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Photocatalytic degradation kinetics and mechanism of environmental pharmaceuticals in aqueous suspension of TiO_2: A case of β-blockers

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ABSTRACT

This study investigated the photocatalytic degradation of three β-blockers in TiO_2 suspensions. The disappearance of the compounds followed pseudo-first-order kinetics according to the Langmuir–Hinshelwood model and the rate constants were 0.075, 0.072 and 0.182 min^{-1} for atenolol, metoprolol and propranolol, respectively. After 240 min irradiation, the reaction intermediates were completely mineralized to CO_2 and the nitrogen was predominantly as NH_4^+. The influence of initial pH and β-blocker concentration on the kinetics was also studied. From adsorption studies it appears that the photocatalytic degradation occurred mainly on the surface of TiO_2. Further studies indicated that surface reaction with •OH radical was principally responsible for the degradation of these three β-blockers. The major degradation intermediates were identified by HPLC/MS analysis. Cleavage of the side chain and the addition of the hydroxyl group to the parent compounds were found to be the two main degradation pathways for all three β-blockers.

1. Introduction

The presence of active pharmaceutical ingredients (APIs) in the aquatic environments was reported as early in the 1980s [1]. Pharmaceutical compounds in surface waters is an emerging environmental issue and provides a new challenge to drinking water, wastewater and water reuse treatment systems [2]. Most of the APIs administered to patients are excreted either as metabolites or as the unchanged parent compounds. The persistence of their residues in surface waters is of great concern in particular because of their potential impact on ecosystem and public health [3,4]. β-Blockers are a class of drugs used to treat a variety of cardiovascular diseases, such as a hypertension, coronary artery disease and arrhythmias, by blocking the action of epinephrine and norepinephrine on the β-adrenergic receptor in the body, primarily in the heart [5].

The occurrence of β-blockers has been reported in sewage treatment plant effluents as well as in surface waters in the United Stated [6,7], Canada [8–10] and Germany [11,12]. Conventional wastewater treatment using activated sludge [13] is not effective in removing these compounds completely. Recently, several studies have reported the degradation of β-blockers using advanced oxidation processes (AOPs) [14–18]. Heterogeneous photocatalysis, one example of AOPs, can achieve complete oxidation of organic and inorganic species [19,20]. Studies have been reported on direct photolysis [8,21] suggesting that engineered UV systems may provide an alternative treatment option, as well.

The formation of reactive oxygen species (ROSs), such as •OH, $•O_2^-$, $•HO_2$ and H_2O_2, on the surface of photocatalysts induced by UV light results in mineralization of a large variety of organic compounds. Thus, three β-blockers, atenolol, metoprolol and propranolol, having a common $–CH(OH)CH_2NHCH(CH_3)_2$ side chain bound directly to an aromatic ring, have been selected to investigate their photocatalytic degradation kinetics and mechanism. The kinetics of photocatalytic degradation of atenolol, metoprolol and propranolol in TiO_2 suspension was studied at different initial pH value and compound concentrations. The contribution of different ROSs was also examined in detail by using different scavengers. Destruction mechanisms of the three β-blockers were elucidated based on the identification of degradation products by HPLC/MS–MS.

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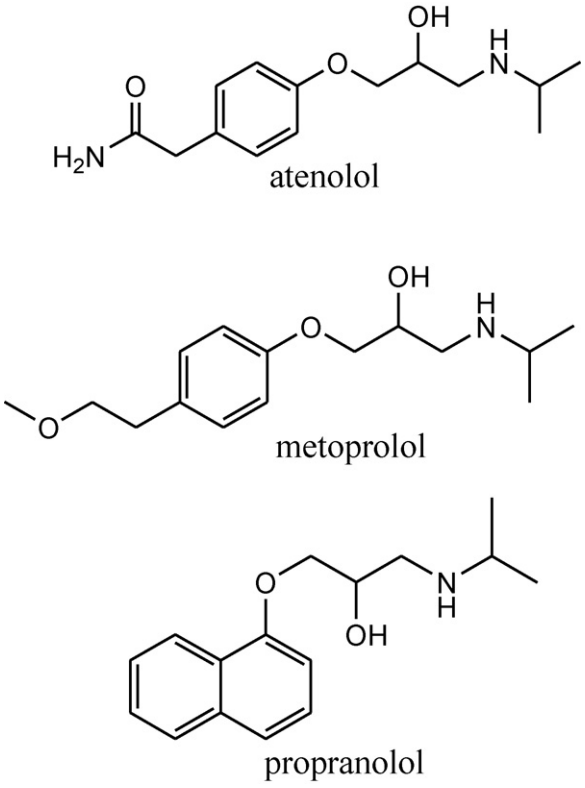


Fig. 1. Chemical structures of three β-blockers used in this study.

2. Experimental

2.1. Materials and reagents

Atenolol, (±)-metoprolol (+)-tartrate salt and propranolol hydrochloride (Sigma–Aldrich) were used as received (≥99% purity, the structures are shown in Fig. 1). HPLC grade water was obtained from a Millipore Milli-Q® System, which was treated by constant illumination with a Xe arc lamp at 172 nm to keep total organic carbon concentration below 13 μg L^{-1}. Acetonitrile and methanol (HPLC grade) were purchased from Sigma.

2.2. Photocatalytic procedures

The adsorption and photocatalytic degradation of β-blockers was carried out in a Pyrex reactor (150 mL) with a double-walled cooling-water jacket to keep the temperature of solutions constant throughout all experiments. The light source was a high-pressure mercury lamp (GGZ-125, Shanghai Yaming Lighting, E_{max} = 365 nm) with a power consumption of 125 W, housed in one side of the photocatalytic reactor to provide the irradiation. Prior to illumination, a suspension of 150 mL β-blockers adding 2.0 g L^{-1} (0.3 g) of photocatalyst (Degussa P25) was stirred in the dark for 30 min to achieve the adsorption–desorption equilibrium. Then, the UV light was turned on for the photocatalytic degradation experiments. The reaction solutions were sampled (3 mL) at fixed time intervals, filtered through 0.2 μm Millipore filters and analyzed. All experiments were carried out at room temperature. The kinetic data are presented as means from triplicate experiments, and the errors are below 5%.

2.3. Analysis

For kinetic analysis, concentrations of the three β-blockers were determined using an Agilent 1200 series HPLC under the following conditions: Kromasil C18 column, 250 × 4.6 mm i.d., performed at 30 °C. The mobile phase was 15% CH_3OH, 15% CH_3CN and 70% phosphate buffer solution (10 mM, pH value 3.0). The mobile phase rate was 1 mL min^{-1}.

Total organic carbon (TOC) was measured, after filtering the suspensions, using a Shimadzu TOC-5000 analyzer (catalytic oxidation on Pt at 680 °C).

A Dionex ion chromatograph equipped with a conductimetric detector was employed to analyze the concentration of ions. The determination of ammonium ions was performed by adapting a CS12A column using 25 mM methanesulphonic acid as the eluent, with flow rate of 1 mL min^{-1}. Under these conditions the ammonium ion retention time was 3.9. The anions were analyzed using an AS9HC anionic column. A mixture of $NaHCO_3$ (12 mM) and K_2CO_3 (5 mM) was used as the eluent at a flow rate of 1 mL min^{-1}. The retention times obtained were 6.63 and 9.58 min for nitrite and nitrate ions, respectively.

For the determination of intermediate reaction by-products, a Shimadazu high performance liquid chromatography (HPLC) system with a Kromasil C18 column, 250 × 4.6 mm i.d., SIL-HT autosampler, LC-10 AT vacuum pump and API 3000 mass analyzer was used. HPLC separations were performed at 0.5 mL min^{-1} with linear gradient elution as following: from 90% A (5 mM formic acid solution) and 10% B (CH_3OH) to 40% A and 60% B within 40 min. An electrospray interface (ESI) was used for the MS and MS–MS measurements in positive ionization mode and full scan acquisition between m/z 100–350. The collision energy varied according to the requirement of the different measurements, and the other parameters were set as follows: the source block and desolvation temperatures were 130 °C and 400 °C, respectively, the desolvation and nebulizer gas (N_2) flow rate were set as 6 L min^{-1} and argon was used as a collision gas at 250 kPa.

3. Results and discussion

3.1. Photocatalytic degradation kinetics

The photocatalytic degradation kinetics of the three β-blockers was investigated, and the results summarized in Fig. 2. These three β-blockers were degraded completely within 40 min irradiation, using a TiO_2 concentration of 2.0 g L^{-1}, an initial concentration of 100 μM and pH of 7.0. The degradation kinetics fit the Langmuir–Hinshelwood model:

$$-\frac{dc}{dt} = \frac{kKC}{1+KC} \quad (1)$$

where when the concentration is very low (i.e. $KC \ll 1$), Eq. (1) simplifies to a pseudo-first-order kinetic law:

$$-\frac{dc}{dt} = k_1 C \quad (2)$$

And then k_1 is the pseudo-first-order rate constant. These rate constants were calculated as 0.075, 0.072 and 0.182 min^{-1} for atenolol, metoprolol and propranolol, respectively.

To further evaluate treatment of three β-blockers and mineralization of the intermediates, TOC and inorganic ions were determined during the photocatalytic degradation (Fig. 2). After 240 min irradiation the residual for atenolol, metoprolol and propranolol was 9.8%, 8.4% and 2.0% (as TOC), respectively. Nitrogen in the compounds could be reduced to NH_3 (NH_4^+ in acidic media) or oxidized to nitrite and/or nitrate ions. During the course of the reaction up to 88.1%, 91.4% and 95.0% of the nitrogen was released as NH_4^+ ions, while 4.9%, 4.1% and 4.1% was detected as NO_3^-, respectively. These results are consistent with others, where the nitrogen in heterocyclic aromatic rings was transformed to both NH_4^+ and NO_3^- species, while secondary, tertiary and quaternary nitrogen

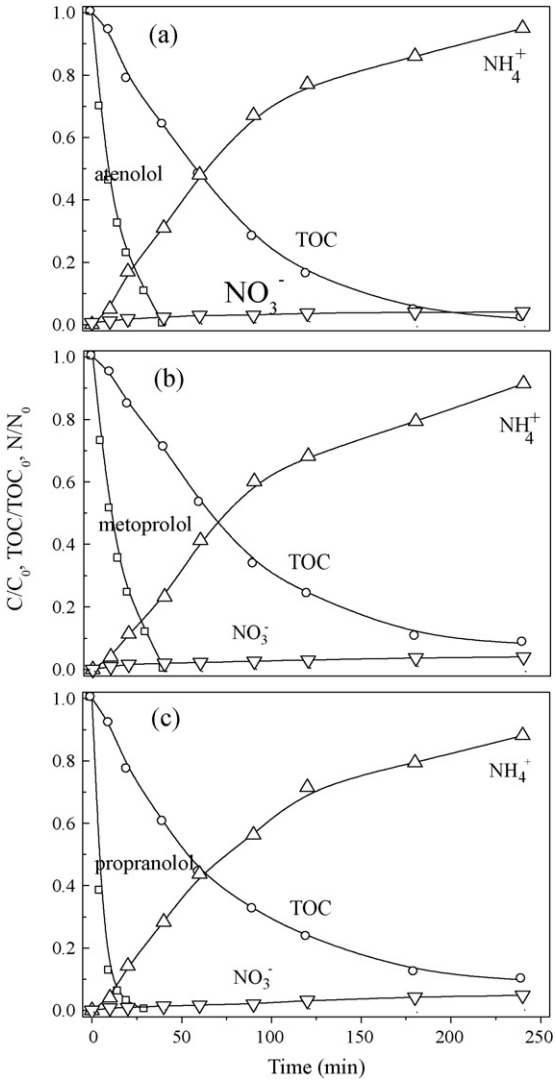


Fig. 2. Photocatalytic degradation of 100 μM β-blockers at 2 g L^{-1} TiO_2 concentration and pH value 7.0; disappearance of initial compound, TOC and evolution of ammonium, nitrite and nitrate ions for atenolol (a), metoprolol (b) and propranolol (c).

atoms were photo-converted predominantly to NH_4^+ ions [22]. No NO_2^- was found after the photocatalytic treatment although there is trace amounts of NO_2^- observed as an intermediate during the degradation of three β-blockers.

3.2. Effect of the initial pH value

The pK_a values of the three β-blockers have been reported to be 9.3, 9.2 and 9.2 for atenolol, metoprolol and propranolol, respectively [23]. This suggests that the –OH group on the side chain loses a proton. Therefore, the effect of the initial pH value on the photocatalytic degradation rate was studied by adjusting the initial pH value of the reaction solution, with either dilute solution of HCl or NaOH. The results, summarized in Fig. 3, show that the k_1 values for atenolol and metoprolol are similar and that of propranolol is quite different. This suggests that the photocatalytic degradation rate is determined by aromatic ring moiety of the compounds. For atenolol and metoprolol, increasing pH, the degradation rate constants increased somewhat. However, for propranolol, a more complex relationship between the reaction rate and pH was observed. For propranolol, the dramatic increase of

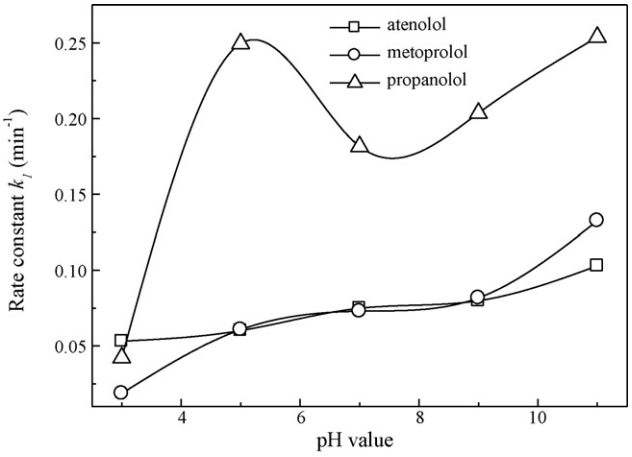


Fig. 3. Effect of initial pH values on the photocatalytic rates of atenolol (□), metoprolol (○) and propranolol (△) with 100 μM and 2 g L^{-1} TiO_2 concentration.

the rate constant obtained at pH value 5.0 may be due to attack on the naphthalene rings, with higher electron density and possible adsorption onto the positive surface of TiO_2 in weak acidic solution.

To better understand the different photocatalytic degradation rates, adsorption kinetics of three β-blockers were also determined. The adsorption kinetics with time at different pH values were shown in Fig. 1S. These data can confirm that, in weak alkaline media, all three β-blockers easily adsorbed onto TiO_2; however, the propranolol was also efficiently adsorbed at pH value 5.0. These findings are consistent with the degradation rates shown in Fig. 3 at the different pH values.

3.3. Effect of the initial concentration

The dependences of the degradation rate constants on the initial concentrations of three β-blockers were also investigated and summarized in Fig. 4. The rate constants all decreased with increased initial concentration, from 0.133, 0.149 and 0.229 min^{-1} at 50 μM to 0.044, 0.026 and 0.078 min^{-1} at 200 μM for atenolol, metoprolol and propranolol, respectively. This is not unexpected, for the higher initial concentrations more substrates occupies more active sites of TiO_2 suppressing for formation of reactive oxygen species, and at the higher substrates concentrations more photons are absorbed

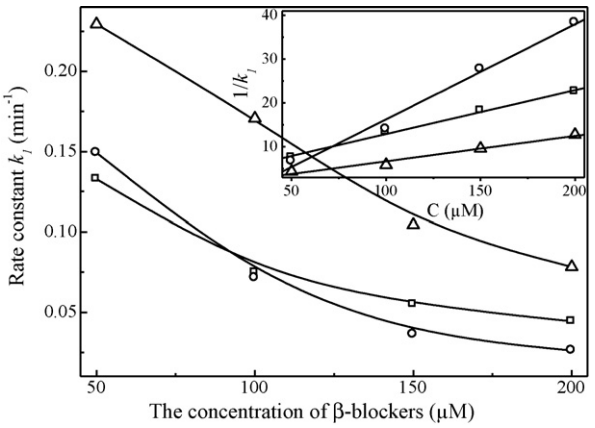


Fig. 4. Effects of initial concentration of β-blockers on the photocatalytic rate constants for atenolol (□), metoprolol (○) and propranolol (△) at 2 g L^{-1} TiO_2 concentration and pH value 7.0. Inset: the relationship between $1/k_1$ and initial concentration of atenolol (□), metoprolol (○) and propranolol (△) at 2 g L^{-1} TiO_2 concentration and pH value 7.0.

Table 1
Scavengers used, oxidizing species quenched and k_1 for β-blockers after quenched by scavengers.

β-Blockers	Scavengers	ROSs quenched	k_1 (min^{-1})	R^2
Atenolol	No scavengers	–	0.075	0.999
	Isopropanol	•OH	0.004	0.990
	Methanol	h^+ and •OH	0.003	0.990
Metoprolol	No scavengers	–	0.072	0.999
	Isopropanol	•OH	0.005	0.990
	Methanol	h^+ and •OH	0.004	0.988
Propranolol	No scavengers	–	0.182	0.991
	Isopropanol	•OH	0.041	0.990
	Methanol	h^+ and •OH	0.006	0.998

by the organic chemicals and the efficiency of the TiO_2 decreases [24].

According to the Langmuir–Hinshelwood adsorption model (by combining Eq. (1) with Eq. (2)), it follows that:

$$k_1 = \frac{kK}{1 + KC} \tag{3}$$

and is linearized:

$$\frac{1}{k_1} = \frac{C}{k} + \frac{1}{kK} \tag{4}$$

with an intercept of k^{-1} and a slope k^{-1} K^{-1} [25,26]. Where k_1 is the pseudo-first-order rate constant (min^{-1}) mentioned above, while k is the intrinsic reaction rate constant ($\mu M\,min^{-1}$) and K is the Langmuir–Hinshelwood adsorption constant of β-blockers over TiO_2 surface (μM^{-1}) in aqueous environments. Three satisfactory linear correlation coefficients were obtained as 0.998, 0.994 and 0.987 for atenolol, metoprolol and propranolol, respectively, between $1/k_1$ and the concentration of β-blockers given in the inset of Fig. 4. Thus, using the slope and the intercept values, the intrinsic reaction rate constants, k, were calculated as 10.0, 4.61 and 17.2 $\mu M\,min^{-1}$, while the Langmuir–Hinshelwood adsorption constants, K, were 0.034, 0.040 and 0.064 μM^{-1}, for atenolol, metoprolol and propranolol, respectively. These high adsorption constants results suggest that the degradation of β-blockers occurred mainly on the surface of TiO_2 by oxidation reactions with photohole (h^+) or •OH radicals. This seems to contradict the data for the adsorption onto TiO_2 in neutral solution and further studies are needed to determine the exact nature of this step in the reactions.

3.4. The contribution of different ROSs

To determine the relative contribution of surface reaction with h^+ or •OH radicals and other ROSs, such as $•O_2^-$, $•HO_2$ and H_2O_2, on degradation kinetics, different scavengers were employed. Isopropanol (0.1 M) was added in the reaction solutions to scavenge •OH radicals and 0.1 M methanol was selected as scavenger of both h^+ and •OH radicals [27–29], as shown in Fig. 5. The pseudo-first-order rate constants with or without addition of various scavengers are summarized in Table 1.

The degradation of three β-blockers was significantly suppressed in the presence of isopropanol and methanol. The pseudo-first-order rate constants decreased from 0.075, 0.072 and 0.182 min^{-1} to 0.004, 0.005 and 0.041 min^{-1} for atenolol, metoprolol and propranolol, respectively, with the addition of isopropanol. These results suggest that 94.7%, 93.1% and 77.5% of the degradation rate of these three β-blockers resulted from reaction of the •OH radicals. The addition of methanol resulted in an additional decrease of the overall rate to 0.003, 0.004 and 0.006 min^{-1}. Overall these data showed that 96.0%, 94.4% and 96.7% of the degradation rate results from the h^+ and •OH radicals. Thus the contribution of

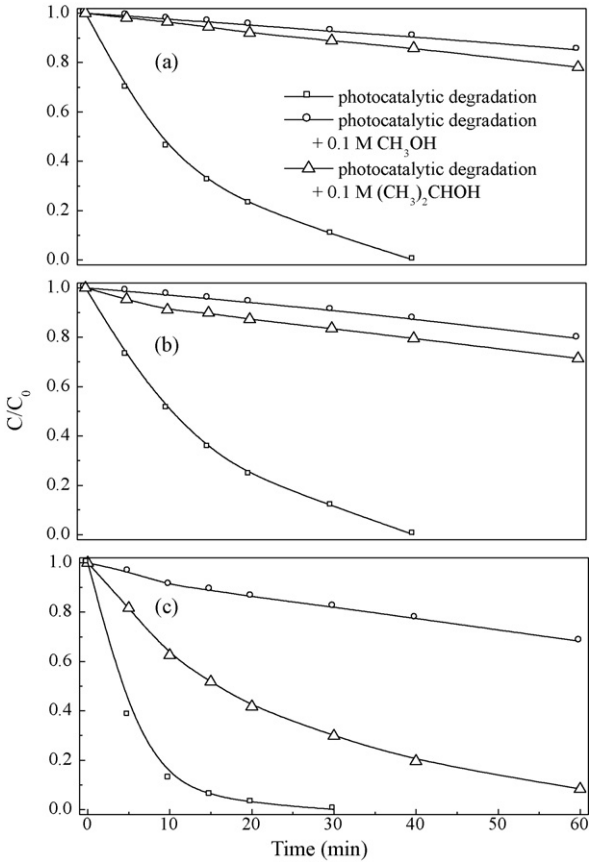


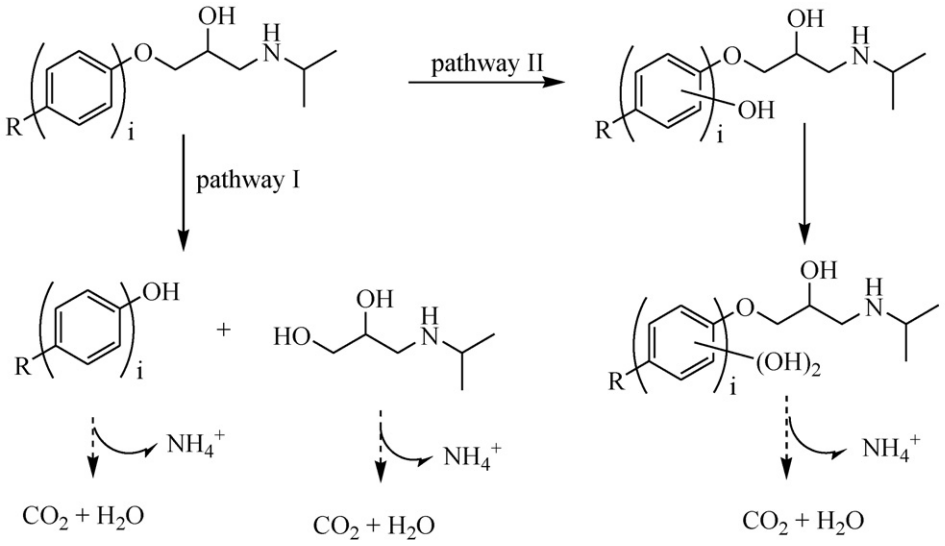
Fig. 5. The photocatalytic disappearance of 100 μM β-blockers without or with scavengers during photocatalytic degradation of atenolol (a), metoprolol (b) and propranolol (c) with 2.0 g L^{-1} TiO_2 and pH value 7.0.

h^+ in the degradation rate was calculated as 1.3%, 1.3% and 19.2%, for atenolol, metoprolol and propranolol, respectively. The remaining 4.0%, 5.6% and 3.3% portion of the overall degradation rate may result from reaction of the other ROSs for these three compounds. Additionally, it is worthwhile to point out that h^+ may also contribution to the photocatalytic degradation of propranolol as a result of increased adsorption on the surface of TiO_2, compared to atenolol and metoprolol in neutral solution (the adsorption isotherms of three β-blockers on TiO_2 surface are shown in Fig. 2S, Supplementary Material).

3.5. Preliminary reaction mechanism

In addition to the photocatalytic degradation kinetics of the three β-blockers, the intermediates formed in these reactions were also investigated. The experiments were conducted using 100 μM solutions of the parent compounds buffered at pH value 7.0. The solutions were sampled and analyzed by HPLC/MS–MS at different irradiation times. The identifications of the breakdown products formed during photocatalytic degradation of β-blockers were based on the analysis of the total ion current (TIC) and the corresponding mass spectra.

The degradation intermediates for atenolol are shown in Table 1S (Supplementary Material). The products with m/z = 152 may be due to the cleavage of side chain, while a corresponding molecule with m/z = 134 was also identified as an amino-diol. Three separate intermediates with m/z = 283, corresponding to the addition of 16 mass units to the parent compound, were observed, which may be attributed to monohydroxylated intermediates. Five intermediates with m/z = 299 and four intermediates



* i= the number of aromatic rings, and R = the substituted group on aromatic ring. atenolol: i =1, R = NH_2COCH_2-; metoprolol: i = 1, R = $CH_3OCH_2CH_2$-; propranolol: i = 2, R = H.

Fig. 6. General scheme of degradation pathways followed by β-blockers.

with m/z = 315 were also detected, which correspond to the dihydroxylated and trihydroxylated intermediates, respectively. Additionally, two tetrahydroxylated intermediates with m/z = 331 were observed later in the photocatalytic process. All of the degradation intermediates were detected during photocatalytic degradation and the relative peak area of all intermediates exhibited the same trends. The peak areas initially increased dramatically and then decreased rapidly at longer irradiation times.

The degradation products for metoprolol were summarized in Table 2S (Supplementary Material). The intermediate with m/z = 134, amino-diol, was again identified. Like atenolol, two monohydroxylated intermediates with m/z = 284, ten dihydroxylated intermediates with m/z = 300, three trihydroxylated intermediates with m/z = 316 and two tetrahydroxylated intermediates with m/z = 331 were detected. At the same time, all the identified degradation intermediates for metoprolol exhibited an initial increase in relative concentration followed by a rapid decrease with increasing irradiation time.

The degradation products of propranolol are also summarized in Table 3S (Supplementary Material). The intermediate with m/z = 145 (naphthol) formed from side chain cleavage was found, as well as the intermediate with m/z = 134. Moreover, one monohydroxylated intermediate (m/z = 161) of naphthol was also found. Seven intermediates with m/z = 276, corresponding to the addition of 16 mass units to the parent compound, were attributed to monohydroxylated intermediates. More monohydroxylated intermediates were produced than for atenolol or metaprolol, likely due to the increased number of available sites on the naphthalene ring for hydroxyl radical addition. In addition, five dihydroxylated intermediates with m/z = 292 and seven trihydroxylated intermediates with m/z = 308 were also detected. During the photocatalytic degradation process, the changes of the peak areas of major identified degradation intermediates for propranolol are also studied, and the change trends are very similar to that of atenolol and metoprolol.

From these results two main photocatalytic degradation pathways appear to account for the degradation of the three β-blockers (Fig. 6). The cleavage of side chain is pathway 1. The intermediate with m/z = 134, amino-diol, was identified for all three β-blockers, and the corresponding phenols produced by atenolol and propranolol were also found. The addition of –OH is degradation pathway II, which resulted in the formation of monohydroxy intermediates with m/z = 283, 284 and 276 for atenolol, metoprolol and propranolol, respectively. Additionally, the polyhydroxy intermediates were also formed in photocatalytic degradation process. Then, these intermediates follow a further degradation and finally release nitrogen predominantly as NH_3/NH_4^+.

4. Conclusions

The photocatalytic degradation kinetics of three β-blockers in aqueous solution was investigated in detail. The results showed that propranolol degraded much more efficiently than atenolol and metoprolol. The half-lives of three β-blockers are 18.9, 19.9 and 7.8 min for atenolol, metoprolol and propranolol, respectively. For the three β-blockers studied, their degradation intermediates were mineralized completely and the nitrogen atoms converted predominantly into NH_4^+ and a lesser extent into NO_3^- within 240 min. The effects of initial pH value and initial concentration of substrates on degradation kinetics were also investigated. The results indicated that the adsorption of β-blockers on TiO_2 surface determined their photocatalytic degradation rates and surface reaction on TiO_2 played a significant role in the degradation of all three β-blockers. Further, studies indicated that $^{\bullet}OH$ are responsible for the major degradation of all these three β-blockers, the other ROSs and h^+ play minor roles during this process. However, the contribution of h^+ to the photocatalytic degradation of propranolol is also very important. At last, based on the identified the degradation intermediates, two main photocatalytic degradation pathways of three β-blockers were proposed, including the cleavage of side chain and the hydroxylation addition to the parent compounds.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jhazmat.2010.03.079.

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