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# Pt–$TiO_2$-assisted photocatalytic degradation of the cytostatic drugs ifosfamide and cyclophosphamide under artificial sunlight

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## HIGHLIGHTS

- Ifosfamide and cyclophosphamide were photooxidized at Pt–$TiO_2$ under solar light.
- The photocatalytic oxidation of drugs were more effective for Pt–$TiO_2$ then $TiO_2$.
- Photocatalytic oxidation of IF and CF occurred in the different pathways.
- The main oxidants in the photocatalytic oxidation were hydroxyl radicals in bulk solution.

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## ABSTRACT

The aim of this work was to develop an effective photocatalytic technique for the removal of two cytostatic drugs from water. To this end, the kinetics, efficiency and decomposition pathway of the photocatalytic decay of ifosfamide (IF) and cyclophosphamide (CF) was investigated. The samples of Pt-doped (0.15 at.%) and undoped $TiO_2$ photocatalysts were prepared by a simple sol–gel method and then structurally characterized. The effects of operating parameters such as loading of photocatalyst, drug concentration, and photoactivity in solar and visible light were studied. The degradation processes in both drugs followed a pseudo-first-order kinetics. A degradation mechanism was proposed based on the identification of inorganic intermediates ($NH_4^+$, $Cl^-$, $PO_4^{3-}$) and organic by-products. The results showed that $PO_4^{3-}$ ions released during the decomposition of drugs were adsorbed on the photocatalyst, but this phenomenon had no negative effect on its photoactivity. The experimental results of the reactive species quenching showed that ·OH radicals were the predominant oxidant species participated in reaction, and the oxidation of drugs occurred in the bulk solution. Moreover, Pt-doped $TiO_2$ was more effective at generating ·OH radicals than $TiO_2$, probably due to the significantly promoted electron/hole separation in the modified photocatalyst. The results also demonstrated that the decomposition pathways of IF and CF differed.



## 1. Introduction

The number of patients receiving anticancer chemotherapy treatment based on cytostatic drugs is steadily increasing. Because the majority of anticancer compounds cannot be eliminated through conventional wastewater treatment processes, these compounds are often detected in the influents of WWTP [1–3]. Cyclophosphamide (CF) and ifosfamide (IF) are among the most frequently used anticancer agents [4,5]. IF and CF were detected in untreated and treated wastewater at concentrations of 0.3–100 ng/L [1,6,7]. Furthermore, the aforementioned drugs at a concentration of ~100 ng/L did not degrade during a 24-h incubation in activated sludge. The low adsorption potential of activated sludge is also to be expected because of the low octanol–water partition coefficient of cytostatic drugs (log Kow for CF and IF is 0.63 and 0.86, respectively). Ternes et al. [8] confirmed that there was almost no adsorption of CF and IF on the primary activated sludge of WWTP. Due to the above, the concentration of cytostatic drugs in surface waters is expected to rise. It is a disturbing trend since these compounds are classified as carcinogens (IARC) and pose a potential risk to the ecosystem and human health. The exposure concentrations of cytostatic drugs are several orders of magnitude lower than the concentrations at which acute eco-toxicological effects have been reported. However, one major concern with

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antineoplastics is the possibility that the cancer risk may exist at any level of exposure. Limited knowledge is available on the chronic health effects related to the consumption of drinking water containing trace amounts of pharmaceuticals or their metabolites. For all the above reasons, these compounds should be removed from water. The application of non-biological procedures, such as advanced oxidation processes (AOPs), may be a possible solution to this problem. Among AOPs, ozonation [9], UV/$H_2O_2$, UV/$Fe^{2+}$/$H_2O_2$ [10], photocatalysis with commercial $TiO_2$ [5,11], and electrolysis at a BDD anode [12] have been proposed as treatments for the cytostatic drugs IF, CF, 5-FU, trofosfamide and metotrexate. In the case of cyclophosphamide, its degradation rate constant in ultrapure water with molecular ozone was low ($kO_3 = 3.3 \pm 0.2\ M^{-1}\ s^{-1}$), while the extent of oxidation was linearly correlated to ozone exposure. The kinetic rate constant for the reaction of cyclophosphamide with hydroxyl radicals was estimated at $2.0 \times 10^9\ M^1\ s^1$ [13].

On the other hand, $TiO_2$-assisted photocatalytic degradation showed a remarkable effect on the degradation of drug dissolved in ultrapure water. The results demonstrated that commercially available $TiO_2$ photocatalyst (Degussa P-25) efficiently removed IF within 10 min in deionized water at environmentally relevant drug concentrations of 100 μg/L under UV-A light irradiation. The study conducted to elucidate the photocatalytic oxidation mechanism revealed that ·OH free radicals were the primary reactive oxygen species responsible for the degradation of oxazaphosphorine drugs (IF and CF). At higher initial oxazaphosphorine concentrations (20 mg/L), although the target compounds were completely degraded, >50% of TOC remained after 6 h of reaction time, indicating that several by-products formed.

The previous published study investigated the photocatalytic oxidation of CF and IF in the presence of commercial photocatalyst P-25. However, $TiO_2$ is only photoactive under the UV light irradiation due to its wide band gap energy (3.20 eV for anatase). Therefore, the modification of $TiO_2$ aimed at reducing the band gap of the photocatalyst, which should increase its quantum efficiency in the visible light region, is beneficial [14]. The doping of $TiO_2$ with a noble metal [15] allows us to extend the light absorption of the band gap in this semiconductor to the visible light, and to enhance the photo-conversion yield by inhibiting the electron hole recombination [16]. However, the efficient absorption of visible light does not appear to be a decisive factor that determines the visible-light photocatalytic activity of Pt–$TiO_2$. The visible-light absorption is clearly necessary to initiate photoreactions, but the visible-light photocatalytic activity of catalytic material also appears to be substrate-dependent [17].

In this paper, we present the Pt-doped $TiO_2$ photocatalyst with the low amount of dopant (0.15 at.%) obtained by a simple sol–gel method. We also describe the photocatalytic activity of this catalyst in relation to the degradation of two cytostatic drugs. The activity of Pt–$TiO_2$ photocatalyst was compared to undoped $TiO_2$. The drug decomposition process was studied under simulated sunlight and visible light. The degradation mechanism and the formation of by-products were investigated in detail. To our knowledge, this is the first comprehensive investigation of the photocatalytic oxidation of cytostatic drugs in Pt–$TiO_2$/solar light photocatalytic system.

## 2. Experimental methods

### 2.1. Chemical materials

Titanium (IV) isopropoxide (97%) was obtained from Aldrich Chemical, while 99% pure $H_2PtCl_6$ (Aldrich Chemical) was used as platinum source in the preparation procedure without further purification. *Para*-benzoquinone was obtained from Sigma–Aldrich (Steinheim, Germany), while 2-propanol was purchased from Chempur (Poland). The standards of ifosfamide (IF) and cyclophosphamide (CF) were purchased from Sigma–Aldrich (Steinheim, Germany). Acetonitrile (ACN) was HPLC grade, while sodium sulfate, sodium chloride, NaF, acid sulfate, sodium hydroxide, potassium phosphate, potassium nitrate, and ammonium sulfate were obtained from POCH S.A. (Gliwice, Poland).

### 2.2. Synthesis of Pt–$TiO_2$

Pt–$TiO_2$ photocatalyst was prepared by the standard sol–gel method. A volume of 50 ml titanium (IV) isopropoxide was added by drops to 0.14 g of the dopant precursor hydrogen hexachloroplatinate(IV) hexahydrate dissolved in 100 mL of distilled water. The solution was stirred for 1 h at room temperature, and then dried for 24 h at 80 °C and calcinated for 2 h at 400 °C. Undoped $TiO_2$ powder was prepared according to the above procedure, except for the addition of $H_2PtCl_6$. To remove the residue $Cl^-$ ions, Pt–$TiO_2$ was mixed for 24 h with distilled water. The concentration of $Cl^-$ ions released from the prepared catalyst equaled 0.2 mg per 1 g of Pt–$TiO_2$.

### 2.3. Characterization of Pt–$TiO_2$

The crystal structure of the Pt–$TiO_2$ powder samples was examined by X-ray diffraction (XRD) using a diffractometer (DRON-3) with Cu Kα radiation. The measurements of surface area were carried out by the Brunauer–Emmett–Teller (BET) method using gaseous $N_2$ (Micromeritics Gemini). The morphological and elemental composition analysis of the photocatalyst were performed by scanning electron microscopy (S-3400N, HITACHI, Japan) with a tungsten source and variable chamber pressure (VP-SEM) equipped with EDX (energy dispersive X-ray spectroscopy). The secondary electrons mode was utilized with an accelerating voltage of 20 kV. The UV–vis diffuse reflectance spectra (DRS) were obtained by means of a Shimadzu UV-2101PC spectrophotometer. The photoluminescence spectrum (PL) of the catalyst was obtained by LS-5OB Luminescence Spectrophotometer equipped with the Xenon discharge lamp as an excitation source, and a R928 photomultiplier as a detector. Obtained samples were excited with 320 nm. The excitation radiation was falling on the sample surface at an angle of 90°. Additionally, the emission filter was applied to block UV radiation about 390 nm.

### 2.4. Photocatalytic apparatus setup

The photocatalytic experiments were performed in a 50-ml batch reactor equipped with a magnetic stir bar. The reactor was placed in a Suntest CPS+ solar simulator (Atlas Matrial Testing Technology LLC) equipped with cooling system, a Xe-arc lamp as the light source and UV special Glass filters to mimic solar irradiation, where $\lambda > 290$ nm (550 W/$m^2$). In some experiments, a filter was utilized to block the wavelengths shorter than 420 nm (visible light). The temperature was maintained at 25 °C. The removal of IF or CF from the aqueous environment was estimated by measuring decomposition rates of both drugs during irradiation in the presence of an appropriate amount of photocatalyst. In order to catalyze the reaction, $TiO_2$, Pt–$TiO_2$ were used. Prior to irradiation, the suspension was stirred in the dark for 30 min to reach the adsorption equilibrium between the photocatalyst surface and the target compounds. One-milliliter aliquots of the aqueous suspension were collected at regular time periods during irradiation and then filtered through 0.22 μm syringe filters to remove the photocatalyst particles. The concentrations of IF and CF were esti-