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Technical Article

Evaluation of concerning emergent compounds characteristics and simultaneous biosorption through multivariate technique

Avaliação das características de compostos emergentes e biossorção simultânea por meio de técnica multivariada

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ABSTRACT

Adsorption is one of the most efficient technologies for the removal of Concerning Emergent Compounds (CECs), also known as Organic Micropollutant (OMP). However, the use of activated carbon in developing countries is still costly. Thus, lignocellulosic residues are used as a base for making new adsorbent materials. This study assessed the relationship between the multicomponent adsorption of CECs in lignin-based adsorbents and the characteristics of the compounds. For this, 27 target compounds were prepared in an aqueous solution and submitted to the adsorption in 3 different materials. All the samples were analyzed in ultra-performance liquid chromatography coupled with mass spectrometry. The results were evaluated with the aid of the multivariate least squares regression (PLS-R) technique. It was observed that the adsorption of pharmaceuticals on activated carbons is a complex process governed by the properties of the adsorbed molecules, and the removal efficiency could be altered by external properties (e.g., adsorbent properties, pH, and organic matter). Even if it was reached an excellent average percentage removal (5.44 – 128.91%), the influence of other organic compounds could not be neglected. Unfortunately, to obtain a good understanding of the interactions between the single chemical molecule and the adsorbents, it would be necessary to study the process for each compound separately from the others and then consider the matrix effect due to the mixing of various pharmaceuticals with very different properties.

Keywords: biosorbent; CEC removal; partial least squares regression; spiked solution.

RESUMO

A adsorção é uma das tecnologias mais eficientes para a remoção de Compostos Emergentes Preocupantes (CEC), principalmente porque não produz produtos secundários de degradação e não é de difícil aplicação. O uso de carvão ativado em países em desenvolvimento ainda é caro, principalmente em razão de sua produção. Nesse contexto, este estudo avaliou a relação entre a adsorção multicomponente de CEC em adsorventes à base de lignina e as características dos compostos. Em detalhe, 27 compostos alvo foram preparados em solução aquosa e submetidos à adsorção em três materiais diferentes (dois de base lignocelulósica e um carvão ativado granular). Todas as amostras foram analisadas em cromatografia líquida de ultraeficiência acoplada à espectrometria de massas. Os resultados foram avaliados com o auxílio da técnica de regressão multivariada por mínimos quadrados (PLS-R). Observou-se que a adsorção de produtos farmacêuticos de Micropoluentes Orgânicos (OMP) em carvões ativados é um processo complexo, governado não apenas pelas propriedades das moléculas adsorvidas, e que a eficiência de remoção pode ser alterada por propriedades externas (por exemplo, propriedades adsorbents, pH, matéria orgânica). Mesmo que se atingisse uma excelente porcentagem média de remoção (5,44 – 128,91%), a influência de outros compostos orgânicos não poderia ser desprezada. Infelizmente, para se obter uma boa compreensão das interações entre a molécula química única e os adsorventes, seria necessário estudar o processo para cada composto separadamente dos outros e então considerar o efeito de matriz em razão da mistura de vários fármacos com substâncias muito diferentes.

Palavras-chave: biosorventes; remoção de CEC; regressão dos mínimos quadrados; amostras fortificadas.

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INTRODUCTION

At present, one of the main concerns worldwide is the growth of water pollution by Considering Emergent Compounds (CECs), also known as Organic Micropollutant (OMP), that emerge from industrial, agricultural, and urban human activities (FERREIRA *et al.*, 2017). These compounds could be persistent organic pollutants, owing to their resistance to conventional chemical, biological, and photolytic processes (DONNER *et al.,* 2013; EBELE ABDALLAH, HARRAD, 2017; GRANDCLÉMENT *et al.,* 2017). As a result, they have been detected in rivers (BARONTI *et al.,* 2000; RODRIGUEZ-MOZAZ *et al.,* 2015; BERTELKAMP *et al.,* 2016; ARCHER *et al.,* 2017; WEE *et al.,* 2019; LIU *et al.,* 2020), lakes (CHÈVRE, 2014; YAN *et al.,* 2018; GOLOVKO *et al.,* 2020), oceans (XIE *et al.,* 2012; PEREIRA *et al.,* 2016), and even drinking water (QUINLIVAN LI; KNAPPE, 2005; JONGH *et al.,* 2012; KENNEDY *et al.,* 2015) worldwide. This results in a severe environmental and public health problems mainly due to their toxicity and potential hazardous health effects (e.g., carcinogenicity, mutagenicity, and bactericidal) on living organisms, including human beings (DONNER *et al.,* 2013; YAN *et al.,* 2014). Dyes (YANG; AL-DURI, 2005; MOROSANU *et al.,* 2019; KITTAPPA *et al.,* 2020), chemicals (BOLONG *et al.,* 2009), and Pharmaceutically Active Compounds (PhACs) (SANTOS *et al.,* 2013; ARCHER *et al.,* 2017) are some of the most common recalcitrant CECs.

As a matter of fact, the activated carbon application for the removal of these compounds from environmental matrices is increasing year by year, as well as the production of these materials (FREIHARDT; JEKEL; RUHL, 2017). The consumption of activated carbon is the highest in the United States and Japan, which together consume 2 – 4 times more activated carbons than European and Asian countries. In 2005, the per capita consumption per year was 0.5 kg in Japan, 0.4 kg in the United States, 0.2 kg in Europe, and 0.03 kg in the rest of the world (KNOPP *et al.,* 2016).

The removal of CECs by adsorption seems to be an effective removal technique applied until present (ZIETZSCHMANN *et al.,* 2019). It is due to the other techniques, such as advanced oxidation (WERT *et al.,* 2007; SHU *et al.,* 2016), biological (REUNGOAT *et al.,* 2011; LÓPEZ-SERNA *et al.,* 2019) and physicochemical processes (LIU; KANJO; MIZUTANI, 2009), that could transform the target compounds in by-products or metabolites which are sometimes more dangerous than their predecessor molecules (FATTA-KASSINOS; VASQUEZ; KÜMMERER, 2011; GARCÍA-GALÁN *et al.,* 2016; SHU *et al.,* 2016). However, the commercial activated carbon is associated with high production costs, which may be difficult for its application in larger treatment plants, especially in developing countries.

In this way, the synthesis of adsorbent materials, optimized for the removal of this concerning class of contaminants, could be the answer to this unclaimed problem. The use of environment-friendly adsorbents could give an uncalculated source of raw material, with countless ways to use as a bottom line (YE *et al.,* 2013; GONZÁLEZ-GARCÍA, 2018). Besides, the production of biosorbents could value a waste that is not well used (e.g., pruning of trees and forest residues in general) (GONZÁLEZ-GARCÍA, 2018).

The lignin, naturally present in barks, is a hydrophobic macromolecule that contains several functional groups such as alcohols, aldehydes, ketones, carboxylic acid, phenolic, and ether linkages. These groups have a strong ability to bind toxic metal ions or CECs by utilizing an electron pair to form complexes in solution (MONTANÉ; TORNÉ-FERNÁNDEZ; FIERRO, 2005).

Studies observe that lignin-based biosorbents have similar or even higher removal percentages of CECs than commercially activated carbon materials (MONTANÉ; TORNÉ-FERNÁNDEZ; FIERRO, 2005; MORO *et al.,* 2017; CALISTO *et al.,* 2017; ALVES; MOTA; PINHEIRO, 2020). In addition, adsorption capacities on biosorbents are generally much improved after modification, while reaction methods are outstanding means to produce better lignocellulose-based materials (SUHAS; CARROTT; RIBEIRO; CARROTT, 2007; ALVES; PINHEIRO *et al.,* 2018; QUESADA *et al.,* 2019). This study aimed to evaluate the relationship between the competitive adsorption of CECs in lignin-based materials and the characteristics of the compounds.

MATERIAL AND METHODS

Target compounds and adsorbents

To simplify the study of the adsorption phenomena, we prepared a set of experiments using a spiked solution of ammonium acetate/ammonia at pH 8 with 27 CECs, specifically 25 PhACs and 2 metabolites, typically found in Wastewater Treatment Plants (WWTPs) (COLLADO *et al.,* 2014): azithromycin, ciprofloxacin, erythromycin, ofloxacin, sulfamethoxazole, trimethoprim, carbamazepine, fluoxetine, venlafaxine, *O*-desmethylvenlafaxine, bezafibrate, atorvastatin, gemfibrozil, diclofenac, ketoprofen, amlodipine, irbesartan, valsartan, atenolol, famotidine, ranitidine, metoprolol, metoprolol acid, furosemide, iopromide, loratadine, and salbutamol. All the target compounds were purchased from Sigma-Aldrich® with a purity higher than 99%.

The spiked water was prepared with a final concentration of 20 $\mu g.L^{-1}$ of each PhAC from an initial stock solution of 500 $\mu g.L^{-1}$. To use variables to explain the adsorption, the physicochemical characteristics of the target compounds were calculated by using Marvin Beans Software (Table 1) (Calculation software, MarvinSketch 5.5, ChemAxon, 2017).

The experiments were performed with two biosorbents and one commercially activated carbon: SP (pinus barks with addition of sulfur groups), KP (pinus barks with addition of potassium groups), and granular activated carbon (GAC). The preparation of the biosorbents was performed by direct reactions of oxidation by sulfuric acid and potassium hydroxide, as described in previous works (ALVES; PINHEIRO *et al.,* 2018). The stock solutions of the sorbents were prepared in ammonium acetate/ammonia (pH 8) in a suspension of 2 $g.L^{-1}$ and were stored overnight for complete wetting.

D_{80} determination

The batch experiments were conducted with the adsorbent suspensions that were prepared from an initial concentration of 2, 0.3, 0.2, 0.1, 0.05, 0.02, or 0.005 $g.L^{-1}$. The tests were conducted in duplicate at 25°C for 48 h. Finally, the concentration of the PhACs after the adsorption was measured and the theoretical mass of adsorbent needed to remove 80% of each selected compound (D_{80}) was calculated according to the methodology proposed by Zietzschmann *et al.* (2014). Thus, the two removals that were closer to 80% were applied in linear interpolation.

Data analysis

The removal of CECs in the batch adsorption system was analyzed by the mean and the relative standard deviation. Normality of the data was checked with the Shapiro–Wilk test, while the homoscedasticity was confirmed with Bartlett's test, both with a level of significance of 5%. In addition, the removals were compared with Analysis of Variance (ANOVA).

Table 1 – Physical and chemical characteristics of the target compounds (Calculation software, MarvinSketch 5.5, ChemAxon, 2017).

Compound	Type	Speciation Form	Characteristics			Speciation at pH 8 (%)				Hydrogen Bonds		Polar Surface Area (A²)	Molecular Ratio	
			[g.mol⁻¹]											
			MW	Log K_{ow}	Log D	Neutral	Positive	Negative	Pos/ Neg	H-Donnor	H-Acceptor	PSA	O/C	H/C
Azithromycin	Antibiotic	Cation	748.99	0.8	−1.73	0.29	99.67	0.00	0.02	7	11	180.08	0.235	0.089
Ciprofloxacin	Antibiotic	Cation/ Anion	331.35	1.57	−1.16	0.10	0.47	17.27	82.17	1	6	72.88	0.296	0.093
Erythromycin	Antibiotic	Cation	733.94	1.22	0.69	29.35	70.62	0.00	0.00	6	12	193.91	0.421	0.159
Ofloxacin	Antibiotic	Anion	361.37	1.51	−0.89	0.37	0.00	98.43	0.12	0	8	73.32	0.592	0.112
Sulfamethoxazole	Antibiotic	Anion	253.28	1.04	−0.03	1.43	0.00	98.47	0.00	1	5	98.22	0.285	0.108
Trimethoprim	Antibiotic	Neutral	290.32	1.05	0.99	87.46	12.54	0.00	0.00	2	7	105.51	0.308	0.136
Carbamazepine	Antidepressant	Neutral	236.27	3.22	3.22	100.00	0.00	0.00	0.00	1	1	46.33	0.266	0.140
Fluoxetine	Antidepressant	Cation	309.33	4.19	2.39	1.55	98.45	0.00	0.00	1	4	21.26	0.468	0.152
Venlafaxine	Antidepressant	Cation	277.31	2.25	1.3	11.00	89.00	0.00	0.00	2	2	32.7	0.157	0.134
O-Desmethylvenlafaxine	Antidepressant metabolite	Cation	263.38	2.22	1.26	10.78	88.06	0.09	1.06	3	2	43.7	0.167	0.131
Bezafibrate	Lipid-lowering	Anion	361.82	3.52	−0.04	0.01	0.00	99.99	0.00	1	5	75.63	0.266	0.123
Atorvastatin	Lipid-lowering	Anion	558.65	5	1.61	0.02	0.00	99.98	0.00	3	6	14.62	0.202	0.089
Gemfibrozil	Lipid-lowering	Anion	250.34	4.22	1	0.03	0.00	99.97	0.00	0	3	46.53	0.280	0.089
Diclofenac	Anti-inflammatory	Anion	296.15	3.97	0.45	0.01	0.00	99.99	0.00	1	5	49.33	0.190	0.066
Ketoprofen	Anti-inflammatory	Anion	254.29	3.46	−0.08	0.01	0.00	99.99	0.00	0	3	26.56	0.250	0.074
Amlodipine	Antihypertensive	Cation	408.90	3.00	0.19	4.98	95.02	0.00	0.00	2	7	99.88	0.250	0.200
Irbesartan	Antihypertensive	Neutral	428.54	5.74	4.23	66.57	0.01	33.41	0.00	0	6	47.59	0.053	0.094
Valsartan	Antihypertensive	Anion	435.53	5.63	0.77	0.02	0.00	99.98	0.00	0	7	112.7	0.167	0.102
Atenolol	β-Blocker	Cation	266.34	0.16	1.24	2.11	97.89	0.00	0.00	3	4	84.58	0.213	0.136
Famotidine	β-Blocker	Neutral	337.45	−0.57	−2.24	48.31	46.00	2.91	0.00	4	8	238.22	0.250	1.875
Ranitidine	β-Blocker	Cation	314.40	1.93	0.64	0.00	38.47	0.00	61.53	2	7	112.10	0.231	1.692
Metoprolol	β-Blocker	Cation	267.37	1.49	−0.18	2.11	97.89	0.00	0.00	2	3	50.72	0.400	0.093
Metoprolol Acid	β-Blocker metabolite	Cation/ Anion	267.33	1.13	−1.87	2.11	0.00	0.00	97.89	2	4	50.72	0.381	0.126
Furosemide	Diuretic	Anion	330.74	1.66	−1.76	0.02	0.00	99.98	0.00	2	6	122.63	0.555	0.077
Iopromide	X-ray contrast	Neutral	791.12	−0.72	−0.72	99.92	0.08	0.00	0.00	6	11	175.64	0.121	0.084
Loratadine	Antihistamine	Neutral	382.89	4.48	4.48	99.98	0.00	0.02	0.00	0	3	34.35	0.078	0.089
Salbutamol	Bronchodilator	Cation	239.15	0.61	−1.06	2.06	96.17	0.03	1.74	3	3	72.72	0.089	0.067

Fonte: Elaboração dos autores, 2022.

CECs quantification

The analysis of the selected PhACs, under positive (PI) and negative (NI) electrospray ionization, was performed following the methodology proposed by Gros, Rodríguez-Mozaz and Barceló (2012) in a Waters Acquity Ultra-Performance™ Liquid Chromatography System (UPLC) (Milford, MA, USA) coupled to a 5500 QTRAP hybrid triple quadrupole-linear ion trap mass spectrometer (Applied Biosystems, Foster City, CA, USA) with a turbo Ion Spray source.

An Acquity HSS T_3 column (50 mm × 2.1 mm i.d., 1.8 µm particle size) was used for the compounds analyzed in PI mode, whereas an Acquity BEH C_{18} column (50 mm × 2.1 mm i.d., 1.7 µm particle size) was applied for the NI mode. Both columns were obtained from Water Corporation. The solvents, elution gradient, volume of injection, and the transitions monitored were described by Gros, Rodríguez-Mozaz and Barceló (2012). The samples were analyzed in triplicate without pretreatment before the injection in the UPLC-QTRAP system.

Prediction and determination of preponderant adsorption characteristics

A multivariate statistical analysis based on Partial Least Squares Regression (PLS-R) was used to determine the physical and chemical characteristics of the PhACs (Table 1) that influence the most on the adsorption process.

The PLS-R results were evaluated by comparing the predicted removals with the sum of the squares for error of each analysis set and found a good correlation between matrices model (Q^2). Also, we observed R^2 value, which is used to evaluate the goodness of fit and determine if the projection had a significance level of

0.05 or better. Also, it was found that the test has the capacity to highlight the most important Variable In the Projection (VIP). In other words, it is possible to characterize which variables influence the adsorption process with greater capacity.

The multivariate test is performed to assess the cross-correlation and single correlation between the characteristics of the study compounds and PhACs removal and to find the relative importance of each parameter/relationship in the adsorption. In this way, it is possible to statistically report which characteristics are most important in the experiments to evaluate the predictivity of the multiple linear regression model.

The PLS-R analysis was performed using XLSTAT® software with a single variable behavior, named as PLS-1 – single compound characteristics versus CECs removal.

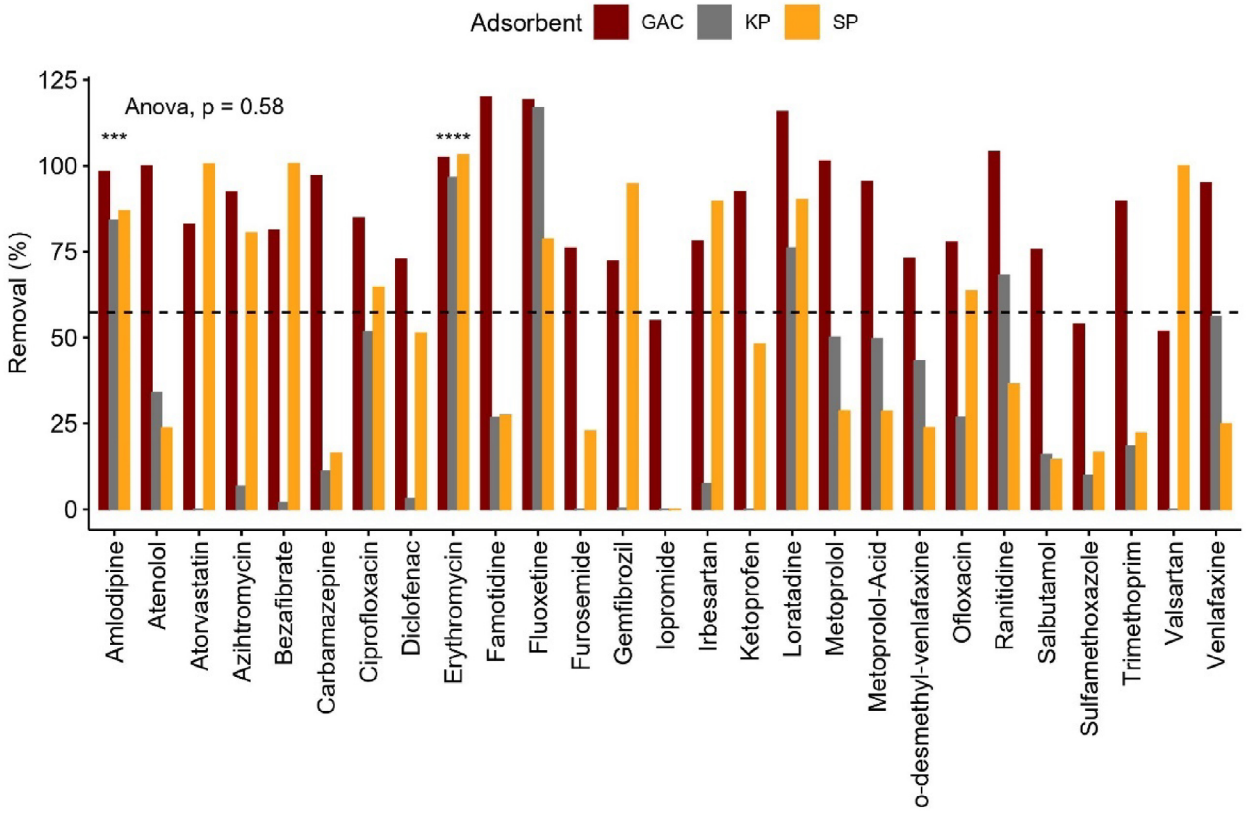
RESULTS AND DISCUSSION

Removal of PhACs from aqueous solution in batch adsorption

When analyzing the batch tests for each compound individually, it is possible to notice that the adsorption capacity of the PhACs is different depending on the adsorbent (Figure 1). For example, the removal of valsartan was 99.85% for SP and 51.67% for GAC. And for ketoprofen, the higher removal was observed for the commercial material (92.38%), followed by SP (47.97%). Both compounds were not adsorbed in KP. Another example is atenolol, which presented a removal of 99.82% for GAC, followed by 33.94% for KP and 23.53% for SP.

The Shapiro–Wilk (W = 0.97215, p-value = 0.07446) and Bartlett (Bartlett's K^2 = 17.649, df = 26, p-value = 0.8882) tests revealed that the data exhibited normal distribution and homoscedasticity at 5% of significance. The average removal in all adsorbents of each compound showed no significant difference (57.34%) (ANOVA, p = 0.58), except for amlodipine and erythromycin which differ at a significance level of 0.05% and 0.001%, respectively.

The compounds that were adsorbed more than 50% (minimum of 51.61%) for all adsorbents were ciprofloxacin, amlodipine, erythromycin, fluoxetine, and loratadine. However, the latter three, as well as famotidine, metoprolol, ranitidine, atorvastatin, and bezafibrate, presented a removal above 100% in some cases, ranging from 100.38% to 119.95%, which may be due to analytical interference. In contrast, some compounds, such as sulfamethoxazole, carbamazepine, salbutamol, and iopromide, which were adsorbed less than 17% by the biosorbents, showed a lower removal for KP and SP. In addition, the compounds such as valsartan, diclofenac, ketoprofen, furosemide, atorvastatin, bezafibrate,



GAC: granular activated carbon; KP: pinus barks with potassium; SP: pinus barks with sulfur; ns: not significant
***Significant at 0.05%.
****Significant at 0.001%. The dashed line represents the mean of all data.
Source: Authors' elaboration, 2022.

Figure 1 – Mean of the PhACs removal (%) and adsorbent material.

gemfibrozil, and iopromide showed a removal lower than 5.00% for KP (0.00 – 3.08%), with the latter showing no removal for SP.

Similar behavior was already described in other studies, in which sulfamethoxazole was poorly removed in spiked water (JARIA *et al.*, 2020) or had a maximum removal of 31% in treated wastewater (RUHL *et al.*, 2014). Also, iopromide was less adsorbed compared with 22 other PhACs in spiked water (ALVES; CABRERA-CODONY *et al.*, 2018). Both sulfamethoxazole and iopromide are hydrophilic. In contrast, fluoxetine and loratadine, which are less hydrophilic, showed to be more absorbable (ALVES; CABRERA-CODONY *et al.*, 2018). However, there are reports of removal values higher than the observed values in this research; for example, diclofenac has been removed from 34% to 94% (RUHL *et al.*, 2014).

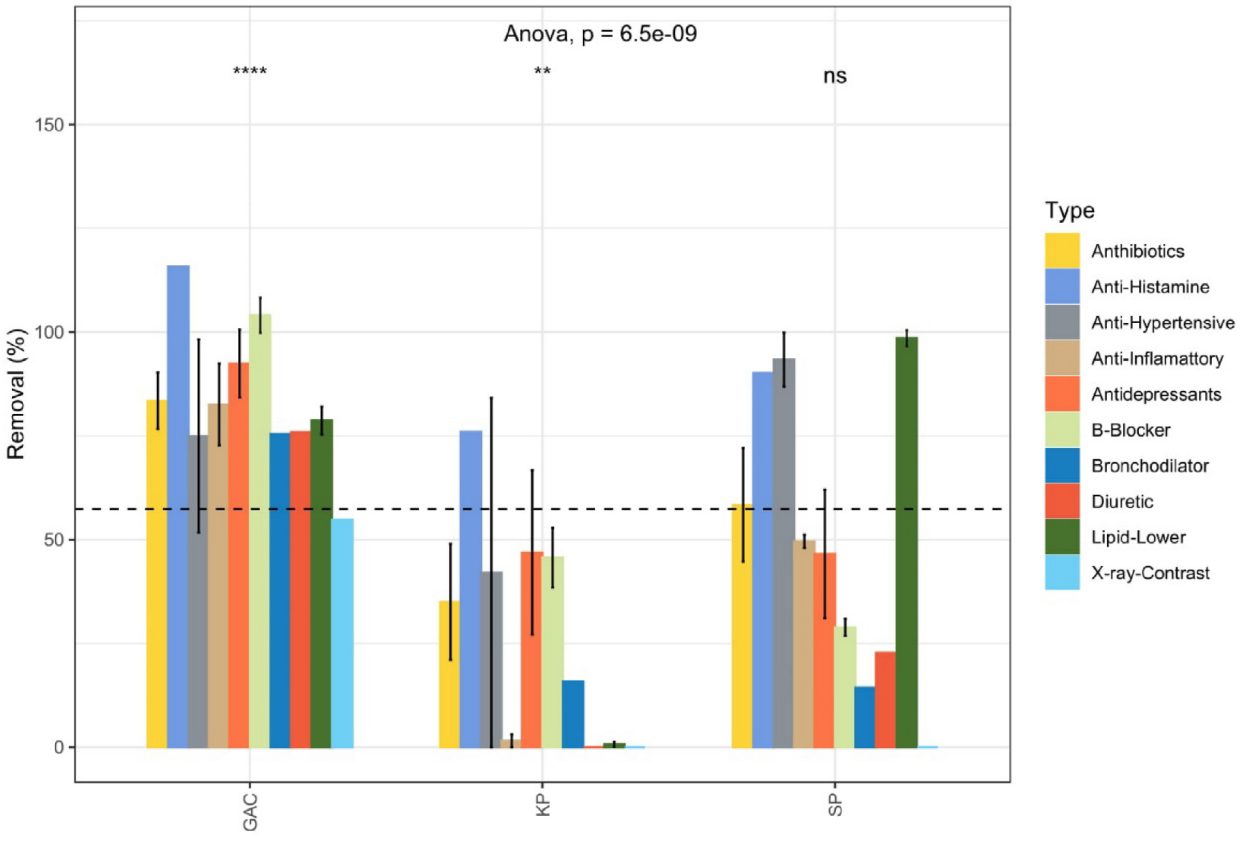
It is important to note that this study tested a mix of 27 CECs. The literature highlights that when there is a mixture of CECs, it is possible to observe a decrease in the adsorption capacity, indicating that there is competition for adsorption sites in multi-component solutions (JUNG *et al.*, 2015; NIELSEN; BANDOSZ, 2016). For example, carbamazepine adsorption reduced at least 50% when analyzed in a mixture with other PhACs (CALISTO *et al.*, 2017). In another study, it was found that sulfamethoxazole decreased an average of 77% when in a solution with carbamazepine and trimethoprim in comparison with the single solution (NIELSEN; BANDOSZ, 2016).

The variability in the percentage adsorption for each material was higher for the antibiotics, antihypertensives, and antidepressants than the other classes (Figure 2). This is probably due to the different molecular characteristics of the analyzed PhACs. X-ray contrast showed lower removal (mean of 18.26%), followed by diuretics (mean of 32.88%) and bronchodilator (mean of 35.23%).

Adsorbent material efficiency

Observing the behavior of adsorbent material on average removal, it can be noted that the GAC had highest mean removal (87.23%) compared to the environment-friendly and alternative materials such as SP (53.17%) and KP (31.61%). The variability of each adsorbent can be indicative of its selectivity; thus, the greater the internal deviation, the more selective the material and consequently the less choice for an application in WWTP, since the compounds present are of varied molecular classes and characteristics.

Compounds removals are observed in different adsorbent materials; however, with considerable deviation, the selectivity of the materials was as follows: GAC (18.33%) < SP (33.75%) < KP (33.95%). Thus, the most selective



GAC: granular activated carbon; KP: pinus barks with potassium; SP: pinus barks with sulfur; ns: not significant in relation to the mean of all data.
**Significant at 0.1%.
****Significant at 0.001%. The dashed line represents the mean of all data.
Source: Authors' elaboration, 2022.

Figure 2 – Removal (%) of the PhACs classes and adsorbent material.

adsorbent was the KP, the material with more limitations in future application. The SP adsorbent presented similar deviation to its homolog material KP, and the commercial adsorbent (GAC) showed less selectivity which is applicable more in future real situations.

Comparing the means with a variance test (p = 6.5e-09), it was found that SP does not have a significance difference, while GAC and KP show statistically significant difference with 0.001% and 0.1%, respectively. However, SP shows promising mean removal efficiency. Thus, it is further suggested to investigate and improve the efficiency for some therapeutic class (e.g., bronchodilator and diuretics).

D80 masses

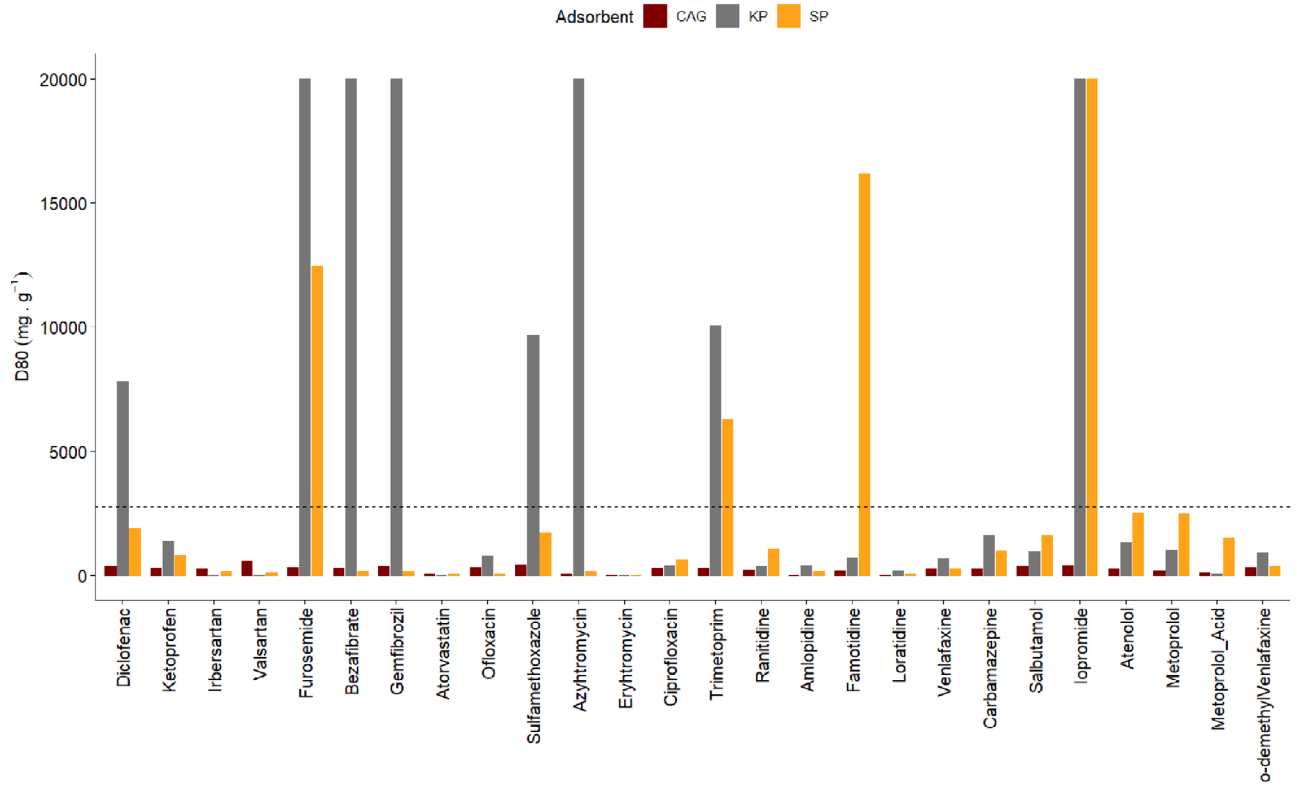
The D_{80} doses may be defined as the sorbent mass capable to remove 80% of the CECs contamination. The smaller the mass, the better the adsorption effectivity. Figure 3 shows the D_{80} values for each target compound by adsorbent. This dose extremely varied for each study compound, ranging from 2.52 to 20.000 $mg.L^{-1}$.

The PhACs more easily adsorbed in most of the adsorbents (average D_{80} < 100 $mg.L^{-1}$) were mainly positively charged compounds, such as erythromycin < atorvastatin < loratadine < ofloxacin for the SP; erythromycin < amlodipine < loratadine < azithromycin < atorvastatin < metoprolol acid for CAG; and valsartan < erythromycin < irbesartan < atorvastatin < metoprolol acid for KP. In contrast, compounds with average D_{80} > 120 $mg.L^{-1}$ were mainly neutrally charged and hydrophobic (log K_{ow} >1.23).

Two PhACs, i.e., venlafaxine and metoprolol, and its main metabolites, i.e., *O*-desmethylvenlafaxine and metoprolol acid, were selected to assess the adsorption of pharmaceutical metabolites compared to their parent compounds. The D_{80} average value of venlafaxine was 380.99 $mg.L^{-1}$ for all the materials and 525.35 $mg.L^{-1}$ for its metabolite (*O*-desmethylvenlafaxine), meaning that the metabolite was less adsorbed than the parent compound, particularly for KP (D_{80} = 905.97 $mg.L^{-1}$). Metoprolol has an average D_{80} of 1221.15 $mg.L^{-1}$, while its metabolite, i.e., metoprolol acid, has an average D_{80} of 551.35 $mg.L^{-1}$, indicating that the metabolite was adsorbed with the higher efficiency, especially in KP (62.31 $mg.L^{-1}$). All the D_{80} values are presented in supplementary material.

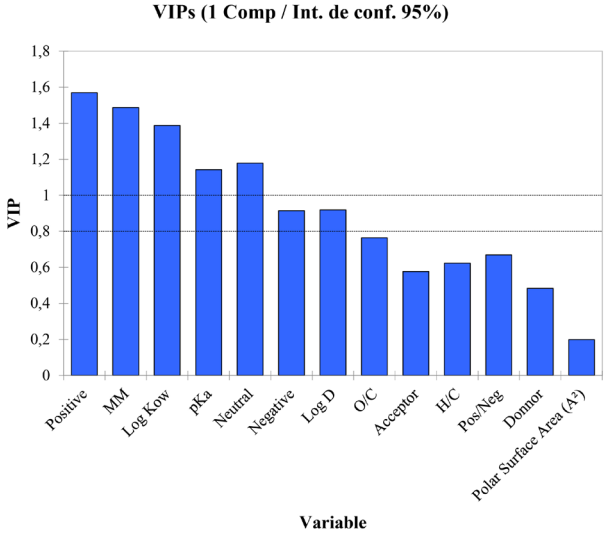
Correlations on compound characteristics versus CECs removal

To get further insight into the parameters ruling the biosorption of PhACs, PLS-R analysis was used as multivariate statistical analysis. PLS-R has been reported previously in the literature as a useful method of predicting pharmaceutical rejection during nanofiltration and the influence of physicochemical characteristics of membranes in this process (FLYBORG *et al.*, 2017). The same approach has been applied in this work to analyze the importance of the physical



GAC: granular activated carbon; KP: pinus barks with potassium; SP: pinus barks with sulfur. The dashed line represents the mean of all data.
Source: Authors' elaboration, 2022.

Figure 3 – D_{80} values for each compound and studied material ($mg.g^{-1}$).



Source: Authors' elaboration, 2022.

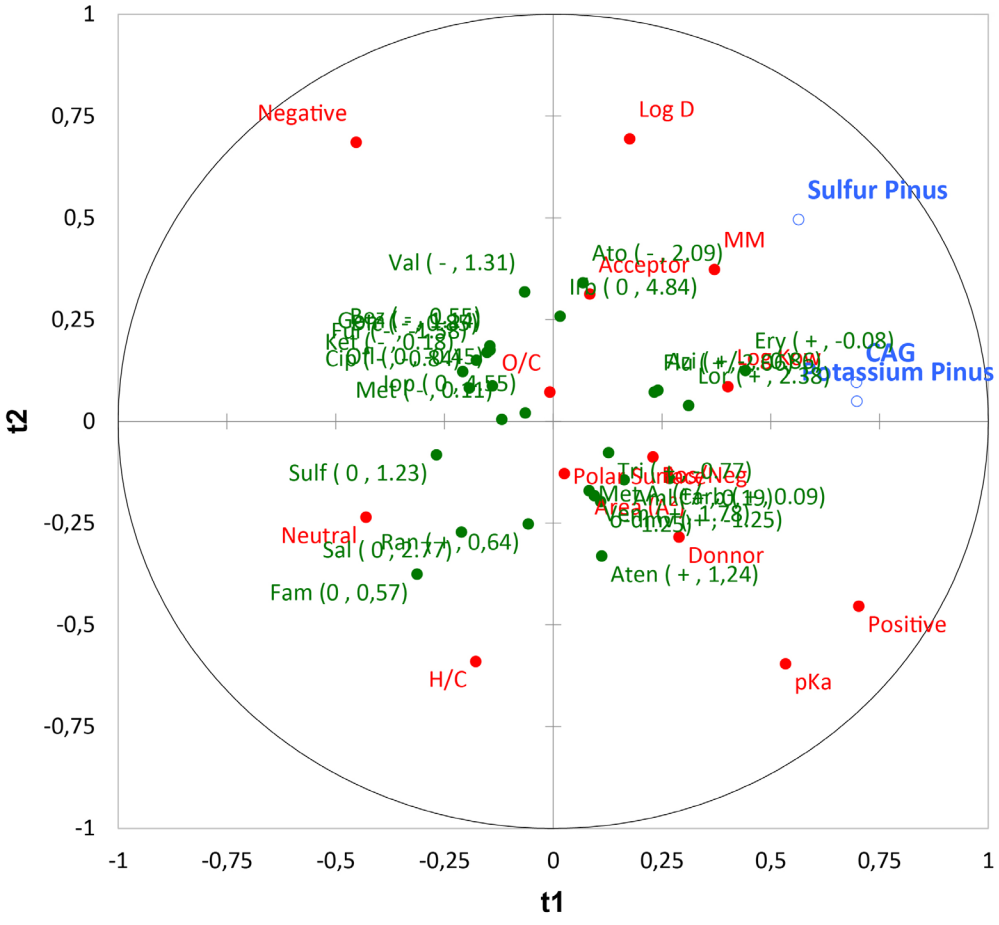
Figure 4 – The variables importance in the projection (VIPs) for the most explainable component at 95% of confidence.

and chemical characteristics of 27 compounds for their removal in 2 biosorbents and 1 commercial GAC.

The VIPs of the study characteristics over the pharmaceutical removal are shown in Figure 4. The higher the VIP, the higher its relevance in the adsorption of PhACs. As shown in Figure 4, the most important variable in the prediction of CECs removal, in order of its relevance, was as follows: the positively charged compound > MM > log K_{ow} > pKa.

The biplot of the PLS-R analysis with correlation matrices of adsorbent characteristics (denoted by red), adsorbent mean removal (denoted by blue), and pharmaceutical removals (denoted by green) is shown in Figure 5. The reason of the CAG and SP materials for being the best removals in the experimental study was explained by VIPs. The molecular effect was observed only for the SP material, with biplot showing very close to this variable.

The charge of the PhACs also has an impact on the removal efficiency. In case of experiments performed in spiked water, PhACs that, at the working conditions (pH 8), predominate as cationic (fluoxetine > loratadine > erythromycin > amlodipine > azithromycin > atorvastatin) were better removed than those as anionic (ketoprofen > diclofenac > furosemide) and



Source: Authors' elaboration, 2022.

Figures 5 – PLS-R biplot correlating the two autovectors t1 and t2.

neutral (famotidine > salbutamol > sulfamethoxazole > iopromide). An average removal was 58.4%, 34.4%, and 23.6% for cationic, anionic, and neutral compounds, respectively. However, the highest percentage removal (average of the three batch experiments) was observed for fluoxetine (128.91 ± 27.99%), while the lowest percentage removal was observed for iopromide (5.45 ± 9.00%), both being anionic and neutral compounds, respectively.

The most important VIP, based on the molecular physicochemical characteristics, was the cationic speciation (positive), followed by molecular weight (MW) and log K_{ow}. This confirmed that the cationic compounds are better adsorbed than anionic and neutral compounds. In competitive matrices, either the compounds or the adsorbent can play an important role. Therefore, further studies with the characteristics of the adsorbents are necessary.

The predictive average of the capability of the multiple linear regression mathematical models (both adsorbents) was 56% in the relationship between physicochemical characteristics of the target compounds and the removal of the pharmaceuticals in the experiment. The predictive power can be a powerful tool to predict removal scenarios depending on the characteristics of the target compounds and can be improved to better understand how to make an adsorbent with better removal capabilities.

The characteristics such as pKa, H/C ratio, and polar surface area are not related to the adsorbents, whereas the characteristics such as MW, cationic ionization, and log K_{ow} are more correlated with the materials.

As reported in the literature, oxygen acts as a good tool for the selection of an adsorbent material and has the potential to remove micropollutants (QUINLIVAN; LI; KNAPPE, 2005). However, this cannot be observed in this experiment. de Ridder *et al.* (2010) observed in their work on prediction of removal of micropollutants in activated carbon that there is a strong linear tendency between the removal and log K_{ow} of the study compounds. Kennedy *et al.* (2017) in their study on a full-scale WWTP removal prediction for CECs showed that statistical values depended more on the low concentrations than the background organic matter of the specific compound.

The PLS-R was extremely useful to preserve Pearson's relations between physicochemical characteristics and removals. It may facilitate the interpretation of the data. It can be pointed out that there are processes of exclusion of molecules with large molecular mass in adsorbents with low volume of mesopores and that oxygenated surfaces increase the efficiency of removal of the pharmaceuticals, especially the positively charged ones. The use of this technique in a similar application has been reported in the literature only a few times (FLYBORG *et al.,* 2017); however, none reported with such a large number of variables, considering the characteristics related to adsorption. This is a pioneer application in the observation of the preponderance of physicochemical characteristics in the removal of pharmaceuticals through adsorption into adsorbent materials.

PLS-R analysis is an excellent tool as it has the ability to access a large data matrix, directing the explanations of the phenomena involved through the VIPs. It is also possible to evaluate direct and private relationships through the biplot. The PLS-R analysis shows that the physicochemical properties of the pharmaceuticals are important in the adsorption of adsorbent material in complex aqueous solution. This study was the first to report the use of PLS-R analysis to analyze data matrices of micropollutant removal by adsorption in AC. Its predictive capability could be used to assist in the selection of future adsorbent materials.

CONCLUSIONS

The aim of this study was to assess whether pharmaceuticals removal by ecofriendly materials in spiked water is achievable, especially by observing the SP. Three different materials were included in the survey, and the target compounds were venlafaxine, salbutamol, iopromide, trimethoprim, ofloxacin, sulfamethoxazole, ciprofloxacin, metoprolol, azithromycin, carbamazepine, erythromycin, fluoxetine, loratadine, metoprolol acid, *O*-desmethylvenlafaxine, valsartan, furosemide, ketoprofen, irbesartan, diclofenac, gemfibrozil, atorvastatin, and bezafibrate. It was found that:

- The adsorption of pharmaceuticals adsorbent materials is a complex process governed by the properties of both the adsorbent and the adsorbed molecules. Even though a good average percentage removal was achieved, the influence of other organic compounds cannot be ignored and need to be studied further;
- Unfortunately, to obtain a good understanding of the interactions between the single chemical molecule and the adsorbents, it would be necessary to study the process for each compound separately from the others and then consider the matrix effect due to the mixing of various pharmaceuticals with very different properties.

The multivariate technique findings include:

- The technique can be used as an excellent tool, since it is able to summarize and perform with a large data matrix, directing the explanations of the phenomena involved through the VIPs, and it is also possible to evaluate direct and private relationships through biplot;
- The characteristics of the materials could be more relevant and explain more accurately the phenomena of adsorption of micropollutants, which needs to be studied and tested in PLS-R approach;
- The physicochemical characteristics of the molecules appear to be relevant in reaction medium that has strong competition with natural organic matter;
- It is the first time in the literature that the use of PLS-R to analyze data matrices of micropowder removal by adsorption in activated carbon, as also with lignocellulosic-based materials, has been reported. Its predictive power needs to be better exploited to assist in the selection of future adsorbent materials.

CONTRIBUIÇÃO DOS AUTORES

Alves, T.C.: Conceptualization, Data Curation, Formal Analysis, Writing – First Draft, Resources, Supervision, Validation, Visualization. Pinheiro, A.: Writing – Review and Editing. Rozza, G.: Research, Methodology, Project Management. Supervision, Validation, Visualization, Writing – First Drafting.

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