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A Review on Conventional and Advanced Water Treatments in Ibuprofen Removal

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Abstract

Nonsteroidal anti-inflammatory drugs (NSAIDs) represent a group of pharmaceutical compounds that are most frequently detected in the aqueous medium. Development of analytical equipment for the detection of organic compounds at low concentration levels, contributed to the detection of NSAIDs in drinking water as well. It is considered that the presence of this group of pharmaceutical components in drinking water is caused by soil washing and via effluents from wastewater treatment plants (WWTPs). Ibuprofen is one of the most frequently detected pharmaceutical components in influents of WWTPs. Although the concentration levels of various classes of pharmaceutical active components are low, their continuous intake can lead to harmful consequences for aquatic systems. Based on the conducted studies, ibuprofen is currently one of the most commonly used non-steroidal anti-inflammatory drugs worldwide. This paper presents an overview of the detection of ibuprofen in the aquatic media, conventional methods for the treatment of ibuprofen in water, as well as advanced oxidation processes for the treatment of water in order to eliminate ibuprofen.

Keywords: Nonsteroidal Anti-Inflammatory Drugs; Pharmaceutical Compound; Wastewater

Introduction

Ibuprofen, (2-(4-isobutylphenyl) propionic acid, is a pharmaceutical component used in the treatment of rheumatic diseases, muscle pain, and influenza. After oral intake, it is excreted in the form of various conjugates, such as 2-hydroxy ibuprofen, 2-carboxy ibuprofen and carboxyhydrotropic acid, which have high toxicity and endocrine disrupting effects on humans and animals [1]. Ibuprofen is currently one of the most commonly used non-steroidal anti-inflammatory drugs worldwide. The annual consumption of ibuprofen in selected European countries is about 300 tons in Germany, 162 tons in the United Kingdom and 58 tons in Poland, while the consumption of ibuprofen in Norway and Denmark is significantly lower [2]. The high prevalence of ibuprofen and metabolites in environment is a consequence of the high daily therapeutic dose, which is from 600 to 1200 mg day-1. In the human body, about 15% of ibuprofen is excreted in its original form or in the form of conjugates or metabolites such as hydroxyibuprofen (2-OH and 3-OH) and carboxyibuprofen. Conjugates of ibuprofen with glucuronide can hydrolyze in the environment [3,4].

Ibuprofen was detected at different concentration levels in the aqueous media. Detected ibuprofen in influents of wastewater treatment plants in China, Greece, Korea, Sweden, and the Balkan region in the range of 0.004 to 603 μg L^{-1}. In addition to detection in aqueous matrices, ibuprofen was detected in soil in the range of 321 to 610 μg kg^{-1} Ashfaq M [5] and a concentration of 0.213 μg L^{-1} in soil irrigated with wastewater containing this pharmaceutical [6]. The average concentration of ibuprofen in groundwater in Europe is 3 ng L^{-1} with a maximum detected concentration of 395 ng L^{-1} [7]. The concentration of ibuprofen residues in wastewater in Canada was 45 μg L^{-1} Guerra [8], in Pakistan it was in the range of 703–1673 μg L^{-1}, while 1.38 μg L^{-1} was detected in South Africa and 5.78 μg L^{-1} in Belgium [5,9]. Ibuprofen concentrations detected in sludge were 0.009 μg kg^{-1} in South Africa, and a range of 2053 to 6064 μg kg^{-1} was quantified in Pakistan [10].

In surface water, ibuprofen was detected at concentrations of 0.98 μg L^{-1} in Canada, 0–67 μg L^{-1} in Greece, < 15–414 μg L^{-1} in Korea, 5.0–280 μg L^{-1} in Taiwan, up to 8.0 μg L^{-1} in France and up to 1417 μg L^{-1} in China [7,11]. Aymerich [12] reported that the concentrations of carboxyibuprofen, 1-hydroxyibuprofen and 2-hydroxyibuprofen in wastewater treatment plant influent were 20, $1{,}1 \cdot 10^3$ and 7,8 ng L^{-1}, respectively. Literature data on the toxicity and impact of ibuprofen on aquatic organisms are still limited. Changes have been recorded after acute exposure to ibuprofen in concentrations significantly higher than are detected in the environment, and lethal effects are possible. Although the acute toxicities of nonsteroidal anti-inflammatory drugs based on EC50 values, in the range of 10 to 100 mg L^{-1} are low, the changes that occur after prolonged exposure to analgesics can cause cyto- and geno-toxic effects and an unbalanced oxidative status of the cell [13]. Parolini M [14] assumed that organisms have the ability to transform the original component into more toxic intermediates. Such a fact was studied by Kayani M [15] for ibuprofen conjugated with diacylglycerol. Parolini M [14] showed that chronic exposure to environmental concentrations of ibuprofen (0.2, 2.0 and 8.0 μg L^{-1}) caused moderate genetic and cellular damage in the zebra mussel, *Dreissena polymorpha*, a reference biological model that is sensitive to different groups of pharmaceutical compounds, including antibiotics.

Han S [16] investigated the chronic toxicity of ibuprofen to three fresh species, *Oryzias latipes*, *Daphnia magna* and *Moina macrocopa* and their effects on hormone balance in vitro using *H295R* cells. Analyzing the results, ibuprofen caused increased production of 17β-estradiol and aromatase activity and decreased testosterone production. Additionally, ibuprofen at concentrations of 0.1 μg L^{-1} caused a delay in oviposition in the fish species *Oryzias latipes*. De Lange [17] indicate that ibuprofen in concentrations of 1 to 100 ng L^{-1} reduces activity in the crab *Gammarus pulex*. Wang L [18] investigated the effect of ibuprofen concentrations detected in the environment on *D. magna*. Total number of eggs and total number of litters in females, as well as body length were significantly reduced after exposure to ibuprofen. It was shown that in low concentrations of ibuprofen (0.5 μg L^{-1}) the expression of the analyzed genes is inhibited, while higher concentrations (50 μg L^{-1}) induced their expression. The third gene expression was inhibited during a shorter exposure time (6 h) and induced during a longer exposure time (48 h). Ibuprofen toxicity has been widely investigated using the *Microtox* test, which allows the evaluation of toxic components in bioluminescent organisms, *Allivibrio fischeri*. Di Nica [19] showed two different IC50 values after 15 minutes of exposure to ibuprofen, 19.1 and 37.5 mg L^{-1}. The negative effects of ibuprofen on various types of aquatic organisms require the implementation of a monitoring program for the quantification of ibuprofen in water media and the determination of the total use of ibuprofen, as well as the need to conduct detailed toxicological tests.

Conventional Technologies for the Treatment of Ibuprofen in Wastewater

Conventional technologies for the treatment of effluents are not effective due to the impossibility of complete removal of color from water, as well as pollutants that have a low or no tendency towards adsorption or evaporation processes. The other disadvantage of the mentioned treatments is the transfer of pollutants from one phase to another, which creates the problem of disposal of the generated waste. Biological treatments require a large operating space and application of chemicals that are toxic, possess less flexibility in design and operation. Although many organic pollutants are degraded in this way, many other pollutants are resistant to biological degradation due to their complex chemical structure and synthetic organic origin. On the other hand, chemical methods involve the application of a large amount of chemicals and produce a large volume of sludge that requires additional treatment. Various physical methods such as processes based on membrane filtration (nanofiltration, reverse osmosis, electrodialysis) and adsorption techniques are used worldwide. The most important disadvantage of membrane processes is their duration and the problem of periodic replacement of membranes, as well as the consumption of energy used to achieve high pressures of water passing through the membranes, the costs of which must be included in any economic analysis. Adsorption is also one of the popular methods being investigated. Activated carbon is widely used as an adsorbent in wastewater treatment. However, the operating costs of using activated carbon are high. The problems of regeneration and the problems of separation from wastewater after application are the two most important challenges in the application of this type of material [20].

Dissolved organic contaminants can be oxidized by biological treatment. Biological treatments involve the application of microorganisms that consume organic components [21]. Processes with activated sludge are the most commonly applied biological methods for the degradation of pharmaceuticals from wastewater due to their long hydraulic retention time (HRT). Various factors affect the efficiency of the activated sludge process such as: temperature, dissolved oxygen, pH, retention time, organic load, microorganisms and presence of harmful substances [22]. In contrast to chlorination, the biological method with activated sludge is considered an environmentally friendly method. However, it requires high energy consumption, is difficult to monitor operationally and generates a large volume of sludge [23]. Activated sludge processes are ineffective for wastewater where the chemical oxygen demand value is greater than 400 mg L^{-1} [24]. Biological treatments are not suitable for removing high concentrations of pollutants in wastewater. In scientific studies, the primary sedimentation technique eliminated ibuprofen in values of 12 to 45 % [1,25]. The concentration after primary treatment was reduced from 20 to 43 % with biological treatment [26]. In the paper of Stumpf [27] a removal percentage of 75% was determined for ibuprofen in the case of applying a biological process with activated sludge. Specific pharmaceutical components found after secondary treatment can be eliminated by tertiary techniques such as adsorption with activated carbon, membrane separation and electrodialysis. However, the effectiveness of these methods varies significantly. Therefore, it is necessary to examine the application of new methods and new materials in the removal of pharmaceutical residues from aquatic waste matrices [21].

The most important mechanisms for the removal of pharmaceutical components during the application of conventional wastewater treatment are based on biotransformation/biodegradation and abiotic removal by adsorption on sludge. Considering the low values of Henry's constant of most pharmaceutical compounds detected in wastewater, the volatilization process can be neglected [28]. The efficiency of removing pharmaceutical compounds depends on physicochemical characteristics such as hydrophobicity and biodegradability and on operational parameters (retention time, sludge retention time (SRT)) in the system and temperature. A higher value of SRT allows the growth of slower bacteria and thus a more diverse microbial biocenosis is obtained than at lower values of SRT. Clara [29] showed in their study the efficiency of removing ibuprofen, bezabirate and diclofenac using SRT reactors. While ibuprofen and bezabirate were degraded to a large extent from 80-100 %, diclofenac proved to be highly resistant to biodegradation during conventional treatment with activated sludge. With the increase of SRT, no significant changes in the biodegradation process were achieved.

Technologies based on membrane bioreactors (MBR) are considered suitable for the removal of various organic micropollutants. However, some organic components pass through the MBR system without reduction in concentration. In wastewater treatment plants in Spain, significant reductions were not achieved for ibuprofen, ketoprofen, naproxen, mefenamic acid and gemfibrozil [30,31]. The low percentage of removal can be explained by the acidic structure of the pharmaceutical compounds (negative charge of the molecules at pH 7) which is associated with the low solid-liquid phase partition coefficient Kd, which results in their presence in the aqueous phase. Acetaminophen, ibuprofen, acetylsalicylic acid, salicylic acid, estrone, estriol, and estradiol were effectively removed by conventional activated sludge treatment.

Suárez [32] investigated the possibility of applying conventional treatment with activated sludge in a pilot plant with a synthetic mixture of selected pharmaceuticals for a long period of time. The removal of ibuprofen in the anoxic reactor increased from 16% (up to 200 days) to 75% (after 340 days). The aforementioned studies point to the fact that the behavior of micropollutants in biological treatments depends on the type of bacteria used in the interaction with the target pollutant.

Advanced Photocatalitic Processes for Ibuprofen Degradation

Conventional wastewater treatments are not designed for a satisfactory removal of pharmaceutical contaminants, therefore it is necessary to apply advanced treatments [30]. In the paper of Yuan [33] a new composite material with carbon nanotubes and TiO_2 (CNT/TiO_2) with different ratio of urea from 1 to 5% was presented for the degradation of ibuprofen at a wavelength of 410 nm. Ibuprofen degradation increased with increasing pH value from 2 to 5 from 48.7% to 87.9% and 53% to 89% for the used photocatalysts, while the degradation efficiency decreased with increasing pH value. A higher degradation rate of ibuprofen was defined at lower pH values and the decomposition was mainly carried out by superoxide radicals. Achilleos [34] investigated the photocatalytic degradation and mineralization of ibuprofen and carbamazepine in the aqueous phase with TiO_2 and solar radiation. Degussa P25 titanium dioxide achieved the highest conversion of ibuprofen and carbamazepine during 120 minutes of photocatalytic treatment. About 65% and 61% of ibuprofen were degraded with the optimal mass of TiO_2 catalyst under UV-A and solar irradiation, respectively.

In the paper of Méndez-Arriaga [35] complete elimination of ibuprofen was achieved with UV/TiO_2. The maximum conversion of ibuprofen at a concentration of 200 mg L^{-1} was achieved with a concentration of 1 g L^{-1} TiO_2 after 240 minutes of irradiation. The first order decomposition constant was 9.1×10^{-3} min^{-1}. Wang [36] synthesized Ag-

$AgBr/TiO_2$ composite, whose photocatalytic activity was investigated for the degradation of ibuprofen under visible light. LED lamps with different wavelengths and colors at 465 nm, 523 nm and 589 nm were used as a source of radiation. Up to 98%, 80%, 97% and 62% degradation of ibuprofen was observed after 2 h of irradiation for white, blue light (465 nm), green light (523 nm) and yellow light (589 nm), respectively. Higher ibuprofen removal efficiency was achieved with white and blue LED light compared to yellow and green LED light. This fact can be explained due to efficient charge transfer and separation of photoexcited charge transfers. Ibuprofen mineralization was achieved up to 80% under LED irradiation after 6h, as well as reduction of toxicity and aromaticity of degradation products. The photocatalyst was highly active in the deactivation of *Escherichia coli* compared to conventional photocatalysts Ag–AgBr/P25 and pure titanium dioxide. In the paper of Eslami [37], a new titanium dioxide photocatalyst coated on polycarbonate (NS-TiO_2) was synthesized using a simple sol-gel method. NS-TiO_2 was successfully deposited on a polycarbonate (PC) substrate using a simple and efficient deposition method. UV light was used as a source of radiation. The photocatalytic activity of the newly formed photocatalyst NS-TiO_2 on PC was investigated for the degradation of ibuprofen and naproxen in a photocatalytic reactor under sunlight. The effects of operational parameters such as: light intensity, initial concentration and contact time were investigated.

The optimal parameters for achieving the maximum degradation of ibuprofen are: light intensity of 8.36 mW cm^{-2}, initial concentration of 10 mg L^{-1} and contact time of 120 min, which achieved a maximum degradation of 83%. Chen [38] investigated the synergistic UV/TiO_2/Fenton process in the degradation of ibuprofen. Decomposition of ibuprofen is significantly higher in the UV/TiO_2/Fenton system than in separated UV, UV/H_2O_2, Fenton, Photo-Fenton and photocatalytic processes at neutral pH. Kinetic analysis showed that ibuprofen is degraded in two stages according to pseudo-first-order kinetics. The application of various advanced oxidation treatments is effective for the treatment of wastewater with a pH value between 5.17 and 9.06. Higher concentrations of hydrogen peroxide lead to faster decomposition of ibuprofen, while the Fe^{2+} concentration of 0.20 mmol L^{-1} is optimal. The optimal ratio of hydrogen peroxide and Fe^{2+} is 1:40. UV-A as a source of radiation was chosen as the most optimal in terms of application in real systems. The optimal value of titanium dioxide was 1 g L^{-1}.

Choina [39], applied the photocatalyst titanium dioxide doped with zirconium for the decomposition of ibuprofen by changing the operational parameters such as the initial concentration of ibuprofen, the concentration of the catalyst, the pH value and the repeated application of the photocatalyst. At the same time, more degradation products are generated. The concentration of formed intermediates decreases as a result of applying a larger mass of catalyst after 180 minutes of photocatalytic degradation. The results showed that the newly formed Zr/TiO_2 photocatalyst has a higher photocatalytic activity on lower photocatalyst masses than pure TiO_2. The degradation of ibuprofen is more pronounced when the pH value decreases from 9 to 2. After doping, the catalyst behaves as a hydrophobic substance. Polar hydrophilic intermediates are generated.

In their second research, Choina [40] applied zinc oxide nanoparticles of different sizes for the degradation of ibuprofen and tetracycline using low mass of photocatalyst and pharmaceutical and photocatalyst to substrate ratio. The synthesis of zinc oxide was carried out using water and ethanol as solvents, which formed two types of nanoparticles, ZnOw and ZnOe. The influence of pH value, zinc oxide and pollutant concentration, as well as the influence of adsorption, were investigated in detail. Smaller zinc oxide particles are more active than larger ones due to specific surface area and adsorption. Adsorption of pharmaceutical components on ZnO is improved at low pharmaceutical concentrations (<5 mg L^{-1}). The photocatalytic degradation of ibuprofen in an acidic environment significantly decreased by about 50% in contrast to the efficiency of tetracycline removal. After 180 minutes of photocatalytic treatment, only 8% and 5% of ibuprofen were removed using ZnO_e and ZnO_w, respectively. The low photocatalytic activity of ZnO is explained by the increase in electrostatic repulsions between the protonated surface of zinc oxide and ibuprofen molecules. Ibuprofen adsorption increased at pH 9 and a significant decrease was observed at pH 3.

Jallouli [41] investigated the degradation of ibuprofen using ultraviolet diodes (LEDs) with titanium dioxide. Samples of ultrapure water and treated effluent from a municipal wastewater treatment plant, as well as wastewater from the pharmaceutical industry with a high concentration of diclofenac (230 mg L^{-1}) were applied in the tested TiO_2/UV-LED system.

Three operating parameters such as pH, mass of catalyst and number of LEDs were optimized. Ibuprofen mineralization was monitored by determining the dissolved oxygen in the samples. Bioassays were conducted using the aquatic species *Vibrio fischeri* to determine the potential acute toxicity of primary and treated wastewater. Titanium dioxide has been shown to be effective for the removal of ibuprofen from ultrapure and pharmaceutical wastewater, and less effective for removal from municipal wastewater. Acute toxicity with treatment was reduced by 40% for all investigated matrices, while the degree of mineralization increased.

In the study of Lei Z Dong [42] due to non-toxicity and stability, graphene quantum dots (GQDs) were modified on silver vanadate ($AgVO_3$) nanoribbons by hydrothermal technique. The newly formed photocatalyst showed good efficiency in the number of photogenerated electron-holes under visible light. Due to this favorable property, an improvement in photocatalytic efficiency was achieved in the degradation of ibuprofen under visible light compared to pure $AgVO_3$. Optimum activity was achieved with a 3% GQD ratio, with the highest separation of photogenerated electron-hole pairs. The concentration of ibuprofen is reduced after a short period of time. After 60 minutes, the reduction of total organic carbon was more than 80%, while after 180 minutes complete mineralization was achieved. The photocatalyst showed good recyclability after four consecutive cycles. The stability of the composite was monitored for 180 minutes of treatment during each cycle. The degradation efficiency was 98% during all four analyzed cycles, due to the high photostability of the formed 3 wt % GQD/$AgVO_3$ nanoribbon. Table 1 shows an overview of the photocatalytic studies of ibuprofen in water.

Radiation source	Photocatalyst	Process parameters	Reference
24 LED lamp with visible light of 410 nm, power 10 W	CNT/TiO_2	t=150 min c_0=5 mg L^{-1} ratio of doping with urea (1-5%) pH 2-11	[33]
9 W UV-A lamp (350–400 nm)	TiO_2	t=120 min c_0=5-20 mg L^{-1} c_k=50–3000 mg L^{-1} c_{H2O2}=0,07–1,4 mM pH 3–10	[34]
3 pilot reactors with solar radiation	TiO_2	t=0,5-1,5 day c_o=20-200 mg L^{-1} c_k=0,1-1 g L^{-1}	[35]
LED photoreactor	Ag–AgBr/TiO_2 composite	t=120 min c_0=10 mg L^{-1} c_K= 0,5 g L^{-1}	[36]
350 W Xenon lamp	NS-TiO_2	t=37-100 min c_0=2,5-10 mg L^{-1}	[37]
400 W photochemical reactor (254- 350 nm)	UV/TiO_2/Fenton process	t=30 min c_o=0,05-0,15 mol L^{-1} c_k=0,02-5,0 g L^{-1} pH 4,22-11,65	[38]
6 UV–Vis lamps (15 W, 320-400 nm)	TiO_2 Degussa P25	t=180 min c_o=5-60 mg L^{-1} c_k=10-40 mg L^{-1} pH 3 and 9	[39]
4 UV–Vis lamps (15 W, 320-400 nm)	ZnO_e and ZnO_w	t=180 min c_o= 5- 40 mg L^{-1} c_k=10 mg L^{-1} pH 7 to 9	[40]
UV-LED reactor (λ_{max} = 382 nm)	TiO_2	t=90 min c_o=6-213 mg L^{-1} c_k= 0,5- 1,5 g L^{-1} pH 3-9	[41]

Table 1: Photocatalytic treatment of ibuprofen in water.

Conclusion

The review presents the detection of ibuprofen in the aquatic medium, shortcomings in the application of conventional methods for the treatment of ibuprofen in water, as well as the possibility of applying advanced oxidation processes in water treatment in order to eliminate ibuprofen. The disadvantage of applying conventional procedures for the treatment of ibuprofen is the insufficient removal from water. The lack of conventional treatment can be overcome by combining conventional treatment with advancced oxidation processes to improve water treatment efficiency. However, the application of advanced oxidation processes is still based on laboratory studies and has not found adequate application in WWTPs.

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