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# Assessing the persistence of pharmaceuticals in the aquatic environment: Challenges and needs

Qingwei Bu [a, b, *], Xiao Shi [a], Gang Yu [b, **], Jun Huang [b], Bin Wang [b]

[a] School of Chemical & Environmental Engineering, China University of Mining & Technology-Beijing, Beijing 100083, PR China
[b] School of Environment, State Key Joint Laboratory of Environmental Simulation and Pollution Control, Beijing Key Laboratory for Emerging Organic Contaminants Control, Tsinghua University, Beijing 100084, PR China

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ABSTRACT

Chemical's persistence is known to be an important parameter applied for decades to identify persistent organic pollutants in hazard and/or risk assessments. Nevertheless it is greatly challenged in the case of emerging contaminants such as pharmaceuticals because the persistence of these chemicals could be more affected by environmental conditions. This fact brings more challenges to the current system for evaluating the persistence of chemical contaminants. In this paper, challenges in assessing the persistence of pharmaceuticals were identified, and more importantly research needs were addressed based on the existing data and knowledge.



## 1. Introduction

Chemical's persistence is defined by its ability to retain in the environment, which is an important parameter applied for decades to identify persistent organic pollutants (POPs) or persistent, bioaccumulative and toxic (PBT) chemicals. One of the well-known practices is that the persistence attribute is employed as one of the most important parameters in Stockholm Convention for selecting POP candidates. The criteria for chemical persistence have been established under many regulatory frameworks to select chemicals of concern based on their transformation half-lives in the individual medium such as air, water, soil and sediment. For instance, both United Nations Environmental Program and Canadian Environmental Protection Agency set half-lives of 60 and 180 days as the criterion for chemical persistence in water and soil, respectively [1,2]. The above criteria have been demonstrated to be effective during screening of traditional POPs or PBT chemicals [3,4].

Persistence is usually assessed as an inherent property of a chemical [3] by using the well-established test guidelines in the lab [5–7]. By contrast, as the quantitative measure of persistence, transformation half-life of a chemical in the environment could be contributed by diverse processes, such as hydrolysis, biodegradation, direct or indirect photolysis, redox reactions. These processes are highly dependent on environmental conditions, e.g. temperature, salt, redox status, microorganism activity, and sunlight exposure [8]. Thus, the transformation half-life of a chemical in the environment is determined by a combination of chemical-specific characteristics and environmental conditions.

The traditional POPs regulated under Stockholm Convention are usually inherently persistent, as they are stable and cannot be transformed easily unless under strong artificial conditions [9–17]. Thus, the persistence of these chemicals in the environment is more dependent on its intrinsic properties. However, for some emerging contaminants that are not as persistent as traditional POPs, the persistence may be more affected by environmental conditions. And it is hard for scientists and managers to accurately quantify the transformation rates of a chemical in the environment and further to judge the persistence by using the lab test of persistence.

Pharmaceuticals are among these chemicals that the transformation could depend to a large extent on environmental conditions [18]. While the widespread presence of pharmaceuticals in

* Corresponding author. School of Chemical & Environmental Engineering, China University of Mining & Technology, Beijing 100083, PR China.
** Corresponding author. School of Environment, Tsinghua University, Beijing 100084, PR China.
*E-mail addresses:* qingwei.bu@cumtb.edu.cn (Q. Bu), yg-den@tsinghua.edu.cn (G. Yu).
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various environmental matrices were well documented during the last two decades [19–23], limited knowledge on their environmental fate (e.g. persistence) is available now. In this paper, we seek to address the challenges and needs in assessing the persistence of pharmaceuticals by comparing existing persistence data obtained both in the filed and the lab. To this end, a brief overview of the persistence data was conducted and we found that few pharmaceuticals were investigated for their persistence properties. Three of them (i.e. carbamazepine, diclofenac and ibuprofen) were in accordance with the aim of the present study. Although during recent years related studies on the fate of pharmaceuticals in other matrices, for example soils [24,25], are increasing, the data were still limited to make the comparison. Thus at now we focused on persistence studies for pharmaceuticals in the aquatic environment, because these chemicals are mostly polar ones and emitted with the discharge of wastewater as water-borne contaminants. We hope this paper will be a turning point for assessing the persistence of pharmaceuticals in the environment on a sound basis.

## 2. Persistence of pharmaceuticals in the aquatic environment

Persistence could be inferred from the continuous presence of a chemical in the environment distant from the emission source through long-term monitoring or biomonitoring. However, this may not apply for pharmaceuticals in environments. Pharmaceuticals were frequently detected with high residue concentrations in the aquatic environment, probably due to their continuous emission from sewage treatment plants which is significantly faster than their environmental removal rates. In view of this, pharmaceuticals were considered as a group of pseudo-persistent contaminants [26].

Another popular evidence for persistence screening is the slow rate of transformation in the laboratory simulation tests or field studies with good designs (that is preferred). Table 1 lists the degradation half-lives of three well studied pharmaceuticals in the aquatic environment or water-sediment systems, including carbamazepine, diclofenac and ibuprofen. The difference of between half-lives obtained in the lab and the field is striking. The variations of these observed values with location and time (or season) are worthy to note. For carbamazepine, most evidence either obtained in the lab or the field showed its half-life exceeded the persistence criteria of 60 days in waters. However, the long half-life of 1200 days observed by Zou et al. [27] in the field is remarkable and requires more attention. Vice versa the extremely fast photolysis with half-life of 3.5 days observed in the lab is impressive [28]. All of the investigated half-lives indicated that diclofenac is not persistent in the environment, although the observed values of half-life vary between studies. Yamamoto et al. [28] reported a surprisingly prolonged photolysis half-life of 413 days for ibuprofen, while most studies showed that ibuprofen with half-life shorter than the persistence threshold.

## 3. Challenges and research needs

As important human benefits, the use and subsequent release of pharmaceuticals are unavoidable to the environment. Hence there are increasing concerns about the presence of pharmaceuticals in environments, and assessing the persistence of these active pharmaceutical ingredients is among the most important issues for understanding their environmental fate. Here the challenges and research needs were identified according to the available information at present.

On the one hand, significant difference is observed for values of half-life obtained in lab simulation tests from field studies (Table 1), which will challenge the extrapolation of half-life from the lab to the field. To address this challenge, the following studies should be of need. (1) It is of great importance to develop sophisticated methods for determining the persistence of pharmaceuticals (or chemicals) in the field, which is the firstly important step for accurate quantification of persistence and further assessing the possibility of extrapolation of half-life from the lab to the field. Using the mass balance model in a well-defined river or lake system is one of the most important approaches for determining persistence in the field and was well documented [29–31,33–37]. Most studies

**Table 1**
Persistence, expressed as transformation half-life in the aquatic environment or water-sediment systems for three well-studied pharmaceuticals.

| Pharmaceuticals | Test type | Half-life, days | Date | Locations | References |
|---|---|---|---|---|---|
| Carbamazepine | Lab | 3.5[a] | August, 2006 | Tokushima, Japan[c] | Yamamoto et al. [28] |
| | Lab | 88[a] | May, 2007 | Tokushima, Japan[c] | Yamamoto et al. [28] |
| | Lab | 125[b] | September, 2006 | Tamiya River, Japan[d] | Yamamoto et al. [28] |
| | Lab | 233[b] | October, 2007 | Tsumeta River, Japan[d] | Yamamoto et al. [28] |
| | Field | 63 | August-September, 1999 | Lake Greifensee, Switzerland | Tixer et al. [29] |
| | Field | 1200 | Spring, 2013 | Lake Norra Bergundasjön, Sweden | Zou et al. [27] |
| Diclofenac | Lab | 0.008[a] | July, 1999 | Wädenswil, Switzerland[c] | Poiger et al. [30] |
| | Field | <30 | February, 1998 | Lake Greifensee, Switzerland | Buser et al. [31] |
| | Field | <8 | October, 1997 | Lake Greifensee, Switzerland | Buser et al. [31] |
| | Field | 8 | August-September, 1999 | Lake Greifensee, Switzerland | Tixer et al. [29] |
| | Field | 10 | Spring, 2013 | Lake Norra Bergundasjön, Sweden | Zou et al. [27] |
| | Field | 21 | Late spring, 2013 | Lake Boren, Sweden | Zou et al. [32] |
| Ibuprofen | Lab | 25[a] | August, 2006 | Tokushima, Japan[c] | Yamamoto et al. [28] |
| | Lab | 413[a] | May, 2007 | Tokushima, Japan[c] | Yamamoto et al. [28] |
| | Lab | 19[b] | September, 2006 | Tamiya River, Japan[d] | Yamamoto et al. [28] |
| | Lab | 20[b] | October, 2007 | Tsumeta River, Japan[d] | Yamamoto et al. [28] |
| | Field | 4.6 | September, 2005 | Trinity River, USA | Fono et al. [33] |
| | Field | 32 | August-September, 1999 | Lake Greifensee, Switzerland | Tixer et al. [29] |
| | Field | <5.6 | Late spring, 2013 | Lake Boren, Sweden | Zou et al. [32] |
| | Field | <27 | Late autumn, 2013 | Lake Boren, Sweden | Zou et al. [32] |
| | Field | <7.2 | Early winter, 2013 | Lake Boren, Sweden | Zou et al. [32] |

[a] Photolysis half-life.
[b] Biodegradation half-life.
[c] The location denotes where the test chemicals exposed to sunlight.
[d] The location denotes where the test water sampled.

established mass balance equations with the assumption of steady state, while chemical flows in the real environment are largely time dependent, especially for pharmaceuticals [38–40]. To overcome the problems of spatial and temporal variability, Zou et al. [18,27,32] developed and applied a framework by using the technique of chemical benchmarking. Nonetheless, it is difficult to select proper benchmark chemicals for pharmaceuticals with varying emission patterns in reality. Thus, a dynamic mass balance model would be just the foundation and research need for the future development of methods of determining the persistence in the field. Once one can measure the persistence in the field accurately, (2) comparing the persistence determined in lab tests with that measured in the field will be possible, and further the possibility of lab-to-field extrapolation should be assessed.

Another challenge is due that the persistence of pharmaceuticals varies with time and location (Table 1). This is easy to understand as many factors influencing the persistence are time or location dependent, for example, the diversity of microorganisms among different locations, in the case of biodegradation. As a result, (1) it emphasized the need of determining the temporal and spatial variation of persistence in the real environment, as they may be different location from location even in the same river [41]; Based on the results, (2) the influence mechanism of environmental conditions on persistence of pharmaceuticals should be classified, which is also important for establishing the lab-to-field extrapolation method in the future; and (3) since pharmaceuticals (as well for other chemical contaminants) display a distribution of persistence (expressed as half-life) as a function of time and location, the traditional pass-fail system based on a “single cut-off line” is flawed. There is a need of setting new criteria for judging the persistence in the environmental reality. A possible solution is to compare the persistence with cut-off values based on a probability distribution curve.

Moreover the continued presence of pharmaceuticals in the aquatic environment could be explained by the continuous release or the inherent persistence, which also challenges the traditional regulatory actions for these chemicals. Hence efforts on differentiating the reason for their continuous presence in the environment are welcomed. This will result in completely different actions for contamination control. For example, for a pharmaceutical with large use volume but fast transformation, the control actions should include avoiding abuse (e.g. the case of antibiotics), proper disposal of unused drugs and so on. For pharmaceuticals that are inherently hard to degrade, search for alternatives would be part of the choices.

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