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Adsorption of ethinylestradiol (EE2) on polyamide 612: Molecular modeling and effects of water chemistry

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ABSTRACT

This study demonstrates that ethinylestradiol (EE2), a priority estrogenic contaminant in water, can be rapidly and selectively removed from aqueous solutions using industrial-grade polyamide 612 (PA612) particles as adsorbents. Isothermal studies showed that non-porous low surface area (20 $m^2\ g^{-1}$) PA612 particles had a maximum adsorption capacity of 25.4 mg g^{-1} for EE2 in water, which is higher or comparable to the results obtained with two benchmark activated carbon (AC) adsorbents (10.4–27.6 mg g^{-1}). The adsorption of EE2 on PA612 followed pseudo-second order kinetics with a high adsorption rate exceeding those of the ACs by 5.3- to 22.4-fold. Computational chemistry calculations and molecular modeling showed that the strong binding affinity between EE2 and PA612 originates from the hydrophobic partitioning of EE2 solutes and hydrogen bonding interactions on PA612 amide groups. PA612 showed high adsorption selectivity for EE2 in water with highly consistent adsorption capacities for EE2 under the influence of a range of water chemistry parameters, including water salinity (NaCl, 1 mM–1 M), metal ions (K(I), Ca(II), and Zn(II); 0.1 M), natural organic matter (humic acids, 0.2–5 mg L^{-1}), and pH level (4.8–9.1).

1. Introduction

Ethinylestradiol (EE2) is a synthetic hormone that is extensively used in modern formulations of combined oral contraceptives and hormone replacement therapy for treatment of osteoporosis, menstrual disorders, and prostate cancer (Datapharm, 2008; USFDA, 2012a). A survey on best-selling drugs published by Pharmacy Times® in 2010 found that EE2 was used as an active pharmaceutical ingredient in five of the top 200 prescribed drugs in the U.S. under the brand names of Ortho Tri-Cyclen® Lo 28, Loestrin® 24 Fe, TriNessa® 28, Ocella®, and Yaz® 28 (Bartholow, 2011). Orally ingested EE2 undertakes extensive metabolism in liver, principally via oxidation at C17 ethinyl triple bond and aromatic hydroxylation at C2/C4 on steroid nucleus, prior to excretion via urine and feces. Human metabolism transforms EE2 into biologically inactive sulfate and glucuronide forms (Bolt, 1979); however, partial degradation in sewage treatment plants (STPs) and natural environment deconjugates EE2 metabolites and renders them estrogenically active again (Limpiyakorn et al., 2011). In fact, treated sewage effluents constitute the major source of environmental EE2 due to the inadequate removal of EE2 in STPs (Braga et al., 2005; Desbrow et al., 1998; Johnson and Sumpter, 2001). Field surveys have frequently

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detected EE2 in STP effluents and natural waters receiving inputs from STPs (Kolpin et al., 2002; Williams et al., 2007; Ying et al., 2002).

The presence of EE2 in environmental waters has raised international concerns due to its ultra-high estrogenicity and ubiquitous occurrence. The Endocrine Disruptor Knowledge Base (EDKB) (USFDA, 2012b), which is jointly published by the U.S. Food and Drug Administration (FDA) and National Center for Toxicological Research, identifies EE2 as the most potent estrogenic chemical in all endocrine-disrupting chemicals discovered to date. Endocrine-disrupting effects of EE2, both *in vivo* (Thorpe et al., 2003) and *in vitro* (Harris et al., 2011; Thorpe et al., 2009; Vajda et al., 2008), have been observed in freshwater fish species in both laboratory and field studies at low nanogram per liter levels. Environmental benchmark concentration as low as 0.35 ng L^{-1} has been recommended for EE2 in water bodies to prevent vitellogenin induction in freshwater fish species (Caldwell et al., 2008). With more scientific evidences being established from ongoing research, water authorities have generally adopted a precautionary approach for EE2 as a priority estrogenic contaminant in water (Blockwell et al., 2007; Middleton et al., 2008; Owen and Jobling, 2012). In January 2012, the European Commission announced a proposal to limit EE2 in European water bodies to an annual average below 0.035 ng L^{-1} under its Water Framework Directive, which has sparked wide debate due to the potentially high treatment costs (McKie, 2012; Owen and Jobling, 2012; Worstall, 2012). In Australia, the risk of human exposure to EE2 through affected drinking water is a realistic concern in water-stressed regions where drinking water supply is augmented by recycled water produced from municipal wastewater effluents (Ying et al., 2004). The Australian Guidelines for Water Recycling recommend a maximum level of 1.5 ng L^{-1} EE2 in drinking water augmented with recycled water, which represents the lowest threshold in a suite of ten targeted estrogens due to the high estrogenicity of EE2 (Middleton et al., 2008).

Adsorption is a proven technology that has found wide application in water treatment and purification (Degrémont, 2007). The appeal of this technology can be attributed to its generally low cost and reliable performance. Rapid adsorptive interactions often enable instantaneous removal of contaminants from source water on a continuous-flow basis, and high production rates can be achieved with good system hydrodynamics. Activated carbon (AC) is by far the most widely used adsorbent in water treatment applications, and has been recently studied for the removal of estrogens from water (Clouzot et al., 2008; Ho et al., 2011; Silva et al., 2012). ACs generally exhibit high adsorption capacities for contaminants in water due to their porous microstructures and resultant large surface areas (Bansal and Goyal, 2005). Nevertheless, the regeneration of exhausted AC adsorbents often proves to be a difficult task. The common industry practice is to either dispose used AC adsorbents to landfill sites or send them to specialized off-site AC regeneration plants where thermal or steam reactivation is carried out at high temperatures (600–950 °C) (Marsh and Rodríguez-Reinoso, 2006; Norit, 2010; Wang et al., 2005).

In our recent work we developed a reversible polymeric adsorption process for the removal of EE2 from water using industrial-grade nonporous aliphatic polyamide particles (Han et al., 2012a). The high adsorption capacity of polyamide 612 (PA612) for EE2 was noted in comparison to a macroreticular polymeric adsorbent and an extensive range of literature data on the adsorption removal of EE2 from water. In this work, we aim to gain a fundamental understanding of the adsorption mechanisms and further demonstrate the high adsorption capacity, fast adsorption kinetics, and adsorption selectivity by testing the PA612 adsorption process under the influence of a range of water matrix constituents. Molecular characteristics of EE2 and PA612 amide groups were studied by quantitative structure–property relationship (QSPR) analysis. Intermolecular hydrogen bonding interactions between EE2 and PA612 were studied in an aqueous environment by quantum mechanical modeling. To put the results into context, the adsorption characteristics of PA612 were comparatively studied with two benchmark AC adsorbents for the removal of EE2 from water. The high adsorption capacity and fast adsorption kinetics of EE2 on PA612 were highlighted, and the PA612 adsorption process was tested under the influence of a range of representative water chemistry parameters at or above environmentally relevant conditions.

2. Experimental

2.1. Materials and reagents

PA612 (Orgasol® 3501) and AC adsorbents (Darco® 12 × 20 and Norit® 1240W) were supplied by Arkema Inc. (France) and Norit B.V. (The Netherlands), respectively. Ethinylestradiol (CAS No. 57-63-6, ≥98%), humic acids (technical grade), disodium hydrogen phosphate (Na_2HPO_4, ≥99%), citric acid (99%), sodium hydroxide (NaOH, 97%, powder), and trifluoroacetic acid (TFA, HPLC, ≥99%) were purchased from Sigma–Aldrich. Potassium chloride (KCl, reagent grade), sodium chloride (NaCl, reagent grade) were supplied by Scharlau Chemie. Calcium chloride ($CaCl_2$, ≥93%) and magnesium chloride ($MgCl_2$, H_2O wt.% <5%) were purchased from Sigma–Aldrich. Zinc nitrate hexahydrate ($Zn(NO_3)_2 \cdot 6H_2O$, reagent grade) was purchased from Ajax Finechem.

2.2. Adsorption isotherms and kinetics

Agitated batch adsorption experiments were conducted to establish the adsorption equilibrium of EE2 on PA612 and AC adsorbents. The aqueous solubility of EE2 is 9.2–9.7 mg L^{-1} at 25 °C under pH neutral condition (Hurwitz and Liu, 1977; Shareef et al., 2006). EE2 working solutions were diluted from 0.02 mM EE2 stock solutions with measured concentrations of 5.8–6.1 mg L^{-1}. Adsorbents were added into a series of EE2 aqueous solutions (30–3000 μg L^{-1}, ca. 0.1–10 μM) at a constant dosage of 0.2 g L^{-1}. The mixed solutions were agitated at 250 rpm in an incubator shaker for 24 h to reach adsorption equilibrium at 25 °C. The adsorption kinetics of EE2 was studied by adding PA612 or AC adsorbents into 500 mL of EE2 solution (200 μg L^{-1}) at a dosage of 0.2 g L^{-1}. The solution was then agitated at 250 rpm for 8 h while samples were collected intermittently to monitor the EE2 concentration in the solution. All samples were immediately filtered by 0.2-μm regenerated cellulose filters (13 mm, Phenomenex) prior to chromatography analysis. In a set of control experiments, EE2 adsorption in