VACUUM-ULTRAVIOLET PHOTOLYSIS OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDs) ibuprofen, ketoprofen, diclofenac and naproxen are detected even in natural waters. Their degradation was achieved through the generation of reactive oxygen containing species (ROS, such as •OH, HO_2• and $•O_2^-$) by using a xenon excimer lamp ($\lambda_{max.}$ = 172 ± 14 nm). The effect of the initial drug concentration, dissolved molecular oxygen, methanol as •OH scavenger and the effect of these pharmaceuticals on each other were investigated. According to the results, not only the reactions based on •OH, but the reactions with other ROS and excited water molecules should also be taken under consideration for the interpretation of the transformation of the four investigated NSAIDs.

INTRODUCTION

The drugs investigated in this work, ibuprofen (IBU), ketoprofen (KETO), diclofenac (DICL) and naproxen (NAP) (Fig. 1) belong to the group of non-steroidal anti-inflammatory drugs (NSAIDs). Due to the improper annihilation and disposal of these medicines they are frequently detected in the aquatic environment. The maximal detected concentration in natural waters are 2.8 μg dm^{-3} for IBU, 0.99 μg dm^{-3} for KETO, 1.2 μg dm^{-3} for DICL and 1.5 μg dm^{-3} for NAP [1-3].

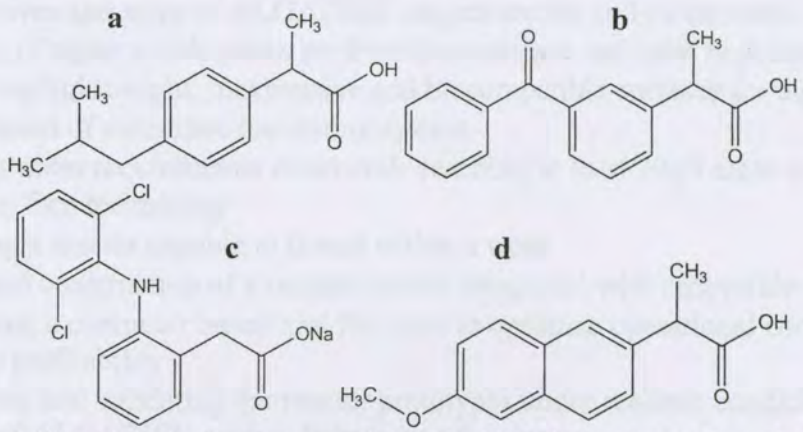
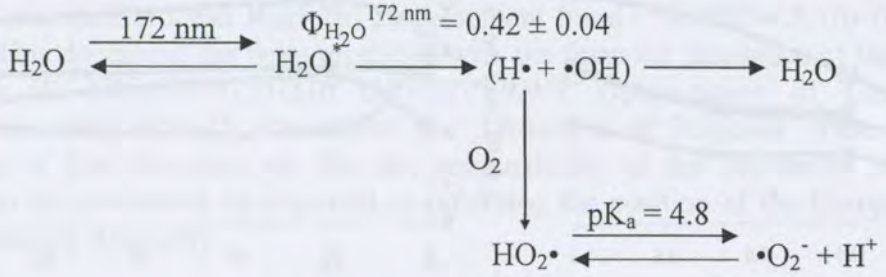


Figure 1. The chemical structure of a) IBU, b) KETO, c) DICL and d) NAP

Therefore, new water treatment techniques are needed, which are more efficient than the conventional ones in the elimination of such persistent chemicals. The methods based on the generation of various reactive oxygen containing species (ROS, mainly •OH), like vacuum-ultraviolet (VUV) photolysis are promising: they can mineralize effectively the contaminant molecules [4]. Water is the main absorber of the VUV light, resulting in excited water molecules (H_2O^*). Hydrogen atoms and hydroxyl radicals are formed via homolytic bond dissociation with a quantum yield of: $\Phi_{H_2O}^{172\ nm} = 0.42 \pm 0.04$ [5]. Dissolved molecular oxygen might prevent the recombination of these radicals by scavenging H• (Scheme 1).



Scheme 1. The VUV photolysis of water

The formed HO_2• as well as its conjugate base pair, the $•O_2^-$ might react with the NSAIDs or with •OH (Table 1). The first reaction increases, while the second one decreases the rate of transformation of the target molecules. The degradation rate of the contaminants depends greatly on the reaction rate coefficients (k) and on the concentrations of the various species involved in these reactions.

Table 1. The reaction rate coefficients (k) of the four NSAIDs and some radicals with •OH

substrate	k ($\times 10^9$ mol^{-1} dm^3 cm^{-1})	reference
HO_2•	6.6	[6]
$•O_2^-$	10	[7]
IBU	7.4	[8]
KETO	8.4	[9]
DICL	18	[8]
NAP	24	[10]

MATERIALS and METHODS

All of the used chemicals were of analytical purity (IBU, KETO, DICL sodium salt: Sigma-Aldrich, ≥ 98%, NAP: Fluka, 98%, acetic acid: Sigma-Aldrich, ≥ 99%, methanol (MeOH), acetonitrile: Scharlau, HPLC-grade). The solutions of the NSAIDs were prepared using MilliQ water produced by MILLIPORE Synergy185 (resistivity: 18 MΩ cm^{-1}). The experiments were carried out in a circulated system (flow rate: 375 cm^3 min^{-1}), where a xenon excimer lamp ($\lambda_{max.}$ = 172 ± 14 nm, P = 20 W, Osram) was centered in a water-cooled, double-walled tubular glass reactor. The irradiated solutions (250 cm^3) were thermostated at 25°C. The effect of dissolved molecular oxygen was investigated by saturating the irradiated solution with N_2, air or O_2 (gas flow rate: 855 cm^3 min^{-1}).

During the kinetic experiments the samples were analyzed using an Agilent 1100 type HPLC equipped with a diode array detector. An eluent of a 50-50% mixture of 1% aqueous acetic acid and acetonitrile was used. The separation of the degradation products was carried out on a C18 (LichroCHART 125-4.5 μm) Agilent column at 0.8 cm^3 min^{-1} flow rate of eluent.

RESULTS

Although the k values of the reactions of the four NSAIDs and •OH decrease in the order: NAP > DICL > KETO > IBU, the initial transformation rates (r_0) follow the order: KETO > IBU ≈ DICL > NAP (Table 1 vs. Fig. 2.a). Therefore, it seems that the transformation of these drugs is not determined only by •OH.

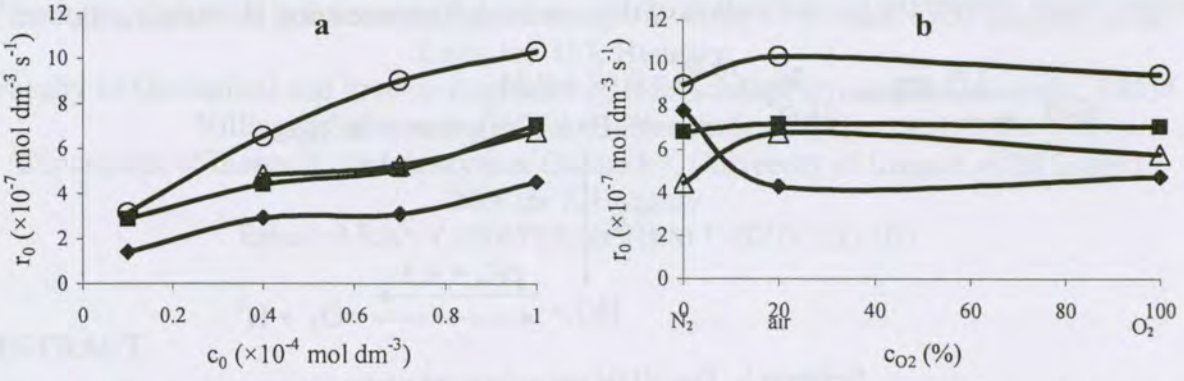


Figure 2. The initial transformation rates (r_0) of KETO (○), DICL (■), IBU (Δ) and NAP (♦) a) vs. their initial concentration, in the presence of oxygen, b) vs. the concentration of dissolved molecular oxygen, c_0 being 1×10^{-4} mol dm^{-3}

Dissolved molecular oxygen does not have the same effect on pharmaceuticals having different chemical structure (Fig. 1 vs. Fig. 2.b). It decreases strongly the r_0 of NAP, but increases that of IBU and KET. At the same time it has no effect on the rate of transformation of DICL. This is likely because of the way of transformation of the NSAIDs depends greatly on the structure of the target molecule.

The presence of another organic substrate causes a decrease of the r_0 of the target substance likely because of the competition for the reactive species (Table 2). MeOH, the commonly used •OH scavenger could produce the same effect only in an around 1000 times higher concentration than NSAIDs, although, the k of the reaction of MeOH with •OH is only with one order of magnitude lower than the values listed in Table 1 ($k = 1.0\times10^9$ mol^{-1} dm^3 s^{-1}[11]). Additionally, dissolved molecular oxygen strongly enhanced the decrease of r_0 in the case of IBU and KETO. Consequently, besides the •OH based reactions, the reactions with other formed ROS and excited water molecules might also have a relative high contribution to the transformation of these target substances during the VUV photolysis of their aqueous solution.

Table 2. The initial transformation rates of the four NSAIDs ($c_0 = 1\times10^{-4}$ mol dm^{-3}) affected by the presence of methanol ($c_0 = 0.1$ or 1 mol dm^{-3}) or another drug ($c_0 = 1\times10^{-4}$ mol dm^{-3})

substrate	r_0 ($\times 10^{-7}$ mol dm^{-3} s^{-1})						
	-	IBU	KETO	DICL	NAP	0.1 mol dm^{-3} MeOH	1 mol dm^{-3} MeOH
IBU	6.8	-	1.8	-	-	2.7	-
KETO	10.3	5.9	-	7.4	7.5	8.0	4.0
DICL	7.2	-	3.3	-	6.0	3.6	1.9
NAP	4.5	-	3.2	2.5	-	3.0	1.7

CONCLUSIONS

Dissolved molecular oxygen has various effects on the VUV photolysis of NSAIDs having different molecular structure. The transformation of the NSAIDs can not be interpreted only with the reactions based on •OH, the reactions with other ROS and excited water molecules should also be taken under consideration.

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