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Waterless Urinals Remove Select Pharmaceuticals from Urine by Phase Partitioning

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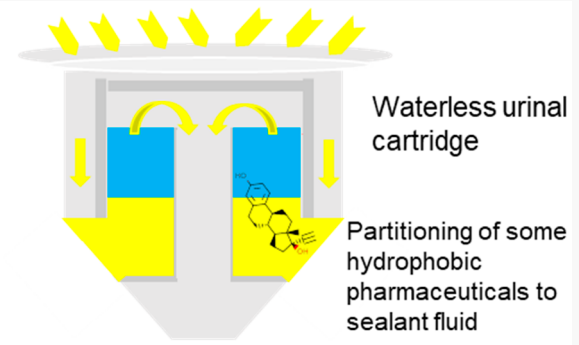
ABSTRACT: We investigated the potential for waterless urinal sealants fluids to remove pharmaceuticals from urine. ^{1}H NMR, FTIR, and GC/MS characterization of the fluids indicated that they are mostly composed of aliphatic compounds. Removal of ethinyl estradiol was >40% for two of the three sealant fluids during simulated urination to a urinal cartridge but removal of seven other compounds with greater hydrophilicity was <30%. At equilibrium with Milli-Q water, ≥ 89% partitioning to the sealant phase was observed for three compounds with pH adjusted log K_{ow} (log D_{ow}) > 3.5. At equilibrium with synthetic urine, removal ranged widely from 2% to 100%. K_{ow} was poorly correlated with removal for both matrices at equilibrium, but D_{ow} was correlated with removal from synthetic urine for two of the three sealants, indicating that ionization and hydrophilicity control partitioning between the urine and sealant phases. To improve removal during urination, where equilibrium is not achieved, we increased the hydraulic retention time 100-fold over that of typical male urination. Removal of specific hydrophobic compounds increased, indicating that both hydrophobicity and kinetics control removal. Removal of ethinyl estradiol was ≥90% for all sealants in the increased hydraulic retention time experiment, demonstrating the potential for implementation to female urinals.



1. INTRODUCTION

Domestic wastewater treatment plants are well designed to remove nutrients (i.e., nitrogen and phosphorus), organic carbon, and suspended solids, but poorly remove many pharmaceuticals.[1,2] Pharmaceuticals may persist in aquatic ecosystems, bioaccumulate, proliferate antibiotic resistance, are chronically toxic, or disrupt the endocrine system of aquatic organisms.[3−8] Further, treated wastewater and wastewater sludge is often used to irrigate and fertilize cropland, which may be human, environmental, animal, or crop toxicological threats.[9−11]

Human urine is one source of pharmaceuticals in wastewater.[12,13] Lienert et al.[2] measured 42 active pharmaceutical ingredients in urine and found that 70 ± 35% was excreted as active ingredients and metabolites. A similar study by the same authors investigated 212 pharmaceutical active ingredients and found that 64 ± 27% were excreted in urine as the parent drug and metabolites.[14] Hence, water bodies receiving treated wastewater typically contain pharmaceuticals in the range of low ng/L to several μg/L which originate in human use, incomplete metabolism, excretion into wastewater, and poor removal by wastewater treatment.[12,15−17]

Because pharmaceuticals in wastewater influents are relatively dilute and diverse in chemical structure and properties, nonselective removal or oxidation technologies have been the focus of research related to reducing effluent load. Advanced oxidation processes and activated carbon have the potential to reduce wastewater effluent pharmaceutical loads, but each has their respective trade-offs.[18,19] Activated carbon removes hydrophobic pharmaceuticals well but may be cost prohibitive considering fouling from high concentrations of wastewater organic matter. UV/advanced oxidation is energy intensive and may produce disinfection byproducts such as bromate.[20]

Urine first interacts with a toilet in many parts of the world, and urine has pharmaceutical concentrations 10^2 to 10^3 times greater than wastewater entering the treatment plant.[13] Therefore, rather than treating pharmaceuticals in a dilute wastewater influent, we propose treatment before dilution with greywater. Urine separation is one technique to reduce the pharmaceutical load in wastewater, but urine separation only diverts pharmaceuticals from the wastewater, rather than achieving removal or treatment and consequently separated urine still must be treated before release.[21] Taking advantage of waterless urinals might be one potential technique in removing pharmaceuticals from the urine.

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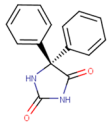
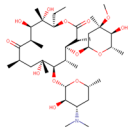
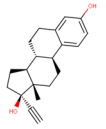
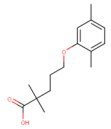
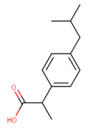
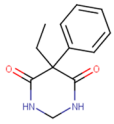
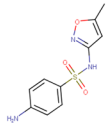
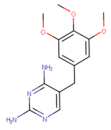
Table 1. Chemical Characteristics of Eight Pharmaceuticals Investigated

Pharmaceutical	Chemical structure	Molecular weight (Da)	pK_a[a]	Log K_{ow}[a]	Log D_{ow} at pH 6.6[a]	Max UV abs. (nm)[b]	Use
Dilantin		252	8.5	2.15	2.14	254	Anticonvulsant
Erythromycin		734	9.0	2.6	0.62	205	Antibiotic
Ethinyl estradiol		296	10.3	3.9	3.9	274	Hormone
Gemfibrozil		250	4.4	4.39	2.41	274	Lipid regulator
Ibuprofen		206	4.9	3.84	2.29	264	Anti-inflammatory
Primidone		218	11.5	1.12	1.12	264	Antiepileptic
Sulfamethoxazole		253	6.2	0.79	0.43	267	Antibacterial
Trimethoprim		290	7.2	1.28	0.53	264	Antibacterial

[a]Chemicalize.org[26] [b]Maximum UV absorbance wavelengths were determined experimentally by scanning the UV/vis range.

Waterless urinals are primarily used to conserve potable water and do not require flushing but utilize a sealant fluid that serves as a barrier to sewer gas. The sealant must be less dense than urine (float on the surface of the urine), be immiscible in urine (reduced loss to sewer and increased replacement interval), and be nonvolatile (minimal loss to room air).[22] We believe that the sealants are most likely composed of oily fluids because they are relatively inexpensive, meet the specified criteria, and are part of several related patents.[23,24] Thus, it may be expected that chemical partitioning to these sealants would be well described by partitioning in an octanol−water system because octanol contains a nonpolar carbon chain, which has similar thermodynamic properties to alkanes. Octanol−water partitioning coefficients are readily available for most pharmaceuticals, and in such systems, more hydrophobic molecules partition to the octanol phase, and more hydrophilic compounds partition to the aqueous phase. Because urine directly interacts with this fluid, and because the sealant fluids are likely to partition relatively hydrophobic compounds, we believe there may be an opportunity to reduce the environmental loading of anthropogenic pharmaceuticals using waterless urinals.

The objective of this research was to evaluate the efficacy of various commercial waterless urinal sealants for removal of pharmaceuticals from urine. Three commercial sealants and eight pharmaceuticals with log K_{ow} from 0.8 to 4.4 were selected. We characterized the sealants using proton nuclear magnetic resonance (^{1}H NMR), Fourier-transform infrared spectroscopy (FTIR), and derivatization gas chromatography−mass spectrometry (GC−MS) and investigated (i) pharmaceutical partitioning during simulated urination, (ii) partitioning in a clean system at equilibrium, and (iii) partitioning from synthetic urine at equilibrium. We followed up simulated urination experiments by attempting to increase pharmaceutical removal during urination by increasing the contact time between urine and sealant.

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Table 2. Physical and Chemical Properties of Sealants in This Study

Sealant	Brand	Manufacturer model	Color[a]	Odor[a]	Kinematic viscosity (cSt) at 25 °C	Density (g/mL)	Volatile organic carbon content[a] (g/L)
A	American Standard	6156100.020	Dark blue	none	30.5	0.907	NA
B	Blueseal	1114	Royal blue	Berry	15.5	0.834	<10
C	Zurn	ZGS-128OZ	Green	Lemon	25.6	0.906	0

[a]Provided by the manufacturers' material safety data sheets.

2. MATERIALS AND METHODS

2.1. Reagents, Pharmaceuticals, and Sealants. Artificial urine was prepared according to DIN EN 1616:1999.[25] The chemical composition was; 25.0 g/L urea ($CO(NH_2)_2$), 9.0 g/L sodium chloride (NaCl), 2.5 g/L disodium hydrogen orthophosphate anhydrous (Na_2HPO_4), 2.5 g/L potassium dihydrogen orthophosphate (KH_2PO_4), 3.0 g/L ammonium chloride (NH_4Cl), 2.0 g/L creatinine ($C_4H_7N_3O$), and 3.4 g/L anhydrous sodium sulfite (Na_2SO_3). The pH of the solution was adjusted to 6.6 ± 0.1 using 0.1 M hydrochloric acid (HCl).

Eight pharmaceuticals were selected to include a range of hydrophobicity (log K_{ow} from 0.8 to 4.4) and because they are environmentally relevant (Table 1).[8,9] Pharmaceuticals were purchased from Sigma-Aldrich (St. Louis, MO) except sulfamethoxazole, from MP Biomedicals (Solon, OH) and erythromycin from Acros Organics (Morris Plains, NJ). All pharmaceuticals were >98% purity. Individual 10 mM stock solutions were prepared in high performance liquid chromatography (HPLC) grade methanol (Fisher Chemical, Fairlawn, NJ). Other HPLC solvents were HPLC grade and from the Fisher Scientific (Lenexa, KS) and Sigma-Aldrich (St. Louis, Missouri). Stock solutions were spiked into ≥18.2 MΩ-cm water (Milli-Q) and synthetic urine that was prepared weekly at a concentration of 100 μM of each pharmaceutical. The pH of the synthetic urine (=6.6) was measured using a Thermo Fisher pH probe and meter (Waltham, MA). Marvin was used to obtain the pH and pK_a adjusted K_{ow} (log D_{ow}) for each pharmaceutical (Supporting Information, SI, Figure S1). Marvin was provided by ChemAxon under an academic use license and uses an established summation of fragments method to estimate partitioning coefficients.[26−28]

Three commercial waterless urinals sealants were examined (Table 2): American Standard (A) (Xela Innovations, Glendale, WI, U.S.A.), BlueSeal (B) (Waterless Co., Inc., Vista, CA, U.S.A.) and, Aqua Green Urinal Sealant (C) (Zurn Industries, Sanford, NC, U.S.A.).

2.2. Urine Simulation Experiments. We conducted experiments to determine partitioning between synthetic urine and waterless urinal sealants during simulated urination. We simulated human urination by passing synthetic urine spiked with pharmaceuticals through commercial waterless urinal cartridges filled with sealants. A Cole-Parmer peristaltic pump (Masterflex L/S Compact 24-VDC drive) with two pump heads (Masterflex L/S Easy-Load II) was used to pump synthetic urine from a 40 L high-density polyethylene (HDPE) carboy. Tubing size of L/S 24 (Masterflex L/S Platinum-Cured Silicon) was used to pump 420 mL of synthetic urine over 21 s to the cartridge.[29,30] Waterless urinal cartridges from Sloan (Part Number: WES-150, Franklin Park, IL) filled with 100 mL of sealant, per the cartridge manufacturer's instructions, were used. The pump was electronically started every 10 min for a total of 10 h. The effluent of the cartridge was directed to waste except every 2 h when samples were collected in 50 mL amber bottles and stored at 4 °C until analyzed. Similar experiments were conducted to determine if increased hydraulic retention time (1% of the initial simulated urine flow, 12 mL/min for 1 h) would increase removal of pharmaceuticals.

We also conducted experiments to calculate loss of sealant during simulated urination. We followed the same procedure to simulate urination as described above, but with Milli-Q water pumped to the cartridge, because it was observed during ongoing experimentation that hydraulic disturbance is the primary cause for loss rather than dissolution, and because dissolution of urine constituents into the sealant may confound measurements of the cartridge mass. We filled waterless urinals cartridges with deionized water and 100 mL of sealant according to the manufacturer's instructions. We measured the mass of the cartridge before and after 100 simulated urinations. The change in mass of the cartridge was assumed to be representative of sealant loss and replacement with Milli-Q water, and was used to calculate the loss of sealant. The density of the sealants was measured in the laboratory to calculate the loss of sealant (Table 2).

2.3. Partitioning Experiments. For equilibrium experiments, 125 mL separatory funnels were separately filled with 50 mL of one of three sealants and 50 mL of Milli-Q water spiked with 100 μM of eight pharmaceuticals. The experiment was conducted separately for individual pharmaceuticals. The mixture of sealant and pharmaceutical was vigorously shaken for 60 s and placed in a prong clamp. Two mL aliquots of the aqueous phase were collected from the bottom of the separatory funnel at 2, 6, 9, 12, 24, 48, and 72 h to determine the time to reach equilibrium. pH of each compound when mixed with Milli-Q water and pH at 24 h for each sealant/pharmaceutical pair were measured to determine the change in pH during the partitioning. The aliquots were collected in 2 mL amber autosampler vials and stored in the dark at 4 °C until analyzed. The same procedure was followed for urine partitioning experiments at equilibrium but with artificial urine rather than Milli-Q water. Conductivity of the aqueous phases was measured in the absence of pharmaceuticals after 24 h of equilibration to determine if the sealants contained high concentrations of salts. Conductivity ranged from 5.5 to 14 μs/cm, which was not expected to result in significant ion-pair partitioning effects.[31,32]

2.4. Analytical Methods. We characterized three commercially available waterless urinal sealant fluids using ^{1}H NMR, FTIR, derivatization GC/MS, and viscosity. ^{1}H NMR spectra were obtained using Varian 400-MHz NMR (Agilent-Varian, Santa Clara, CA). Sample preparation for ^{1}H NMR was based on Fang et al.[33] Briefly, in a 5 mm NMR tube, 20 μL of a sealant was dissolved in 630 μL of deuterated chloroform and 20 μL of deuterated dimethyl sulfoxide prior to analysis. IR spectra were obtained using Thermo Nicolet 6700 FT-IR (Thermo Fisher Scientific, Waltham, MA) equipped with diamond attenuated total internal reflection (ATR). The sample was directly spread onto the ATR with a pipet and the

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IR spectra was scanned in the wavelength range of 500−4000 cm^{-1} using 30 scans per sample at a resolution of 4 cm^{-1}.

GC/MS analysis was performed using an Agilent 7890A GC coupled to a 5975C quadrupole MS equipped with Agilent 7630 auto sampler (Agilent Technologies, Santa Clara, CA). Prior to injection, fatty acids were converted to their methyl esters through acid catalyzed trans-esterification in the presence of methanol and boron trifluoride.[33] Further GC/MS sample preparation and analytical methods are provided in the SI. Viscosity of the sealants were measured using a Lab-line Saybolt viscometer (Lab-line Instruments Inc. Chicago, IL) following standard method AASHTO:T72−10[34]

Pharmaceutical concentrations were analyzed with an Agilent 1260 Infinity HPLC using a method similar to Yoon et al.[35] Separations were performed on a ZORBAX Eclipse plus C_{18} column from Agilent Technologies (4.6 mm I.D, 150 mm length, and 5 μm). The mobile phase for dilantin, ethinyl estradiol, primidone, trimethoprim, and sulfamethoxazole was 45:55 v/v methanol/0.01 M phosphoric acid (H_3PO_4) in water, and the total run time was 10 min. 50:50 v/v acetonitrile/0.01 M H_3PO_4 in water was the mobile phase for gemfibrozil and ibuprofen with a run time of 25 min. Erythromycin was determined using 60:40 v/v acetonitrile:0.025 M ammonium dihydrogen phosphate ($NH_4H_2PO_4$) in water (pH of 7.0) as the mobile phase with a column temperature of 25 °C. The flow rate was 1.0 mL/min for all methods. The column was operated at 30 °C for all other methods. Wavelengths used for quantitation were based on maximum absorbance of the individual compounds measured with a ThermoFisher Scientific UV−vis (Waltham, Massachusetts) instrument set to scan from 200 to 700 nm. Maximum UV absorbance bands for each compound are provided in Table 1. An example chromatogram is shown in Figure S2. Method detection limits for the eight compounds were <1 μM based on three times the signal-to-noise ratio.

2.5. Statistical Methods. Logarithmic regressions were performed in Microsoft Excel. Spearman rank correlations were conducted in R using the cor.test function.[36] ANOVA followed by posthoc Tukey's Honest Significance Tests were performed in R to compare the difference between the means of simulated urination experiments.[36] The level of significance was set to $\alpha < 0.05$.

3. RESULTS AND DISCUSSION

3.1. Sealant Characterization. We initially used ^{1}H NMR to characterize three waterless urinal sealants and identify primary chemical components that may interact with pharmaceuticals. For two sealant fluids (sealants A and C) we observed strong signals at 2.02 and 5.29 ppm, and at 4.19 and 5.15 ppm, which are consistent with saturated and unsaturated fatty acids, and triacylglycerols, respectively (Figure S3A). Fatty acids and their glycerol esters are the primary component of vegetable oil, and the spectra matched well with published spectra of vegetable oil.[37−39] For sealant B, signals at 1.2 and 0.85 ppm were observed, consistent with alkane groups (Figure S3B).[37] We did not observe fatty acids or glycerol ester components for sealant B. The spectra matched well with the published spectra of mineral oil.[40] The spectra and assignment of peaks are shown in Table S1. Detailed resonance assignments are provided in Table S1. We preliminarily concluded that sealants A and C were composed primarily of vegetable oil and sealant B was primarily composed of mineral oil and we attempted to confirm using FTIR and derivitization GC/MS.

With FTIR, we observed strong signals at 1743, 1168, and 1090 cm^{-1} in the spectra of sealants A and C. Again, the spectra is representative of fatty acid esters (Figure 1).[41] We

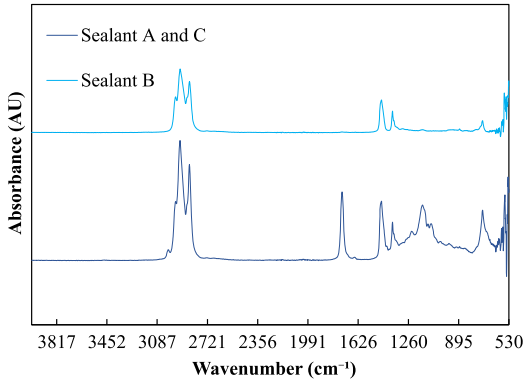

Figure 1. FTIR spectra of sealants A, B, and C. Spectra for A and C are offset for clarity.

did not observe representative signals of fatty acids or triacylglycerols in the spectra for sealant B (Figure 1). However the instrument library (Thermo Scientific OMNIC Spectra) identified that sealant B's spectra matched well with mineral oil (87 match score), and that sealant A and C's spectra matched linoleic acid (i.e., free fatty acids present in vegetable oil, ≥ 70 match score).

We then attempted to derivatize the fatty acids present in the sealants to make them amenable to GC/MS analysis. We observed the same chromatographic peaks for sealants A and C and NIST spectral library matches indicated that the two primary peaks were likely to be octadecanoic and tridecanoic acids. The primary peak had principal mass fragments of 55 and 59 m/z (Figure S4A,C) with the former fragment likely representing $C_4H_7^+$ (alkene fragment) and the latter, H_3COOC^+ (methyl ester fragment). The other chromatographic peak had mass fragments of 74 and 87 m/z (Figure S4A,C), with 74 m/z likely representing McLafferty rearrangement of the ester[42] and the 87 m/z representing $H_3COOCCH_2CH_2^+$. No discernible chromatographic peaks were observed for sealant B after derivatization (Figure SI4B), agreeing with the conclusion that sealant B does not contain groups that terminate in a carboxylic acid and thus cannot be trans-esterified (i.e., mineral oil or another higher alkane).

Other bulk properties of the sealants are shown in Table 2. Notably, the kinematic viscosity and specific gravity of the fluids further support the hypothesis that the fluids are primarily composed of naturally occurring oils that have been processed to provide the relatively pure products—likely vegetable oil (sealants A and C) and mineral oil (sealant B).

3.2. Partitioning of Pharmaceuticals to Commercially Available Waterless Urinal Sealant Fluids during Simulated Urination. Because the characteristics of the sealants closely match what is required to partition hydrophobic functional groups from water, we believed the sealants may incidentally remove some pharmaceuticals and conducted experiments to determine if sealant fluids removed pharmaceuticals under simulated urination conditions. We simulated partitioning of pharmaceuticals to in-use waterless urinal sealants by simulating urination with a peristaltic pump,

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which pumped synthetic urine[25] spiked with 100 μM of eight pharmaceuticals into a commercially available waterless urinal cartridge filled with 100 mL of three separate sealants. Although 100 μM is likely to be greater concentration than would be observed in human urine, this concentration was chosen to facilitate HPLC quantitation. Further, the percent removal in partitioning experiments is generally independent of the initial concentration and was assumed to be so here. We tested only a single urinal cartridge because we purchased two from separate manufacturers which were similar in flow design, volume of sealant contained, and likely contact duration between urine and sealant. We simulated a high-use urinal by pumping urine every 10 min and collected samples of the aqueous effluent of the cartridge. Between simulated urinations, the urine from the previous cycle was in contact with the sealant for 10 min, although only at the relatively small sealant/urine interfacial area.

Removal was unchanged over five sets of samples that were collected over 10 h, indicating that the sealant was not saturated with pharmaceuticals during 60 simulated urinations. Due to the observed variability in some replicates during the 10 h sampling period (likely due to unstable flow conditions inside the cartridge), we collected most samples in replicates of five at the final sampling time of 10 h in an attempt to reduce experimental error. Additionally, there was a strong chromatographic interference from sealant fluid carryover for erythromycin, likely due to the high flow rate of simulated urination, which caused us to remove it from these results. Pharmaceutical removal from the urine after 10 h of intermittent simulated urination is shown in Figure 2. Removal

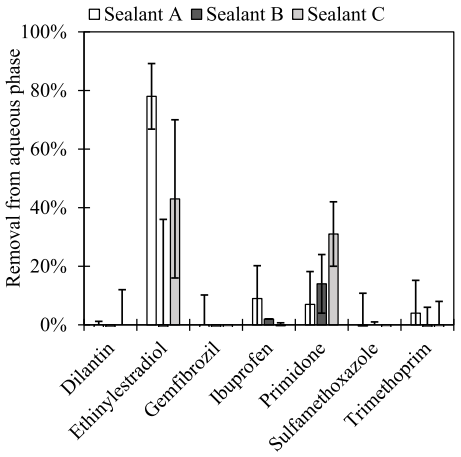

Figure 2. Pharmaceutical removal during simulated urination to a waterless urinal cartridge containing three separate sealant fluids. Error bars indicate the standard deviation of five samples from the same experiment.

ranged from 0% to 78%, and ethinyl estradiol was removed to the greatest extent of the seven pharmaceuticals (>40% by two sealant fluids). Removal of ibuprofen and trimethoprim was <10% and primidone was <32% for the three sealant fluids. Dilantin, gemfibrozil, and sulfamethoxazole were not removed to a measurable extent.

We expected removal to be well represented by octanol–water partitioning coefficients because octanol contains a nonpolar carbon chain which is similar in structure and thermodynamic properties to the sealants (i.e., we expected compounds with greater D_{ow} would be removed to a greater extent by the sealants) and because these partitioning coefficients are readily available for all pharmaceuticals. Notably, the compound with the greatest log D_{ow}, ethinyl estradiol (=3.9), was removed to the greatest extent by sealant A and C, as was expected. However, logarithmic regressions between removal and log D_{ow} were generally not good representations of the data (R^2 = 0.12 to 0.25). We attribute this to the short residence time in the cartridge (<10 s) and low interfacial surface area, where the stream of urine likely flows through the cartridge as a stream, rather than as high surface area droplets, and to the large urine volume to sealant volume ratio, which precludes significant contact with the sealant. Sealant B removed little or none of the compounds tested, which may be because it is less polar than vegetable oil (sealants A and C contain ester groups not present in sealant B), which may have further decreased the miscibility of the sealant and the water, causing a further decrease in interfacial surface area.

During simulated urination, droplets of sealant of approximately 1 mm were observed from the outlet of the waterless urinal cartridge. An additional experiment was conducted to measure loss of sealant, and the loss of sealant was between 2.5 and 3.2 mL/100 urination events for two of the sealants. Loss of sealant during the urination indicates that some pharmaceutical mass is lost to the sewer, dissolved in fine droplets of sealant. However, the capacity of pharmaceuticals in the sealant fluid is likely limited only by attractive forces between the solvent and solute, which are unchanged at low concentrations of solute. Therefore, combined with the finding that removal was unchanged over 60 urinations, the removal of pharmaceuticals which are well retained by the sealant fluid from the waste stream is limited the greatest by the replacement rate.

3.3. Pharmaceutical Partitioning at Equilibrium. To further explore the mechanisms that control partitioning we conducted two equilibrium experiments. First, we measured partitioning between a clean matrix (i.e., Milli-Q water) and the sealants, followed by an experiment to determine if urine constituents and pH impact partitioning due to protonation/deprotonation of the pharmaceuticals. Pharmaceuticals were spiked into Milli-Q water or synthetic urine and agitated with the urinal sealant fluids. For both matrices, equilibrium was achieved for all compounds in less than 12 h based on no further concentration change in the aqueous phase at later sampling points. Data shown and discussed were at equilibrium, having been sampled at 72 h.

For the clean matrix, partitioning of eight pharmaceuticals from Milli-Q water to the sealant phase ranged from 0 to 100% (Figure 3). Ethinyl estradiol, gemfibrozil, and ibuprofen were removed to the greatest extent, with removal of >89% for all sealants. Trimethoprim was removed poorly (<10%). Sealant A and C generally removed pharmaceuticals similarly, while sealant B again appeared to interact contrarily, with 100% removal of primidone, compared to no removal for sealants A and C. We also observed a chromatographic interference for dilantin, likely from partitioning of coloring agents in sealant B, which was not observed for the other sealants.

Initially we generated logarithmic regressions between log K_{ow} and removal for each sealant, which resulted in weak regression coefficients (R^2 = 0.11 to 0.40). However, we observed changes in the pH of Milli-Q water measured at 24 h (Table S3). Because the sealant dominated buffering of the Milli-Q water (i.e., pH with pharmaceutical within ~1 pH unit

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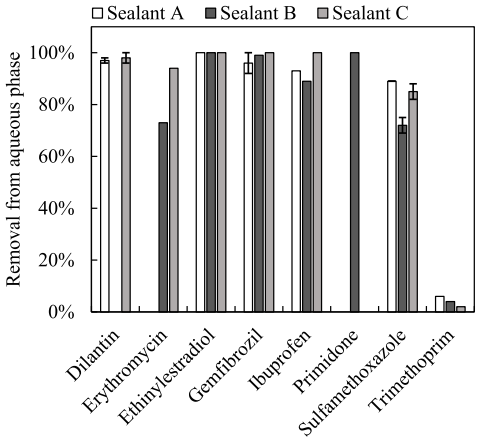

Figure 3. Equilibrium pharmaceutical phase partitioning between Milli-Q water and waterless urinal sealants. Error bars indicate the range and bars indicate the average of duplicate samples, when measured. A chromatographic interference was observed for dilantin and sealant B. No removal was observed for erythromycin and sealant A and for primidone and sealant A and C.

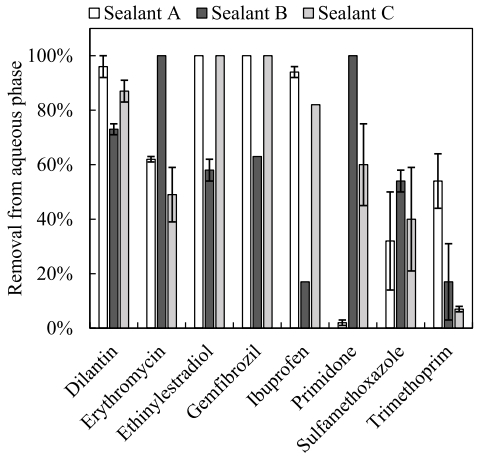

Figure 4. Equilibrium pharmaceutical phase partitioning between pH 6.6 buffered synthetic urine and waterless urinal sealants. Error bars indicate the range and bars indicate the average of duplicate samples, when measured.

of sealant/Milli-Q system without pharmaceutical), rather than the dissolved pharmaceutical, we calculated D_{ow} at the final experimental pH and again generated logarithmic regressions. Log D_{ow} and log K_{ow} values were the same for all compounds except erythromycin and trimethoprim, and therefore correlation between log D_{ow} and removal again resulted in relatively weak regression coefficients (R^2 = 0.21 to 0.63), although modestly improved from K_{ow}. Compounds with log D_{ow} > 3.5 (ethinyl estradiol, gemfibrozil, and ibuprofen) were removed ≥89% by all sealants, and dilantin (log D_{ow} > 2) was removed >95%. Removal of compounds with log D_{ow} < 1.3 was more variable. Sulfamethoxazole (log D_{ow} = 0.78) was removed well (72% to 89%) for all three sealants and primidone (log D_{ow} = 1.12) was not removed for sealant A and C, except in the case previously mentioned, where sealant B completely removed primidone. As expected, trimethoprim was removed ≤6%, but erythromycin was removed ≥73%, except in one case, where erythromycin was not removed to a measurable extent by sealant A. Because we generally observed that decreasing D_{ow} resulted in reduced removal, we conducted Spearman rank correlations between D_{ow} and removal, and found correlation coefficients of 0.79, 0.56, and 0.75, with p-values of 0.022, 0.146, and 0.029 for sealants A, B, and C, respectively. The correlations were stronger than logarithmic regressions, but, D_{ow}/K_{ow} were generally not useful in explaining partitioning from this clean system. We also used SPARC[43] to predict hexadecane−water partitioning coefficients because it was thought that they may better represent the sealant fluids (Tables S3 and S5). However, correlation was not improved and neither octanol nor hexadecane were perfect representations of the sealant fluid.

We hypothesized that ionization and pK_a play an important role in partitioning, so we conducted additional experiments in artificial urine. Pharmaceuticals were spiked into pH 6.6 buffered synthetic urine and agitated with the urinal sealant fluids. Partitioning to the sealant ranged from 2% to 100% (Figure 4). In some cases, lower D_{ow} compared to K_{ow} resulted in the expected reduction in partitioning to the sealant (e.g., sealant B, gemfibrozil, ibuprofen, sulfamethoxazole), but in other cases, changes in partitioning did not follow any expected trend (e.g., increased primidone partitioning to sealant C despite K_{ow} = D_{ow}). This may partially be explained by the presence of some free fatty acids in sealants A and C, which contain carboxylic acids (pK_a ≈ 5) which may electrostatically interact with polar functional groups present in the pharmaceuticals. Additionally, we did not observe the same chromatographic interference for dilantin for sealant B, perhaps because specific coloring compounds contained in the sealant were less water-soluble at pH 6.6. (Figure 4).

Despite some unexpected trends when comparing Milli-Q and synthetic urine partitioning to the sealants, a similar overall trend was observed in that greater pharmaceutical K_{ow} generally resulted in greater removal. The correlation was again weak (R^2 = 0.0 to 0.73), but when accounting for pharmaceutical ionization (D_{ow}), correlations between removal by sealant A and C and log D_{ow} were acceptable for sealants A and C (Figure 5). Spearman rank correlations between log D_{ow}

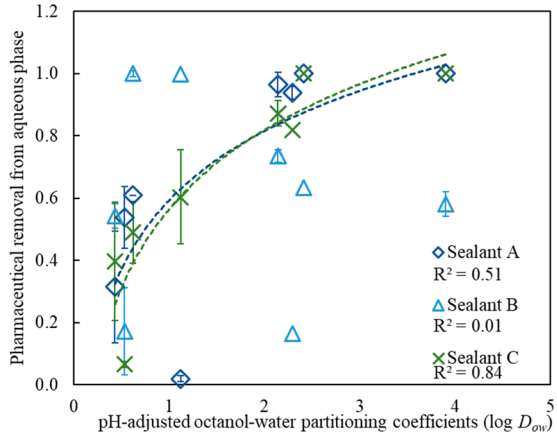

Figure 5. Correlation between pharmaceutical removal and log D_{ow}. Error bars indicate the range of duplicate samples, when measured.

and removal, and found ρ = 0.82, 0.06, and 0.95, with p-values of 0.011, 0.88, and 0.0004 for sealants A, B, and C, respectively. Correlation for sealants A and C from both logarithmic regressions and Spearman rank correlations were acceptable, suggesting that hydrophilicity controls partitioning to these two waterless urinal sealants. Correlations were again weak for sealant B, further demonstrating that this sealant is comprised

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of a significantly different chemical structure than sealants A and C.

3.4. Potential Adaptations to Waterless Urinals to Increase Removal of Pharmaceuticals. Removal was greater in equilibrium tests than simulated urination and for two of the three sealants, we conclude that partitioning from urine to the sealant fluid is a function of the hydrophobicity and ionization of the compound, represented by D_{ow}, and of the sealant itself. While determining the duration of quiescence required to achieve equilibrium, the shortest duration for which we allowed the sealant to equilibrate was 2 h, and we found that most of the compounds that would eventually be removed well, were removed <50%. We postulated that contact time and contact area between the aqueous phase and the sealant phase control the kinetics of pharmaceutical partitioning. Should waterless urinals be deployed in the future to intentionally reduce wastewater and environmental pharmaceutical loading (e.g., hospitals), adaptations would be required to overcome low removal.

We conducted one additional experiment to determine if increasing the hydraulic retention time (HRT) of the cartridge would increase the removal of pharmaceuticals. We again simulated urination but with reduced flow rate from the initial simulated urine experiment (1% or 12 mL/min). Because we did not observe significant changes in removal over time in the experiments with greater flow rate, we only sampled the cartridge effluent after 1 h (720 mL loaded). Altering the flow rate caused significant washout of chromatographically interfering compounds, and erythromycin and trimethoprim were removed from the analysis. Show in Figure 6, a

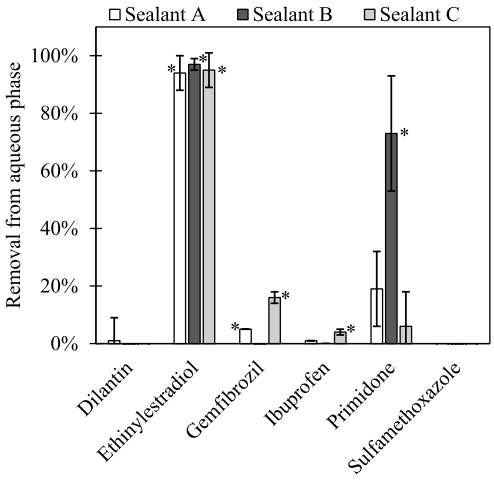

Figure 6. Urine simulation experiment using reduced flow rate (12 mL/min, 1% of initial simulated urination experiment). Error bars indicate the standard deviation of four samples. Asterisks indicate a statistically significant increases compared to simulated urination (1200 mL/min).

statistically significant increase in removal was observed for most pharmaceutical/sealant pairs with D_{ow} > 2.2 (ethinyl estradiol, ibuprofen, and gemfibrozil, *p*-values provided in Table S2). For some pharmaceutical/sealant pairs, removal decreased but not to an appreciable extent, and dilantin and sulfamethoxazole were not removed to a measurable extent in either experiment. All sealants achieved ≥90% removal of ethinyl estradiol, nearly 20% greater for sealant A and 50% greater for sealant C than the experiment with a more typical urination flow rate. Removal of primidone (D_{ow} = 1.12) also increased significantly for sealants A and B, but decreased for sealant C. Thus, increased retention time tended to increase the removal for specific compounds which were amenable to removal at higher flow rates, but was not overall effective at increasing removal of compounds which were poorly removed at higher flows.

3.5. Implications. We showed that some hydrophobic compounds are removed well from urine by partitioning to waterless urinals sealants, and that removal was not changed over 60 urinations. Removal is controlled partially by kinetics and strongly by hydrophobicity, and likely limited by urine/sealant interfacial area. In particular, ethinyl estradiol was well removed and adaptations of waterless urinals to women's toilets may result in significant decreases of anthropogenic hormones in the environment.

On the basis of the results presented here, we believe that pharmaceuticals are likely partitioned to urinal sealants deployed in active restrooms. Because the cartridges can become clogged over time with mineral precipitates, manufacturers recommend that the cartridges are discarded as solid waste, generally with the sealant still present inside, although some is lost to the sewer slowly over weeks and we have observed in follow-on research that will be the subject of a separate publication, that poorly managed waterless urinals may have no sealant present. Loss of the sealant to the sewer presents a missed management opportunity to divert pharmaceuticals from the wastewater stream, and diversion through typical municipal solid waste streams represents a missed opportunity to use the aliphatic sealants as incinerator fuel while simultaneously destroying the pharmaceuticals.

Increasing the HRT in this research was not substantially effective at increasing removal, likely because the urine is polar and flows through the cartridge as a stream with low contact area. To better capture pharmaceuticals and increase their diversion, one approach may be to increase the interfacial area of the sealant and urine retained between urinations, or, dispersing the urine into fine droplets.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.est.9b06205.

Additional methodological information, raw statistical data, and raw instrumental spectra (PDF)

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Notes

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