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# Effectiveness of degradation and removal of non-steroidal pharmaceuticals which are the most frequently identified in surface water

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**ABSTRACT**

Pharmaceuticals are quite common but very harmful environmental contaminants. Major part of them are non-steroidal compounds. Data on the risk connected with the presence of such contaminants in surface waters are scattered; however, it was confirmed that one of the important sources of these micropollutants are wastewater treatment plants. Because of this preventive action not only monitoring should be recommended. For recommendation, detailed knowledge not only on effects but also on removal efficiencies is necessary. The aim of this study is to describe the possibilities of degradation and removal of 10, the most frequently present in surface waters, non-steroidal pharmaceuticals. Removal effectiveness of pharmaceutical can be in the range from several to even 100% and is affected by properties of individual compounds, treatment technology, and technological parameters. The most effective processes seem to be advanced oxidation processes.

*Keywords:* Pharmaceuticals; Toxicity; Removal; Biodegradation; Physical processes; Chemical processes

## 1. Introduction

Pharmaceuticals are particularly harmful for the water organisms because they are biologically active substances which affect metabolic pathways. Major part of them are non-degradable compounds because of the fact that they are designed to be resistant in the acid environment of gastric juices and also to be long lasting. Pharmaceuticals are not completely metabolized in the organisms, thus they are discharged to wastewaters and to the environment both in the form of by-products and as a baseline active substances [1,2]. Pharmaceuticals are more than 4,000 active compounds, whereas the amount of commercial products reaches 10,000. Major part (about 34%) of the medicines which are available on the world market are the non-steroidal compounds [1]. According to the report of IWW [3], the non-steroidal pharmaceuticals which have been the most frequently found in the aquatic environment of all UN regional groups are diclofenac, carbamazepine, ibuprofen, sulfamethoxazole, naproxen, trimethoprim, paracetamol, clofibric acid, ciprofloxacin, and ofloxacin. Because of their properties, pharmaceuticals are included in the list of the emerging pollutants in European Union. In 2010, pharmaceuticals in the environment, called environmental persistent pharmaceutical pollutants, were suggested as an emerging issue in a Strategic Approach to International Chemicals Management. This indicates that scientific and political committees have noted the seriousness of the situation. As it was found in the ISDE Nomination Report [2], with exception of downstream wastewater treatment plants (WWTPs), concentrations of pharmaceuticals in surface waters are rather low (<0.1 μg/L), although it does not mean they are safe. It however clearly indicates the serious problem which is connected with discharging the WWTPs effluents to the environment. It simultaneously indicates the way to deal with the problem—we can "catch" and remove a major part of harmful pharmaceuticals at WWTP. It is also possible in the case of other abundant source of micropollutants—landfills. The importance of WWTPs and landfills for the pollution of surface waters by pharmaceuticals is shown in Fig. 1.

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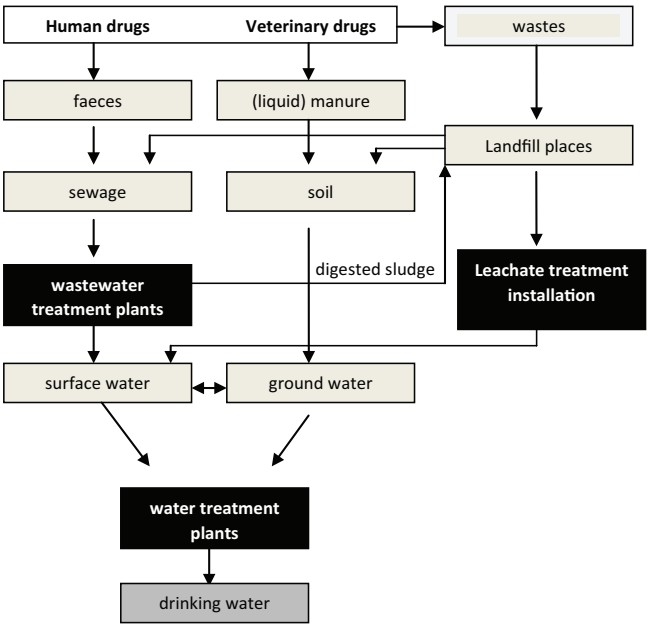



Fig. 1. Possible ways of the pharmaceuticals release into surface water.

Despite this obvious fact that prevention is better than treatment, most research and review articles are focused on toxicological properties of the pharmaceuticals or on effectiveness of their removal in particular processes. They also usually describe the groups of the pharmaceuticals set based on their medicinal properties. There are a few articles which concern both threats for living organisms and remediation techniques. The aim of this study is to describe the possibilities of degradation and removal of 10, the most frequently present in surface waters, non-steroidal pharmaceuticals.

## 2. Physicochemical and toxicological properties of the non-steroidal pharmaceuticals, the most frequently present in surface waters

Table 1 presents selected physicochemical properties of the non-steroidal compounds, the most frequently present in surface water samples, according to the report of IWW [3].

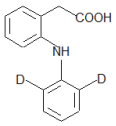
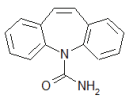
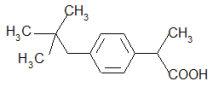
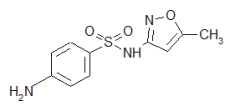
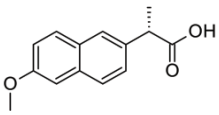
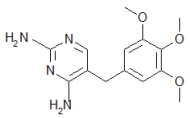
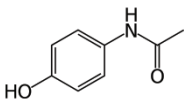
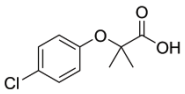
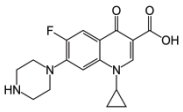
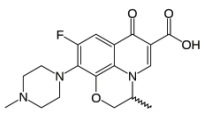
They differ a lot in terms of water solubility (from 2.37 mg/L for diclofenac to 30,000 mg/L for ciprofloxacin) and affinity to solid particles (defined based on log Kow value). The log Kow values in all cases are lower than 4.0. It means that all compounds considered in the article do not show high adsorption potential, and they are likely to stay in the aqueous phase.

Data on toxicological properties of the described chemicals are included in Table 2. Both the data on chronic and acute toxicity for water organisms (fish, invertebrates, algae, or plants) have been included. Taking into account aquatic toxicity EC50 or LC50 given in the study by USFW [5] (super toxic, <0.01 mg/L; extremely toxic, 0.01–0.1 mg/L; highly toxic, 0.1–1 mg/L; moderately toxic, 1–10 mg/L; slightly toxic, 10–100 mg/L; practically nontoxic, 100–1,000 mg/L; and relatively harmless, >1,000 mg/L), the considered pharmaceuticals can be classified as in Table 3. As can be seen from the collected data, based on acute toxicity parameters for water organisms, the considered pharmaceuticals can be classified mainly as slightly and moderately toxic. Highly toxic ones are only sulfamethoxazole and ofloxacin. These two compounds are antibiotics, but they differ a lot in terms of water solubility and log Kow.

The organisms which were the most sensitive to the pharmaceuticals were various depending to the compound. This is connected with the fact that drugs which are considered in the article belong to various groups of chemicals. Acute effects are usually rather low because of the fact that pharmaceuticals are mainly designed to act in human or other mammalian organisms, not for water ones, for example, antiepileptic drug carbamazepine acts by blocking the voltage-dependent sodium channels of excitatory neurons or by increasing inhibitory effect of gamma-aminobutyric acid. This acid has been found in fish and aquatic invertebrates but no in algae [6]. This is the reason why *Danio rerio* is the organism which is the most sensitive to carbamazepine. Despite the mechanism of action, carbamazepine is however also toxic for green algae *Selenastrum capricornutum*. No observed effect concentration (NOEC) values for the considered pharmaceuticals are at level from 0.006 mg/L (sulfamethoxazole, algae) to 100 mg/L (ciprofloxacin and trimethoprim, fish). In most cases, the concentrations of the pharmaceuticals observed in effluents (Table 4) are lower than NOEC values. It, however, does not mean that effluents are safe for water environment. It should be emphasized that chronic tests on NOEC usually last only for 7–21 d and do not take into consideration cumulative effects and generation of the metabolites. In the environment, pharmaceuticals pose a serious risk. This is the reason why we should not only control the concentrations in surface waters but in particular consider various removal methods (both biological and physicochemical). Concentrations of 10, the most frequently used, pharmaceuticals in WWTPs influents and landfill leachates (Table 4) vary a lot. It is difficult to find correlation between the type of influent and concentration of pharmaceuticals. Also no correlation can be found in the case of landfill leachates. The problem, especially when we consider landfill leachates, is that the available data are insufficient. Available data suggest that one of the most abundant pharmaceuticals in influents and landfill leachates are ibuprofen and paracetamol, thus these kinds of wastewater can be reservoirs of over-the-counter medicines. The less abundant ones are, for example, trimethoprim and ofloxacin. These data cannot be however considered to be reliable for all influents and landfill leachates and should be experimentally examined for individual installations.

When we consider the possibilities of pharmaceuticals biodegradation, it is important to know also the toxicity for the bacteria, because they are the main group of microorganisms involved in treatment processes. Available data indicate that pharmaceuticals discussed in the article affect microorganisms (bioluminescent inhibition EC50) at concentrations equal to at least several mg/L, for example, ibuprofen 11.3 mg/L, naproxen 18.5 mg/L, and carbamazepine 28.3 mg/L [7]. Carbamazepine NOEC for *Vibrio fischeri* was found to be 8.9 mg/L (bioluminescence) [8], whereas EC50 for these bacteria was equal to 64 mg/L. In ready biodegradability test percentages of transformations were stated for the following pharmaceuticals: paracetamol, 57%–99%; ibuprofen,

Table 1
Characteristics of pharmaceuticals which are the most frequently analyzed in surface waters [4]

| Compound | IUPAC name | Structure | Group | Water solubility, mg/L | Log Kow |
|---|---|---|---|---|---|
| Diclofenac | o-N-(2,6 Dichloroplenyl) aminophenylacetic acid |  | Analgesics | 2.37 (at 25°C) | 1.90 |
| Carbamazepine | Benzo[b][1]benzaze-pine-11-carboxamide |  | Antiepileptic | 17.7 | 1.51 |
| Ibuprofen | (RS)-2-[4-(2-methylprophyl)phenyl] propanoic acid |  | Analgesics | 21 (at 25°C) | 2.48 |
| Sulfamethoxazole | 4-Amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide |  | Antibiotics | 610 (at 37°C) | 0.89 |
| Naproxen | (2S)-2-(6-Methoxy-2-naphthyl) propanoic acid |  | Analgesics | 15.9 (at 25°C) | 3.18 |
| Trimethoprim | 5-[(3,4,5-Trimethoxyphenyl)methyl] pyrimidine-2,4-diamine |  | Antibiotics | 400 (at 25°C) | 0.91 |
| Paracetamol (acetaminophen) | N-Acetyl-p-amino-phenol |  | Analgesics | 14,000 (at 25°C) | 0.46 |
| Clofibric acid | 2-(4-Chlorophe-noxy)-2-methylpropanoic acid |  | Lipid-lowering | 583 (at 20°C) | 2.57 |
| Ciprofloxacin | 1-Cyclopropyl-6-fluoro-4-oxo-7-piperazin-1-ylquinoline-3-carboxylic acid |  | Antibiotics | 30,000 (at 20°C) | 0.28 |
| Ofloxacin | 9-Fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-[1,4]oxaz-ino[2,3,4-ij]quinoline-6-carboxylic acid |  | Antibiotics | 28,300 | –0.39 |

10%–60% to >90%; diclofenac, 22%–93%; ciprofloxacin, 0%; trimethoprim, 4%; and sulfamethoxazole, 0%–4% [9].

## 3. Degradation and removal of the considered pharmaceuticals in WWTPs

As can be seen from Fig. 1, major part of pharmaceuticals can be potentially removed or degraded before discharge into the environment from WWTPs and treatment units situated in dumping sites. Municipal wastewater is regarded to be a main source of pharmaceuticals and their metabolites in water environment. Especially high loads of pharmaceuticals are discharged to sewer systems from hospitals. Spare and expired compounds may also drain off the landfills and migrate to the ground and surface waters. Sources of the veterinary pharmaceuticals are mainly farms. Part of them is treated with sewage, but the ones present in manure can be rinsed off to the surface water; they also can infiltrate to the groundwater. The significant limitation, both in the monitoring of these compounds in the environment and in their degradation or removal, is the fact that despite the basic form of bioactive substance also the by-products of different chemical properties occur in wastewater. It was proved that bioconversion of pharmaceuticals (and other xenobiotics)

Table 2
Data on chronic and acute toxicity of selected pharmaceuticals to water organisms

| Compound | Levels of long-term toxic effects (96 h and more) for water organisms, mg/L | | Levels of acute toxicity for water organisms, mg/L | | Reference |
|---|---|---|---|---|---|
| Diclofenac | NOEC (Rainbow throut) | 0.320 | EC50 (*Lemna minor*) | 7.5 | [9,12–17] |
| | NOEC (*Danio rerio*) (20 d) | 5 | EC50 (48 h) (*Daphnia magna*) | 22.4–68 | |
| | LOEC (*Oncorhynchus mykiss*) (28 d) | 0.001 | LC50 (*O. mykiss*) | 1–4 | |
| | LOEC (*D. rerio*) (20 d) | 15 | | | |
| | NOEC (*Ceriodaphnia dubia*) (diclofenac sodium) | 1 | | | |
| | NOEC alga | 10 | | | |
| Carbamazepine | NOEC (*D. rerio*) | 12.5 | EC5 (*Desmodesmus subspicatus*) | 85 | [7,8,18] |
| | NOEC (*D. magna*) | 0.4 | | | |
| | NOEC (*S. capricornutum*) (96 h) | 0.52 | EC50 (*Selenastrum capricornutum*) (96 h) | 48.9 | |
| | NOEC (*Chlorella vulgaris*) | 11.8 | | | |
| | NOEC (*Pseudokirchneriella subcapitata*) | 0.5 | | | |
| | | | EC50 (*D. magna*) | 157 | |
| | | | EC50 (*C. dubia*) | 77.7 | |
| | | | LC50 (*D. rerio*) | 35.4 | |
| Ibuprofen | NOEC (*Lepomis macrochirus*) | 10 | EC50 (*S. capricornutum*) (96 h) | 2.3 | [7,12,19–21] |
| | LOEC (*Jordanella floridae*) | 0.1 | EC50 (*D. subspicatus*) | 342 | |
| | NOEC (*Americamysis bahia*) | 30 | EC50 (*D. magna*) (48 h) | 108 | |
| | NOEC (*D. magna*) | 40–72 | LC50 (*L. macrochirus*) | 173 | |
| | NOEC (*S. capricornutum*) (96 h) | 0.52 | | | |
| | NOEC (*Lemna gibba*) | 1 | | | |
| | NOEC (*P. subcapitata*) | 40.7–72.9 | | | |
| Sulfamethoxazole | NOEC fish | >8 | EC50 (*P. subcapitata*) | 0.52 | [9,17] |
| | NOEC (*Daphnia* sp.) | 0.25 | IC50 (*Brachionus calyciflorus*) (48 h) | 0.63 | |
| | NOEC alga | 0.006 | | | |
| | | | EC50 (*D. magna*) (48 h) | 149.3 | |
| | | | EC50 (*D. magna*) (96 h) | 85.4 | |
| | | | LC50 (*Oryzias latipes*) (96 h) | 562.5 | |
| Naproxen | LOEC (*J. floridae*) | 0.1 | EC50 (*S. capricornutum*) (96 h) | 3.7 | [7,17,21,22] |
| | NOEC (*Lumbriculus variegatus*) (96 h) | 3.2 | EC50 (*P. subcapitata*) (96 h) | 39 | |
| | LOEC (*D. magna*) (21 d) | 0.15–0.47 | EC50 (*D. magna*) (48 h) | 174 | |
| | NOEC (*S. capricornutum*) (96 h) | 0.52 | LC50 (*Hyalella azteca*) (96 h) | 383 | |
| | NOEC (*P. subcapitata*) (72 h) | 6.2 | LC50 (*L. macrochirus*) (96 h) | 560 | |
| | LOEC (*P. subcapitata*) (72 h) | 12 | | | |
| Trimethoprim | NOEC fish | 100 | EC50 algae or water plants | 16–110 | [9,17,23,24] |
| | NOEC (*Poecilia reticulata*) | 3–25 | EC50 (*Daphnia* sp.) | 123 | |
| | NOEC (*D. magna*) | 3.12 | EC50 (*D. magna*) (48h) | 167.4 | |
| | NOEC (*S. capricornutum*) (96 h) | 25.5 | LC50 (*O. latipes*) 96 h | > 100 | |
| Paracetamol (acetominophen) | LOEC (*O. latipes*) | 95 | EC50 (*Scenedesmus subcapitatus*) (72 h) | 134 | [25–27] |
| | NOEC (*D. magna*) (survival) | 5.72 | | | |
| | LOEC (*S. capricornutum*) | >0.032 | EC50 (*D. magna*) (96 h) | 26.6 | |
| | | | LC50 (*O. latipes*) (96 h) | >160 | |
| Clofibric acid | NOEC (*D. rerio*) | 70 | EC50 (*S. subcapitatus*) (72 h) | 89 | [17,23,27,28] |
| | NOEC (*Palaemonetes pugio*) | <1 | EC50 (*D. magna*) (48 h) | 72 – >200 | |
| | LOEC aquatic plants | >1.0 | LC50 (*Gambusia holbrooki*) (96 h) | 7.7 | |
| | NOEC (*P. subcapitata*) | 75 | | | |
| | NOEC (*C. dubia*) | 0.64 | | | |
| Ciprofloxacin | NOEC fish | 100 | EC50 (*C. vulgaris*) (96 h) | 20 | [9,17,23] |
| | NOEC (*Daphnia* sp.) | 60 | EC50 (*P. subcapitata*) (72 h) | 2.97 | |
| | LOEC (L. gibba) | 0.3 | EC50 (*Daphnia* sp.) | >10 | |
| | | | EC50 (*D. magna*) (48 h) | >60 | |
| | | | LC50 (*D. rerio*) (96 h) | >100 | |
| Ofloxacin | NOEC (*D. rerio*) | 26.7 | IC50 (*P. subcapitata*) (72 h) | 1.44 | [23,27] |
| | NOEC (*C. dubia*) (7 d) | 10 | IC50 (*B. calyciflorus*) (48 h) | 0.53 | |
| | LOEC (*L. gibba*) | 0.3 | EC50 (*D. magna*) (24 h) | 31.75 | |
| | | | LC33.5 (*D. rerio*) (96 h) | 1,000 | |

LOEC, Lowest observed effect concentration.

in living organisms has two stages. The first stage includes mainly adsorption and transport into cytoplasm, and it is followed by oxidation, reduction, and hydrolysis or other reactions (e.g., of synthesis with glukoron acid, sulfates, and amino acids [10]. They can also undergo abiotic degradation. These processes can also be used for removal of xenobiotics, including pharmaceuticals in treatment units. The effectiveness of removal of most medicines in WWTPs can be in the range of 0%–98% (Table 5). Ibuprofen and naproxen, the most abundant of the examined compounds in the influent, were efficiently removed from wastewater in WWTP. During treatment of wastewater, the part of pharmaceutics undergo biodegradation, another part is adsorbed onto solid particles (both organic and inorganic). The compounds which are sorbed are accumulated in sludge. The part of pharmaceuticals and their metabolites retain in treated wastewater. The fates of individual compounds depend on the type of wastewater treatment and the properties of the pharmaceuticals, for example, it was proved that the acid pain-killer medicines such as ibuprofen and diclofenac in neutral environment hardly ever are sorbed on solid particles whereas the alkaline pharmaceutics are easily sorbed onto sludge.

The crucial issue, however, is to identify the processes (biological and abiotic) which are involved in medicines removal from wastewater.

Table 3
Classification of 10 the most frequently used pharmaceuticals according to their acute toxicity

| Pharmaceutical | Toxicity classification to water organisms | The most sensitive to pharmaceutical group of organisms |
|---|---|---|
| Diclofenac | Moderately toxic | Fish |
| Carbamazepine | Slightly toxic | Fish |
| Ibuprofen | Moderately toxic | Algae |
| Sulfamethoxazole | Highly toxic | Algae |
| Naproxen | Moderately toxic | Algae |
| Trimethoprim | Slightly toxic | Algae or water plants |
| Paracetamol | Slightly toxic | Invertebrates |
| Clofibric acid | Moderately toxic | Fish |
| Ciprofloxacin | Slightly toxic | Invertebrates |
| Ofloxacin | Highly toxic | Rotifers |

### 3.1. Biodegradation of selected pharmaceuticals

Pharmaceuticals such as considered in the article can be biologically degraded both under aerobic and anaerobic conditions. The pharmaceuticals described in the article were divided into three groups: highly toxic for water organisms (sulfamethoxazole and ofloxacin), moderately toxic (diclofenac, ibuprofen, naproxen, and clofibric acid), and slightly toxic (carbamazepine, trimethoprim, paracetamol, and ciprofloxacin).

#### 3.1.1. Aerobic processes

Removal of the considered pharmaceuticals occurred both in activated sludge systems and in biological beds. Not only classical processes were used but also hybrid and supported with physicochemical processes were considered.

Table 4
Data on landfill leachate, influent, and effluent concentrations of selected pharmaceuticals

| Compound | WWTPs influent, μg/L | WWTPs effluent, μg/L | Landfill leachate, μg/L | Reference |
|---|---|---|---|---|
| Diclofenac | 0.123 ÷ 3.0 | 0.06 ÷ 5.45 | 1.183 ÷ 3.19 | [30–35] |
| Carbamazepine | 0.59 ÷ 1.18 | 0.1 ÷ 1.5 | 0.008 ÷ 1.415 | [33–35] |
| Ibuprofen | 0.193 ÷ 39.8 | 0.013 ÷ 2.1 | 0.07 ÷ 124 | [32,33,35–37] |
| Sulfamethoxazole | <0.04 ÷ 0.391 | <0.038 ÷ –0.211 | Not detected | [32,38,39] |
| Naproxen | 0.6 ÷ 40.7 | Not detected ÷ 12.5 | <0.001 ÷ 2.0 | [33–35,37] |
| Trimethoprim | 0.025 ÷ 2.775 | <0.002 ÷ 1.26 | Not detected | [32,38] |
| Paracetamol (acetaminophen) | 1.746 ÷ 43.223 | 0.02 ÷ 4.319 | 2.7 ÷ 117 | [32,39,40] |
| Clofibric acid | 0.15 ÷ 0.34 | 0.15 ÷ 0.88 | 2.658 ÷ 2.879 | [33,35] |
| Ciprofloxacin | <0.019 ÷ 5.876 | <0.038 ÷ 0.211 | 0.269 | [32,35,41] |
| Ofloxacin | <0.005 ÷ 0.51 | <0.0086 ÷ 0.2 | No data available | [31,41] |

Table 5
Removal effectiveness of selected pharmaceuticals in WWTPs

| Pharmaceuticals | Concentration, μg/L [42] | | | Concentration, μg/L [43] | |
|---|---|---|---|---|---|
| | Primary effluents | Secondary effluents | Final effluents | Influent | Effluent |
| Ibuprofen | 17 ÷ 30 | <0.01 ÷ 0.02 | 0.01 ÷ 0.02 | 1.681 ÷ 33.764 | 0.380 |
| Naproxen | 12 ÷ 15 | <0.010 ÷ 0.013 | 0.013 ÷ 0.027 | 0.838 ÷ 1.173 | 0.170 ÷ 0.370 |
| Sulfamethoxazole | 0.65 ÷ 1.900 | 0.480 ÷ 1.500 | 0.370 ÷ 1.500 | 0.003 ÷ 0.115 | 0.010 ÷ 0.019 |
| Carbamazepine | 0.160 ÷ 0.260 | 0.19 ÷ 0.340 | 0.180 ÷ 0.310 | 0.950 ÷ 2.593 | 0.826 ÷ 3.117 |
| Diclofenac | <0.120 | <0.096 | <0.063 | 0.069 ÷ 1.500 | 0.058 ÷ 0.599 |

*3.1.1.1 Activated sludge* Highly toxic for water organisms, antibiotic sulfamethoxazole, was efficiently removed from wastewater (at initial concentration of 2 μg/L) under 12 h retention times both by suspended and granular activated sludge. Removal efficiencies for this pharmaceutical were 73% and 84%, respectively. Granular activated sludge was more effective in sulfamethoxazole removal because of higher concentration of biomass involved in biological processes. It was stated that removal mechanism of sulfamethoxazole was not by sorption, but by biological processes [44]. The second highly toxic compound considered in the article—ofloxacin—was also removed from the wastewater by activated sludge; however, the mechanism of the removal differed from the one for sulfamethoxazole. Ofloxacin was removed from wastewater mainly by sorption on activated sludge (granular activated sludge; sequencing bath bioreactor: 1 h feeding, ca. 2–7.5 h aeration; settling). Phenomenon of pharmaceutical release back to the wastewater was also observed; moreover, inhibition of nitrifying bacteria was stated [45].

In the case of moderately toxic diclofenac and clofibric acid, removal efficiency by classical activated sludge was poor. It was equal only 9% in the case of diclofenac and 45% in the case of clofibric acid [46]. Ibuprofen and naproxen were better susceptible to degradation. In classical activated sludge process, removal efficiencies for these compounds were higher than 74% [46]. The parameters of the process were as follows: influent concentration of compounds, 1 μg/L and hydraulic retention time (HRT), 48 h. Also, Gagnon and Lejeunesse [47] observed higher efficiency of ibuprofen removal by activated sludge (>95%) than diclofenac (5% ÷ 10%). Such pharmaceuticals as ibuprofen and diclofenac show high susceptibility to degradation by nitrifying activated sludge, even under low temperature (12°C) [48].

Slightly toxic carbamazepine was removed by classical activated sludge in 5% ÷ 21% under the same conditions as indicated above [46,47]. The results obtained by Zupanc et al. [46] and Gagnon and Lejeunesse [47] were confirmed also by Okuda et al. [49]. In conventional activated sludge system, they have obtained carbamazepine removal efficiency lower than 30%. Increase in this compound degradation effectiveness was, however, obtained by final ozonation.

Trimethoprim, despite its antibacterial properties, was removed by nitrifying activated sludge in 50% ÷ 70% and in 1% ÷ 25% by only heterotrophic activated sludge. It was probably connected with longer solid retention times in nitrifying activated sludge systems compared with the non nitrifying ones [50]. Paracetamol is also well degraded by activated sludge as with ciprofloxacin. Quintelas et al. [51] stated that removal efficiency of paracetamol at concentration within the range of 0.4 to 1 mg/L ranged from 93.3% to 98.8% and decreased as the initial concentration of the pharmaceutical increased. High removal efficiency of paracetamol by activated sludge was also stated by Karaman et al. [52]. They found that paracetamol can be decomposed among others by *Pseudomonas aeruginosa* present in activated sludge. Ciprofloxacin removal efficiency by activated sludge (anaerobic/aerobic sequential reactor system, HRT 10 d, organic load rate 0.19 g chemical oxygen demand/L/d) was 83% [53]. The results described above indicate that activated sludge effectively removes most compounds considered in the article. The removal effectiveness is connected with concentration of bacteria, species composition, and initial concentration of the compound and retention time.

*3.1.1.2. Biological beds* In biological bed systems, pharmaceuticals also can be effectively removed from wastewater. Based on the results available in research literature, it can be suggested that removal efficiency of pharmaceuticals in fixed bed reactors should be expected at level similar to the one in classical activated sludge systems. For example, Göbel et al. [54], in the case of sulfamethoxazole, stated that both classical activated systems and fixed bed reactor ensure similar removal effectiveness. In system with rotating discs (under lower oxygen concentration than in classical fixed bed reactor), lower removal efficiency was achieved [55]. In the case of slightly toxic compounds, such as trimethoprim, removal was at level <25% in rotating disk contactors. When concentration of oxygen available for bacteria was higher, removal efficiency increased [54]. While according to the results obtained by Delgado et al. [56], carbamazepine (at initial concentration 200 μg/L) was removed in biological rotating contactors at 20%, whereas removal efficiency of other organic compounds was at level 95% (at wastewater flow rate equal to 70 mL/min). The obtained results indicate that removal efficiency of carbamazepine in suspended biomass systems (activated sludge) and attached biomass systems (biological beds) is similar. No results of other considered pharmaceuticals removal in biological beds efficiency are available in scientific literature.

*3.1.2. Membrane biological reactors (MBRs) and hybrid processes*

Good effects of pharmaceuticals removal can be obtain using MBRs. The research works in MBRs were conducted, among others, by Cecconet et al. [57] (Table 6). Removal effectiveness by MBRs can reach even 99%; however, in the case of carbamazepine (slightly toxic) and diclofenac (moderately toxic) is minimal (it was also confirmed by Tiwari et al. [58]—Table 7). It was however rather high for highly toxic sulfamethoxazole.

Table 6
Effectiveness of selected pharmaceuticals removal from wastewaters in MBRs [57]

| Kind of wastewater | Scale | Compound | Removal effectiveness, % |
|---|---|---|---|
| Municipal | Technical | Paracetamol | 99 |
| | | Ibuprofen | 99 |
| Synthetic | Laboratory | Carbamazepine | Minimal |
| | | Ibuprofen | 100 |
| | | Diclofenac | Minimal |
| Hospital | Pilot | Ibuprofen | 100 |
| | | Naproxen | 82.3 |
| | | Trimethoprim | 80.1 |
| | | Sulfamethoxazole | 78.5 |

Comparison of selected pharmaceuticals removal by conventional activated sludge and MBRs (Table 8) indicates that in some cases MBRs slightly enhance removal of pharmaceuticals. Especially spectacular results were obtained in the case of sulfamethoxazole and ofloxacin, but in the case of the remaining compounds increases of the removal were not so spectacular.

Research studies on ibuprofen and diclofenac removal from wastewater performed by Langenhoff et al. [59] have indicated that in pilot membrane reactor installation (at initial concentration from 50 to 300 mg/L and wastewater flow from 10 to 25 $m^3$/h) ibuprofen was almost completely removed (to concentration lower than 0.01 g/L). Under the same conditions, diclofenac was also effectively removed from wastewater; however, its complete removal required use of activated carbon. The results showed that both diclofenac and ibuprofen were degraded. Bacteria species *Phanerochaete chrysosporium* were identified to be involved in degradation process. Luo et al. [60] used moving bed biofilm reactor (MBBR) technology with polyurethane sponge as a carrier medium. They have obtained removal efficiency of ibuprofen in 80% and of naproxen in 90%. They have stated that both biodegradation and sorption processes were involved in removal of pharmaceuticals. Sorption was important mechanism in the case of such pharmaceutical removal as carbamazepine and diclofenac. However, effectiveness of the carbamazepine and diclofenac biodegradation was at level 20%. According to the authors, removal efficiency of MBBR process was similar to the one obtained in conventional activated sludge and MBR.

Table 7
Effectiveness of pharmaceutical removal from wastewater by classical activated sludge and MBRs [58]

| Compound | Susceptibility for the biodegradation, % | Removal efficiency, % | |
|---|---|---|---|
| | | CAS | MBRs |
| Highly toxic | | | |
| Sulfamethoxazole | 50 ÷ 90 | 51.9 | 81 |
| Ofloxacin | 0 | 75 | 93.5 |
| Moderately toxic | | | |
| Diclofenac | 5 ÷ 45 | 50 | 32 |
| Naproxen | 55 ÷ 85 | 94 | 95 |
| Ibuprofen | 90 ÷ 100 | 99 | 99 |
| Slightly toxic | | | |
| Carbamazepine | <40 | <25 | 28 |
| Ciprofloxacin | 0 | – | 89 |
| Paracetamol | 100 | 99.1 | 99.8 |
| Trimethoprim | 90 | 90 | 90 |

CAS, Classical activated sludge.

Table 8
The efficiency of pharmaceutics removal from wastewater in various treatment processes [73]

| Pharmaceutical | Comparison of the efficiency of pharmaceuticals removal, ng/L | | |
|---|---|---|---|
| | Activated sludge | MBBR | Coagulation and flocculation |
| Carbamazepine | 220 | 349 | 238 |
| Diclofenac | 1.358 | 1.254 | 1.579 |

Pharmaceuticals can also be removed from wastewater in other types of hybrid systems: activated sludge or methane digestion and adsorption on biologically activated carbon. This process involves not only biodegradation but also adsorption on activated carbon. Research conducted by Sbardella et al. [61] showed that during 10 min contact of wastewater with a bed of activated carbon it is possible to remove about 55% of trimethoprim. In the case of ciprofloxacin, ofloxacin, and sulfamethoxazole removal rate were up to 22%, 30%, and 35%, respectively.

Other method of pharmaceutical removal is bioelectrochemical systems. These systems use microorganisms which catalyze oxidation/reduction reactions both organic and inorganic electrons donors/acceptors on their anodic or catodic electrodes [57].

Interesting removal technology of pharmaceuticals was proposed by Del Álamo et al. [62]. They have investigated advanced bio-oxidation process with rotating contactors and white rot fungi using synthetic and municipal wastewater. Research was conducted under laboratory scale. Clofibric acid, carbamazepine, diclofenac, ibuprofen, and sulfamethoxazole at concentration of 50 μg/L were spiked to the wastewater; HRT was equal to 1 d. This biological process was more effective than the conventional ones. It allowed for pharmaceuticals removal efficiency in the range from 50% to 95%, and such compounds which are known as not well biodegradable (carbamazepine and diclofenac) were removed in 56% and 61%, respectively.

### *3.1.3. Anaerobic processes*

Research on anaerobic fates of pharmaceuticals is largely limited to the compounds adsorbed on biomass of microorganisms treating wastewater. Research studies on degradation of considered pharmaceuticals under anaerobic conditions are less frequent than these on aerobic conditions. In the case of highly toxic sulfamethoxazole, it was stated that anaerobic digestion allows for removal of >99% pharmaceutical present in sludge after 10–35 d in batch laboratory-scale experiments [63]. These results were confirmed by Narumiya et al. [64] who demonstrated that sulfamethoxazole was almost completely (>90%) degraded during methane digestion of sewage sludge. Under the same conditions, the second highly toxic pharmaceutical ofloxacin was moderately degraded (30%–50%) [64].

Among slightly toxic compounds, carbamazepine was not degraded under anaerobic conditions, whereas trimethoprim was almost completely degraded (>90%) [64]. The results for carbamazepine were not confirmed by Zhou et al. [65]. They stated that during mesophilic (37 ± 2°C) and thermophilic (55 ± 2°C) methane digestion (solid retention times 10–20 d under mesophilic and 7–20 d under thermophilic conditions) at initial concentration of 5 μg/L removal efficiency for carbamazepine was about 48% ÷ 61% [65]. Efficiency of carbamazepine removal under anaerobic conditions (by 73%) could be enhanced by ultrasounds [66].

When we consider moderately toxic compounds (diclofenac, ibuprofen, naproxen, and clofibric acid), the results were as follows. In the studies by Zhou et al. [65,67]

clofibric acid was removed under anaerobic conditions in 57%–65% or 98%. Diclofenac was removed in 95% [67]. Also ibuprofen was well degradable under anaerobic conditions both mesophilic and thermophilic [68]. The same results were obtained for naproxen [67]. Under mesophilic methane digestion, naproxen was completely removed through primary biodegradation. Wolfson et al. [69] identified that naproxen under anaerobic conditions is removed via acetogenesis and synthropic acetate oxidation by methanogenic consortia.

### *3.2. Physicochemical processes of pharmaceuticals removal from wastewater*

Taking into consideration the fact that conventional methods of wastewater treatment are not always sufficiently effective in the removal of the pharmaceuticals, they should be supported by third treatment step involving physicochemical processes. The increase of the level of pharmaceuticals elimination is possible by additional wastewater treatment in the process of sorption on activated carbon or advanced oxidation (ozonation, UV radiation, and Fenton's reagent) as well as by using membrane processes (nanofiltration [NF], reverse osmosis [RO]) [70]. Also other processes, such as coagulation, are used. Mechanism of action and effectiveness of removal vary depending of wastewater characteristics and process parameters.

#### *3.2.1. Coagulation*

Coagulation process with PIX or other coagulating agents is used in WWTPs for removal of phosphorus. Coagulants also cause removal of turbidity, thus removal of colloids which do not settle down under the gravity force occurs. In the case of pharmaceuticals, removal coagulation is not very effective [71]. The results of the pharmaceuticals removal during coagulation obtained by various authors differ a lot. As it was stated by Gerrity and Snyder [42], effectiveness of removal of carbamazepine, diclofenac, ibuprofen, naproxen, sulfamethoxazole, and trimethoprim during coagulation did not exceed 15%. According to the Carballa et al. [72], during coagulation with $FeCl_3$ removal efficiency was as follows: diclofenac (70%) > naproxen (20%) > carbamazepine = ibuprofen (not removed from wastewater). According to the Gerrity and Snyder [42], the effectiveness of the pharmaceuticals removal was correlated with the value of log Kow and it increased as the hydrophobicity of individual compounds increased. The results obtained by Carballa et al. [72] suggest however that log Kow values are not so important in the case of pharmaceuticals removal by coagulation as suggested by Gerrity and Snyder [42]. The diclofenac which is characterized by log Kow equal to 1.90 was the one which was effectively removed. However, ibuprofen and carbamazepine which were not removed had also low log Kow values 2.48 and 1.51, respectively. The conclusion is that log Kow characterizes probably more reliably way adsorption, but no coagulation. Comparison of the effectiveness of selected pharmaceuticals removal from wastewater by activated sludge, coagulation, and MBBRs is presented in Table 8.

In the case of coagulation, the effectiveness of pharmaceuticals removal is connected not only with hydrophobicity but also with the dose of coagulant and conditions of the reaction environment.

*3.2.1.1. Adsorption* Adsorption is a promising process in the case of pharmaceuticals removal; however, the effectiveness of various adsorbents in medicines removal varies a lot. The adsorbent which is especially efficient in pharmaceuticals removal is activated carbon. This sorbent efficiently removes, for example, such compounds as diclofenac and carbamazepine (the ones that are not susceptible for biodegradation). Removal efficiency in the case of these pharmaceuticals was in the range 96% ÷ 100%. In the case of highly toxic sulfamethoxazole, removal efficiency was in the range from 2% to 62%.

The disadvantage of the method is necessity of replacing or regeneration of activated carbon [71]. Activated carbon can be produced from various materials which have various adsorption capacities toward pharmaceuticals. Ahmed and Hameed [74] researched sorption of pharmaceuticals on various sorbents (commercial activated carbon, biochar, and the adsorbents produced from waste materials) which were packed in filter beds. The authors analyzed the effect of the following parameters on the removal efficiency: flow rate, bed length, and initial concentration of chemical compound. It was stated that the parameters which were the most significantly affected in the pharmaceutical removal were initial concentration of compound and flow rate. Commercial activated carbon was more effective in pharmaceuticals removal than biochar and adsorbents prepared based on waste materials. Physicochemical properties of pharmaceuticals also affected removal efficiency. The amount of pharmaceuticals adsorbed on activated carbon was close to 185 mg/g (for diclofenac). The amounts of the pharmaceuticals considered in this article which were adsorbed on various adsorbents obtained by various authors are given in Table 9. The results presented in the Table 9 are cited after Ahmed and Hameed [74]. According to the presented data, the pharmaceutical which was less adsorbable were naproxen and ciprofloxacin.

Teeba et al. [75] also confirmed efficiency of granulated activated carbon (GAC) (commercial and prepared from dates) for removal of ciprofloxacin depended on initial concentration and flow rate (flow rates were 0.5, 1.0, and 1.5 mL/min; bed length 15–25 cm; and initial concentration 75, 150,and 225 mg /L). They have put the thesis that as the flow rate decreases adsorbate have enough time to penetrate through the pores which increases the amount of pharmaceutical which is adsorbed. High flow rate decreases thickness of the liquid film around adsorbent particles. As a result, low resistance of mass transfer occurs. Simultaneously, high rate of mass transfer is observed.

Table 10 summarizes the results obtained for adsorption with powdered (PAC) and GAC.

When GAC was used, removal efficiency was the highest and was in the range 98% ÷ 100% (in the case of PAC, removal efficiency depended on the dose of the carbon).

#### *3.2.2. Membrane processes*

Effectiveness of membrane processes in pharmaceuticals removal depends on the membrane pore sizes. Hypertensis processes, such as microfiltration (MF) and ultrafiltration (UF) are not efficient in medicines removal. It is connected with the fact that pore sizes are relatively high in these cases, and limit for MW is 100,000 and 2,000 Da, respectively. Because

Table 9
Parameters of adsorption of selected pharmaceuticals adsorbed on adsorbents [74]

| Compound | Adsorbent | Bed length, cm | Initial concentration mg/L | Sorption capacity, mg/g |
|---|---|---|---|---|
| Highly toxic | | | | |
| Sulfamethoxazole | Carbon nanotube | 15 | 40 | 92.00 |
| Moderately toxic | | | | |
| Diclofenac | Commercial carbon | 4 | 10 | 184.7 |
| Ibuprofen | Raspberry carbon | 3.0 | 10 | 46.14 |
| | Peach stones carbon | 15.0 | 10 | 55.00 |
| | Granulated active carbon | 3 | 20 | 48.57 |
| Naproxen | Raspberry carbon | 3.0 | 10 | 46.29 |
| | Bone char | 15.0 | 10 | 0.113 |
| | Granulated active carbon | 3 | 20 | 47.67 |
| Clofibric acid | Raspberry carbon | 3 | 10 | 45.75 |
| | Granulated active carbon | 3 | 20 | 46.53 |
| Slightly toxic | | | | |
| Paracetamol | Olive stones carbon | 2.9 | 6.7 | 88.40 |
| Ciprofloxacin | Granulated active carbon | 25 | 150 | 2.094 |
| | | 25 | 150 | 1.328 ÷ 2.094 |
| | | 15 | 150 | 1.587 |
| | | 20 | 150 | 1.482 |
| | | 25 | 75 | 0.856 |
| | | 25 | 225 | 1.514 |

Table 10
The efficiency (%) of selected pharmaceutical removal from wastewater by using powdered and granulated activated carbon [76,77]

| | Powdered activated carbon (PAC) – dose, mg/L | | | | | PAC | GAC |
|---|---|---|---|---|---|---|---|
| Pharmaceutical | 8 | 23 | 43 | 1.5 | 50 | n.d. | – |
| Diclofenac | 96 | 98 | 99 | 38 ÷ 46 | – | 98 ÷ 99 | >98 |
| Carbamazepine | 98 | 99 | 100 | – | – | >80 | 23 |
| Sulfamethoxazole | 2 | 32 | 62 | 36 | 56 | 2 ÷ 62 | – |

n.d., Not detected.

the pharmaceuticals usually have Da lower than 500 relatively easily penetrates through the membranes of these types. But, if they are in the form adsorbed on solid particles or on colloids, then they can be separated also on UF and MF membranes. Significantly more effective in pharmaceuticals' removal are high-pressure NF membranes, NF, and RO, because limit value of MW for these membranes are about 250 and 100 Da, respectively. Snyder et al. [78] analyzed various membrane methods under technical and semi-technical scales. They have stated that hydrophobic compounds with aliphatic substituted aromatic ring structures and high values of pKa are effectively removed by MF and UF membranes. Neutral and hydrophilic compounds were not removed by MF and UF processes. Effective removal of all pharmaceuticals was achieved during NF and RO processes [78]. In Table 11, effectiveness of selected pharmaceuticals removal with membrane processes is presented. The results indicate that RO is the most effective process in pharmaceuticals removal from water solutions, and those are wastewater.

Table 11
The efficiency of pharmaceutics removal in the membrane processes, % [42,78]

| Pharmaceuticals | Effectiveness of membrane separation | | | | |
|---|---|---|---|---|---|
| | MF | UF | NF | RO | UF/MBR |
| Diclofenac | <20 | <20 | 50 ÷ 80 | >80 | <20 |
| | | | 55 | 95 | 0 ÷ 66 |
| Ibuprofen | <20 | <20 | 50 ÷ 80 | >80 | 50 ÷ 80 |
| | | | 34 ÷ 96 | 96 | 97 ÷ 100 |
| Naproxen | <20 | <20 | 20 ÷ 50 | >80 | >80 |
| | | | 26 | 97 | 36 ÷ 99 |
| Sulfamethoxazole | <20 | 20–50 | 50 ÷ 80 | >80 | 20 ÷ 50 |
| | | | 13 ÷ 19 | 94 ÷ 99 | 52 ÷ 81 |
| Carbamazepine | <20 | <20 | 50 ÷ 80 | >80 | 20 ÷ 50 |
| | | | 7 ÷ 95 | 91 | 14 ÷ 20 |
| Trimethoprim | <20 | <20 | 50 ÷ 80 | >80 | |
| | | | 13 ÷ 19 | – | 47 ÷ 90 |
| Ofloxacin | – | – | >95 | 95 | – |

Effectiveness of membrane separation is connected not only with the properties of membrane but also on the characteristics of dissolved substances, medium, and process environment. Effectiveness of separation depends not only on molecular weight and particles size but also on hydrophobicity and hydrophilicity as well as on charge characteristics and chemical structure [79–81]. Hydrophobic compounds are removed with higher rate than others [82]. Also surface charge (ζ potential) and surface morphology affects membrane effectiveness [79].

Because of the membrane characteristics, research concerning pharmaceutical removal is focused mainly on NF and RO. The results obtained in various studies indicate that retention rate for pharmaceutical are often higher than 80% (Table 12). Separation mechanism is complex. It is believed that mechanisms which dominate are interaction between dissolved matter and membrane, electrostatic repulsion, as well adsorption. Effectiveness of separation is also affected by pH. Characteristic is "rejection of ions" caused by electorstatic repulsion between electrically charged compounds and surface charge of the membrane. Non-charged particles are mostly rejected because of their sizes, which are higher than membrane pores [65].

Table 12
Removal of selected carbamazepine by various AOPs methods [84]

| Compound | Effectiveness, % | Process parameters | Reference |
|---|---|---|---|
| Carbamazepine | >90 | $O_3$ | [85] |
| Diclofenac | >90 | (5 mg/L): 15 min | |
| Sulfamethoxazole | >90 | $O_3$ | [71] |
| Diclofenac | 100 | | |
| Carbamazepine | >90 | | |
| Ibuprofen | 50–80 | $O_3$ | [42] |
| Diclofenac | >80 | (2.5 mg/L): 24 | |
| Carbamazepine | >80 | min | |
| Sulfamethoxazole | >80 | | |
| Naproxen | | | |
| Ibuprofen | 83 | $O_3$ (5 mg/L) + | [71] |
| Diclofenac | >99 | $H_2O_2$ (3.5 mg/L) | |
| Carbamazepine | >99 | | |
| Sulfamethoxazole | 98 | | |
| Diclofenac | >80 | UV + $H_2O_2$ | |
| Sulfamethoxazole | >80 | | |
| Naproxen | >80 | | |
| Sulfamethoxazole | 100 | No data | |
| Diclofenac | 100 | | |
| Ofloxacin | 100 | $O_3$ | [73] |
| Sulfamethoxazole | >99 | $O_3$ + $H_2O_2$ | [71] |
| Diclofenac | >99 | | |
| Carbamazepine | >99 | | |
| Sulfamethoxazole | 51 | UV | |
| Diclofenac | 100 | | |
| Carbamazepine | 23 | | |
| Ibuprofen | 34 | $UV_{254}$: 10 min | [86] |
| Diclofenac | 100 | | |
| Carbamazepine | 23 | | |
| Sulfamethoxazole | 51 | | |
| Ibuprofen | <20 | UV 40 mJ/cm$^2$ | [73] |
| Carbamazepine | <20 | | |
| Erythromycin | <20 | | |
| Naproxen | <20 | | |
| Acetaminophen | 20–50 | | |
| Diclofenac | 50–80 | UV 40 mJ/cm$^2$ | |
| Sulfamethoxazole | 50–80 | | |
| Carbamazepine | 20–50 | UV 450 mJ/cm$^2$ | |
| Ibuprofen | 20–50 | | |
| Ofloxacin | 89 | UV/$H_2O_2$ | [87] |

*3.2.3. Photolysis*

A major determinant in organic compounds decomposition during direct photolysis is adsorption of photon by particle of pollutant. It is possible only when emission spectrum of radiation totally, or partially, overlap with adsorption spectrum of the compound. Effectiveness of the process is affected by the presence of other dissolved organic compounds, pH, presence of substances which cause turbidity and color, as well as intensity and frequency of electromagnetic radiation. Susceptibility of pharmaceuticals for photolytic degradation is differentiated, for example, diclofenac is susceptible to photolysis. During exposition which lasted several minutes about 98% ÷ 100% of this pharmaceutical was removed. Simultaneously carbamazepine was degraded maximally in 23% [83]. The results are similar to the ones obtained by Giannakis et al. [73]. The authors obtained complete degradation of diclofenac after exposition to UV-C radiation for 10 min. Despite the fact that UV photolysis can be effective method for removal of selected compounds, it generally is not cost-effective because a lot of pharmaceuticals are resistant to UV radiation [42].

*3.2.4. Ozonolysis*

Ozonolysis is the most frequently used in water treatment installations. At present, this process is also proposed as an effective tertiary treatment of wastewater. Ozone can react with the organic particles directly or indirectly. Ozone is very effective in pharmaceuticals removal. In the case of some pharmaceuticals (e.g., ibuprofen) ozonation should be supported by adding $H_2O_2$, to multiplying the effect [42]. Tertiary treatment by ozonation is used among others in Switzerland. It allowed for more than 80% removal of carbamazepine and diclofenac at dose of ozone equal to 3.5 mg $O_3$/L. Diclofenac and carbamazepine are the compounds which are the most effectively removed by ozonation [71]. Also sulfonamide antibiotics are considered as very reactive with ozone. In the studies by Giannakis et al. [73], removal of ofloxacin by ozonation reached 100%. Complete mineralization by ozone is believed as non-practical because of the energy demand and potential generation of by-products [42].

*3.2.5. Advanced oxidation processes*

Mechanism of organic compounds oxidation by advanced oxidation processes (AOPs) is due the generation of free radicals, mainly the hydroxyl ones. They are generated in chemical or photochemical reactions. In alkaline or neutral environment, ozone should be used, but in acidic environment, $O_3/H_2O_2$, UV/$O_3$, UV/$H_2O_2$, $O_3$/UV/$H_2O_2$, and $Fe^{2+}/H_2O_2$ are recommended. The most frequently used photochemical processes are photo-Fenton and photocatalysis; however, use of processes in wastewater treatment is

limited because of turbidity and color of the medium. AOPs are the most frequently used for treatment of industrial wastewater, for example, from textile or cosmetics industry. AOPs are also sometimes used as tertiary treatment method for municipal wastewater. In the case of selected pharmaceuticals (sulfamethoxazole, diclofenac, and carbamazepine), reaction rate coefficients were in the range of $10^9$–$10^{10}$/M·s. These compounds are considered as the most suitable for oxidation in AOPs processes. Effectiveness of $UV/H_2O_2$ process in degradation of sulfamethoxazole and diclofenac was in the range 99.6% ÷ 100%. Similar results (about 99% degradation) were obtained during $O_3/H_2O_2$ oxidation for sulfamethoxazole, diclofenac, and carbamazepine [71]. AOPs are highly effective but also energy consuming. Under optimal conditions, however, reaction time is relatively short. AOPs should be matched with the contaminants present in wastewater, for example, diclofenac which is well removed by $UV/H_2O_2$ is not so effectively removed by Fenton's reagent. After 2 h of photo-Fenton removal efficiency of diclofenac was no higher than 75% [71]. Effectiveness of various AOPs in degradation of selected pharmaceuticals is listed in Table 12.

## 4. Conclusions

At present, pharmaceutical in surface waters are mainly present as by-products which were not completely metabolized in organisms. They are classified as "emerging contaminants", compounds which are persistent in the environment. Despite the fact that concentrations of pharmaceuticals in surface water are usually at level of several micrograms in liter, toxicological tests show the negative effect of these micropollutants on living organisms. This negative effect is confirmed by LOEC and NOEC as well as lethal doses or effect concentration values. Because of the fact that wastewater effluents and landfill leachates were considered as important sources of surface water pollution by pharmaceutical, various physicochemical processes can be used for removal of them from effluents and to control discharges of medicines into the environment. The processes which can be used are coagulation, flotation, adsorption, membrane processes, and AOPs. They can be integrated with biological treatment. Removal effectiveness of pharmaceutical can be in the range from several to even 100% and is affected by properties of individual compounds, treatment technology and technological parameters. The most effective processes seem to be AOPs. Side effect of these technologies is, however, potential of by-products generation. By-products can be more toxic than pharmaceuticals. During coagulation, adsorption, and membrane processes no by-products are formed, but simultaneously no degradation of micropollutants occurs. These processes only move the pollutants from one phase to another, for example, from water phase to suspended solids. In membrane processes, concentration of pollutants occurs. It should be emphasized that research studies usually are focused only on degradation or toxicity of individual compounds whereas in wastewater or leachate they are present as mixtures of the compounds. Effectiveness of the pharmaceuticals removal in technical scale can differ from the results of laboratory studies.

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