Available online at www.sciencedirect.com
ScienceDirect
Chemosphere 69 (2007) 1765–1774
CHEMOSPHERE
www.elsevier.com/locate/chemosphere

Fate of cancerostatic platinum compounds in biological wastewater treatment of hospital effluents

Katharina Lenz [a,b], Gunda Koellensperger [a], Stephan Hann [a,*], Norbert Weissenbacher [b], Susanne N. Mahnik [b], Maria Fuerhacker [b]

[a] *Department of Chemistry, Division of Analytical Chemistry, University of Natural Resources and Applied Life Sciences, Muthgasse 18, A-1190 Vienna, Austria*

[b] *Institute of Sanitary Engineering and Water Pollution Control, University of Natural Resources and Applied Life Sciences, Muthgasse 18, A-1190 Vienna, Austria*

Received 14 February 2007; received in revised form 24 May 2007; accepted 25 May 2007
Available online 10 July 2007

Abstract

The present work focuses on the fate of two cancerostatic platinum compounds (CPC), cisplatin and carboplatin, as well as of two inorganic platinum compounds, $[PtCl_4]^{2-}$ and $[PtCl_6]^{2-}$ in biological wastewater treatment. Laboratory experiments modelling adsorption of these compounds onto activated sludge showed promising specific adsorption coefficients K_D and K_{OC} and Freundlich adsorption isotherms. However, the adsorption properties of the investigated substances were differing significantly. Adsorption decreased following the order cisplatin > $[PtCl_6]^{2-}$ > $[PtCl_4]^{2-}$ > carboplatin. Log K_D-values were ranging from 2.5 to 4.3 , log K_{OC} from 3.0 to 4.7.

A pilot membrane bioreactor system (MBR) was installed in a hospital in Vienna and fed with wastewater from the oncologic inpatient treatment ward to investigate CPC-adsorption in a sewage treatment plant. During three monitoring periods Pt-concentrations were measured in the influent (3–250 μg l^{-1} Pt) and the effluent (2–150 μg l^{-1} Pt) of the treatment plant using ICP-MS. The monitoring periods (duration 30 d) revealed elimination efficiencies between 51% and 63% based on averaged weekly input–output budgets. The derived log K_D-values and log K_{OC}-values ranged from 2.4 to 4.8 and from 2.8 to 5.3, respectively. Species analysis using HPLC-ICP-MS proofed that mainly carboplatin was present as intact drug in the influent and – due to low log K_D – in the effluent of the MBR.

Keywords: Hospital wastewater; Cancerostatic platinum compounds; Activated sludge; Adsorption

1. Introduction

Cancerostatic platinum compounds (CPC) are very successfully used in anti-cancer chemotherapy (Roberts and Thomson, 1979; Kuemmerer and Helmers, 1997; Desoize and Madoulet, 2002). However, they are regarded as one important anthropogenic source of platinum in the environment. Although these substances represent a minor fraction of platinum compared to emissions from car catalytic converters, they have a significantly higher toxicological and cancerogenic impact than catalyst-born inorganic platinum. The most frequently used CPC cisplatin (*cis*-diaminedichloroplatinum(II)) is classified as probably carcinogenic to humans (group 2A) by the International Agency for Research on Cancer (IARC, 1987). Carboplatin (*cis*-diammine 1,1-cyclobutanedicarboxylato-platinum(II)) and oxaliplatin ([(1R,2R)-1,2cyclohexanediamine-*N*,*N*′]oxalate(2-)-O, O′-platinum), the two other frequently administrated divalent square-planar platinum-complexes may be carcinogenic as well (Luo et al., 1999; Gebel, 2000).

After administration during anti-cancer chemotherapy, considerable portions of the CPC are eliminated via the patients' urine (Vermorken et al., 1984; Elferink et al., 1987; Graham et al., 1998; Allen et al., 1998) and reach the wastewater. However, so far only few studies dealt with the

* Corresponding author. Tel.: +43 1 36006 6086; fax: +43 1 36006 6059.
E-mail address: stephan.hann@boku.ac.at (S. Hann).

0045-6535/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.chemosphere.2007.05.062

fate of CPC in the wastewater system. Preliminary investigations indicated that the most plausible mechanism of CPC-elimination from the liquid phase was adsorption to activated sludge during wastewater treatment (Lenz et al., 2005a).

The European Community bans the discharge of chemicals and metabolites with carcinogenic or mutagenic potential into the wastewater system (Council Directive 80/68/EWG, 1991; Council Directive 76/464/EWG, 2000). In wastewater from oncologic in-patient treatment wards cytostatic agents and many other pharmaceuticals are present in highly concentrated form, which facilitates their systematic elimination. Accordingly, wastewater treatment at the major CPC source, i.e. the hospitals is crucial, since separate collection and treatment of oncologic wastewater might be the most effective approach of elimination. However, since the number of outward cancer treatment is increasing CPC-loads excreted into municipal wastewater should not be disregarded (Mahnik et al., 2002).

As the chemical and toxicological properties of CPC are strongly related to their chemical form (Miller and House, 1989a,b, 1990), CPC – metabolism in the water cycle is of major importance for the behaviour and elimination of CPC in sewage treatment plants. Based on the results of recent studies concerning CPC in patient excretions and CPC metabolism in the sewage system (Tang et al., 1997; Graham et al., 2000; Hann et al., 2003; Hann et al., 2005), it can be assumed, that 75% of the administered amount of cisplatin enters sewage treatment as highly active *cis*-$[PtCl(H_2O)(NH_3)_2]^+$ (monoaquacisplatin). Because of its stability in model experiments simulating wastewater, carboplatin is expected to reach sewage treatment as parent drug, whereas oxaliplatin is supposed to be exclusively present as biotransformation products. Hence, only for cisplatin and carboplatin laboratory experiments with the parent drugs and different amounts of chloride are representative for these compounds in wastewater (Hann et al., 2005).

In the present work adsorption of cisplatin, carboplatin and two inorganic platinum compounds, $[PtCl_4]^{2-}$ and $[PtCl_6]^{2-}$ was addressed by laboratory batch experiments with activated sludge. Moreover, for the first time CPC-adsorption to activated sludge was investigated in a pilot membrane bioreactor system (MBR), which was fed with wastewater from the oncologic in-patient treatment ward of a hospital in Vienna. In addition to the detection of the total amount of platinum, species analysis was performed in selected samples. The aim of the present paper was the investigation of the fate (metabolism, adsorption) of CPC in biological wastewater treatment and the assessment of a MBR as a selective method for elimination of high concentrations of CPC in hospital wastewater.

2. Materials and methods

2.1. Standards and reagents

Cisplatin, $[PtCl_4]^{2-}$ and $[PtCl_6]^{2-}$ were obtained from Sigma-Aldrich (Schnelldorf, Germany), Carboplatin was purchased at British Pharmacopoeia Chemical Reference Substance (Stanmore, UK). Purified water obtained using a reagent I grade water (>18 $M\Omega\,cm^{-1}$ according to ISO 3696 water specifications) purification system (HQ, USF, Vienna, Austria) was further purified in a quartz sub-boiling system (Milestone-MLS, Leutkirch, Germany). For preparation of HPLC eluents suprapure formic acid (VWR, Darmstadt, Germany), sub-boiled ammonium hydroxide (Aldrich, Milwaukee, WI, USA) and methanol (HPLC gradient grade, VWR) were used. Stock solutions containing chloride were prepared using sodium chloride (VWR). Analytical reagent grade HCl (37%, VWR), used for decomposition and sample stabilisation and HNO_3 (65%, VWR), used for decomposition were additionally cleaned by sub-boiling distillation in an ultrapure quartz apparatus (Milestone-MLS, Leutkirch, Germany). Calibration standards for determination of the total amount of platinum were prepared by diluting a 1000 $mg\,l^{-1}$ Pt single element standard solution (VWR). A 1000 $mg\,l^{-1}$ indium single element standard solution (Standard for ICP, VWR) served as internal standard for the analysis of platinum by ICP-MS. All solutions and eluents were prepared using ultrapure sub-boiled water. All bottles used were made of polyethylene (PE) except of HPLC-eluent containers, which were made of glass.

2.2. Laboratory adsorption experiments

Two test series were carried out with two replicates per each sample. The experiments were performed using PE-bottles, which were, in a first step, investigated for both, possible platinum adsorption and possible platinum contamination. For investigations on platinum adsorption the PE-bottles were filled with HQ-water, charged with different concentrations of the investigated substances (30–3000 $\mu g\,l^{-1}$), and agitated for 24 h. For investigations on possible platinum contamination the PE-bottles were filled with municipal wastewater (Pt-concentration < limit of detection) and agitated for 24 h. The experiments showed that both, platinum adsorption and contamination via the used PE-bottles was negligible.

In the first series, PE-bottles containing 40 $mg\,l^{-1}$ of municipal wastewater were charged with 0.35 $g\,l^{-1}$ activated sludge (dry weight). Prior to incubation the investigated platinum compounds were added to the wastewater in terms of stock solutions resulting in varying initial concentration (from 30 up to 3000 $\mu g\,l^{-1}$ of each substance). Stock solutions (1 $mg\,ml^{-1}$ of each platinum compound) comprising 61 $mg\,l^{-1}$ chloride were used at the age of at least 48 h. The chloride concentration and age of the solutions have been chosen, since the resulting species distribution represents the best simulation of hospital wastewater containing excretions of patients treated with cis- and carboplatin. In a solution containing 50 $mg\,l^{-1}$ Cl^- cisplatin is present as 31.5% cisplatin, 61% as the sum of $[PtCl(H_2O)(NH_3)_2]^+$ (monoaquacisplatin) and *cis*-$[PtCl(OH)(NH_3)_2]$ (monohydroxocisplatin), and 7.5% as the sum of *cis*-$[Pt(H_2O)_2$-