent, and its operation condition are a prerequisite key during the analytical method. A very popular SPE column for the analysis of drug residues in aqueous samples is the Oasis HLB column. Oasis HLB is suitable for wide variety of pharmaceutical pollutants analysis, it has both lipophilic and hydrophilic properties, but also a wide range of physicochemical qualities that are problematic to analyse simultaneously with other stationary phases based on one type of interaction [13]. The typical analytical techniques used to determine NSAIDs in water are liquid chromatography (HPLC) and gas chromatography (GC) [13, 14]. The precise determination of analytes requires the use of advanced analytical systems. In many cases, the derivatization of analytes is necessary to obtain more detectable compounds (Fig. 2) [14].

In the case of gas chromatography as a determination method, the derivatization of analytes is used to increase the volatility of the analyte, while in the case of liquid chromatography, the derivatization is used to introduce chromophore groups into the analyte. A very interesting option is a fully automated alkaline-induced salting-out homogeneous liquid-liquid extraction (SHLLE) procedure coupled with in-line organic-phase detection by an optical probe (SHLLE), which is based on the addition of a salting-out agent to a homogeneous sample solution containing a water-miscible organic solvent. This method usually involves a separate step followed by manual handling of the organic phase [15].

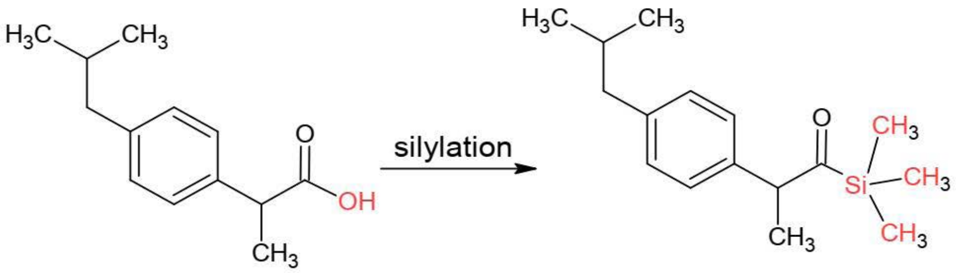


Figure 2. Derivatization of ibuprofen by the silylation reaction

Pharmaceuticals content in surface water

The widespread and relatively high concentration of some pharmaceutics in aquatic ecosystems raises concerns about the environmental risks of this class of pollutants to aquatic organisms, especially to fish. Despite the increasing knowledge, a thorough understanding of the environmental risks of very common pharmaceutics and their metabolites on aquatic organisms are still insufficient. Table 1 shows the concentration ranges of common pharmaceuticals in surface waters reported in the literature.

Table 1. Pharmaceutical contamination of surface waters

Compound	Concentration [μg/L]	Location	Reference
Ibuprofen	1.2–19.2	various	[16]
Naproxen	1.84–39.6	South Africa	[17]
Diclofenac	10.1–104	South Africa	[17]
Ketoprofen	2.90–28.4	Durban, South Africa	[18]
Paracetamol	up to 103	Vistula river near Warsaw	[19]
Diazepam	< 0.3–42	Nigeria	[20]
Valsartan	< 1–3330	Nigeria	[20]
17β-estradiol	up to 0.087	Brazil	[21]
Progesterone	up to 0.026	Brazil	[21]

Toxicity of pharmaceuticals to aquatic organisms

The toxicity of pollutants depends on the group of aquatic organisms and species. A general scale of toxicity applied to aquatic invertebrates is presented in Table 2.

Tables 3 and 4 show the effective concentration (EC) and lethal concentration (LC) for various aquatic organisms for two commonly used NASIDs.

Methods of advanced treatment of wastewater

Typical techniques used in wastewater treatment plants (WWTPs) may not be sufficient to adequately treat the wastewater from active pharmaceutical ingredients. Ibuprofen, naproxen, and diclofenac are included in the list of the top ten high priority pharmaceutical persistent pollutants (class I) [20]. Therefore, the development of a low cost and efficient removal technology for active pharmaceutical ingredients from wastewater is an urgent requirement of our society. The following are technological processes that can be used to remove persistent contaminants in the water, including residues of active pharmaceutical substances.

Coagulation and sedimentation processes

Coagulants are added to the wastewater to bring the non-sedimenting particles together and initiate or accelerate the precipitation process. The coagulation combined with the sedimentation process is used typically in water and wastewater treatment as a basic pre-treatment stage. It has the potential to remove colloidal particles and precipitates. Coagulation combined with sedimentation has many advantages, such as easy operation and well-known technology, however, many dissolved organic drug ingredients are not easily eliminated by this method. Small particles are not removed efficiently by sedimentation and other steps are required. According to many authors, preliminary treatments and primary settling are generally fairly inefficient at removing pharmaceutics from wastewaters (efficiency < 10% only) [28].

Table 2. Qualitative description of toxicity of pollutants to aquatic invertebrates [22]

LC50 or EC50 [mg/L]	Category description
<0.1	Very high toxicity
0.1 – 1	Highly toxic
>1; <10	Moderately toxicity
>10; <100	Slightly toxicity
>100	Practically non-toxic

Table 3. Toxicity of diclofenac to various aquatic organisms

Target	Exposure time	Index	Concentration [mg/L]	Reference
Phytoplankton	96 h	EC$_{50}$	14.5	[23]
Zooplankton	96 h	EC$_{50}$	22.4	[23]
Dunaliellatertiolecta	96 h	EC$_{50}$	185.7	[24]
Desmodesmussubspicatus	72 h	EC$_{50}$	72 mg/L	[24]
Oncorhynchus mykiss	28 days	EC$_{50}$	> 5 µg/L	[24]
Lemna minor	168 h	EC$_{50}$	148 mg/L	[25]
Daphnia magna	-	EC$_{50}$	100 mg/L	[25]

Table 4. Toxicity of ibuprofen to various aquatic organisms

Target	Exposure time	Index	Concentration [mg/L]	Reference
Daphnia magna	48 h	EC$_{50}$	108	[26]
Lemna minor	7 days	EC$_{50}$	4.01	[26]
Thamnocephalusplatyurus	24 h	LC$_{50}$	19.6	[26]
Phymorhynchus carinatus	72 h	LC$_{50}$	0.017	[27]
Tachysurusfulvidraco	24 h	EC$_{50}$	0.005	[27]
Daphnia similis	48 h	EC$_{50}$	97	[27]

Flotation process

Flotation uses highly dispersed tiny bubbles as carriers to adhere to the wastewater pollutants and this way remove suspended particles of secondary effluent. This process produces a large number of small bubbles by injecting air into wastewater, forming floating floc with smaller density than wastewater. Air dissolved in wastewater during flotation is a very effective solid-liquid separation process used in water treatment, as an alternative to sedimentation ideal for treating water with light particles [6].

Activated carbon adsorption

Activated carbon absorption is one of the most important processes in wastewater treatment because of its ability to adsorb a wide variety of persistent organic compounds. This process is very effective but relatively expensive. Active carbon has a large specific surface area, multilevel pore structure, high adsorption capacity, and is chemically stable. Its activity can be classified both, as physical and chemical interactions. Physical adsorption is reversible, and there is no selectivity to adsorbate.

The methods based on sorbents are widely used for advanced water treatment because they can be recycled and have a wide range of applications. This method of wastewater treatment is currently one of the most important stage for removing pharmaceutical contaminants [29].

Advanced oxidation

Advanced oxidation processes (AOPs) are powerful tools in water purification and wastewater treatment, containing pharmaceutics, dyes, pesticides, and other deleterious pollutants like nanomaterials. There are many kinds of reagents and techniques such as wet air oxidation, Fenton reagent (Fe^{2+}/H_2O_2), and zero-valent iron application (ZVF/H_2O_2), electrochemical oxidation and ozonation, photocatalytic oxidation, ultrasound oxidation. After several decades of studies on AOPs, these technologies have proven their efficiency for the removal of a wide variety of pollutants in general and pharmaceutics in particular [30].

Biological treatment

Biological wastewater treatment consists of using microbial communities (mainly bacteria), which degrade and mineralize organic pollutants. However, pharmaceuticals and their conjugates due to their often refractory or toxic properties are not efficiently eliminated by conventional biological treatment plants. Poor removal efficiencies have been documented for compounds with complex molecular structures, like naproxen or ibuprofen [31]. Figure 3 shows different treatment efficiencies for municipal wastewater containing pharmaceutical substances. The very wide ranges of the observed values result from the technologies used, wastewater treatment time, temperature, pH, and other factors.

Conventional wastewater plants most often use activated-sludge, which has become the most popular treatment among biological technologies. In this technology, the microbial biomass is used in form of flocs that are subsequently separated from purified wastewater by simple sedimentation and recycled back into the bioreactor (aeration chamber). This floc-based technology has basically replaced once-popular trickling filters and rotating biological discs where bacteria are immobilised in biofilms growing on stable immersed substrates. However, several new technologies both aerobic and anaerobic using bacteria immobilized in biofilms (including granular sludge) have recently been gaining popularity in particular for the treatment of industrial wastewaters [32].

Compared to the activated sludge, biofilms offer many advantages. Their density is usually higher than that of activated-sludge flocs, which makes the separation of the biomass from the treated water easier. Microbial biomass growing in biofilms may be more concentrated in the reactor hence higher loads can be treated. However, from the point of view of eliminating pharmaceuticals, the most interesting property of biofilms lies in still another aspect.

Large refractory molecules cannot be degraded by a single bacterial strain since their breakdown and mineralization is a process involving many stages. For each successive reaction bacteria with specific metabolic capabilities are needed. Activated-sludge flocs have a looser structure compared to biofilms and are often disintegrated under intense mixing and aeration. Since biofilms are denser and more long-lasting, cells with complementary functions can be gathered together in a direct vicinity one to each other creating synergistic microconsortia [33, 34]. Under such conditions, the breakdown and mineralization of refractory molecules may proceed more efficiently since intermediate products, which could slow down the whole process, do not accumulate.

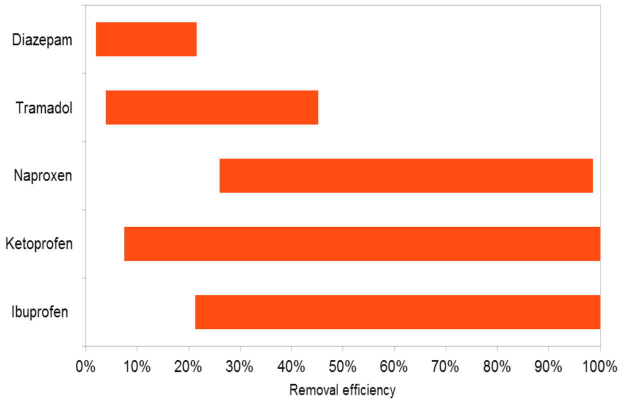


Figure 3. Removal efficiencies from the liquid phase in conventional wastewater plant [30]

Conclusions

Every year huge amounts of pollutants, including pharmacological substances, are introduced into surface waters. Municipal wastewater contains a wide variety of pollutants and the applied wastewater treatment technologies do not guarantee their full purification. Global population growth combined with the development causes significant environmental pollution. The pharmaceutical industry is currently one of the branches of the economy with the greatest dynamics of development. At the same time, excessive consumption of pharmaceuticals is observed, especially in developed countries. This situation causes a significant impact on the aquatic environment with substances with strong biological effects. Additionally, there is a risk that inadequately treated sewage will contaminate rivers being the source of raw water for waterworks. The basic conclusion of our work is that there is an urgent need to monitor the content of pharmaceutical substances in surface waters in Poland. Another issue is to determine the effectiveness of wastewater treatment in the context of these substances. Our surmise indicates that the content of these pollutants in surface waters is still significantly below the critical limits (EC_{50} or LC_{50}), but there is a great risk that the degradation of waters will increase in the future. On the other hand, the fact that the acute toxicity limits are not exceeded does not mean that there is no risk to any particular species of aquatic organism. The long-term impact of pollutants on aquatic organisms can disturb aquatic ecosystems, leading to reproductive problems, physiological changes, and extinction of more sensitive species with community-level consequences. The conclusion resulting from the presented paper is that large wastewater treatment plants should assess the effectiveness of the applied technologies in the context of pharmaceutical removal. This estimation should be the basis for modification of the technological process in those treatment plants, where the degree of pharmaceutical elimination is ineffective.

Author Contributions

Conceptualization, Marek Chyc, Krzysztof Wiąckowski; methodology, Marek Chyc, Krzysztof Wiąckowski; software, Jowita Sawczak; validation, Marek Chyc, Krzysztof Wiąckowski; formal analysis, Krzysztof Wiąckowski; investigation, Jowita Sawczak, Marek Chyc; resources, Jowita Sawczak, Marek Chyc; data curation, Marek Chyc, Krzysztof Wiąckowski; writing—original draft preparation, Marek Chyc; writing—review and editing, Marek Chyc, Krzysztof Wiąckowski, Jowita Sawczak; visualization, Marek Chyc, Jowita Sawczak; supervision, Marek Chyc; project administration, Marek Chyc, Krzysztof Wiąckowski; funding acquisition, Marek Chyc, Krzysztof Wiąckowski, Jowita Sawczak.

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