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A model assessment of the importance of direct photolysis in the photo-fate of cephalosporins in surface waters: Possible formation of toxic intermediates

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Abstract

The direct and indirect photodegradation of six cephalosporins was predicted using a photochemical model, on the basis of literature values of photochemical reactivity. Environmental photodegradation would be important in surface water bodies with depth $\leq 2-3$ m, and/or in deeper waters with low values of the dissolved organic carbon ($\text{DOC} \leq 1 \text{ mg C L}^{-1}$). The half-life times would range from a few days to a couple of weeks in summertime. In deeper and higher-DOC waters and/or in different seasons, hydrolysis could prevail over photodegradation. The direct photolysis of cephalosporins is environmentally concerning because it is known to produce toxic intermediates. It would be a major pathway for cefazolin, an important one for amoxicillin and cefotaxime and, at $\text{pH} < 6.5$, for cefapirin as well. In contrast, direct photolysis would be negligible for cefradine and cefalexin. The DOC values would influence the fraction of photodegradation accounted for by direct photolysis in shallow water, to a different extent depending on the role of sensitisation by the triplet states of chromophoric dissolved organic matter.

Keywords: cephalosporins; emerging pollutants; environmental photochemistry; direct photolysis.

1. Introduction

The occurrence of pharmaceuticals in surface waters is a matter of concern, because of their adverse effects on living organisms and drinking water supplies. Many pharmaceuticals are only partially degraded in wastewater treatment plants (WWTPs), the outlets of which are thus important point sources of these xenobiotics (Kümmerer, 2009; Pal et al., 2010; Kosjek and Heath, 2011). In particular, antibiotics have been detected in the ng L^{-1} to $\mu\text{g L}^{-1}$ range in surface waters, where the possible bioaccumulation and the induction of drug resistance in bacteria may affect environmental and human safety (Corvaglia et al., 2008; Xu et al., 2011; Manzetti and Ghisi, 2014; Lee et al., 2014; Iliev et al., 2015; Jahne et al., 2015).

Cephalosporins are a widely used class of β -lactam antibiotics in human and veterinary medicine (Ball, 1999), and they are detected at significant concentration at the inlet and outlet of WWTPs (Rossmann et al., 2014). Their degradation in surface waters mainly occurs through abiotic

pathways (hydrolysis and photochemistry), while biodegradation may be important in sediment (Jiang et al., 2010). The kinetics of cephalosporin hydrolysis is minimum under ~neutral conditions (Yamana and Tsuj, 1976), thus photodegradation can be a competitive pathway in surface waters (Wang and Lin, 2012).

Photodegradation is usually divided into direct photolysis and indirect photochemistry. The involvement of both processes in surface-water conditions has been shown for cephalosporins (Xu et al., 2011, Wang and Lin, 2012) and other antibiotics (Li et al., 2011 and 2014; Lian et al., 2015; Niu et al., 2013). In direct photolysis, a xenobiotic undergoes transformation triggered by sunlight absorption (Pace and Barreca, 2013). In indirect photochemistry, sunlight is absorbed by naturally-occurring photosensitisers such as chromophoric dissolved organic matter (CDOM), nitrate and nitrite (Tai et al., 2012). Photosensitisers produce reactive transients including HO[•], ¹O₂ and CDOM triplet states (³CDOM*). The radicals HO[•] are produced by photolysis of nitrate and nitrite, and through different processes that may or may not involve H₂O₂ upon CDOM irradiation (Page and McNeill, 2011). The transients ³CDOM* and ¹O₂ are produced by CDOM photochemistry, while the carbonate radicals (CO₃^{-•}) are formed upon oxidation of carbonate and bicarbonate by HO[•] and of carbonate by ³CDOM* (Canonica et al., 2005).

Wang and Lin (2012) have observed that cephalosporin direct photolysis produces intermediates that are more toxic than the parent compounds. It is thus very important to assess the significance of direct photolysis in surface-water environments and to identify the conditions where it may be favoured. To our knowledge, the photodegradation of cephalosporins has been studied in the laboratory (Jiang et al., 2010; Xu et al., 2011; Wang and Lin, 2012) but not in the field, and a direct extrapolation of laboratory results to surface-water conditions may be problematic because of *e.g.* very different water column depths (Vione, 2014). To tackle this problem, we used a model approach to describe phototransformation. Model calculations are based on literature photoreactivity parameters for each compound (direct photolysis quantum yields and second-order reaction rate constants with transients), and on environmental conditions such as water chemistry and depth. The environmental conditions are thus predicted where *i*) cephalosporin phototransformation can be important compared to *e.g.* hydrolysis, and *ii*) direct photolysis accounts for an important fraction of the photochemical transformation.

2. Methods

2.1. Source data

Table 1 reports the available photoreactivity parameters of the cephalosporins under investigation. The direct photolysis quantum yield was measured under real sunlight for amoxicillin (AMO; Andreozzi et al., 2004), and using a solar simulator for the other compounds (Wang and Lin, 2012). The availability of photolysis quantum yields and second-order reaction rate constants with HO[•] is important for photochemical modelling because, differently from the first-order rate constants,

second-order ones and quantum yields can be extended over a much wider range of conditions that go far beyond the laboratory ones. Pulse radiolysis of water plus competition kinetics with SCN^- has been used to derive the HO^\bullet second-order reaction rate constants of AMO (Song et al., 2008) and cefazolin (CFZ; Dail and Mezyk, 2010). Comparable results were obtained for AMO by Andreozzi et al. (2005), upon UV irradiation of H_2O_2 and competition kinetics with benzoic acid. The rate constants of cefalexin (CFX), cefradine (CFD) and cefotaxime (CTX) with HO^\bullet have been measured by Wang and Lin (2012) with the Fenton reaction, using acetophenone as model compound.

2.2. Photochemical modelling and toxicity predictions

The assessment of the phototransformation kinetics was carried out with the APEX software (Aqueous Photochemistry of Environmentally-occurring Xenobiotics). It predicts photochemical half-life times as a function of water chemistry and depth, for compounds with known direct photolysis quantum yields and second-order reaction rate constants with transient species (Vione, 2014; Bodrato and Vione, 2014). APEX is based on a photochemical model, validated by comparison with field data of phototransformation kinetics in surface freshwaters (Maddigapu et al., 2011; De Laurentiis et al., 2012; Marchetti et al., 2013). Its time unit is a summer sunny day (SSD), corresponding to fair-weather 15 July at 45°N latitude. Further information is reported in the Supplementary Material (hereafter SM).

Insight into acute and chronic toxicity was obtained with the software ECOSAR (Ecological Structure Activity Relationship, <http://www.epa.gov/oppt/newchems/tools/21ecosar.htm>, last accessed April 2015), which gives a standard toxicity profile based on acute and chronic endpoints for fish, daphnid and algae (acute: median lethal concentrations for fish and daphnid, median effective concentrations for algae; chronic: geometric mean of the no observed effect concentration and of the lowest observed effect concentration for all organisms).

3. Results and Discussion

The data reported in Table 1 show that the direct photolysis quantum yield is available for all the investigated compounds (two values are reported for cefapirin, CFP, which undergoes an acid-base equilibrium with $\text{pK}_a = 5.44$; Wang and Lin, 2012). Unfortunately, the reaction rate constant with HO^\bullet is not available for CFP. Because the known HO^\bullet rate constants for the compounds of interest are all higher than $5 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$, in a conservative approach this value was taken as a reasonable lower limit for the reaction rate constant(s) between CFP (both forms) and HO^\bullet .

The rate constant with $^1\text{O}_2$ is known for AMO alone ($1.4 \cdot 10^4 \text{ M}^{-1} \text{ s}^{-1}$; Xu et al., 2011). It is very low, which excludes an important role of the $^1\text{O}_2$ reaction for AMO degradation in surface waters. Even in the case of the anti-inflammatory drug acetaminophen, which has a $^1\text{O}_2$ reaction rate

constant in the $10^7 \text{ M}^{-1} \text{ s}^{-1}$ range, the $^1\text{O}_2$ reaction is only a secondary one (De Laurentiis et al., 2014). In the case of another cephalosporin, ceftazidime, indirect evidence by kinetic comparison with N_3^- suggests that the $^1\text{O}_2$ rate constant could be around $10^6 \text{ M}^{-1} \text{ s}^{-1}$ (Deby-Dupont et al., 1998). This is also not enough for the process to be important in surface waters, compared to *e.g.* HO^\bullet reaction. Therefore, it might be reasonable to neglect the $^1\text{O}_2$ reaction as a significant sink for cephalosporins in aqueous environments.

Xu et al. (2011) have investigated the role of direct photolysis and reactions with HO^\bullet , $^1\text{O}_2$ and $^3\text{CDOM}^*$ in the phototransformation of AMO with several humic and fulvic acids. Although the reaction rate constants have not been worked out, by use of scavengers it was concluded that $^3\text{CDOM}^*$ accounted for 60-70% of AMO phototransformation. Direct photolysis and reaction with $^\bullet\text{OH}$ accounted for 10-20% each, while reaction with $^1\text{O}_2$ was negligible (coherently with the low reaction rate constant). Considering the experimental parameters and conditions used by Xu et al. (irradiation under simulated sunlight, optical path length in solution of a few centimetres, reported organic matter concentrations) and the known values of photolysis quantum yield and HO^\bullet reaction rate constant for AMO (see Table 1), the APEX software was used to simulate the experimental system. The experimentally observed role of triplet-sensitised transformation could be reproduced well with $k_{\text{AMO},^3\text{CDOM}^*} = 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$ as the second-order reaction rate constant between AMO and $^3\text{CDOM}^*$. This value is comparable to those of triplet sensitisation for fenuron, isoproturon and metoxuron, which also undergo important transformation by $^3\text{CDOM}^*$ in surface waters (Canonica et al., 2006; Canonica, 2007). For the other cephalosporins under investigation, because of the unavailability of reactivity data, it was hypothesised that the rate constants with $^3\text{CDOM}^*$ may vary within $2 \cdot 10^7 - 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$. This is for instance the approximate rate constant range of several phenylurea herbicides with reactive triplet states (Fabbri et al., 2015), and it also takes into account the fact that $^3\text{CDOM}^*$ from different environments may react differently (Vione et al., 2014).

There is evidence that the radical $\text{CO}_3^{\bullet-}$ may play a role in the phototransformation of CFX, CFD and CTX in natural waters (Wang and Lin, 2012), which will be taken into account when discussing the model results for these compounds.

3.1. Model assessment of cephalosporin direct and indirect phototransformation

Figure 1a shows the modelled photochemical half-life time of AMO ($t_{1/2}^{\text{AMO}}$), the cephalosporin for which the most complete photoreactivity data set is available, as a function of water depth and DOC under summertime irradiation conditions. The $t_{1/2}^{\text{AMO}}$ would vary from a few days to ~ 1.5 months. The half-life time would increase with depth, because in a deep water body the elevated photoactivity of the well-illuminated surface layer is compensated for by the limited irradiance in the lower depths. The depth effect also explains why the modelled half-life times in environmental waters are considerably higher than in laboratory experiments (Xu et al., 2011), where optical path lengths of a few cm are usually employed compared to some metres for surface waters.

Interestingly, $t_{1/2}^{AMO}$ increases up to a plateau with increasing DOC. High-DOC waters contain elevated DOM and CDOM, which have variable effects on the main phototransformation processes (direct photolysis and reaction with HO[•] and ³CDOM*). Direct photolysis would be inhibited at high DOC because of competition for sunlight irradiance between the substrate and CDOM (Jasper and Sedlak, 2013). Reaction with HO[•] would be inhibited as well, because of scavenging by DOM (usually not offset by the generation of HO[•] by CDOM; Kim and Zoh, 2013). In contrast, ³CDOM*-mediated processes are favoured at high DOC (Ukpebor and Halsall, 2012). Figure 1a suggests that the inhibition of HO[•] and direct photolysis has an important effect on $t_{1/2}^{AMO}$ for low DOC, at all water depths. As DOC increases, the increasing role of the ³CDOM* reactions causes the AMO half-life times to level off.

In addition to photodegradation, one should consider that cephalosporins undergo hydrolysis in aqueous solution. The process is catalysed under both acidic and basic conditions and it is slowest at pH values around neutrality (Yamana and Tsuj, 1976). The hydrolysis half-life time of AMO ($t_{1/2}^{AMO,hydr}$) under ~neutral conditions is around 10 days (Xu et al., 2011), which corresponds to a first-order hydrolysis rate constant $k^{AMO,hydr} = \ln 2 (t_{1/2}^{AMO,hydr})^{-1} \approx 0.07 \text{ day}^{-1}$. Figure 1b reports the relative weight (RW) of photochemical reactions in AMO transformation, calculated as $RW_{Photochemistry} = k^{AMO,phot} (k^{AMO,phot} + k^{AMO,hydr})^{-1}$. Here $k^{AMO,phot}$ is the (APEX-modelled) first-order degradation constant of AMO, accounted for by all the summertime photochemical processes. AMO phototransformation would prevail over hydrolysis ($RW_{Photochemistry} \geq 0.5$) in shallow waters ($d \leq 2 \text{ m}$), independently of the DOC, and in low-DOC waters ($\leq 1 \text{ mg C L}^{-1}$) independently of depth. Under different conditions, hydrolysis would be the main AMO transformation process.

Figure 1c reports the fraction of AMO phototransformation accounted for by direct photolysis, as a function of depth and DOC. At low depth, where photochemistry would be important compared to hydrolysis, direct photolysis would account for 30-50% of the overall phototransformation and it would be maximum around 2-4 mg C L⁻¹ DOC. Reaction with HO[•] would be the main transformation process at lower DOC, and reaction with ³CDOM* would prevail at higher DOC. Under high-depth and high-DOC conditions the direct photolysis fraction would be quite low, but in these circumstances the whole AMO photochemistry would be slower than hydrolysis. Other water parameters (e.g. nitrate, nitrite, inorganic carbon) would be scarcely important for AMO direct photolysis.

Figure 2 shows the modelling results for CFZ. The photochemical $t_{1/2}^{CFZ}$ is here reported as a function of depth and DOC, under the hypotheses that $k_{CFZ,^3CDOM^*} = 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (2a) and $k_{CFZ,^3CDOM^*} = 2 \cdot 10^7 \text{ M}^{-1} \text{ s}^{-1}$ (2b). In the former case CFZ would be slightly more photolabile than AMO (because of the higher importance of the direct photolysis, *vide infra*), but the overall trend is similar to the AMO one and has the same explanation. An important difference can be noticed between the $t_{1/2}^{CFZ}$ values of Figures 2a and 2b, in particular as far as deep and high-DOC waters are concerned. The reason is that the ³CDOM* reactions are very important (up to 75% of total

phototransformation) in the high-depth and high-DOC conditions of Figure 2a ($k_{CFZ,^3CDOM^*} = 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$), but they are always minor in the case of Figure 2b ($k_{CFZ,^3CDOM^*} = 2 \cdot 10^7 \text{ M}^{-1} \text{ s}^{-1}$).

The relative weight of photochemistry in the overall transformation of CFZ (photochemistry + hydrolysis) is shown in Figure S1 (SM). It was used $k^{CFZ,hydr} = 0.05 \text{ day}^{-1}$ (Yamana and Tsuj, 1976), and it can be concluded that photochemistry would prevail over hydrolysis in summertime for $d \leq 2-3 \text{ m}$ and/or $\text{DOC} \leq 1-1.5 \text{ mg C L}^{-1}$. The assumed value of $k_{CFZ,^3CDOM^*}$ ($2 \cdot 10^7$ or $2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$) would not change the above conclusions significantly, while hydrolysis would prevail in any case under high-depth and high-DOC conditions.

Figure 2c reports the fraction of CFZ phototransformation accounted for by direct photolysis, as a function of depth and DOC, under the hypothesis that $k_{CFZ,^3CDOM^*} = 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$. The qualitative trend is similar to the AMO one, but the direct photolysis would play a more important role in the case of CFZ. It would account for approximately 60-80% of total photodegradation in shallow and low-DOC waters, and it would be maximum for 2-4 mg C L^{-1} DOC. Figure 2d reports the CFZ direct photolysis fraction as a function of DOC and of $k_{CFZ,^3CDOM^*}$, for $d = 1 \text{ m}$. Interestingly, for low values of $k_{CFZ,^3CDOM^*}$ the direct photolysis fraction tends to a plateau at elevated DOC, where the minor $^3\text{CDOM}^*$ process would be unable to decrease the relative role of photolysis.

Direct photolysis is predicted to be very important for CFZ. The process is known to yield toxic intermediates, and there was an interesting correlation between the time trends of toxicity and of the intermediate 5-methyl-1,3,4-thiadiazole-2-thiol (Wang and Lin, 2012). Coherently with these findings, the ECOSAR software suggests that CFZ would be non-toxic for all the considered endpoints, while 5-methyl-1,3,4-thiadiazole-2-thiol would be quite toxic for algae and daphnid (but less for fish). Significant chronic effects for algae/daphnid are predicted at levels of hundreds ppb.

Figure 3 reports the direct photolysis fraction as a function of DOC and $k_{I,^3CDOM^*}$, where I = CFD (3a), CFX (3b) or CTX (3c). It was assumed $d = 1 \text{ m}$. The plots show that, independently of the environmental conditions and of the $k_{I,^3CDOM^*}$ values, the direct photolysis would be negligible (relative importance <1%) for both CFD and CFX. In contrast, the importance of the CTX direct photolysis would be approximately comparable to that of AMO. Table 1 shows that CFD and CFX have higher photolysis quantum yields than CTX. However, radiation absorption by CFD and CFX becomes very low above 310 nm, while that of CTX is higher and it is extended up to about 340 nm (see the absorption spectra reported in Figure S2 in SM). As already observed for CFZ, the direct photolysis fraction of CTX would be maximum at 2-4 mg C L^{-1} DOC if $k_{CTX,^3CDOM^*} = 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$, and it would increase with DOC (up to a plateau or a very broad maximum) for low $k_{CTX,^3CDOM^*}$. The corresponding photochemical half-life times under low-DOC conditions would be $\leq 10 \text{ SSD}$ for CFD and CTX and $\leq 14 \text{ SSD}$ for CFX, with little effect of $k_{I,^3CDOM^*}$. Half-life times in the same range are predicted for elevated DOC and high $k_{I,^3CDOM^*}$ values, but the model foresees 1-2 months if $k_{I,^3CDOM^*}$ is low. In the latter case, hydrolysis would be a major transformation process (Yamana and Tsuj, 1976).

CFD, CFX and CTX could undergo significant reaction with $\text{CO}_3^{\bullet-}$ (Wang and Lin, 2012), which would decrease the relative weight of their direct photolysis. Photolysis of CFD and CFX would be in any case negligible, but the effect of $\text{CO}_3^{\bullet-}$ on CTX could be important. By applying APEX modelling to the experimental data of Wang and Lin (2012), concerning CTX phototransformation in river water under simulated sunlight (with cm-range optical path lengths and the reported water chemistry values), one gets $[\text{CO}_3^{\bullet-}] \approx 1.5 \cdot 10^{-14}$ M. If direct photolysis and $\text{CO}_3^{\bullet-}$ reaction are the main processes of CTX transformation in irradiated river water, one gets $k_{\text{CTX}, \text{CO}_3^{\bullet-}} \approx 5 \cdot 10^7 \text{ M}^{-1} \text{ s}^{-1}$ (which would be an upper limit for the relevant rate constant). In this scenario and in the low-DOC conditions of Figure 3c, the reaction with $\text{CO}_3^{\bullet-}$ would account for about 50% of CTX phototransformation. The CTX direct photolysis fraction would be proportionally decreased from 30-40% to 15-20%. Moreover, the $\text{CO}_3^{\bullet-}$ reaction would account for ~25% phototransformation at 5 mg C L⁻¹ DOC, and for ~15% at 10 mg C L⁻¹ DOC.

The case of CFP is peculiar, because this compound undergoes an acid-base equilibrium in the environmental pH range ($\text{pK}_a = 5.44$; Wang and Lin, 2012), which affects significantly its photochemical fate. Figure 3d reports the direct photolysis fraction of CFP as a function of pH and of $k_{\text{CFP}, ^3\text{CDOM}^*}$, with fixed $d = 1$ m and $\text{DOC} = 2$ mg C L⁻¹. The direct photolysis fraction would decrease slightly with increasing $k_{\text{CFP}, ^3\text{CDOM}^*}$, because of the growing importance of the $^3\text{CDOM}^*$ process. However, $^3\text{CDOM}^*$ would play a limited role for $\text{DOC} = 2$ mg C L⁻¹, which accounts for the limited impact of $k_{\text{CFP}, ^3\text{CDOM}^*}$. The CFP direct photolysis would be more important at acidic pH (up to ~80% of total phototransformation), where the CFP acidic form prevails, and it would become a secondary process for $\text{pH} > 6.5$. The rationale is that the acidic form of CFP undergoes direct photolysis to a higher extent than the basic one (Wang and Lin, 2012). Coherently, the CFP photochemical half-life times (all photoprocesses) under summertime irradiation conditions and with the above depth and DOC values would be ~1 week at pH 5 and ~2 weeks at pH 7.

4. Conclusions

The photodegradation of cephalosporins could be important in shallow water bodies ($d \leq 2-3$ m) and/or at low DOC levels (≤ 1 mg C L⁻¹), where phototransformation would prevail over hydrolysis under summertime irradiation conditions. Among photochemical processes, the direct photolysis of these compounds has been shown to produce toxic intermediates and it is, therefore, of high environmental concern. Photolysis would be negligible for CFD and CFX, a major pathway for CFZ, and it would be important for AMO, CTX and CFP. For CFP, however, the photolysis process would be minor at $\text{pH} > 6.5$.

Other conditions favouring the direct photolysis of cephalosporins would depend on the $^3\text{CDOM}^*$ reactions. If triplet-sensitised transformation is important (elevated rate constant, as in the case of AMO), the direct photolysis fraction would be maximum for $\text{DOC} = 2-4$ mg C L⁻¹. If $^3\text{CDOM}^*$ reactions are not important, the direct photolysis fraction would increase with DOC. For

hydrolysis not to be more important than photochemistry, the concerned water bodies should be quite shallow ($d \leq 2-3$ m). In the case of CTX, the direct photolysis fraction at low DOC could be significantly decreased by the reaction with $\text{CO}_3^{\bullet-}$.

Little to nothing is unfortunately known about the toxicity of intermediates formed in other photochemical pathways (OH^\bullet , $\text{CO}_3^{\bullet-}$, $^3\text{CDOM}^*$). Such pathways could be important or even prevail depending, most notably, on the water DOC values. Experimental work regarding *i*) the accurate evaluation of missing kinetic parameters of photochemical concern and of hydrolysis rates in real aqueous media, and *ii*) the study of the nature, toxicity and formation yields of the intermediates of indirect photoreactions will be required for a more precise assessment of the environmental impact of cephalosporin transformation.

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Table 1. Direct photolysis quantum yields (Φ_{DP}) and second-order reaction rate constants with HO^\bullet of the cephalosporins under investigation. The structures of the investigated compounds are reported in Scheme S1 of the Supplementary Material (SM). CFP data are reported for two pH values, because CFP undergoes an acid-base equilibrium with $\text{pK}_a = 5.44$ (Wang and Lin, 2012). In this case, modelling took into account the fractions of the two forms which occurred at both pH values. n/a: not available.

Compound	Φ_{DP}	$k_{\text{Compound},\text{HO}^\bullet}, \text{M}^{-1} \text{s}^{-1}$
Amoxicillin (AMO)	$6 \cdot 10^{-3}$ (a)	$6.9 \cdot 10^9$ (c)
Cefalexin (CFX)	$9.1 \cdot 10^{-2}$ (b)	$7.1 \cdot 10^9$ (b)
Cefradine (CFD)	$7.6 \cdot 10^{-2}$ (b)	$1.1 \cdot 10^{10}$ (b)
Cefotaxime (CTX)	$1 \cdot 10^{-3}$ (b)	$8.1 \cdot 10^9$ (b)
Cefazolin (CFZ)	$6.0 \cdot 10^{-2}$ (b)	$6.5 \cdot 10^9$ (d)
Cefapirin (CFP)	$7 \cdot 10^{-3}$ (pH 7) (b)	n/a
	$1.6 \cdot 10^{-2}$ (pH 5) (b)	

(a) Andreozzi et al. (2004).

(b) Wang and Lin (2012).

(c) Song et al. (2008).

(d) Dail and Mezyk (2010).

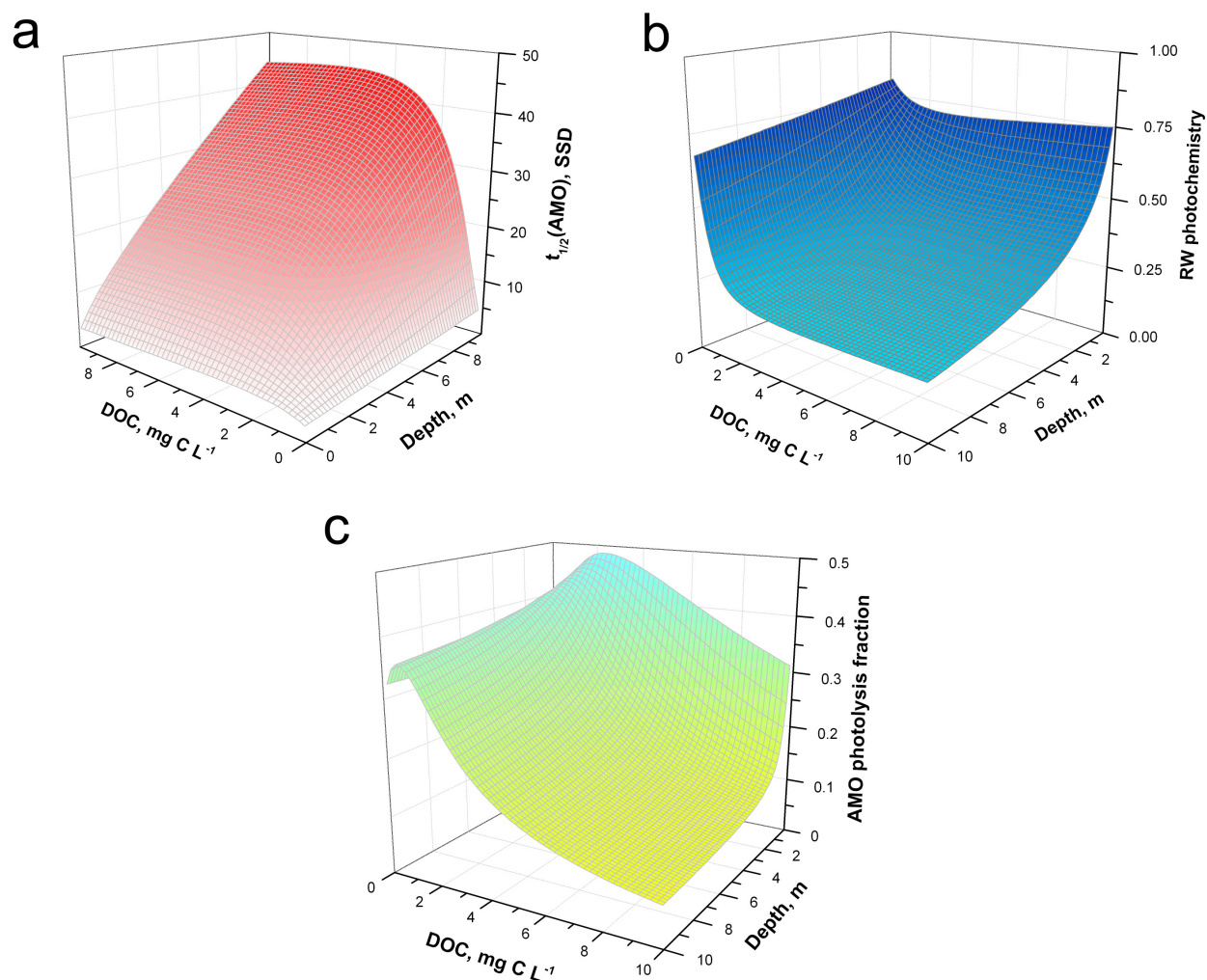


Figure 1. (a) AMO half-life time (SSD units) vs. water depth and DOC. (b) Relative weight (RW) of the photochemical processes in the overall CFZ degradation (photochemistry + hydrolysis), vs. depth and DOC. (c) Fraction of AMO phototransformation accounted for by direct photolysis, vs. depth and DOC. Other water conditions: 0.15 mM nitrate, 1 μM nitrite, 1 mM bicarbonate, 10 μM carbonate.

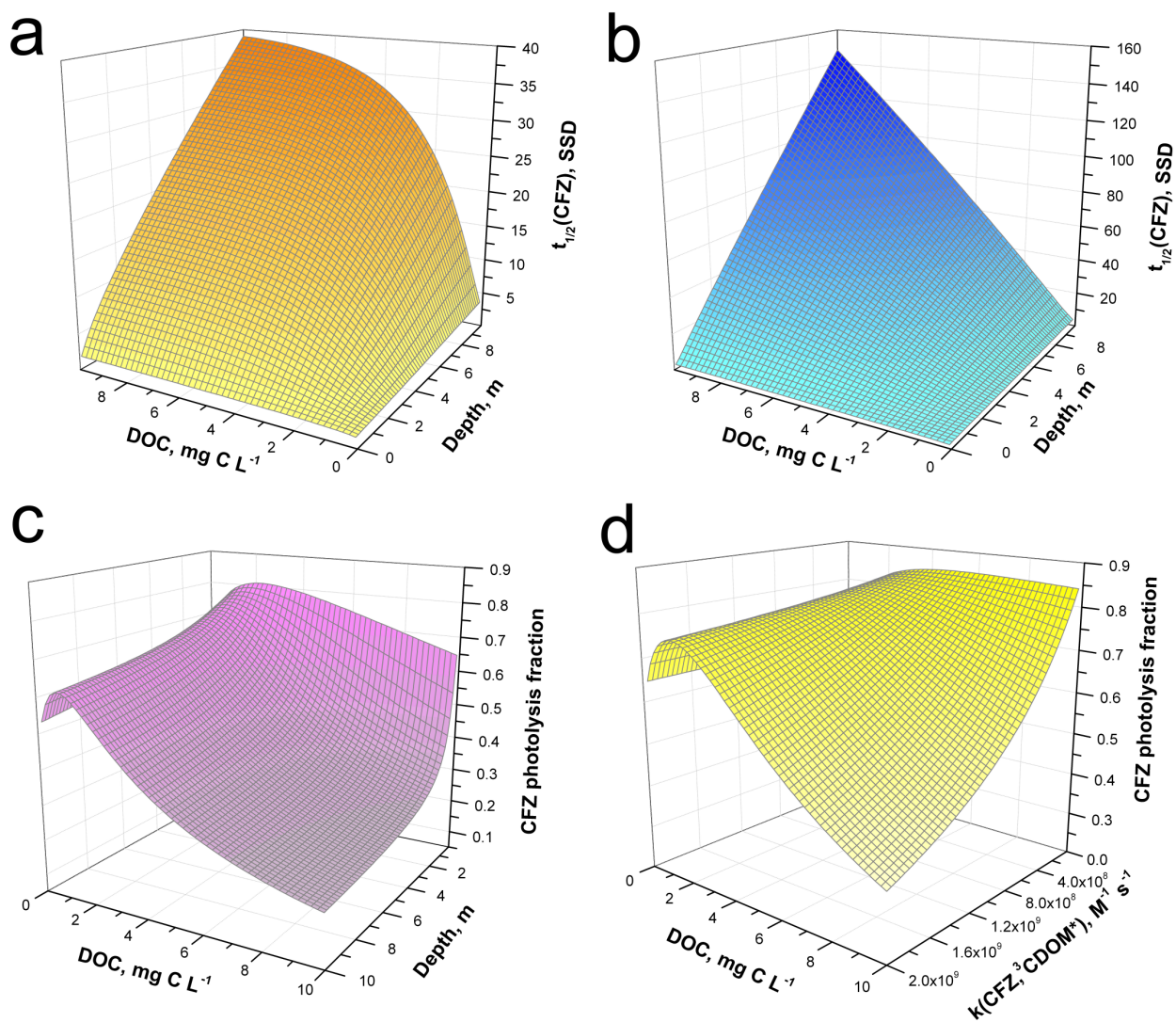


Figure 2. (a) Half-life time of CFZ vs. depth and DOC, if $k_{\text{CFZ},^3\text{CDOM}^*} = 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$. (b) As before, with $k_{\text{CFZ},^3\text{CDOM}^*} = 2 \cdot 10^7 \text{ M}^{-1} \text{ s}^{-1}$. (c) Direct photolysis fraction of CFZ vs. depth and DOC, with $k_{\text{CFZ},^3\text{CDOM}^*} = 2 \cdot 10^9 \text{ M}^{-1} \text{ s}^{-1}$. (d) Direct photolysis fraction of CFZ vs. DOC and $k_{\text{CFZ},^3\text{CDOM}^*}$, for depth $d = 1 \text{ m}$. Other water conditions as for Figure 1.

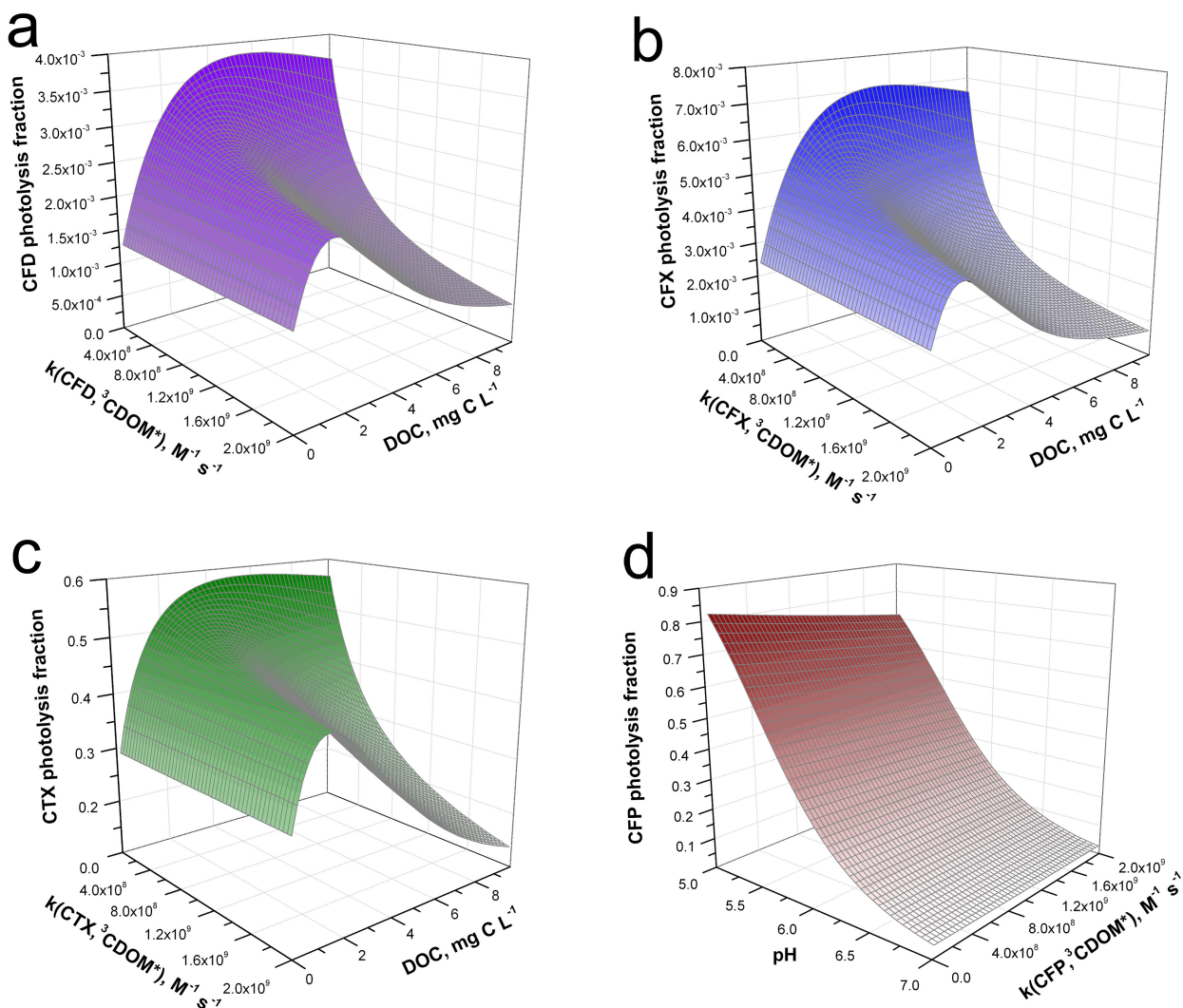


Figure 3. Fractions of phototransformation accounted for by direct photolysis, vs. DOC and $k_{I,3CDOM^*}$, for $I =$ (a) CFD, (b) CFX and (c) CTX. (d) Fraction of CFP phototransformation accounted for by direct photolysis, vs. pH and $k_{CFZ,3CDOM^*}$, for DOC = 2 mg C L⁻¹. Other water conditions as for Figure 1, plus 1 m depth.