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PHOTO-TREATMENT OF AQUEOUS SOLUTIONS OF FIVE MEDICINES

Stavros Georgopoulos, George Kostoulas, Vassiliki Repousi & Maria Papadaki*
Department of Environmental Engineering, School of Engineering, University of Patras, 2 Georgiou Seferi St. Agrinio, Greece

ABSTRACT

In this work we investigated the effect of sunlight and its combination with TiO2 and sea-salt for the removal of five medicines, i.e. Zinadol, Zyrtec , Pricefil, Pariet and Panadol. Aqueous solutions of the ready for consumption medicine were subjected to direct photolysis and TiO2 photocatalysis with and without untreated sea-salt in the average concentration that it is encountered in the sea (3.5% w/w). The samples were exposed to sunlight for up to a few months and they were analysed via UV measurements and TOC analyses. Direct photolysis of the medicines resulted in some degradation of all medicine solutions in all cases but in the case of Panadol. The photocatalyst TiO2 seemed to play a more complex role, depending on the employed medicine and on whether NaCl was present or not. In all photocatalytic measurements without NaCl, UV absorption was constantly reducing; however, TOC was usually increasing after being reduced for some time, thus indicating desorption of intermediate products in the aqueous solution. This was not the case however, in NaCl-containing photolytically treated solutions; NaCl increased their resistance to degradation. Therefore, these medicines cannot be removed naturally from sea-water. Photocatalysis seems to be a very good method for Panadol minaralisation.

Keywords: *pharmaceuticals in waste-waters, Zinadol, Zyrtec, Pariet, Pricefil, Panadol photolysis, photocatalysis.*

I. INTRODUCTION

The traditional biological wastewater treatment methods cannot remove or degrade water pollutants such as medicines, pesticides, herbicides and other organic compounds used as active ingredients employed for the treatment of disease. Hundreds of tons of pharmaceuticals are released annually into the environment unchanged or as metabolites. It is noteworthy that the majority of pharmaceuticals have been detected at concentrations ranging from ng L^{-1} up to g L^{-1}.

For example, in Italy, macrolides, particularly clarithromycin and spiramycin, and quinolones, particularly ciprofloxacin and l-floxacin/o-floxacin, were found to be the most abundant antibiotics in untreated wastewaters. Several of them were not removed in sewage treatment plants and still remained in the treated wastewater; a total estimate of 7–14 tons of active ingredients were discharged annually into the aqueous environment through this route(Zuccato et al 2010). In Istanbul, Turkey the occurrence of 14 mostly used pharmaceuticals from different classes (antibiotics, b-blockers, nonsteroidal anti-inflammatory drugs, and stimulant) and hormones in surface water wasstudied. An important drinking water source, Buyukcekmece Lake and main rivers flowing into the lake were selected for the monitoring of the compounds. The most frequently detected compounds in those were caffeine and antibiotics (amoxicillin, ciprofloxacin, erythromycin and sulfamethoxazole)Aydin and Talinli (2013).In a study performed by Ferrer and Thurman (2012) is reported that compounds such as carbamazepine, bupropion, lamotrigine, diphenhydramine, gemfibrozil, metoprolol, propanolol, sulfamethoxazole, thiabendazole, trimethoprim, venlafaxine and their respective metabolites were the most common pharmaceuticals detected in water. The highest concentrations measured in water samples were those corresponding to anti-convulsants, anti-depressants, psychiatric drugs and beta-blockers. Sui et al (1015) in a detailed review present numerous studies reporting the increasing groundwater contamination by frequently detected antibiotics, anti-inflammatories, lipid-regulators and a number of other pharmaceuticals and personal care products. In a subsequent article Ebele et al, 2017 review the implications which such contaminants can have in the freshwater aquatic environment. Given their, persistence, bioaccumulation and toxicity criteria. Blair et al 2013.

There are several thousands of medicines prescribed in USA, for instance, according to U.S. FDA Orang book 2019.However, for the majority of those there are no toxicity and ecotoxicity data or knowledge about their fate in the environment. This is usually because either there are not any approved protocols for the measurement of their concentration and toxicity, or the existing methods are unreliable, tedious and time-consuming(Dong et al 2013). As a result, the establishment of maximum permissible limits for their concentration in water is rendered a formidable task.

Pharmaceuticals have been specially designed so as to be capable to change the biochemical and physiochemical functions of biological systems when administered in small quantities (Boillot et al 2006). They usually have the common characteristics of xenobiotic entities, thus they are resistant to biological degradation (Petrie et al 2015).
The inability of known biological processes for treating municipal wastewater for complete degradation of pharmaceuticals, has created the need to upgrade them further comprising alternative methods of treatment such as the advanced oxidation processes (AOPs). The basic function of AOPs is based on the production of free radicals which act as powerful oxidisers which degradade organic pollutants transforming them into inorganic products (mineralization)(Parsons 2014).

In recent years, there have been many studies on the pharmaceutical sector using some AOPs, such as heterogeneous photocatalysis, photolysis, ozonation, oxidation with Fenton, photolysis in the presence of H_2O_2 and to a lesser extent sonolysis, electrolysis and wet oxidation (Baran et al 2006; Klavarioti et al 2009).

In this work we investigate the effect of sunlight and its combination with TiO_2 for the removal of five amply used medicines, i.e. Zinadol (antibiotic; active ingredient: cefuroxime axetil), Zyrtec (allergy medication; active ingredient: Cetirizine dihydrochloride), Pricefil (antibiotic; active ingredient:cefprozil monohydrate),Pariet (treatment of stomach ulsers; active ingredient: rabeprazole sodium) and panadol (painkiller and febrifuge; active ingredient: acetaminophen). Studies on the toxicity and/or ecotocxicity of all but the latter compound are practically non-existent. A number of toxicity studies do exist for acetaminophen and a summary of such data is presented by Kosma et al (2010) and Brausch et al (2012).

In any case, the toxicity of a chemical can be substantially different of the toxicity of its metabolites (which are often more toxic than the original compounds (Vlastos et al 2010; Sakkas et al 2007;Konstantinou et al 2010). Therefore, the study and the development of methods for persistent-compound removal and mineralisation is an effective way to eliminate potential or unknown toxic effects. One additional reason for aiming at processes which result in their mineralisation is offered by Archer et al 2017. As they report after having taken extensive measurements upstream and downstream of wastewaters treatment plants, in addition to the limited removal of those compounds, negative mass balances of compounds and their metabolites indicating possible back-transformation of the mother pharmaceuticals in the course of the wastewater treatment. Along these lines, the scope of this research is two-fold. First, to get some guidance on the potential efficiency of applied photo-treatment processes for the removal of such compounds from sewage treatment plants and next to assess the effect of natural sunlight on their removal from fresh and sea-waters. For this purpose, and in order to account for potential synergies, tablets of the aforementioned five medicines, as supplied by the producer pharmaceutical company were dissolved in water and subjected to photo-treatment, as explained next. The aforementioned medicines are widely prescribed in Greece.

II. METHOD & MATERIAL

Tablets of the first four medicines, as supplied by the producer pharmaceutical company (Zinnat 500 mg, GlaxoSmithKline, Zyrtek film-coated tablets 10 mg UCB, Pariet 20 mg JANSSEN-CILAG and Pricefil 500 mg VIANEX S.A.) were dissolved in 1 L of double-distilled water, each. The solution was then filtered and used as it was for photolysis measurements or mixed with TiO_2 Degussa P-25 for photocatalytic experiments. Four series of experiments were performed for each solution, one for the study of the effects of direct photolysis and one for the study of photocatalysis in fresh water (use of distilled water and the medicine with or without catalyst) and surrogate sea water with addition of sea-salt (Chion-XIΩN A.B.E.E) to form a 3.5% w/w NaCl solution. A number of 10 ml sterilised transparent glass vials were half-filled with 5 ml of solution, each, and they were sealed and placed under

direct sunlight. The vials employed in the photocatalytic measurements were shaken regularly and they were opened for aeration twice a day, in the early morning and late evening hours, when the outside temperature was low. The samples remained in the sun for 45-91 days.

The samples were subsequently analysed using a Hitachi U-2000 UV Spectrophotometer 1212301-10 with cuvettes made of quartz of 3.5 ml capacity. The total organic carbon (TOC) content of each solution was also measured by means of combustion catalytic oxidation / NDIR method on a Shimadzu TOC-V CSH analyser. The first measurement for all series of measurement was taken 1 hour after filtering. During this hour the stock involving catalyst was subjected to vigorous agitation in the dark.

For paracetamol, a single 500 mg of effervescent panadol tablet (GlaxoSmithKline)was fully dissolved under continuous vigorous agitation,in the appropriate quantity of double distilled water, so as to form a solution of 60 mg of paracetamol per litre of solution, at ambient temperature. The UV spectrum and the TOC of the solution was measured. Subsequently, the mixture was split in two parts: one for the photolytic and the other for the photocatalytic experiments. For the photocatalytic experiments TiO_2, Degussa P-25 was added to form a concentration of 1g L^{-1}. The solution was then split in sterilised bottles in the same way as the above mentioned medicines and was also treated in an identical way, except for the length of treatment, which, in this case, lasted for up to 5 months.

III. RESULT AND DICUSSION

Although differences were observed between different medicines, it was broadly found that in all cases UV absorption was reduced as a function of treatment time, although TOC removal was very slow in all cases. The solutions containing NaCl however, presented a distinctly different behaviour. More specifically, as can be seen in Figure (1a), photocatalytic treatment reduces absorption at longer wavelengths, indicating decomposition of larger molecules. Figure (2a), shows the UV absorption of the samples subjected to photolytic treatment. As can be seen, absorption at larger wavelength drops with time but not as fast as in the measurements with catalyst. Figures (1c) and (1d), display a substantially different initial absorption spectrum, which practically remains unaltered for the 25 days that the study lasted.

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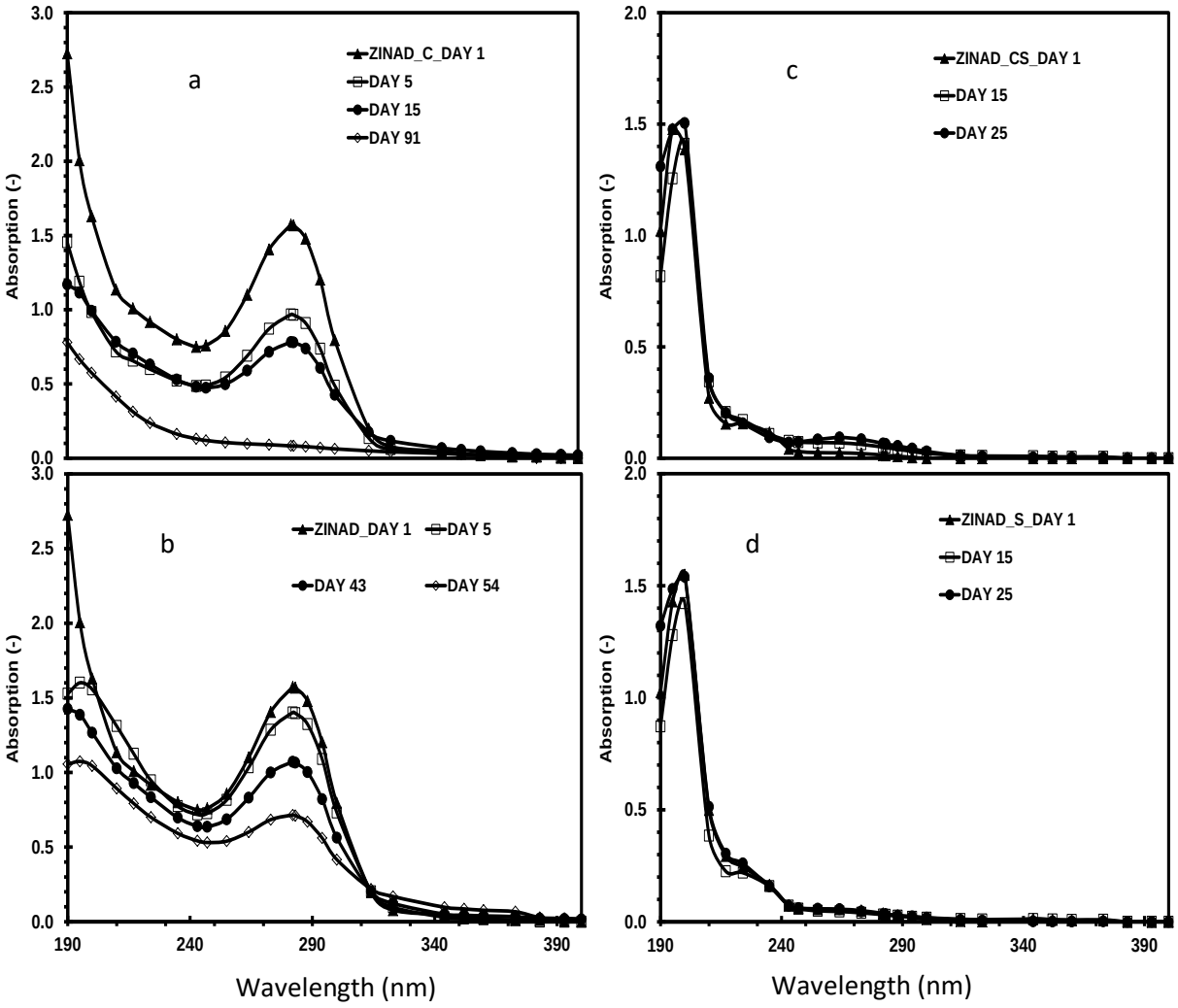

Figure 1: UV absorption of aqueous solution of Zinadol for four different time lengths, as a function of wavelength (a) with TiO_2 catalyst (index C), (b) without any catalyst, (c) with catalyst and salt (index CS) and (d) with salt only (index S). Initial concentrations for (a) and (b) similar, but not the same; for (c) and (d) the same, but different from those of (a) and (b).

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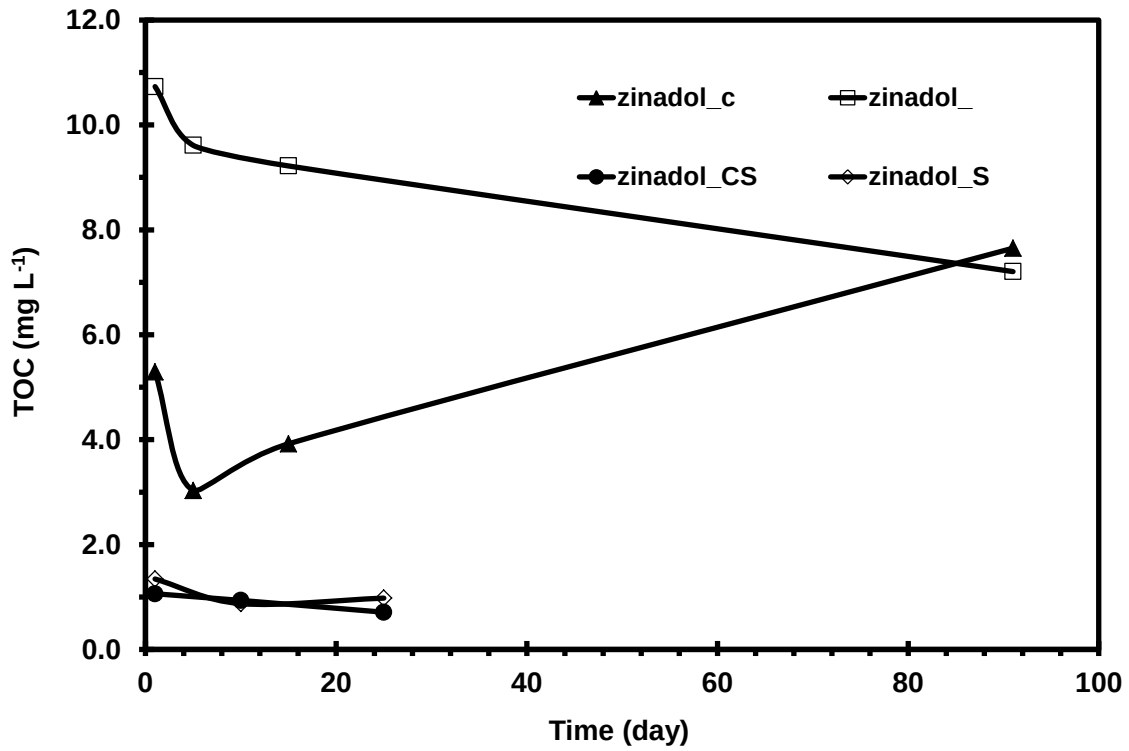

Figure 2: TOC of the aqueous solutions of Zinadol shown in Figure 1, as a function of time; (▲) with TiO_2 catalyst (index C); (□) without any catalyst;(●) with catalyst and salt (index CS) and (◊) with salt only (index S).

Figure 2 shows the TOC history of the respective measurements. By comparison of the TOC concentration of time zero for the photolytically and the photocatalytically treated samples, it becomes obvious that there is a strong adsorbance of molecules on the catalyst; as reported earlier, the two solutions had very similar-but not identical initial concentration. As can be seen in Figure 2, the photolytic treatment results in a constant drop of the solution TOC, which reaches a 30% TOC removal in 3 months. At the same time, the photocatalytically treated sample shows that organic carbon is released in the solution, most likely because of organic molecules desorption. It is plausible, taking into account Figure 1a, that the desorbed molecules are products of decomposition of the original molecules and smaller than those. The TOC concentration of the samples containing NaCl, with or without catalyst, displays a similar stability, without much drop of TOC concentration.

The phototreatment of Zyrtec presents some analogies with that of Zinadol. The two pairs of solutions, i.e. photocatalytic and photolytic without NaCl and plotolytic and photocatalytic with NaCl hadvery similar concentrations and similar to each other, but not identical. As can be seen in Figure 3, the UV absorption indicates that solutions containing NaCl, with or without TiO_2 have a small degradation in 25 days. Figure 4 shows that organic molecules which were originally adsorbed on the catalyst are later desorbed in the solution, while photolytic treatment also results in TOC reduction. Again, the presence of NaCl makes solutions more resistant to TOC reduction.

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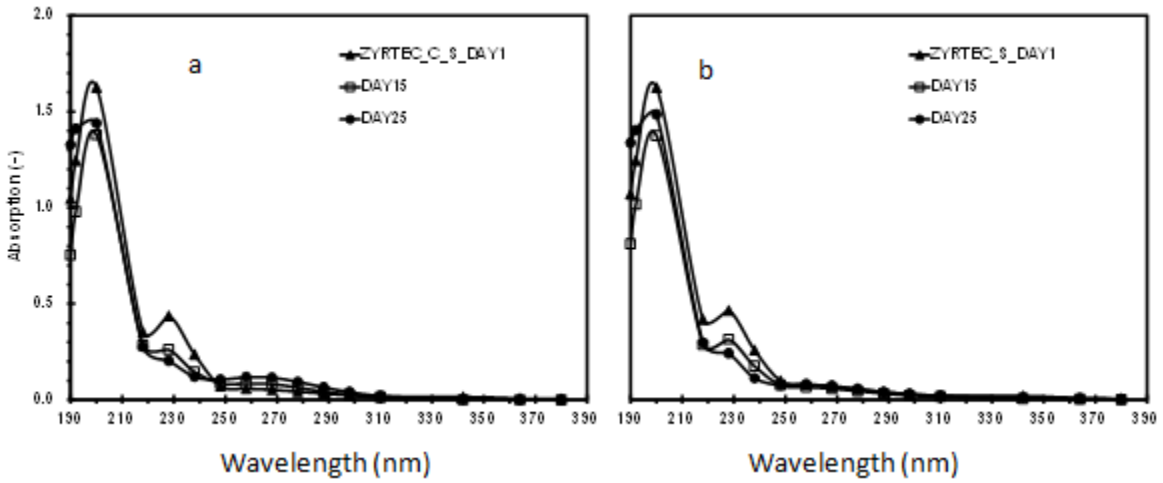

Figure 3:UV absorption of aqueous solution of Zyrtek as a function of wavelength for different time-lengths exposure; (a) with TiO_2 and sea-salt (index C_S) and (b) with sea-salt only (index S).

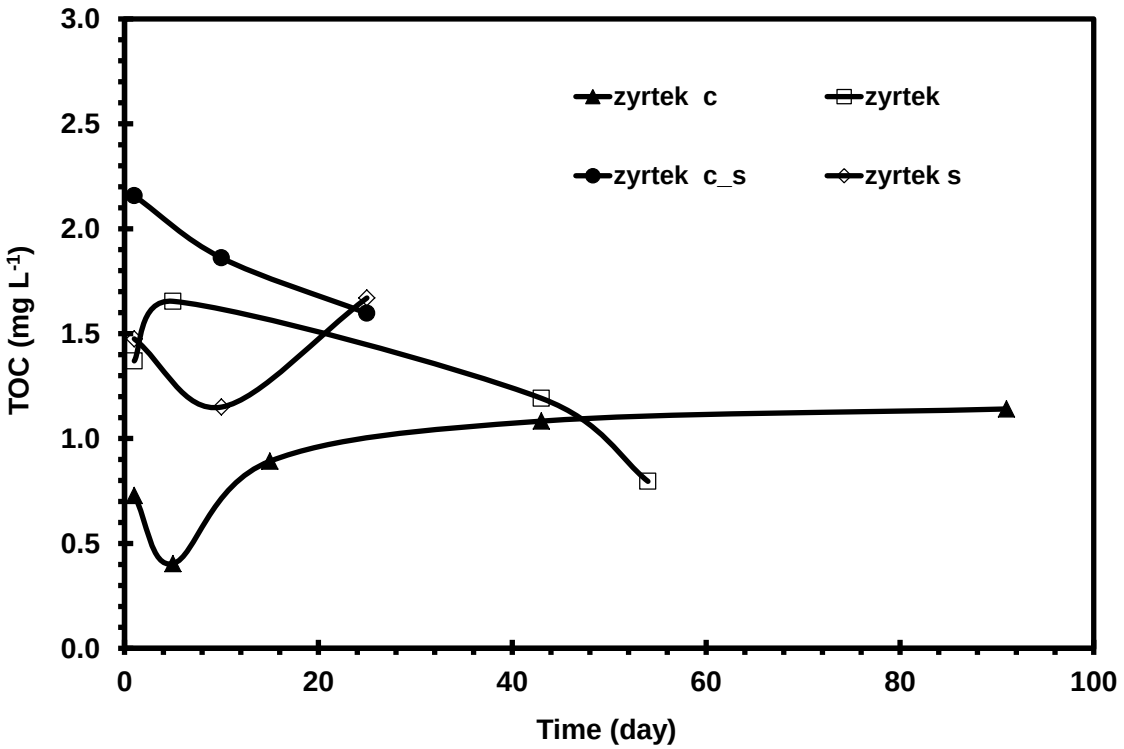

Figure 4:*TOC of the aqueous solution of Zyrtek, as a function of time; (▲) with TiO_2 catalyst (index C);(□) without any catalyst;(●) with catalyst and salt (index CS); (◊) with salt only (index S).*

Figure 5 shows the UV absorption history of the four solutions of Pariet at selected wavelengths. As can be seen in Figures (5a) and (5b) UV absorption reduces with time in both photolytic and photocatalytically treated samples, with the catalytic treatment reducing much more effectively absorption in shorter wavelengths. In this case,the UV absorption of samples containing NaCl, also reduces with time. The TOC history for all four measurements is shown

in Figure (6a). As can be seen in Figure (6a), strong absorption of organics on the catalyst is observed in this case, which is followed by some desorption of plausibly smaller molecules later on in time. Again, the presence of NaCl has a similar effect on the phototreatment of the samples as in the previously shown medicines.

Figure (6b) shows the TOC history for the fourth medicine, ie. Pricefil. This medicine shows a very small reduction of TOC in the photocatalytically treated solutions over the course of 91 days. No product desorption in the solution is evident. The photolytically treated samples show a gradual TOC reduction, while NaCl seems to prevent TOC reduction as in all aforementioned cases.

The phototreatment of paracetamol, shown in Figure 7 where the UV absorption at different wavelengths is shown as a function of time. As can be seen in Figure (7a), photolytic treatment had no effect so ever on the sample UV absorption at any wavelength. This was confirmed by the TOC measurement of those samples, which remained intact through out the expose period. On the other hand, TiO_2 photocatalysis was very effective, as the TOC of the sample was reduced from 80 mg L^{-1} to 14 mg L^{-1} within a month, in winter time. The reduction of TOC was accompanied by the UV absorption drop as a function of time, at all shown wavelengths, as can be seen in Figure (7b).

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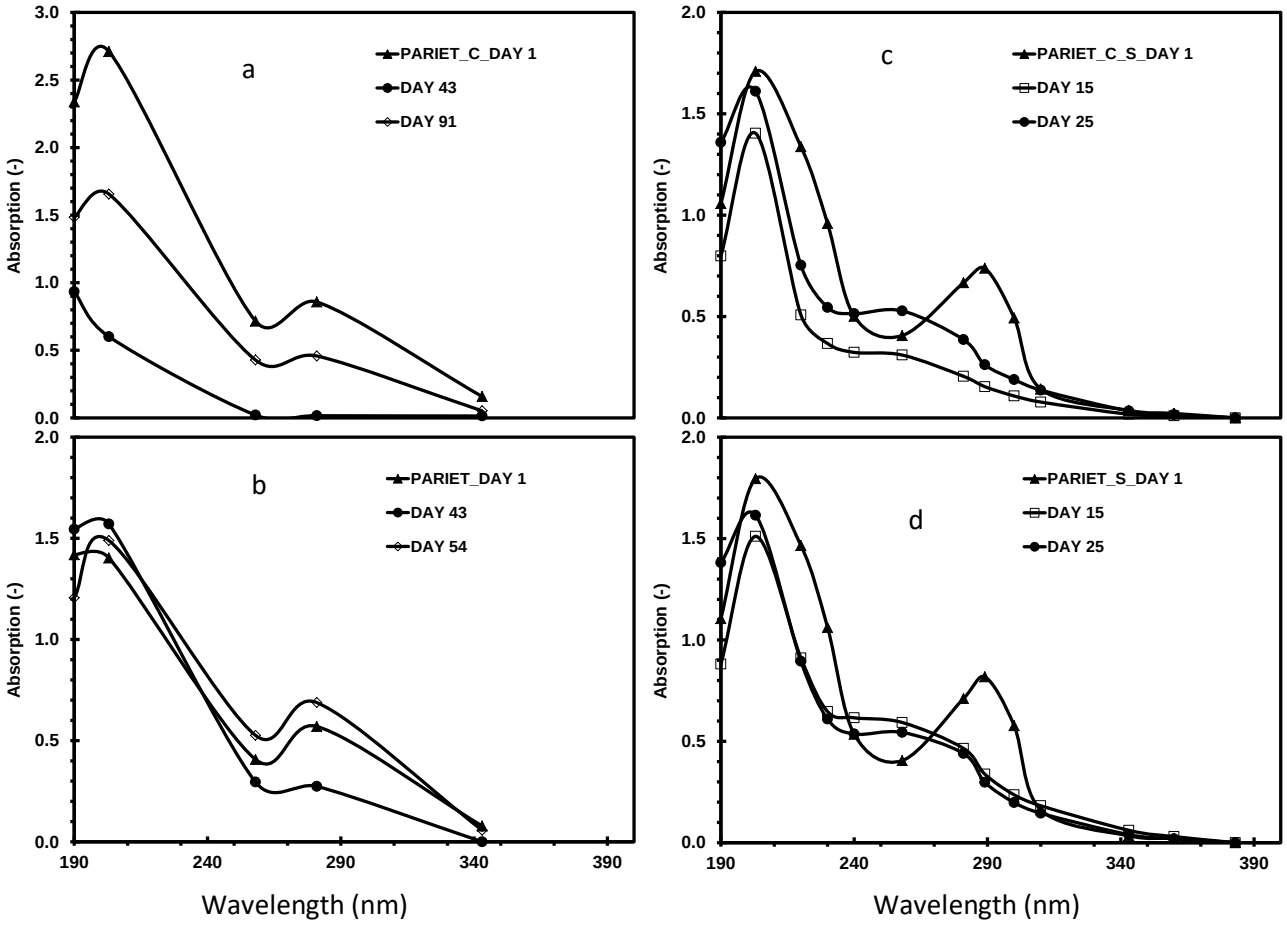

Figure 5:UV absorption of aqueous solution of Pariet for four different time lengths, as a function of selected wavelength: (a) with TiO_2 catalyst (index C), (b) without any catalyst, (c) with catalyst and salt (index CS) and (d) with salt only (index S). Initial concentrations for (a) and (b) different; for (c) and (d) the same, but different from those of (a) and (b).

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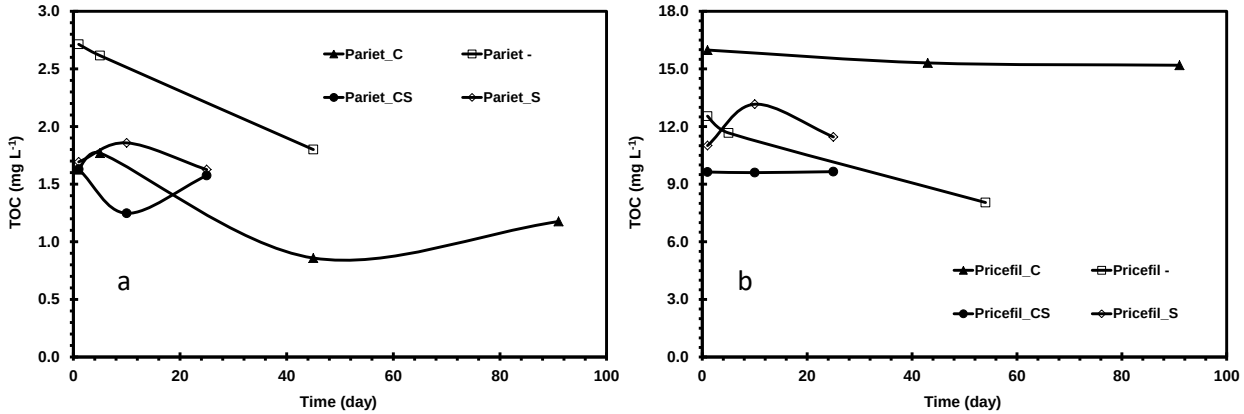

Figure 6:TOC of the aqueous solution of (a) Pariet, and (b) Pricefil, as a function of time; (▲) with TiO_2 catalyst (index C);(□) without any catalyst;(●) with catalyst and salt (index CS); (◊) with salt only (index S).

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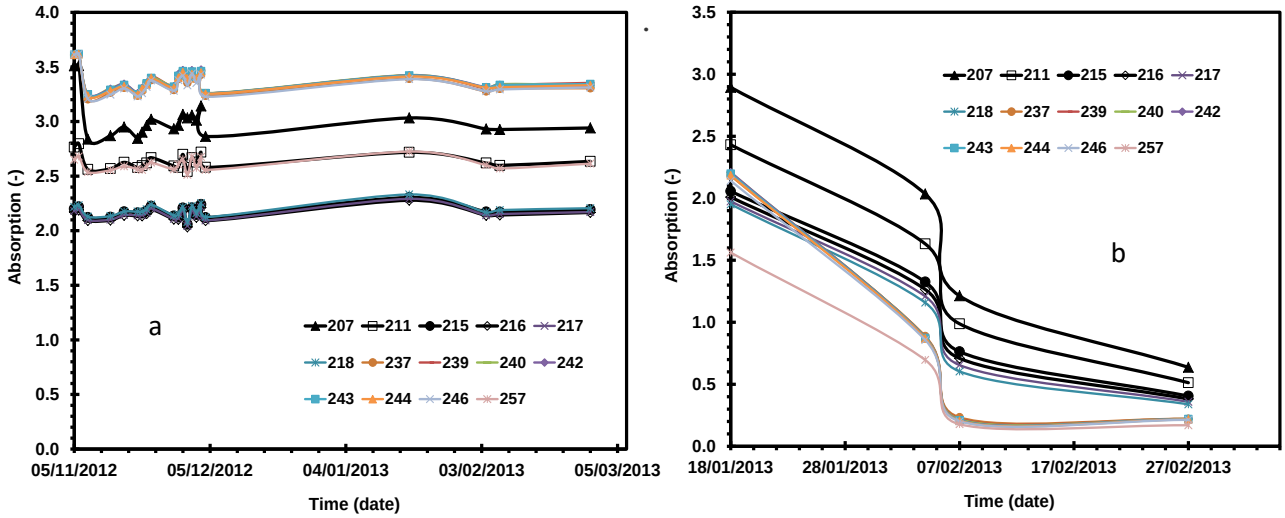

Figure 7:UV absorption of the aqueous solution of (a) photolytically treated Panadol and (b) photocatalytically treated Panadol at different wavelengths, as a function of time

IV. CONCLUSION

Direct photolysis of the medicines examined here resulted in some degradation of all medicine solutions in all cases but in the case of Panadol. This indicates, that the sun can reduce TOC in natural waters exposed to sunlight; However, further research is required, as it is not known whether TOC reduction meets a plateau; additionally, as in many other cases, photolysis, may be proven inefficient as a technological application for the treatment of wastewaters containing those medicines. Panadol solutions cannot be treated by photolysis.

This was not the case however, in NaCl-containing photolytically treated solutions. Therefore, these medicines cannot be removed naturally from sea-water.

The photocatalyst TiO_2seemed to play a more complex role, depending on the employed medicine and on whether NaCl was present or not. In all photocatalytic measurements without NaCl, UV absorption was constantly reducing; however, TOC was usually increasing after some reduction had taken place, thus indicating desorption of intermediate products in the aqueous solution .Further research is required in order to identify the photocatalytic products released into the solution and their toxicity. Again, the four first medicines displayed a more persistent behaviour in the presence of NaCl. Photocatalysis seems to be a very good method for Panadol minaralisation.

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