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Photolysis and photocatalysis of ibuprofen in aqueous medium: characterization of by-products via liquid chromatography coupled to high-resolution mass spectrometry and assessment of their toxicities against *Artemia Salina*

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The degradation of the pharmaceutical compound ibuprofen (IBP) in aqueous solution induced by direct photolysis (UV-A and UV-C radiation) and photocatalysis (TiO_2/UV-A and TiO_2/UV-C systems) was evaluated. Initially, we observed that whereas photocatalysis (both systems) and direct photolysis with UV-C radiation were able to cause an almost complete removal of IBP, the mineralization rates achieved for all the photodegradation processes were much smaller (the highest value being obtained for the TiO_2/UV-C system: 37.7%), even after an exposure time as long as 120 min. Chemical structures for the by-products formed under these oxidative conditions (11 of them were detected) were proposed based on the data from liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS) analyses. Taking into account these results, an unprecedented route for the photodegradation of IBP could thus be proposed. Moreover, a fortunate result was achieved herein: tests against *Artemia salina* showed that the degradation products had no higher ecotoxicities than IBP, which possibly indicates that the photocatalytic (TiO_2/UV-A and TiO_2/UV-C systems) and photolytic (UV-C radiation) processes can be conveniently employed to deplete IBP in aqueous media. Copyright © 2014 John Wiley & Sons, Ltd.

Keywords: photodegradation; ibuprofen; high-resolution mass spectrometry; liquid chromatography; characterization of by-products

Introduction

The presence of various pharmaceutical pollutants in the environment has received much attention because of their unknown impact on flora and fauna present in aquatic systems.[1,2] These compounds have been detected in natural aquatic environments at trace concentrations (from $ng\,L^{-1}$ to $\mu g\,L^{-1}$).[3–7] The major sources of these pollutants arise from emissions of production sites, direct disposal of over plus drugs in households and hospitals, excretion of urine or feces after drug administration to humans/animals and water treatment in fish farms.[8]

To improve the efficiency of removal of pharmaceutical compounds in aqueous media, novel and powerful technologies have been developed, especially the so-called advanced oxidation processes (AOPs). Moreover, there has been a growing interest in the detection and identification of degradation products resulting from the application of AOPs.[9,10] Among the AOPs, the following processes are noteworthy: photolysis,[11–16] photocatalysis,[17] electrochemistry and photoelectrochemistry.[18,19] However, many challenging issues still remain, which are mainly related to the fact that products arising from the degradation of pollutants may present higher toxicity than their predecessors. This possibility has been properly assessed by studies with brine shrimp (*Artemia salina*), an organism that is particularly sensitive to the degree of toxicity of organic compounds in solution.[20–24]

The compound 2-[3-(2-methylpropyl)phenyl] propanoic acid, commercially available as ibuprofen (IBP), is one of the most consumed pharmaceuticals worldwide.[25] It is a nonsteroidal agent, analgesic, antipyretic and anti-inflammatory, used for the treatment of fever and to relieve pain in general.[25] Once administered, only 15% is eliminated as the original form, while 26% is excreted as hydroxy-IBP and 43% as carboxy-IBP (Fig. 1).[26]

There are reports on the presence of IBP and its metabolites in effluents from sewage treatment plants and surface waters. A

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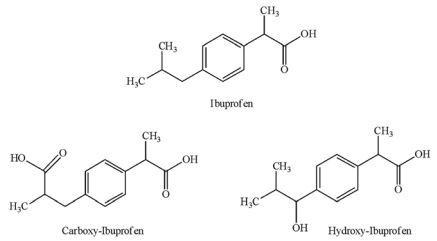

Figure 1. Chemical structures of ibuprofen (IBP), hydroxy-ibuprofen and carboxy-ibuprofen.

survey conducted between 2006 and 2010 confirmed the presence of IBP in concentrations ranging from 65 to 7100 ng L^{-1} in sewage treatment plants and raw sewage effluents and up to 360 ng L^{-1} in freshwater.[27] The lower concentration of IBP reported in surface waters is probably due to a combination of factors such as photolysis, biotransformation, sorption, volatilization and dispersion in the environment.[28]

Studies have demonstrated that IBP is partially removed in treatment stations; in some cases, a removal rate of 70% can be obtained, especially when using biological oxidation.[29] However, the main metabolites (carboxy-IBP and/or hydroxy-IBP) persist after the biological treatment as toxic by-products that may affect the aquatic environment.[26–30] Even reaching moderate levels of removal (70%), IBP is not easily depleted by conventional biological processes; as a consequence, an inconveniently long withholding time (usually days) is required to attain higher degradation rates. Therefore, a series of new technologies have been applied in order to more effectively reduce the presence of IBP in the environment, such as photodegradation, solar photodegradation,[30–34] biological treatment[35–43] and other AOPs.[44–47]

Although some studies involving the removal of IBP from aqueous solution have been reported, detailed information regarding the overall degradation process remains scarce. The present study aims, therefore, to investigate the degradation of IBP in a watery medium induced by two distinct methods: direct photolysis (by employing UV-A and UV-C irradiation) and photocatalysis (by using the TiO_2/UV-A and TiO_2/UV-C systems). The detection and identification of recalcitrant by-products, possibly formed under these oxidative conditions, via liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS) are the main focus of the present paper. Additionally, the level of ecotoxicity of such compounds is appraised in tests against *A. salina*.

Experimental section

Chemicals

Ibuprofen ($C_{13}H_{18}O_2$, nominal mass 206.1307), whose chemical structure is shown in Fig. 1, was purchased from Sigma-Aldrich (St. Louis, MO, USA). Solvents for analytical determinations were methanol (chromatographic grade, JT Baker) and ultrapure water. Ultrapure water, from a Millipore Milli-Q system (Milford, MA, USA), was employed to prepare all solutions. Commercial TiO_2 (99% anatase), acquired from Sigma-Aldrich company (St. Louis, MO, USA), was used as a catalyst in the photocatalytic experiments.

Degradation experiments

The experiments were conducted in a jar-test apparatus (model 218/LDB06, Nova Ética, Jundiaí, São Paulo, Brazil). Three distinct types of assays were performed: photocatalysis (using TiO_2 and UV radiation simultaneously), photolysis (with UV radiation solely) and hydrolysis (with no TiO_2 and UV radiation). In the photocatalysis and photolysis experiments, two different types of UV radiation, UV-C and UV-A, were tested. UV-C and UV-A radiations were provided by the following lamps, respectively: germicidal (power: 9 W, emission wavelength range: 200–280 nm, model: PL-S, manufacturer: Philips) and dark light (power: 9 W, emission wavelength range: 315–400 nm, model: LY9-H, manufacturer: Ecolume). Each photocatalytic or photolytic experiment was performed using three UV lamps (UV-A or UV-C) simultaneously with a total nominal power of 27 W. The three UV lamps were placed together into a cylindrical quartz tube, which was immersed in the aqueous solution of IBP. A volume of 2.0 L of this solution, prepared at an abnormally high concentration of 5 mg L^{-1}, was transferred to the rectangular container of the jar-test vessel (2.5 L volumetric capacity). The concentration of the IBP solution (5 mg L^{-1}), although much higher than those typically found in environmental samples, was chosen to make the subsequent chromatographic analysis easy, with no need of extraction and pre-concentration steps. The solution, kept protected from external light, was stirred for about 30 min before the beginning of the degradation tests. Control experiments (results not shown) indicated that the amount of IBP adsorbed by the TiO_2 material in the dark for 120 min was negligible. All tests were conducted within a narrow range of temperature (24–25 °C), which certainly has negligible effects on the course of the photodegradation processes.[48]

In the photocatalysis experiments, 240 mg of TiO_2 (comprising a dosage of about 120 mg L^{-1}) was used. The reaction flasks (jar-test containers) were externally coated with a refractory material applied to ensure that ambient radiation would not dissipate into the medium. During the degradation experiments, the jar-test instrument was operated with a rotational speed of 250 rpm, corresponding to a gradient velocity of 400 s^{-1}. The tests were conducted in batch mode for a period of 2 h, during which aliquots were collected at intervals of 0, 5, 10, 15, 30, 60 and 120 min.

The aliquots collected during the photocatalysis experiments were centrifuged at 4000 rpm for 10 min (centrifugal model 80–20, Centribio, São Paulo, Brazil) to remove any suspended material (TiO_2). The supernatant was then recovered and stored protected from light at a temperature lower than 4 °C. The aliquots collected from the photolysis and hydrolysis tests were also maintained under identical conditions until the moment of the total organic carbon (TOC) and chromatographic analyses. Because of their high polarity, the degradation products are certainly more soluble in water than IBP (the structures proposed for all by-products will be displayed later in this paper). Hence, the occurrence of precipitation of any by-product during the centrifugation step is quite unlikely.

Total organic carbon analyses

Total organic carbon (TOC) analyses were carried out on a TOC analyzer (Shimadzu, model TOC-VCPH, Kyoto, Japan). The TOC content of each collected aliquot was obtained by the indirect method that corresponds to the difference between the total carbon and inorganic carbon values.

Ecotoxicity tests against *Artemia Salina*

The ecotoxicity tests with brine shrimp (*A. salina*) were carried out following a previous protocol.[49] By following this procedure, an aqueous solution of sea salt (at 38 g L^{-1}) was prepared, filtered

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and added to a small (15 cm diameter) round plastic container. Subsequently, many *A. salina* eggs were added in only one-half of this container, which was kept protected from light for 24 h, whereas the opposite half was continuously irradiated by a 100 W lamp. After the eggs hatched, the *A. salina* organisms migrated to the lit side. A small portion of this solution with the adult individuals was then collected and transferred to a cylindrical glass vial (3 cm diameter) and the volume completed to 1.0 mL by adding the aforementioned salt solution. Afterwards, 4.0 mL of a given aliquot, collected from the degradation experiments, was put into the vial (at the end the total volume in each vial was 5.0 mL). The vial was then left to stand under light for a period of up to 24 h. After this time, the percentage of the immobilized organisms was determined. The assays with each aliquot were conducted in triplicate to estimate the accurate toxicity of each by-product.

Liquid chromatography coupled to mass spectrometry

The analyses were performed on a liquid chromatographer (LC) coupled to a hybrid mass spectrometer (MS) system. The liquid chromatographer (Prominence LC-20 AD; Shimadzu Corporation, Kyoto, Japan) was equipped with a binary pump and an autosampler (SIL 20 AC; Shimadzu Corporation, Kyoto, Japan). The mass spectrometer (IT-TOF; Shimadzu Corporation, Kyoto, Japan) provides high sensitivity and accuracy with a resolving power over 10.000 at mass-to-charge (*m/z*) 1000. The mass spectrometer was equipped with an electrospray ionization (ESI) source operating in both the negative (−3.5 kV) and positive modes (+4.5 kV) modes. Direct infusion analyses were conducted by simultaneously operating the electrospray source in the positive and negative modes and adjusting the nebulizer gas (N_2) to a flow rate of 1.5 L min^{-1}. The interface and curved line dessolvation were operated at a constant temperature of 200 °C. An *m/z* range of 50–500 was recorded. The samples were directly introduced into the ESI source by injecting 5 μL of sample via the LC autosampler. For the LC-HRMS analyses, the mass spectrometer was set to operate under the conditions specified earlier. The chromatographic conditions were as follows: an ACE C18 column (2.1 × 100 mm × 3 mm particle diameter) was used, whereas water (A) and methanol (B) (at assorted proportions) were employed as the mobile phases at a flow rate of 0.2 mL min^{-1}. The gradient program started with 30% B, rising to 50% B in 4 min, then to 100% B in 3 min, which was then held for 3 min. At the end of the chromatographic run, the column was re-equilibrated to the initial conditions and stabilized for 4 min, which led to a total run time of 14 min. The injection volume was 5 μL.

Results and discussion

Kinetics of ibuprofen degradation

All aliquots were analyzed by direct infusion ESI-HRMS in both the positive and negative modes (see Experimental Section for more details). However, because by-products were detected exclusively in the negative mode of acquisition, only this set of data will be presented and discussed herein. Hence, Fig. 2 shows the continuous decrease in the concentration of IBP as a function of reaction time observed for the photocatalysis, photolysis and hydrolysis tests. The results from the hydrolysis experiments (conducted in the absence of TiO_2 and UV radiation) indicated that IBP is quite stable in aqueous solution.

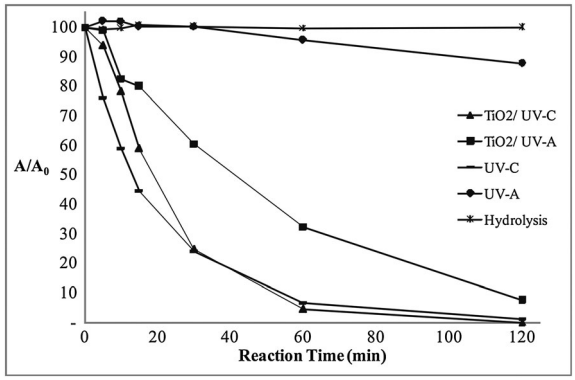

Figure 2. Relative concentration of ibuprofen achieved for different systems: photolysis (UV-A and UV-C), photocatalysis (TiO_2/UV-A and TiO_2/UV-C) and hydrolysis. The concentrations of IBP were determined via extracted-ion chromatograms for deprotonated ibuprofen (*m/z* 205.1235). An initial IBP concentration of 100 was arbitrarily assigned in each assay.

The heterogeneous photocatalytic and direct photolytic systems operating under UV-C irradiation promoted the removal of IBP with high efficiencies, at rates reaching 100% and 98.9%, respectively, after 120 min of exposure. The reason for the high degradation rates achieved upon application of the photolytic system is probably due to the overlapping of the emission spectrum of the UV-C lamp (100–280 nm with a maximum emission at 254 nm) with the absorption spectrum of IBP (absorption up to 240 nm with a λ_{max} at 222 nm).[50] This effect can also be attributed to the *in situ* generation of $OH^{\bullet}$ radicals directly from the homolysis of water molecules by the 185 nm irradiation.[51] Although the use of TiO_2 seems not to make a remarkable difference regarding the removal of IBP, its beneficial effects will be discussed following this paper.

The TiO_2/UV-A and TiO_2/UV-C photocatalytic systems showed similar capacities in promoting the depletion of IBP (the first one was able to degrade 92.6% of the original IBP after a treatment time of 120 min). Conversely, the direct photolysis with UV-A radiation exhibited a much lower efficiency (roughly 12.5%) than the analogous assay with UV-C (98.9%). This result indicates that the catalyst (TiO_2) is of prime importance to achieve higher degradation yields when UV-A radiation (that mimics solar radiation and is generated by means of a dark lamp; see Experimental Section for more details) is employed. The low removal efficiency achieved by the application of direct UV-A photolysis can be easily explained considering that neither IBP can absorb in the emission region of the UV-A lamp (315–400 nm with λ_{max} = 360 nm) nor $OH^{\bullet}$ radicals can be generated upon the homolysis of H_2O molecules by the UV-A irradiation. This set of findings therefore indicates that the depletion of IBP induced by the TiO_2/UV-A system is mostly caused by hydroxyl radicals ($OH^{\bullet}$), quite reactive species that are generated *in situ* by the interaction of H_2O molecules with the positive holes (h^+) at the valence band of excited TiO_2 catalyst.

Table 1 shows the rate constants (*k*) and half-life times ($t_{1/2}$) calculated for the degradation of IBP induced by the photocatalytic (TiO_2/UV-A and TiO_2/UV-C) and photolytic (UV-A and UV-C) systems. The experimental data, i.e. the relative concentration of IBP as a function of time, achieved for each one of the four systems, were properly adjusted by a first-order kinetic model. Hence, in all the first-order kinetic plots, i.e. ln (C_t/C_o) (C_o and C_t refer to the concentrations of IBP at the beginning and at a given reaction time, respectively) *versus* time, correlation coefficients (R^2) ranging from 0.943 to 0.994 (for the UV-A and TiO_2/UV-A

Table 1. Kinetic parameters obtained for the degradation of ibuprofen in aqueous solution induced by four distinct systems: TiO_2/UV-C, UV-C, TiO_2/UV-A and UV-A

Degradation system	R^2	k (min^{-1})	$t_{1/2}$(min)
TiO_2/UV-C	0.991	0.054	12.83
UV-C	0.987	0.037	18.73
TiO_2/UV-A	0.994	0.021	33.00
UV-A	0.943	0.001	693.00

A first-order model was used to adjust the experimental data.

systems, respectively) were achieved. An accurate analysis of Table 1 reveals that although the TiO_2/UV-C and UV-C processes yielded similar degradation rates after an identical treatment time (120 min, see previous discussion), the photocatalytic systems are more efficient to deplete IBP than the analogous photolytic processes, given that $t_{1/2}$ (TiO_2/UV-A) $< t_{1/2}$ (UV-A) and that $t_{1/2}$ (TiO_2/UV-C) $< t_{1/2}$ (UV-C). As previously stated, the superior performance of the photocatalytic systems can be related to the ability of the TiO_2 material (upon exposure to UV radiation) to generate a substantial amount of hydroxyl radicals, which promote a prompt and nonspecific attack towards target molecules present in the reaction medium.

Furthermore, it is important to state that in all experiments (photolytic and photocatalytic), the maximum variation between the pHs of the initial and final solutions was about 0.25 units. The solution pH is a complex factor that can affect photocatalytic reactions in many ways. For instance, factors such as the ionization state of TiO_2 surface, the influence of electron holes on $OH^{\bullet}$ generation and the reduction of surface area by the agglomeration of TiO_2 particles are affected by the solution pH.[52] This small difference between the pHs of the initial and final solutions could not cause therefore remarkable changes in the reaction kinetics.

Mineralization

Although impressive IBP degradation rates (over 90%) were achieved by the employment of the TiO_2/UV-C, TiO_2/UV-A and UV-C systems (Fig. 2), the TOC data revealed that IBP was not mineralized to a similar extent, even after a treatment time as long as 120 min. For instance, the highest mineralization rate was only 37.7% achieved upon the application of the TiO_2/UV-C system. Moreover, the mineralization rates derived from direct photolysis (UV-C and mainly UV-A) were negligible. These findings indicate that whereas most of the original IBP was not mineralized, recalcitrant by-products were generated under these conditions. The fact that the direct photolysis processes are unable to reduce the TOC content in solution strongly indicates that such refractory by-products absorb neither UV-A nor UV-C radiation. It is also evident that the highest rates of mineralization obtained by the photocatalytic systems (TiO_2/UV-C and TiO_2/UV-A) can be attributed again to their superior ability to promote the *in situ* generation of hydroxyl radicals upon exposure of the TiO_2 catalyst to UV radiation.

Identification of by-products: proposal of a degradation route

The aliquots collected during the photocatalysis and photolysis experiments were firstly analyzed via direct infusion HRMS in the negative ion mode. Some examples of the mass spectra recorded are depicted in Fig. 3. Note the continuous decrease in the relative abundance of the ion ascribed to be the deprotonated form of IBP (*m/z* 205.1235). This finding thus indicates the continuous consumption of IBP by the photolytic and photocatalytic systems. A meticulous search in these mass spectra revealed the presence of 11 ions clearly distinguishable from the 'background'. Based on the HRMS data, molecular formulae for these ions, which were ascribed to be the deprotonated forms of degradation products possibly formed under these conditions, are displayed in Table 2. A maximum error of 8 ppm between the experimental and theoretical accurate masses of IBP and its by-products was observed. All these intermediates were detected at least in one of the aliquots of the photocatalytic (TiO_2/UV-C and TiO_2/UV-A) or photolytic (UV-C and UV-A) processes. Extracted-ion chromatograms (Fig. 4) were obtained for each one of these 11 ions to confirm the formation of by-products in solution. Under the chromatographic conditions employed, some by-products co-eluted (**1** and **6** as well as **7** and **8**), whereas other ones (**8**, **9** and **11**) eluted at very close retention times (Fig. 4). In spite of these chromatography limitations, the HRMS data allowed the proposition of chemical structures for each one of these by-products.

Based on these results as well as on the well-known reactivity of hydroxyl radical towards organic molecules in aqueous medium, a route for the photodegradation of IBP could thus be proposed, as outlined in Fig. 5. Hence, hydroxylated derivatives were identified by the increase of one or more oxygen atoms in the molecular formulae of IBP or some of its intermediates, with no alterations in the double bond equivalence. Among the by-products detected (**1–11**) several isomeric structures can be postulated. The correct structure (or structures), however, could not be firmly established herein based on the information provided by HRMS. Moreover, the fragmentation profile (not shown) of each ionic species (deprotonated forms of **1–11**) was useless to accomplish this task as in the MS/MS product ions arising from loss of water were dominant. For a matter of simplicity, however, only one among the several isomers possibly formed under these conditions are represented in Fig. 5. Some intermediates were proposed to be formed by successive hydroxylation starting from IBP ($C_{13}H_{18}O_2$). That is the case of **1** ($C_{13}H_{18}O_3$), (represented as two isomeric forms: α-hydroxy-carboxy-IBP and α-hydroxy-isopropyl-IBP), **2** ($C_{13}H_{18}O_4$) and **3** ($C_{13}H_{18}O_5$). Another by-product (**5**, $C_{12}H_{18}O_6$) was proposed herein to arise from hydroxylation of **4** ($C_{12}H_{18}O_5$). In addition, other by-products were suggested to be generated via alternative pathways. For instance, intermediates **4** ($C_{12}H_{18}O_5$) and **6** ($C_{12}H_{18}O$) were possibly formed by decarboxylation of **3** ($C_{13}H_{18}O_5$) and **1** ($C_{13}H_{18}O_3$), respectively. In sequence, by-product **6** ($C_{12}H_{18}O$) could undergo hydroxylation and loss of 2-propanol to yield intermediate **9** ($C_9H_{10}O$). By-product **7** ($C_9H_{10}O_3$) could be formed by two consecutive hydroxylations of **9** ($C_9H_{10}O$). It is also suggested that the subsequent oxidation of the alcohol function of **9** ($C_9H_{10}O$) could furnish intermediate **8** ($C_9H_8O_3$). Lastly, the acyclic intermediates **10** ($C_6H_{10}O_3$) and **11** ($C_5H_{10}O_3$) could be generated by successive hydroxylation of intermediates **8** and **5** that could ultimately lead to the opening of their aromatic rings. These intermediates (**10** and **11**) could be easily mineralized under these oxidative conditions. It is important to mention that some of these intermediates (**1**, **2**, **6**, **8** and **9**) have been previously reported by several research groups.[25,32,36,38,45,51,53,54]

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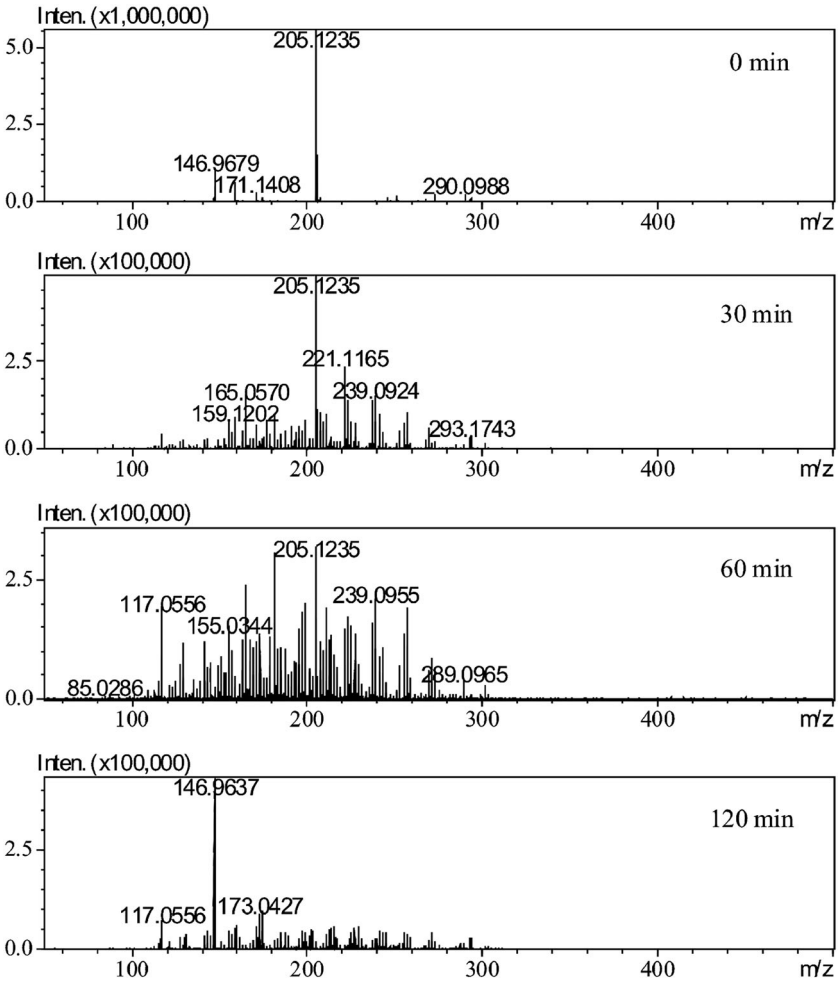

Figure 3. High resolution mass spectrometry (HRMS) recorded for aliquots collected from the TiO_2/UV-C system after the following reaction times: 0, 30, 60 and 120 min. The molecular formulae for some of the intermediates observed in these mass spectra are shown in Table 2. Note that relative abundance of the ion of *m/z* 235.1235 (deprotonated IBP) decreases as a function of reaction time.

Table 2. High-resolution mass spectrometry data and the molecular formulae calculated for the by-products generated during the photodegradation of ibuprofen in water

Compound	Molecular formula	Molecular mass (M)[a]	$[M-H]^-$ (theoretical)	$[M-H]^-$ (experimental)	Error (ppm)	Double bond equivalence
IBP	$C_{13}H_{18}O_2$	206.1307	205.1234	205.1235	0.47	5
1	$C_{13}H_{18}O_3$	222.1256	221.1183	221.1165	−5.88	5
2	$C_{13}H_{18}O_4$	238.1205	237.1132	237.1138	2.38	5
3	$C_{13}H_{18}O_5$	254.1154	253.1076	253.1082	3.16	5
4	$C_{12}H_{18}O_5$	242.1154	241.1081	241.1088	2.70	4
5	$C_{12}H_{18}O_6$	258.1103	257.1031	257.1033	0.92	4
6	$C_{12}H_{18}O$	178.1358	177.1285	177.1295	5.64	4
7	$C_9H_{10}O_3$	166.0630	165.0557	165.0570	7.72	5
8	$C_9H_8O_3$	164.0473	163.0401	163.0388	7.73	6
9	$C_9H_{10}O$	134.0732	133.0653	133.0651	−1.50	5
10	$C_6H_{10}O_3$	130.0630	129.0557	129.0563	4.64	2
11	$C_5H_{10}O_3$	118.0630	117.0557	117.0556	1.00	1

[a]Accurate mass calculated by the LCMS solutions software.

The evolution of each intermediate (**1–11**) formed during the photodegradation processes could then be monitored by LC-HRMS. The results from the extracted-ion chromatograms (Fig. 4) were handled to build plots of the relative concentration of each by-product (a value of 100 was attributed to the highest concentration) *versus* reaction time for all the four

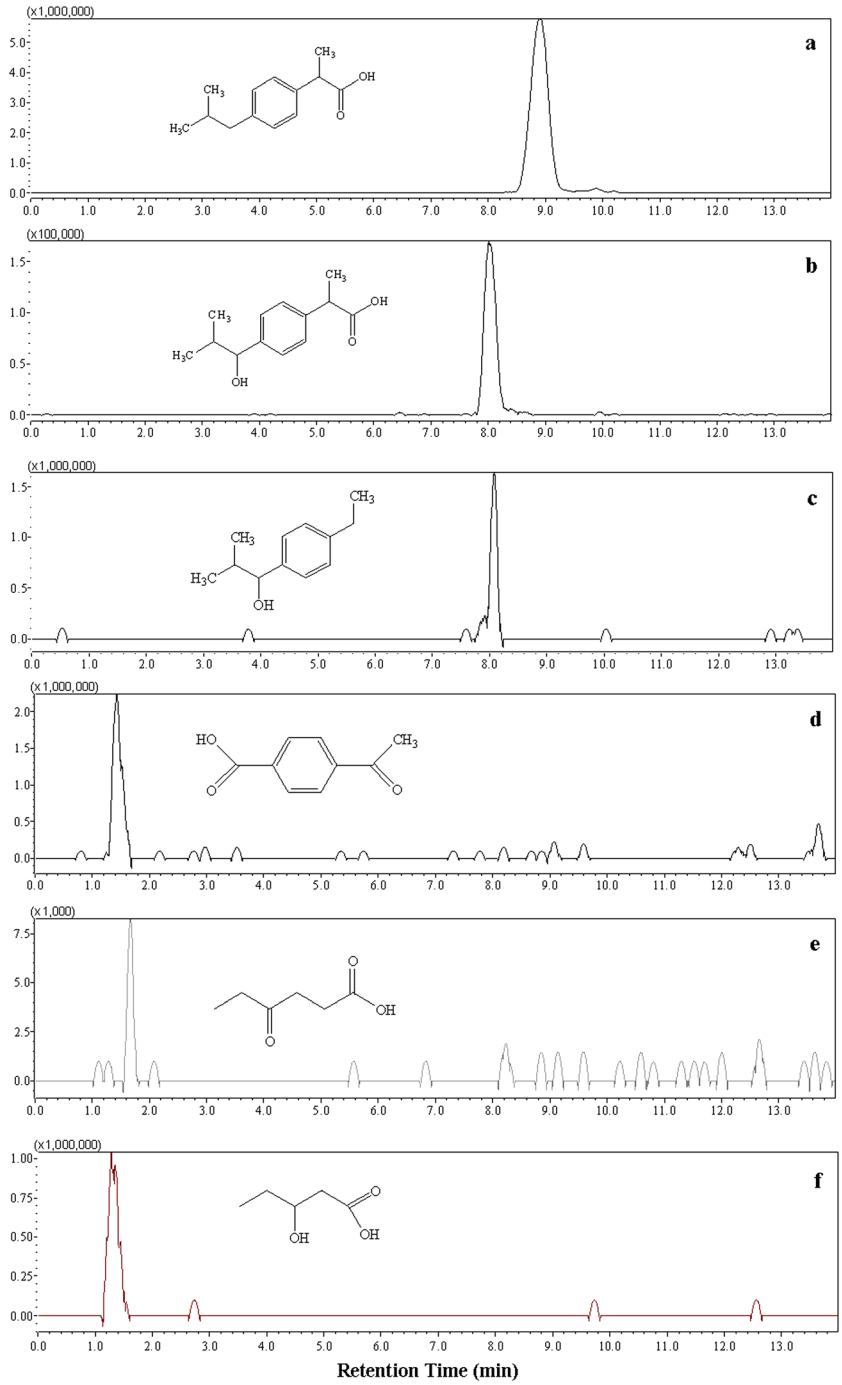

Figure 4. Extracted-ion chromatograms for the following ions [deprotonated forms of ibuprofen (IBP) and degradation products]: (a) *m/z* 205.1235 (IBP), (b) *m/z* 221.1165 (**1**), (c) *m/z* 177.1295 (**6**), (d) *m/z* 163.0388 (**8**), (e) *m/z* 129.0563 (**10**) and (f) *m/z* 117.0556 (**11**). The analyses refer to an aliquot collected after submitting an aqueous solution of IBP to the TiO_2/UV-C system for 60 min.

degradation processes evaluated (Fig. 6). Hence, for the TiO_2/UV-C photocatalytic system practically only intermediates **10** and **11** remained in solution after 120 min of exposure (Fig. 6(a)). The remarkable ability of the TiO_2/UV-C system to generate hydroxyl radicals possibly caused the prompt depletion of the other intermediates (**1–9**), thus preventing their accumulation and detection. For the UV-C direct photolysis (Fig. 6(b)), however, several intermediates (**1**, **6**, **7**, **8**, **10** and **11**) were persistent in solution after identical treatment time. These findings seem to confirm the results from TOC analyses, which revealed that higher mineralization rates were achieved by the TiO_2/UV-C photocatalytic system. For the tests involving the TiO_2/UV-A system (Fig. 6(c)), only intermediates **7**, **8** and **3** were not persistent. Conversely, after 120 min of treatment by UV-A photolysis, intermediate **1** was by far predominant (Fig. 6(d)). This result suggests that UV-A radiation is not energetic enough to excite **1** and thus to cause its conversion into the subsequent intermediates (**2–11**), as observed for the other systems (TiO_2/UV-C, TiO_2/UV-A and UV-C) evaluated herein.

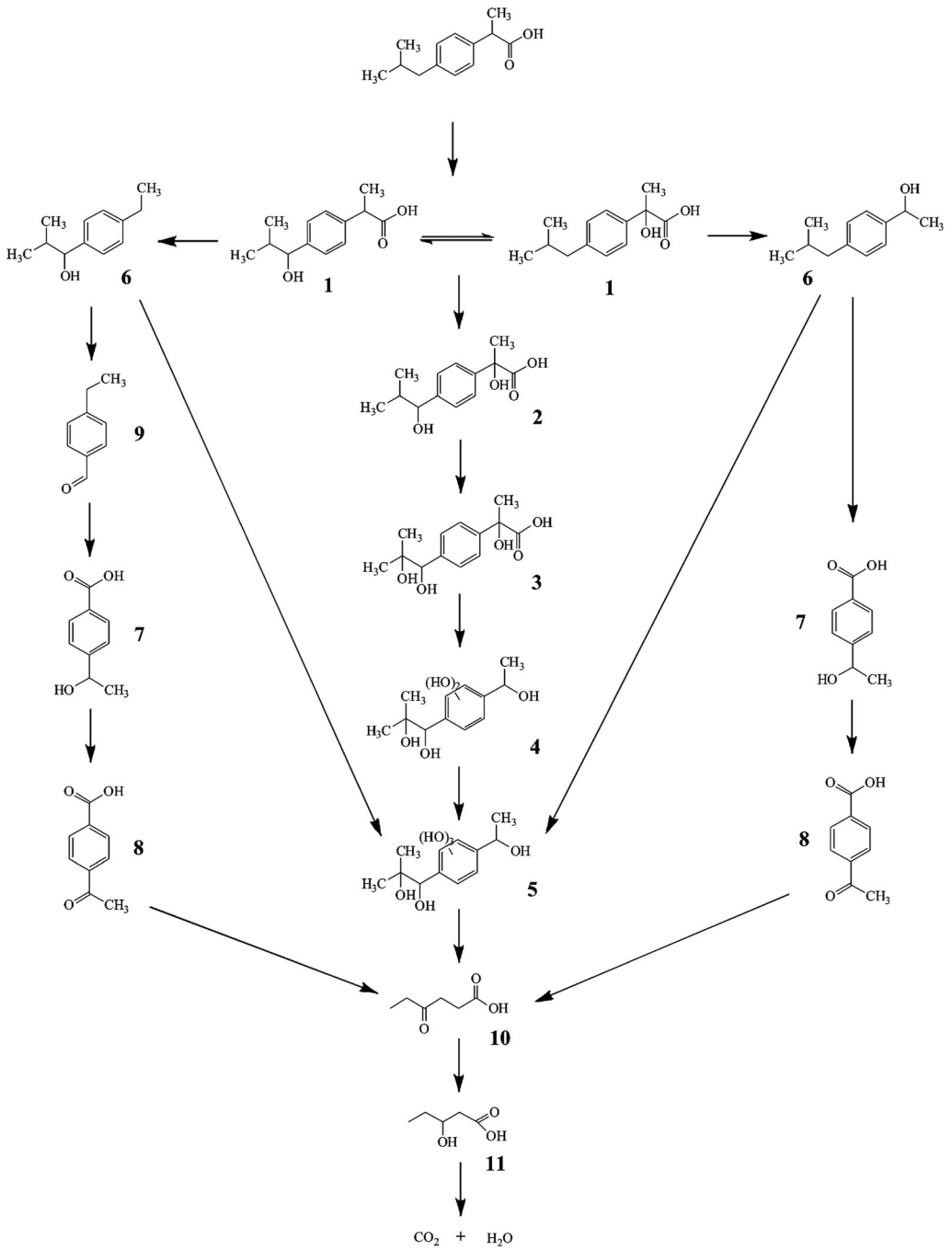

Figure 5. Proposed route for the photodegradation of ibuprofen in water as induced by the photolytic (UV-A and UV-C) and photocatalytic (TiO_2/UV-A and TiO_2/UV-C) systems. Isomeric structures can also be proposed for the degradation products. However, to facilitate visualization, only the structures **1–11** are displayed herein.

Toxicity assessment

Although several reports have described the degradation of IBP, little is known about the possible by-products generated and their degree of toxicity. As can be observed in Fig. 6, after the complete disappearance of IBP, many compounds still remain in solution, which may have a potential impact on the environment and possibly on human health. To evaluate the toxicity of IBP and its transformation products, toxicity tests against *A. salina* were conducted. These tests were performed with all aliquots taken during the degradation reactions (0, 5, 10, 15, 30, 60 and 120 min), and the mortality rates determined in each case. A control test with saline solution was also conducted (see Experimental Section for further details).

At the end of these tests, a fortunate result emerged: just as observed for the IBP solution, the aliquots collected after an exposure time of 120 min (taken from the reaction vessels of the four degradation systems: TiO_2/UV-C, TiO_2/UV-A, UV-C, UV-A) exhibited a very low toxicity against *A. salina* (mortality rates of about 5%). This finding ensures that both the photocatalytic and photolytic systems can therefore be conveniently used to degrade IBP as toxic by-products are probably not formed under these conditions.

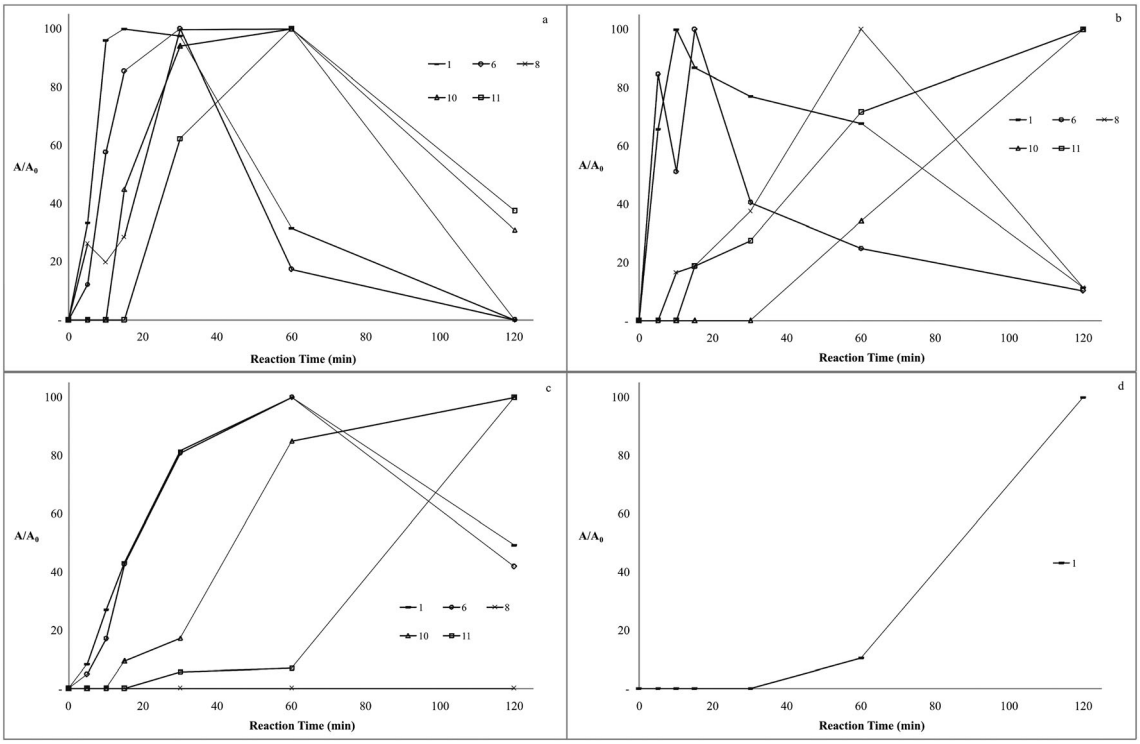

Figure 6. Plots of the relative concentrations of by-products (**1**, **6**, **8**, **10**, **11**) as a function of reaction time for the following systems: (a) TiO_2/UV-C, (b) UV-C, (c) TiO_2/UV-A and (d) UV-A. A value of 100 was attributed to the maximum concentration of each by-product. To facilitate visualization, only 5 among the 11 by-products detected are plotted.

Conclusions

The degradation of IBP, one of the most consumed pharmaceuticals worldwide, in aqueous medium by typical photocatalytic (TiO_2/UV-C and TiO_2/UV-A) and photolytic (UV-A and UV-C) systems was investigated herein. It was verified that all the systems (excepting UV-A) were able to cause an almost complete degradation of IBP after a reaction time of 120 min. However, it was also demonstrated that among the systems evaluated, the TiO_2/UV-C photocatalytic process was the most efficient in promoting both the degradation and mineralization of the substrate. Results from high-resolution MS analyses allowed the detection and characterization of 11 by-products, many of them persistent even after an exposure of as long as 120 min. These intermediates were proposed to be formed via a prompt attack of hydroxyl radicals, reactive species produced *in situ* under the conditions of both the photocatalytic and photolytic processes, on the original substrate as well as on the subsequent by-products. Based on these results, an unprecedented route for the photodegradation of IBP in aqueous medium could be proposed. This route comprised mainly the successive oxidation of the original IBP until its final conversion into CO_2 and H_2O (mineralization). Tests against *A. salina* revealed that the 120-min aliquots collected from the four systems contained compounds with no higher toxicities than IBP. This fortunate result therefore ensures that any of these systems (excluding UV-A) can be used to deplete IBP in water bodies.

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