Sorption, Photodegradation, and Chemical Transformation of Naproxen and Ibuprofen in Soils and Water

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Abstract

Pharmaceutically active compounds (PhACs) are released into the environment where they undergo soil sorption, photodegradation, and chemical transformation into structurally similar compounds. Here we report on studies of naproxen (NAP) and ibuprofen (IBP), two widely-used nonsteroidal anti-inflammatory drugs (NSAIDS), in soils and water. Organic matter (OM) was observed to play an important role in each of these processes. Sorption was observed to be stronger and nonlinear in higher OM soils while weaker but still significant in lower OM, higher clay soils; the amphiphilic nature of these two PhACs combined with the complex charged and nonpolar surfaces available in the soil was observed to control the sorption behavior. Simulated solar photodegradation rates of NAP and IBP in water were observed to change in the presence of humic acid or fulvic acid. Structural analogs of each compound were observed as the result of chemical transformation in both photoexposed aqueous solutions and non-photoexposed soil. Two of these transformation products were detected as both soil and photo transformation products for both PhACs. OM was observed to influence the chemical transformation of both pharmaceuticals.

40 Graphical Abstract:

41
42 Capsule:

43 Organic matter present in water and soil played a critical role in sorption, photodegradation, and
44 chemical transformation of ibuprofen and naproxen.

1. INTRODUCTION

The twentieth century saw tremendous growth in the development, availability, and use of pharmaceuticals to treat disease. As a result, trace levels of pharmaceutically active compounds (PhACs) are currently found in municipal drinking water and natural streams around the world (Barnes et al., 2008; Benotti et al., 2008; Cunningham, 2008; Focazio et al., 2008; Jelić et al., 2012; Kolpin et al., 2002; Lapworth et al., 2012; Li, 2014). PhACs enter natural water systems after passing through wastewater treatment plants that have proven to be relatively inefficient at removing them (Cunningham, 2008; Khetan and Collins, 2007; Li, 2014; Snyder et al., 2003; Ternes et al., 2004). Measured concentrations of PhACs in natural waters are typically well below medical dosage levels, but studies of ecosystem risk have indicated adverse effects to both aquatic and non-aquatic organisms (Daughton and Ternes, 1999; Halling-Sorenson et al., 1998; Khetan and Collins, 2007).

Because of their continuous use and release from wastewater treatment plants, PhACs are considered to be pseudo-persistent contaminants (Daughton and Ternes, 1999). Once entering the environment, they can persist either in their original form or as structurally similar transformation products (Daughton and Ternes, 1999; Snyder et al., 2003). Two of the predominant processes that determine the environmental fate of PhACs are (1) sorption to soils and sediments and (2) photodegradation in aquatic environments. Both can result in the formation of PhAC transformation products.

Soils and sediments are the ultimate repository for PhACs discharged into the environment. The binding of PhACs to natural soils and sediment has been the subject of recent reports (Löffler et al., 2005; Matamoros and Bayona, 2006; Thiele-Bruhn, 2003; Tolls, 2001; Yamamoto et al.,

2009). The chemical structure of the PhAC, the texture of the soil, and the presence of reactive groups in the soils such as organic matter and mineral oxide surfaces are critical in influencing the binding of PhACs to soils (Loffler et al., 2005). Other factors such as soil exchange capacity and soil solution pH are also important (Schwarzenbach et al., 2003). Previous studies have looked at sorption of ibuprofen and reported lower soil sorption coefficients for this acidic PhAC (Loffler et al., 2005) especially as compared to basic PhACs (Yamamoto et al., 2009). There is evidence that PhACs can be attenuated during transport by soil materials into groundwater from surface water (Bradley et al., 2014). Degradation occurring in the soil environment has been observed to result in PhAC transformation products due to chemical transformations of the parent compound (Dodgen et al., 2014; Li et al., 2014).

Sunlight exposure often leads to the photodegradation of PhACs present in surface waters via both direct and indirect processes. Direct photodegradation occurs when the UV absorption spectrum of the PhAC (at environmentally relevant pH levels) overlaps with the solar spectrum (>290 nm). Indirect photodegradation can occur in natural waters when dissolved organic matter absorbs sunlight, producing reactive oxygen species (including singlet oxygen, the superoxide ion, and hydroxyl radicals) and/or is excited to the triplet state, $^3\text{DOM}^*$, which can then transfer energy to the PhAC via triplet-triplet energy transfer (TTET) (Cooper et al., 1989; Guerard et al., 2009). At the same time, DOM can inhibit photoexposure (Boreen et al., 2004; Walse et al., 2004) via sunlight filtration as well as by quenching photochemical reactions. Sunlight exposure has been found to result in PhAC transformation products including those that are more persistent and more ecotoxic (Fatta-Kassinos et al., 2011).

Naproxen and ibuprofen (NAP and IBP, Fig. 1) are two drugs widely used for treatment of pain and inflammation. Studies have shown that after human use, 72% of the excreted NAP (Runkel

et al., 1972) is present as either the original or a conjugated form (which is easily cleaved in water to release the original pharmaceutical). IBP is more extensively metabolized; studies indicate that 15% (Food and Drug Administration, 2007) of excreted IBP is in the free or conjugated form. Both PhACs have been detected globally in water samples, including sewage treatment plant (STP) influent at 3.2 ppb NAP (Yu et al., 2006) and 7.1 ppb IBP (Pal et al., 2010), and in German rivers (Ternes, 1998) at up to 0.39 ppb NAP and 0.53 ppb IBP.

NAP and IBP are both amphiphilic molecules with aromatic (nonpolar) and carboxylic acid (polar/anionic, pH-dependent) functional groups (Fig. 1). The log octanol-water partitioning coefficients (log K_{ow}) for NAP (3.2) and IBP (3.6) indicate that both are somewhat hydrophobic. Both PhACs also have a carboxylic acid group that is deprotonated at environmentally-relevant

pH levels (5-8) and so are primarily in anionic, conjugate base forms in the aquatic and soil environments. The log D_{OW} values (NAP, 1.7; IBP, 2.2) take this pH-dependent ionization into consideration and indicate that while the deprotonated forms of NAP and IBP are less hydrophobic than their neutral forms, they still maintain some of their nonpolar character. This amphiphilic nature suggests potentially complex interactions between NAP and IBP with natural sorption surfaces, including SOM, mineral surfaces, and in tissues of aquatic organisms.

In this study we investigated the soil sorption, solar photodegradation, and chemical transformation of NAP and IBP as part of an assessment of the environmental fate of these PhACs. Organic matter was observed to affect each of these processes. Sorption studies were conducted in soil samples with different OM and clay mineral contents. Based on previous studies, we hypothesized that NAP and IBP would preferentially sorb to organic-rich soils because of their nonpolar moieties. Photodegradation of NAP and IBP, such as that which would occur in surface waters, was investigated with and without the addition of Suwanee River Humic Acid (SRHA) and Fulvic Acid (SRFA); we hypothesized that these reactive fractions of DOM would aid in the photodegradation of IBP, which does not directly absorb sunlight, but would reduce the rate of photodegradation of NAP, which does. NAP and IBP were monitored in all solutions by high performance liquid chromatography (HPLC); transformation products were detected and identified by liquid chromatography with tandem mass spectrometry (LC-MS/MS).

2. MATERIALS AND METHODS

2.1 Soil Materials:

Sorption studies were performed on clean soils collected from Francis Marion National Forest, a US Forest Service-managed pristine forested watershed near Charleston, SC, USA. A- and B-horizon soils were collected from areas with no apparent sources of anthropogenic contamination. In all cases, the A-horizon soils were collected from near-surface to a depth of approximately 15 cm below ground surface (b.g.s.). The B-horizon soils were collected from a depth of 25-40 cm b.g.s. A- and B-horizon soils used in all experiments were collected at the same location for each soil series sampled at this site. These soils were air-dried for 24 h in a laboratory at 21°C and 60% relative humidity. After 24 h, large clods were gently broken into smaller pieces by hand and roots and rock fragments were removed. Finally, the soil samples were homogenized, stored in plastic bags, and sealed in air-tight plastic containers pending further use.

2.2 Soil Characterization:

Each soil was characterized for organic matter content (OM) by a thermal oxidation method (Swift, 1996), particle size fractionation using both sieving and a particle size analyzer (Gee and Or, 2002), and soil pH in de-ionized water or 10 mM CaCl₂ solutions (Thomas, 1996). Predominant minerals that made up the clay-sized fractions of the soils were determined using reflectance spectroscopy (Biehl and Stoner, 1985; Clark, 1999; White and Roth, 1986) and a spectroradiometer (LabSpec benchtop analyzer, ASD, Boulder, CO). Dried (105 °C, 24 h) and hydrogen peroxide treated (for OM removal) clay-sized fractions (< 63 µm) of all soil samples

were measured for reflectance in the near-infrared range (0.7-2.5 μm). The measured spectra was matched with USGS Digital Spectral Library (Clark et al., 2003) using ENVI software environment (Excelis, Inc., Boulder, CO) to make qualitative assessments of predominant minerals present in the soils.

2.3 Sorption Studies:

The reactivity of NAP and IBP (Sigma Aldrich, St. Louis, MO) in different soils was assessed using batch sorption experiments. In these experiments, a known concentration of NAP or IBP was spiked into a pre-cleaned PyrexTM media storage bottle containing 0.5-10 g of soil and 50-500 mL of 10 mM CaCl_2 solution prepared in deionized water. The soil:solution ratio (ranging from 1:5 to 1:1000) was adjusted based on expected strength of sorption (e.g., lower soil:solution ratio was used when sorption was expected to be strong and vice versa). This method allowed the final equilibrium concentration of NAP or IBP to be within 20-80% of initial concentration applied to the soil solution (Vulava et al., 2000). The pH levels of both initial and final solutions were measured. Sample blanks were also run in a setup identical to the batch sorption experiments, but with no soil included in the batch reactor. Batch reactor experiments using high-OM soils were also performed in a dark box to exclude ambient indoor light.

The bottles were shaken in a reciprocating shaker for 7 d in the dark to ensure equilibrium between soil and PhACs. This equilibration time was determined from initial kinetic sorption experiments in which a constant concentration (10 or 20 mg/L) of PhAC solution (100 mL) was applied to several bottles containing 10 g of soil; bottles were removed for sampling at specified time intervals (2 h to 14 d). To separate soil from the bulk solution, the samples were filtered using 0.45 μm MilliporeTM MillexTM PES syringe filters (recovery > 98%). The filtrate was

analyzed for the PhAC and any transformation products using HPLC as described in a following section.

2.4 Photoexposure Studies:

PhAC solutions of 500 ppb, 50 ppb or 5 ppb of NAP and IBP, with and without the addition of 10 or 25 ppm Suwannee River Fulvic Acid Standard II (SRFA) or Humic Acid Standard II (SRHA) (IHSS, St. Paul MN) were prepared for photoexposure studies. All solutions were prepared in 5 mM phosphate buffer solution ($\text{pH} = 7.0$) in distilled water and sonicated to ensure full dissolution before photoexposure. Solutions were stored in the dark in amber glass bottles at 5 °C until photoexposure. Control samples were stored in the dark at ambient room temperature.

Photoexposure was carried out using a solar simulator photoreactor (LuzChem SolSim, Ottawa, Ontario, Canada) at 400,000 Lux, calibrated to match the standard AM1.5 spectrum, with diffuser table. Solutions were contained in quartz vials (3.5 mL) with PTFE-lined septa (NSG Precision Cells Inc., Farmingdale, NY) during photoexposure. Vials were tightly capped to prevent the release of volatile phototransformation (PT) products. At predetermined time points, aliquots of each aqueous solution (0.3 mL) were transferred via 0.5 mL glass syringes (Hamilton, Reno NV) into individual amber glass HPLC vials for HPLC analysis in the following manner: the syringe pierced the septum on the quartz vial, an 0.3 mL aliquot was withdrawn, and then the syringe pierced the septum on the HPLC vial to avoid sample contact with open air and the potential loss of PT products due to volatilization. Each sample was prepared in triplicate to ensure reproducibility. Temperature change during photoexposure was observed to be negligible.

2.5 HPLC Analysis:

HPLC analysis was carried out on an Agilent LC 1200 with diode array detection. Separation was achieved with a C8 column (Agilent Eclipse Plus, 4.6×150 mm, 3.5 µm particle size) using the following 1.0 mL/min mobile phase gradient: t = 0-1 min, 55% buffer (20 mM formic acid, pH = 3.0): 45% acetonitrile; t = 1-4 min, gradient to 20% buffer: 80% acetonitrile; t = 4-8 min, isocratic hold at 20% buffer:80% acetonitrile. The column was held at ambient temperature and allowed to re-equilibrate for 2 min between injections; an injection volume of 100 µL was used. With these conditions, limits of detection of ~1 pbb for NAP and ~10 ppb IBP (both at 230 nm) were achieved. Four wavelengths were monitored to ensure detection of all major transformation products: 214 nm, 230 nm, 254 nm and 280 nm. The transformation products were preliminarily identified by comparison of retention times and UV absorbance spectra with standard solutions (1-(6-methoxy-2-naphthyl)ethanol, 2-acetyl-6-methoxynaphthalene, and 4-isobutylacetophenone, Alfa Aesar, Ward Hill, MA), followed by confirmation with atmospheric pressure chemical ionization – liquid chromatography – mass spectrometry (APCI-LC-MS/MS).

2.6 APCI-LC-MS/MS Analysis:

Confirmation of the identities of NAP and IBP transformation products was carried out using a Velos Pro LC-MS (Thermo Scientific) system with a heated atmospheric pressure chemical ionization (APCI) source. The isocratic LC method included a C8 column (Agilent Eclipse Plus, 4.6×150 mm, 3.5 µm particle size) with a mobile phase of 60% aqueous 0.1% formic acid and 40% acetonitrile with 0.1% formic acid, mobile phase flow rate 1.0 mL/min, and an injection volume of 1 µL.

APCI parameters included source heater/vaporizer temperature of 350 °C, sheath gas flow rate of 60 (arb units), auxiliary gas flow rate of 20 (arb units), sweep gas flow rate of 5 (arb units), discharge current of 5.00 μ A, and capillary temperature of 200 °C. Other settings for the ion trap and APCI were optimized using LTQ Tune software.

The MS/MS analysis was carried out at a normalized collision energy of 35% and $Q=0.250$. MS/MS data of soil and photoexposed samples was compared to that of standard materials.

3. RESULTS AND DISCUSSION

3.1 Soil Sorption:

The soils characterized in this study had disparate properties: OM content 0.4% to 9% ($f_{OC} = 0.004-0.9$), clay mineral content 6-20%, and soil pH 4.5-6.5. The clay mineral composition was primarily kaolinite (up to 85%) and smectite (up to 15%) with a small amount ($<0.5\%$) of Fe-oxides, primarily hematite with some goethite. In all cases, the A-horizon soils had higher f_{OC} and lower clay content than the B-horizon soils. Recent studies have shown the organic matter is comprised of diverse collections of humic substances and could be extremely variable within the same soil (Sutton and Sposito, 2005). The structure of the OM in these soils was not characterized. It was expected that the complex humic and fulvic acid fractions of the soil OM would be the most chemically reactive due to the presence of numerous carboxylic acid, amine, and alcohol functional groups within the aromatic fractions (Oades, 1989; Schwarzenbach et al., 2003). During sorption experiments, soil solution pH remained constant and approximately the same as the soil pH (± 0.5) in this study.

Both compounds sorbed more strongly to A-horizon soils than to the B-horizon soils. The sorption isotherms (plot of PhAC in solution, c_i mg/L vs. PhAC sorbed, q_i mg/kg, Fig. 2) indicated a linear relationship in B-horizon soils, while a non-linear relationship was observed in A-horizon soils due to stronger sorption at lower PhAC concentrations and weaker sorption at higher concentrations (Fig. 2). However, in all cases, sorption was five to ten times stronger in A-horizon soils as compared to that in B-horizon soils, indicating that SOM played a significant role in binding both NAP and IBP to soil components. At the soil solution pH, the deprotonated carboxylic acid functional group (Fig. 1) of both PhACs likely adsorbed to charged portions (protonated amines) of the SOM as well as to some amphoteric mineral oxide surfaces (e.g., Fe-, Al-oxides) present in the soils (Kleber et al., 2007; Schwarzenbach et al., 2003). Sorption in B-

horizon soils indicated that other mineral components play an important in sorption of NAP and IBP (Stumm and Morgan, 1996). The deprotonated forms of NAP and IBP likely bonded with the charged inorganic surfaces via simple electrostatic attraction or the stronger chemisorption (Schwarzenbach et al., 2003). The soil solution pH also played a very important role in influencing the charge on various soil components. At pH 5 ± 0.2 , the predominantly deprotonated NAP and IBP sorbed more strongly to the amphoteric Fe oxide surfaces than to the permanent negatively charged clay mineral surfaces (Chiou, 2003; Figueroa and MacKay, 2005; Zhang and Huang, 2007); the positive charge on these Fe oxides would have offered simple ligand exchange sites for NAP and IBP under these conditions (Gu et al., 1994; Gu and Karthikeyan, 2005).

The sorption isotherms did not exhibit sorption maxima, indicating that sorption sites were not saturated at the concentrations studied. The Freundlich isotherm model ($q_i = K_f c_i^n$, where K_f is the Freundlich constant and n is the Freundlich exponent) strongly fit the sorption isotherms ($R^2 > 0.90$). K_f was higher for both compounds in A-horizon soils than in B-horizon soils (data not shown); $n < 1$ in all A-horizon soils and $n \cong 1$ in all B-horizon soils. When $n < 1$, the isotherm concaved downwards, indicating that as sorbate concentrations increased, the sorbates were bound to the soil components with weaker free energies. This behavior is commonly observed in sorption of polar organic solutes on charged surfaces (Chiou, 2003). When $n = 1$, the isotherm was linear, indicating constant sorption free energies at all sorbate concentrations (Schwarzenbach et al., 2003). Such isotherms are common when sorption involves either uncharged sorbent surfaces or nonpolar organic compounds. Since both NAP and IBP were primarily anionic at the soil solution pH, their n values were more likely a reflection of the nature of a sorbent that was low in OM and high in clay mineral and Fe oxide content. The solid-water distribution coefficient $K_d (= q_i/c_i)$, calculated from the sorption isotherms data, decreased with

increasing concentration in all A-horizon soils and was nearly constant in the B-horizon soils, confirming the trends observed in the sorption isotherms. There were weak but positive linear correlations between K_d and f_{OC} and K_f and f_{OC} , indicating that both compounds preferentially partitioned to soils with larger SOM content.

3.2 Transformation products formed during soil sorption studies:

During batch sorption experiments in A-horizon soils ($f_{OC} = 0.09$), small amounts of NAP and IBP transformation products were observed (NAP-T2 and IBP-T1, Fig. 3) which were identified by APCI-LC-MS/MS (S1). NAP-T2 (2-acetyl-6-methoxynaphthalene) is the decarboxylated ketone analog of NAP while IBP-T1 (4-isobutylacetophenone) is the same analog of IBP. These transformation products were observed at significantly lower concentrations than the parent compound – approximately 10^5 and 10^4 times lower than concentrations for NAP and IBP, respectively, too low to impact sorption of the parent compounds – and were directly correlated

with the equilibrium solution concentrations of the parent PhACs (Fig. 4). Transformation products previously observed as the result of biodegradation of naproxen (Quintana et al., 2005; Wojcieszynska et al., 2014) and ibuprofen (Matamoros et al., 2008) were not observed in this study. IBP-T1 and NAP-T2 have been observed in other phototransformation studies (DellaGreca et al., 2003; Jacobs et al., 2011; Marotta et al., 2013; Ruggeri et al., 2013). Toxicity studies have shown these compounds, both aromatic ketones, to be more ecotoxic than the parent PhACs (DellaGreca et al., 2003; Ruggeri et al., 2013), raising concerns about their production during environmental processes.

3.3 Photodegradation:

283 When exposed to simulated sunlight, naproxen (5 ppb) underwent relatively rapid direct solar
284 photodegradation following a pseudo-first order rate law (half-life, $t_{1/2} = 53$ min). Ibuprofen (50
285 ppb) was observed to photodegrade much more slowly, also following pseudo-first order kinetics
286 ($t_{1/2} = 44$ h). Both results were expected; NAP's absorption spectrum overlaps with the solar
287 spectrum ($>290\text{nm}$), promoting direct photodegradation, while IBP's spectrum does not overlap
288 (Fig. 5).

289

290 The addition of both SRFA and SRHA to NAP in aqueous solution ($\text{pH}=7.0$) resulted in an
291 overall decrease NAP's rate of photodegradation (Fig. 5). The addition of 10 ppm SRFA led to
292 an even slower rate ($t_{1/2} = 4$ h) than the addition of 25 ppm SRFA ($t_{1/2} = 2$ h), indicating the

possible occurrence of competing photosensitization and photo inhibition. In the case of SRHA, the addition of both 10 ppm and 25 ppm both resulted in the same, slower rate ($t_{1/2} = 4$ h). The degradation in dark control samples of each solution was observed to be negligible over this time frame.

Additions of SRFA and SRHA to IBP solutions were observed to increase the photodegradation rate by one to three times over that of buffered IBP alone, indicating that DOM acted primarily as a photosensitizer and promoted indirect photodegradation (Fig. 6). A smaller concentration of SRHA (10 ppm) resulted in a higher rate of photodegradation ($t_{1/2} = 15$ h) than the higher 25 ppm ($t_{1/2} = 20$ h) indicating the possibility of competing photosensitization and photo inhibition with more concentrated SRHA. The rates for both 10 ppm and 25 ppm SRFA were equal to each other

and similar to the SRHA values ($t_{1/2} = 17$ h). The degradation in dark control samples of each solution was again observed to be negligible over this time frame.

3.4 Transformation products formed during photoexposure studies

Photodegradation of NAP was observed to produce two transformation products, the decarboxylated alcohol analog 1-(6-methoxy-2-naphthyl) ethanol (NAP-T1) and the ketone analog (NAP-T2) (Fig. 3). Both compounds have been reported to form during photoexposure as a result of the decarboxylation of NAP followed by the formation of a radical, oxidation to NAP-T1, and further oxidation to NAP-T2 (Musa and Eriksson, 2008).

A solution containing 50 ppb NAP with 10 ppm SRHA was also photoexposed under the same conditions (ten times higher than the concentration exposed in Fig. 6, higher concentration was required to quantify the transformation products). In this solution, NAP's half-life was observed to be 5 h, the same as that observed for 5 ppb NAP with 10 ppm SRHA. After 5 h of photoexposure, the concentration of NAP-T1 formed was 4 ppb, or 8% of the original NAP concentration, while the amount of NAP-T2 product formed was also 4 ppb (8%), resulting in a total 16% conversion of NAP to transformation products at the half life.

After up to 90 h of photoexposure, only one transformation product was observed for IBP (IBP-T1, Fig. 3). This photochemical transformation of IBP has been reported to proceed through the decarboxylation of IBP followed by the formation of a radical (Musa and Eriksson, 2007) and subsequent oxidation. IBP-T1 is comparable to NAP-T2, as both are aromatic ketone analogs of the parent PhAC. We did not observe the alcohol analog for IBP that is comparable to NAP-T2. This was expected, as the isobutyl group on IBP is a much weaker electron donor than the ether

linkage on NAP, causing the alcohol analog of IBP to be less stable than the NAP alcohol analog.

A solution containing 500 ppb IBP (ten times higher than the concentration exposed in Figure 6) with 10 ppm SRHA was also photoexposed under the same conditions in order to quantify the trace production of IBP-T1. At this concentration, IBP was observed to photodegrade at the same rate as 50 ppb IBP with 10 ppm SRHA ($t_{1/2} = 15$ h). After 15 h of photoexposure, the concentration of IBP-T1 formed was 11 ppb, or 2% of the original IBP concentration. IBP-T1 directly absorbs sunlight and is therefore susceptible to direct photodegradation, unlike IBP. However, IBP-T1 is structurally stable and has been observed by others in field samples. One study determined that levels of up to 40 ng/L of this compound were present in sewage waters in Sweden (Zorita et al., 2007) and 197 ng/L in the influent of a wastewater treatment plant (Manso et al., 2014), indicating that it is indeed being formed and persisting in natural waters and therefore potentially impacting the aquatic environment. As an aromatic ketone, this raises concerns about ecotoxic risk.

3.5 Correlation between transformation products formed in soil and photoexposed aqueous samples

While the transformation products observed here have been previously reported as phototransformation (PT) products, in this study two of them (NAP-T2 and IBP-T1) were also observed to be soil transformation (ST) products. The identity of each transformation product was confirmed by comparison to standards using APCI-LC-MS/MS (see Supplementary Data).

NAP and IBP were not exposed to light during soil sorption experiments and these transformation products were observed only in A-horizon soils, those containing OM, but not in B-horizon soils, which do not. The transformation process occurring in the soil is not known at this time. Biological transformation of PhACs in soil is a possibility, as the soil was not sterilized before sorption studies. However, the products of biological transformation processes are generally more polar than the parent pharmaceutical (Boxall et al., 2004). For naproxen and ibuprofen, reported biotransformation products include hydroxyl and carboxyl analogs (Matamoros et al., 2008; Wojcieszynska et al., 2014). These products were not observed in this study; the ketone and alcohol analogs observed here were less polar than the parent PhAC. Recent reports of dark hydroxyl radical formation in arctic soils (Page et al., 2013) indicate the possibility that hydroxyl radical mediated transformation could contribute to soil transformation as it does with DOM-mediated phototransformation.

These observations indicate that processes occurring in soil resulted in less polar, more ecotoxic transformation products with more similarity to phototransformation products than to those formed as a result of biological transformation. Further study is needed to determine the process that transforms NAP and IBP into these products in soil.

4. CONCLUSIONS

Organic matter, both in soil and dissolved in aqueous solution, was observed to play an important role in the sorption, photodegradation, and chemical transformation of both NAP and IBP.

Sorption of both NAP and IBP was strong in soils that had higher OM content and weaker but still significant in soils that were more clay- and Fe oxide-rich. This led to the conclusion that the

368 aromatic moieties of the compounds were strongly interacting with aromatic fractions of natural
369 OM present in soils. The permanent negative charge in clay minerals was not observed to have
370 significantly contributed to sorption of these compounds.

371 Two soil transformation products were observed, NAP-T2 and IBP-T1. These transformation
372 products were observed in A-horizon soils, which have high OM contents. The processes leading
373 to this chemical transformation of NAP and IBP in soils is not known at this time.

374 NAP and IBP both underwent photodegradation in simulated sunlight. The half-life of IBP
375 photodegradation in all solutions was longer than that of NAP, indicating that IBP is more likely
376 to be persistent in surface waters than NAP. While the addition of SRHA and SRFA had an
377 overall inhibitory effect on the rate of NAP photodegradation, the IBP degradation rate was
378 observed to increase in the presence of DOM as indirect photodegradation was promoted.

379 Two PT products for NAP and one for IBP were identified: the two ketone analogs observed in
380 soil samples were also observed in photoexposed samples, along with an alcohol analog of
381 naproxen. Higher amounts of these products were observed in photoexposed solutions than in
382 soil samples.

383 The combination of the sorption, photodegradation, and transformation results led to the
384 conclusion that OM is an important factor in the environmental fate of both NAP and IBP. More
385 studies of the processes involved in soil transformation are needed, as the products identified
386 here have been observed to have higher ecotoxicity than the parent PhACs. These combined
387 results indicate that the environmental processes occurring once these PhACs enter the
388 environment can have a notable impact on the quality of the water resources in our communities.

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