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Influence of Inorganic Ions and Organic Substances on the Degradation of Pharmaceutical Compound in Water Matrix

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Abstract: The paper determined the influence of inorganic substances and high-molecular organic compounds on the decomposition of diclofenac, ibuprofen, and carbamazepine in the process of photocatalysis conducted with the presence of Titanium dioxide (TiO_2). It was determined that the presence of such ions as CO_3^{2-}, HCO_3^-, HPO_4^{2-} as well as SO_4^{2-} inhibited the decomposition of carbamazepine, whereas the efficiency of diclofenac degradation was decreased only by the presence of CO_3^{2-} and HCO_3^- anions. In case of ibuprofen sodium salt (IBU), all investigated anions influenced the increase in its decomposition rate. The process of pharmaceutical photooxidation conducted in suspensions with Al^{3+} and Fe^{3+} cations was characterized by a significantly decreased efficiency when compared to the solution deprived of inorganic compounds. The addition of Ca^{2+}, Mg^{2+} and NH_4^+ affected the increase of reaction rate constant value of diclofenac and ibuprofen decomposition. On the other hand, high molecular organic compounds present in the model effluent additionally catalysed the degradation process of pharmaceutical compounds and constituted an additional sorbent that enabled to decrease their concentration. Toxicological analysis conducted in deionized water with pharmaceutical compounds' patterns proved the production of by-products from oxidation and/or reduction of micropollutants, which was not observed for model effluent irradiation.

Keywords: pharmaceuticals; photocatalysis; cations and anions; organic compounds; toxicological assessment

1. Introduction

Pharmaceutical compounds constitute one of the largest groups among organic micropollutants that are present in the aquatic environment [1]. Municipal effluents into which these compounds are transported along with waste products from people taking them, inappropriately utilized expired or unused medication a well as surface effluents from farming areas on which they were applied are considered their main source [2,3]. It is estimated that the pharmaceutical market of the European Union comprises approximately 3000 different substances [4], and this number keeps increasing. Wastewater treatment plants that apply conventional wastewater treatment methods based mainly on activated sludge methods that enable to decrease the concentration of high molecular organic compounds and biogenic compounds do not guarantee a complete elimination of pharmaceutical micropollutants [5] classified as hardly biodegradable substances [6].

One of the methods that guarantees high removal rates of organic substances including pharmaceutical compounds [7–9] is the process of heterogenic photocatalysis conducted with the application of catalysts of a different type; out of them nanomolecules of Titanium dioxide (TiO_2) are described in the literature most frequently [10].

The mechanism of reactions occurring on the surface of a catalyst during the process of photochemical oxidation is divided on five stages, i.e., photoexcitation, diffusion, trapping, recombination, and oxidation [11]. The course of these stages involve the oxidation and reduction of compounds adsorbed in active centres of semiconductors by means of highly reactive free hydroxyl radicals OH$^\bullet$. The process of micropollutants adsorption may be hindered by the presence of organic or inorganic compounds that block active centres on the catalyst surface. Chládková et al. [12] indicated that common inorganic anions Cl$^-$, NO$_3^-$ and SO$_4^{2-}$ can be competitively adsorbed on the surface of the photocatalyst and decrease the photodegradation rate of organic caompunds. On the other hand, some inorganic compounds such as sulfate ions can be immobilized on the surface of TiO$_2$ nanoparticles and improve the photocatalytic activity of the formed composite [13].

Pharmaceuticals which are biologically active compounds—apart from their therapeutic effect—may also demonstrate a toxic character against aquatic organisms; therefore, in case of water streams' treatment there exists the need for a comprehensive assessment of the removal rate of micropollutants by the application of analytical methods that enable to explicitly identify pharmaceuticals and products formed during their natural or assisted decomposition. Additionally, there exists the necessity for a toxicological analysis of the formed decomposition by-products. In this case, the widespread use of biotests conducted on a variety of indicator organisms, i.e., on bacteria, crustacea, fresh- and saltwater fish as well as on vascular plants [14–17]. Special attention should be paid to tests conducted on bioluminescent organisms that prove sensitivity towards a wide range of toxicants including pharmaceutical compounds [18] that enable to obtain results in a very short period of time [19].
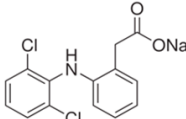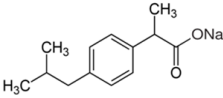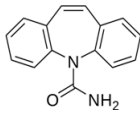
This paper describes the efficiency of removal of three medications most frequently identified in the aquatic environment, i.e., diclofenac, ibuprofen, and carbamazepine, from water suspensions in the process of heterogenic photocatalysis with the presence of selected inorganic compounds and organic substances. The process of photochemical oxidation and reduction was conducted in the presence of TiO$_2$ as a catalyst of this process. The kinetics of the process was described by means of Langmuir-Hisherwood equation. The efficiency of the process was also assessed on the basis of the decrease in concentration of pharmaceutical micropollutants as well as toxicological measurements of the subprocess suspensions with the use of bioluminescence bacteria *Aliivibrio fischeri* (Microtox$^\circledR$ test). It enabled to comprehensively assess the degree of pollutants mineralization process as well as to establish potential toxicity against living organisms that may prove generation of by-products of oxidation process of pharmaceuticals.

2. Materials and Methods

2.1. Materials and Reagents

Patterns of pharmaceutical micropollutants used during the research were from the group of nonsteroidal anti-inflammatory analgesics supplied as diclofenac sodium salt (DCF) and ibuprofen sodium salt (IBU) as well as a psychoactive drug—carbamazepine (CBZ) from Sigma-Aldrich (Poznań, Poland) (Table 1). Their percentage of purity exceeded 98%. TiO$_2$ applied as a catalyst into the process of heterogenic photocatalysis was purchased from Evonik Degussa GmbH (Hanau, Germany) and labelled by the manufacturer with the symbol of P25. Additionally, methanol and acetonitryle by Avantor Performance Materials Poland S.A. (Gliwice, Poland) was used in this research.

Table 1. Characteristics of tested pharmaceutical compounds.

Pharmaceutical Compound	Diclofenak Sodium Salt	Ibuprofen Sodium Salt	Carbamazepine
Structural formula			
Molecular formula	$C_{14}H_{10}Cl_2NNaO_2$	$C_{13}H_{17}NaO_2$	$C_{16}H_{12}N_2O$
CAS No.	15307-79-6	31121-93-4	298-46-4
Molecular weight, g/mol	318.13	228.26	236.30
Solubility in water, mg/L	50	100	17
pK_a	4.15	4.91	2.30

2.2. Study Subject

Water solutions with the addition of pharmaceutical compounds of the concentration of 1 mg/L constituted the subject of the study. High concentrations of DCF, IBU and CBZ that exceeded the usual environmental concentrations were applied due to the increase of accuracy of the conducted analytical measurements. The influence of inorganic ions on the efficiency of oxidation and reduction of micropollutants was determined by the addition of 1 mol/L inorganic salts, i.e., NaCl, Na_2CO_3, $NaHCO_3$, Na_2SO_4, Na_2HPO_4 and $AlCl_3$, $FeCl_3$, $CaCl_2$, $MgCl_2$, NH_4Cl to the water solutions. In order to determine the influence of organic substances on the degradation of pharmaceutical micropollutants, the process was conducted with the use of synthetic effluent after mechanical and biological treatment conducted on conventional wastewater treatment plant (WWTP) with the addition of pharmaceuticals patterns. The solution was prepared by adding 152 mg of dry stock and 226 mg of casein peptone to 1 L of tap-water. The mixture was heated to reach 100 °C, and after cooling it down to 21 ± 2 °C the inorganic compounds were introduced, i.e., NH_4Cl (20 mg/L), NaCl (7 mg/L), $CaCl_2 \cdot 6H_2O$ (7.5 mg/L), $MgSO_4 \cdot 7H_2O$ (2 mg/L), K_2HPO_4 (40 mg/L), KH_2PO_4 (16 mg/L). The prepared mixture was diluted 10 times. The physical and chemical characteristics of the obtained solution are presented in Table 2.

Table 2. Characteristics of the water matrix.

Indicators of Pollution	Model Effluent
pH	7.10
Conductivity, $\mu S/cm$	772.12
UV-VIS absorbance ($\lambda = 254$ nm), cm^{-1}	0.063
ChZT, mg O_2/L	32.21
BOD_5, mg O_2/L	5.23
$N-NH_4$, mg/L	1.58
$N-NO_3$, mg/L	3.50
Total organic nitrogen (TON), mg/L	6.60
$P-PO_4$, mg/L	0.40
TOC, mg/L	21.38
IC, mg/dm^3	50.54

2.3. Photocatalysis Process

The process of heterogenic photocatalysis was conducted in a laboratory glass sequential batch reactor with a volume of 700 mL by Heraeus (Hanau, Germany) (Figure 1) equipped with a medium-pressure mercury vapour UV lamp (150 W) placed in a cooling jacket. The cooling process of the lamp was performed by means of tap water and enabled to keep a constant temperature of the conducted process that did not exceed 20 ± 1 °C. The UV lamp emanated radiation with a wavelength λ_{exc} equal to 313, 365, 405, 436, 546 and 578 nm. Thus, the water suspensions were irradiated with UV-A and visible light. The dose of catalyst applied to the reaction mixture reached the level of 50 mg/L, whereas the time of contact of the catalyst with the mixture before UV irradiation process (dark mixing

inside the reactor) was set to 15 min. This step ensured the adsorption of micropollutants on the surface of TiO$_2$, what constitutes the basis for a proper run of photocatalytic oxidation and/or reduction of pharmaceuticals. To ensure proper mixing of the reactor content during the process and to avoid catalyst sedimentation, the reactor was placed on a magnetic stirrer.

The UV lamp was placed into the reactor after she obtained a stable intensity of irradiation (90 s after the UV lamp was light up). On the other hand, an aeration pump of capacity of 4 L air per minute was applied to oxidate the system. The separation of catalyst from the post-reaction mixture was conducted through the process of microfiltration with the application of a filtration set equipped with membrane filters of 0.45 membrane pore sizes by Merck Milipore (Darmstadt, Germany), with vacuum pump by AGA Labor (Warsaw, Poland).
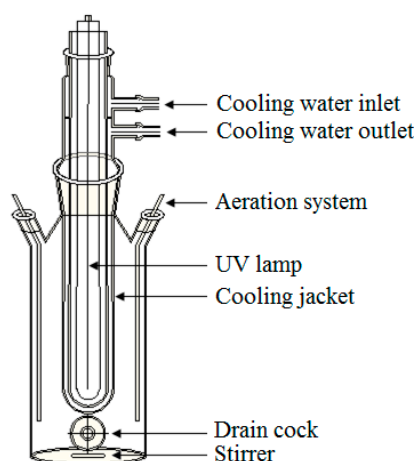

Figure 1. Scheme of the photocatalytic batch reactor.

The kinetics of the photocatalysis process was calculated with the Langmuir-Hinsherwood equation, as a correlation between the concentration of the pharmaceutical micropollutant in the investigated solutions and the time devoted to the UV irradiation (Equation (1)):

$$r = \frac{dC}{dt} = k \left(\frac{KC}{1 + KC} \right) \tag{1}$$

With the assumption that the degradation process of the pharmaceutical compound becomes a pseudo-first order reaction, the reaction rate constant may be established as a linear regression slope (Equation (2)):

$$\ln \left(\frac{C_t}{C_0} \right) = -kt \tag{2}$$

where: k constitutes the reaction rate constant of the pharmaceutical compound degradation (min^{-1}), K is an equilibrium constant of the drug adsorption on the catalyst surface, whereas C_0, C_t is the drug concentration in the water matrix before the commencement of the irradiation process ($t = 0$) and after a given time indicated as t.

The awareness of a reaction rate constant k enables to identify the half life $t_{\frac{1}{2}}$ on the basis of the Equation (3):

$$t_{\frac{1}{2}} = \frac{\ln 2}{k} \tag{3}$$

2.4. Analytical Procedure

To facilitate chromatographic identification of analytes out of the water samples with a volume of 20 mL (pH = 7) the investigated pharmaceuticals were separated with the solid phase extraction (SPE)

in a single-use columns Supelclean™ ENVI-8 volume 6 mL (1.0 g) by Supelco (Poznań, Poland) filled with octylsilyl bad (C_8). Before the extraction stage the bad was rinsed with 5 mL of methanol and conditioned with 5 mL of deionised water with pH = 7. Then, the water sample was applied onto the extraction column with a constant flow at the level reaching 1 mL/min. After the extraction the column bad was dried for 5 min at vacuum. The extract was eluted with 3 mL of methanol and then dried in a nitrogen stream. High-performance liquid chromatography HPLC equipped with UV-VIS detector by Varian (Warsaw, Poland) was incorporated for micropollutant determination. The identifications of the analytes were conducted by the use of Hypersil GOLD column by Thermo Scientific (Warsaw, Poland) of length equal to 25 cm, diameter of 4.6 mm and granulation of 5 μm. Detector wavelength (λ) necessary to obtain the required sensitivity was established at 220 nm. The mobile phase consisted of a mixture of acetonitryl and water in the ratio 85:15 (v/v), in which the flow rate reached 1 mL/min. Sample injections were performed manually with a micro-syringe of 50 μL by Hamilton.

Degradation by-products of the tested pharmaceutical compounds, generated during photocatalysis ware estimated using Saturn 2100 T gas chromatograph (GC) coupled with mass spectrometer (MS) of ion trap type with electron ionization (EI) by Varian (Warsaw, Poland). Chromatograph was equipped with 30 m × 0.25 mm SLB™-5 ms capillary column of 0.25 μm film thickness by Supelco (Poznan, Poland). Helium 5.0 was used as the carrier gas. The temperature of ion trap and ion source was 180 °C.

2.5. Toxic Bioassay

Toxicological assessment of the process was performed with Microtox® biotest that incorporates bioluminescent bacteria *Aliivibrio fischeri* as bioindicators. The test was carried out according to the Screening Test procedure by MicrotoxOmni system in the Microtox analyser Model 500 by Modern Water (Warsaw, Poland). The bacterial species *Aliivibrio fischeri* demonstrate high sensitivity across a wide variety of organic and inorganic toxic substances [20]. The test result was presented by a percentage of bioluminescence inhibition which is a result of inhibition of metabolic processes of bioindicators when exposed to a toxic substance for 15-min in reference to a control sample test constituting 2% NaCl solution.

3. Results and Discussion

3.1. Influence of Inorganic Anions

Figure 2 presents the rates of concentration decrease of pharmaceuticals present in deionized water suspensions with selected anions added as sodium salts. The preliminary investigations were conducted to assess the adsorption process of the investigated pharmaceutical compounds on the photocatalyst particles for the contact time equal to 15 min. This step initiated the placement of micropollutants around active centres of semiconductor which were supposed to accelerate their degradation after the implementation of UV irradiation process. The absorption of pharmaceutical compounds on the photocatalyst surface depends on the chemical structure of the compound and the type of semiconductor [21]. The 19% decrease of DCF concentration, 37% IBU and 12% CBZ was observed for P25 TiO_2. It is necessary to highlight the fact that the process was conducted in suspensions with pH 7, so being around the pH value of isoelectric point of the type of TiO_2 used in this study [22,23]. In these conditions, the surface of semiconductor particles has a neutral charge. Therefore, the phenomenon of adsorption of pharmaceutical substances with a negative electrostatic charge is intensified and at the same time it increases the level of their elimination. Thus, it may be assumed that the higher degree of adsorption of IBU being a weak acid was a result of the mutual attraction between the surface of the catalyst and the negatively charged pharmaceutical particles.
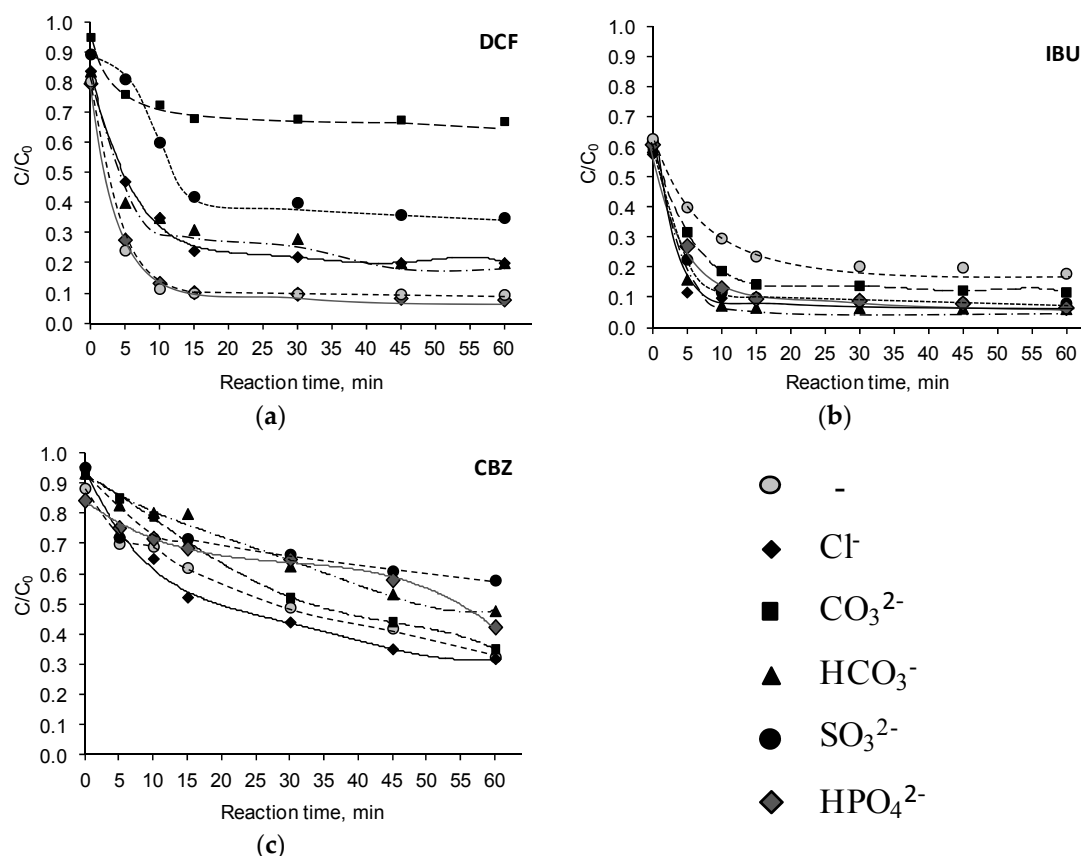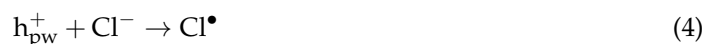
Figure 2. Influence of selected anions on the photocatalytic degradation of pharmaceuticals (**a**) diclofenac sodium salt (DCF); (**b**) ibuprofen sodium salt (IBU) and (**c**) carbamazepine (CBZ) present in water suspensions.

It was established that adding Cl^-, CO_3^{2-}, HCO_3^- and SO_4^{2-} ions leads to a decrease of the DCF adsorption degree on the photocatalyst surface (Figure 2, reaction time 0 min). The start of irradiation of the reaction mixture with UV resulted in the decrease of the drug removal to 80%, 34%, 80% and 65% subsequently after 60 min of irradiation, whereas in a solution without salts the removal exceeded 90% (Figure 2a). The mechanism of the process of heterogeneous photocatalysis assumes that the decomposition of compounds by reaction with $OH^\bullet$ radicals occurs only when these compounds are adsorbed on the surface of the photocatalyst, or are directly in close proximity [24]. Competitive adsorption of inorganic ions on the surface of the photocatalyst preclude the adsorption of pharmaceutical compounds, leading to a reduction in the efficiency of their photochemical decomposition.

The inhibition of the oxidation and reduction of the pharmaceutical substance was caused mainly by a competitive adsorption of Cl^-, CO_3^{2-}, HCO_3^- and SO_4^{2-} anions in the active centers on the catalyst surfaces. In the case where different ions react with positively charged electron holes, the intensity of the generation of hydroxyl radicals, which are mainly responsible for the distribution of contaminants, is lowered [25]. This affects the inhibition of the reaction of oxidation and/or reduction of compounds. For example, Cl^- ions may react with "holes" of valence bands of TiO_2 particles that leads to creating $Cl^\bullet$, $HClO$ or Cl_2 according to Equations (4)–(6) [26]. These radicals and compounds are well-known oxidants. Their ability to decompose organic compounds is closely connected with the chemical structure of the compounds and their functional groups (alkyl, alcohol, amide, acid, etc.) [27]. In the case of DCF, the formed oxidizing agents did not affect the increase in the decomposition of the pharmaceutical compound. This fact may be caused by the deprotonation of HOCl to yield ClO^- at a pH value above 6. It should be recalled that the experiments were conducted at pH 7. ClO^-
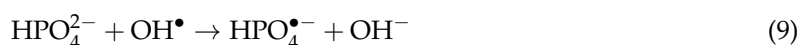
ions have in general a negligible reactivity, especially in the reaction with ionized forms of organic compounds [28].

$$h_{pw}^+ + Cl^- \rightarrow Cl^\bullet \tag{4}$$

$$OH^\bullet + Cl^\bullet \rightarrow HClO \tag{5}$$

$$Cl^\bullet + Cl^\bullet \rightarrow Cl_2 \tag{6}$$

The decrease of efficiency of the process was far higher with the presence of such ions as CO_3^{2-}, HCO_3^- and SO_4^{2-} rather than Cl^-. It is presumably connected with the higher value of the Van der Waals radius for carbonates, bicarbonates, sulphates in comparison to chlorides, which results in the higher efficiency to block active centres of a catalyst [29]. The decrease of efficiency of the photochemical degradation process of low- and high-molecular weight compounds was also proved in a wide range of other papers on this subject [30–35]. Moreover, the irradiation of the sulphate ions resulted in the generation of reactive sulphate anion radicals $SO_4^{\bullet-}$ being able to decompose organic compounds [36]. The obtained research results show the superiority of the adsorption process of the SO_4^{2-} ions on the surface of TiO_2 and the inhibition of the decomposition process of DCF over the drug oxidation through $SO_4^{\bullet-}$ radicals. Among the investigated ions, only the HPO_4^{2-} ions did not influence the oxidation and reduction of DCF. The removal degree of that compound obtained in the considered irradiation time of 60 min of both suspensions with and without the addition of HPO_4^{2-} ions was very similar. The DCF concentration in the solution containing HPO_4^{2-} ions decreased by 80% after 60 min of UV irradiation, while in the solution without any inorganic additive the DCF concentration decreased by 50%.

Different correlations were observed in case of IBU (Figure 2b). Both the addition of Cl^-, CO_3^{2-}, HCO_3^-, HPO_4^{2-} as well as SO_4^{2-} increased the efficiency of the process and the obtained removal rates for this medication exceeded 92%. Only in case of CO_3^{2-} ions did the removal rate for IBU reach 88%. On the other hand, for the solution with no salt, the micropollutant removal rate reached only 82%.

The increase in the intensity of the drug degradation for the solution containing Cl^- ions was observed during the photocatalytic CBZ oxidation. This may be related to the generation of chlorinated oxidants, which supported the decomposition of the pharmaceutical by $OH^\bullet$ radicals. The remaining anions inhibited the processes of oxidation and reduction of this micropollutant. Both ions CO_3^{2-}, HCO_3^-, HPO_4^{2-} as well as SO_4^{2-} have the ability to catch $OH^\bullet$ radicals as a result of Reactions (7)–(10) [37]:

$$CO_3^{2-} + OH^\bullet \rightarrow CO_3^{\bullet-} + OH^- \tag{7}$$

$$HCO_3^- + OH^\bullet \rightarrow CO_3^{\bullet-} + OH^- \tag{8}$$

$$HPO_4^{2-} + OH^\bullet \rightarrow HPO_4^{\bullet-} + OH^- \tag{9}$$

$$SO_4^{2-} + OH^\bullet \rightarrow SO_4^{\bullet-} + OH^- \tag{10}$$

The obtained radicals show the potential ability to decompose organic compounds, which was already mentioned in the case of $SO_4^{\bullet-}$ radicals, which enhance the degradation of drugs that contain a large number of nitrogen atoms [38] or carboxylic groups [39]. However, in the case of compounds which do not have carboxylic groups or contain fully oxidized nitrogen atoms, the presence of additional radicals may have an effect that is completely contrary. This was already confirmed in the case of CBZ oxidation and reduction.

The data analysis from the kinetics assessment of the photocatalysis occurring in the presence of ions Cl^-, CO_3^{2-}, HCO_3^-, HPO_4^{2-} and SO_4^{2-} proved a significant difference between the rapidity of pharmaceutical compounds' degradation observed during the preliminary period of the process (up to 15 min) and the rapidity of the process observed after the 15th minute of UV radiation (Table 3). These differences may result from a competitive sorption of inorganic compounds and by-products of pharmaceuticals decomposition on the surface of catalyst as well as the inhibition of the oxidation and/or reduction of pharmaceuticals. As an example, the mechanism of DCF decomposition in a

solution with $NaHCO_3$ runs very rapidly within the first 5 min of UV irradiation, with the half-life of the compound reaching 11.9 min, and after 15 min of irradiation the oxidation process stops and the reaction rate constant decreases by almost three times. The reason behind this observation may be so called scavenging of hydroxyl radical by HCO_3^- ions and producing carbonate radicals according to Reaction (8) or blockage of active centres of photocatalyst. Further irradiation of the solution results in re-acceleration of the oxidation and/or reduction of DCF, whereas the half-life of the compound decreases from 63.2 to 56.4 min. However, it is not possible to explicitly indicate if any further decomposition of the medication is caused by the reaction with $OH^\bullet$ radicals or $CO_3^{\bullet-}$ radicals. A similar correlation was observed in case of the degradation of CBZ in the presence of Na_2SO_4. SO_4^{2-} ions cause significant inhibition of the degradation process of the micropollutant due to their sorption in the active centres of semiconductor between 5 and 15 min of UV irradiation, whereas the half-life reaches 612.8 min.

Table 3. Half-life of investigated pharmaceutical compounds during photocatalysis in the presence of selected anions.

Pharmaceutical Compound	Ions	Reaction Time, (min)	Reaction Rate Constant k, (min^{-1})	R^2	Half-Life $t_{\frac{1}{2}}$, (min)
DCF	-	0–15	0.1395	0.89	8.4
		15–60	0.0039	0.93	767.9
	Cl^-	0–15	0.0808	0.98	11.6
		15–60	0.0128	0.89	166.9
	CO_3^{2-}	0–15	0.0209	0.87	38.0
		15–60	0.0010	0.96	1077.8
	HCO_3^-	0–5	0.0736	0.99	11.9
		5–15	0.0255	0.99	63.2
		15–60	0.0330	0.88	56.4
	SO_4^{2-}	0–15	0.0512	0.95	14.3
		15–60	0.0130	0.96	119.9
	HPO_4^{2-}	0–15	0.1375	0.94	8.1
		15–60	0.0197	0.96	150.2
IBU	-	0–15	0.0647	0.98	18.9
		15–60	0.0170	0.93	127.2
	Cl^-	0–10	0.1603	0.99	7.7
		10–60	0.0101	0.84	293.1
	CO_3^{2-}	0–15	0.0970	0.97	13.3
		15–60	0.0147	0.95	178.8
	HCO_3^-	0–15	0.1490	0.88	10.1
		15–60	0.0043	0.98	797.0
	SO_4^{2-}	0–15	0.1231	0.91	11.2
		15–60	0.0147	0.93	206.1
	HPO_4^{2-}	0–15	0.1261	0.97	10.3
		15–60	0.0245	0.95	123.5
CBZ	-	0–60	0.0153	0.98	59.6
	Cl^-	0–15	0.0384	0.97	16.07
		15–60	0.0114	0.98	17.85
	CO_3^{2-}	0–60	0.0165	0.99	47.4
	HCO_3^-	0–15	0.0099	0.78	59.70
		15–60	0.0114	0.97	52.90
	SO_4^{2-}	0–5	0.0558	0.99	11.53
		5–15	0.0006	0.98	612.75
		15–60	0.0049	0.99	87.30
	HPO_4^{2-}	0–15	0.0134	0.94	37.40
		15–60	0.0104	0.87	50.70

3.2. Influence of Inorganic Cations

A further stage of the investigations assessed the influence of selected cations, i.e., Al^{3+}, Fe^{3+}, Ca^{2+}, Mg^{2+}, NH_4^+, on the photochemical decomposition of micropollutants. Taking into consideration the fact that Cl^- ions only negatively influenced the DCF degradation while stimulating the oxidation and reduction of the other pharmaceuticals, the chloride salts of the above mentioned cations were

applied into the water suspensions of micropollutants. The obtained results were presented in Figure 3. The cations applied to the suspensions insignificantly influenced the adsorption rate of the micropollutants present in the water on the TiO_2 surface. Only in the case of IBU did the presence of Al^{3+} and Fe^{3+} ions decrease the sorption efficiency with the drug decrease rate reaching 16% and 14% correspondingly.
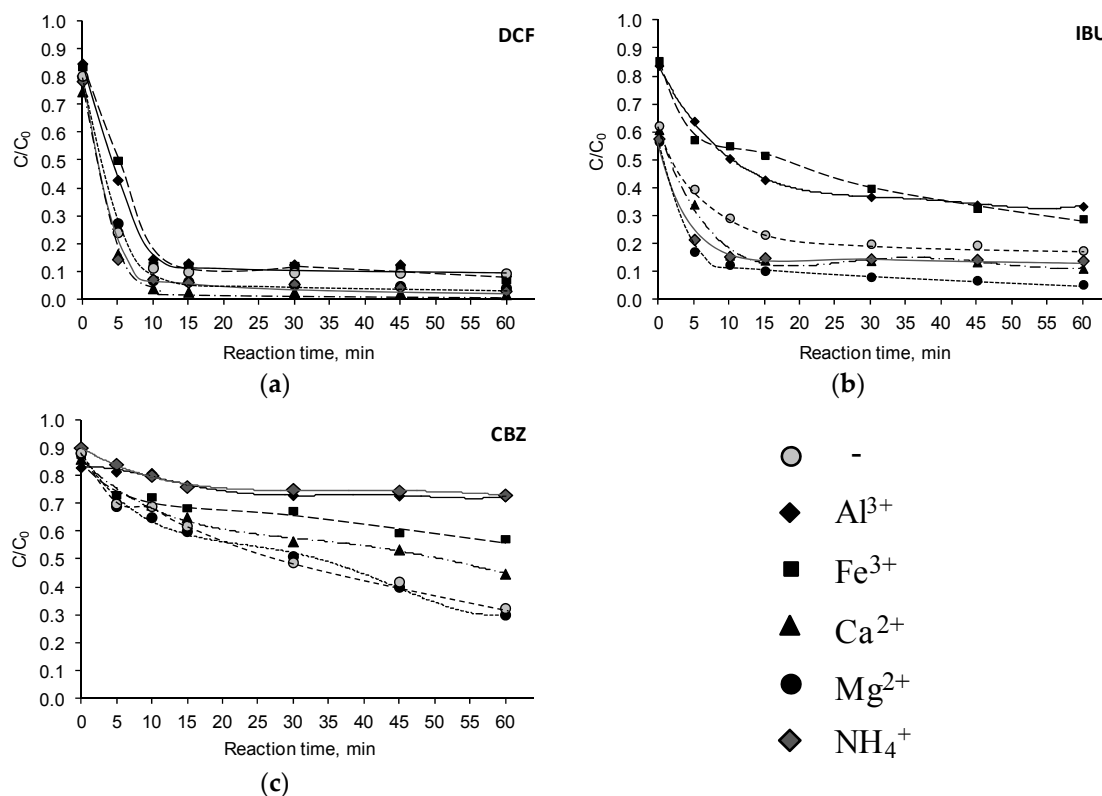

Figure 3. Influence of different cations on the photocatalytic degradation of pharmaceuticals (**a**) DCF; (**b**) IBU and (**c**) CBZ present in water suspensions.

Additionally, it was determined that the presence of Al^{3+} and Fe^{3+} ions also decreases the efficiency of photochemical degradation of all investigated pharmaceutical compounds. In research [40] it was confirmed that Al^{3+} ions can precipitate on the surface of a photocatalyst and block its photoactivity. Fe^{3+} ions can also attract electrons emerging in the process of photoactivation of photocatalyst particles according to Equation (11) and lead to the decrease of the intensity of $OH^{\bullet}$ radicals' generation.

$$Fe^{3+} + e^- \rightarrow Fe^{2+} \tag{11}$$

In the case of the solution with $AlCl_3$ the pharmaceuticals' removal rates obtained after 60 min of UV irradiation during photocatalysis reached correspondingly 91% for DCF, 66% for IBU and only 28% for CBZ. On the other hand, the micropollutants' removal rates in suspensions with $FeCl_3$ obtained more than 92% for DCF, 71% for IBU and 43% for CBZ.

It was observed that the addition of Ca^{2+}, Mg^{2+}, NH_4^+ ions to suspensions with DCF and IBU facilitated their oxidation and/or reduction taking place during the photochemical process. The DCF removal rate reached the highest value exceeding 98% in the solution with Ca^{2+} cations. The most significant decrease for IBU concentration equal to 94% was obtained during the process conducted with the presence of Mg^{2+}. Research presented in [41] proved that there is no influence of Ca^{2+}, Mg^{2+} ions on the process of photocatalytic decomposition of inorganic compounds; thus, it may be

deduced that the increase of IBU removal rate is a result of adding Cl^- anions to the solution that were stimulating the decomposition of this pharmaceutical.

Conducted tests indicated that the decomposition of DCF in the process of heterogeneous photocatalysis was intensified in the presence of Ca^{2+}, Mg^{2+}, NH_4^+ cations, whereas Al^{3+} and Fe^{3+} cations inhibit the course of the oxidation and/or reduction reactions of the pharmaceutical. The influence of Cl^-, CO_3^{2-}, HCO_3^- and SO_4^{2-} anions on the photochemical degradation of DCF was not as significant as in the case of anions.

In case of CBZ decomposition only, Mg^{2+} ions did not have a significant influence on the reaction course. Similarly to Al^{3+} and Fe^{3+} cations, the presence of Ca^{2+} and NH_4^+ ions decreased the removal rate of the compound which for the solution with Ca^{2+} equalled to 56% whereas for the process conducted with the presence of NH_4^+ it equalled only to 27%. On the other hand, the process conducted with no inorganic compounds enabled to remove this micropollutant by 60%.

Table 4 presents reaction rate constants and half-lives of pharmaceutical compounds determined for different time periods of heterogenic photocatalysis of suspensions containing selected cations.

Table 4. Half-life of investigated pharmaceutical compounds during photocatalysis in the presence of selected cations.

Pharmaceutical Compound	Ions	Reaction Time, (min)	Reaction Rate Constant k, (min^{-1})	R^2	Half-Life $t_{\frac{1}{2}}$, (min)
DCF	Al^{3+}	0–10	0.1760	0.98	4.5
		10–60	0.0172	0.92	151.3
	Fe^{3+}	0–10	0.1904	0.93	3.8
		10–30	0.0013	0.96	2137.1
		30–60	0.0539	0.89	50.8
	Ca^{2+}	0–15	0.2241	0.94	5.5
		15–60	0.0243	0.88	173.3
	Mg^{2+}	0–10	0.2436	0.99	3.6
		10–60	0.0171	0.92	197.9
	NH_4^+	0–10	0.2365	0.94	4.7
		10–60	0.0286	0.99	115.9
IBU	Al^{3+}	0–15	0.0447	0.99	20.0
		15–60	0.0165	0.88	95.1
	Fe^{3+}	0–15	0.0309	0.77	30.8
		15–60	0.0385	0.98	35.9
	Ca^{2+}	0–15	0.1023	0.94	12.3
		15–60	0.0143	0.76	182.1
	Mg^{2+}	0–10	0.1494	0.90	9.4
		10–60	0.0267	0.93	106.0
	NH_4^+	0–10	0.1307	0.92	10.3
		10–60	0.0030	0.90	853.8
CBZ	Al^{3+}	0–30	0.0043	0.98	116.76
		30–60	0.0002	0.97	1921.25
	Fe^{3+}	0–15	0.0161	0.95	33.49
		15–60	0.0042	0.98	89.85
	Ca^{2+}	0–60	0.0094	0.94	99.9
	Mg^{2+}	0–60	0.0160	0.97	57.6
	NH_4^+	0–15	0.0111	0.99	72.4
		15–60	0.0026	0.97	371.9

The shortest micropollutant half-lives were obtained for the processes conducted during the first 10 and 15 min of irradiation of the suspensions containing DCF. Thus, it can be deduced that the negative influence caused by adding the inorganic compounds occurred only during the further stages of the degradation processes of this micropollutant. It should be highlighted that the DCF oxidation and reduction processes carried out with $FeCl_3$ undergo significant inhibition between 10th and 30th minute of the process. The half-live of the compound exceeds 2137 min. The decomposition of IBU was the most rapid in the first 10 min of irradiation of the solution that included $MgCl_2$. On the other hand,

the longest CBZ half-life that reaches 1921.3 min was observed between the 30th and 60th minute of the process with the presence of AlCl$_3$.

3.3. Influence of Organic Substances

The influence of high-molecule organic compounds present in the solution of the model effluent as a dry stock and casein peptone on the degradation of the pharmaceutical compounds was also assessed. Figure 4 presented a comparison of the decrease in pharmaceutical concentration during the UV irradiation of suspensions based on deionised water (Figure 4a) and model WWTP effluent. It was observed that the significant reduction of the micropollutant concentration already began during the sorption stage. It may be concluded that the pharmaceutical substances sorbed both on the surface of TiO$_2$ particles and on the organic compounds present in the model WWTP effluent. It resulted in the decrease of the DCF concentration rate of 68%, IBU of 77% and CBZ of more than 23%. The start of the irradiation process enabled for more than 96% degradation of DCF in the first 10 min of the process, in which the half-life of the compound reached only 7.4 min (Table 5). The same situation was observed for IBU and its more than 96% decrease in concentration rate after 15 min of its photocatalytic oxidation, with its half-life not exceeding 18.3 min. Further irradiation of the reaction mixture influenced the decrease of the reaction rate constant for DCF and IBU and the increase in half-life of the compounds to 253.7 and 110.6 min correspondingly.
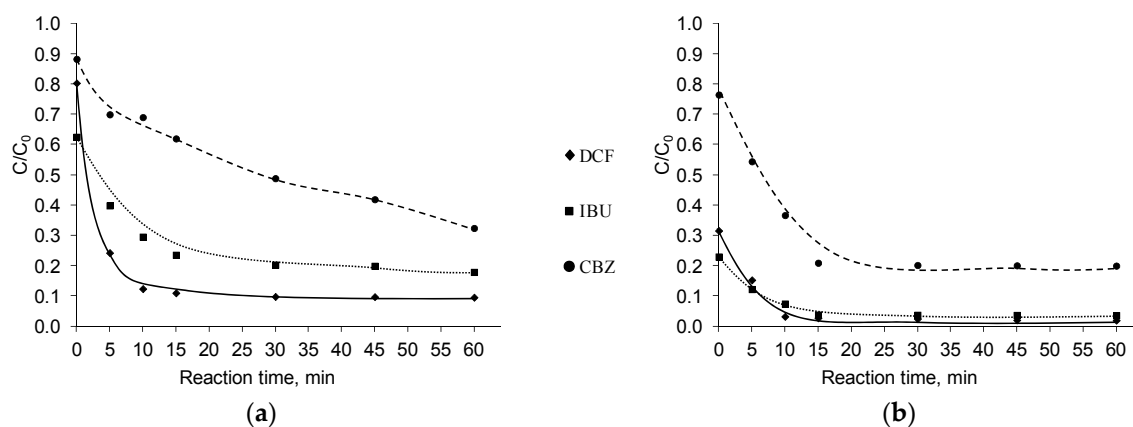

Figure 4. Degradation of pharmaceutical in (**a**) deionised water suspensions and (**b**) model WWTP effluent.

Table 5. Reaction rate constant and half-life of pharmaceutical compounds in the process of photocatalytic oxidation of the model effluent.

Pharmaceutical Compound	Reaction Time, (min)	Reaction Rate Constant k, (min^{-1})	R^2	Half-Life $t_{\frac{1}{2}}$, (min)
DCF	0–10 10–60	0.2303 0.0167	0.96 0.82	7.4 253.7
IBU	0–15 15–60	0.1189 0.0360	0.99 0.99	18.3 110.6
CBZ	0–15 15–60	0.0858 0.0029	0.99 0.78	10.6 782.7

The decomposition of CBZ occurred more slowly. For the first 15 min of the process, the result of k was almost three times lower than the reaction rate constant observed during the first stage of the DCF decomposition, whereas the concentration decrease of the pharmaceutical substance reached only 79%. The established half-life was obtained from 10.6 min till the 15th minute of UV irradiation

of the solution, and then it was prolonged up to 782.7 min. It proves the significant inhibition of the oxidation and reduction processes of this micropollutant.

The increased efficiency of the micropollutants' decomposition in the model effluent in relation to the suspensions prepared with the use of deionized water may be a result of the presence of nitrite and nitrate that may indirectly constitute an additional source of OH$^\bullet$ radicals [42–44] according to Reactions (12)–(14). Therefore, it can be deduced that the presence of other organic compounds including biogenic compounds facilitates the degradation process of pharmaceutical micropollutants. This deduction enables to anticipate a high efficiency in removal of these types of substances from the real effluent of wastewaters.

$$NO_3^- \xrightarrow{h\gamma} O^{\bullet -} + NO_2^\bullet \tag{12}$$

$$NO_2^- \xrightarrow{h\gamma} O^{\bullet -} + NO^\bullet \tag{13}$$

$$O^{\bullet -} + H^+ \xrightarrow{h\gamma} OH^\bullet \tag{14}$$

3.4. Toxicological Assessment of Treated Water Solution

The last stage of the research investigated the toxicological influence of the post-reaction suspensions. The increase of toxic effect was observed for the start of the photochemical decomposition of pharmaceutical compounds in suspensions based on deionised water (Figure 5). It is correlated with the by-products from the micropollutant degradation processes that influence the decrease of the metabolic processes of the tested organisms. The slight increase of toxicity for DCF and IBU was observed only at the beginning of the process, i.e., up to 15 min. Water of such characteristics is classified as non-toxic [45,46]. As a result of the further conduct of the process, a gradual decrease in water toxicity was observed, whereas negative values of bioluminescent inhibition of bacteria prove the existence of the stimulation of their metabolic processes. This shows probable evidence on a complete mineralization of micropollutants into H_2O and CO_2 or to the generation of products of their decomposition that influence the intensification of the oxidation process of luciferin into oxiluciferin that occurs in the organisms of the bioluminescent bacteria [47] and is responsible for generating radiation with a wavelength of about 490 nm [48].
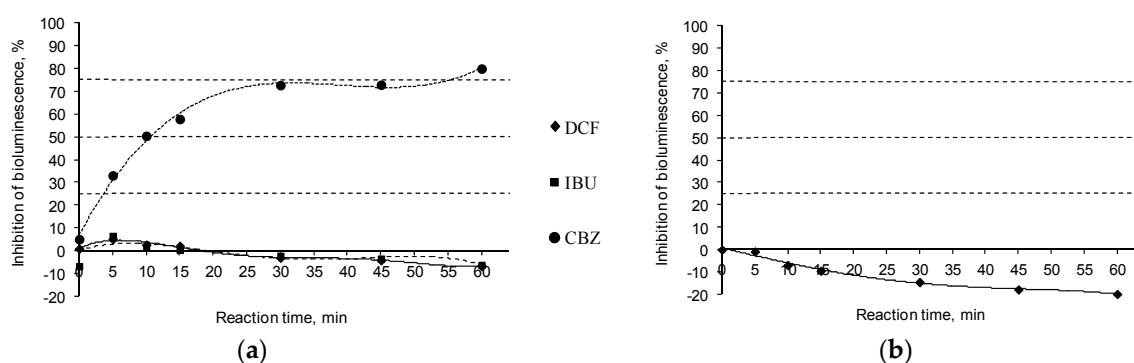

Figure 5. Change in toxicity of (**a**) deionised water suspensions and (**b**) model WWTP effluent.

A significant increase in toxicity was observed for the irradiation of deionised water solution with CBZ. After 15 min of irradiation, the collected samples were classified as toxic, whereas after 60 min the post-reaction solution was characterised with high toxicity. The obtained results prove an incomplete decomposition of CBZ and production of oxidation by-products of this pharmaceutical substance that significantly deteriorates the quality of the treated water. Research presented in [49] show the possibility to produce a wide array of by-products of CBZ degradation during different processes of water treatment, among which the UV radiation is also enumerated. These compounds are characterised by higher biological activity that causes the increase in their toxic influence on other tested organisms [50].

No toxic response was observed during the irradiation process of the model effluent solution. The stimulation of the bacteria bioluminescence was observed in sample after 5 and 60 min of irradiation. It is connected with the high rate of micropollutant removal. Moreover, it may be concluded that by-products from the incomplete mineralization of pharmaceutical compounds underwent oxidation and/or reduction or adsorbed themselves on the substrates surfaces, which are a part of the model effluent, and composed complexes, for example: micropollutant–organic compound.

The generation of different oxidation by-products of DCF, IBU and CBZ was established during the GC-MS analysis of analyst present in water samples after their UV irradiation. The analysis was carried out for water suspension without the addition of organic and inorganic compounds. The by-products were identified based on the obtained mass spectrum. The possible degradation pathways of DCF ware illustrated in Figure 6. The decomposition of this pharmaceutical compound leads to the formation of nine by-products which were mainly present in samples after 5, 10 and 15 min of UV irradiation. Products of IBU decomposition ware shown on Figure 7. The CBZ decomposition by-products presented in Figure 8 were generated during the whole irradiation process.
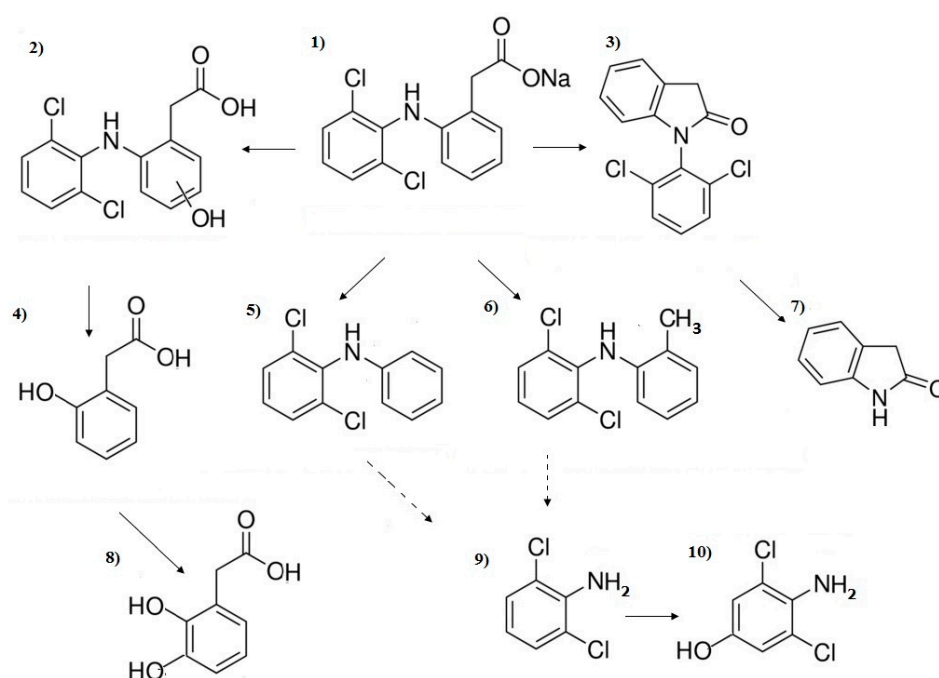

Figure 6. Possible degradation pathway of **1** diclofenac sodium salt where **2** 4′-hydroxydiclofenac, **3** 1-(2,6-dichlorophenyl)-2-indolinone, **4** 2-hydroxyphenylacetic acid, **5** 2-dichlorodiphenylamine, **6** *N*-(2,6-dichlorophenyl)-2-aminotoluene, **7** 2-indolinone, **8** 2,3-dihydroxyphenylacetic acid, **9** 2,6-dichloroaniline and **10** 4-amino-3,5-dichlorophenol.
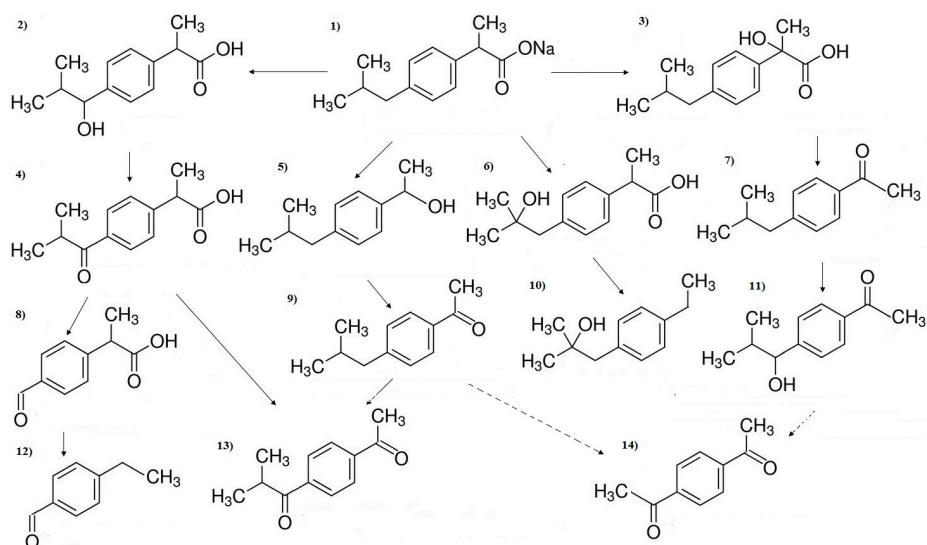
Figure 7. Possible degradation pathway of **1** ibuprofen sodium salt where **2** 1-hydroxyibuprofen **3** 2-hydroxy-2-[4-(2-methylpropyl)phenyl]propionic acid, **4** 2-(4-isopropylcarbonylphenyl)propanoic acid, **5** 1-(4-isobutylphenyl)-1-ethanol, **6** 2-hydroxyibuprofen, **7** 1-[4-(2-methylpropyl)phenyl] ethanone, **8** 2-(4-formylphenyl)propanoic acid, **9** 1-(4-isobutylphenyl)-1-ethanone, **10** 1-ethyl-4-(2-hydroxy)isobutyl benzene, **11** 4-(1-hydroxy-2-methylpropyl)acetophenone, **12** 4-ethylbenzaldehyde, **13** 1-(4-acetylphenyl)-2-methyl-1-propanone and **14** 4-acetylbenzoic acid.
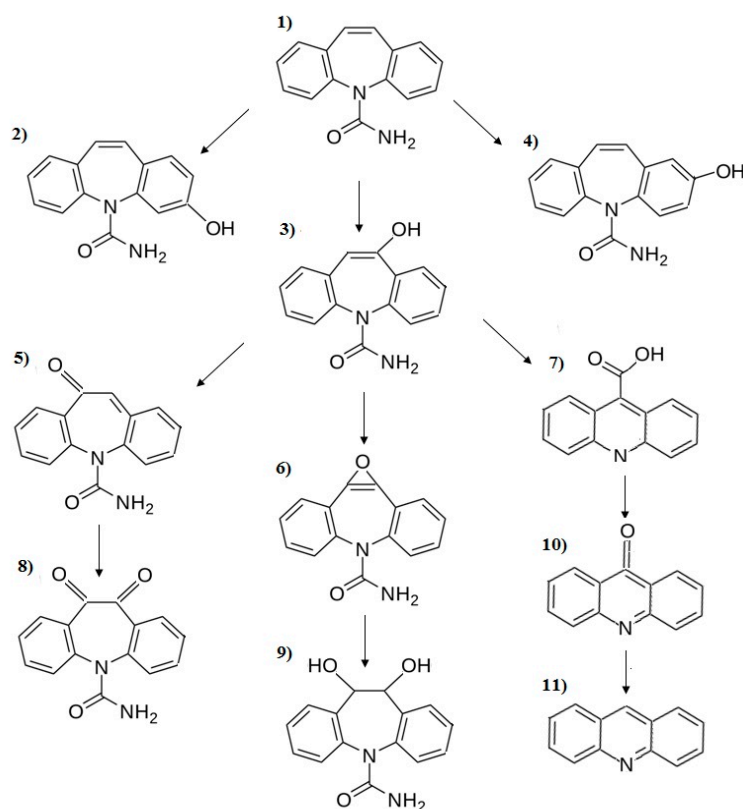
Figure 8. Possible degradation pathway of **1** carbamazepine where **2** 3-hydroxycarbamazepine, **3** 10,11-dihydro-10-hydroxycarbamazepine, **4** 2-hydroxycarbamazepine, **5** oxcarbazepine, **6** carbamazepine 10,11-epoxide, **7** acridine-9 carboxylic acid, **8** diketo-oxcarbazepine, **9** dihydrocarbamazepine-10,11-*trans*-diol, **10** acridine and **11** acridine.

4. Conclusions

On the basis of the conducted investigations on the assessment of the decomposition rate of DCF, IBU and CBZ in the process of photocatalytic oxidation in the presence of inorganic compounds, it was concluded that the efficiency of micropollutants' decomposition strictly depends on the type of pharmaceutical compound as well as on the inorganic ions themselves. In DCF suspensions, a significantly decrease in the compound was observed in the presence of Cl^-, CO_3^{2-}, HCO_3^- and SO_4^{2-} ions. The decomposition of CBZ was most effective in deionised water with Cl^-, whereas the presence of CO_3^{2-}, HCO_3^-, HPO_4^{2-} and SO_4^{2-} inhibited the reaction course of the compound decomposition in an explicit way. A contrary relation was observed for IBU. In this case, all anions facilitated the process of its photochemical oxidation and/or reduction. The presence of Al^{3+} and Fe^{3+} cations affected the decrease of the process efficiency for all investigated pharmaceutical compounds. For DCF and IBU in suspensions containing Ca^{2+}, Mg^{2+} and NH_4^+, the increase of the reaction rate constant of compounds' decomposition was observed in comparison to a solution with no inorganic compounds added. The highest removal rate of micropollutants was observed for the model effluent that exceeded 96% for DCF and IBU and reached 79% for CBZ. The presence of inorganic compounds with high molecular weight catalyses the degradation process of pharmaceutical compounds and constitutes an additional sorbent that is able to significantly reduce their concentration. The toxicological analysis conducted in the deionised water showed generation of by-products of the oxidation and/or reduction of pharmaceutical micropollutants that deteriorate the quality of the treated aqueous streams. This was explicitly visible for the oxidation of a solution with CBZ which characterised itself with high toxicity after 60 min of the process. The presence of organic compounds affects the decrease of water toxicity, which is visible in the stimulation of metabolic processes of bacterium *Aliivibrio fischeri*. The gas chromatography-mass spectrometry (GC-MS) analysis allowed for the estimation of the possible photocatalytic degradation pathways of the examined pharmaceutical compounds.

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