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Supported ionic liquids for the removal of cyclophosphamide from aqueous solutions

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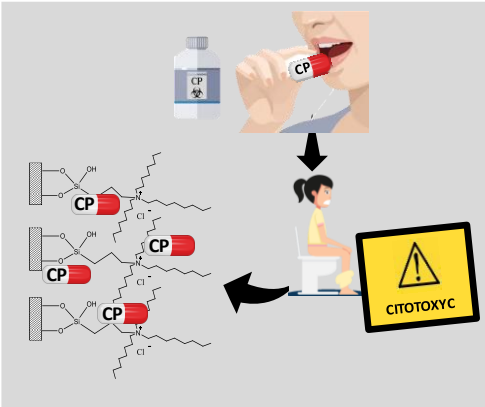

The incidence of cancer is increasing and with it also the consumption of anti-cancer drugs. As with other drugs, these compounds are not completely metabolized and are excreted through the urine, ultimately reaching waste water treatment plants (WWTPs). Anti-cancer drugs are emerging pollutants, reinforcing the need for developing effective treatment or removal strategies. This work aims to contribute to the development of an efficient material for the removal of anti-cancer drugs, namely cyclophosphamide (CP), from urine. This strategy envisages the removal of anti-cancer drugs at the entrance point to avoid the contamination of water streams. To this end, six supported ionic liquids (SILs) were synthesized and characterized. A preliminary study was carried out to address the efficiency of these materials for the removal of CP from aqueous solutions. Kinetic and adsorption isotherms were determined for the best materials, and future studies will be carried out with urine samples.

Nowadays, cancer is one of the most relevant causes of death worldwide. It is expected that the incidence of this disease will increase in the following years and, therefore, the use of anticancer drugs (cytostatics) will continue to rise. Oral therapy is being used as an alternative and/or complement to traditional chemotherapy, and therefore most of the cytostatic drugs are consumed by outbound patients [1]. Among these, cyclophosphamide (CP) is one of the most used cytostatic drugs to treat cancer – Figure 1.

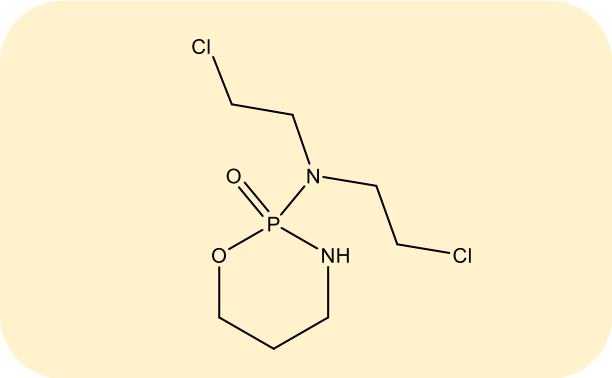

Figure 1. Molecular structure of cyclophosphamide (CP).

CP as well as other cytostatics are not completely metabolized by humans, being excreted by urine (ca. 25% of the consumed drugs) [2]. These compounds ultimately reach waste water treatment plants (WWTPs) that are unable to efficiently remove or treat them [3]. Thus, the development of materials that could be used as adsorbents of cytostatic drugs from the urine of oncologic patients, i.e. at their entrance point and before they reach WWTPs, is highly relevant to avoid the entrance of such pollutants into the environment.

The main objective of this work is to prepare and identify low-cost materials functionalized with ionic liquids capable of efficiently removing cytostatics from urine samples. Supported ILs (SILs) were already described as efficient materials to remove other pharmaceutical compounds, such as nonsteroidal anti-inflammatory drugs (sodium diclofenac, ibuprofen, naproxen, and ketoprofen) from aqueous samples [4], but were never investigated for the removal of cytostatic drugs. In this work, experiments were carried out with CP, as a main representative of cytostatic drugs. Six SILs (SilprMImCl, SilprNMe$_2$BzCl, SilprNEt$_3$Cl, SilprN(C$_8$)$_3$Cl, SilprNMe$_2$BuCl, SilprNBu$_3$Cl) were synthesized and characterized by SEM, ^{13}C solid NMR, elemental analysis and surface charge (pzc) assays. Preliminary adsorption studies (at a fixed drug concentration, material weight and solution volume) of CP from aqueous solutions were carried out to identify the most efficient SILs. After identifying the best SILs (SilPrNBu$_3$Cl, SilPrNEt$_3$Cl and SilPrN(C$_8$)$_3$Cl), kinetic and adsorption isotherms were determined. CP was quantified by DAD-HPLC in all experiments.

The experimental values obtained were adjusted to two kinetic models, in which the pseudo-second order model was found as the best model to describe the experimental data. The experimental values were also adjusted by two equilibrium isotherm models: the Langmuir model [5] and the Freundlich model [6]. The experimental results were better described by the Langmuir model, where the maximum concentrations of adsorbate in equilibrium in the solid phase (q_{mL}) were found to be 0.0161, 0.0173 and 0.0163 mg.g^{-1} for SilprNEt$_3$Cl, SilprNBu$_3$Cl, and SilprN(C$_8$)$_3$Cl, respectively. The results obtained show that these materials can effectively remove the studied drug from aqueous solutions. Further investigations on these materials performance, to remove cytostatic drugs from urine samples, are ongoing.

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