The Possible Production of Harmful Intermediates Is the "dark Side" of the Environmental Photochemistry of Contaminants (Potentially Adverse Effects, and Many Knowledge Gaps)

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The possible production of harmful intermediates is the "dark side" of the environmental photochemistry of contaminants (potentially adverse effects, and many knowledge gaps)

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Photochemical reactions, *i.e.*, transformation processes triggered by sunlight, help surface waters to get rid of a variety of contaminants, and particularly of biorecalcitrant compounds. Unfortunately, in some cases, the photodegradation of a contaminant is offset by the production of harmful intermediates (*e.g.*, toxic, mutagenic, or endocrine-disrupting compounds).[1,2] The potential of a contaminant to produce harmful intermediate(s) is highly affected by environmental conditions, which are related both to the availability of sunlight and, at least as importantly, to features such as water chemistry and depth. For instance, the photochemical transformation of the anti-inflammatory drug ibuprofen into the toxic by-product 4-isobutylacetophenone (IBAP) is favored in waters rich in dissolved organic matter (DOM), but minimized in DOM-poor environments.[3]

Indeed, photochemical transformation is the combination of several reaction pathways, each with its own peculiarities. First, we have to distinguish between direct photolysis (where the contaminant absorbs sunlight and the absorption process triggers transformation) and indirect photolysis. The latter is triggered by so-called photochemically-produced reactive intermediates, *i.e.*, photogenerated transient species that react with the contaminants to transform them, and includes species such as the hydroxyl ($^\bullet OH$) and carbonate ($CO_3^{\bullet-}$) radicals, singlet oxygen ($^1O_2$), and the triplet states of chromophoric dissolved organic matter ($^3CDOM^*$). Direct photolysis and each indirect photolysis pathway are affected by the environmental conditions to a different extent: for instance, low DOM and elevated nitrate/nitrite favors $^\bullet OH$ radical formation (and $CO_3^{\bullet-}$ radicals if water is rich in inorganic carbon), while high organic matter generally favors $^3CDOM^*/^1O_2$ reactions and inhibits $^\bullet OH$, $CO_3^{\bullet-}$ radical reactions and direct photolysis. Coupled to this is the added complexity that the photogeneration of toxic intermediates from breakdown of parent contaminants takes place via specific preferential pathways. For example, ibuprofen degrades photochemically to IBAP mainly by both direct photolysis and reaction with $^3CDOM^*$, while reaction with $^\bullet OH$ radicals degrades ibuprofen but with little IBAP formation.[3]

By knowing the photochemical reactivity of a given contaminant (absorption spectrum, photolysis quantum yield, reaction rate constants with different transient species) and the potential formation

yield of a harmful intermediate *via* a particular photoreaction pathway, it is possible to predict the formation of the intermediate as a function of the environmental conditions. Such predictions can be used to show the potential of surface water bodies to degrade contaminants given their particular water chemistry. Figure 1 shows the mapped potential of water bodies in France and Switzerland to photochemically produce the transformation intermediates dihydroxycarbamazepine and 4-chlorophenol from carbamazepine and clofibric acid, respectively.
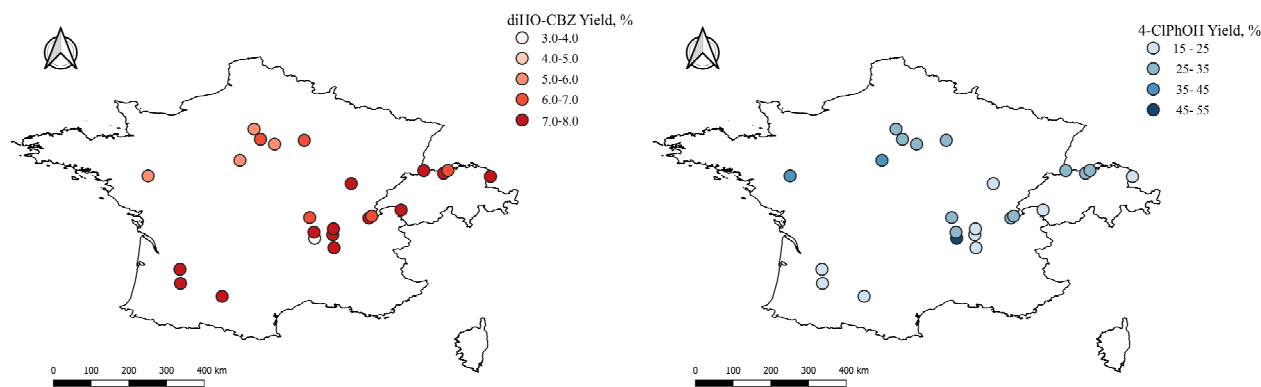

Figure 1: Maps of the formation yields in sunlit river water of (left) 10,11-dihydro-10,11-trans-dihydroxycarbamazepine from carbamazepine, and (right) 4-chlorophenol from clofibric acid. The calculation procedure is described in previous work.[4] Many sites of central-southern France have the highest potential to produce the former intermediate, and the lowest potential to produce the latter.

The prediction approach described here could allow for relatively easy identification of those water bodies where the formation yield of harmful intermediate(s) could be high if parent compound contamination is present. Such vulnerable water bodies should be prioritized for the assessment and environmental impact of parent contamination. This method could also open up the way to the definition of environmental vulnerability, in the context of photochemical reactions.[4]

Currently, photoreaction pathways are well known for only a small selection of contaminants. Moreover, the characterization and quantification of the formation yields of intermediates faces several challenges, which include the following:

(i) Consider all Photochemical Transformation Pathways: Many phototransformation studies focus on direct photolysis and reactions with $^{\bullet}$OH radicals, and an incomplete understanding of all potential photolytic degradation pathways is known. Processes triggered by reactions with the

transients $^3CDOM^*$, $CO_3^{\bullet-}$ and $^1O_2$ are often neglected, although they have high potential to produce harmful by-products.

(ii) The detection of by-products using the most popular techniques (LC-MS, GC-MS) provides identification but not quantification, unless the molecule is commercially available or already synthesized for other purposes (*e.g.*, by the manufacturer of the original contaminant).

(iii) Ecotoxicological studies take typically more time compared to analytical determinations, thus there are many identified by-products that lack toxicological data.

In summary, there is a huge predictive potential that cannot be properly exploited due to lack of input data. While it is unrealistic to think that a solution will be obtained soon, positive steps forward could include:

(a) The development of standard photochemical degradation study protocols. In standard assessments of the photodegradation of parent contaminants, important pathways are often overlooked or imprecisely characterized. Work should begin to define and standardize how photodegradation studies should be carried out, to capture meaningful and precise data.

(b) Prioritizing data generation for compounds with known toxic by-products. For compounds that are significantly photodegraded and produce known harmful intermediates (*e.g.*, phenylurea herbicides are transformed by $^{\bullet}OH$ into toxic N-formyl species),[5] efforts could focus on yield measurement under different conditions using available analytical standards, possibly through an *ad hoc* synthesis of standards for quantitative measurements or the supply of analytical standards from the parent company of the original contaminant. Manufacturers can identify major photodegradation by-products with standard tests that are suitable for direct photolysis but less so for indirect photolysis. Indirect photolysis by-products important for peculiar environments might escape detection, because it is difficult to define one representative condition for all water bodies.

(c) Using *in-silico* methods to assess the ecotoxicology of the identified transformation intermediates.[2] Although approximated, this approach can include virtually any organic compound and provide acute and chronic toxicity data for aquatic organisms (*e.g.*, fish, crustaceans and algae). Therefore, it could tackle a field where insufficient knowledge is currently available, and could suggest priorities for laboratory studies.

(d) Setting up specific photochemical-reaction ecotoxicology tests: To screen which photoreaction pathways have the most potential to produce harmful compounds from a parent contaminant, one could test the reaction mixtures arising from each separate photodegradation pathway. This screening approach could be used to identify the problematic photoprocesses creating ecotoxicologically relevant by-products and could be an important step forward.

In conclusion, the many knowledge gaps around the full photochemical reactivity of a given contaminant under different aquatic conditions hinders the ability to predict the formation of intermediate by-products as a function of water chemistry. The approaches suggested here could help tackle this problem, leading to the possibility of mapping the potential of a surface water body to produce harmful photodegradation intermediates and aid in the identification of vulnerable water bodies.

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