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Fate of pharmaceuticals—photodegradation by simulated solar UV-light

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Abstract

The fate of pharmaceuticals in surface waters under solar irradiation was investigated. Photodegradation of pharmaceuticals caused by sun irradiation may be of major significance in the natural elimination process. Based on a data compilation from the literature, the lipid lowering agent metabolite clofibric acid, the iodinated X-ray contrast media iomeprol, which contribute to the adsorbable organic halogen compounds, and the antiepileptic drug carbamazepine were selected. The irradiation experiments were carried out in batch experiments with simulated UV–sunlight. The photodegradation of the pharmaceuticals showed a pseudo-first-order kinetics. The objective of this investigation was to demonstrate that the extent of photoinduced degradation of pharmaceuticals can vary significantly for the different pharmaceuticals and it strongly depends on the water constituents present in solution. The influences of different initial pharmaceutical concentrations, the presence of other pharmaceuticals like carbamazepine or clofibric acid and the presence of natural organic matter on the photochemical degradation rate of pharmaceuticals in aqueous solutions were investigated. Analyses of the pharmaceuticals and their photodegradation products were carried out by high performance liquid chromatography with diode-array and fluorescence detection.

Keywords: X-ray contrast media; Iomeprol; Carbamazepine; Clofibric acid; Natural organic matter; Aquatic systems

1. Introduction

In recent years, the occurrence and fate of pharmaceutical residues in the environment has become a subject of public interest. The reason why these medical substances are of environmental concern can be deduced from their specific biological effects not only on patients, also on aquatic biota. Due to the variety and amount of their applications pharmaceuticals belong to the environmentally relevant compounds (Halling-Sørensen et al., 1998; Ternes, 1998). When applying pharmaceuticals to humans, many of their constituents are excreted unchanged through urine and faeces or as metabolites via municipal sewage system, many pharmaceutical compounds can frequently be found in effluents of wastewater treatment plants, in rivers and lakes. Balances of the input and the output of drugs and diagnostic agents in sewage treatment plants reveal that many pharmaceuticals are not removed quantitatively. Therefore sewage treatment plants act as point sources for surface water contamination. Recent studies have shown that a multitude of drugs is found in aquatic systems (Heberer et al., 1998; Möhle et al., 1999; Hirsch et al., 2000; Roßknecht and Hetzenauer, 2000; Ternes and Hirsch, 2000).

In particular, clofibric acid (Heberer et al., 1997; Sacher et al., 1998; Daughton and Ternes, 1999; Stumpf et al., 1999)—a therapeutically active metabolite of the

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lipid regulating substances ethofyllinclofibrate, etofibrate and clofibrate ethyl—shows a highly persistent behavior in the aquatic environment and has already been found in ground water and in drinking water as well as in the North Sea with concentrations ranging from 0.5–7.8 ng/l (Buser et al., 1998a). Tap water samples from Berlin were found to contain clofibric acid at concentrations between 10 and 165 ng/l (Stan et al., 1994; Heberer and Stan, 1996; Heberer et al., 1997; Heberer et al., 1998). Carbamazepine is a widely prescribed antiepileptic drug. It is ubiquitously present in the aquatic environment with typical average concentration of 2.1 μg/l in sewage treatment plant effluents and 0.25 μg/l in rivers and streams (Germany) (Halling-Sørensen et al., 1998; Ternes, 1998). Carbamazepine seems to be a permanent contamination in the rivers Rhine, Main, Danube and Neckar, whereby the concentration especially in river Rhine amounted up to 1 μg/l (Sacher et al., 1998). Removal in sewage treatment plants was found to be extremely low (7%) (Ternes, 1998; Möhle et al., 1999). As carbamazepine is not totally removed during ground passage this compound has also been detected in raw water of water works using bank filtrate for drinking water production (Sacher et al., 1998). Among all pharmaceuticals used in hospitals, iodinated contrast media are, concerning weight, the most frequently applied substances. The annual applied amount in Germany lies in the order of 360 t (Steger-Hartmann et al., 1999; Jekel and Wischnack, 2000; Putschew et al., 2000; Putschew et al., 2001). The relevance in terms of quantity becomes obvious, considering the fact that for one medical examination about 100 g of X-ray contrast media (≈30 g absorbable organic iodinated compounds (AOI)) are applied to the patients. After intake, the contrast media are excreted mainly non-metabolized within a few hours and find their way to the public sewage system. During wastewater treatment the elimination of the contrast agents is poor. Degradation experiments show that iodinated contrast media are released almost quantitatively in unmetabolized form by a municipal sewage treatment plant (Steger-Hartmann et al., 1998; Kalsch, 1999; Ternes and Hirsch, 2000). X-ray contrast media have been detected even in Lake Constance in concentrations up to 10 ng/l as well as in drinking water (Gartiser et al., 1996; Kümmerer et al., 1998; Hirsch et al., 2000; Roßknecht and Hetzenauer, 2000).

The solar radiation spectrum and the molar absorption coefficients of carbamazepine, iomeprol and clofibric acid show a large, small and almost no overlap respectively (Figs. 1 and 2). This adds basic photochemical aspects to the environmental interest of the selected compounds. Because of their low biodegradability and chemical properties, photodecomposition becomes significant as pathway of natural elimination. For example diclofenac was not detected in lake sediments and also showed negligible adsorption onto sediment particles in laboratory experiment. Further experiments

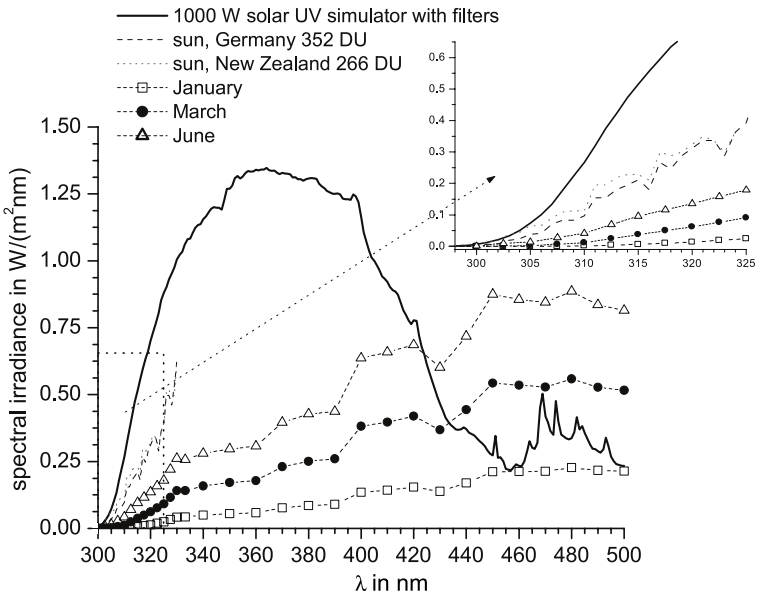


Fig. 1. The spectral irradiance of the sun in New Zealand and Germany at cloudless sky, zenith angle $\varphi = 34.3°$, ozone layer thickness in DU, measured by Seckmeyer and McKenzie (1992), the calculated spectral irradiance for central Europe (January, March and June) by Frank and Klöpffer (1988) and the measured spectral irradiance of the solar UV simulator used in this work by Schindelin et al. (1997).

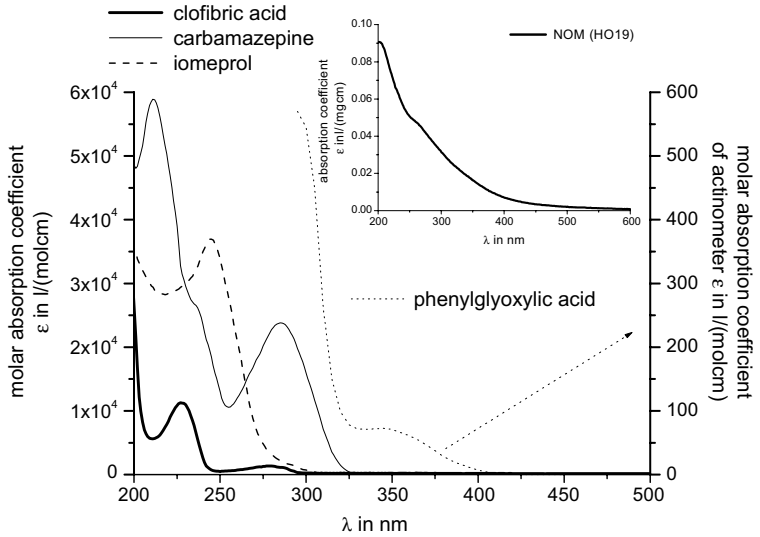


Fig. 2. Molar absorption coefficients of the pharmaceuticals (carbamazepine, clofibric acid and iomepol) in Milli-Q water and of the actinometer (phenylglyoxylic acid) in ACN:MilliQ water = 3:1 (v/v). The absorption coefficients of NOM (HO19) in l/(mg cm).

showed its minimal biological degradation and rapid photodegradation under natural sunlight (Buser et al., 1998b). Also quinolones, which are chemotherapeutical agents with antibacterial activity, were found to degrade photochemically under simulated sunlight (Burhenne et al., 1999).

Whereas visible sunlight ($400 < \lambda < 750$ nm) hardly causes photochemical reactions, solar UV-B radiation ($280 < \lambda < 315$ nm) and partially solar UV-A radiation ($315 < \lambda < 400$ nm) induce various direct and indirect photochemical processes in the top level of surface waters, which can lead to a degradation of anthropogenic micropollutants (Zepp et al., 1995). A photon absorbed by an organic molecule causes an electronic excitation of the molecule following the basic photochemical law of Grotthus and Draper (Gilbert and Baggott, 1991). The excitation can be followed by a primary photochemical process leading in most cases to an unstable intermediate. The formation of stable products may involve a long series of thermally controlled reactions. This type of direct photochemical reaction of an organic substance is called photolysis and requires an absorption spectrum that overlaps the spectrum of the incoming radiation (Braun et al., 1991).

It is well known that natural organic matter (NOM) plays an important part in sunlight induced photochemical processes in surface waters. NOM can act as inner filter, as radical scavenger and as precursor of reactive species. One important characteristic of humic substances lies in their ability to initiate the photochemical transformation of organic compounds in natural water and their eventual degradation. After being activated by solar UV photons, natural organic substances can produce reactive species, such as singlet oxygen, solvated electrons, superoxide anion, hydroxyl radicals and others. These reactive species are able to degrade anthropogenic organic compounds. In addition, photochemically activated NOM can react directly with anthropogenic organic compounds to form bound residues (Fischer et al., 1987; Cooper et al., 1989; Hoigné et al., 1989; Gjessing and Källqvist, 1991; Frimmel, 1994; Frimmel, 1998).

In this work, we intended to assess the importance of these direct and indirect photochemical processes for the degradation rate of pharmaceuticals and a diagnostic agent in surface waters by simulated UV–sunlight. The influences of NOM, different initial pharmaceutical concentrations and the presence of other drugs on the photochemical degradation rate of pharmaceuticals were investigated.

2. Experimental

2.1. Chemicals and materials

The pharmaceuticals clofibric acid and carbamazepine were purchased from Sigma-Aldrich (Deisenhofen, Germany); iomeprol was a courtesy from Byk Gulden (Konstanz, Germany); *p*-benzoquinone, hydroquinone, phenol, 4-chlorophenol and benzoyl formic acid were purchased from Fluka (Deisenhofen, Germany) (all p.a. quality). The chemicals used in the experiments were KH_2PO_4 (p.a.), NH_4Ac (p.a.) and acetic acid (HAc) (100%, p.a.) from Merck (Darmstadt, Germany), methanol (MeOH) and acetonitrile (ACN) (both HPLC

Table 1
Characteristic data of non-diluted brown water (HO19), filtered through 0.45 μm pore size polycarbonate membrane (Nucleopore)

pH (2 °C)	3.9
Electrical conductivity (2 °C)	45 μS/cm
Redox potential (2 °C)	353 mV
O_2 (2 °C)	8.81 mg/l
Spectral absorption coefficient A (254 nm)	99.8 1/m
Spectral absorption coefficient A (436 nm)	7.7 1/m
ρ(DOC)	21.1 mg/l
ρ(TOC)	24.32 mg/l
$\rho(NO_3^-)$	1.24 ± 0.154 mg/l
$\rho(SO_4^{2-})$	1.41 ± 0.497 mg/l
$\rho(Cl^-)$	2.27 ± 0.894 mg/l
ρ(Fe)	404.6 ± 0.35 μg/l
ρ(Ca)	1.98 ± 0.015 mg/l
ρ(Mg)	484.6 ± 3.84 μg/l

The TOC was determined in the unfiltered sample.

reagents) from Baker (Griesheim, Germany). NOM was taken from Lake Hohloh, a brown water lake in the south west of Germany (Hohlohsee, Black Forest). Water from Lake Hohloh (HO..) has a high concentration of dissolved organic carbon (DOC) and humic substances. The sampling day was 5 February 2001. It was the 19th sample collected in a series and therefore obtained the code HO19. The measured basic characteristic data of the non-diluted brown water HO19 are given in Table 1.

2.2. Sample preparation

The model stock solutions were prepared by dissolving clofibric acid, carbamazepine and iomeprol in Milli-Q water (demineralized water, additionally treated by activated carbon filtration and ion exchange, ρ(DOC): < 0.1 mg/l, electrical conductivity: 0.055 μS/cm). After addition of the pharmaceuticals, the samples were stirred for several hours to ensure a complete dissolution. Then the stock solutions were filtered (0.2 μm cellulose nitrate filter). The stock solutions were protected from solar irradiation and stored in a refrigerator. Their ages were kept less than one month. After dilution with Milli-Q water, the pH was adjusted to 7.0. Before being filled into the irradiation vessels, the solution was equilibrated with humidified air in order to get similar concentrations of oxygen and bicarbonate in all samples. For experiments with model solutions containing NOM, filtered HO19 water (0.45 μm cellulose nitrate filter) and a stock solution of carbamazepine in Milli-Q water were mixed and diluted with Milli-Q water to get the final pharmaceutical concentration.

2.3. Irradiation experiments

The samples were irradiated using a solar UV simulator (Oriel Corp., Stratfort, CT) with additional filters of the type WG 295, 6 mm (Schott Glaswerke, Mainz, Germany) and an atmospheric attenuation filter (Oriel Corp., Stratfort, CT) installed in the radiation beam to match the spectrum of the Xenon lamp to the typical solar UV-spectrum. The scheme of the solar simulator used for irradiation experiments is shown in Fig. 3. The radiation source was a 1000-W Xe short-arc lamp. The spectral irradiance of the simulated solar radiation with the WG 295 filter and the atmospheric attenuation filter in the radiation beam was determined by spectral radiometry (Schindelin, 1998) in combination with polychromatic actinometry. The spectral irradiance of natural sunlight in Germany (48° N) and in New Zealand (45° S) (Seckmeyer and McKenzie, 1992), the calculated spectral irradiance for central Europe (Frank and Klöpffer, 1988; Webb, 1991) and the spectral irradiance of the solar UV simulator measured by Schindelin (Bissen et al., 2001) are shown in Fig. 1. The spectrum of the solar UV simulator contained relatively

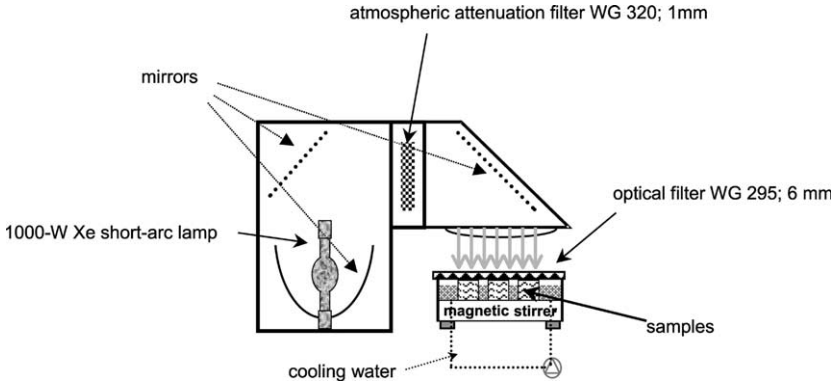


Fig. 3. Scheme of the solar UV simulator used for the irradiation experiments with model solutions.

small portions of the visible light compared to the real sunlight, while the cut-off wavelength in the UV-range was situated nearly at the same wavelength as in real sunlight. The intensities in the UV-range of the solar UV simulator are much higher than those of the real sunlight. Up to nine samples were irradiated simultaneously from above in a homogeneous light field. The sample volumes were 20 ml with an additional stirrer bar volume of 0.848 ml. The optical pathlength of the samples was 1.727 cm with a surface area of 12.07 cm^2. The samples were cooled (20 °C) by circulating water and stirred magnetically. The incident photon flux $\dot{n}_p$ was determined by chemical polychromatic actinometry, using phenylglyoxylic acid dissolved in ACN:MilliQ water = 3:1 (v/v), which functions as an actinometer by the photochemical decarboxylation of phenylglyoxylic acid to benzaldehyde and carbon dioxide (Defoin et al., 1986). The incident radiation between 290 and 400 nm was absorbed by the chemical actinometer phenylglyocylic acid (Figs. 1 and 2). The wavelength dependence of the quantum yield ϕ_λ for the chemical actinometer (phenylglyoxylic acid) in ACN:MilliQ water = 3:1 (v/v) is given in Defoin et al. (1986) and Schindelin (1998). The experimental setup and the evaluation of the results of the polychromatic actinometry were done following Braun et al. (1991) and Bossmann et al. (1998). The photon flux $\dot{n}_p$ measured by polychromatic actinometry with phenylglyoxylic acid was verified by the spectral radiometry (Schindelin, 1998). The photon flux $\dot{n}_p$ in the UV range ($\lambda \leqslant 400$ nm) of the solar UV simulator measured by polychromatic actinometry with phenylglyoxylic acid was 3.10×10^{-4} Einstein/(m^2 s) and with the spectral radiometry 3.08×10^{-4} Einstein/(m^2 s) (Schindelin, 1998). In the experiments the photon flux in the UV radiation range $\lambda < 320$ nm (UV-B: $280 < \lambda < 315$ nm) was 1.26×10^{-5} Einstein/(m^2 s), which is 1.9 times higher than the solar irradiation on a horizontal area at the earth's surface under cloudless conditions measured on 7/29/1991 in Neuherberg, Germany by Seckmeyer and McKenzie (1992) (zenith angle $\varphi = 34.3°$, 352 Dobson Units (DU) for the ozone layer thickness with 1 DU = 2.69×10^{16} molecules/cm^2). Table 2 gives an extended comparison of the incident photon flux of the solar simulator with the photon flux of natural solar radiation measurements (Frank and Klöpffer, 1988; Webb, 1991; Seckmeyer and McKenzie, 1992). The incident photon flux $\dot{n}_p$ of the radiation was much higher for the UV range ($\lambda \leqslant 320$ nm) than for the total UV range ($\lambda \leqslant 400$ nm) relating to real sunlight conditions. The proportion factors of simulation to reality depend on the measuring position and especially on the time of the sunlight measurements.

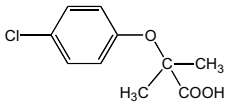
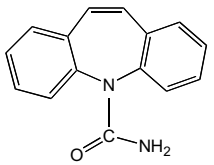
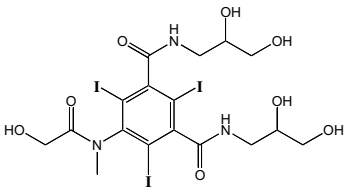
2.4. Analysis

The UV-absorbance of clofibric acid, carbamazepine, iomeprol, phenylglyocylic acid and NOM (HO19) was measured by a UV–visible spectrophotometer Cary 50 Conc (Varian), equipped with a quartz cell having a pathlength of 1 cm. The spectral absorbances are measured with baseline correction with a scan rate of 600 nm/min and a data point interval of 1 nm. The absorption coefficients of the pharmaceuticals, the actinometer and the NOM are given in Fig. 2. The concentrations of clofibric acid, carbamazepine and iomeprol were measured by high performance liquid chromatography using a HP 1090 LC (Hewlett Packard) equipped with an ODS-Hypersil column (125 mm × 4 mm, particle size: 5 μm, Agilent) with diode-array and fluorescence detection. The operating conditions for the HPLC/DAD/FLD measurements are shown in Table 3. The DOC concentrations were measured by a TOC 5000

Table 2
Incident photon flux $\dot{n}_p$ of the 1000 W solar UV simulator determined by chemical polychromatic actinometry and spectral radiometry and the comparison with the photon flux of natural solar radiation

Spectral area	UV	
	($\lambda \leqslant 320$ nm)	($\lambda \leqslant 400$ nm)
1000 W solar UV simulator		
Incident photon flux $\dot{n}_p$ from polychromatic actinometry	1.26×10^{-5} Einstein/(m^2 s)	2.45×10^{-4} Einstein/(m^2 s)
Refer back to data from:	Ratio of simulation to reality:	
Neuherberg, Germany	1.9	
Lauder, New Zealand (Seckmeyer and McKenzie, 1992)	1.6	
Reading, England (Webb, 1991)	2.1	
March, Europe—model	11.7	4.0
June, Europe—model	4.3	2.3
September, Europe—model	7.6	3.6
December, Europe—model (Frank and Klöpffer, 1988)	114	18.7

Table 3
Operating conditions for HPLC/DAD/FLD measurements

Pharmaceutical	Eluent/gradient programme			Detector DAD/FLD
	Time [min]	%B	Flow [ml/min]	
Clofibric acid 	A: 5 mM KH_2PO_4, 0.001% HAc, MillQ B: 0.001% HAc, MeOH:ACN = 1:1			
	0.0	50.0	1.0	DAD: 197, 228, 279 nm,
	3.0	50.0	1.0	FLD: $\lambda_{ex} = 230$ nm,
	5.0	55.0	1.0	$\lambda_{em} = 307$ nm
	7.0	55.0	1.0	
	Oven temperature: 35 °C			
Carbamazepine 	A: 5 mM NH_4Ac, MilliQ B: 5 mM NH_4Ac, ACN: H_2O = 99:1			
	0.0	5.0	1.0	DAD: 212, 286 nm
	10.0	80.0	1.0	
	12.0	100.0	1.0	
	Oven temperature: 40 °C			
Iomeprol 	A: 5 mM NH_4Ac, MilliQ B: 5 mM NH_4Ac, ACN:H_2O = 99:1			
	0.0	2.0	1.0	DAD: 240, 254 nm
	5.0	2.0	1.0	
	10.6	3.5	1.0	
	Oven temperature: 40 °C			

Carbon Analyzer (Shimadzu). The AOX measurements were done by an ECS 1200 (Euroglas Analytical Instrument). For the determination of AOX 50 mg activated carbon were added to each sample according to DIN 38409-14 (1985). After shaking for 24 h the samples were filtered. The covered filters containing the loaded activated carbon were inserted into the AOX-furnace. The AOX concentration was measured by using a pyrolytic microcoulometer according to DIN 38409-14 (1985). The relative standard deviation of the concentration values was <8%. Total concentrations of dissolved metals were measured by ICP-AES (inductively coupled plasma-atomic emission spectrometry) on a Vista-Pro CCD Simultaneous ICP-OES (Varian) at 240.489 and 258.588 nm (iron, Fe), 315.887 and 422.673 nm (calcium, Ca) and 279.553 and 285.213 nm (magnesium, Mg). Yttrium ($\rho(Y) = 2$ mg/l) served as internal standard measured at 377.433 nm. The separation of I^-, IO_3^- and iomeprol was performed by LC (Sykam, Germany) using an IonPac® AS9-SC (250 mm × 4 mm, Dionex) analytical column. Iodine was detected on-line with ICP-AES at 178.215 nm, with a detection limit of 50 μg/l. A solution containing 8 mM $NaHCO_3$ and 8 mM Na_2CO_3 dissolved in demineralized water was used as mobile phase. The flow rate was 1 ml/l, and the injection volume of the sample was 500 μl. The concentrations of the inorganic anions were determined by ion chromatography (Metrohm 690 Ion Chromatograph).

2.5. Kinetic analyses

The concentration of pharmaceuticals was followed as a function of irradiation time (between 8 and 70 h). The concentrations of the pharmaceuticals showed an exponential decrease during irradiation (Fig. 4). The data were fitted by a pseudo-first-order kinetic law (Eq. (1)), where c_0 and c_t are the concentrations at time 0 and t, k is the pseudo-first-order degradation rate constant (in 1/min) and t is the irradiation time in minutes.

$$c_t = c_0 \times e^{-k \times t} \quad (1)$$

For calculation of the degradation rate constant k of the photochemical degradation, only the concentration values with $\rho_t/\rho_0 \geqslant 0.7$ were used, because the degradation products influenced the rate in the sequel by scavenging reactive intermediates and by competitive spectral absorption (Schindelin et al., 1997). The fitting was done by the least squares method. Between six and ten data points were used for the computation. The coefficient of determination R^2 was higher than 0.98 in all cases.

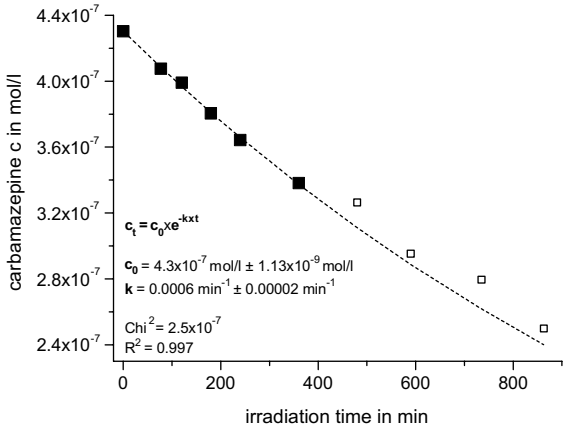


Fig. 4. Decrease of carbamazepine ($c_0 = 4.3 \times 10^{-7}$ mol/l, $\rho_0 = 0.102$ mg/l) during the irradiation time with a data fit by first-order kinetics, where c_0 and c_t are the concentrations at time 0 and t. Only the concentration values with $c_t/c_0 \geqslant 0.8$ were used for the fit here.

3. Results and discussion

The photochemical degradation of clofibric acid was found to decrease from $c_0 = 0.94$ mmol/l to $c = 0.67$ mmol/l within 70 h. The clofibric acid concentration decreased, but the DOC and the AOX concentration did not decrease so rapidly (Fig. 5). This is attributed to the formation of intermediates such as hydroquinone, *p*-benzoquinone, phenol and 4-chlorophenol. All these intermediates were assigned according to the retention times of the liquid chromatography and the UV spectra based on comparison with standards. The concentrations of hydroquinone and *p*-benzoquinone were too low for a quantification. Sometimes we were not able to detect benzoquinone because of its conversion to dihydroxybenzene (hydroquinone) during sampling. The concentrations of phenol and 4-chlorophenol as intermediates during the photochemical degradation progress are shown in Fig. 5. At the beginning of the irradiation experiments more 4-chlorophenol than phenol was formed. During the irradiation the concentration of the intermediates like phenol and 4-chlorophenol increased. The AOX concentration up to 22 h of irradiation reflected the theoretical value of clofibric acid. After 22 h of irradiation time other chlorinated substances beside clofibric acid and 4-chlorophenol contributed to the AOX concentration. The AOX concentrations at the higher irradiation time were lower than the sum of clofibric acid and 4-chlorophenol. A reason for that could be the volatility of chlorophenol and the period of time which passed until the AOX measurements were done. The measured ρ(DOC) concentrations in mg/l were higher than the calculated DOC concentrations, based on the sum of determined clofibric acid, 4-chlorophenol and phenol (Fig. 5). The reason could therefore be the formation of other intermediates

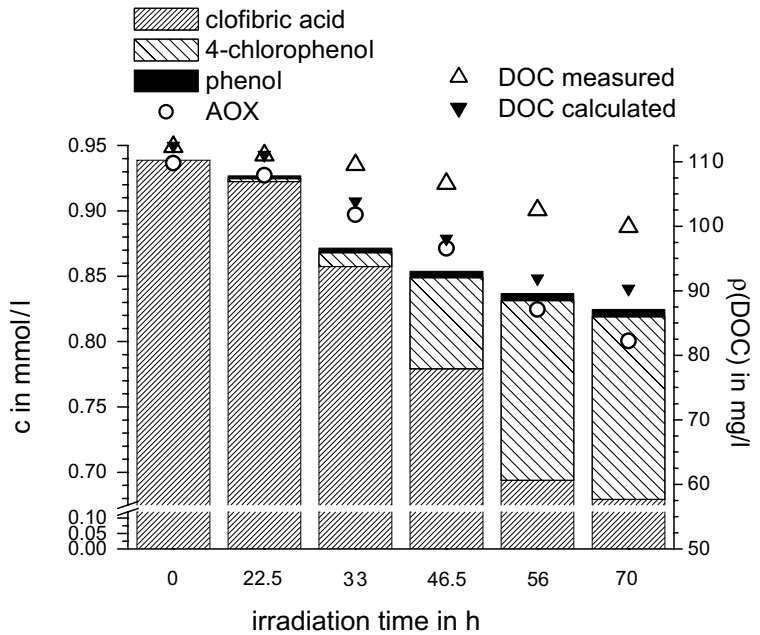


Fig. 5. Concentrations during photochemical degradation of clofibric acid ($c_0 = 0.94$ mmol/l), AOX, the intermediates 4-chlorophenol and phenol and the ρ(DOC) measured and calculated (total sum of clofibric acid, 4-chlorophenol and phenol).

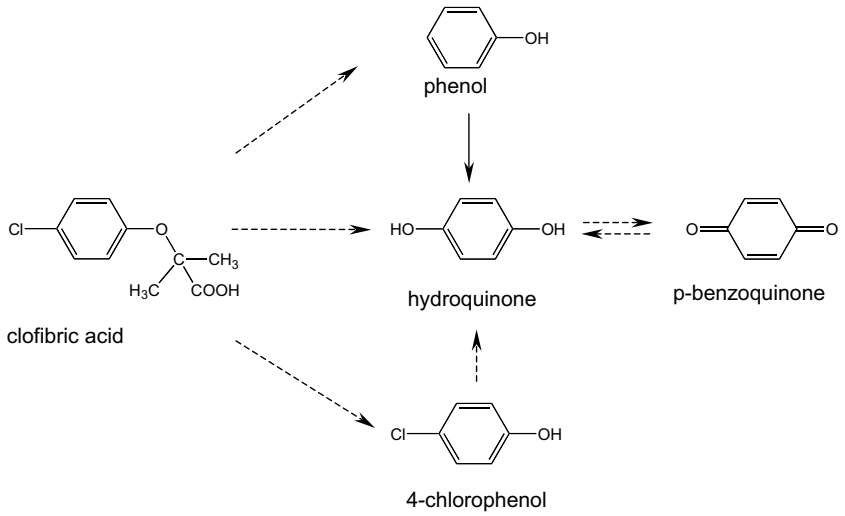


Fig. 6. Formation scheme of the photochemical degradation products of clofibric acid.

which were not measured by the investigated analytical methods. A possible scheme for the formation of the intermediates like 4-chlorophenol, phenol, hydroquinone and *p*-benzoquinone during the photochemical degradation of clofibric acid is shown in Fig. 6.

The presence of NOM from Lake Hohloh (HO19) increased the photochemical degradation rate of carbamazepine (Fig. 7). According to the photon flux absorbed by carbamazepine, the rate constant of the direct photolytic degradation should have decreased with increasing NOM concentration due to the inner filter effect of NOM. For example the photolysis of 4-quinolone antibiotics in presence of humic acids showed a decrease in the degradation kinetics, but no additional degradation products (Volmer et al., 1997). Also the photodegradation rate of pesticides with low pressure mercury lamp was lower in the presence of NOM than in distilled water because of competitive light absorption by colored NOM. In this case the NOM played the role of a light filter (Frimmel and Hessler, 1994). The measured basic characteristic data of the non-diluted brown water HO19 are given in Table 3. The degradation rates of carbamazepine increased rapidly with increasing DOC concentrations up to 7 mg/l. Consequently, the faster degradation of carbamazepine in the presence of NOM must be caused by NOM-induced reactions. These reactions can happen via reactive species formed by irradiated NOM like singlet oxygen ($^1O_2$), superoxide anion ($^{\bullet}O_2^-$), hydrogen peroxide (H_2O_2) and solvated electrons (e_{aq}^-). It is also reasonable to assume a direct reaction of excited NOM with carbamazepine by electron transfer or energy transfer. At DOC concentrations exceeding 7 mg/l, the increase of the degradation rates of carbamazepine induced by NOM was smaller and became nearly constant for DOC concentrations exceeding 12 mg/l (Fig. 7). In addition, the photochemical degradation rate was nearly constant up to DOC concentration of 20 mg/l of NOM due to scavenging of reactive species (Fig. 7).

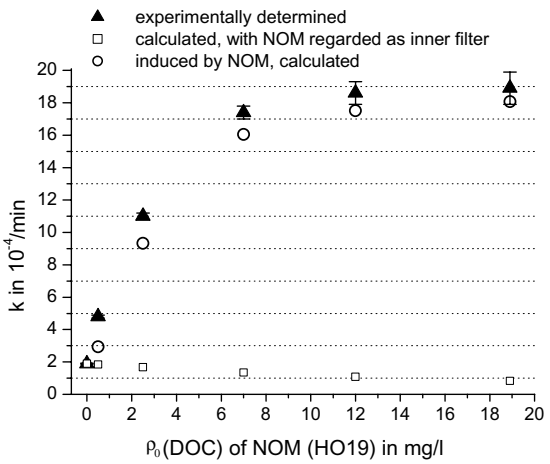


Fig. 7. Experimentally determined photochemical degradation rate constants of carbamazepine ($\rho_0 = 0.5$ mg/l, $c_0 = 2.1 \times 10^{-6}$ mol/l) at different initial concentrations of NOM (HO19, Lake Hohloh sampling number), calculated photochemical degradation rates with NOM acting as inner filter and the NOM induced degradation (differences of determined values and calculated values).

The inner filter effect of the NOM lowers the photochemical degradation rates of some substances, because of the competitive absorption of the incident photon flux. The photon flux absorbed by pharmaceuticals in the presence of NOM and the photon flux absorbed by the NOM (see Fig. 8) could be calculated.

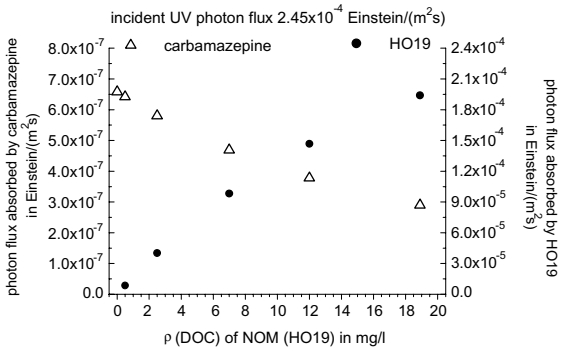


Fig. 8. Photon fluxes absorbed by carbamazepine and NOM in the irradiated samples of the UV solar simulator. Values calculated from the measured data of irradiance and absorbance taking into account the competitive absorption of both components.

The photon flux absorbed by the substance S is defined as:

$$\dot{n}_{P,S} = \dot{n}_{P,0} \times (1 - 10^{-\varepsilon_\lambda \times c_S \times d}),$$

$\dot{n}_{P,0}$: incident photon flux.

In the case of polychromatic irradiance the spectral photon flux is defined as:

$$\dot{n}_{P,\lambda} = \frac{d\dot{n}_P}{d\lambda}$$

In the case of polychromatic irradiation the spectral photon flux, which is absorbed by a substance S in presence of NOM is defined as:

$$\dot{n}_{P,\lambda,S} = \frac{d\dot{n}_{P,S}}{d\lambda} = \frac{\varepsilon_{\lambda,S} \times c_S}{\varepsilon_{\lambda,S} \times c_S + \varepsilon_{\lambda,NOM} \times c_{NOM}} \times \dot{n}_{P,\lambda,0} \times (1 - 10^{-(\varepsilon_{\lambda,S} \times c_S + \varepsilon_{\lambda,NOM} \times c_{NOM}) \times d})$$

$\dot{n}_{P,S}$—the absorbed spectral photon flux of the substance S, $\dot{n}_{P,\lambda,0}$—incident spectral photon flux, $\varepsilon_{\lambda,S}$—molar absorption coefficient of the substance S at the wavelength λ, d: pathlength.

The total absorbed photon flux of the substance S is obtained by integration over the complete absorbed wavelength range.

$$\dot{n}_{P,S} = \int_{\lambda_{min}}^{\lambda_{max}} \dot{n}_{P,\lambda,S}\, d\lambda$$

$$\dot{n}_{P,S} = \int_{\lambda_{min}}^{\lambda_{max}} \frac{\varepsilon_{\lambda,S} \times c_S}{\varepsilon_{\lambda,S} \times c_S + \varepsilon_{\lambda,NOM} \times c_{NOM}} \times \dot{n}_{P,\lambda,0} \times (1 - 10^{-(\varepsilon_{\lambda,S} \times c_S + \varepsilon_{\lambda,NOM} \times c_{NOM}) \times d})\, d\lambda$$

or simplified:

$$\dot{n}_{P,S} \cong \sum_i \dot{n}_{P,i,S} \Delta\lambda = \sum_i \frac{\varepsilon_{i,S} \times c_S}{\varepsilon_{i,S} \times c_S + \varepsilon_{i,NOM} \times c_{NOM}} \times \dot{n}_{P,\lambda,0} \times (1 - 10^{-(\varepsilon_{i,S} \times c_S + \varepsilon_{i,NOM} \times c_{NOM}) \times d}) \Delta\lambda$$

i—running variable for the absorbed wavelength range.

A theoretical degradation rate of pharmaceuticals in the presence of NOM was calculated with:

$$k_{NOM} = \frac{\dot{n}_{P,NOM}}{\dot{n}_{P,\text{without NOM}}} \times k_{\text{without NOM}}$$

k_{NOM}—theoretical rate of the degradation of pharmaceuticals in the presence of NOM, $k_{\text{without NOM}}$—rate of the degradation of pharmaceuticals in pure water in absence of NOM (determined by experiment), $\dot{n}_{P,NOM}$—photon flux absorbed by pharmaceuticals in the presence of NOM, $\dot{n}_{P,\text{without NOM}}$—photon flux absorbed by pharmaceuticals in the absence of NOM.

The theoretical degradation rate constants for the photochemical degradation of the pharmaceuticals in the presence of other drugs were calculated in the same way. The absorbed photon fluxes by carbamazepine and clofibric acid in the irradiated samples of the UV solar simulator were calculated from the measured data of irradiance and absorbance taking into account the competitive absorption of both components. The measured degradation rate constants of carbamazepine ($\rho_0 = 0.5$ mg/l, $c_0 = 2.1 \times 10^{-6}$ mol/l) and the calculated photochemical degradation rates in the presence of different initial concentrations of clofibric acid acting as a competitive inhibition (as an inner filter) are shown in Table 4. The clofibric acid absorbs almost nothing of the incoming radiation ($\lambda > 295$ nm). Therefore the calculated photochemical degradation rates of carbamazepine in the presence of the different initial concentrations of clofibric acid are nearly the same. For initial concentrations of 1 and 5 mg/l clofibric acid, the degradation rate constants of carbamazepine achieved only 58% and 11% of the calculated ones considering the competitive inhibition as an inner filter. The measured degradation rate constants of clofibric acid ($\rho_0 = 5$ mg/l, $c_0 = 2.3 \times 10^{-5}$ mol/l) and the calculated photochemical degradation rates of clofibric acid in the presence of different initial concentrations of carbamazepine are shown in Table 5. The extinction coefficients of carbamazepine at the wavelength of the incoming radiation are higher than those of clofibric acid. Therefore the competitive inhibition of carbamazepine was greater than that of clofibric acid. In the presence of initial concentrations of 0.5 mg/l ($c_0 = 2.1 \times 10^{-6}$ mol/l) and 1 mg/l ($c_0 = 4.2 \times 10^{-6}$ mol/l) carbamazepine the measured degradation rates of clofibric acid were about 50% and 62% lower than the calculated photochemical degradation rates of clofibric acid. The comparison of calculated and

Table 4
Experimentally determined and calculated photochemical degradation rate constants of carbamazepine ($\rho_0 = 0.5$ mg/l, $c_0 = 2.1 \times 10^{-6}$ mol/l) at different initial concentrations of clofibric acid acting as competitive inhibitor (as an inner filter)

	$k \times 10^{-4}$ in 1/min at different initial concentrations of clofibric acid		
		$\rho_0 = 1$ mg/l $c_0 = 4.6 \times 10^{-6}$ mol/l	$\rho_0 = 5$ mg/l $c_0 = 2.3 \times 10^{-5}$ mol/l
Carbamazepine ($\rho_0 = 0.5$ mg/l, $c_0 = 2.1 \times 10^{-6}$mol/l) experimentally determined	1.9 ± 0.03	1.1 ± 0.02	0.2 ± 0.03
Carbamazepine ($\rho_0 = 0.5$ mg/l, $c_0 = 2.1 \times 10^{-6}$mol/l), calculated with clofibric acid as inner filter (competitive absorption)	1.9	1.89	1.88

Table 5
Experimentally determined photochemical degradation rate constants of clofibric acid ($\rho_0 = 5$ mg/l, $c_0 = 2.3 \times 10^{-5}$ mol/l) at different initial concentrations of carbamazepine acting as competitive inhibitor (as an inner filter)

	$k \times 10^{-4}$ in 1/min at different initial concentrations of carabamazepine		
		$\rho_0 = 0.5$ mg/l $c_0 = 2.1 \times 10^{-6}$ mol/l	$\rho_0 = 1$ mg/l $c_0 = 4.2 \times 10^{-6}$ mol/l
Clofibric acid ($\rho_0 = 5$ mg/l, $c_0 = 2.3 \times 10^{-5}$ mol/l) experimentally determined	0.9 ± 0.04	0.4 ± 0.01	0.3 ± 0.01
Clofibric acid ($\rho_0 = 5$ mg/l, $c_0 = 2.3 \times 10^{-5}$ mol/l) calculated with carbamazepine as inner filter (competitive absorption)	0.9	0.80	0.78

measured degradation rates showed that the competitive inhibition is not only an inner filter effect. There must also be a scavenging of reactive intermediates and/or a stabilization of the compounds by formation of complexes.

The photodegradation of iomeprol led to different intermediates found at lower retention times in the liquid chromatogram. However, they could not be identified. During irradiation of iomeprol the equivalent AOI concentration decreased more slowly (Fig. 9) than the equivalent iomeprol concentration. During the irradiation of iomeprol, which belongs to the triiodinated substances, the concentration of I^- increased (Fig. 9). This indicates the production of other iodinated intermediates and the loss of the iodine during irradiation.

In all irradiation experiments, the concentration of the pharmaceuticals decreased nearly exponentially with irradiation time. Thus a pseudo-first-order rate constant could be determined according to Eq. (1). The higher the rate constant is, the faster the degradation is. In the absence of NOM and other drugs, the pharmaceuticals were degraded due to photolysis (i.e. via direct photochemical reactions) by simulated UV solar radiation. Carbamazepine showed the strongest absorption of the incoming radiation (simulated or natural sunlight) (Fig. 2) compared to iomeprol and clofibric acid, but it showed the lowest degradation rate constants (Fig. 10). The importance of the photolysis versus indirect photochemical degradation reactions depends on the absorption spectrum of the chemicals and on the quantum yield of their photolysis. The initial pharmaceutical concentrations had a considerable influence on the degradation rate constants (Fig. 10). The degradation rate constant from the first-order kinetics was higher for lower initial concentrations of a pharmaceutical than for higher initial concentrations of the pharmaceutical. A reason could be the complete absorption of the incident photon flux by the higher initial pharmaceutical con-

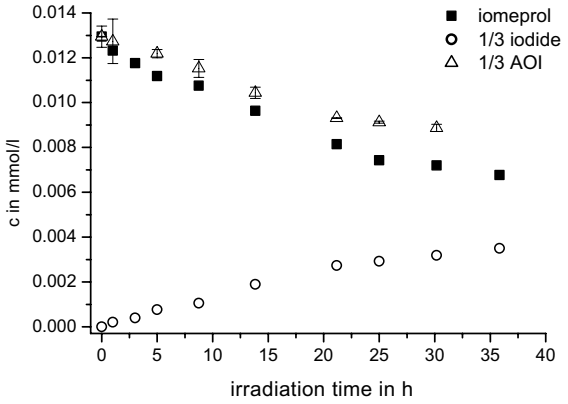


Fig. 9. Decrease of iomeprol ($c_0 = 0.013$ mmol/l) during the irradiation time. Concentrations of AOI and iodide during photochemical degradation of iomeprol.

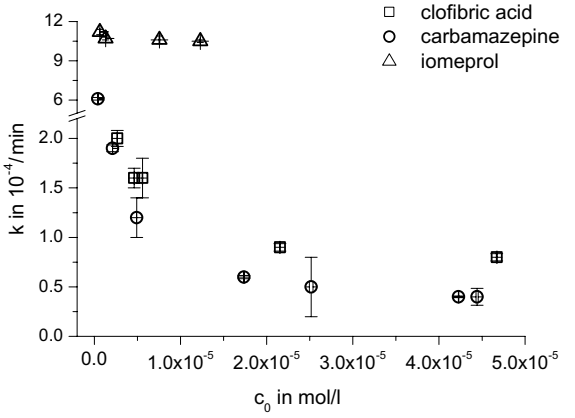


Fig. 10. Photochemical degradation rate constants of carbamazepine, clofibric acid and iomeprol at different initial concentrations of the pharmaceuticals in Milli-Q water determined with the solar UV simulator.

centrations over a shorter pathlength. So the absorbed photon flux of the lower and higher initial pharmaceutical concentrations was probably not proportional to the initial concentration of the pharmaceuticals. The dependence of the degradation rate constants on the initial concentration of pharmaceuticals shows that the degradation of the pharmaceuticals could not properly be fitted in a satisfactory way according to first-order kinetics.

An exponential relation between the degradation rate constant of carbamazepine and the initial concentration was found (Fig. 11). This can be explained by the lower transmission of the samples at higher concentrations of carbamazepine. The incident light was absorbed over a shorter distance. A calculation of the rate constants for the degradation, which was corrected for an inner filter effect also leads to an exponential relation. The k value of $c_0 = 4.26 \times 10^{-7}$ mol/l ($\rho_0 = 0.1$ mg/l) was the reference for the calculation, because the transmission values in the range of $290 < \lambda < 400$ nm were 0.98–1 for the pathlength of 1.7 cm. The values of the calculated degradation rate constants were much lower than the measured ones (Fig. 11). A reason for the difference between the measured and the calculated degradation rate constants could be the good stirring of the samples during irradiation. The stirring of the samples caused a better average transmission for the irradiation and led to a better degradation in the experimental setup than the calculated one, which was based on a stagnant solution. During irradiation of carbamazepine degradation products were produced, in very low concentrations.

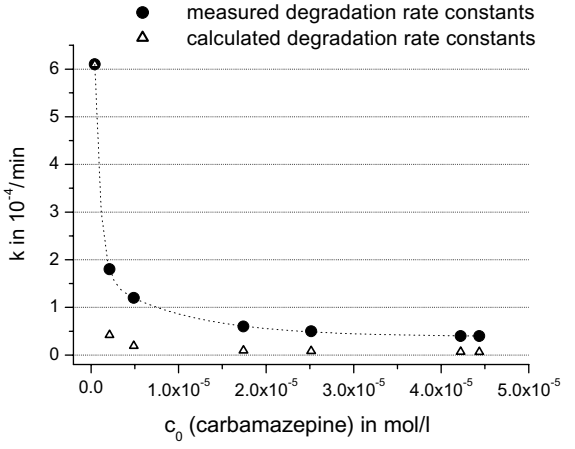


Fig. 11. Photochemical degradation rate constants of carbamazepine at different initial concentrations in Milli-Q water determined with the solar UV simulator and the calculated degradation rate constants considering the lower transmission (reference k value $c_0 = 4.26 \times 10^{-7}$ mol/l).

4. Conclusions

The environmentally relevant pharmaceuticals, carbamazepine, clofibric acid and iomeprol, could be photodegraded successfully. Carbamazepine absorbed most of the incoming radiation (simulated or natural sunlight) in relation to the other tested pharmaceuticals, but has the lowest degradation rate constants. During the irradiation of carbamazepine degradation products (intermediates) of carbamazepine were found. Clofibric acid absorbs only little of the incoming radiation (sun or solar simulator), but is degraded over the intermediates 4-chloropenol, hydroquinone, *p*-benzoquinone and phenol. There is also a degradation of the iodinated contrast agents with simulated sunlight, which can be measured by increasing iodide concentrations and decreasing AOI concentrations. During the degradation of iomeprol, new intermediates are formed. Further experiments should be done for the identification of these intermediates. The importance of the direct photolysis versus indirect photochemical degradation reactions depends on the absorption spectrum of the chemicals and on the quantum yield of their photolysis.

NOM from lake Hohloh (HO19) is enhancing the photochemical degradation of carbamazepine. Low concentrations of NOM accelerate the degradation due to the photochemical formation of reactive species by NOM. However, at higher concentrations of NOM, the acceleration of the degradation decreases. It can be concluded that NOM can act as inner filter, as radical scavenger and/or as precursor of reactive species. Other scavenging substances and effects have still to be investigated.

The theoretical degradation rate constants for the photochemical degradation of the pharmaceuticals in

the presence of other drugs were measured and calculated. The measured degradation rate constants of carbamazepine and clofibric acid in the presence of different initial concentrations of other pharmaceuticals, which were acting as a competitive inhibition, were lower than the calculated ones, which were corrected for the inner filter effect. Hence, there must be also a scavenging effect of reactive intermediates.

As a consequence, in comparison to the slow biodegradation photodecomposition of these pharmaceuticals by natural sunlight can be of major significance in the photic zone of aquatic systems. The presence of NOM can lead to a faster degradation of carbamazepine by the production of photochemically induced reactive species. On the other hand the degradation of carbamazepine or clofibric acid can be inhibited by clofibric acid or carbamazepine respectively.

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