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ORIGINAL ARTICLE

A solid-phase extraction approach for the identification of pharmaceutical–sludge adsorption mechanisms

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Abstract It is important to understand the adsorption mechanism of chemicals and active pharmaceutical ingredients (API) on sewage sludge since wastewater treatment plants are the last barrier before the release of these compounds to the environment. Adsorption models were developed considering mostly hydrophobic API–sludge interaction. They have poor predictive ability, especially with ionisable compounds. This work proposes a solid-phase extraction (SPE) approach to estimate rapidly the API–sludge interaction. Sludge-filled SPE cartridges could not be percolated with API spiked mobile phases so different powders were tested as SPE sludge supports. Polytetrafluoroethylene (PTFE) was selected and tested at different PTFE/sludge ratios under eight different adsorption conditions with three API ionisable compounds. The PTFE/sludge mixtures with 50% or less sludge could be used in SPE mode for API sorption studies with methanol/water liquid phases. The results gave insights into API–sludge interactions. It was found that π–π, hydrogen-bonding and charge–charge interactions were as important as hydrophobicity in the adsorption mechanism of charged APIs on sludge.

1. Introduction

The fate and effects of active pharmaceutical ingredients (API) in the environment have raised the need for a risk assessment and safety evaluation. The requirement for environmental risk assessment was first triggered by pesticides and herbicides sprayed in fields and the environment [1] and then considered for humans active pharmaceutical ingredients (API) that could be released into the environment. Their molecular form or metabolites could affect living organisms, including humans even at very low concentrations [2].

Municipal and hospital wastewater treatment plants are important sources of release of pharmaceuticals into the environment

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[3,4]. Wastewater treatment plants are the last barriers before the pharmaceuticals are released into the aquatic environment. Some pharmaceuticals are not biodegraded by the wastewater treatment plant processes [5]. In this case, the API partitioning between the residual sludge and aqueous phase, K_d (the partition coefficient) is a key indicator to determine the fate of these pharmaceuticals in the environment. K_d is defined as the ratio of the concentration of the pharmaceutical in soil or sludge over its concentration in the aqueous phase:

$$K_d = [API]_{sludge}/[API]_{aq} \quad (1)$$

K_d measurement is time and resource consuming and existing soil models fail to provide accurate prediction for the partitioning into sewage sludge. Various soil models based on the organic carbon partitioning theory have been developed for different types of chemicals but not specifically for APIs or for ionisable compounds, with the largest model training set including 52 compounds [6]. A sludge model has been developed based on 10 hydrophobic compounds measured in sludge but none of them are APIs [7]. Sewage sludge is a complex matrix mainly made of organic matter and nutrients from residual solids produced during wastewater treatment [8]. Little is known about binding mechanisms occurring in sewage sludge.

The main assumption is that hydrophobic interactions are the key mechanism of interaction occurring in sludge. Most soil models are based on the organic carbon partition coefficient, K_{OC} and are converted to K_d via the fraction of organic carbon, f_{OC} in the sludge [9]:

$$K_d = K_{OC} * f_{OC} \quad (2)$$

The existing interaction models are mainly based on soil models. These models might be suitable for neutral organic compounds where hydrophobic interactions predominate. However, they fail to give reliable predictions for ionisable compounds. Many pharmaceuticals are ionisable compounds and therefore hydrophobicity may not be the only mechanism of interaction, hence the theoretical models become limited. The understanding of binding mechanisms in the sewage sludge matrix needs to be expanded [10–13]. More robust and accurate models for K_d predictions involving hydrophobic as well as more polar dipole, π–π and charge–charge (Coulomb) interactions must be built to predict the partitioning of APIs with sewage sludge, sediment and soil.

Solid-phase extraction (SPE) is a commercially available technique that uses a number of stationary phase chemistries to extract analytes from a wide variety of different liquid matrices [14]. The main advantage of SPE is its ease of use. SPE is not time consuming and generally requires only small volumes of extraction solvents. All interaction mechanisms can be used and combined offering possible mixed modes of interaction to favour the extraction of one class of compounds or another [15]. The selection of the stationary phase is associated with the desired class of compounds, hence the mechanism of interaction must be known [16].

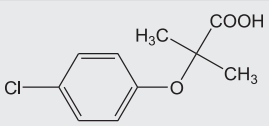
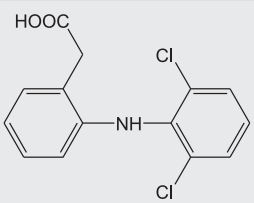
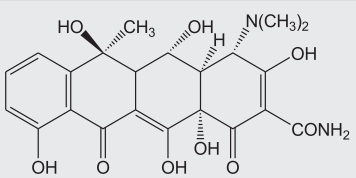
This work used the SPE technique to gain insights into the mechanism of interaction between APIs and sewage sludge. Three ionisable pharmaceuticals: clofibric acid, diclofenac and oxytetracycline, covering the range of low [17,18], medium [19] and high [20] K_d values, respectively, were selected for the study. The behaviour of these three pharmaceuticals was tested on commercially available SPE cartridges to order to obtain insights into the possible interaction mechanisms in the sludge. Sewage sludge could not be used directly as an SPE stationary phase as the aqueous eluent phase could not percolate through any wet sludge sample. To overcome this issue, various sludge–SPE packing mixtures were used as the stationary phase. Four SPE packing materials were tested as possible candidates. Bare silica was chosen for its well known packing properties in HPLC [16]. Silicon carbide was evaluated as it is used in many different environmental applications [20–22]. Polytetrafluoroethylene (PTFE or Teflon®) was selected for its very low polarity and non-adsorptive properties. Lastly, polyether ether ketone (PEEK) was chosen for its chemical stability, being commonly used as plastic connecting tubing in liquid chromatography.

2. Materials and methods

2.1. Chemicals and solvents

Clofibric acid (98.6%), diclofenac (99%) and oxytetracycline (97%) were all purchased from Sigma Aldrich (Gillingham. Dorset, UK) and were chosen for their acidic or zwitterionic character and their widespread and long term use explaining their frequent presence in the environment. The physico-chemical properties of the APIs are listed in Table 1. As seen by the pK_a values, clofibric acid and diclofenac are in a molecular form at low pH, such as pH 2 (condition 8) and in a negatively charged (carboxylate anion) form at intermediate and high pHs, such as pH 7.2 (condition 7). Oxytetracycline is a bulky compound always bearing charges: at low pH its tertiary amine group is positively charged. At pH 4.5, the isoelectric

Table 1 Physico-chemical properties of the three active pharmaceutical ingredients used as test solutes.

Compound	Clofibric acid	Diclofenac	Oxytetracycline
Structure			
Pharmaceutical class	Lipid regulator	Analgesic, anti-inflammatory	Antibacterial, antibiotic
MW	215	296	460
Log K_{ow}[a]	2.7	4.1	1.6
pK_a	3.0	4.15	3.3, 7.3, 9.1
Log K_d	1.5 [16]	1.5–2.7 [16,17]	3.5 [18]

[a]Predicted by ACDLab program.