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Letter

Decontamination of Organic Pollutants from Aqueous Media Using Polymer-Free Bioinspired Materials

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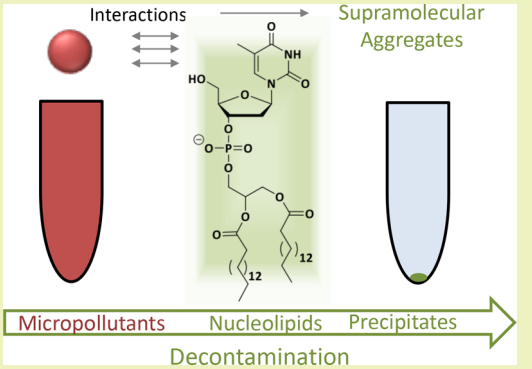
ABSTRACT: The occurrence of organic pollutants into water resources, including pharmaceutics, personal care products, pesticides, and/or hormones, is a major issue for all biological species. The impacts of these contaminants on both human beings and the environment are not yet fully understood, and the water pollution has raised a major public concern for many worldwide health authorities. In this letter, we propose a new strategy allowing the decontamination of organic pollutants based on polymer-free bionspired materials. A simple incubation of contaminated samples with nucleolipids allows a quantitative decontamination.



KEYWORDS: *Nucleolipids, Wastewater decontamination, Multiple pollutants, Supramolecular aggregates*

INTRODUCTION

Organic pollutants are hazardous molecules, such as pesticides, organic materials, detergents, or pharmaceutical residues, found in the air, soil, or water. These substances, resulting from human activities, can have a strong toxic or ecotoxic impact for all or part of organisms or ecosystems, including human beings even at high dilutions in the range of microgram, nanogram, or picogram per liter. In many cases organic pollutants are only degraded partially after water treatment, and degradation byproducts are sometimes more toxic than the original molecules.[1] Regarding pharmaceutical residues, different drugs are found in drinking water.[2,3] For example, after body metabolization, drugs are rejected in the sanitation systems in their initial form or metabolite.[4] Importantly, certain substances, which do not show adverse effects as single molecules, can exhibit toxic effects at low concentrations when they are combined with cocktails of organic pollutants.[5]

Today, despite different wastewater treatments and processes, the presence of residual contaminants remains a major worldwide societal concern, and new decontamination strategies are needed to address this pollution issue.[6−9] Here, we introduce a novel approach and a promising alternative to conventional decontamination systems. We demonstrate that polymer-free bioinspired materials made of nucleolipids (NLs) upon powder application tightly trap pharmaceuticals and/or pesticides residues to their aggregates (Figure 1). We also show that NLs aggregates can anchor cocktails of organic pollutants combining pesticides and drugs providing decontaminated aqueous samples.

In this context, we hypothesized that the use of supramolecular aggregates resulting from the self-assembly of nucleolipids could serve as a biomaterial allowing the trapping of organic pollutants. These NL-based biomaterials offer several advantages to polymeric sorbents as they possess properties nonachievable by polymers. The nontoxicity and the self-assembly properties of the nucleolipids render them ideal amphiphilic adjuvants for trapping pharmaceutics contaminants.[10] Also, their degradation provides nontoxic natural biomolecules, such as nucleosides, phosphates, and lipids.

To demonstrate our approach, we selected propranolol and diclofenac, which are poorly removed after wastewater treatments.[11−13] Propranolol is a beta blocker widely prescribed in hypertension cases, and diclofenac is a nonsteroidal anti-inflammatory drug. Both of them belong to the family of pharmaceutically active compounds (PhACs), and they are widely used worldwide. Despite the fact that PhACs are found in wastewater at low concentrations (in the range of nanograms to low micrograms per liter, i.e., 0.1 or 4 $\mu g \cdot L^{-1}$ for

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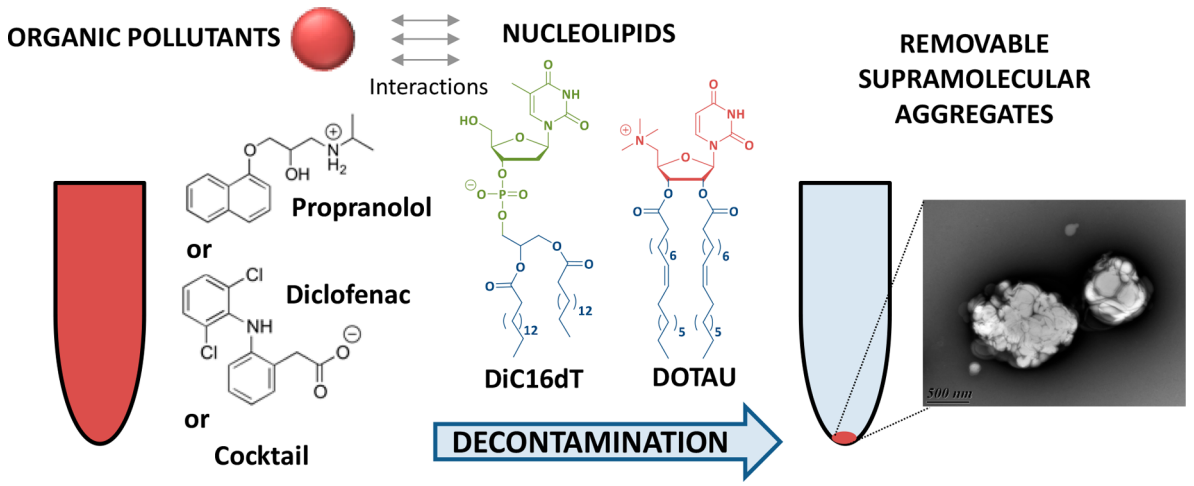

Figure 1. Schematic illustration of the removal of organic pollutants from aqueous samples using nucleolipids (NLs) biomaterials. Interactions between organic pollutants (propranolol, diclofenac, or cocktails) and nucleolipids allow the formation of removable supramolecular aggregates (TEM image, right). As a result, the decontamination of the aqueous sample can be achieved.

propranolol and diclofenac, respectively),[14] their occurrence in water and the environment has been widely discussed in the past decade.[15] Water treatment plants are not specifically designed to remove PhACs leading to large quantities of residual contaminants in drinking water,[16,17] and several approaches are currently under investigation, including nanofiltration[18,19] or nucleic acid-based technologies involving aptamers,[20] for example. To remove these contaminants from water, we selected nontoxic and biodegradable nucleolipids,[21] which have been extensively investigated in the field of biomedicine for drug delivery and tissue engineering applications.[22] On the basis of their properties,[23−25] we hypothesized that the amphiphilic character, the nucleobase, and functions would favor their interaction with diclofenac and propranolol and stabilize nucleolipid−drugs aggregates (see Figure ESI4). Also, it was expected that these aggregates should be removed from the aqueous phase by simple decantation and/or filtration processes. In this context, two nucleolipids have drawn our attention: 3′-1,2-dipalmitoyl-*sn*-glycerol phosphate thymidine (DiC16dT)[23] and *N*-[5′-(2′,3′-dioleoyl)uridine]-*N*′,*N*′,*N*′-trimethylammonium (DOTAU).[26] They possess opposite charges (negative for DiC16dT and positive for DOTAU).

EXPERIMENTAL SECTION

Materials. Propranolol and diclofenac were acquired from Sigma-Aldrich. DiC16dT and DOTAU were synthesized according to procedures previously described.[21,26] Trivorex (commercialized neutralizing absorbent polymers) was acquired from PREVOR.

Calibration Solution of Propranolol, Diclofenac, and Trivorex. Here, 7 mg of drugs or nucleolipids were added in 7 mL of deionized water (stock solution: 1 mg·mL^{-1}). The λ_{max} were determined by spectra measurements for each compound. Different solutions were prepared with their stock solution and dosed in quartz of of 100 μL with a Jacso V-630 UV-spectrophotometer. Epsilon (molar extinction coefficient) of each compound was determined at 258, 266, 276, and 289 nm ($A = a \times C + b$ where A is the absorbance, C the concentration, and a is extinction coefficient (cm^{-1}·μg^{-1}·mL), and b is the value of the absorbance with a value of C equal to 0 (Table ESI1). Trivorex does not absorb in a deionized water solution. The same protocol was used in tap water.

Decontamination of Propranolol by DiC16dT and Diclofenac by DOTAU. Simple method experiments were achieved in triplicate. Here, 10 mg of DiC16dT was dissolved in 50 mL of propranolol (50 μg·mL^{-1} in deionized water or in tap water). Then, 600 μL was filtered on a 0.22 μm Millex-GS MF-Millipore membrane. Spectra of these samples were measured by a UV spectrophotometer with quartz cells of 100 μL. The final concentrations of propranolol as well as the percentage of decontamination were calculated via a multicomponent mode method (eqs 1 and 2, Supporting Information).[27] The same protocol was realized replacing DiC16dT by Trivorex. The decontamination of diclofenac (20 μg·mL^{-1}: work solution) was realized by using DOTAU or Trivorex following the same protocol.

Decontamination of Propranolol and Diclofenac Mixture: Complex Methods. Two series of samples (a and b) were studied in triplicate. Sample a: 10 mg of a nucleolipid was dissolved in 50 mL of an aqueous solution containing the contaminant. Then, 10 mg of the other nucleolipid was added after either 10 or 15 min. The decontamination efficacy was measured by a UV spectrophotometer (quartz cells, 100 μL) after filtration (600 μL was filtered on a 0.22 μm Millex-GS MF-Millipore membrane). This protocol was established for both drugs ([propranolol] = 50 μg·mL^{-1} and [diclofenac] = 20 μg·mL^{-1}). Sample b: 10 mg of both nucleolipids were added simultaneously to 50 mL of the solution containing the contaminant. After incubation, 600 μL was filtered on a 0.22 μm Millex-GS MF-Millipore Membrane. The spectra were recorded by a UV spectrophotometer with quartz cells of 100 μL. This system was established for both drugs ([propranolol] = 50 μg·mL^{-1} and [diclofenac] = 20 μg·mL^{-1}).

Data Analysis. The parametric ANOVA test was used to detect significant differences between the decontamination methods, and afterthat the normality (Shapiro−Wilk test) and homoscedasticity (Bartlett test) were tested. When the ANOVA test was significant (p-value < 0.05), the Tukey posthoc test was used (ns = not significant, p > 0.05; ∗ = low significance, p < 0.05; ∗∗ = very significant, p < 0.005; ∗∗∗ = highly significant, p < 0.0005).

Cocktail Decontamination. The 13 organic pollutants were solubilized at concentrations at least higher than 10 times their limits of quantification (LOQ) in 500 mL of water (see concentrations in Tables ESI2 and ESI3). Three replicates of 50 mL of this solution were analyzed after decontamination using DiC16dT. These samples were analyzed by LCMS. Contaminants and their concentrations are detailed in Tables ESI2 and ESI3.

LCMS Analysis. *Liquid Chromatography.* The chromatographic separation was carried out with an HTC PAL automatic sampling system (CTC Analytics AG, Zwingen, Switzerland) coupled with a Dionex Ultimate 3000 HPLC system (ThermoFisher Scientific, Les Ullis, France) equipped with two pumps (charging and elution) and a VIM (valve interface module) to elute the SPE online backflush.

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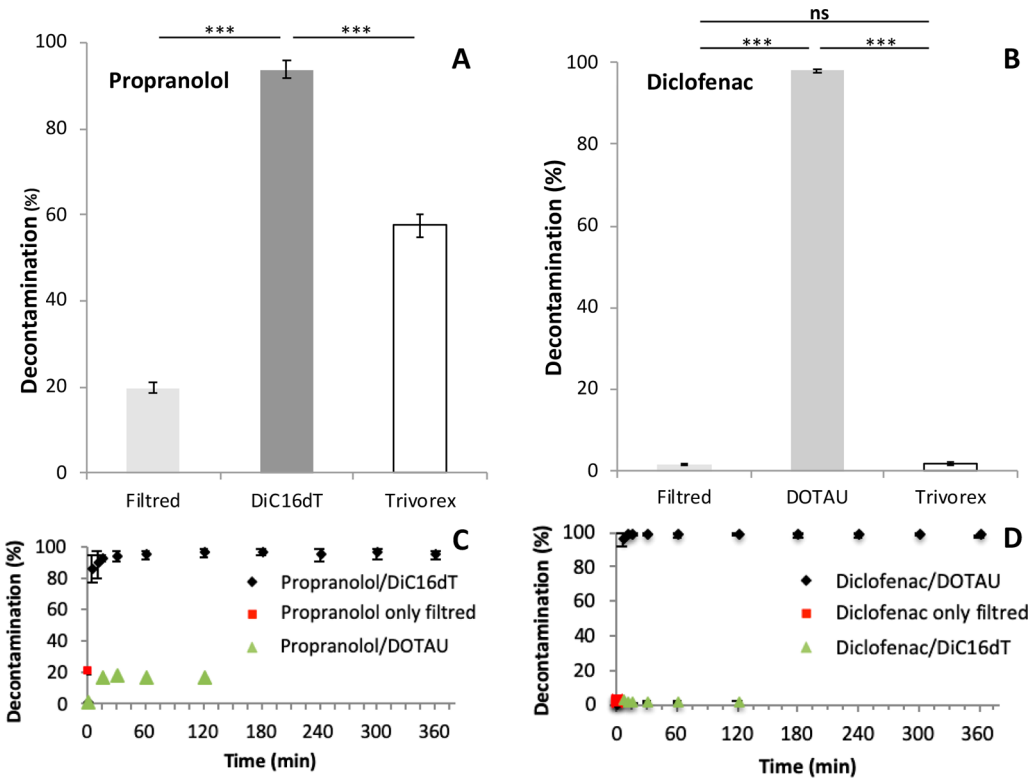

Figure 2. Removal efficacies of propranolol (A) and diclofenac (B). Propranolol decontamination in deionized water by filtration only (0.22 μm) (filtered), by DiC16dT and filtration (DiC16dT), by DOTAU and filtration (DOTAU), by Trivorex and filtration (Trivorex). Diclofenac decontamination in deionized water by filtration only (0.22 μm) (filtered), by DOTAU and filtration (DOTAU), and by Trivorex and filtration (Trivorex). Decontamination efficacies versus incubation time of propranolol (C) and diclofenac (D).

Mass Spectrometry. The assays were performed in positive mode with a Q-Exactive (ThermoFisher Scientific, Les Ullis, France) equipped with a HESI (heated electrospray ionization) source (ThermoFisher Scientific, Les Ullis, France). The acquisition and exploitation of the results were carried out with Xcalibur software (ThermoFisher Scientific, Les Ullis, France). The signal corresponding to each of the contaminants was validated according to its m/z (with a tolerance of 5 ppm) and retention time and manually reintegrated if necessary. Calibration lines were obtained for each molecule in LC-MS grade water with concentrations up to two times the initial concentration of the test solution. The parameters of these calibration lines (slope, intercept, and linear regression coefficient) were obtained using Excel software, which was used to quantify each molecule in the samples.

ITC Analysis of Propranolol by DiC16dT. The calorimetric measurements were performed using a MicroCal ITC200 instrument (Malvern, Orsay France). The propranolol solution was used at a concentration of 50 $\mu g \cdot mL^{-1}$, and the DiC16dT solution at 1 $mg \cdot mL^{-1}$. The working cell (205.8 μL) was filled with the propranolol solution and the reference cell with water. The injection syringe was filled with the DiC16dT solution. The titration schedule consisted of 16 consecutive injections of 4 μL with an interval of 180 s between each injection. The corresponding reference blank experiments were also performed, namely, titration of the water in the propranolol solution and titration of the DiC16dT solution in the water. To avoid the presence of bubbles, all samples were degassed before starting the measurements. The syringe was constantly stirred at 400 rpm. Temperature was kept constant at 25 °C. The first injection was carried out without taking into account the corresponding observed heat because the first injection was had errors as a result of the diffusion of solution across the syringe tip during the pretitration equilibrium period.

Under the assumption of a one-site binding model with the ligand in the sample cell, thermodynamic parameters as enthalpy (ΔH), entropy (ΔS), and the equilibrium binding constant were calculated. Data analysis was performed with MicroCal Analysis software. The binding affinity (K) and enthalpy (ΔH) at a constant temperature (T) are measured.

RESULTS AND DISCUSSION

Removal of Propranolol and Diclofenac. In the first series of experiments, the decontamination of aqueous solutions (deionized water or tap water) containing either propranolol or diclofenac was realized in two different conditions: (i) Trivorex (as a control) or (ii) nucleolipids. In a typical experiment, 10 mg of either nucleolipids or Trivorex was added as a powder to 50 mL of contaminated solutions ([propranolol] = 50 μg/mL; [diclofenac] = 25 μg/mL). After incubation upon stirring, 600 μL of this solution was filtered (Millex-GS 0.22 μm, MF-Millipore). Then, the concentrations of pollutants as well as the removal efficacy were determined using a spectrophotometer (see Supporting Informtion). Figure 2 shows the decontamination efficacies obtained for propranolol or diclofenac in distilled water under the following conditions: filtration alone, in the absence of a removing agent; addition of a nucleolipids (DOTAU or DiC16dT), followed by filtration; addition of Trivorex, followed by filtration. A high removal efficacy is observed for the solution containing propranolol in the presence of DiC16dT (93.69% ± 2.04%) and for the solution containing diclofenac in the presence of DOTAU (98.03% ± 0.51%). These decontamination efficiencies are significantly higher than those obtained with Trivorex, respectively, 55% ± 5% (for propranolol) and less than 5% (for diclofenac). Noteworthy, in similar conditions, filtration alone on a cellulose membrane gives a very poor decontamination (19.80% ± 1.22%) for propranolol, which has

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an affinity for the cellulose membrane, and no decontamination for diclofenac (1.86% ± 0.17%). Also, the use of Trivorex commonly used as an absorbent in hospitals was inefficient to remove both propranolol and diclofenac, with removal yields lower than 60% and 2%, respectively. In order to determine the optimum incubation time, the removal efficiency versus incubation time was investigated for both contaminants. As shown in Figure 2C and D, the maximum decontamination is observed only after a few minutes. Here, 98.03% ± 0.51% and 93.69% ± 2.04% of removal efficiencies are observed for propranolol and diclofenac after 10 and 15 min, respectively. Importantly, the removal efficacies were also investigated in tap water. In these conditions, the propranolol decontamination by DiC16dT shows slower kinetics than in distilled water (max decontamination in tap water reached at 2 h versus 15 min in pure water, see Figure ESI2). DiC16dT allows for a better decontamination in tap water than in distilled water (max decontamination in tap water 99.28% ± 0.95% versus 93.69% ± 2.04% in distilled water).

In order to evaluate the removal efficacy of nucleolipid mixtures, two different protocols were investigated: (a) simultaneous addition of both nucleolipids or (b) step by step addition method (see Supporting Information). As shown in Figure ESI3, simultaneous addition of both nucleolipids provides a higher efficacy (72.71% ± 2.44%) than a simple filtration (20.03% ± 1.14%) but a lower removal efficiency than DiC16dT (98.21% ± 0.72%). In the case of diclofenac decontamination, both protocols remain efficient (removal efficacies above 90%, see Figure ESI3).

To evaluate the binding properties of nucleolipids interacting with their organic pollutant, thermodynamic parameters were determined by isothermal titration calorimetry (ITC). The ITC data reveal a relevant favorable binding reaction between DiC16dT and propranolol (Figure 3). The ITC titration peaks are negative, in agreement with an exothermic binding reaction. Likely, the positive parts of the first peaks involve a reorganization of DiC16dT. Such a behavior is similar to the endothermic ITC data reported by Pector et al. on lipid derivative DiC14−amidine.[28] To avoid the DiC16dT reorganization, the last nine peaks were fitted with a "one-set-of-sites" model (Figure 3). Thus, the binding constant value (K) obtained in these conditions is 8.46×10^5 ($\pm 1.72 \times 10^6$) M^{-1}, while the enthalpy is −9.27 (±0.15) kJ/mol and the entropy is 80 J/mol/deg. Importantly, these results (negative enthalpy, positive entropy, and high binding affinity constant) show a favorable formation of complexes, which are enthalpically and entropically driven. Hence, the favorable interactions (van der Waals forces, $\pi-\pi$ stacking, etc.) between nucleolipids (DiC16dT) and pollutants (propranolol) would explain the formation of aggregates entrapping the pollutants.

Removal of Cocktail of 13 Organic Pollutants. Wastewater effluents contain a mixture of toxic xenobiotics contaminating aquatic environments and soils. It has been reported that the exposure to a mixture of organic pollutants can induce toxicity, including cytogenotoxicity, hematological and histopathological, in the case of pharmaceutic pollution, for example.[29] Animal and human exposure to multiple organic pollutants is a major concern regarding the possible combined effects of multiple pollutants ("cocktail effect").[30] Hence, an important aim of this study was to evaluate our polymer-free bionspired materials on water contaminated with 13 organic pollutants selected among the main family of residues,

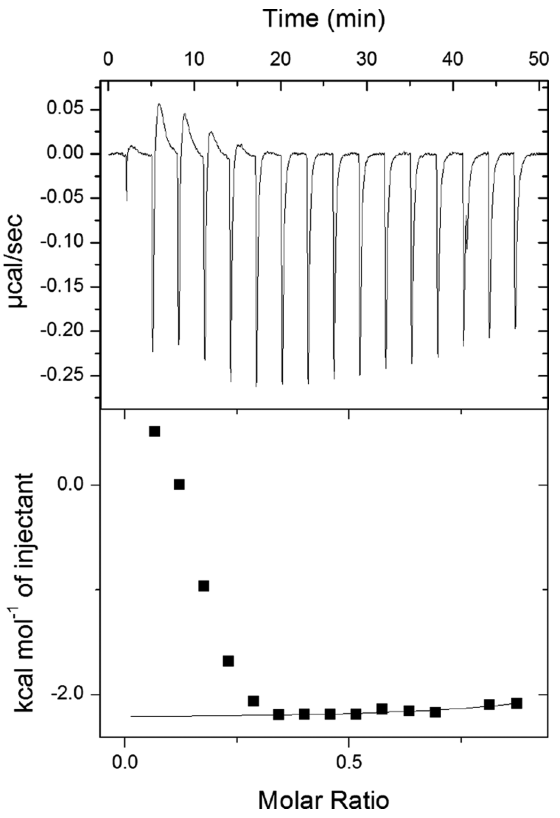

Figure 3. Representative ITC data for the titration DiC16dT (injectant) to propranolol. The top plot of power versus time was integrated to yield the bottom plot of molar enthalpy versus molar ratio of DiC16dT−propranolol.

including anticonvulsants, antibiotics, endocrine disruptors, antidepressants, beta blockers, and pesticides (Table ESI2). Removal studies of each of these compounds were performed similarly to those for propranolol using DiC16dT. Noteworthy, in order to mimic the actual concentrations found in groundwater,[31] the concentrations of the pollutants used in the cocktail decontamination experiments were in the range from 0.1 to 4 $\mu g \cdot L^{-1}$ (see Table ESI2 with a total concentration of 14 $\mu g \cdot L^{-1}$). As shown in Figure 4, DiC16dT was highly efficient for removing the cocktail with a global removal efficacy higher than 95%. Nine pollutants showed a quantitative uptake (higher than 97%) by DiC16dT, whereas four contaminants were partially decontaminated (40% < removal efficacies < 77%). These results demonstrate that nonpolymer biomaterials can at globally remove major organic pollutants at environmental concentrations simultaneously when present in cocktails suggesting that they can contribute to the removal of a wide range of organic pollutants during water and wastewater treatment.

CONCLUSION

In summary, a simple method for the decontamination of aqueous samples containing organic pollutants has been reported. Thanks to the formation of supramolecular aggregates by the nucleolipids, the removal of pollutants such as propranolol or diclofenac was successfully achieved at room temperature in distilled and tap waters. As illustrated with the cocktail decontamination experiments, nucleolipids show high removal efficacy for mixtures containing actual concentrations of anticonvulsants, antibiotics, endocrine

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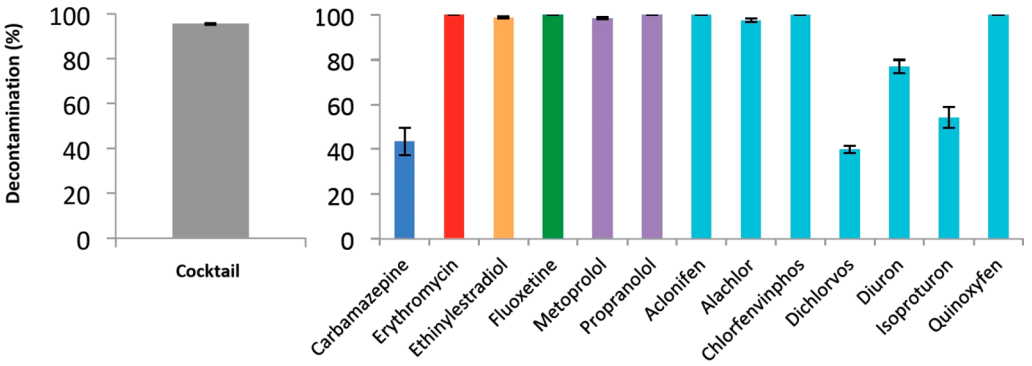

Figure 4. (Left) Global removal efficacies of the cocktail containing 13 organic pollutants (gray) using DiC16dT as sorbent. (Right) Decontamination efficacies of each contaminant in the cocktail (deep blue, anticonvulsants; red, antibiotics; orange, endocrine disruptors; green, antidepressants; purple, beta blockers; and light blue, pesticides).

disruptors, antidepressants, beta blockers, and pesticides. The performance levels observed in removing organic pollutants from water using polymer-free biomaterials could help to solve a major public pollution concern worldwide.[32,33]

■ ASSOCIATED CONTENT

Supporting Information

This material is available free of charge via the Internet The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acssuschemeng.0c04329.

Methods, kinetic of decontamination, LCMS results, absorbance calibration curves, and complementary TEM images (PDF)

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Notes

The authors declare no competing financial interest.

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