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Use of a clay mineral and its nonionic and cationic organoclay derivatives for the removal of pharmaceuticals from rural wastewater effluents

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Highlights

- Significant occurrence of pharmaceuticals (PPs) in a rural wastewater treatment facility
- Use of clay and organoclay as adsorbents for PPs showing different organic moieties
- Removal of PPs from a wastewater solution appears efficient at low concentration

- Electrostatic interaction seems to be the main driving force for PPs adsorption

Keywords

Rural water treatment, emerging pollutants, pharmaceuticals, adsorption, organoclay

Abstract

A Na^+ exchanged montmorillonite clay (Na-Mt) and its organoclay derivatives prepared with benzyldimethyltetradecylammonium (BDTA) cationic and polyoxyethylene(20)oleyl-ether (Brij-O20) non-ionic surfactants were used for first time at our knowledge as adsorbents the removal diverse pharmaceuticals (PPs) from samples collected in a rural wastewater facility (town of Josnes in France). The selected facility showed a poor efficiency for the elimination of PPs that were permanently release to the environment. Although involving different interactional mechanisms, the whole adsorbents Na-Mt, nonionic Brij-Mt and cationic BDTA-Mt organoclays, could remove the entire PPs of various chemical nature in a low concentration regime (ng L^{-1}), where electrostatic interactions mainly controlled the adsorption. Thus, the organic PPs cations were preferentially adsorbed onto Na-Mt and $Brij_{0.4}$-Mt (with its dual hydrophilic-hydrophobic nature) while anionic PPs showed a bold affinity to BDTA-Mt. The hydrophobic environment generated by the intercalation of surfactants within the interlayer space of organoclays conferred a versatility for the adsorption of numerous PPs through weak molecular forces (Van der Waals and/or pi-pi interactions). The study confirmed the proper efficiency of the studied layered materials including organoclays and emphasized about their promising interests in water remediation strategy.

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1. Introduction

Constructed wetlands and lagoon-based systems represent elegant and low-cost water remediation technologies used by numerous small communities in Europe (Zhang and Li, 2011; Verlicchi and Zambello, 2014; Thiebault et al., 2016a; Thiebault et al., 2016b; Kania et al., 2018). While constructed wetlands assisted by phyto-planted filters appear quite sophisticated with the design of several stages of vertical-flow filters including the action of sludge, the lagoon type is quite simple leaning against the presence of micro-organisms combined with solar UV radiation for the removal of diverse organic contaminants. However, this easy set-up purification system which requires little maintenance mainly suffers from a lack of efficiency in wintertime when the biological activity and solar radiation are weak. Thus the incapacity of the lagoon type waste water treatment plants to completely eliminate organic pollutants including pharmaceutical products (PPs) and in particular the hydrophobic ones leads to their continuous discharge in the aquatic network with concentrations that can spread out from a few to several hundred ng L^{-1} (Kolpin et al., 2002; Tixier et al., 2003; Zhang et al., 2007; De Oliveira and Guégan, 2016; De Oliveira et al., 2017; De Oliveira et al., 2018). Besides their presence in top surface water in such concentration range, the toxicity of PPs was widely confirmed by numerous studies emphasizing their hazardous behaviours, and the consequences of mixtures or cocktails of PPs (including those based on hormones). The exposure of ecosystems to PPs may cause various perturbations in different species such as about the changes of gender in fish and amphibian species for instance and even possible hazardous effects to humans. The conjugate toxicity of multiple PPs associated with other contaminants can also be drastically superior than the effects of only one pollutant.

Industrial techniques bearing on chemical and physical processes such as oxidation, UV irradiation or the use of activated carbons show excellent results for the removal of organic

contaminants but are traditionally limited for the production of drinking water. Indeed, moreover of their expensive costs, both UV degradation and oxidation generate metabolites or by products of which side effects are still hard to predict. In contrast, adsorption based on porous materials appears as the most efficient and simplest way to eliminate micro-pollutants (Guégan, 2011; Carli et al., 2015; Guégan et al., 2015; Thiebault et al., 2016a; Thiebault et al., 2016b; Guégan et al., 2017; Guégan, 2019; Guégan et al., 2020). Among the possible adsorbents, raw clay minerals represent interesting materials with a reasonable cost, and appropriate adsorption properties with a large specific surface area, and capacity to exchange ions but show their limits to the hydrophobic PPs. With the intercalation of both cationic and non-ionic surfactants within the interlayer space of raw clay minerals, hybrid layered materials, organoclays are formed (Madejová et al., 2016; Slaný et al., 2019). Organoclays, with their hydrophobic nature and abilities to exchange ions, show adsorption properties for numerous organic products including PPs for various experimental conditions mimicking those of the natural context (Guégan et al., 2015; De Oliveira and Guégan, 2016; De Oliveira et al., 2018; Guégan, 2019). If the sorption onto raw clay minerals of PPs at low starting concentrations (µg L^{-1} and ng L^{-1}) sampled from wastewater has been investigated (Thiebault et al., 2016a), no similar experiments have been performed onto organoclays where the reactivities of the hybrid materials to PPs need to be determined for any possible uses or applications in water remediation strategies.

In the light of the well-known adsorption efficiency of organoclays to pharmaceuticals, this study aims for the first time at our knowledge at both evaluating and understanding the adsorption of some pharmaceuticals sampled from a wastewater treatment facility (lagoon based system in a rural community: the town of Josnes, located in the department of Loir-et-Cher in the region of Centre-Val de Loire in France) onto organoclays. These hybrid layered materials were prepared by benzyldimethyltetradecylammonium cationic (BDTA) and

polyoxyethylene (20) oleyl ether (Brij-O20) nonionic surfactants. The efficiency of the studied organoclays for the removal of PPs was studied by UHPLC/MRM MS and compared to an untreated montmorillonite. This present study addresses also the interests of organoclays in complement of lagoon-based system potential for a complete removal of PPs.

2. Materials and Methods

2.1. Origin of the samples

The samples of contaminated water of PPs were taken from the lagoon-based wastewater treatment plant of the town of Josnes, located in the department of Loir-et-Cher in the region of Centre-Val de Loire (France). The wastewater treatment plant, set up in 1991, deals with the waste/discharge of a population estimated at 893 people in 2015 (INSEE) of which 23.7% of them are older than 60 years old and thus are subject to consume PPs.

Figure 1: Lagoon-based system (with a schematic representation of its functioning) as wastewater treatment plant of the town of Josnes located in the Region Centre in France.

The rural wastewater treatment lagoon consists to a succession of three tanks before water being released into the environment (Figure 1). The first one (B1) is aerated and combines a decantation step for heavy particles while the others (B2 and B3) are simple tanks without any aeration. The lagoon-based system is therefore a succession of three basins in which different types of algae and processions bacteria favour and contribute to the degradation of organic molecules. While showing the advantage of being less expensive than other conventional treatment plants, one of the main inconvenient of the lagoon-based system concerns the continuous release of algae and bacteria in effluents.

2.2. Sampling and samples preparation

A sampling campaign was conducted on January 30, 2018. Two sampling points were selected, a first sample taken in the first basin B1 (Figure 1) and a second at the exit of the wastewater treatment (after the third tank B3). A total of 20 litters of sewage water were collected at both points for the adsorption experiments. In situ pH and conductivity measurements were done during the collection of the samples.

Solutions were first 0.22 μm filtered for the removal of microorganisms that may degrade the pharmaceutical substances and solid particles that can adsorb molecules. Then a concentration procedure by solid phase extraction (SPE) was achieved prior any UHPLC/MRM MS analyses and after interaction with sorbents. This step was necessary to concentrate the molecules in the solution in order to amplify their signal and to be above the limit of detection of several spectroscopic techniques (De Oliveira and Guégan, 2016; Thiebault et al., 2016a; Thiebault et al., 2016b; De Oliveira et al., 2017; Guégan et al., 2020).

2.3. Adsorbents

Wyoming sodium montmorillonite (Mt), obtained from the Source Clay Minerals Repository, University of Missouri (Columbia, MO) was used in this study as a starting material. The

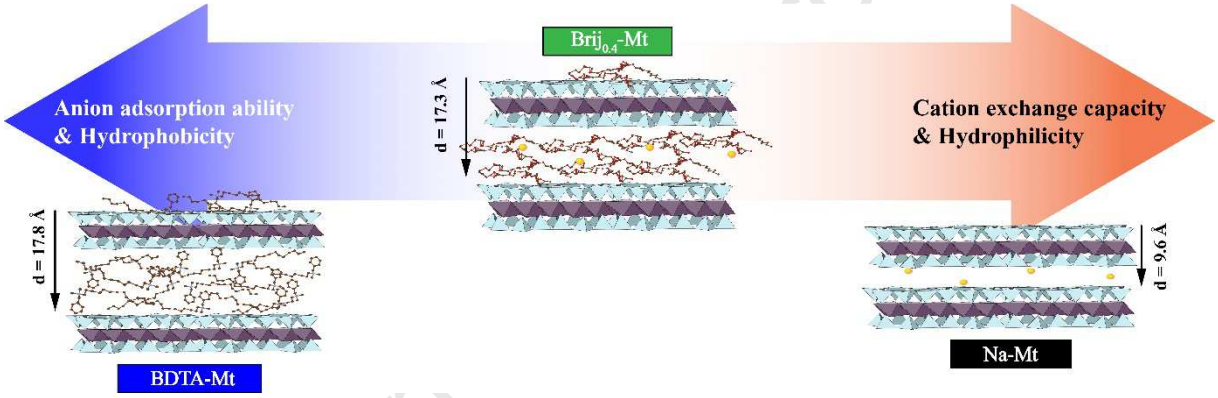
structural formula can be expressed as: $(Ca_{0,12}\ Na_{0,32}\ K_{0,05})[Al_{3,01}\ Fe(III)_{0,41}\ Mn_{0,01}\ Mg_{0,54}\ Ti_{0,02}][Si_{7,98}\ Al_{0,02}]O_{20}(OH)_4$. Mt was fractioned to < 2 μm by gravity sedimentation, purified and Na^+ exchanged. This Na-Mt clay mineral shows a cation exchange capacity (CEC) of 76.4 meq per 100 g clay.

The preparation of the organoclays is well described in the literature and consists in the chemical modification of Na-Mt by surfactants (BDTA and Brij-O20). Both benzyldimethyltetradecylammonium (BDTA) and polyoxyethylene (20) oleyl ether (Brij-O20) surfactants which were supplied from Sigma Aldrich Chemical. The cationic surfactant (BDTA) of which chemical formula is: $CH_3(CH_2)_{13}N(Cl)(CH_3)_2CH_2C_6H_5$, has a molar mass of 368.04 g mol^{-1}, and was conventionally used as organic modifier for the preparation of cationic organoclays. Brij-O20 ($C_{18}H_{35}(OCH_2CH_2)_{20}OH$) nonionic surfactant, has high molar mass of 1150 g mol^{-1}, characterized a CMC of 25μM and a Hydrophilic-Lipophilic Balance (HLB) of 15.3 over 20. BDTA-Mt cationic organoclay was prepared by mixing (at 300 rpm for 24 h, at 25°C) aqueous solutions of BDTA surfactant at a concentration of 1 CEC and Na-Mt suspensions which was stoichiometrically intercalated and exchanged with the Na^+ cations located within the interlayer space. In contrast, Brij-O20 surfactants, prepared at 25°C and at a concentration 1.13 x 10^{-3} mol L^{-1}, keep the Na^+ cations in the layered structure of the hybrid materials ($Brij_{0.4}$-Mt) and are adsorbed through ion-dipole interaction. Organoclays were prepared based on previous studies of the group when the concentrations of the surfactants was investigated and improved for a high adsorption efficiency for several PP molecules (De Oliveira et al., 2017; Guégan, 2019).

The BDTA-Mt and $Brij_{0.4}$-Mt organoclays were intensively characterized by complementary techniques and the data were published elsewhere (De Oliveira and Guégan, 2016; De Oliveira et al., 2017; De Oliveira et al., 2018; Guégan, 2019; Guégan et al., 2020). In contrast to Na-Mt showing a hydrophilic character, the organoclays with the intercalation of

161 surfactants in a lateral bilayer arrangement, display a hydrophobic behaviour with a wide
162 expansion of the interlayer space (Figure 2). By keeping the Na^+ cations and the HLB value of
163 a Brij-O20, $Brij_{0.4}$-Mt display a dual hydrophilicity/hydrophobicity behaviour with still the
164 possibility to exchange the Na^+ cations (30% of them) for further adsorption. BDTA-Mt with
165 a slight excess of organic cations display an organophilic behavior with the ability to adsorb
166 some anion (De Oliveira and Guégan, 2016; De Oliveira et al., 2017; De Oliveira et al., 2018;
167 Guégan, 2019; Guégan et al., 2020).

168



169

170 Figure 2: Schematic representation of the different adsorbents with a lateral bilayer
171 arrangement of the surfactants expanding the interlayer space at large value in contrast to the
172 starting Na-Mt. Na-Mt shows a cation exchange capacity and hydrophilic character. BDTA-
173 Mt shows an ability to adsorb anion species and hydrophobicity properties, and $Brij_{0.4}$-Mt
174 display a dual hydrophilic-hydrophobic behaviour through the presence of the whole
175 compensating Na^+ cations and the non-ionic surfactant (De Oliveira et al., 2018; Guégan,
176 2019; Guégan et al., 2020) .

177 2.4. Experimental techniques

178 Chromatographic separation was achieved with an Ultimate 3000 RSLC (Thermo Fisher
179 Scientific Inc., CA, USA) liquid chromatography system equipped with a binary pump and a

Nucleodur C18 Gravity column (150 mm × 2 mm ; 1.8 μm, Macherey-Nagel) supplemented by a guard column. Separation was performed at a flow rate of 0.4 mL min^{-1} and the temperature was maintained at 30 °C. Two solvents were used as mobile phase: ultrapure water (solvent A) and ACN (solvent B) both acidified with 0.1% of formic acid. The elution gradient was a transition from 95% to 5% of A in 16.2 min followed by 3.3 min of 100% of B and then a return to the initial conditions (95% of A) during 10 min for a total analysis time of 29 min. The chromatography system was coupled to a TSQ Endura triple quadrupole mass spectrometer equipped with a heated electrospray ionization (H-ESI) interface (Thermo Scientific Inc., San Jose, CA, USA). The concentration of pharmaceuticals products before and after being in contact with the adsorbents: clay mineral and organoclays was performed by UHPLC/MRM MS with an electrospray ionization source operating in positive mode, with an electrospray voltage of 3600 V, a vaporizer temperature of 450 °C, ion transfer temperature of 325 °C, sheath gas of 50 Arb, auxiliary gas of 20 Arb, and sweep gas of 1 Arb.

2.5. Adsorption of pharmaceuticals products

A total of thirty pharmaceuticals molecules of particular interest were pre-selected as target substances for the adsorption experiments with Na-Mt, BDTA-Mt and $Brij_{0.4}$-Mt due to their high consumption level by the population, their low global removal rate by wastewater treatment, as well as their high occurrence in the environmental aquatic medium as previously discuss and their proven toxicity for organism. Only twelve out of the total of thirty PPs were selected due to their easier detection in the wastewater. The selected molecules were: atenolol, codeine, doxepin, metoprolol, trimethoprim, oxazepam, carbamazepine, sulfamethoxazole, bezafibrate, diclofenac, salicylic acid and ibuprofen. At the pH of the wastewater (pH=7.8), PPs display three different major electrical form according to their pKa (Table 1). Atenolol, codeine, doxepin and metoprolol are in their cationic form whereas trimethoprim, oxazepam and carbamazepine are neutral and sulfamethoxazole, bezafibrate, diclofenac, salicylic acid

and ibuprofen are mainly anionic. The other characteristics: Log P, solubility in water of the PPs are listed in the Table 1.

Table 1: Physicochemical properties of the selected 12 PPs

Major electrical form at a pH of 7.8	PPs	Weight (g mol^{-1})	Solubility (mg L^{-1})	Chemical formula	Log P	pK_a
Cationic	Atenolol	266.3	1.33×10^4	$C_{14}H_{22}N_2O_3$	0.57	9.67/14.08
	Codeine	299.4	9.00×10^3	$C_{18}H_{21}NO_3$	1.2	9.19/13.78
	Doxepin	279.4	3.19×10^1	$C_{19}H_{21}NO$	4.29	9.76
	Metoprolol	267,4	1.69×10^4	$C_{15}H_{25}NO_3$	1.88	9.67/14.09
Neutral	Trimethoprim	290,4	4.00×10^2	$C_{14}H_{18}N_4O_3$	0.91	7.16/17.33
	Oxazepam	286.7	1.79×10^2	$C_{15}H_{11}ClN_2O_2$	2.01	-1.5/10.61
	Carbamazepine	236,2	1.77×10^1	$C_{15}H_{12}N_2O$	2.45	-3.8/15.96
Anionic	Sulfamethoxazole	253,2	6.10×10^2	$C_{10}H_{11}N_3O_3S$	0.89	1.97/6.16
	Bezafibrate	361.8	1.55×10^0	$C_{19}H_{20}ClNO_4$	3.97	0.84/3.83
	Diclofenac	296,1	2.37×10^0	$C_{14}H_{11}Cl_2NO_2$	4.51	-2.1/4.15
	Salicylic acid	138.1	2.24×10^3	$C_7H_6O_3$	1.96	-6.3/2.79
	Ibuprofen	206.3	2.10×10^1	$C_{13}H_{18}O_2$	3.5	4.85

Batch adsorption experiments were conducted at ambient temperature (25°C) with a solid-to-liquid ratio constant of 2:1 (100 mg of adsorbent and 50 mL of solution), and at a similar pH to that of the field of 7.8 with the use of NaOH and HCl solutions at 1 mol L^{-1} each. Samples were shaken on a rotary shaker at 300 rpm during 24 h in order to reach the equilibrium and then centrifuged at 5000 rpm for 25 min. Both supernatants and adsorbents after being in contact with the solution were extracted and analysed through UHPLC/MRM MS. The removal percentage (% R) and amount of each adsorbed pharmaceuticals at time t (q_t, mol g^{-1}) was calculated by the difference between the initial and equilibrium concentrations following the equations 1 and 2 respectively.

$$\% R = \frac{(C_0 - C_t)}{C_0} \times 100 \quad (1)$$

$$q_t = \left(\frac{(C_0 - C_t) \times V}{m}\right) \times \frac{1}{M} \quad (2)$$

219

220 where C_0 and C_t (g L^{-1}) are respectively the initial and equilibrium concentrations of PP at a
221 time t = 24h, m is the amount of sorbent (g), V the volume of the solution (L) and M the
222 molar mass of the PP (g mol^{-1}).

223

3. Results

3.1. Determination of the initial concentration of PPs

The concentration of the 12 selected pharmaceuticals of the two collected samples is shown in Table 2. From the selected PPs, salicylic acid and ibuprofen, in a first basin, show concentration of about 4.74 and 11.07 μg L^{-1} respectively and their preponderance can be explained by a large consumption of these nonsteroidal anti-inflammatory PPs by the population of Josnes. Besides a large concentration of these two PPs in a first basin, the lagoon-based system displays a certain efficiency with a removal reaching 88-93%, underlining here the impact of biodegradation and photodegradation processes, leading to a release at concentration of about 300-4000 ng L^{-1} in an effluent (at the exit of the third basin). However, for other molecules such as oxazepam, trimethoprim and doxepin, the wastewater treatment show its limits with a poor degradation, nor removal of the PPs with removal rates of only 1-15%. Surprisingly, a negative removal was determined in the case of carbamazepine and was already observed in previous studies (Andreozzi et al., 2002; Andreozzi et al., 2003) and can be explained by (i) the difference of the residence times between the first basin and at the exit of the third one, (ii) the recalcitrance of PPs, and (iii) a possible combination or formation of PPs through depredated products (Verlicchi and Zambello, 2014). If one excludes carbamazepine, the average value for the removal of the whole PPs reaches 38.24 % with a release of the PPs at concentration above 100 ng L^{-1}, pointing out a moderate overall elimination performance for PPs (selected in this studied) of the wastewater treatment based on the lagoon system.

Table 2: Measured concentration (in ng L^{-1}) of the 12 PPs detected in the first basin and in the effluent of the wastewater treatment lagoon. Removal rate (%) are calculated between the two selected sampling points. (+) PP under cationic form, (0) PP under neutral form and (-) PP under anionic form at pH of 7.8

PPs (electrical charge)	1st basin	Effluent	Removal (%)
Atenolol (+)	2077.8 ± 37	1083.2 ± 132	47.86
Codeine (+)	966.4 ± 44	360.9 ± 99	62.65
Doxepin (+)	684.0 ± 220	590.4 ± 150	13.68
Metoprolol (+)	812.3 ± 111	485.2 ± 26	40.26
Trimethoprim (0)	867.9 ± 53	845.3 ± 81	2.60
Oxazepam (0)	388.2 ± 54	381.5 ± 12	1.72
Carbamazepine (0)	82.8 ± 17	171.5 ± 55	-107.12
Sulfamethoxazole (-)	1366.0 ± 69	1170.7 ± 68	14.29
Bezafibrate (-)	1788.5 ± 218	1316.7 ± 85	26.37
Diclofenac (-)	2242.9 ± 96	1585.5 ± 139	29.31
Salicylic acid (-)	4746.6 ± 222	315.2 ± 189	93.35
Ibuprofen (-)	11027.5 ± 149	1260.2 ± 33	88.57

3.2. Adsorption onto the adsorbents

The results (q_t and % R) of the adsorption experiments from wastewater solutions and for the three selected adsorbents are listed in tables for the first basin (Table 3) and for the effluents (Table 4). The q_t values for Na-Mt after being in contact with a solution collected from the first basin spread out from 2.89 x 10^{-11} to 1.65 x 10^{-8} mol g^{-1} for carbamazepine and salicylic acid, respectively. While not being present in the same initial concentrations, the adsorption rate related to the molecules are not correlated to their adsorbed amounts. Bezafibrate and salicylic acid represent the minimum and maximum values of the %R which is calculated at 5.94% and 96.25%. The total adsorbed amount is estimated at 3.51 x 10^{-8} mol g^{-1} for a

removal average of 43.65%. For BDTA-Mt, the adsorbed amount values are between 1.01 x 10^{-10} and 2.48 x 10^{-8} mol g^{-1} respectively for carbamazepine and ibuprofen. The adsorption rate is between 9.45% and greater than 99% respectively for codeine and diclofenac, with a total of 5.30 x 10^{-8} mol g^{-1} and an average of 66.38%. For $Brij_{0.4}$-Mt, q_t values are between 1.50 x 10^{-10} and 1.70 x 10^{-8} mol g^{-1} for carbamazepine and salicylic acid. The adsorption rate spreads out from 24.42% and 98.80% for bezafibrate and salicylic acid and the total amount adsorbed is 4.08 x 10^{-8} mol g^{-1} for an average of 67.02%.

Since the PPs do not evolve in the same way to the wastewater treatment, some of them were preferentially degraded while others are less altered. Thus, it leads to different molecular proportions that totally vary from one sampling point to another and consequently affects the results of the interactions between the adsorbents and the analytes with those different initial conditions. Na-Mt shows for the effluents some adsorbed amounts ranging from 9.49 x 10^{-11} to 9.49 x 10^{-10} mol g^{-1} related to codeine and doxepin molecules respectively. The minimum adsorption rate is 10.36% for sulfamethoxazole and maximum for doxepin with 89.67%. BDTA-Mt shows q_t values ranging from 8.15 x 10^{-11} to 2.70 x 10^{-9} mol g^{-1} for codeine and diclofenac. These molecules also correspond to the minimum and maximum adsorption rates of 13.53% and more than 99% respectively. Values for $Brij_{0.4}$-Mt are between 3.47 x 10^{-10} and 1.74 x 10^{-9} mol g^{-1} for the carbamazepine and sulfamethoxazole molecules. The adsorption rate is between 33.52% and 95.48% for bezafibrate and carbamazepine. The total amounts adsorbed are about 6.17 x 10^{-9}, 1.30 x 10^{-8} and 1.07 x 10^{-8} mol g^{-1}, representing an average adsorption percentage of 40.56%, 68.82% and 65.47% for Na-Mt, BDTA-Mt and $Brij_{0.4}$-Mt respectively.

286 Table 3: Adsorbed amount q_t (mol g^{-1}) and removal percentage (%R) of 12 PPs detected in the
287 first basin of the wastewater treatment lagoon for the starting clay material (Na-Mt), the
288 cationic (BDTA-Mt) and the non-ionic ($Bij_{0.4}$-Mt) organoclays. (+) PP under cationic form,
289 (0) PP under neutral form and (-) PP under anionic form at pH of 7.8

PPs (electrical charge)	Na-Mt		BDTA-Mt		$Brij_{0.4}$-Mt	
	q_t (mol g^{-1})	%R	q_t (mol g^{-1})	%R	q_t (mol g^{-1})	%R
Atenolol (+)	$2.03 \times 10^{-9} \pm 0.06$	51.98	$4.97 \times 10^{-10} \pm 0.46$	12.74	$2.32 \times 10^{-9} \pm 0.58$	59.38
Codeine (+)	$8.14 \times 10^{-10} \pm 0.98$	58.15	$1.32 \times 10^{-10} \pm 1.06$	9.45	$1.17 \times 10^{-9} \pm 0.07$	83.8
Doxepin (+)	$1.11 \times 10^{-9} \pm 0.29$	90.44	$8.81 \times 10^{-10} \pm 0.12$	72.00	$1.12 \times 10^{-9} \pm 0.01$	91.82
Metoprolol (+)	$8.50 \times 10^{-10} \pm 1.11$	55.94	$7.78 \times 10^{-10} \pm 0.80$	51.22	$1.20 \times 10^{-9} \pm 0.30$	79.16
Trimethoprim (0)	$1.01 \times 10^{-9} \pm 0.02$	67.84	$7.31 \times 10^{-10} \pm 1.13$	48.88	$1.39 \times 10^{-9} \pm 0.22$	92.74
Oxazepam (0)	$1.17 \times 10^{-10} \pm 0.23$	17.21	$5.55 \times 10^{-10} \pm 0.06$	81.99	$3.32 \times 10^{-10} \pm 0.47$	48.98
Carbamazepine (0)	$2.89 \times 10^{-11} \pm 1.58$	16.48	$1.01 \times 10^{-10} \pm 0.10$	57.52	$1.50 \times 10^{-10} \pm 1.72$	85.62
Sulfamethoxazole (-)	$2.25 \times 10^{-10} \pm 0.89$	8.36	$2.14 \times 10^{-9} \pm 0.04$	79.18	$1.73 \times 10^{-9} \pm 0.34$	64.16
Bezafibrate (-)	$1.47 \times 10^{-10} \pm 1.10$	5.94	$2.41 \times 10^{-9} \pm 0.01$	97.71	$6.04 \times 10^{-10} \pm 3.38$	24.42
Diclofenac (-)	$4.16 \times 10^{-10} \pm 0.92$	11.00	$3.81 \times 10^{-9} \pm 0.02$	>99	$1.05 \times 10^{-9} \pm 0.13$	27.71
Salicylic acid (-)	$1.65 \times 10^{-8} \pm 0.004$	96.25	$1.62 \times 10^{-8} \pm 0.009$	94.20	$1.70 \times 10^{-8} \pm 0.05$	98.80
Ibuprofen (-)	$1.18 \times 10^{-8} \pm 0.005$	44.22	$2.48 \times 10^{-8} \pm 0.02$	92.74	$1.27 \times 10^{-8} \pm 0.17$	47.64

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291

292

293 Table 4: Adsorbed amount q_t (mol g^{-1}) and removal percentage (%R) of 12 PPs detected in the
294 effluent of the wastewater treatment lagoon for the starting clay material (Na-Mt), the cationic
295 (BDTA-Mt) and the non-ionic ($Bij_{0.4}$-Mt) organoclays. (+) PP under cationic form, (0) PP
296 under neutral form and (-) PP under anionic form at pH of 7.8

PPs (electrical charge)	Na-Mt		BDTA-Mt		$Brij_{0.4}$-Mt	
	q_t (mol g^{-1})	%R	q_t (mol g^{-1})	%R	q_t (mol g^{-1})	%R
Atenolol (+)	$5.85 \times 10^{-10} \pm 0.40$	28.75	$2.50 \times 10^{-10} \pm 0.23$	12.28	$1.16 \times 10^{-9} \pm 0.14$	57.23
Codeine (+)	$9.49 \times 10^{-11} \pm 5.73$	15.75	$8.15 \times 10^{-11} \pm 3.40$	13.53	$5.23 \times 10^{-10} \pm 0.22$	86.80
Doxepin (+)	$9.49 \times 10^{-10} \pm 1.40$	89.67	$7.64 \times 10^{-10} \pm 1.00$	72.34	$1.02 \times 10^{-9} \pm 0.05$	96.44
Metoprolol (+)	$6.81 \times 10^{-10} \pm 1.24$	75.00	$6.14 \times 10^{-10} \pm 3.75$	67.62	$5.49 \times 10^{-10} \pm 0.72$	60.56
Trimethoprim (0)	$9.48 \times 10^{-10} \pm 0.15$	65.12	$7.21 \times 10^{-10} \pm 2.54$	49.54	$1.26 \times 10^{-9} \pm 0.07$	86.63
Oxazepam (0)	$1.51 \times 10^{-10} \pm 1.73$	22.68	$5.01 \times 10^{-10} \pm 0.17$	75.25	$3.77 \times 10^{-10} \pm 0.46$	56.67
Carbamazepine (0)	$2.05 \times 10^{-10} \pm 0.64$	56.38	$2.82 \times 10^{-10} \pm 0.51$	77.65	$3.47 \times 10^{-10} \pm 0.17$	95.48
Sulfamethoxazole (-)	$2.40 \times 10^{-10} \pm 0.19$	10.36	$2.09 \times 10^{-9} \pm 0.11$	90.46	$1.74 \times 10^{-9} \pm 0.09$	75.39
Bezafibrate (-)	$2.56 \times 10^{-10} \pm 0.41$	14.09	$1.76 \times 10^{-9} \pm 0.02$	96.46	$5.92 \times 10^{-10} \pm 2.07$	32.52
Diclofenac (-)	$6.38 \times 10^{-10} \pm 6.71$	23.82	$2.70 \times 10^{-9} \pm 0.05$	>99	$1.07 \times 10^{-9} \pm 0.11$	40.13
Salicylic acid (-)	$6.99 \times 10^{-10} \pm 0.55$	61.22	$7.26 \times 10^{-10} \pm 4.64$	90.51	$1.03 \times 10^{-9} \pm 0.04$	63.64
Ibuprofen (-)	$7.28 \times 10^{-10} \pm 0.99$	23.84	$2.48 \times 10^{-9} \pm 0.02$	81.24	$1.04 \times 10^{-9} \pm 0.008$	34.14

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4. Discussion

4.1. First basin solution interaction

The electrical charge of PPs was recognized to be one of the key parameters in the adsorption, as well as the zeta potential of adsorbents. At a pH of wastewater in the lagoon (pH=7.8), only atenolol, codeine, doxepin and metoprolol are organic cations. Based on the pKa values of the other PPs, trimethoprim, oxazepam and carbamazepine are neutral, while sulfamethoxazole, bezafibrate, diclofenac, salicylic acid and ibuprofen are organic anions. The impact of the electrical charge of PPs (and the long ranged electrostatic interaction) has been pointed out to be one of the major parameters for the adsorption onto montmorillonite and their organoclay derivatives (De Oliveira et al., 2018). If we exclude salicylic acid and ibuprofen (due to an order of magnitude of concentration higher than the other molecules for the first sampling point), the adsorbed amounts for Na-Mt highlight its affinity for protonated molecules. Atenolol, codeine, doxepin and metoprolol as well as trimethoprim with positive functional groups, are preferentially adsorbed compared to neutral molecules such as carbamazepine or anions such as bezafibrate, sulfamethoxazole or diclofenac. This trend is also confirmed with the mean value of sorption for the cationic PPs (i.e. atenolol, codeine, doxepin and metoprolol) which reaches 64.13% while for the anionic PPs (bezafibrate, sulfamethoxazole and diclofenac) the value falls down to about only 8.43 % and 33.84 % for neutral PPs (trimethoprim, oxazepam and carbamazepine). This supports the establishment of cationic exchanges between the inorganic cations of Na-Mt and the amine moieties of the cationic molecules (Bekçi et al., 2006; Thiebault et al., 2016a; Thiebault et al., 2016b). Also, it suggests surface complexation with donor-acceptor electron between negatively charged site (aluminol and silanol groups located on the edges of Na-Mt) and protonated groups of pharmaceutical substances as interactional mechanisms (Gao et al., 2008).

The large adsorption of anionic substances such as salicylic acid and ibuprofen onto Na-Mt can be explained by the large concentrations of PPs in the collected wastewater samples. Indeed, salicylic acid and ibuprofen are respectively quantified at 4.7 μg L^{-1} and 11 μg L^{-1}, which induces a concentration gradient or flux favourable to the adsorption of these molecules at the expense of the others PPs. In addition, with surface complexation process or cations exchanges involved, organic cations are first adsorbed forming an organic brush or coating likely to screen up the repulsion forces and allows adsorption of anionic PPs through other molecular interactions as similar as organoclays (i.e. enhancing the adsorption efficiency through intercalation of organic molecules). Moreover, with a conductivity of 1193 μS cm^{-1} in the wastewater, it is not excluded that an association or the formation of organic complexes between PPs occur and favour the adsorption of PP anions.

$Brij_{0.4}$-Mt displays similar interactional mechanisms as Na-Mt and the adsorption of the cationic substances appears quite favourable. However, the introduction of non-ionic surfactant in the interlayer spacing confers enhanced adsorption properties than the raw clay mineral (Van der Waals and the hydrogen bonding interaction). The sorption of PPs occurs at larger amounts than Na-Mt, in particular for the neutral (i.e. carbamazepine) and anionic compounds (i.e. sulfamethoxazole, bezafibrate, diclofenac, salicylic acid and ibuprofen). $Brij_{0.4}$-Mt appears more efficient in the adsorption of cationic, zwitterionic and neutral substances than both Na-Mt and BDTA-Mt. The mean sorption value for the cationic PPs is 78.54% while for the anionic PPs the value is 52.55 % and 75.78 % for neutral PPs.

BDTA-Mt adsorbs better anionic PPs than cationic ones by setting up electrostatic interactions between the organic ions of the surfactant (alkyl ammonium ion) and the deprotonated functional groups (i.e. acidic groups -COOH) of molecules such as diclofenac or salicylic acid. This affinity allows BDTA-Mt to have a higher total adsorbed amount than the two other adsorbents since the majority of the molecules at high concentration are in an

anionic form. The mean sorption value for the cationic PPs is only 36.35% while for the anionic PPs the value is 95.57% and 62.80% for neutral PPs.

The efficiency of the layered materials for the removal of the PPs matched those of our previous studies (De Oliveira et al., 2018, Guegan et al., 2020) with the use of 'synthetic waters' or experimental conditions quite distant from wasterwater conditions. Indeed, in synthetic waters, important parameters affecting the adsorption such as the ionic strength, temperature, concentration of PPs could be finely controlled allowed us to determine precisely equilibrium isotherms and to discriminate the main interactional mechanism. From these previous works, it appeared that the main driving force for the adsorption was principally electrostatic and other aspects (hydrogen bonding or Van der Waals interaction) played a minor role in the adsorption of PPs. In wastewaters, multiple effects occur with possible competition among PPs and other compounds or possible different kinetics of adsorption with prior adsorption of some chemicals leading to a change of the zeta potential of the adsorbents as well as their chemical nature. Thus, despite its main negative charge, ibuprofen can be adsorbed onto Na-Mt by a high concentration gradient compared to other compounds and certainly due to a possible prior adsorption of other compounds bearing a positive charge allowing a surface complexation of a pharmaceutical. However, the overall affinity adsorbents-PPs is still respected with our previous observations in synthetic water experimental conditions. Ibuprofen, which is mainly in its deprotonated form, shows a higher adsorbed amount and removal rate with the use of cationic organoclay BDTA-Mt. The removal rate falls with $Brij_{0.4}$-Mt and appears minimum with Na-Mt. Also, doxepin is principally adsorbed onto $Brij_{0.4}$-Mt, followed by Na-Mt but can be also be retained by BDTA-Mt due to the neutral behavior of a pharmaceutical at a pH of 7.8 that limits the repulsive forces with the surface of the layered material.

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374 *4.2. Effluent wastewater solution interaction*

375 The results of the adsorption experiments from the effluent highlight for the first time the
376 capacity of organoclays to adsorb, by UHPLC/MRM MS, PPs from wastewater collected in a
377 lagoon system at concentration range of ng L^{-1}.

378 Nevertheless, results are more difficult to interpret for both Na-Mt and $Brij_{0.4}$-Mt in regards to
379 the adsorbed amount of each PPs. No clear trend seems to emerge as to the affinities between
380 molecules and adsorbent. The mean adsorbed amount for cationic and anionic PPs onto Na-
381 Mt are respectively of 5.77×10^{-10} mol g^{-1} and 5.12×10^{-10} mol g^{-1} while for the $Brij_{0.4}$-Mt, the
382 mean adsorbed amount for cationic and anionic PPs are respectively of 8.13×10^{-10} mol g^{-1}
383 and 1.09×10^{-9} mol g^{-1}. Cationic PPs are preferentially adsorbed onto Na-Mt and $Brij_{0.4}$-Mt
384 through cation exchange and surface complexation. Nevertheless, the total adsorbed amount
385 of cationic PPs is slightly equal to that of anionic ones for which repulsive forces exist.
386 However, due to their large flux and large concentration, anionic compounds could be
387 adsorbed. BDTA-Mt seems to be the optimum adsorbent for the removal of anionic PPs.

388 The anionic molecules such as sulfamethoxazole, bezafibrate, diclofenac, salicylic acid and
389 ibuprofen have an average half-life time (half-life times of PPs either under photodegradation
390 condition or in soil) shorter than the cationic molecules atenolol, codeine, doxepin and
391 metoprolol (Andreozzi et al., 2003; Kodešová et al., 2016). Thus, anionic PPs may be subject
392 to be removed or degraded by the wastewater treatment of Josnes than the cationic ones which
393 is confirmed by the calculated %R. Indeed, the anionic molecules are removed up to 50.38%
394 against 41.11% for the cationic molecules. Nevertheless, these anionic species remained at
395 high concentration even in the effluent.

The results about the wastewater treatment system emphasize that neutral molecules such as oxazepam and carbamazepine are among the least well removed and adsorbed onto the layered materials. The absence of apparent charge associated with the possible competition among PPs for the adsorption sites of the sorbents may disadvantage an adsorption. In addition, their half-life time is much longer than previous PPs with values up to several days (Andreozzi et al., 2002; Calisto et al., 2011) which prevent a fast degradation within the wastewater treatment.

5. Conclusions

While Na-Mt appears as an efficient adsorbent to PPs, the use of organoclays display a certain versatility which improve the adsorption of the organic molecules. Indeed, the interests of organoclays bear on the possibility to adsorb a large range of molecules and especially those showing a poor affinity to clay minerals.

The collected wastewaters from the lagoon-based system in Josnes showed a pH relatively high (basic regime) and the concentrations of the pharmaceuticals spread out from 300 to 12000 ng L^{-1}. In those pH conditions, the PPs appeared mainly as organic species, emphasizing the interests of BDTA-Mt which appeared as the most efficient adsorbent for removal of the pharmaceuticals.

The selected wastewater treatment of the municipality of Josnes, based on a lagoon-type system, showed a limited over time removal process leading to the persistence of the pharmaceuticals in the aquatic network. One possible solution to improve the efficiency removal consists to use organoclays and even raw clay minerals as filters between the transition from the different lagoon basins. Indeed, through the experiments carried out, montmorillonite and its organoclay derivatives revealed a high potential for the removal of organic products with diverse physicochemical properties, suggesting a good efficiency in the adsorption of other types of micropollutants for an application shot. In order to characterize the overall efficiency of organoclays over time in a context of wastewater treatment, future research works should focus their efforts on both the influence of other physicochemical parameters such as inorganic ions that can generate a competitive effect among PPs and the degree of recycling and reuse of these layered hybrid materials via adsorption and desorption experiments.

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Highlights

- Significant occurrence of pharmaceuticals (PPs) in a rural wastewater treatment facility
- Use of clay and organoclay as adsorbents for PPs showing different organic moieties
- Removal of PPs from a wastewater solution appears efficient at low concentration
- Electrostatic interaction seems to be the main driving force for PPs adsorption

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The 15th of June 2020

Object: declaration of the scientific contribution of the corresponding author

To whom it should be addressed,

I would like to first answer to the inquiry of the editor about the number of co-authors associated to this work, which I believe deserve to be co-authors of this work. This work is a part of a PhD study of Dr. Tiago De Oliveira whom I was the main scientific PhD supervisor (Dr. Mohammed Boussafir was more an administrative supervisor but partially participated in the supervision of Tiago De Olivieira). Tiago De Oliveira was my master student in 2015 at the University of Orleans in France when I was an associate professor (since 2007, I am now seconded employee from this university). The results of his master project allowed us to publish two papers (one in Journal of Hazardous Materials: https://www.sciencedirect.com/science/article/pii/S0304389416304204 and one in ES&T: https://pubs.acs.org/doi/abs/10.1021/acs.est.6b03393) that I wrote completely the papers and thus was a corresponding author but Tiago was first author since it is the custom to put a student as a first author. Then, Tiago de Oliveira started his PhD in 2015, but in March 2018, I got a position as an associate professor at Waseda in Japan. For almost one year until the defence of a PhD of Tiago De Oliveira in March 2019, I supervised the work and the interpretation of the whole data of his PhD at distance and discussed also about the results of his PhD with Prof. Y. Sugahara. Prof. Sugahara is a specialist of layered materials and already participated in the writing of some papers of have been published already (ACS Omega 2018: https://pubs.acs.org/doi/abs/10.1021/acsomega.8b02049 , Chemosphere 2020: https://www.sciencedirect.com/science/article/pii/S0045653519319605) based on the results of a PhD of Tiago De Oliveira. Some meetings involved the whole co-authors to discuss about the results of the work of Tiago De Oliveira. Finally, I would like to mention my contribution in this study that concerned the design of the experiments, the interpretation of the data, the writing of a manuscript (based on the work of Tiago De Oliveira and his PhD that I completely rewrote), but also the creation of some graphics in order to produce a work with the required criteria to be published in a journal such as Chemosphere.

Attached to the letter, the justification of the scientific contribution of the whole co-authors. Based on your experience, please feel free to consider the contribution of each co-authors and to judge if necessary, to keep them as co-authors or to remove some of them.

Sincerely,
Régis Guégan

Dear Editor,

The study presented in the submitted manuscript is directly based my PhD research directed by Mohammed Boussafir and Régis Guégan at the University of Orléans in France. My contribution to the manuscript is total, starting to the conception of the experimental protocol, the execution of the experiments, the analysis of the samples, the interpretation of results and finishing with the writing of the reported manuscript. As my contribution on this research is major, I am legitimate to be cited as the main author of this scientific article which is based on my PhD research topic.

Tiago De Oliveira

Dear Professor Klaus Kümmerer
Editor

My contribution to this work is manifold. First of all, I am the PhD supervisor of Tiago de Oliveira's work co-supervised by Dr Régis Guegan. I am also in charge of the scientific project that funded his research. With Pr. Régis Guegan, we supervised Tiago's work from experimentation to writing. I thus took part in all the stages of the realization of this scientific article.

Kind regards

Orléans, Jun 12, 2020

Dear editorial,

The results contained in Dr Guegan's manuscript entitled "Use of a clay mineral and its nonionic and cationic organoclay derivatives for the removal of pharmaceuticals from rural wastewater effluents" were obtained by UHPLC/MS MRM mode coupling analyzes. The entire method for quantifying the molecules presented in the article was developed at the Institute of Chemical Organic and Analytic (ICOA) by Dr Destandau and Dr Fougère. In addition, they advise Dr De-Oliveira to carry out the analysis sequences, discuss the results and the solve problems encountered. Our contribution to this research allows us to be present as co-author of this article.

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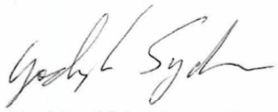
June 9, 2020

Declaration on scientific contribution

Dear Editor

I, Dr. Yoshiyuki SUGAHARA at Waseda University, participated in preparation of the manuscript entitled "Use of a clay mineral and its nonionic and cationic organoclay derivatives for the removal of pharmaceuticals from rural wastewater effluents". I discussed Prof. Guegan on the result interpretation based on my long research carrier on chemistry of layered compounds, since I and Prof. Guégan have been closely corroborated at Waseda University. I was also involved in writing manuscript partially. Based on my contribution to this research I am justified to be s co-author of this article.



Yoshiyuki SUGAHARA

Use of a clay mineral and its nonionic and cationic organoclay derivatives for the removal of pharmaceuticals from rural wastewater effluents

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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: