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Authors: Maldonado-Torres, Sabino, Gurung, Rubi, Rijal, Hom, Chan, Andrew, Acharya, Shishir, et al.

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Fate, Transformation, and Toxicological Impacts of Pharmaceutical and Personal Care Products in Surface Waters

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Sabino Maldonado-Torres[1], Rubi Gurung[1], Hom Rijal[1], Andrew Chan[1], Shishir Acharya[2], Snezna Rogelj[2], Menake Piyasena[1] and Gayan Rubasinghege[1]

[1]Department of Chemistry, New Mexico Tech, Socorro, NM, USA. [2]Department of Biology, New Mexico Tech, Socorro, NM, USA.

ABSTRACT: With the growth of the human population, a greater quantity of pharmaceutical and personal care products (PPCPs) have been released into the environment. Although research has addressed the levels and the impact of PPCPs in the environment, the fate of these compounds in surface waters is neither well known nor characterized. In the environment, PPCPs can undergo various transformations that are critically dependent on environmental factors such as solar radiation and the presence of soil particles. Given that the degradation products of PPCPs are poorly characterized, these "secondary residues" can be a significant environmental health hazard due to their drastically different toxicologic effects when compared with the parent compounds. To better understand the fate of PPCPs, we studied the degradation of selected PPCPs, including ibuprofen and clofibric acid, in aqueous solutions that contained kaolinite clay and were irradiated with a solar simulator. The most abundant degradation products were identified and assessed for their toxicologic impact on selected microorganisms. The degraded mixtures showed lower toxicity than the starting compounds; however, as these degradation products are capable of further transformation and interaction with other PPCPs in natural waters, our work highlights the importance of additionally characterizing the PPCP degradation products.

KEYWORDS: Pharmaceuticals, photo-enhanced toxicology, abiotic transformation, personal care products, photodegradation, secondary residues

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CORRESPONDING AUTHOR: Gayan Rubasinghege, Department of Chemistry, New Mexico Tech, Socorro, NM 87801, USA.
Email: gayan.rubasinghege@nmt.edu

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Introduction

The growing medical and personal needs of the human population have escalated the release of pharmaceutical and personal care products (PPCPs) into the natural environment.[1–3] This has raised major concerns related to the environment and human health. Limited research has been conducted to determine the occurrence and direct health risks of primary PPCP compounds, yet, environmental degradation, transformation, and the fate of PPCPs are poorly understood. Numerous studies have shown that low-dose exposures of environmental chemicals, similar to PPCPs, organic solvents and pesticides, can be linked to various health conditions in the general population, including premature birth and death, cancer, chronic bronchitis, respiratory tract infection, heart disease, and permanent diminution in lung capacity.[2] However, the origin and formation of most of such low-dose toxic compounds, in particular, secondary residues of PPCP degradation, remain unknown. Here, we argue that the lack of knowledge regarding the chemistry of degradation products and their impact on the ecosystem may have misled numerous field and laboratory studies in the past, underestimating environmental abundances—and thus potential health effects—of many pharmaceutical compounds.[3] This deficiency has constrained the established policies and protocols for controlling environmental pollution by PPCPs. To inform such decision-making processes, it has, therefore, become vital to conduct extensive studies of PPCP degradation pathways which specifically focus on abiotic mechanisms under natural conditions and increase our understanding of the fate, the transformation, and the long-term health effects of both PPCPs and their degradation products.

Degradation of PPCPs in Surface Waters

The degradative reactions of PPCPs can be influenced by various environmental factors, including pH, solar irradiation, and the presence of soil particles.[4] The PPCPs released to the environment are in constant interaction with soil particles, a complex mixture of metal oxides and clays. These particles provide a highly reactive surface for rich chemistry to occur.[5] In combination with sunlight, the soil allows for heterogeneous photochemical reactions that can result in hydrolysis, oxidation-reduction, polymerization, and isomerization reactions. To gain insight into the chemistry behind the PPCP reactions in water bodies, we studied the degradation of ibuprofen and clofibric acid, two pharmaceuticals found abundant in water bodies.[6] A comparison of ibuprofen and clofibric acid decays, under various experimental conditions, is shown in Figure 1. Here, the degradation



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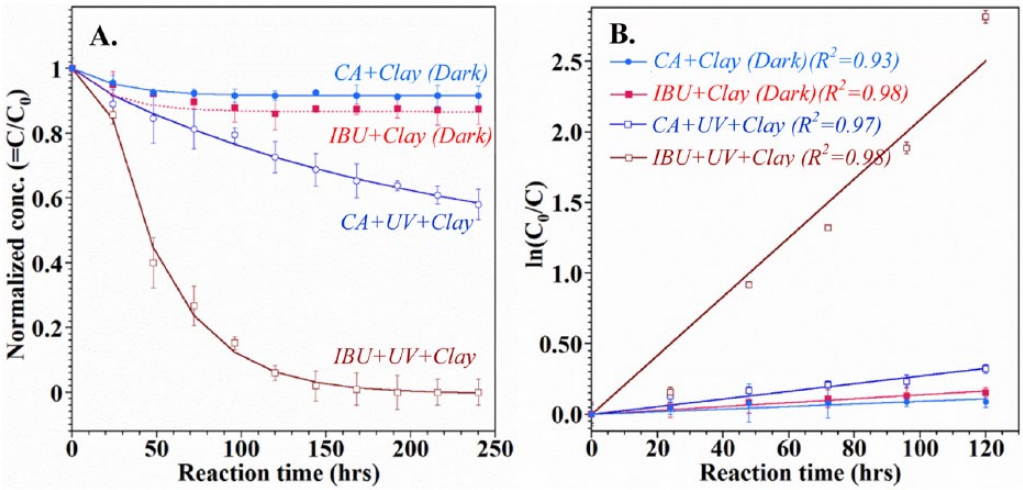


Figure 1. A comparison of kinetics of ibuprofen (IBU) and clofibric acid (CA) decay under various experimental conditions, determined from high-performance liquid chromatography analysis of remaining drug in degraded mixtures. (A) Decay curves for drug. C_0—initial drug concentration; C—drug concentration at reaction time, *t*. (B) Pseudo-first-order kinetics for drug decay. R^2—correlation coefficient.

was monitored using high-performance liquid chromatography analysis of the remaining primary compound. Under dark conditions, the decay of either ibuprofen or clofibric acid was minimal, with only ~10% loss of the initial concentration after 250 hours. Given that no secondary product formation was observed, this loss is ascribed to the (potentially limited) surface adsorption onto clay particles.

The degradation of PPCPs can be significantly influenced by solar radiation via photochemical reactions, including the direct photolysis, formation of hydroxyl radicals, and other transient reactive species.[7] As shown in Figure 1, in the presence of light, ibuprofen exhibited a complete transformation into secondary residues while only 40% of clofibric acid was degraded. Based on kinetic analysis (Figure 1B), the initial rate of degradation was 3- to 6-fold higher in the presence of light compared with its dark counterpart. Thus, the higher degradation rates indicate a rapid transformation of primary PPCP compounds to secondary mixtures, especially during the daytime. Here, we propose that the reported PPCP abundances in fieldwork are only the equilibrium concentrations and that a significant fraction of original PPCPs added to the environment has degraded into their secondary residues. It is also important to highlight the role of clay particles in photodegradation. As discussed in our previous work,[1] the irreversible uptake of PPCPs results in bathochromic shifts of π to π^* and n to π^* transitions. These chemical shifts enhance the overlap of the absorption bands and the emission profile of sunlight, resulting in higher quantum yields, more photo-excited PPCP molecules, and increased reactive oxygen species.

Liquid chromatography coupled with mass spectroscopy was performed to identify these degradation products. The most abundant degradation product of ibuprofen was 4-acetylbenzoic acid.[1,8,9] Also in good agreement with previous work, 4-chlorophenol ($m/z = 128$) was found to be the main photodegradation product of clofibric acid (Figure 2A).[10] As illustrated in Figure 2B, these photodegradation pathways may involve decarboxylation ($-CO_2$) and demethylation ($-CH_3$) of the photo-excited clofibric acid adsorbed onto the kaolinite surface and yield 4-chlorophenol. Because PPCPs are a group of highly diverse chemical compounds, the specific mechanisms and degradation pathways would greatly depend on PPCP's structural, electronic, and photochemical properties.

Toxicologic Effects and Health Hazards

Pharmaceuticals are intrinsically biologically active compounds, yet only few risk assessment studies have been performed in the context of the environment. New evidence is turning up, particularly regarding endocrine-disrupting compounds and raising questions about potential human health risks. In a recent report, Kortenkamp et al[11] evaluated the health risks of phthalates found in children's toys, childcare products, and in products used by women of childbearing age. They concluded that potential health risks of phthalates included the (rat) phthalate syndrome, characterized by malformations of the epididymis and reduced anogenital distance. A recent clinical study reported a univocal depression of testicular function, including testosterone production, after the use of ibuprofen.[12] Authors further showed that exposure to ibuprofen causes selective transcriptional repression in endocrine cells which leads to an elevation of the stimulatory pituitary hormones; this could result in a state of compensated hypogonadism which is associated with adverse reproductive and physical health disorders.[12] Another concern about PPCPs in the environment is their potential bioaccumulation and biomagnification via aquatic food web. Although Li and Lin have recently shown that the irradiated samples of aqueous mixtures of various pharmaceuticals increased their toxic effects on a luminescent bacterium, *Photobacterium phosphoreum*, our understanding of toxic effects of degradation products of PPCPs

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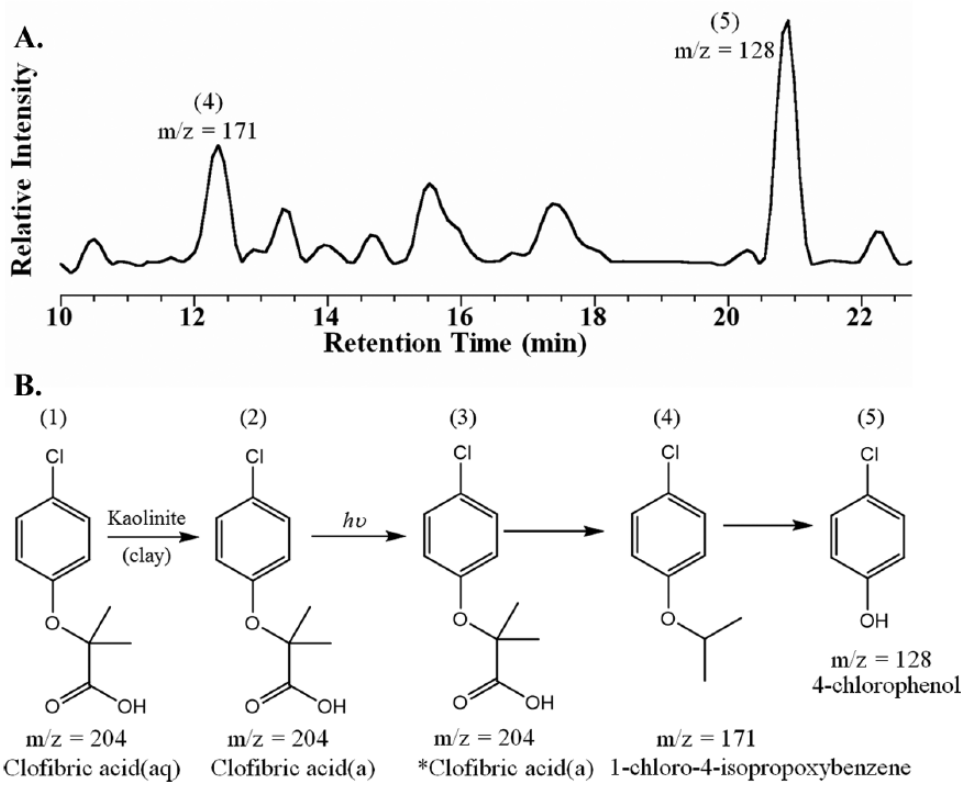


Figure 2. (A) LC-MS (liquid chromatography coupled with mass spectroscopy) analysis of degradation products of clofibric acid from abiotic degradation in the presence of kaolinite on irradiation. Given are *m/z* values of the 2 major degradation products. (B) One possible reaction pathway for the abiotic degradation of clofibric acid in the presence of kaolinite and sunlight.

remains very poor.[13] In our previous work, we evaluated the toxic effects of primary PPCPs and their degradation compounds on several microbial species, including gram-positive and gram-negative bacterial species and algal species.[1] There we reported that 4-acetylbenzoic acid, the major degradation product of ibuprofen, showed a significant inhibition on the growth of micro-green algae, *Chlorella vulgaris*.[1] Furthermore, 4-chlorophenol, the primary degradation product of clofibric acid, has been previously reported to be a highly toxic compound for various organisms including humans.[14] Nonetheless, more comprehensive toxicologic studies are needed to ascertain potential health hazards of these—and other—degradation products.

Conclusions

Our studies demonstrate that PPCPs significantly degrade via abiotic pathways, especially in the presence of clay particles and solar radiation, to generate secondary residues with different toxic effects. However, several limits need to be considered when studying the degradation of PPCPs. The laboratory studies we reported here are isolated experiments that only focus on a single PPCP component at a time. Surface waters have a variety of active compounds that are also undergoing degradation through reactions catalyzed by UV exposure and on the same soil particles. In addition to the photochemical reactions that are occurring in surface water, some reactions are occurring at the biological level as well as between the cocktail of secondary residues found in the same medium. Our current studies aim to help elucidate the possible chemistry of these degradative pathways as well as the toxicologic potential of the most abundant PPCP secondary species.

Author Contributions

GR devised the project, the main conceptual ideas and directed the experimental work. HR and AC performed the degradation studies. SM, RG, and SA carried out the toxicological assays under the supervision of SR and MP. SM and GR wrote the paper with input from all authors.

ORCID iD

Gayan Rubasinghege https://orcid.org/0000-0002-2089-6807

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