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PHOTOCHEMISTRY OF THREE SELECTED PHARMACEUTICALS IN SEAWATER AND RIVER WATER

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ABSTRACT

The aim of these work was to study the direct photolysis of three pharmaceuticals with relatively high potential ecological risk and high consumption-namely, fluconazole, bicalutamide and anastozole promoted by photochemical processes. By conducting experiments in Milli Q water, Baltic Sea Water and Olandsån River Water. To evaluated this process under laboratory conditions, used chemical actinometer for sunlight measurements. The actinometer is the known bicalutamide, fluconazole and anastozole the half life in sunlight ranging from several minutes to 120 minutes. The systems were relatively persistent against sunlight. It has quantum yield invariant with wavelength to 261 nm for fluconazole 271 nm for bicalutamide and 269 for anastozole.

Keywords: Fluconazole, Bicalutamide, Anastozole, Photolysis, Seawater, River water.

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Contribution/ Originality

This study uses new estimation methodology developed by Q-TOF. This study originates new formula of analysis method. This study is one of very few studies which have investigated photolysis of pharmaceuticals. The paper contributes the first logical analysis of the problems solves about pollution of pharmaceuticals in aquatic environment. The paper's primary contribution is finding that pharmaceuticals behavior in the aquatic environment. This study documents to support by YÖK and Stockholm University.

1. INTRODUCTION

Pharmaceuticals have started to attract public attention since the late 1990s [1, 2]. These compounds are excreted as metabolites and unchanged after consumption and may find their way to the environment through discharge of treated and untreated wastewater. It is very difficult to know which of these might pose a threat to aquatic environment. Photodegradation of pharmaceuticals is an area of growing concern. In 2005, the US Pharmacopedia listed over 250

drugs that require protection from ultraviolet (UV) and visible light [3]. Moreover, photolysis of pharmaceuticals has been investigated over the 10 years by several researchers; the β-blocker propranolol [4], acetaminophen, atenolol, carbamazepine, ibuprofen, ifenprodil, indomethacin, mefenamic acid, propranolol [5] and the anti-inflammatory drug diclofenac [6].

Several authors reported the light sensitive of the selected pharmaceuticals (e.g. quinolones, tetracyclines, sulphonamides, tylosin, nitrofuran). However, not all compounds are photo-degradable [7]. Sulphanic acid was found as a degradation product common to most of the sulpha drugs. In the study reports of Boree, et al. [8], photo-degradation of these drugs in natural water samples (e.g. Lake Superior) was attributed solely to direct photolysis [8].

Pharmaceuticals can undergo abiotic transformations in surface waters via hydrolysis and photolysis. As the majority of pharmaceuticals designed for oral intake are resistant to hydrolysis, the photolysis appears as the primary pathway for their abiotic transformation in surface waters [9].

Fluconazole belongs to a class of drugs called azole antifungals. It is used to prevent and treat a variety of fungal and yeast infections. In Sweden, approximately 121 kg of fluconazole is used per year. This figure is based on Apoteket AB`s sales during 2007. Based on the Swedish sales value for fluconazole, in combination with the daily defined dose, the predicted environmental concentration in surface water was calculated to be 20 ng/L according to the European Medicines Agency [9]. Anastrozole is effective and well tolerated in the treatment of advanced breast cancer. Anastrozole total amounts consumed were of 31.70 kg in 2008 [10]. In Sweden, anastrozole consumptions reached 3,12 kg/year in 2008. Bicalutamide is one of the leading non-steroidal anti-androgens used for treatment of prostate cancer. Prostate cancer is the most common cancer of men in the UK and approximately 606.37 kg of bicalutamide is clinical used per year [11]. In France, Bicalutamide total amounts consumed were of 863 kg in 2008 [10]. In Sweden, 300.74 kg bicalutamide sold in 2008 [12]. Despite their regular use, very little information is availabre presently regarding the presence or absence of Bicalutamide in STW effluents or the wider aquatic environment. Pharmaceuticals were initially identified in the mid 1970s associated with waste water treatment plants effluents. Table1. represents that summary of the data on the occurance of fluconazole and anastrozole in the Environment. Kahle et al, 2008 reported that fluconazole was found in all investigated WWTP influents at concentrations between 10 and 110 ngL^{-1} in Swiss STP [13]. Lindberg [14], reported that fluconazole is released at significant levels into the aquatic environment [14]. It was detected (at concentration ranging from 90 to 140 ngL^{-1}) in both raw sewage water and final effluent in Swedish sewage treatment plants. Anastrozole is reported in WWTP effluent of 0.3 ng/L and of 0.12 ng/L and of 0.32 in WWTP influent and with maximum respective concentrations of 0.3-3.7 ng/L hospital effluents. The physicochemical characteristic of the investigated compounds is summarized in Table 2.

Table-1. Summary of the data on the Occurance of Fluconazole and Anastrozole in the Environment

Location	Concentration
Fluconazole	
Wastewater Treatment Plant Influent	0.1-0.39 nM[13, 14]
Wastewater Treatment Plant Effluent	0.09-0.46 nM[13, 14]
Hospital Sewage Water	1.9 nM[13, 14]
Lake Surface Water	<0.03 nM[13, 14]
Anastrozole	
Wastewater Treatment Plant Influent	0.12-0.32[15]
Wastewater Treatment Plant Effluent	0.3-3.7[15]
Hospital Effluent	0.3-3.7[15]

Table-2. Physicochemical characteristic of the investigated compounds

Name	Mol. Formula	MW	Type	pKa
Anastrozole	$C_{17}H_{19}N_5$	293.37	Aromatase inhibitor	11.38
Bicalutamide	$C_{18}H_{14}F_4N_{20}4S$	430.38	Antiandrogen	11.49
Fluconazole	$C_{13}H_{12}F_2N_6O$	306.27	Antifungal	1.76

In sunlight, the rate constant for photolysis (k_{pE}) is given by Dulin and Mill [16].

$$Kp\ (\lambda)=2{,}3W\ (\lambda)\ A/V\varepsilon i\ (\lambda)\ l\ (\lambda)\ \Phi r\ (\lambda) \quad (1)$$

Where W (λ) A/V is the incident light intencity per unit volume of the cell and l (λ) is the cell pathlength that can be determined experimentally for the selected λ value. Integration of equation 1 gives

$$\ln [C_0]/ [C_t]= k_{pE}t \quad (2)$$

where $[C_0]$ and $[C_t]$ refer to concentrations at time zero and Mabey, et al. [17].

Morover, the quantum yield, Φ, was calculated of equation 3.

$$\Phi=0{,}44\ [Pyr]+0{,}00028 \quad (3)$$

$$A\ (\lambda) =\varepsilon i\ (\lambda)\ Ci\ l \quad (4)$$

Ci is the concentration of the compound I of interest in moles per liter (M), l is the path length of the light in the solution commonly expressed in centimeters, εi (λ) is the decadic molar absorption coefficient of the compound I at wavelength A the absorbance of a solution of the compound.

2. MATERIAL METHOD

2.1. Chemicals

Fluconazole, bicalutamide and anastozole were purchased from Toronto Research Chemical (TRC) Inc. Methanol (MeOH) and Acetonitrile (ACN) was obtained from VWR International [18]. All chemicals came from commercial sources and were used without further purifications because analyses by Q-TOF revealed only trace impurities in the samples.

2.2. Analyses

Most analyses were performed by Waters Micromass Q-Tof Premier Mass Spectrometer at room temperature. Separations were made with a 2.1 x 100 mm Acquity Ultra Performance LC

column. A flow rate of 0.6 mL/min was used for all analyses. The composition of the mobile phase was 95:5 H_2O/ACN (v/v), 10 mM Acetic Acid and 5:95 H_2O/ACN (v/v), 10 mM Acetic Acid. The solvent was degassed using an ultrasonic unit. Absorption spectra were recorded on a spectrophotometer (model Hitachi U2010 and 190 nm-1100 nm uv-vis range). Bicalutamide, fluconazole and anastozole in water was investigated under simulated (indoor) sunlight. For indoor photolysis, Bicalutamide, fluconazole and anastozole was photolyzed in water using Heraeus Suntest CPS solar simulator equipped with a xenon lamp. The lamp was fitted with a UV-Suprax optical filter (passing wavelengths ranging from 290 to 800 nm), and the light intensity was set at 765 W/m².

3. METHODS

Experiments by direct photolysis were performed to determine the kinetic order of reaction and photodegradation rate coefficient of Bicalutamide, fluconazole and anastozole. Reaction solutions were made using relevant initial concentration of fluconazole, bicalutamide and anastozole 500 ng/mL found in water. Internal standards are added to the samples. Pharmaceuticals stock solutions were prepared in acetonitrile. Solution were made in ultrapure Milli-Q water, Baltic Sean Water and Olandsån River Water. These experiments were conducted using a solar simulator (Heraeus Suntest CPS), which simulates the radiation of the sun using with xenon lamp. Dark controls were wrapped in aluminum foil and placed in the Suntest. The 5 mL solutions under UV irradiation was taken at each time point and the control sample was taken at the same time. Solutions were then assayed using Q-TOF.

4. RESULTS

The three photolysis tests conducted with MilliQ water in laboratory conductions for the selected pharmaceuticals are shown in Fig 1-2-3. Photolysis of light experiments of pharmaceuticals in Baltic Sea Water is also presented Fig 4. Photolysis of dark experiments of pharmaceuticals in Baltic Sea Water is presented Fig 5. The three pharmaceuticals were relatively stable against sunlight.

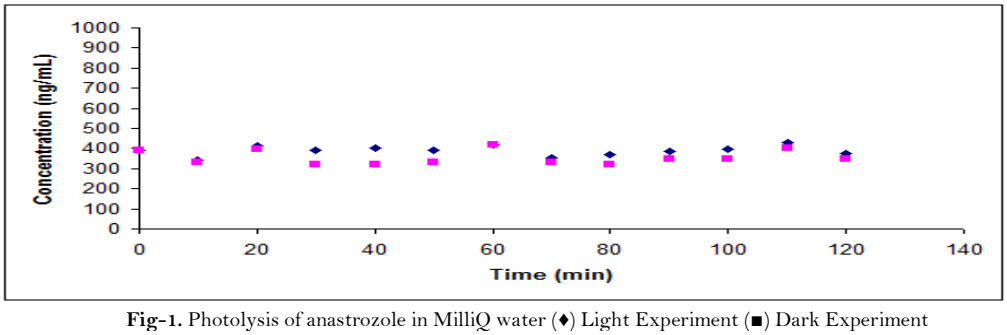

Fig-1. Photolysis of anastrozole in MilliQ water (♦) Light Experiment (■) Dark Experiment

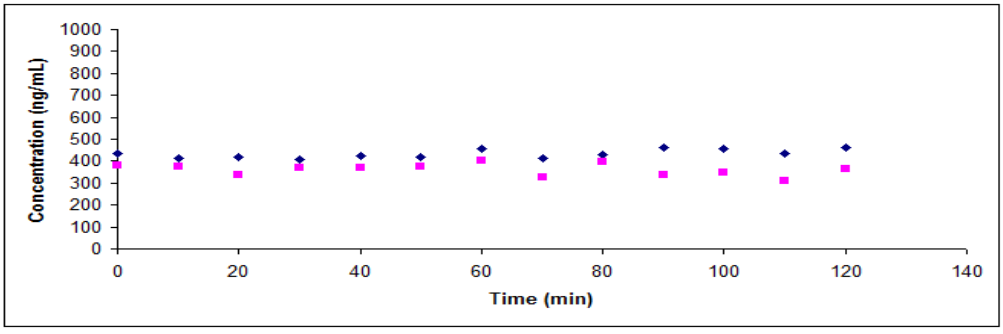

Fig-2. Photolysis of fluconazole in MilliQ water (♦) Light Experiment (■) Dark Experiment

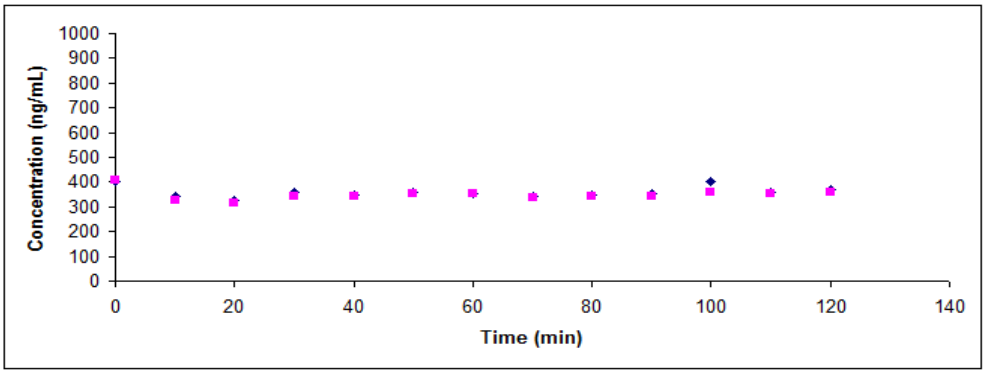

Fig-3. Photolysis of bicalutamide in MilliQ water (♦) Light Experiment (■) Dark Experiment

The stable concentration of the selected pharmaceuticals were also observed in the control samples with Milli-Q water (Fig 1-2-3).

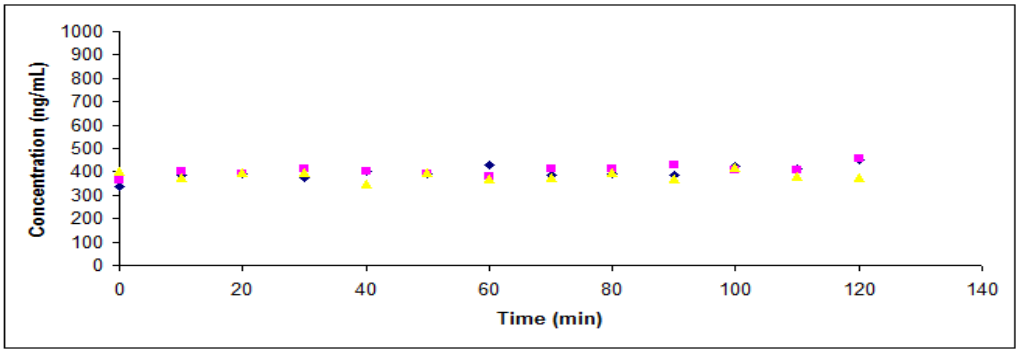

Fig-4. Photolysis of light experiments of pharmaceuticals in Baltic Sea Water (♦) Anastrozole (■) Fluconazole (▲) Bicalutamide

Fluconazole has been detected in wastewater and surface water in the world. According to Peng, et al. [19], there is no biodegradation and adsorption for fluconazole in STPs and largely remained in the final effluent in China [19]. Kahle [13], reported that fluconazole is largely unaffected by wastewater treatment in Sweden [13]. Moreover, no degradation of fluconazole could be observed with in 24 h. For fluconazole, no information on hydrolysis or photolysis is available so far.

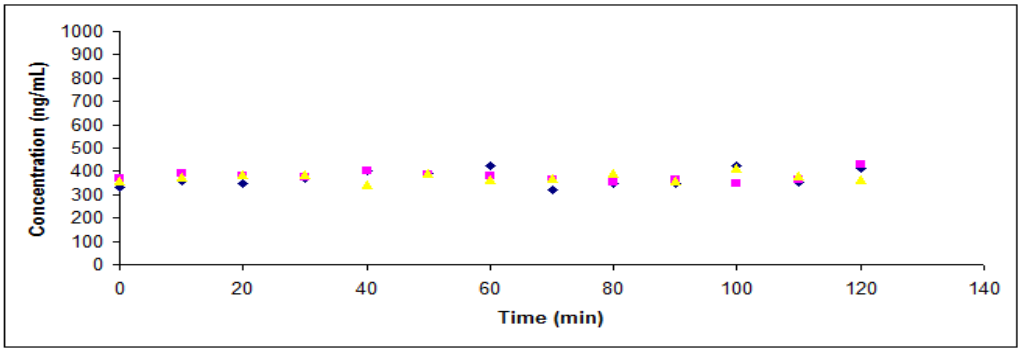

Fig-5. Photolysis of dark experiments of pharmaceuticals in Baltic Sea Water (♦) Anastrozole (■) Fluconazole (▲) Bicalutamide

Anastrozole is lipophilic compound. It has high log K_{ow} and low water solubility. These properties indicated that it is likely to be absorbed by the sewage sludge and sediments. There is little information for treatment strategies for anastrozole. The reason of these gap is the extremely low concentration of the compound that can be detected in natural waterbodies.

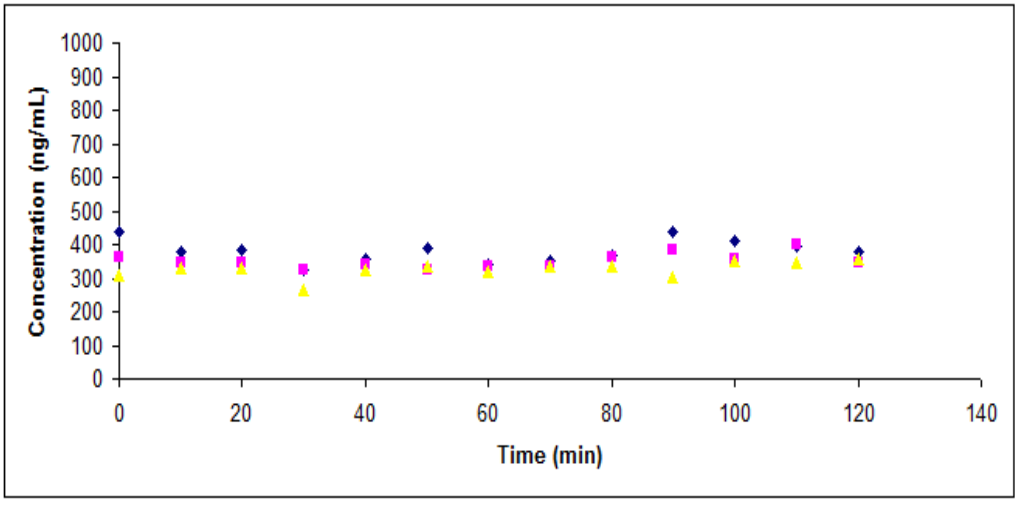

Fig-6. Photolysis of light experiments of pharmaceuticals in Olandsån River Water (♦) Anastrozole (■) Fluconazole (▲) Bicalutamide

The three photolysis tests conducted with Olandsån River Water in laboratory conductions for the selected pharmaceuticals are shown in Fig 6-7. Photolysis of light experiments of pharmaceuticals in Olandsån River Water is also presented Fig 6. Photolysis of dark experiments of pharmaceuticals in Baltic Sea Water is presented Fig 7.

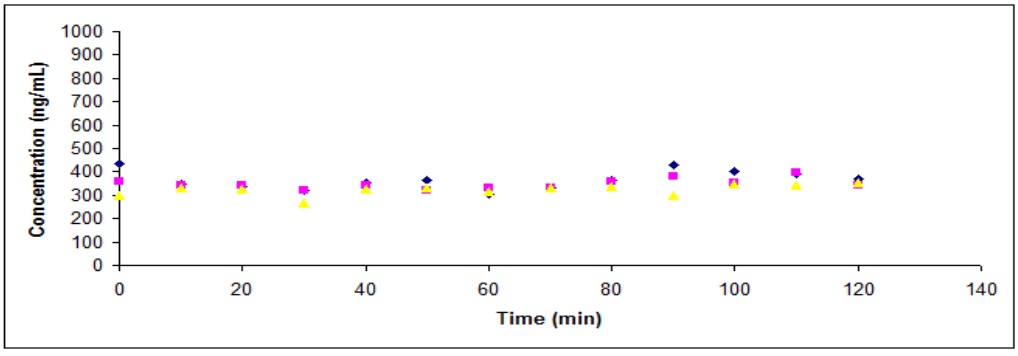

Fig-7. Photolysis of dark experiments of pharmaceuticals in Olandsån River Water (♦) Anastrozole (■) Fluconazole (▲) Bicalutamide

5. CONCLUSIONS

It selected three different pharmaceuticals with relatively high potential ecological risk and high consumption, laboratory experiments were conducted for these drugs, to examine persistence and partitioning in the aquatic environment. It conducted photodegradation experiments using Milli-Q water, Baltic Sea Water and Olandsån River water. The systems were relatively persistent against sunlight. The results of photolysis experiments suggest a negligible photodegradation of the selected pharmaceuticals. Hence, in general, there is still a knowledge gap concerning the generation of metabolites and transformation products of known contaminants. The assessment of their fate is necessary to understand degradation mechanisms during wastewater treatment.

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