Occurence of pharmaceuticals in surface water

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Summary

Pharmaceuticals constitute a large group of human and veterinary medicinal organic compounds which have long been used throughout the world. According to their therapeutic activity they are classified in several groups: antibiotics, analgesics/antipyretic, CNS (Central nervous system) drugs, cardiovascular drugs, endocrinology treatments, diagnostic aid-adsorbable organic halogen compounds. Pharmaceuticals are designed to have a physiological effect on humans and animals in trace concentrations. Pharmaceuticals end up in soil, surface waters and eventually in ground water, which can be used as a source of drinking water, after their excretion (in unmetabolized form or as active metabolites) from humans or animals via urine or faeces. The possible fates of pharmaceuticals once they get into the aquatic environment are mainly three: (i) ultimately they are mineralized to carbon dioxide and water, (ii) the compound does not degrade readily because it is lipophilic and is partially retained in the sedimentation sludge and (iii) the compound metabolizes to a more hydrophilic molecule, passes through the wastewater treatment plant and ends up in receiving waters (which are surface waters, mainly rivers). These compounds exhibit the highest persistence in the environment. In recent years, and in particular after the use of the advanced measurement technologies, many pharmaceuticals have been identified worldwide and detected at ng/L levels (trace concentrations) in the aquatic environment, and are considered as an emerging environmental problem due to their continuous input and persistence in the aquatic ecosystem even at low concentrations.

Keywords: pharmaceuticals, surface water, purification

Introduction

The rapid development of technology and new knowledge in medicine and the chemical industry lead to the increasing production of medicines for human and veterinary use and, finally, to their increasing consumption. Consequently, pharmaceuticals, their metabolites and transformation products are detected in higher concentrations in the environment. Their presence in waste, surface and groundwater, seas and ground has increased in a large number of countries.

After consumption, the drugs are released into the environment by excretion from the body, either in the unchanged form or in the form of metabolites that may have similar or even higher toxicity than the original substance. These metabolites can be further transformed into the wastewater purification process (Lishman et al., 2006).

Primarily, pharmaceuticals end up in the environment via communal wastewater, and at higher concentrations through wastewater from hospitals and drug companies. Large amounts of medicines in the environment also stem from irregularly disposed unused drugs (Nikolaou et al., 2007).

Waste water from the wastewater treatment plant is also polluted with pharmaceuticals that end up in the receivers because they pass through the system without degradation. The wastewater treatment may lead to the transformation of less toxic pharmaceutical metabolites into their more toxic forms and in some cases, a higher concentration of pharmaceuticals is measured at the outflow of the wastewater treatment plant than at the intake stream (Vieno et al., 2007).

Although the stability of pharmaceuticals is low, their presence in the environment is significant because the rate of release of pharmaceuticals into the environment is higher than the rate of their transformation and degradation, and is increasingly the subject of scientific interest and research. This also results in an increasing number of reports on the detection of pharmaceuticals in various environmental samples (Nikolaou et al., 2007, Fent et al., 2006, Mompelat and Tomas, 2006).

In addition, the growing interest in this serious environmental problem is also affected by the development of more advanced and more sensitive chemical analysis methods, such as liquid chromatography and mass spectrometry, which allow the detection of polar organic substances at very low concentrations (Kolpin et al., 2002, Ternes et al., 2001).

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The most commonly used pharmaceuticals in surface waters

When pharmaceuticals reach surface water, they can act toxically at all levels of the biological hierarchy: cell, organs, organisms, populations and ecosystems. Apart from their toxic effects, some pharmaceuticals, such as antibiotics, can cause long-term and irreversible changes in the genome of microorganisms and become resistant to antibiotics at low concentrations. Table 1 shows the most commonly used pharmaceuticals and their concentration in wastewaters.

Analgesics:

- Acetaminophen / Paracetamol: analgesic and antipyretic used to relieve headaches, pains and fever
- Diclofenac: relieves pain, inflammation and menstrual cramps
- Ibuprofen: relieves fever, headache, toothache, back pain
- Ketoprofen, Naproksen: relaxation in rheumatoid arthritis, osteoarthritis, menstrual cramps

Antihyperlipidemics:

- reduce cholesterol and triacylglycerol production and increase the production of saturated fatty acids ("good" cholesterol), include bezafibrate, clofibric acid and gemfibrozil

Antibiotics:

- Ciprofloxacin and Erythromycin: Treatment of infections caused by gram-positive and gram-negative bacteria
- Sulfamethoxazole: an antibiotic often prescribed in combination with trimethoprim and used to treat urinary tract infections, bronchitis and ear infections
- Triclosan: an antimicrobial substance that is found in soaps and toothpaste

EDC (*endocrine disrupting compounds*), substances that directly affect the endocrine system of people and cause major problems with the thyroid, diabetes, osteoporosis and many other hormone-related problems, also represent a great health problem (Bredhult et al., 2007). These are mostly organic synthetic organic chemicals that appear in the anthropological environment (surfactants, pesticides, pharmaceuticals, etc.), while some appear naturally (eg estrone, 17 β-estradiol) (Richardson, 2005; Nieuwenhuijsen, 2005; Andrzejewski et al., 2005; Cancho, Ventura, 2005).

Due to the increasing concentrations of these compounds in wastewaters, three pharmaceuticals: ethinyl estradiol, β-estradiol and diclofenac are found in the so-called. "Priority Pollutant List" of the EU Water Framework Directive (European Commission, 201; Zenker et al., 2014).

Other substances: bisphenol A, caffeine - a natural stimulant in coffee, tea and guarans, antiepileptic carbamazepine. Fig. 1 shows the most common pharmaceuticals in surface waters and their structures.

Table 1. Pharmaceuticals mostly present in wastewaters and their concentrations (Al-Rifai et al., 2007; Gomez et al., 2007; Santos et al., 2007; Vieno et al., 2007)

Antibiotics	Sulfonamides: sulfamethoxazole (0.02-0.58 μg/L) Florokinones: ofloxacin (6-52 ng/L), ciprofloxacin (6-60 ng/L) Bacteriostatic: trimethoprim (0.11-0.37 μg/L) Penicillin group: penicillin G (0.025 μg/L)
Analgesics/Antipyretics	Acetaminophen (10-23.33 μg/L), diclofenac (0.01-510 μg/L), naproxen (0.5-7.84 μg/L), ibuprofen (0.49-990 μg/L), ketoprofen (0.13-3 μg/L) carbamazepine (0.1-1.68 μg/L)
CNS stimulants	Caffeine (3.2-11.44 μg/L)
Cardiovascular disease medicines	Propranolol (0.05 μg/L), atenolol (10-730 ng/L), metoprolol (10-390 ng/L), Chlofibric acid (0.47-170 μg / L), gemfibrozil (0.3-3 μg/L), fezafibrat (0.1-7.60 μg/L)
Endocrinological treatments	17α-ethinylestradiol (1 μg/L), estrone, 17β-estradiol, estriol (10 μg/L)
Diagnostic organic halogen compounds	Iopromide (0.026–7.5 μg/L), Iomeprol (1.6 μg/L)

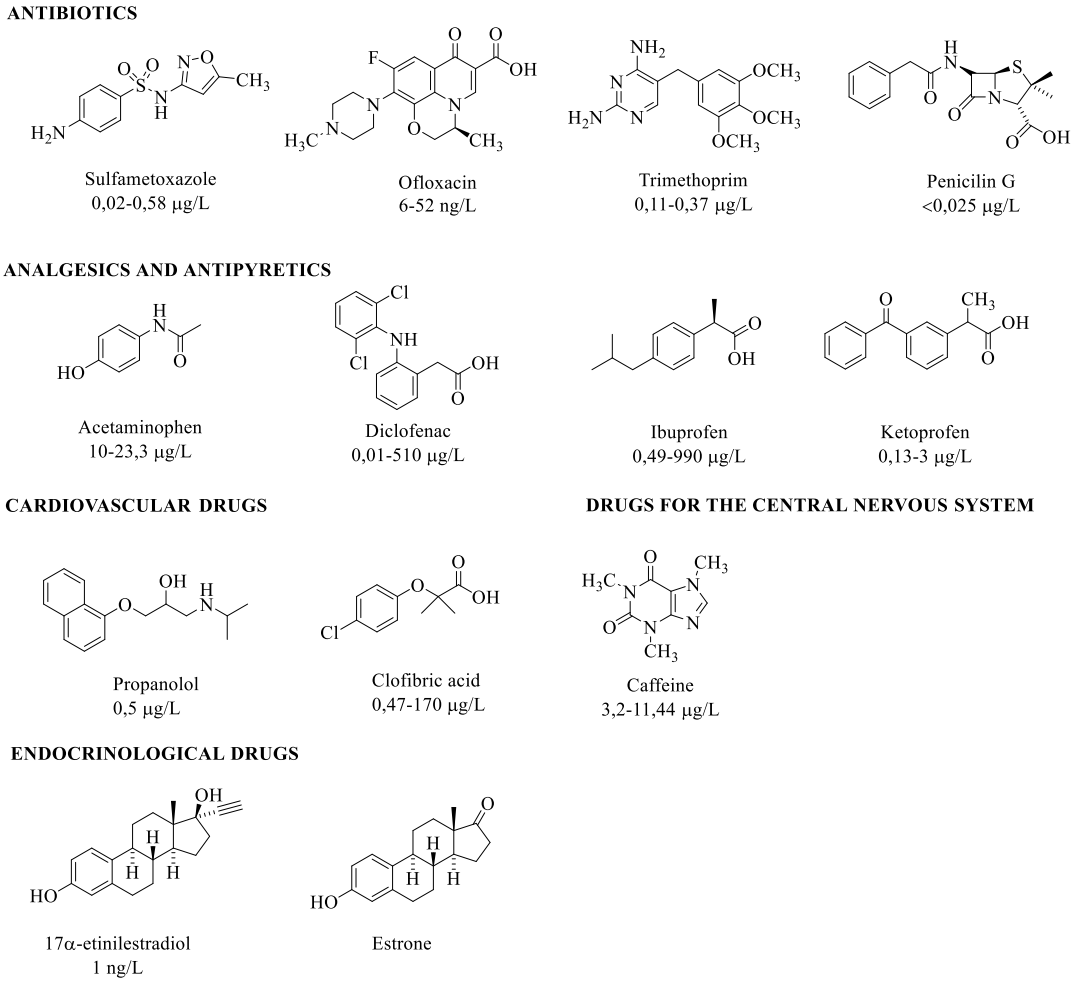

Fig. 1. Pharmaceuticals mostly present in surface waters

Behaviour of pharmaceuticals in surface water

Once they end up in aquatic ecosystems, pharmaceuticals undergo the process of degradation. Biodegradation (microorganisms: bacteria and fungi) and abiotic processes (hydrolysis and photocatalytic degradation) are the most significant degradation processes, and they are determined by physical and chemical properties like octanol / water distribution coefficient, the distribution coefficient, the ionisation constant and the coefficient of organic carbon sequestration (Periša and Babić, 2016). The degradation process results in the reduction in the concentration of the initial molecule of pharmaceuticals and the formation of degradation and transformation products. Transformation implies a change in the structure of the starting molecule of pharmaceuticals, while decomposition results in the formation of new compounds with different molecular mass.

Bacteria are responsible for biological degradation in surface water (Kummerer, 2008). Pharmaceuticals are used by microorganisms as building blocks and in catabolism degradation as the only source of energy and carbon. Unlike catabolic, cometabolic degradation takes place in the presence of growth substrates such as glucose or methanol at low pharmaceutical concentrations. Considering that pharmaceuticals are mainly traceable in surface waters, it can be concluded that cometabolic degradation will be performed (Onesios et al., 2009; Grenni et al., 2013).

Pharmaceuticals can be fully mineralized by the biological degradation to carbon dioxide and inorganic salts, or degradation may be only partial, and in this case, the products may be more stable than the initial molecules of pharmaceuticals with different, new toxic properties.

If pharmaceuticals are resistant to microorganism degradation, the environment may be subjected to abiotic degradation, hydrolysis or photolytic degradation processes.

Although there is paucity of literature on hydrolytic stability of the pharmaceuticals, hydrolysis degradation is significant in some antibiotics that have been found to be unstable in water. According

to Alexy and Kummerer (2006), penicillin leads to the opening of the β-lactam ring by the hydrolysis process or the activity of β-lactamase, a bacterial enzyme.

In surface waters that have access to sunlight, photolytic degradation of pharmaceuticals is most common due to aromatic rings, π-conjugated systems, heteroatoms and nitro, phenolic and naphthoxyl groups that can absorb solar radiation (290-800 nm) and are subject to photolytic degradation (Fatta-Kassinos et al., 2011; Boreen et al., 2003).

By absorbing the photon, the molecule goes into an excited state in which it remains shortly and after physical and chemical relaxation processes returns to its initial state. For photolytic degradation of pharmaceuticals, these processes that cause chemical changes in the initial molecule are essential and thus reduce their concentration in surface waters.

The pharmaceutical structure strongly influences its photolytic degradation.

Different behaviors have been observed in pharmaceuticals belonging to various drug groups, such as pharmaceuticals from the group of nonsteroidal anti-inflammatory drugs (diclofenac) and antibiotics (triclosan). Pharmaceutics belonging to the same group or having a similar structure may also behave quite differently. In natural waters this can be attributed to the dissolved organic matter and nitric ions, which are present in the natural environment (Packer et al., 2003).

Fig. 2 shows the reactions of diclofenac and triclosan photolysis. Diclofenac degradation products are formed by decarboxylation and loss of chlorine and formation of carbon-carbon bonds within the ring to form carbazole. Further products are then formed by degradation of the initial intermediates.

Triclosan decomposition also results in numerous products formation after elimination of chlorine atoms and dehydroxylation (Arnold and McNeill, 2007).

Except for the initial pharmaceuticals, it is important to identify and determine the structure of its degradation products as they may be more stable and toxic than the starting molecule and potentially have a negative effect on the environment.

Physico-chemical processes for surface water purification

Most of the pharmaceuticals that end up in surface water are resistant to these degradation processes due to their harmful and toxic effects on humans and other organisms. For this reason, they should be completely removed and higher priority should be given to research on more sophisticated, non-biological methods of water purification.

A large number of studies are concerned with purification methods using membrane bioreactors (Jones et al., 2007; Masse et al., 2006; Raif et al., 2013) and filtration methods: ultrafiltration, nanofiltration and reverse osmosis (Dolar and Košutić, 2013). However, advanced oxidation processes (AOP's) have been shown to be most effective.

The advanced oxidation processes are processes in which energy, either chemical, electrical, or radiation energy, results in the formation of highly reactive hydroxyl radicals, in an amount sufficient to break down most of the organic compounds. The following processes are included in the AOP: heterogeneous and homogeneous photocatalysis based on near-ultraviolet (UV) radiation, electrolysis, ozonization, processes under the influence of ultrasound in which Fenton reagent is used, but also less conventional methods such as wet oxidation, ionization and microwave radiation (Klavarioti et al, 2009).

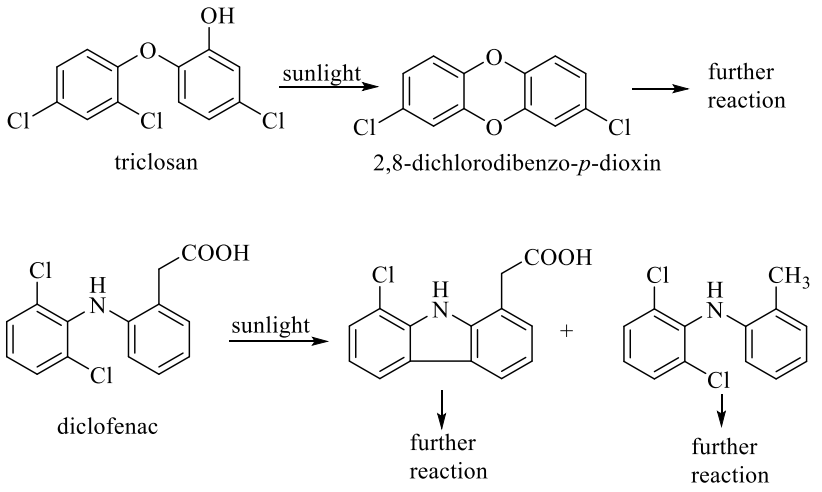

Fig. 2. Selected photolysis pathways for triclosan and diclofenac (Arnold and McNeill, 2007)

Table 2 shows the AOP, mechanism of their activity and the advantages and disadvantages of their application in water purification.

For wastewater from hospitals and pharmaceutical industries where pharmaceutical concentrations are higher and are expressed even in g/L, finding the appropriate purification method is of great importance.

Conclusions

Pharmaceuticals, important group of the so-called new pollutants for which there is no legal regulation on their release into the environment, find different pathways in changing the environment. Considering their resistance to purification by conventional methods such as biological treatment or abiotic processes, more effective invasive purification methods such as advanced oxidation processes are necessary to apply. However, due to expensive equipment, they are often unavailable.

In addition, in order to reduce the unnecessary release of pharmaceuticals into the environment, preventive action is needed, as well as education for pharmaceutical users.

Table 2. *AOP's* mechanism of their action and the advantages and disadvantages of their application in water purification

UV	$R\text{-}R + h\nu \rightarrow R\text{-}R \rightarrow 2R^{\bullet}$ $R\text{-}R^{*} + O_2 \rightarrow R\text{-}R^{\bullet} + O_2^{\bullet}$ $^{3}DOM^{*} + {}^{3}O_2 \rightarrow DOM + {}^{1}O_2$	• Direct irradiation leads to molecular transition from basic to the excited singlet state. The resulting radicals induce chain reactions; e.g. radicals with unsaturated electrons on carbon atom ($R^{\bullet}$) are reacting with dissolved oxygen to form alkylperoxyl ($RO_2^{\bullet}$) and alkoxy ($RO^{\bullet}$) radicals • Photolysis (indirect or sensitized) is preferred in the presence of natural substances in the system (e.g., dissolved organic matter acting as a photosensitizer, producing strong reactive intermediates, e.g. singlet oxygen ($^{1}0_2$) and hydroxyl radical ($HO^{\bullet}$)) • Disadvantages: UV with lamp is expensive
UV/H_2O_2	$H_2O_2 + hv \rightarrow HO^{\bullet} + HO^{\bullet}$ $HO^{\bullet} + H_2O_2 \rightarrow HO^{\bullet}_2 + H_2O$ $HO^{\bullet}_2 + H_2O_2 \rightarrow HO^{\bullet} + H_2O + O_2$	• hydroxyl radicals are formed by photolytic cleavage of H_2O_2 • high concentration of H_2O_2 influences the increase of the free radical movement thus making the process less effective • disadvantages: low formation of radicals caused by low molar extinction coefficient H_2O_2
O_3	$O_3 + R \rightarrow R_{OH}$ $2O_3 + 2H_2O \rightarrow 2HO^{\bullet} + O_2 + 2HO^{\bullet}_2$	• In the absence of light, ozone can directly react with organic substrate (R) by slow and selective reactions or by rapid and non-selective radical reactions in which hydroxyl radicals are formed • Disadvantages: low water solubility O_3, O_3 is selective, formation of byproducts (bromate), high costs
H_2O_2/O_3	$O_3 + H_2O_2 \rightarrow HO^{\bullet} + O_2 + 2HO^{\bullet}_2$	• H_2O_2 promotes decomposition of O_3 by electron transfer • Disadvantages: additional costs for H_2O_2 compared to using only O_3
UV/O_3	$O_3 + h\nu + H_2O \rightarrow H_2O_2 + O_2$ $O_3 + hv \rightarrow O_2 + O(^{1}D)$ $O(^{1}D) + H_2O \rightarrow 2HO^{\bullet}$	• The resulting hydrogen peroxide breaks down by photolysis on the hydroxyl radicals and reacts with the excess of ozone • If $\lambda < 300$ nm, ozone photolysis occurs, producing additional hydroxyl radicals and other oxidants with subsequent increase in efficiency • Disadvantages: high operating costs
$UV/H_2O_2/O_3$	$O_3 + H_2O_2 + h\nu \rightarrow O_2 + HO^{\bullet} + HO^{\bullet}_2$	• By adding light to H_2O_2 / O_3 processes, efficiency is increased with additional formation of hydroxyl radicals • Disadvantages: increased costs
UV/TiO_2	$TiO_2 + h\nu \rightarrow TiO_2 (e^{-}_{ca} + h^{+}_{va})$ $HO^{-} + h^{+}_{va} \rightarrow HO^{\bullet}$ $O_2 + e^{-}_{ca} \rightarrow O^{\bullet}_2{}^{-}$	• When the semiconductor particle wakes up with light energy, energy shortages emerge • Disadvantages: low quantitative yield, catalyst removal and regeneration
Fenton	$Fe^{2+} + H_2O_2 \rightarrow Fe^{2+} + HO^{-} + HO^{\bullet}$	• Fenton processes include the use of H_2O_2 and catalysts, usually iron (Fe^{2+} or Fe^{3+} ion) in the acid medium • Fe^{2+} oxidation leads to the formation of hydroxyl radicals • Disadvantages: low pH (2.8 - 3.0), removal of metal is needed
Photo-Fenton	$Fe^{2+} + H_2O \rightarrow Fe^{2+} + H^{+} + HO^{\bullet}$	• Photo-Fenton processes include solar irradiation or artificial light source. In the presence of light, the process may be more effective by photoreducing Fe^{3+} in Fe^{2+} and creating additional hydroxyl radicals • Disadvantages: low pH (2.8 - 3.0) needed for iron removal. Additional costs for UV radiation • Solar Fenton has attracted additional interest due to solar radiation, which would further reduce process costs

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