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Photodegradation of naproxen and its photoproducts in aqueous solution at 254 nm: A kinetic investigation

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ABSTRACT

The kinetics of photodegradation of the non steroidal anti-inflammatory drug naproxen (+)-S-2-(6-methoxynaphthalen-2-yl)propanoic acid, an emerging organic pollutant, was studied in aqueous solutions under deaerated and aerated conditions. The photolysis experiments were carried out under monochromatic irradiation ($\lambda = 254$ nm) at pH = 7.0 and $T = 25$ °C.

Simplified reaction schemes of photodegradation of naproxen are proposed in absence and in presence of oxygen respectively. The schemes take into account the photolysis of naproxen and its photoproducts and the reactions of the measured species with oxygen dissolved in the liquid bulk. According to these schemes, two kinetic models were developed which correlate the experimental data, for runs performed in absence and in presence of oxygen, with a fair accuracy and allowed to estimate the best values for the unknown kinetic parameters.

The calculated quantum yield of direct photolysis of naproxen under deaerated media is in good agreement with the one previously reported. Under aerated conditions, the generation of singlet oxygen has also been taken into account.

The obtained results, under the adopted conditions, indicated a marked influence of dissolved oxygen on the photodegradation rates of naproxen and the relative distribution of the major reaction intermediates.

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1. Introduction

The reuse of urban wastewater in agricultural field, after a proper treatment, may represent a suitable solution for water shortage in many parts of the world including the Mediterranean area (Post et al., 2008; Angelakis and Bontoux, 2001; Angelakis et al., 1999).

The more stringent standards indicate that, after a first biological process, the effluents have to be submitted to a disinfection procedure mainly to reduce the presence of pathogenic microorganisms under specified limits (Koivunen, 2005; Kretschmer et al., 2000).

Different processes are currently adopted for water sterilisation before the reuse, mainly UV irradiation, ozonation, chlorination and oxidant dosage as peracetic acid (Gehr et al., 2003; Caretti and Lubello, 2003; Radziminski et al., 2002; Paraskeva and Graham, 2002; Liberti et al., 2000).

Generally the water streams are submitted to one of the above-mentioned processes until the presence of total and faecal coliforms is reduced below the limits imposed in the specific country. It is noteworthy to observe that the conditions adopted for sterilization are quite mild and this would suggest a limited conversion of chemical species present.

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Only a little attention, different from country to country, is generally reserved to the presence, at very low concentrations (micrograms/litre or nanograms/liter), of organic micropollutants which can be adsorbed by the plants receiving the treated water streams. The xenobiotics may have bio-accumulating properties when applied to crops through irrigation (Korte et al., 2000; Marty, 1999) or exert toxic effects on the same plants, bacteria and algae (Levine and Asano, 2004; Singh et al., 2004; Dizer et al., 2002; Ono et al., 1996) and may end up in humans through food ingestion (Beek et al., 2000).

Among the classes of micropollutants present in STP effluents, pharmaceuticals have gained during the last decade the attention of many researchers mainly due to the concern of possible effects on living aquatic organisms and humans. Although no conclusive assessments are so far available on this topic, the presence of these unregulated xenobiotics in STP effluents to be reused for irrigation in agricultural field is undesirable based on the precautionary principle. However, before planning the adoption of proper treatments to remove these species from water streams, an evaluation of their fate during the sterilization procedure may be useful. A literature search indicates the existence of some studies in which the reactivity of pharmaceuticals with hypochlorite is investigated at the conditions adopted during the sterilization process for water reuse. For example, it has been reported that acetaminophen is transformed into toxic compounds during chlorination in wastewater treatment plants (Bedner and MacCrehan, 2006a) whereas N-chloramines are produced from the reaction between hypochlorite and fluoxetine or metoprolol (Bedner and MacCrehan, 2006b). Moreover, Della Greca et al. (2009) found that atenolol reacts with hypochlorite with the formation of chlorinated products. Regarding the sterilization based on UV irradiation, Kim et al. (2009a) recently reported the results of an investigation on 30 pharmaceuticals and personal care products found in an effluent from secondary sedimentation tanks in a municipal wastewater treatment plant which were submitted to UV (at 254 nm) treatment. The data given by these authors indicate that at very severe conditions of irradiation with a fluence quite higher than those adopted during the sterilization procedure for reuse, a great part of the studied species were not effectively removed. Moreover, no indications on the photoproducts have been reported in the study.

The presence of naproxen, (+)-S-2-(6-methoxynaphthalen-2-yl)propanoic acid, a non steroidal anti-inflammatory drug (NSAID), has been often documented in different STP effluents at concentration levels between 25 ng l⁻¹ and 33.9 µg l⁻¹ (Santos et al., 2010; Bueno et al., 2009; Vieno et al., 2005; Andreozzi et al., 2003; Metcalfe et al., 2003; Miao et al., 2002; Ternes et al., 1998).

The ecotoxicity of naproxen and its photoproducts was assayed on some aquatic organisms, such as bacteria, microcrustaceans and algae (Isidori et al., 2005; Della Greca et al., 2004). The reported results indicated that some photoderivatives are more ecotoxic than naproxen, both in acute and chronic conditions, whereas genotoxic and mutagenic effects were not found.

The EC₅₀ values of naproxen were respectively 21.2 µg l⁻¹ from the test ToxAlert and 35.6 µg l⁻¹ with the Microtox test (La Farre et al., 2001).

Its behaviour in aqueous solutions under UV irradiation at a wavelength of 254 nm has been recently investigated (Kim et al., 2009a,b). It has been observed that the removal of naproxen, with UV intensity lamps of 0.384 mW cm⁻², was around 30% and 90% in 10 and 73 min respectively. Unfortunately due to the severe conditions adopted, the results achieved during this study could not be used to predict the fate of this species during the sterilization procedure for reuse. Kinetic indications on naproxen removal during irradiation at 254 nm were also reported by others (Pereira et al., 2007a,b; Benitez et al., 2009; Meite et al., 2010). The quantum yield and the photoproduct distribution depend in a sensible way on the adopted conditions (aerobic versus anaerobic medium).

In particular, the quantum yields of direct photolysis (at 254 nm) in water, under aerated media, reported in three previous papers, are not in good agreement: 9.3·10⁻³ ± 2.7·10⁻⁴ mol E⁻¹ (Pereira et al., 2007a,b), 49.8·10⁻³ mol E⁻¹ (Benitez et al., 2009) and 24.0·10⁻³ ± 5.0·10⁻³ mol E⁻¹ (Meite et al., 2010). These discrepancies in the quantum yields can be probably attributed to the influence of the concentration of dissolved oxygen as observed by Meite and coauthors who, under controlled operative conditions (pH 5.5–6.0, T = 25 °C, photon flux 10⁻⁷ E l⁻¹ s⁻¹), estimated the following values of quantum yields: 1.5·10⁻² mol E⁻¹, 2.40·10⁻² mol E⁻¹ and 5.60·10⁻² mol E⁻¹ for dissolved oxygen concentrations of 0.01 mM, 0.26 mM and 1.3 mM respectively.

Moreover, no indications were found in the literature on the products formed during the photolysis/photooxidation of naproxen at 254 nm, whereas detailed reaction schemes may be found for its photolysis/photooxidation in aqueous solution under solar UV irradiation conditions (Musa and Eriksson, 2008; Bosca et al., 2001, 1990; Moore and Chappuis, 1988).

These findings demonstrated the harmful effects of the investigated compounds and suggested the opportunity to consider also the photoderivatives in ecotoxicology assessment of naproxen.

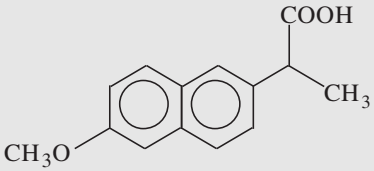
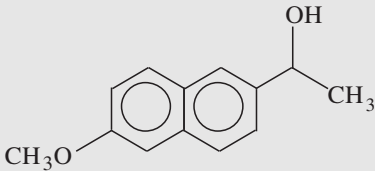
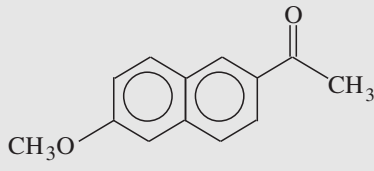
Therefore, the present work aims at a new, and more detailed, characterization of the kinetics of naproxen photodegradation and its photoproducts under UV irradiation at 254 nm in deaerated and aerated aqueous solution at pH = 7.0.

2. Experimental

Naproxen solutions in water were irradiated with a nominal 17 W low-pressure mercury monochromatic lamp emitting at 254 nm (Helios Italquartz) in a 0.420 l (V) annular photoreactor, with a path length (L) equal to 2.20 cm. The reactor was thermostated at 298 K and wrapped with an aluminium foil. At the top, the reactor had more inlets for feeding reactants and gas stream and outlets for withdrawing samples. A scheme of the experimental device has been reported elsewhere (Andreozzi et al., 2000).

The power output of the lamp (I_0) was 2.13·10⁻⁶ ± 1.12·10⁻⁷ E s⁻¹ as measured by hydrogen peroxide actinometry (Nicole et al., 1990). The pH of the aqueous solutions was regulated at 7.0 with perchloric acid and/or sodium hydroxide and monitored by means of an Orion 420A⁺ pH-meter (Thermo).

Table 1 – Chemical structure of naproxen and its major photoproducts along with their molar absorptivities at 254 nm.

		
naproxen	1-(6-methoxy-2-naphthyl)ethanol	2-acetyl-6-methoxynaphthalene
NP	NP	NP
$\epsilon_{\text{NP}}^{254} = 4.18 \cdot 10^3 \text{ M}^{-1} \text{ cm}^{-1}$	$\epsilon_{\text{NP}_1}^{254} = 4.35 \cdot 10^3 \text{ M}^{-1} \text{ cm}^{-1}$	$\epsilon_{\text{NP}_2}^{254} = 3.06 \cdot 10^4 \text{ M}^{-1} \text{ cm}^{-1}$

In all the experiments the solution was preventively sparged with air. During the runs a gaseous stream of air was continuously fed, at a flow rate of 0.3 l min^{-1} , to the irradiated magnetically stirred solution.

The concentration of the dissolved oxygen, reported above as $[\text{O}_2]$, was calculated according to the Henry's law ($P_{\text{O}_2} = H \cdot x$) with $H = 4.38 \cdot 10^4 \text{ atm}$ (Perry and Green, 1997). If an air stream at $P = 1 \text{ atm}$ was used then $x = 4.79 \cdot 10^{-6}$. A value of $2.66 \cdot 10^{-4} \text{ M}$ for the concentration of oxygen dissolved in the liquid bulk can be thus obtained.

The concentrations of naproxen and its photoproducts, 1-(6-methoxy-2-naphthyl)ethanol and 2-acetyl-6-methoxynaphthalene, named as NP, NP₁ and NP₂ respectively (Table 1), were evaluated by HPLC analysis. For this purpose, the HPLC apparatus (Agilent 1100) was equipped with a diode array UV/Vis detector ($\lambda = 220 \text{ nm}$) and a Synergi Max-RP column (Phenomenex), using a mobile phase of 60% aqueous buffer and 20% acetonitrile, flowing at 1.0 ml min^{-1} . One liter of buffer was made by 10 ml of phosphoric acid solution (5.05 M), 50 ml of methyl alcohol and water for HPLC.

For each experimental run, a starting concentration around 10^{-5} M of the selected substrate was used to prepare the aqueous solution.

The molar absorptivities for NP, NP₁ and NP₂ at $\lambda = 254 \text{ nm}$ (ϵ_i^{254}) were calculated by measuring the absorbances of solutions at known concentration ($\text{pH} = 7.0$) with UV–Vis Diode Array spectrophotometer (HP 8452 A) equipped with a quartz cell of a 1 cm path length (Table 1).

Naproxen was purchased from Sigma Aldrich whereas 1-(6-methoxy-2-naphthyl)ethanol and 2-acetyl-6-methoxynaphthalene from Alfa Aesar Co. with a purity 98% w/w. All reagents were used as received.

The experiments were conducted in duplicate with a resulting standard deviation lower than 3.5% and for each reaction time the average value of concentration was reported in the diagrams.

3. Results and discussion

Preliminary runs were carried out at dark under aerated conditions on solutions containing NP, NP₁ and NP₂ species. No reactivity at all was observed (data not shown).

The results of UV₂₅₄-photolysis of NP in aerated aqueous solution are shown in Fig. 1a. A complete removal of this species was achieved, at the adopted experimental conditions, after 30 min of irradiation with the formation of NP₁ and NP₂ as major intermediates.

In a second experiment in which the same solution was submitted to UV irradiation under a continuous feeding of pure oxygen, no appreciable changes were observed in the concentration profiles of NP, NP₁ and NP₂ (data not shown).

That is the UV irradiation at 254 nm of naproxen, in aerated or oxygenated aqueous solutions, converted it mainly into NP₁ which is one of its possible intermediate and this was successively transformed into the corresponding ketone (NP₂).

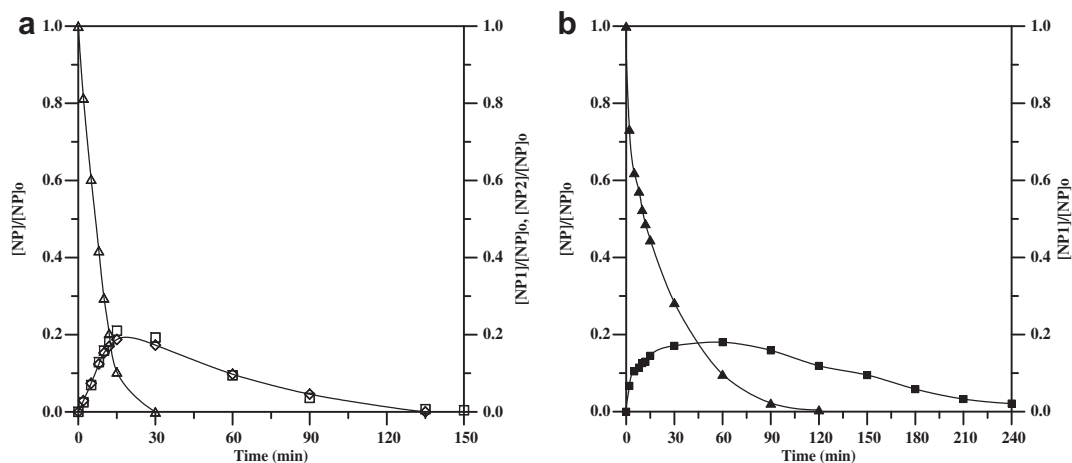


Fig. 1 – UV-photolysis of naproxen under aerated (fig. 1a) and deaerated (fig. 1b) conditions. $\text{pH} = 7.0$. $T = 25^\circ \text{C}$ $[\text{NP}]_0 = 2.3 \cdot 10^{-5} \text{ M}$ (Δ , \blacktriangle) NP, (\square , \blacksquare) NP₁, (\diamond) NP₂.

These results are in agreement with those reported by others on the photodegradation of naproxen but for wavelength irradiations higher than 300 nm (Boscà et al., 1990; Costanzo et al., 1989; Moore and Chappuis, 1988).

To investigate the role exerted by dissolved oxygen, some runs were repeated after having purged oxygen from the solution through a helium bubbling. In Fig. 1b the results collected during one of these runs are reported.

A decrease of the reactivity of both NP and NP₁ was observed with a formation of NP₂ at trace level only. For both aerated and no aerated conditions it can be inferred that the first step of UV₂₅₄-photolysis of NP is always a decarboxylation reaction to give NP₁ which is preferentially oxidized to NP₂, if oxygen is present in the aqueous solution, as occurs for higher wavelengths (Boscà et al., 2001).

It was suggested in the literature that “long lifetime triplet transient states”, formed during the irradiation of NP, transfer readily energy to oxygen molecules, leading to the formation of an excited oxygen state as singlet oxygen (¹O₂) (Quintero and Miranda, 2000; Martinez and Scaiano, 1989). Since no indications were reported on the generation of singlet oxygen for irradiation of NP₁ and NP₂ photoproducts, some attempts were done to evaluate the real occurrence of this species in the reacting system and its effects.

Further runs were thus carried out to analyse the behaviour of both the species, NP₁ and NP₂, either in the absence and presence of oxygen in the solution or when a well known quencher for singlet oxygen (¹O₂) and for triplet transient species, 1,4-diazabicyclo[2,2,2]octane, named DABCO (Mac and Wirz, 2002; Bhattacharyya and Das, 1986; Monroe, 1985; Foote et al., 1970) was added to the oxygenated aqueous solution (Fig. 2a,b and 3 respectively).

The results shown in these figures undoubtedly indicate that both the reactivities of NP₁ and NP₂ species decrease after purging oxygen from the solution (Fig. 2a and 3, full triangles).

The addition of the DABCO seems to slightly reduce the reactivity NP₁ during the UV₂₅₄-photolysis (Fig. 2a, black circles), while it does not influence the consumption profile for UV₂₅₄-photolysis of NP₂ (Fig. 3, black circles). Moreover, no production of NP₂ was evidenced when the UV-photolysis of NP₁ was carried out in aerated condition but in presence of DABCO (Fig. 2b, black circles), probably due to the ability of DABCO to quench NP₁ excited states whose decomposition leads to the formation of NP₂. The irradiation of NP₂ seems not to generate singlet oxygen (Fig. 3, black squares and circles).

4. Kinetic modelling

4.1. UV-photolysis in the deaerated system

On the basis of above-reported observations an attempt to model the system behaviour was firstly done by considering the simple UV₂₅₄-photolysis of the investigated species (NP, NP₁ and NP₂) that occurs when oxygen is purged from the solution.

The following scheme was thus proposed for the UV₂₅₄-photolysis of naproxen in aqueous solution:

According to the results reported in the previous paragraph the proposed scheme accounts for the formation of NP₁ from

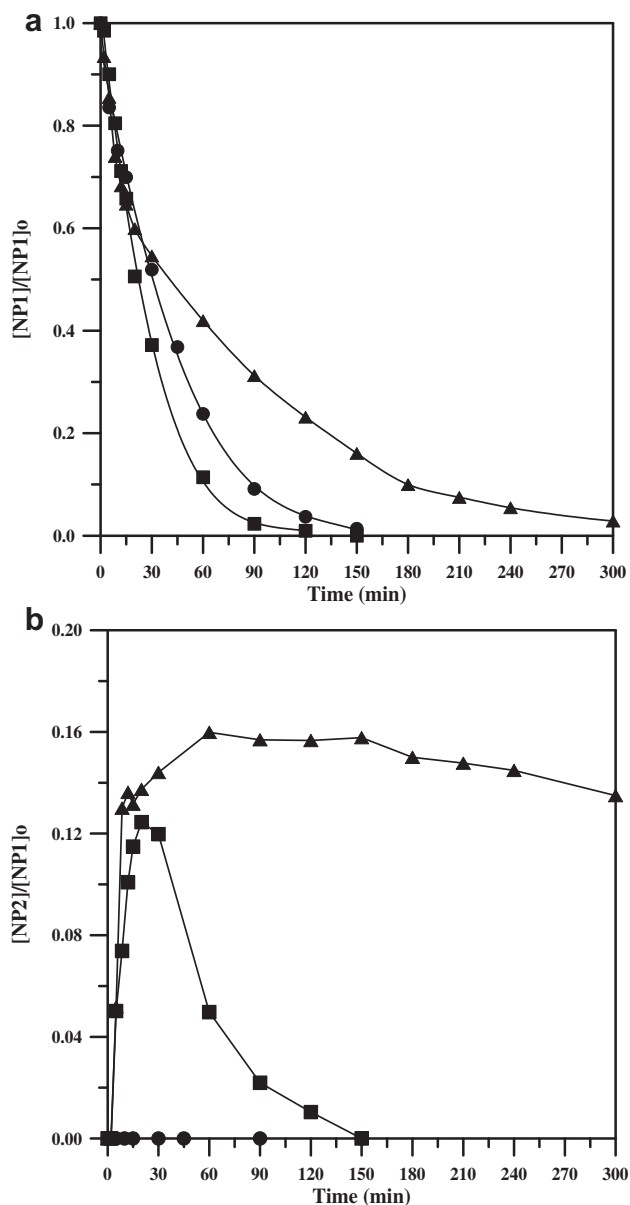


Fig. 2 – UV₂₅₄-photolysis of NP₁ under deaerated (▲), aerated without DABCO (■) and aerated with DABCO (●) conditions. [NP₁]₀ = 2.5 · 10⁻⁵ M. pH = 7.0, T = 25 °C (2a) NP₁ consumption, (2b) NP₂ formation.

UV₂₅₄-photolysis of NP (at a selectivity lower than 1) and for its photolytic decomposition which only in part gives rise to the generation of NP₂. The disappearance of the latter by photolysis was included in the scheme. The formation of unidentified species was foreseen from NP₁ and NP₂ precursors and the photolysis of NP₂. This pathway is consistent with the mechanisms proposed for the NP photodegradation in deaerated media: NP₁ is generated through an electron ejection from the NP singlet excited state followed by decarboxylation. On the other hand, NP excited state could give rise to the formation of radical intermediates which can abstract hydrogen to form other unidentified species (Boscà et al., 2001, 1990).

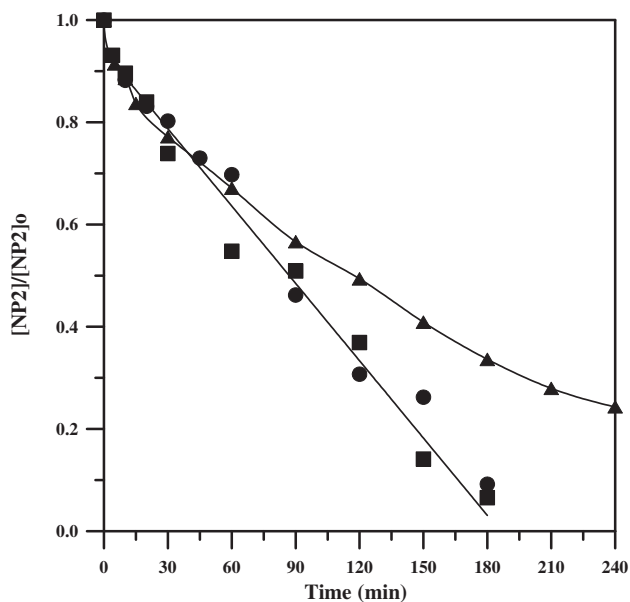


Fig. 3 – UV₂₅₄-photolysis of NP₂ under deaerated (▲), aerated without DABCO (■), aerated with DABCO (●) conditions. [NP₂]₀ = 1.7 · 10⁻⁵ M. pH = 7.0, T = 25 °C.

According to Scheme 1 and taking into account the equation rate for a photolytic process, in which the rate of photolysis of a substrate may be related to the photon flux absorbed by the solution and the quantum yield (Tang, 2003; Leifer, 1988), the following material balance equations could be written for all the involved species and for the pseudo-component X:

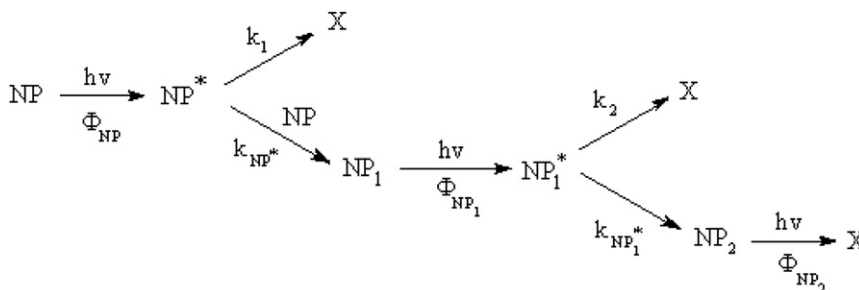
$$\frac{d[\text{NP}]}{dt} = -\frac{I_0 \cdot \Phi_{\text{NP}}}{V} \cdot E \cdot f_{\text{NP}} \quad (1)$$

$$\frac{d[\text{NP}^*]}{dt} = \frac{I_0 \cdot \Phi_{\text{NP}}}{V} \cdot E \cdot f_{\text{NP}} - (k_{\text{NP}^*} \cdot [\text{NP}] + k_1) \cdot [\text{NP}^*] \quad (2)$$

$$\frac{d[\text{NP}_1]}{dt} = k_{\text{NP}^*} \cdot [\text{NP}^*] \cdot [\text{NP}] - \frac{I_0 \cdot \Phi_{\text{NP}_1}}{V} \cdot E \cdot f_{\text{NP}_1} \quad (3)$$

$$\frac{d[\text{NP}_1^*]}{dt} = \frac{I_0 \cdot \Phi_{\text{NP}_1}}{V} \cdot E \cdot f_{\text{NP}_1} - (k_{\text{NP}_1^*} + k_2) \cdot [\text{NP}_1^*] \quad (4)$$

$$\frac{d[\text{NP}_2]}{dt} = k_{\text{NP}_1^*} \cdot [\text{NP}_1^*] - \frac{I_0 \cdot \Phi_{\text{NP}_2}}{V} \cdot E \cdot f_{\text{NP}_2} \quad (5)$$



Scheme 1 – UV₂₅₄-photolysis of NP species under deaerated conditions. X represents unidentified species.

$$[\text{X}] = [\text{NP}]_0 - [\text{NP}] - [\text{NP}_1] - [\text{NP}_2] \quad (6)$$

where

$$E = 1 - e^{-2.3 \cdot L \cdot (\epsilon_{\text{NP}}^{254} \cdot [\text{NP}] + \epsilon_{\text{NP}_1}^{254} \cdot [\text{NP}_1] + \epsilon_{\text{NP}_2}^{254} \cdot [\text{NP}_2] + \epsilon_{\text{X}}^{254} \cdot [\text{X}])} \quad (7)$$

For $\epsilon_{\text{X}}^{254}$ a value of $6.58 \cdot 10^3 \text{ M}^{-1} \text{ cm}^{-1}$ was obtained by measuring the absorbances (A_{tot}) of the samples withdrawn from the reactor at different reaction times and using the following equation:

$$A_{\text{tot}} = \epsilon_{\text{NP}}^{254} \cdot [\text{NP}] + \epsilon_{\text{NP}_1}^{254} \cdot [\text{NP}_1] + \epsilon_{\text{NP}_2}^{254} \cdot [\text{NP}_2] + \epsilon_{\text{X}}^{254} \cdot [\text{X}] \quad (8)$$

The terms f_{NP} , f_{NP_1} and f_{NP_2} can be written as:

$$f_{\text{NP}} = \frac{\epsilon_{\text{NP}}^{254} \cdot [\text{NP}]}{A_{\text{tot}}} \quad f_{\text{NP}_1} = \frac{\epsilon_{\text{NP}_1}^{254} \cdot [\text{NP}_1]}{A_{\text{tot}}} \quad f_{\text{NP}_2} = \frac{\epsilon_{\text{NP}_2}^{254} \cdot [\text{NP}_2]}{A_{\text{tot}}} \quad (9)$$

Applying the steady-state hypothesis for NP* and NP₁* transient species:

$$[\text{NP}^*]_{\text{ss}} = \frac{\left(\frac{I_0}{V} \cdot \Phi_{\text{NP}} \cdot E \cdot f_{\text{NP}}\right)}{k_{\text{NP}^*} \cdot [\text{NP}] + k_1} \quad (10)$$

$$[\text{NP}_1^*]_{\text{ss}} = \frac{\left(\frac{I_0}{V} \cdot \Phi_{\text{NP}_1} \cdot E \cdot f_{\text{NP}_1}\right)}{k_{\text{NP}_1^*} + k_2} \quad (11)$$

the Equations (3) and (5) become:

$$\frac{d[\text{NP}_1]}{dt} = \frac{\left(\frac{I_0}{V} \cdot \Phi_{\text{NP}} \cdot E \cdot f_{\text{NP}}\right)}{[\text{NP}] + k_a} \cdot [\text{NP}] - \frac{I_0 \cdot \Phi_{\text{NP}_1}}{V} \cdot E \cdot f_{\text{NP}_1} \quad (12)$$

$$\frac{d[\text{NP}_2]}{dt} = \frac{\left(\frac{I_0}{V} \cdot \Phi_{\text{NP}_1} \cdot E \cdot f_{\text{NP}_1}\right)}{1 + k_b} - \frac{I_0 \cdot \Phi_{\text{NP}_2}}{V} \cdot E \cdot f_{\text{NP}_2} \quad (13)$$

where $k_a = k_1/k_{\text{NP}^*}$ and $k_b = k_2/k_{\text{NP}_1^*}$

As it is clear from the equations reported above (1, 12 and 13), there are too many unknown parameters (k_a , k_b , Φ_{NP} , Φ_{NP_1} and Φ_{NP_2}) to be estimated by means of the data collected in a single photolytic run starting from an aqueous solution of naproxen. To overcome the difficulties associated with this assessment, the results collected by following the evolution of the more simple subsystems were firstly taken into account. That is, for example, a first attempt was done to estimate the best value of quantum yield Φ_{NP_2} by focussing the attention on the results collected during some photolytic runs in which deaerated aqueous solutions containing NP₂ species were irradiated. Successively, the data collected when NP₁ species

were submitted to photolysis in the absence of oxygen were considered and so on. In each case, the best estimation of the values of the parameters was done, for each subsystem, through an iterative optimization procedure (Marquardt approach) which minimized the squares of the differences between calculated and experimental concentrations of each species (objective function) (Reklaitis et al., 1983):

$$\Omega = \sum_{l=1}^m \sum_{j=1}^n \sum_{i=1}^h (y_{i,j,l} - c_{i,j,l})^2$$

in which the terms y and c are the calculated and experimental concentrations whereas m , n and h are the number of experimental data recorded in each experiment, the number of the involved species and the number of the experiments used in a simple optimization procedure respectively.

The MATLAB routine “ode45”, which is based on the Runge–Kutta method with adaptive step-size, was used to solve the set of ordinary differential equations (ODEs).

The percentage standard deviation for the j -th component was calculated as follows:

$$\sigma_j(\%) = \frac{1}{\bar{c}} \times \sqrt{\frac{\sum_{i=1}^n (y_i - c_i)^2}{n - p}} \times 100$$

where \bar{c} is the average measured concentration, c_i the experimental concentration of j -th component for the i -th reaction time, n the number of the experimental points and p the unknown parameters to be estimated.

The parameter confidence limits were calculated by means of Student's t variable, for a fixed degree of freedom (ν) and a level of confidence as those corresponding to the intersection between the objective function and the straight line:

$$\Omega = \Omega_k \cdot \left(1 + \frac{t^2}{\nu}\right)$$

being Ω_k the value which the objective function assumes for the best estimated value of the k unknown parameter.

In Table 2 the values estimated for all the unknown parameters are shown along with their uncertainties and percentage standard deviations.

The values of quantum yields of direct UV₂₅₄-photolysis for NP₁ and NP₂ species were estimated for the first time in the present paper, whereas the value calculated for Φ_{NP} ($1.297 \cdot 10^{-2} \pm 1.23 \cdot 10^{-3} \text{ mol E}^{-1}$) is in good agreement with that previously reported ($1.5 \cdot 10^{-2} \pm 5.0 \cdot 10^{-3} \text{ mol E}^{-1}$) by Meite et al. (2010). From the comparison of the three parameters Φ_{NP} , Φ_{NP_1} and Φ_{NP_2} it can be assessed that, at the same experimental starting conditions, the photoreactivity at 254 nm follows the order: NP > NP₁ > NP₂ even if the order of molar absorptivities is $\epsilon_{\text{NP}_2}^{254} > \epsilon_{\text{NP}_1}^{254} > \epsilon_{\text{NP}}^{254}$.

Some examples of comparison of experimental and calculated data for the subsystems considered in the estimation procedures are reported in Fig. 4a–b. The analysis of the data reported in Table 2 (low uncertainties on the estimated parameters) and in the figures indicates that the model derived from Scheme 1 adequately describes the behaviour of the investigated system under deaerated conditions.

4.2. UV₂₅₄-photolysis in the aerated system

On the basis of collected experimental results, a new kinetic scheme can be obtained by adding to the reactions already considered for the direct photolysis of NP₁ species in deaerated conditions (Scheme 1, black arrows) those occurring when oxygen is present in the reacting system (Scheme 2, blue arrows):

This scheme is in agreement with the findings previously reported on the photodegradation of NP in presence of oxygen. NP undergoes a photodecarboxylation step, leading to a decarboxy-naproxen radical, which combines readily with dissolved molecular oxygen, in aerated solution, yielding a peroxy radical which further reacts to yield 1-(6-methoxy-2-naphthyl)ethanol and 2-acetyl-6-methoxynaphthalene as major photooxidation products (Boscà et al., 2001) and other photoproducts such as 2-ethyl-6-methoxy-naphthalene and 2-hydroperoxyl-6-methoxy-naphthalene (Hsu et al., 2006; Della Greca et al., 2004). According to these findings, in Scheme 2, under aerated irradiated conditions, NP gives prevalently NP₁ and NP₂ species and minor photoproducts, indicated as X. The NP₁ and NP₂ intermediates undergo a similar photo-oxidation process. Moreover, since there are some evidences that major products generated by the NP photolysis are a source of singlet oxygen (Partyka et al., 2001; Costanzo et al., 1989), it is considered the possibility that NP₁ reacts with oxygen dissolved to produce singlet oxygen via photo-unstable intermediate (Y). The singlet oxygen can be quenched by the aqueous media to its ground state (triplet oxygen) or attack NP₂ species.

Although it was reported in the literature that NP is a moderate singlet oxygen photosensitizer (Martinez et al., 1998; De la Pena et al., 1997) any quantitative attempt done in the present work to include, in Scheme 2, a reaction of singlet oxygen by irradiation of NP failed.

Under aerated conditions, taking into account Scheme 2, the above-described ODEs (1, 12–13), developed for the photodegradation of NP in absence of oxygen, were properly modified and reported below along with the mass balance on Y, Y*, ¹O₂ and X species:

Table 2 – Best estimated values of unknown kinetic constants along with the single ($\bar{\sigma}_i$) and overall ($\bar{\sigma}_{\text{tot}}$) average standard deviations for the UV₂₅₄-photolysis of NP, NP₁ and NP₂, under un-aerated conditions, in aqueous solution at pH = 7.0.

Φ_{NP} (mol E ⁻¹)	Φ_{NP_1} (mol E ⁻¹)	Φ_{NP_2} (mol E ⁻¹)	k_a (mol l ⁻¹)	k_b (dimensionless)
$1.29 \cdot 10^{-2} \pm 1.23 \cdot 10^{-3}$	$3.80 \cdot 10^{-3} \pm 3.20 \cdot 10^{-4}$	$3.73 \cdot 10^{-4} \pm 1.70 \cdot 10^{-5}$	$2.70 \cdot 10^{-2} \pm 5.01 \cdot 10^{-3}$	0.607 ± 0.13
$\bar{\sigma}_{\text{NP}}$ (%)	$\bar{\sigma}_{\text{NP}_1}$ (%)	$\bar{\sigma}_{\text{NP}_2}$ (%)	$\bar{\sigma}_{\text{tot}}$ (%)	
1.26	2.2	0.23	3.06	

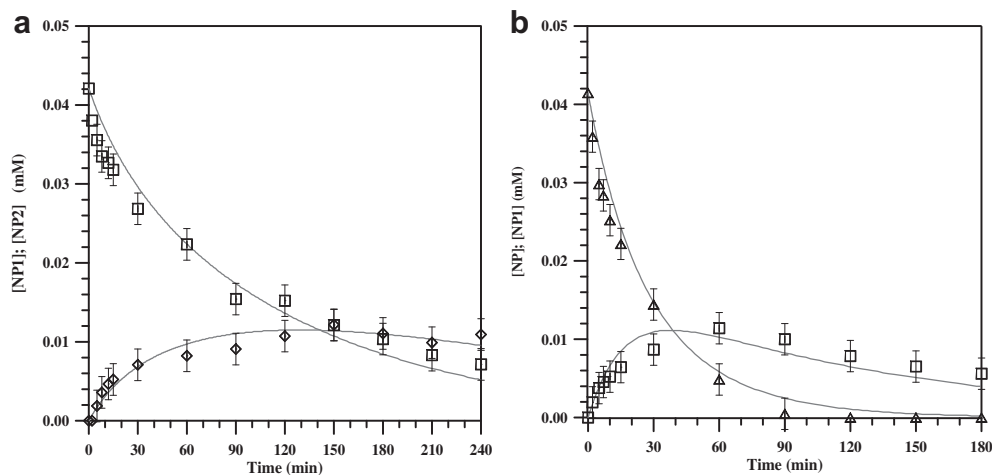


Fig. 4 – Predicted (solid lines) and experimental (symbols: \triangle NP, \square NP₁, \diamond NP₂) concentration-time profile for NP₁ species UV₂₅₄-photolysis under deaerated conditions at pH = 7.0 and T = 25 °C, 4a: [NP₁]_o = 4.21 · 10⁻⁵ M; 4b: [NP]_o = 4.14 · 10⁻⁵ M.

$$\frac{d[\text{NP}]}{dt} = -\frac{I_0 \cdot \Phi_{\text{NP}} \cdot E \cdot f_{\text{NP}}}{V} - (k_{\text{NP}/\text{O}_2} + k'_{\text{NP}/\text{O}_2} + k''_{\text{NP}/\text{O}_2}) \cdot [\text{NP}] \cdot [\text{O}_2] \quad (14)$$

$$\frac{d[\text{Y}]}{dt} = k_{\text{NP}_1/\text{O}_2} \cdot [\text{NP}_1] \cdot [\text{O}_2] - \frac{I_0 \cdot \Phi_{\text{Y}} \cdot E \cdot f_{\text{Y}}}{V} \quad (17)$$

$$\frac{d[\text{NP}_1]}{dt} = \frac{\left(\frac{I_0}{V} \cdot \Phi_{\text{NP}_1} \cdot E \cdot f_{\text{NP}_1}\right)}{[\text{NP}_1] + k_a} \cdot [\text{NP}] - \frac{I_0 \cdot \Phi_{\text{NP}_1} \cdot E \cdot f_{\text{NP}_1}}{V} + k'_{\text{NP}/\text{O}_2} \cdot [\text{NP}] \cdot [\text{O}_2] + -k_{\text{NP}_1/\text{O}_2} \cdot [\text{NP}_1] \cdot [\text{O}_2] \quad (15)$$

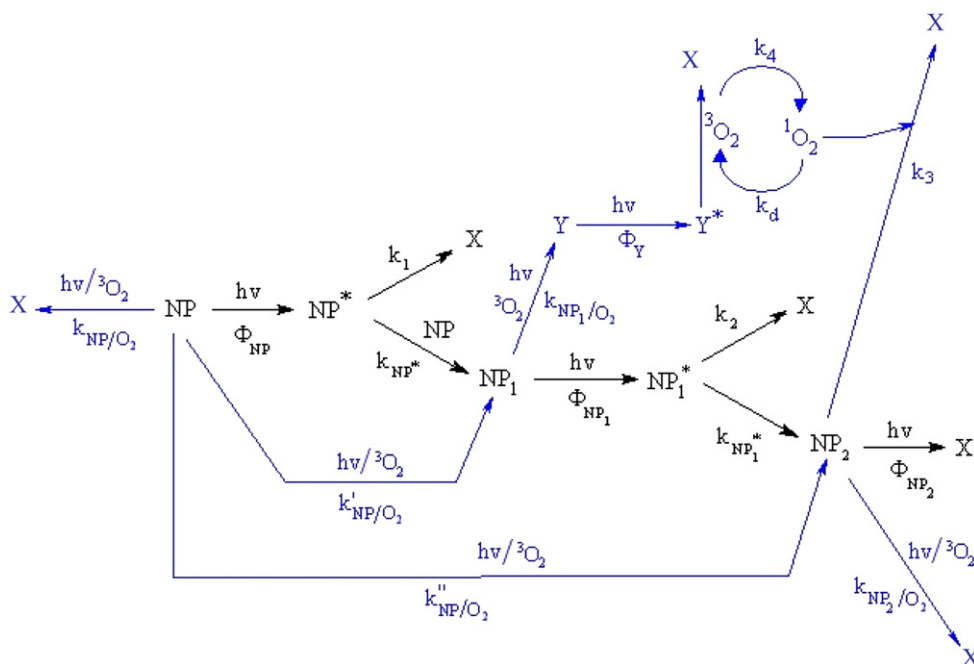
$$[\text{X}] = [\text{NP}]_o - [\text{NP}] - [\text{NP}_1] - [\text{NP}_2] - [\text{Y}] \quad (18)$$

$$\frac{d[\text{NP}_2]}{dt} = \frac{\left(\frac{I_0}{V} \cdot \Phi_{\text{NP}_2} \cdot E \cdot f_{\text{NP}_2}\right)}{1 + k_b} - \frac{I_0 \cdot \Phi_{\text{NP}_2} \cdot E \cdot f_{\text{NP}_2}}{V} + k''_{\text{NP}/\text{O}_2} \cdot [\text{NP}] \cdot [\text{O}_2] + -k'_{\text{NP}_2/\text{O}_2} \cdot [\text{NP}_2] \cdot [\text{O}_2] - k_3 \cdot [\text{NP}_2] \cdot [^1\text{O}_2]_{\text{ss}} \quad (16)$$

where [O₂] indicates the concentration of ³O₂ dissolved in the liquid bulk (see Scheme 2).

The concentrations for ¹O₂ and Y* were calculated assuming a steady-state hypothesis for these species:

$$\frac{d[^1\text{O}_2]_{\text{ss}}}{dt} = -[^1\text{O}_2]_{\text{ss}} \cdot (k_d + k_3 \cdot [\text{NP}_2]) + k_4 \cdot [\text{Y}^*]_{\text{ss}} \cdot [\text{O}_2] = 0 \quad (19)$$



Scheme 2 – UV₂₅₄-photolysis of NP species under aerated (blue arrows) and deaerated (dark arrows) conditions. X and Y represent unidentified species. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3 – Best estimated values of unknown kinetic constants along with the single ($\bar{\sigma}_i$) and overall ($\bar{\sigma}_{\text{tot}}$) average standard deviations for the UV₂₅₄-photolysis of NP, NP₁ and NP₂, under aerated conditions, in aqueous solution at pH = 7.0.

k_{NP/O_2} ($\text{M}^{-1} \text{s}^{-1}$)	$k'_{\text{NP}/\text{O}_2}$ ($\text{M}^{-1} \text{s}^{-1}$)	$k''_{\text{NP}/\text{O}_2}$ ($\text{M}^{-1} \text{s}^{-1}$)	$k_{\text{NP}_1/\text{O}_2}$ ($\text{M}^{-1} \text{s}^{-1}$)	$k_{\text{NP}_2/\text{O}_2}$ ($\text{M}^{-1} \text{s}^{-1}$)	k_3 ($\text{M}^{-1} \text{s}^{-1}$)	Φ_Y (mol E^{-1})
$0.817 \pm 6.67 \cdot 10^{-2}$	$0.172 \pm 4.50 \cdot 10^{-2}$	$0.283 \pm 3.67 \cdot 10^{-2}$	$0.175 \pm 2.83 \cdot 10^{-2}$	$4.33 \cdot 10^{-2} \pm 8.33 \cdot 10^{-3}$	$7.07 \cdot 10^9 \pm 2.30 \cdot 10^8$	$3.31 \cdot 10^{-3} \pm 5.96 \cdot 10^{-4}$
$\bar{\sigma}_{\text{NP}}$ (%)	$\bar{\sigma}_{\text{NP}_1}$ (%)			$\bar{\sigma}_{\text{NP}_2}$ (%)		$\bar{\sigma}_{\text{tot}}$ (%)
1.46	3.04			1.57		6.10

$$\frac{d[Y^*]_{\text{ss}}}{dt} = -k_4 \cdot [\text{O}_2] \cdot [Y^*]_{\text{ss}} + \frac{I_0 \cdot \Phi_Y}{V} \cdot E \cdot f_Y = 0 \quad (20)$$

with

$$f_Y = \frac{\epsilon_Y^{254} \cdot [Y]}{A_{\text{tot}}} \quad (21)$$

$$A_{\text{tot}} = \epsilon_{\text{NP}}^{254} \cdot [\text{NP}] + \epsilon_{\text{NP}_1}^{254} \cdot [\text{NP}_1] + \epsilon_{\text{NP}_2}^{254} \cdot [\text{NP}_2] + \epsilon_X^{254} \cdot [X] + \epsilon_Y^{254} \cdot [Y] \quad (22)$$

$$E = 1 - e^{-2.3 \cdot L \cdot (\epsilon_{\text{NP}}^{254} \cdot [\text{NP}] + \epsilon_{\text{NP}_1}^{254} \cdot [\text{NP}_1] + \epsilon_{\text{NP}_2}^{254} \cdot [\text{NP}_2] + \epsilon_X^{254} \cdot [X] + \epsilon_Y^{254} \cdot [Y])} \quad (23)$$

It was reasonably assumed that $\epsilon_{\text{NP}_1}^{254} = \epsilon_{\text{NP}_2}^{254} = 4.35 \cdot 10^3 \text{ M}^{-1} \text{ cm}^{-1}$. For the kinetic constant of physical quenching of singlet oxygen (k_d) a value of $2.5 \times 10^5 \text{ s}^{-1}$ was considered (Wilkinson et al., 1993).

Also in this case, several kinetic constants were present for which no values were known “a priori” (k_{NP/O_2} , $k'_{\text{NP}/\text{O}_2}$, $k''_{\text{NP}/\text{O}_2}$,

$k_{\text{NP}_1/\text{O}_2}$, $k_{\text{NP}_2/\text{O}_2}$, k_3 , Φ_Y) and the same procedure “step-by-step”, previously adopted for deaerated process, was adopted for their estimation. Firstly, the $k_{\text{NP}_2/\text{O}_2}$ value was separately estimated using experimental data collected during photolytic run of aerated solutions containing NP₂ species ($t = 0$, $[\text{NP}_2]_0 = 1.15 \cdot 10^{-5} \text{ M}$). Successively, the data collected from two runs, at different starting NP₁ concentrations ($[\text{NP}_1]_0 = 2.00 \cdot 10^{-5}$ and $4.40 \cdot 10^{-5} \text{ M}$), when aerated solutions were submitted to photolysis, were used to estimate the best values for $k_{\text{NP}_1/\text{O}_2}$, k_3 , Φ_Y parameters. Finally, the model was applied to the data collected from three photolytic runs with different NP initial concentrations, ($[\text{NP}]_0 = 1.40 \cdot 10^{-5}$, $2.40 \cdot 10^{-5}$ and $4.50 \cdot 10^{-5} \text{ M}$), carried out on aerated solution of NP, with the purpose to identify the best values for k_{NP/O_2} , $k'_{\text{NP}/\text{O}_2}$, $k''_{\text{NP}/\text{O}_2}$ constants.

The kinetic values found for all the unknown parameters along with their uncertainties and percentage standard deviations for the photodegradation of NP ad its photoderivatives

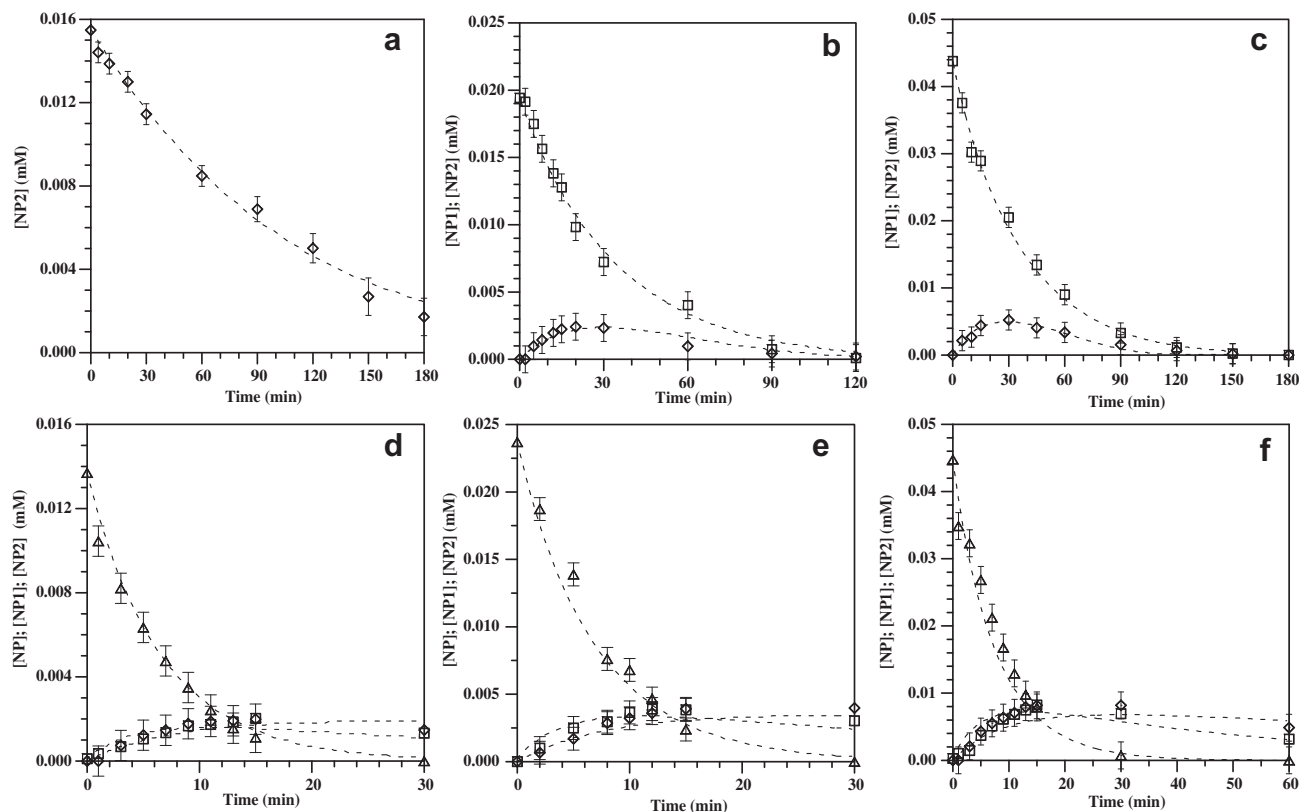


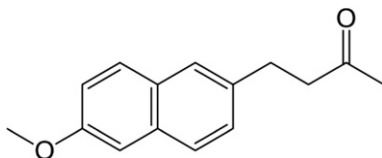
Fig. 5 – Predicted (dashed lines) and experimental (symbols: \triangle NP, \diamond NP₁, \diamond NP₂) concentration-time profile for NP_i species UV₂₅₄-photolysis under aerated conditions at pH = 7.0 and T = 25 °C, 5a: $[\text{NP}_2]_0 = 1.15 \cdot 10^{-5} \text{ M}$; 5b: $[\text{NP}_1]_0 = 1.94 \cdot 10^{-5} \text{ M}$; 5c: $[\text{NP}_1]_0 = 4.38 \cdot 10^{-5} \text{ M}$; 5d: $[\text{NP}]_0 = 1.37 \cdot 10^{-5} \text{ M}$; 5e: $[\text{NP}]_0 = 2.37 \cdot 10^{-5} \text{ M}$; 5f: $[\text{NP}]_0 = 4.48 \cdot 10^{-5} \text{ M}$.

under aerated conditions are shown in Table 3. The overall percentage standard deviations and those on the NP_i species, are lower than those associated to the experimental determination of the concentrations of the measured species.

The kinetic constants values for the photoreactions of oxygen with NP to give NP₁ (k'_{NP/O_2}) and NP₂ (k''_{NP/O_2}) are very similar and close to the value estimated for the attack of oxygen to NP₁ under irradiation (k'_{NP_1/O_2}). Their reaction rates are obviously influenced by the concentration of oxygen dissolved in the aqueous bulk.

This fact is in agreement with Meite's results (Meite et al., 2010) who reported that the value of the quantum yield of naproxen photolysis at 254 nm, estimated by using a simple model of the type $\ln[C]/[C]_0 = -2.3 \cdot \epsilon_\lambda \cdot l \cdot \Phi_\lambda \cdot I_0(\lambda) = -k_{app} \cdot t$, increases at increasing oxygen concentration in the liquid bulk. This observation may explain the discrepancies found in the literature for naproxen quantum yield values reported by different Authors (Meite et al., 2010; Benitez et al., 2009; Pereira et al., 2007a,b).

The k_3 parameter is the kinetic constant for the attack of singlet oxygen to NP₂ species leading to unknown species. The estimated value for it ($7.07 \cdot 10^9 \pm 2.30 \cdot 10^8 \text{ M}^{-1} \text{ s}^{-1}$) is not very different from that ($4.0 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$) reported in the literature for the reaction between singlet oxygen and nabumetone (Martinez and Scaiano, 1989), which is structurally very similar to NP₂:



The k_3 value is four order larger than the rate constant for interaction of NP with singlet oxygen ($1.1 \cdot 10^5 \text{ M}^{-1} \text{ s}^{-1}$) reported by others (Packer et al., 2003) thus indicating that NP does not compete with NP₂ for this reacting species.

A visual comparison of the calculated and experimental concentration data for the NP, NP₁ and NP₂ species is shown in the figures reported below (Fig. 5a–f). A good capability of the model to simulate the system behaviour appears from the analysis of these diagrams.

5. Conclusions

The kinetics of photodegradation of naproxen was investigated under both deaerated and aerated media at pH = 7.0 and T = 25 °C.

Simplified reaction schemes of photodegradation of naproxen were proposed, in absence and in presence of oxygen, which take into account the photolysis reactions of naproxen and its derived photoproducts and contemporary the reactions of the measured species with oxygen dissolved in the liquid bulk. According to these schemes, two proper kinetic models were developed to simulate the system behaviour.

In particular, when oxygen was admitted in the reacting solution, the generation of singlet oxygen and its reactions with some of the intermediates identified or simply put forward in the solution were considered.

The proposed kinetic models predict the experimental data with a good accuracy and allowed to estimate, for the first time, the best values for the unknown kinetic parameters.

The calculated quantum yield of direct photolysis of naproxen under deaerated media ($1.29 \cdot 10^{-2} \pm 1.23 \cdot 10^{-3} \text{ mol E}^{-1}$) is in good agreement with the one previously reported by others ($1.50 \cdot 10^{-2} \pm 5.0 \cdot 10^{-3} \text{ mol E}^{-1}$).

The obtained results, under the adopted conditions, indicated a marked influence of dissolved oxygen on the photodegradation rates of naproxen and the relative distribution of the major reaction intermediates. The estimated kinetic constants values for the attack of oxygen to NP and NP₁, under irradiation, are very similar.

The calculated value for the kinetic constant of singlet oxygen attack to NP₂ ($7.07 \cdot 10^9 \pm 2.30 \cdot 10^8 \text{ M}^{-1} \text{ s}^{-1}$) was found to be close to the value of $4.0 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$ reported for the reaction between singlet oxygen and nabumetone which is structurally very similar to NP₂.

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