

## Ceftriaxone Degradation using Titanium Dioxide (TiO<sub>2</sub>) Nanoparticles: Toxicity and Degradation Mechanism

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### Abstract

Ceftriaxone is a third generation of cephalosporin antibiotics that commonly used in patients with ulcer. Ceftriaxone residues in the environment are degraded using Titanium dioxide (TiO<sub>2</sub>) nanoparticles. Degradation of ceftriaxone using TiO<sub>2</sub> nanoparticles was influenced by environmental conditions, such as light sources, pH of solution, the mass of TiO<sub>2</sub> nanoparticles, and the length of radiation. The remained ceftriaxone was analyzed by using spectrophotometer UV-visible. The toxicity of the solution after degradation process was tested on *Escherichia coli* and the type of products resulted was analyzed using Liquid Chromatography-Mass Spectrophotometry (LC-MS). The optimum conditions in degrading 50 mL 250 ppm ceftriaxone was radiation under a mercury UV lamp (white), pH 8, and 100 mg of TiO<sub>2</sub> nanoparticles for 9 hours. Degradation degree of ceftriaxone obtained was 96.52%, producing a simpler compounds that not toxic to *E. Coli*.

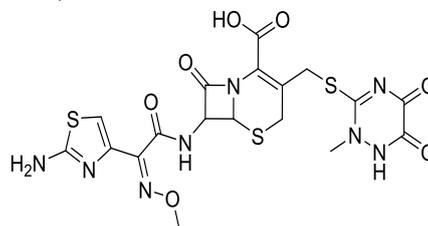
**Keywords:** TiO<sub>2</sub> nanoparticles, ceftriaxone, photo catalyst, degradation.

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### 1. INTRODUCTION

The use of antibiotics is now a major concern for many parties, especially the government, health workers, and researchers. This is due to the increasing number of bacterial infectious diseases including those with Diabetes Mellitus (DM) who have ulcers (Sari *et al.*, 2018) and gangrene (Rosa *et al.*, 2019). A treatment that is commonly used in these cases is ceftriaxone antibiotics. Ceftriaxone is a third-generation of cephalosporin antibiotic (Figure 1). Sari *et al.* (2018) showed that the use of ceftriaxone in patients with ulcer was not rational because its use was not effective yet, both from the type and from dosage of the drug. The irrational use of antibiotics can increase the amount of antibiotic residues in the surrounding environment, causing antibiotic resistance (Utami, 2011).

The usage of oxidation system of antibiotic compounds with catalysts is one of the efforts to control the amount of antibiotic residues in the environment (Jiang *et al.*, 2016). The catalysts that are often used in solution system with sunlight (photocatalyst) are titanium dioxide (TiO<sub>2</sub>) and zinc oxide (ZnO) (Ambrosetti *et al.*, 2015). Ambrosetti *et al.* (2015) reported that TiO<sub>2</sub> was more effective and efficient in degrading pollutants, for instance rhodamine B (Saputro *et al.*, 2016), diazinon pesticides (Usman *et al.*, 2017), and direct red-23 dyes (Fitriyani *et al.*, 2017), in the environment.



**Figure 1.** Ceftriaxone structure

The process of ceftriaxone degradation using TiO<sub>2</sub> is influenced by several factors including the type of light source, the degree of acidity (pH) of the solution, the amount of TiO<sub>2</sub>, and the length of exposure (Ambrosetti *et al.*, 2015). The product of ceftriaxone degradation with TiO<sub>2</sub> is still unknown. Thus, this study examined the type of antibiotic degradation product of ceftriaxone and the toxicity of the result of degradation using TiO<sub>2</sub> against *Escherichia coli* bacteria.

## 2. MATERIALS AND METHODS

### Instruments and Materials

The instruments used in this study were Liquid Chromatography Mass Spectrometry (LC-MS.), UV-Visible spectrophotometers (Thermo Scientific, Genesys 10S UV-Vis), magnetic stirrers (IKA C-MAG HS 7), centrifuges (Health), reactors which is equipped with UV Blue Light Blue lamps (Gaxindo, T5 6W BLB) and UV white mercury (Philips, HPL-N 125W), micropipettes 10-100  $\mu$ L (Dragon Lab), and other glassware. Materials used in this study were ceftriaxone (injection preparations, OGB dexta), TiO<sub>2</sub> P25 degussa (25 nm anatase, Merck), distilled water, sodium dihydrogenphosphate (NaH<sub>2</sub>PO<sub>4</sub>, Merck), sodium hydrogenphosphate (Na<sub>2</sub>HPO<sub>4</sub>, Merck), *Escherichia coli* (*E. coli*), disc paper (Oxoid), and agar media (KGaA).

### Ceftriaxone Standard Solution Preparation

Standard solution of 500 ppm Ceftriaxone was prepared by dissolving 100 mg Ceftriaxone in 200 mL distilled water. The solution was taken as many as 25; 10; 5; 2.5; and 1 mL then was diluted to 50 mL in order to obtain a solution with a concentration of 250; 100; 50; 25; and 10 ppm.

### Scanning Maximum Wavelength and Standard Curve of Ceftriaxone

Scanning maximum wavelength of ceftriaxone was performed by using UV-visible spectrophotometer with wavelength range of 200-400 nm on 500 ppm ceftriaxone solution. The maximum wavelength was used to measure the absorbance of 250; 100; 50; 25; and 10 ppm ceftriaxone solution. The absorbance values were used to create a standard curve of ceftriaxone, and it was obtained linear equation  $y = ax + b$ . The

equation was used to determine the concentration of ceftriaxone after degradation.

### Effect of Light Source

25 mL standard solution of 500 ppm ceftriaxone was diluted to 50 mL using phosphate buffer (pH 7) that the concentration of the solution became 250 ppm. The solution was added with 100 mg TiO<sub>2</sub> nanoparticles, then it had been radiated with UV BLB lamps and UV white mercury separately for 5 hours. Separation of TiO<sub>2</sub> nanoparticles was carried out by centrifugation. Ceftriaxone absorption is measured by spectrophotometer at the maximum wavelength obtained.

### Effect of Solution pH

25 mL standard solution of 500 ppm ceftriaxone was diluted to 50 mL with a concentration of 250 ppm using phosphate buffer with pH 5.5; 6; 7; 7.5; and 8. The solution was added with 100 mg TiO<sub>2</sub> nanoparticles, then it had been radiated for 5 hours with the best UV light source. The separation of TiO<sub>2</sub> nanoparticles was carried out by centrifugation. Ceftriaxone absorption was measured by spectrophotometer at the maximum wavelength obtained.

### Effect of TiO<sub>2</sub> Mass

25 mL standard solution of 500 ppm ceftriaxone was diluted to 50 mL with the best pH phosphate buffer until 250 ppm ceftriaxone solution was obtained. The solution was added with TiO<sub>2</sub> nanoparticles with a variation of 50; 75; 100; 125; and 150 mg. Each solution had been radiated for 5 hours with the best UV light source. Separation of TiO<sub>2</sub> nanoparticles was carried out by centrifugation. Ceftriaxone absorption was measured by spectrophotometer at the maximum wavelength obtained.

### Effect of Radiation Time

25 mL standard solution of 500 ppm ceftriaxone was diluted to 50 mL with the best pH phosphate buffer that 250 ppm ceftriaxone solution was obtained. The solution was added with the best amount of TiO<sub>2</sub> nanoparticles. Each solution had been radiated for 5; 6; 7; 8; and 9 hours with the best UV light source. Separation of TiO<sub>2</sub> nanoparticles was carried out by centrifugation. Ceftriaxone absorption was measured by spectrophotometer at the maximum wavelength obtained.

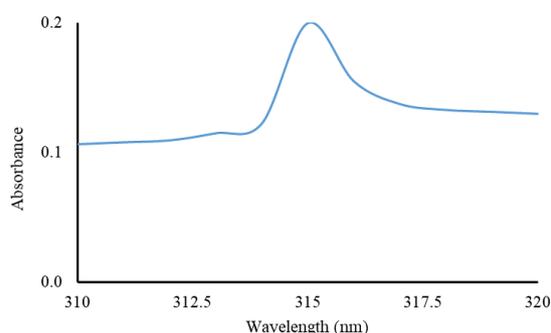
### Toxicity and Prediction of Degradation Products

The solution tested for toxicity was the solution with the lowest absorbance or had the highest percentage of degradation in each variation made. 50  $\mu$ L bacterial suspension and 20 mL sterile Nutrient Agar (NA) media were put in a sterile petri dish. Disc paper with a diameter of 3 mm that had been filled with 20  $\mu$ L of test solution was added to the prepared petri dish. Incubation was carried out for 18 hours at room temperature. The diameter of the inhibitory zone in the clear area of the paper disk was measured using a Vernier caliper. The solution that was analyzed by LCMS to determine the prediction of the product that was formed was ceftriaxone solution with the lowest absorbance or has the highest percentage of degradation of all variations.

### 3. RESULTS AND DISCUSSION

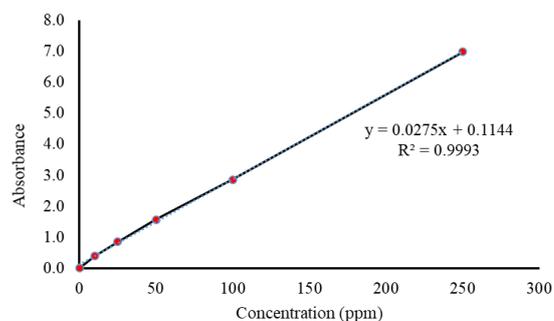
#### Scanning of Maximum Wavelength and Standard Ceftriaxone Curve

The scanning of the maximum wavelength of 500 ppm ceftriaxone solution in the range of 200-400 nm with an interval of 2 obtained a peak at 310-320 nm wavelength. The maximum wavelength was determined with interval 1 at 310-200 nm wavelength. The results obtained showed that the wavelength of 315 nm has the highest absorbance of 0.200 as shown in Figure 2.



**Figure 2.** the scanning of the maximum wavelength of 500 ppm ceftriaxone with interval of 1 in the range 310-320 nm

Absorbance of standard solution of ceftriaxone concentration of 250; 100; 50; 25; and 10 ppm measured with a wavelength of 315 nm. The obtained standard curve showed the equation  $y = 0.0275x + 0.1144$  with  $R^2 = 0.9993$ .



**Figure 3.** Standard curves of ceftriaxone

#### Effect of Light Source

Table 1 showed the results of ceftriaxone degradation with different radiation sources that the degradation percentage of ceftriaxone with white mercury UV lamps is higher than UV BLB lamps. The difference between the two lamps lies in the wavelength that is resulted. The wavelengths produced by the white mercury UV lamp ( $\lambda = 304; 314; 335; 366$  nm) are wider than the wavelength of the UV BLB lamp ( $\lambda = 352$  nm) (Hickel *et al.*, 2018; Maletić *et al.*, 2019). Light sources with different wavelengths ( $\lambda$ ) can produce different photon energies by following the energy equation  $(E) = hc/\lambda$ , where  $h$  is the Planck constant  $= 6.625 \times 10^{-34}$  J s and  $c$  is the speed of light  $= 2.998 \times 10^8$  m/s (Schöpp & Franke, 2014). Thus, the amount of photon energy produced in white mercury UV lamps is more compatible with TiO<sub>2</sub> nanoparticles than UV BLB lamps in degrading ceftriaxone. Photo catalyst of TiO<sub>2</sub> nanoparticles that are exposed to photon energy will be active as photo catalysts characterized by the transfer of electrons from the valence band to the conduction band (Kashiwaya *et al.*, 2018).

**Table 1.** Effect of light sources on ceftriaxone degradation

No.	Light Sources	% Degradation
1	UV-BLB	56.95
2	White mercury-UV	63.38

#### Effect of Acidity

Table 2 showed the degradation percentage of ceftriaxone as a function of pH changing of the solution, that in acidic conditions ( $<7$ ) it was decreased from pH 5.5

to pH 6. Degradation percentage of ceftriaxone will increase after pH 7 up to pH 8. The decrease of degradation percentage happened because the increase of acid pH will decrease the number of H<sup>+</sup> ions. The reduction of H<sup>+</sup> ions in solution will reduce the amount of H radicals thus the degradation percentage will decrease. While, the increase of pH will increase OH<sup>-</sup> ions then it will increase the amount of OH radicals. The process of OH radical formation is faster than H radical therefore the degradation of ceftriaxone compounds in alkaline conditions is better than acidic conditions (Nasikhudin *et al.*, 2018).

**Table 2.** Effect of pH on ceftriaxone degradation

No.	pH	% Degradation
1	5.5	62.84
2	6	62.09
3	7	62.32
4	7.5	66.01
5	8	67.79

**Effect of TiO<sub>2</sub> Mass**

Table 3 showed the increase of degradation percentage (50 mg to 100 mg). However, the degradation percentage tended to be constant at TiO<sub>2</sub> greater than 100 mg. It was suspected due to shielding effect so that excessive use of TiO<sub>2</sub> nanoparticles can reflect UV light or block incoming light (Fitriyani *et al.*, 2017; Saudi and Adel, 2018).

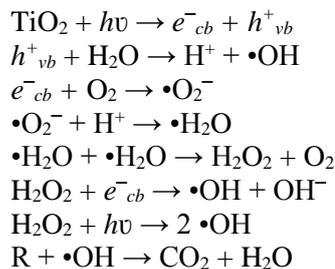
**Table 3.** Effect of TiO<sub>2</sub> nanoparticles mass on ceftriaxone degradation

No.	TiO <sub>2</sub> mass (mg)	% Degradation
1	50	81.85
2	75	83.90
3	100	86.22
4	125	86.41
5	150	87.60

**Effect of Irradiation Time**

The degradation percentage of 50 mL 250 ppm ceftriaxone using TiO<sub>2</sub> nanoparticle catalysts with variations in irradiation time are presented in table 4. The degradation percentage of ceftriaxone continues to increase proportionately to the duration of exposure. It

is because the increasing duration of irradiation given will increase the number of OH radicals (Guo *et al.*, 2019). The formation reaction of OH radicals (Nasikhudin *et al.*, 2018) as follows:



Which R is an organic compound.

**Table 4.** Effect of irradiation time on ceftriaxone degradation

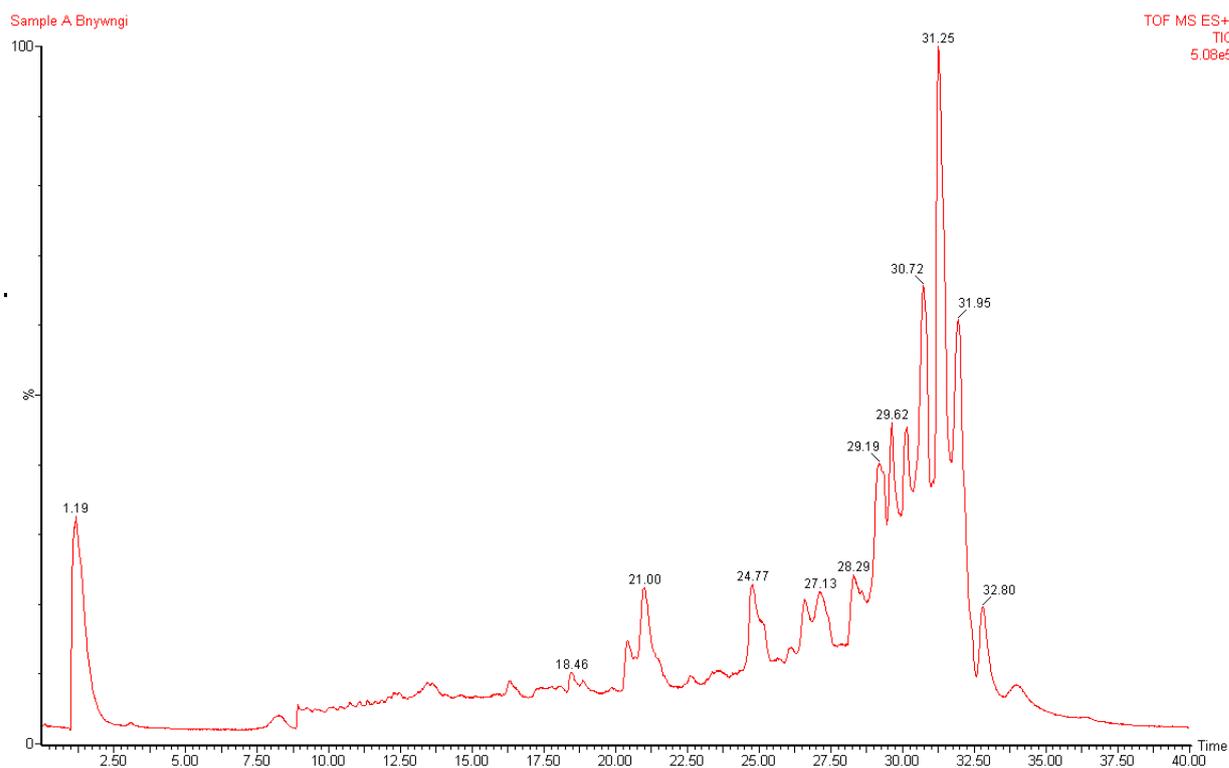
No.	Irradiation Time (hours)	% Degradation
1	5	85.62
2	6	90.12
3	7	91.37
4	8	94.64
5	9	96.52

**Toxicity and Degradation Mechanism**

The results of the toxicity test on the solution after ceftriaxone was degraded from the solution that has the best degradation percentage in each variation are presented in Table 5. The data show a decrease in inhibition zone in *E. coli* bacteria as the degradation percentage of ceftriaxone increased. It is because the increase in degradation percentage will decrease the amount of ceftriaxone. The increasing number of *E. coli* bacteria in a solution with a high degradation percentage indicates that the solution has low toxicity.

**Table 5.** Toxicity testing solution degradation products (% highest degradation) using *Escherichia coli*

No.	Variation	% Degradation	Inhibition Zone (mm)
1	Light Source	63.38	53±6
2	Acidity (pH)	67.79	36±3
3	TiO <sub>2</sub> Mass	86.22	32±7
4	Irradiation Time	96.52	16±4



**Figure 4.** Chromatogram of ceftriaxone solution from degradation under optimum conditions

The solution with the highest degradation percentage in the 9-hours radiation variation period was analyzed using LC-MS to determine the type of product that had been produced after the degradation. Allegedly, the product was used to predict the degradation mechanism of ceftriaxone. Chromatograms that was generated from LC-MS analysis are presented in Figure 4.

Figure 4 shows the presence of other compounds, which were the product of ceftriaxone degradation with TiO<sub>2</sub> nanoparticle catalyst. These other compounds have differences in polarity in mobile phase (liquid) and silent phase (solid), that a separation occurs in LC column. This separation results in different retention times (RT) for each ceftriaxone degradation product. The compounds that have been separated are predicted by looking at the results of mass-to-charge ratio ( $m/z$ ) using MS. The  $m/z$  data generated is presented in table 6.

Some products of ceftriaxone degradation cannot be identified because the  $m/z$  data from the MS analysis requires further analysis including the chromatogram at 24.77 minute with  $m/z = 149.03$ ; minute 30.72 with  $m/z = 633.15$ ; the 31.95 minute with  $m/z =$

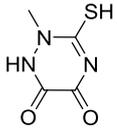
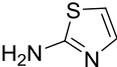
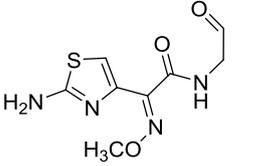
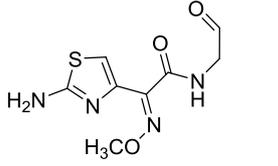
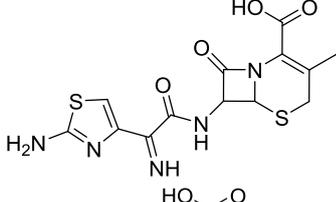
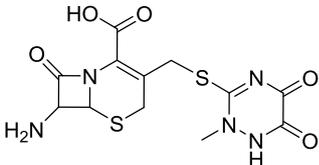
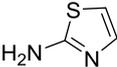
707.16. The results of  $m/z$  at 30.72 and 31.95 minutes exceeded the  $m/z$  value of ceftriaxone which is 554.05. It is suspected due to the coordination bond between ceftriaxone and Ti (IV) ions from the TiO<sub>2</sub> photo catalyst used (Doadrio *et al.*, 2002). In addition, it is suspected that this also happened at 24.77 minutes with  $m/z 149.03$ . Ti (IV) Ion forms a coordination bond with the degradation product of **E** compound.

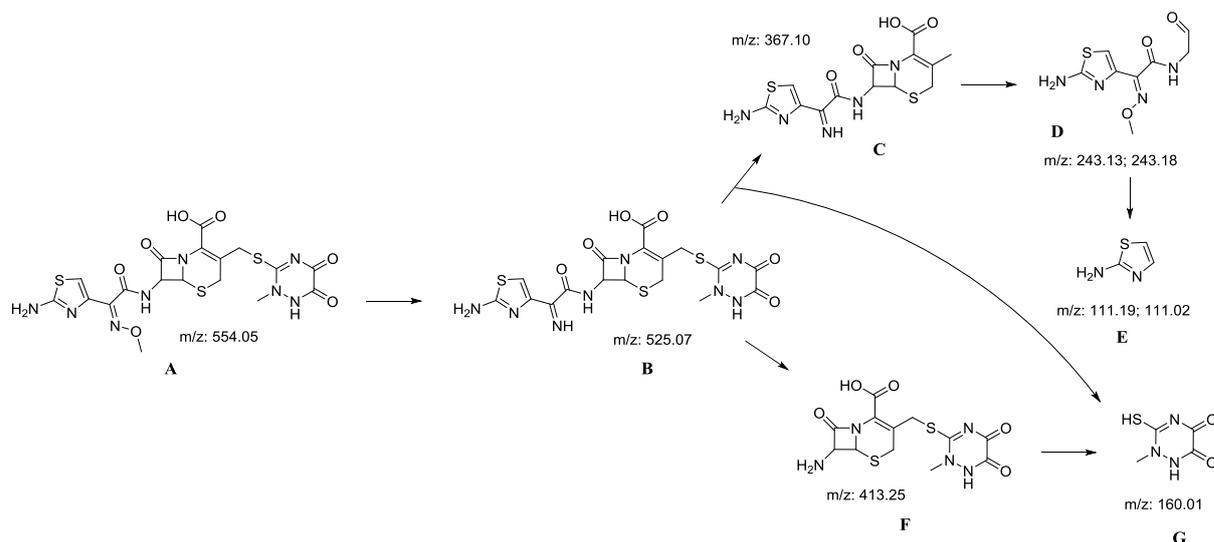
Degradation of ceftriaxone (**A** compound) begins with the interaction of ceftriaxone with photo catalyst TiO<sub>2</sub> forming a coordination bond, then protonated by releasing the methoxy group on the oxime group to form **B** compound ( $m/z$  525). The oxime group is easily damaged because it is influenced by the low ionization energy of free electrons in nitrogen heteroatoms (Zhang *et al.*, 2011). **B** Compound is protonated by removing tio-heterocyclic groups to produce **C** compound ( $m/z = 367.10$ ). The structure of **C** compound is proposed by releasing tio-heterocyclic groups in accordance with the presence of tio-heterocyclic compound fragments with  $m/z$  160.01 symbolized by **G** compound. **C** compound is protonated and causes damage to the rectangular ring on the 7-

aminosefalosporin (7-ACA) fragment (Fenollar-Ferrer *et al.*, 2008; Zhang *et al.*, 2011) by forming **D** compound. Damage to the 7-ACA ring reduces antibiotic/antibacterial activity (Verdino *et al.*, 2017), so that the clear zone produced from this optimum condition solution is the lowest. The structure of **D** compound resulted also corresponds to the fragment which subsequently yields **E** compound with  $m/z$  111. The proposed structure of **E** compound also corresponds to

the fragment of **F** compound with  $m/z$  413.25, which is one of the products of protonation of **B** compound with the release of the carbonyl group at N atoms are bound to C7 at 7-ACA. The end of ceftriaxone degradation was suspected forming  $\text{CO}_2$ ,  $\text{H}_2\text{O}$ , and several other molecules. The mechanism of ceftriaxone degradation with  $\text{TiO}_2$  nanoparticles which has been described previously is presented in Figure 5.

**Table 6.** Predictions of degradation products of ceftriaxone at optimum conditions

Retention Time (min)	$m/z$ [M+H] <sup>+</sup>	Predictions	References
1.19	160.01		(Zhang <i>et al.</i> , 2011)
21.00	111.19		(Zhao <i>et al.</i> , 2018)
24.77	149.03	Unidentified	(Zhang <i>et al.</i> , 2011)
27.13	243.13		(Zhang <i>et al.</i> , 2011)
28.29	243.18		(Zhang <i>et al.</i> , 2011)
29.19	367.10		(Zhang <i>et al.</i> , 2011)
29.62	525.07		(Zhang <i>et al.</i> , 2011)
30.72	633.15	Unidentified	-
31.25	413.25		(Zhao <i>et al.</i> , 2018)
31.95	707.16	Unidentified	-
32.80	111.02		(Zhao <i>et al.</i> , 2018)



**Figure 5.** Mechanism of degradation of ceftriaxone catalyzed by TiO<sub>2</sub> nanoparticles

#### 4. CONCLUSION

The results of research showed the influence of environmental conditions on the performance of TiO<sub>2</sub> nanoparticles in degrading ceftriaxone. The degradation percentage of 50 mL 250 ppm ceftriaxone continued to increase with the optimum conditions which was 96.5149%. The optimum conditions are using 100 mg of TiO<sub>2</sub> nanoparticles at pH 8 with radiation for 9 hours using white mercury lamps as the light source. The solution after degradation process had low toxicity against *E. coli* bacteria because the amount of ceftriaxone remained low. The products of ceftriaxone degradation produces compounds with decreased antibiotic/antibacterial activity as the 7-ACA ring breaks.

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#### REFERENCES

- Ambrosetti B, Campanella L, Palmisano R. 2015. Degradation of antibiotics in aqueous solution by photocatalytic process: comparing the efficiency in the use of ZnO or TiO<sub>2</sub>. *Journal of Environmental Science and Engineering A*. 4(6): 273-281. doi:10.17265/2162-5298/2015.06.001
- Doadrio AL, Mayorga A, Orenga R. 2002. VO<sup>2+</sup> and Cu<sup>2+</sup> Interactions with ceftriaxone and ceftizoxime. HPLC kinetic studies. *J. Braz. Chem. Soc.* 13(1): 95-100. doi:10.1590/S0103-50532002000100015
- Fenollar-Ferrer C, Frau J, Donoso J, Muñoz F. 2008. Evolution of class C β-lactamases: factors influencing their hydrolysis and recognition mechanisms. *Theor Chem Account.* doi:10.1007/s00214-008-0463-2
- Fitriyani YO, Septiani U, Wellia DV, Putri RA, Safni. 2017. Degradasi zat warna direct Red-23 secara fotolisis dengan katalis C-N-codoped TiO<sub>2</sub>. *Valensi*. 3(2): 152-159. doi:10.15408/jkv.v3i2.5792
- Guo Q, Zhou C, Ma Z, Yang X. 2019. Fundamentals of TiO<sub>2</sub> photocatalysis: concepts, mechanisms, and challenges. *Advanced Materials*. 31(50): 1-26. doi:10.1002/adma.201901997
- Hickel ER, Knabben GC, Zotto DD, Carvalho MWM, Bertoldi B, Novaes YR. 2018. Attractiveness of light-emitting diodes (LEDs) of different wavelengths to the South American rice water weevil. *Arg. Inst. Bio.* 85(2018): 1-6. doi:10.1590/1808-1657000382016
- Jiang C, Ji Y, Shi Y, Chen J, Cai T. 2016. Sulfate radical-based oxidation of fluoroquinolone antibiotics: kinetics, mechanisms and effects of natural water matrices. *Water Research*. 106(2016): 507-517. doi:10.1016/j.watres.2016.10.025

- Kashiwaya S, Morasch J, Streibel V, Toupance T, Jaegermann W, Klein A. 2018. The work function of TiO<sub>2</sub>. *Surfaces*. 1(1): 73-89. doi:10.3390/surfaces1010007
- Maletić M, Vukčević M, Kalijadis A, Janković-Častvan I, Dapčević A, Laušević Z, Laušević M. 2019. Hydrothermal synthesis of TiO<sub>2</sub>/Carbon composites and their application for removal of organic pollutants. *Arabian Journal of Chemistry*. 12(8): 4388-4397. doi:10.1016/j.arabjc.2016.06.020
- Nasikhudin, Diantoro M, Kusumaatmaja A, Triyana K. 2018. Study on photocatalytic properties of TiO<sub>2</sub> nanoparticle in various pH condition. *Journal of Physics: Conference Series*. 1011(2018): 1-7. doi:10.1088/1742-6596/1011/1/012069
- Rosa SKD, Udiyono A, Kusariana N, Saraswati LD. 2019. Faktor-faktor yang berhubungan dengan timbulnya gangren pada pasien diabetes mellitus di RSUD KRMT. Wongsonegoro Semarang. *Jurnal Kesehatan Masyarakat*. 7(1): 192-202.
- Saputro ANC, Mulyani B, Nurhayati ND, Kurniawan Y. 2016. Uji kinerja fotodegradasi kain terlapis komposit nanosized Chitosan/TiO<sub>2</sub> terhadap zat warna rhodamine B. *Valensi*. 2(1): 45-54. doi:10.15408/jkv.v2i1.3083
- Sari YO, Almasdy D, Fatimah A. 2018. Evaluasi penggunaan antibiotik pada pasien ulkus diabetikum di instalasi rawat inap (IRNA) penyakit dalam Rsup Dr. M. Djamil Padang. *Jurnal Sains Farmasi & Klinis*, 5(2): 102-111.
- Saudi HA, Adel G. 2018. The Effect of TiO<sub>2</sub> on optical and radiation shielding properties of BaO B<sub>2</sub>O<sub>3</sub> glasses. *Optics*. 7(1): 1-6. doi:10.11648/j.optics.20180701.11
- Schöpp H, Franke S. 2014. Mercury-Vapor Lamps. In R. Karlicek, C.-C. Sun, G. Zissis, & R. Ma (Eds.), *Handbook of Advanced Lighting Technology* (pp. 1-14). Cham: Springer International Publishing.
- Usman MR, Noviyanti AR, Eddy DR. 2017. Photocatalytic degradation of diazinon using titanium oxide synthesized by alkaline solvent. *Indones. J. Chem.*, 17(1): 22-29. doi:10.22146/ijc.23548
- Utami ER. 2011. Antibiotika, Resistensi, dan Rasionalitas Terapi. *El-Hayah*. 1(4): 191-198.
- Verdino A, Vigliotta G, Giordano D, Caputo I, Soriente A, Rosa MD, Marabotti A. 2017. Synthesis and biological evaluation of the progenitor of a new class of cephalosporin analogues, with a particular focus on structure-based computational analysis. *PLoS ONE*. 12(7): e0181563. doi:10.1371/journal.pone.0181563
- Zhang XH, Cao DM, Zhao SY, Gong P, Hei DQ, Zhang HQ. 2011. Gamma radiolysis of ceftriaxone sodium for water treatment: assessments of the activity. *Water Sci. Technol.*, 63(12), 2767-2774. doi:10.2166/wst.2011.485
- Zhao Y, Liang X, Wang Y, Shi H, Liu E, Fan J, Hu X. 2018. Degradation and removal of ceftriaxone sodium in aquatic environment with Bi<sub>2</sub>WO<sub>6</sub>/g-C<sub>3</sub>N<sub>4</sub> photocatalyst. *J Colloid Interface Sci*. 523: 7-17. doi:10.1016/j.jcis.2018.03.078