



Research Article

# Degradation of Ciprofloxacin by Titanium Dioxide (TiO<sub>2</sub>) Nanoparticles: Optimization of Conditions, Toxicity, and Degradation Pathway

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## Abstract

The popular use of ciprofloxacin is often irrational, so it causes environmental pollution such as resistance. The solution to overcome environmental pollution due to ciprofloxacin is degradation by using TiO<sub>2</sub> nanoparticles. TiO<sub>2</sub> nanoparticles performance is influenced by environment such as light source, pH solvent, duration of lighting and TiO<sub>2</sub> nanoparticles mass. The residual levels determination of ciprofloxacin was carried out by using a UV-Vis spectrophotometer. Toxicity test of ciprofloxacin degradation products with TiO<sub>2</sub> nanoparticles used *Escherichia coli* bacteria. Liquid Chromatography Mass Spectrometry (LCMS) was used to determine the type of ciprofloxacin degradation product with TiO<sub>2</sub> nanoparticles. The optimum condition for the ciprofloxacin degradation with TiO<sub>2</sub> nanoparticles is lighting for 5 hours by using a white mercury UV lamp and 50 mg TiO<sub>2</sub> nanoparticles with pH solvent of 5.5. The toxicity of ciprofloxacin degradation product with TiO<sub>2</sub> nanoparticles was low. The smallest degradation product identified with m/z was p-fluoraniline (m/z 111).

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**Keywords:** Degradation; ciprofloxacin; Titanium Dioxide (TiO<sub>2</sub>); nanoparticles; degradation; toxicity

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## 1. Introduction

Ciprofloxacin is a fluoroquinolone class of antibiotics which is quite popular and is widely used in several health services, such as hospitals [1]. Ciprofloxacin is used in diseases caused by bacteria, such as: *Salmonella typhi* which causes typhoid fever [2] and some bacteria that

can cause Urinary Tract Infection (UTI) [3,4]. The use of antibiotics not only treats diseases caused by bacteria, but can also have negative effects if their use is irrational [5]. Irrational use of ciprofloxacin can cause environmental pollution, for example antibiotic resistance [1] which threatens human health [6]. Some of the health problems caused by consuming water contaminated with ciprofloxacin are vomiting, headache, diarrhea, stomatitis, skin and immune system disorders [7]. Moreover, it can interfere with the process of photosynthesis in plants which causes growth to be delayed [8].

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Several attempts have been made to reduce environmental pollution due to the use of ciprofloxacin, namely by deactivating and degrading ciprofloxacin using the microorganism *Xylaria longipes* [9], fenton oxidation [10], and oxidation with the help of a combination of UV light and chlorine gas [11]. The current popular solution in reducing environmental pollution is using a photocatalyst. TiO<sub>2</sub> photocatalysts are able to degrade environmental pollutants such as indigo carmine dyes [12], basic yellow (BY13) [13], diazinon pesticides [14], acetaminophen [15] and amoxicillin antibiotics [16,17]. Research on the degradation of ciprofloxacin using TiO<sub>2</sub> nanoparticles continues. Several researchers used TiO<sub>2</sub> nanoparticles of P25 degussa powder to obtain 100% degraded ciprofloxacin within 30 minutes [18] and 6 minutes [19]. Then several modifications were made to improve the previous results, namely by TiO<sub>2</sub> nanoparticles immobilized on glass plate, the results obtained showed that 100% ciprofloxacin was degraded within 120 minutes [20]. Then in the next study finally added several types of metals such as Fe (percentage of degradation of ciprofloxacin 94.6% for 60 minutes degradation) [21]; Cu (percentage of degradation of ciprofloxacin 97% for 4 hours degradation) [22]; and Ce (percentage of degradation of ciprofloxacin 93.22% for 180 minutes degradation). Several previous studies have shown that with TiO<sub>2</sub> nanoparticles powder is still better than some of the previous modifications [23]. Along with the continuous use of ciprofloxacin will increase the amount of ciprofloxacin pollutants, thus it is necessary to study the degradation of ciprofloxacin with a higher initial concentration.

The degradation process using TiO<sub>2</sub> nanoparticles is influenced by several factors including the light source, the mass of TiO<sub>2</sub> nanoparticles, the pH of the solution, and the duration of irradiation [24]. Each of these factors can affect the degradation product of ciprofloxacin with TiO<sub>2</sub> nanoparticles. This study aims to evaluate the optimum conditions for degradation of ciprofloxacin using TiO<sub>2</sub> nanoparticles which include a UV light source, TiO<sub>2</sub> nanoparticle mass, solution pH, and exposure time. The sources of UV light used were UV BLB lamps and white mercury lamps. Meanwhile, the pH of the solution in acidic conditions is at pH 5.5 and 6; neutral pH (pH 7); and alkaline pH at pH 7.5 and 8. In addition, this study was also to determine the type and toxicity of the degradation products of ciprofloxacin with TiO<sub>2</sub> nanoparticles. The toxicity test in this study used the *Escherichia coli* (*E. coli*) bacteria. The solu-

tion after degradation at optimum conditions was analyzed using LCMS to determine the simpler product type of ciprofloxacin degradation using TiO<sub>2</sub> nanoparticles.

## 2. Materials and Methods

### 2.1 Instruments and Chemicals

The tools in this study used glassware which is common in laboratories and several instruments, namely: magnetic stirrer (IKA C-MAG HS 7), centrifuge (Health), UV reactor with UV BLB (Blue Light Blue) (8 W, wavelength 365 nm, Gaxindo) and UV lamps. white mercury HPL-N (250 W, wavelength 300-700 nm, Philips), UV-Visible spectrophotometer (Thermo Scientific, Genesys 10S UV-Vis), 10-100  $\mu$ L micropipette (Dragon Lab), and Liquid Chromatography Mass Spectrometry (LC-MS). The materials in this study were distilled water, ciprofloxacin (Asclepius Bio-Tech), *Escherichia coli* (*E. coli*) bacteria, 3 mm diameter disc paper (Oxoid), agar medium (KGaA), and several chemicals obtained from Merck, namely TiO<sub>2</sub> nanoparticles P25 Degussa (anatase 85.7% with crystallite size 32.84 nm and rutile 14.3% with crystallite size 22.59 nm) [25], sodium chloride (NaCl), sodium dihydrogen phosphate dihydrate (NaH<sub>2</sub>PO<sub>4</sub>·2H<sub>2</sub>O), and sodium monohydrogen phosphate dihydrate (Na<sub>2</sub>HPO<sub>4</sub>·5H<sub>2</sub>O).

### 2.2 Standard Equation of Ciprofloxacin

500 ppm ciprofloxacin mother solution was prepared by dissolving 100 mg of ciprofloxacin into 200 mL of 0.1 M NaCl solution. 500 ppm mother liquor was used for scanning the maximum wavelength in the range 190-400 nm. 500 ppm mother liquor diluted to 250; 100; 50; 25; and 10 ppm to determine the standard equation for ciprofloxacin. The standard ciprofloxacin equation is used to determine the concentration of ciprofloxacin after degradation.

### 2.3 Optimization of Degradation Condition

Optimization of the degradation conditions of ciprofloxacin with TiO<sub>2</sub> nanoparticles included light source, solution pH, mass of TiO<sub>2</sub> nanoparticles, and irradiation time respectively. The light sources used in the optimization of light sources are UV BLB and white mercury UV lamps. The 500 ppm ciprofloxacin solution was diluted to 250 ppm with phosphate buffer pH 7. The ciprofloxacin solution was then added with 100 mg of TiO<sub>2</sub> nanoparticles and degraded for 5 hours. The

TiO<sub>2</sub> nanoparticles were separated from the solution by centrifugation at 4000 rpm for 30 minutes. The optimum light source will be used to optimize the pH of the solution with variations in the pH of the solution, namely at pH 5.5; 6; 7; 7.5 and 8. The optimum light source and the optimum pH of the solution are used to optimize the duration of irradiation with variations of 5; 6; 7; 8; and 9 hours. The last optimization is the mass of TiO<sub>2</sub> nanoparticles with variations in the mass of TiO<sub>2</sub> nanoparticles used, namely 50; 75; 100; 125; and 150 mg, each of which will be degraded under optimum light source conditions, solution pH, and exposure time.

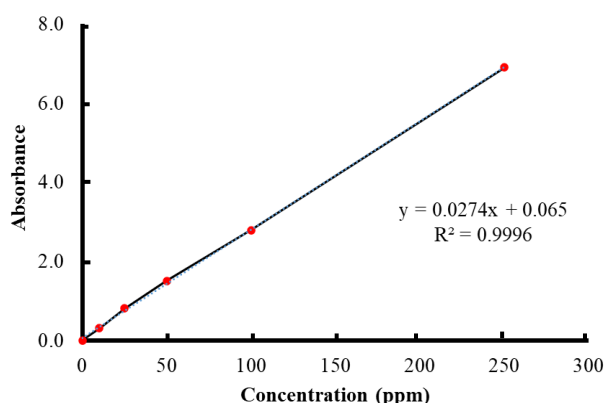
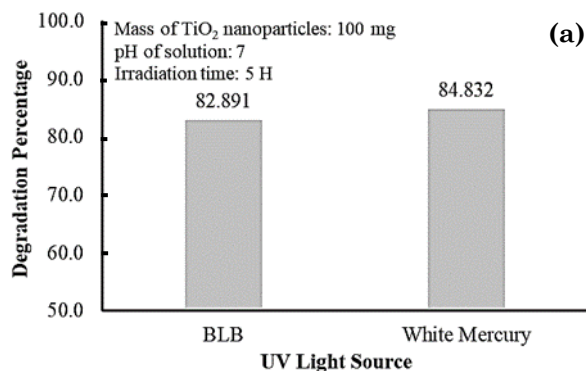


Figure 1. Standard curve of ciprofloxacin.



## 2.4 Toxicity and Degradation Pathway

The toxicity of ciprofloxacin degradation products with TiO<sub>2</sub> nanoparticles at each optimum condition was based on the zone of inhibition against the growth of *E. coli* bacteria. The number of bacteria used was 50 μL in 20 mL Nutrient Agar (NA) media. Disc paper that was added with 20 μL of the test solution was put into a petri dish filled with bacterial suspension. The petri dishes were then incubated at room temperature for 18 hours. The determination of the degradation pathway of ciprofloxacin with TiO<sub>2</sub> nanoparticles will be based on the results of the LCMS analysis of the degradation products with the lowest residual amount of ciprofloxacin of all degradation products.

## 3. Results and Discussion

### 3.1 Standard Equation of Ciprofloxacin

Scanning the maximum wavelength of 500 ppm ciprofloxacin was carried out with two intervals, 2 nm intervals at 190-400 nm wavelengths and 1 nm intervals at 275-285 nm wavelengths. The maximum wavelength obtained is 278 nm, where in different studies the maximum wavelength of ciprofloxacin is 275 nm [26]. The standard ciprofloxacin equation obtained is:  $y = 0.0274x + 0.065$  with

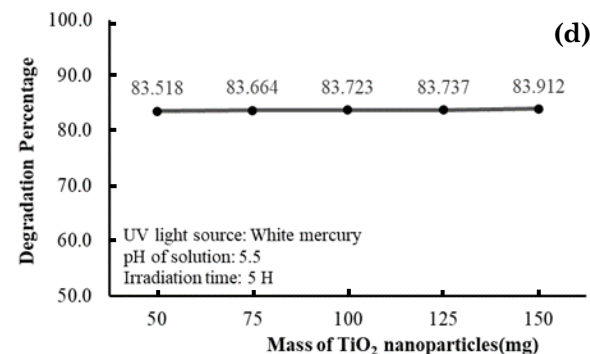
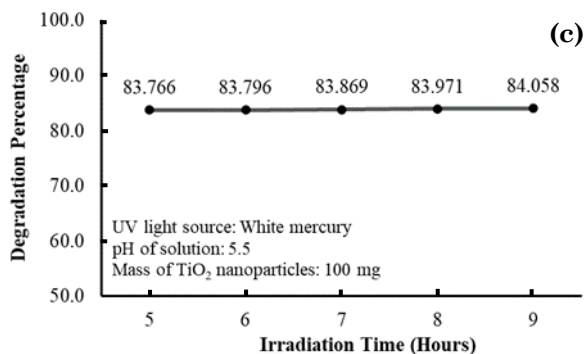
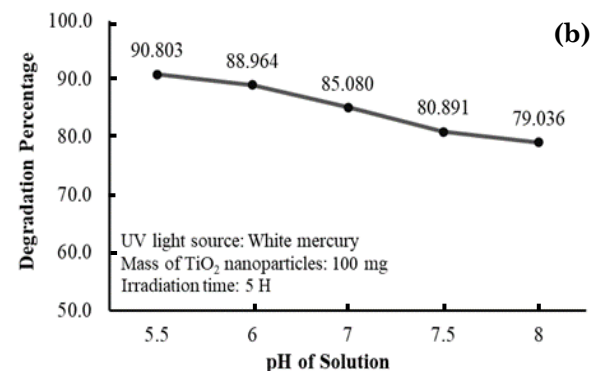


Figure 2. Condition optimization of ciprofloxacin degradation by TiO<sub>2</sub> nanoparticles (a) UV light source; (b) pH of solution; (c) irradiation time; and (d) mass of TiO<sub>2</sub> nanoparticles.

$R^2 = 0.9996$ . The standard curve of ciprofloxacin is shown in Figure 1.

### 3.2 Optimization of Degradation Condition

Optimization of the light source used to degrade ciprofloxacin 250 ppm with  $\text{TiO}_2$  nanoparticles is shown by the ratio of % degradation in Figure 2a. The % degradation yield of 250 ppm ciprofloxacin with  $\text{TiO}_2$  nanoparticles using white mercury UV light sources was higher than using UV BLB light sources. This is because the photon energy originating from a white mercury UV light source is more suitable for activating  $\text{TiO}_2$  nanoparticles in degrading ciprofloxacin [24].

The % degradation yield from optimizing the pH of the solution with a white mercury light source is shown in Figure 2b. The results obtained indicated that pH 5.5 was the optimum condition for degrading ciprofloxacin with  $\text{TiO}_2$  nanoparticles. Acidic conditions in the solution can increase the amount of positive charge on the surface of  $\text{TiO}_2$  nanoparticles. The increase in the positive charge on the surface of  $\text{TiO}_2$  nanoparticles will increase the amount of ciprofloxacin adsorbed on the surface of  $\text{TiO}_2$  nanoparticles with electrostatic bonds [27]. An electrostatic bond is formed between the piperazine ring which has high electrons and the hole on the  $\text{TiO}_2$  surface which is positively charged [28] as shown in Figure 3. In addition, the aromatic amine group on the piperazine ring of ciprofloxacin has a pKa of 4-5 so it is easily ionized under acidic conditions [29] and then it will be degraded. Meanwhile, in alkaline conditions the amount of ciprofloxacin adsorbed onto the  $\text{TiO}_2$  surface decreases the value of % degradation. Similar results showing the best conditions, namely acidic conditions, were shown in the

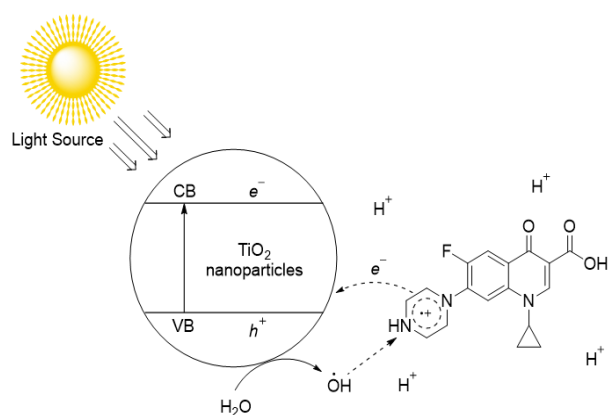


Figure 3. Ciprofloxacin adsorption on  $\text{TiO}_2$  nanoparticles surface.

degradation studies of methylene blue dye [30] and phenol [31]. The interaction of ciprofloxacin with  $\text{TiO}_2$  nanoparticles in acidic conditions when exposed to light [28] is as follows:

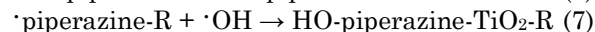
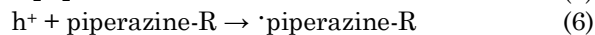
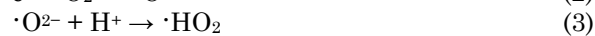


Figure 2c shows the % degradation results of ciprofloxacin with  $\text{TiO}_2$  nanoparticles on optimization of exposure time. The results obtained show similar % degradation values from the variations that were carried out. This is due to the acidic conditions in the solution system so that it can increase the effectiveness of  $\text{TiO}_2$  nanoparticles in degrading ciprofloxacin [27]. Thus, irradiation for 5 hours was able to degrade ciprofloxacin with  $\text{TiO}_2$  nanoparticles optimally.

The same thing was also obtained in the optimization of the mass of  $\text{TiO}_2$  nanoparticles, namely the % degradation value which was not too different. The results of mass optimization for  $\text{TiO}_2$  nanoparticles are shown in Figure 2d. The similar % degradation value indicates that the variation in the mass of  $\text{TiO}_2$  nanoparticles carried out is close to the amount that can cause a shielding effect. The shielding effect occurs when the amount of  $\text{TiO}_2$  nanoparticles used is excessive so that it can block light from reaching the  $\text{TiO}_2$  nanoparticles surface that is in the solution. The existence of this effect resulted in the  $\text{TiO}_2$  nanoparticles in the interior of the solution being only able to absorb ciprofloxacin without degrading it [32].

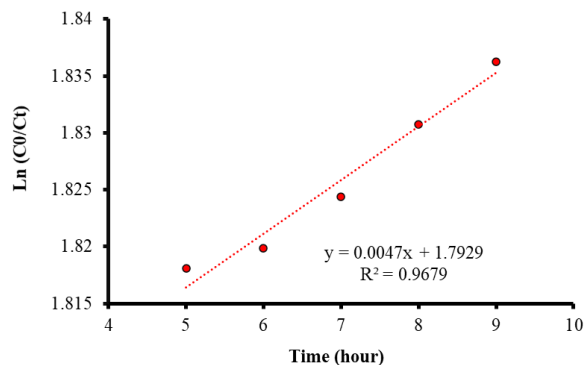


Figure 4. Pseudo-first-order Langmuir-Hinshelwood (L-H) kinetic model plot for degradation ciprofloxacin 250 ppm  $\text{TiO}_2$  nanoparticles.

Thus, the optimum 50 mg TiO<sub>2</sub> nanoparticles were used in accelerating the degradation of ciprofloxacin.

In determining the rate of degradation of ciprofloxacin with TiO<sub>2</sub> nanoparticles using a pseudo-first-order Langmuir–Hinshelwood (L–H) kinetic model [33] with the following equation:

$$\ln\left(\frac{C_t}{C_0}\right) = -k_{obs}t \quad (8)$$

Where  $C_0$  is the initial concentration of ciprofloxacin,  $C_t$  is the concentration of ciprofloxacin at a certain time ( $t$ ), and  $k_{obs}$  is the rate constant for the reaction. The observed reaction rate constant was determined by plotting  $\ln(C_t/C_0)$  against time ( $t$ ) the observed concentration of ciprofloxacin. The plotting results are presented in Figure 4 with the  $k_{obs}$  value of 0.0047 h<sup>-1</sup>. The value of  $k_{obs}$  can vary depending on several factors such as the initial concentration of ciprofloxacin [33].

### 3.3 Toxicity and Degradation Pathway

The toxicity test of ciprofloxacin degradation products used TiO<sub>2</sub> nanoparticles with optimum conditions for each variation. The data obtained are shown in Table 1. Table 1 shows a decrease in the clear zone along with the increase in the degradation of ciprofloxacin. This is influenced by the amount of ciprofloxacin residue after degradation with TiO<sub>2</sub> nanoparticles, where the increasing % of ciprofloxacin degradation indicates that the remaining amount of ciprofloxacin residue is getting smaller. The decrease in the clear zone in Table 1 shows a decrease that is not equivalent to an increase in the percentage of degradation. This is presumably because there is *E. coli* that is resistant to ciprofloxacin [34]. Resistance of *E. coli* to ciprofloxacin is also seen in the growth ratio of *E. coli* shown in Figure 5. Figure 5a shows that the resulting clear zone does not show any *E. coli* growth. In contrast to the clear zone in Figure 5b which shows the

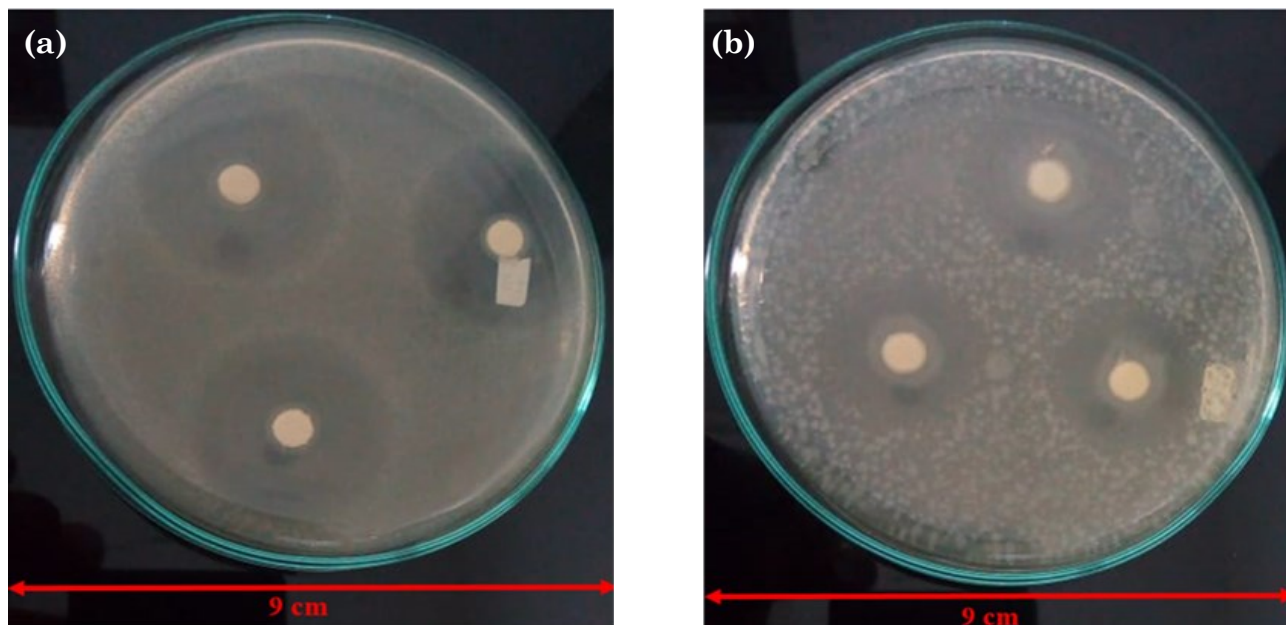
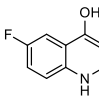
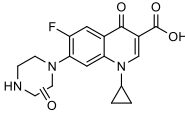
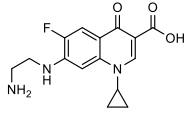
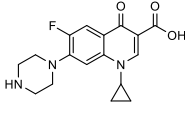
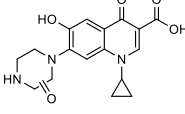
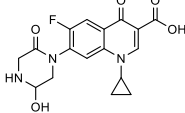
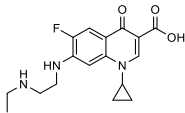
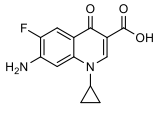
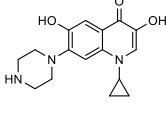
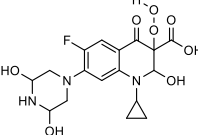
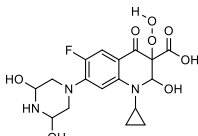

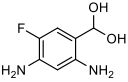


Figure 5. Clear zone of the degradation product of ciprofloxacin (a) degradation percentage 83.52% and (b) degradation percentage 83.77%.

Table 1. Toxicity of degradation ciprofloxacin product by TiO<sub>2</sub> nanoparticles at the optimum conditions of each variation.

Variant		%Degradation (%)	Clear Zone
Mass of TiO <sub>2</sub>	50 mg	83.52	2.8
Irradiation time	5 hours	83.77	2.5
UV light source	White mercury	84.83	2.1
pH of solution	5.5	90.80	1.6

Table 2. Compound product of degradation ciprofloxacin by TiO<sub>2</sub> nanoparticles at optimum condition.

RT	m/z	Molecule Formula	Molecule Structure	References
1.19	164.9352	C <sub>9</sub> H <sub>8</sub> FN <sub>1</sub> O		[37]
9.62	346.1229	C <sub>17</sub> H <sub>18</sub> FN <sub>3</sub> O <sub>4</sub>		[38]
10.52	306.125	C <sub>15</sub> H <sub>16</sub> FN <sub>3</sub> O <sub>3</sub>		[11,38]
10.98	332.1309	C <sub>17</sub> H <sub>18</sub> FN <sub>3</sub> O <sub>3</sub> Ciprofloxacin		[10,11,38]
11.73	344.1103	C <sub>17</sub> H <sub>19</sub> N <sub>3</sub> O <sub>5</sub>		[38]
12.12	362.1118	C <sub>17</sub> H <sub>16</sub> FN <sub>3</sub> O <sub>5</sub>		[38]
12.82	334.1109	C <sub>17</sub> H <sub>20</sub> FN <sub>3</sub> O <sub>3</sub>		[39]
13.36	263.0703	C <sub>13</sub> H <sub>11</sub> FN <sub>2</sub> O <sub>3</sub>		[38]
15.25	301.0835	C <sub>16</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub>		[10]
29.65	522.5985		Unidentified (Complex compound of ciprofloxacin with Ti(IV))	
30.14	550.6289			
31.23	413.2609	C <sub>17</sub> H <sub>20</sub> FN <sub>3</sub> O <sub>8</sub>		[37]
32.033	413.2687	C <sub>17</sub> H <sub>20</sub> FN <sub>3</sub> O <sub>8</sub>		[37]
32.79	111.0223	C <sub>6</sub> H <sub>6</sub> FN		[43]
34.22	172.9619	C <sub>7</sub> H <sub>9</sub> FN <sub>2</sub> O <sub>2</sub>		[42]

growth of *E. coli* around the disc paper. The good growth of *E. coli* indicates that the degradation product of ciprofloxacin with TiO<sub>2</sub> nanoparticles has low toxicity.

The chromatogram resulting from LCMS analysis of the degradation product of ciprofloxacin at optimum conditions with the % degradation value of 90.80% is shown in Figure 6. The chromatogram has several peaks with dif-

ferent retention times indicating that there are several compounds of ciprofloxacin degradation products with TiO<sub>2</sub> nanoparticles. The determination of ciprofloxacin degradation product compounds was based on the mass spectrum results of each peak that appeared on the chromatogram. Some of the degradation product compounds are shown in Table 2. Data in table 2 there are several peaks that cannot be identi-

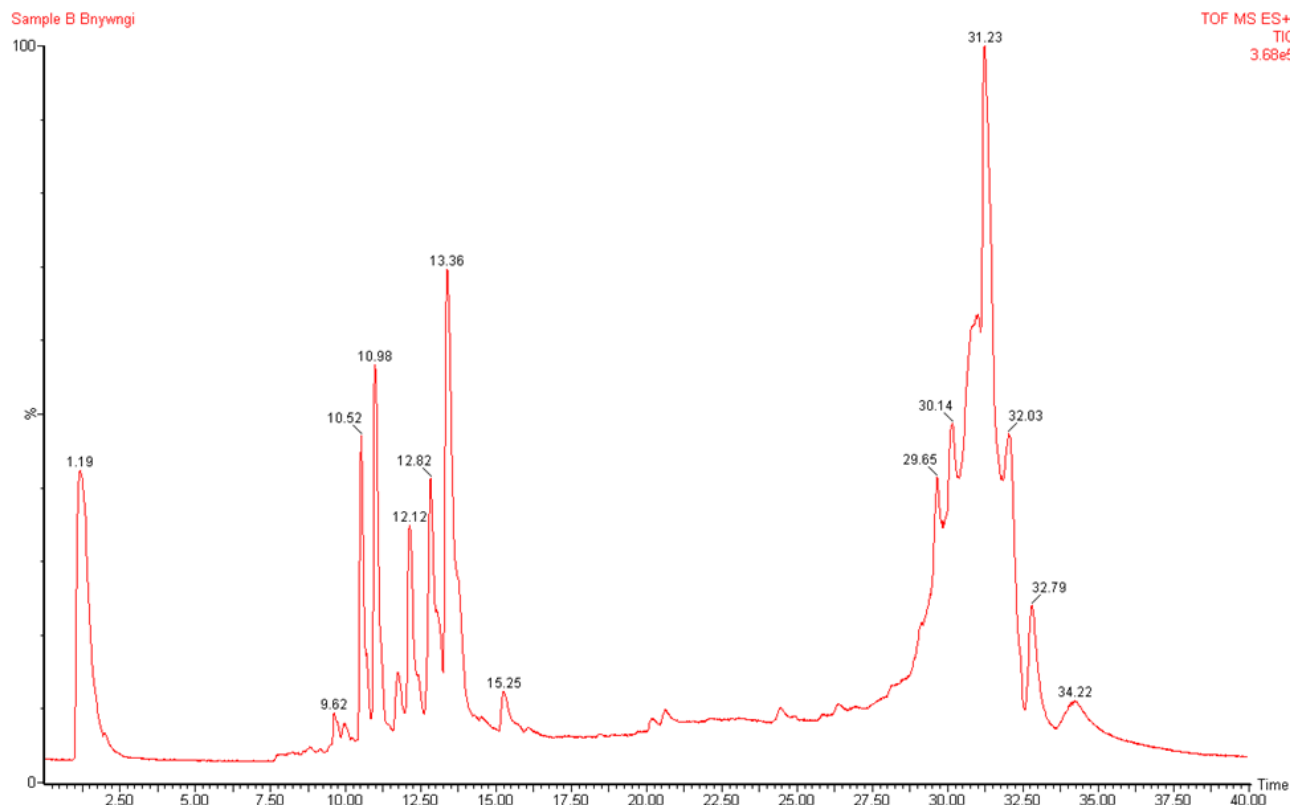


Figure 6. Chromatogram of degradation ciprofloxacin product by TiO<sub>2</sub> nanoparticles at optimum condition.

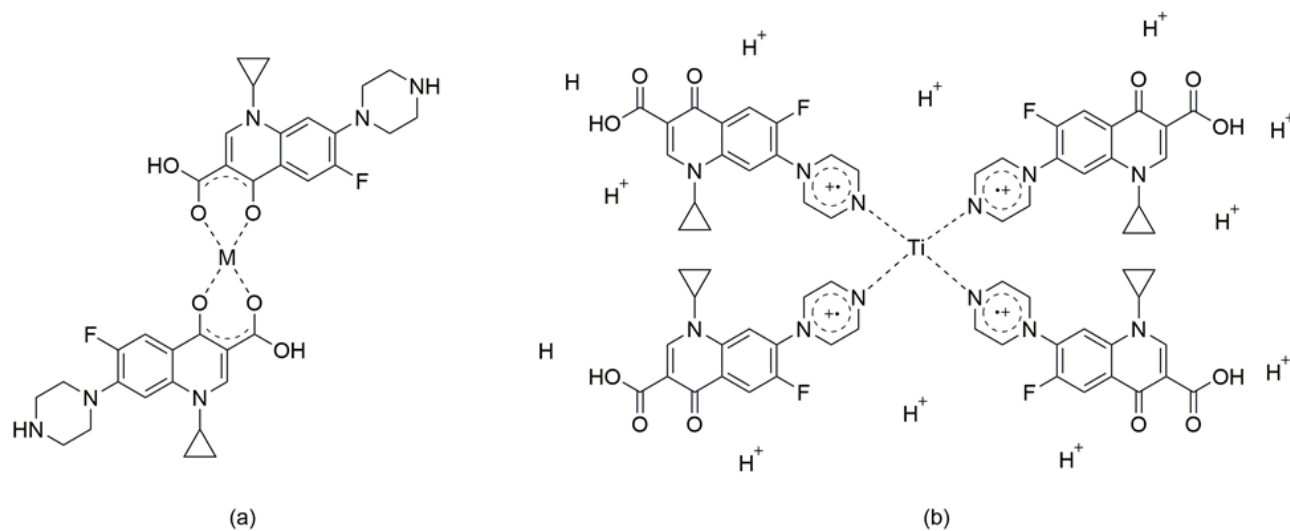


Figure 7. Complex compound of ciprofloxacin (a) with metal in general [36] and (b) with TiO<sub>2</sub> in acidity.

fied, namely the peak at the retention time of 29.65 with  $m/z$  522.5985 and at the retention time of 30.14 with  $m/z$  550.6289.

The peak has  $m/z$  more than  $m/z$  of ciprofloxacin, so it is suspected that during the retention time a complex Ti(IV) compound from  $TiO_2$  nanoparticles with ciprofloxacin was formed. The N and O atoms in ciprofloxacin are able to donate the lone pair to Ti(IV) to form complex compounds. In general, ciprofloxacin complex compounds with metals are formed in carbonyl groups [35,36] as shown in Figure 7a. However, in this study the metal Ti(IV) used also acts as a photocatalyst under acidic conditions so that it is suspected that it can form complex compounds with the structure shown in Figure 7b.

The piperazine ring that approaches the surface of  $TiO_2$  is unstable and easily binds with OH produced by  $TiO_2$ . This is indicated by the structure of compound **A** in Figure 8 which is a degradation product at the retention times of 31.23 and 32.033 with similar  $m/z$  values, namely 413.2609 and 413.2687. Research by Aggelopoulos *et al.* [37] also showed the mechanism pathway for the formation of compound **A** in the presence of  $O_2$  and  $H_2O$  in the solution system and OH which continues to be generated on the  $TiO_2$  surface. The compound **A** initiates the degradation process of ciprofloxacin. The increasing number of electrons in the piperazine ring causes the OH group to be oxidized to compound **B** with  $m/z$  346. In addition, the increasing number of OH on the surface of

$TiO_2$  causes the F atom to be substituted into an OH group in compound **C** with  $m/z$  301 [38]. The piperazine ring in compound **C** is also oxidized to produce compound **D** with  $m/z$  344 which is similar to compound **B**. The resulting **B** compound is degraded in 2 ways to become compound **G** with  $m/z$  306. The first path is compound **B** is reoxidized to become compound **E** that has  $m/z$  362. In contrast to the second path, the piperazine ring undergoes a deformylation reaction which is then followed by a hydrogenation reaction. This reaction causes the termination of the amine (C-N) bonds in the piperazine ring to produce compound **F** ( $m/z$  334) [39]. The carbon chain in compound **F** undergoes a second dissolving reaction of the amine atom (C-N) to produce compound **G**. In addition, compound **G** with an  $m/z$  value of 306 is also produced from compound **E** which undergoes rapid reduction and deformylation reactions [38]. Based on the results also obtained by Guo *et al.* [38] showed that the breakdown of the piperazine ring could break the amine (C-N) bond resulting in compound **H**. Compound **I** with  $m/z$  164 was also identified as a product in the research of Aggelopoulos *et al.* [37]. Compound **I** is thought to be a product of a deamination reaction, desiclopropylation [40], and a reduction or decarboxylation reaction [41]. In addition, the loss of the lateral group in compound **H** results in compound **J** with  $m/z$  172 [42]. The resulting **J** compound then underwent a deamination and decarboxy-

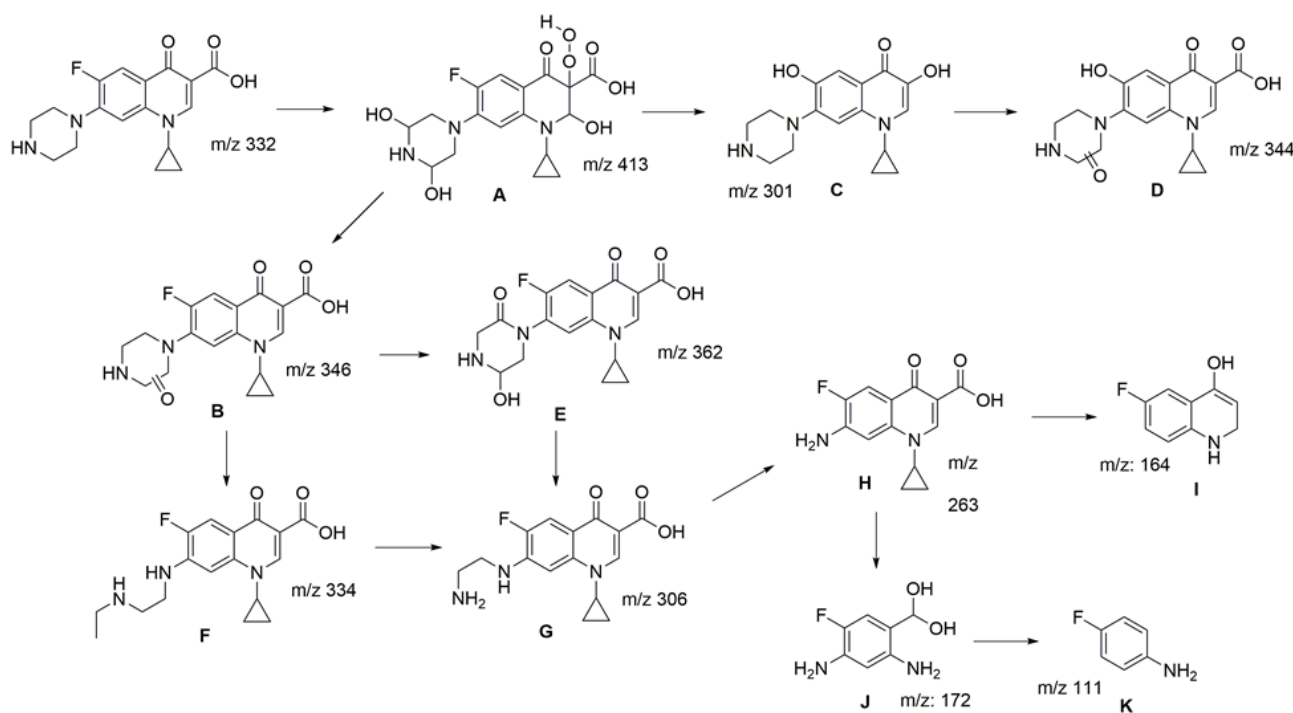


Figure 8. Degradation pathway of ciprofloxacin by  $TiO_2$  nanoparticles.



lation reaction which produced **K** compound with  $m/z$  111 was also identified in the biodegradation of ciprofloxacin using *Labrys portucalensis F11* in the study of Amorim *et al.* [43]. The compound **K** produced with the smallest  $m/z$  was suspected because the initial concentration of ciprofloxacin used was high, resulting in a complex reaction between the ciprofloxacin radical or the intermediate compound radical with other intermediate compounds. The degradation pathway of ciprofloxacin with  $TiO_2$  nanoparticles is shown in Figure 8.

#### 4. Conclusions

This study showed that the optimum conditions for the degradation of 50 mL ciprofloxacin 250 ppm using  $TiO_2$  nanoparticles, namely with a white mercury UV lamp light source, at a pH of 5.5, irradiation time is 5 hours and the mass of  $TiO_2$  nanoparticles used is 50 mg. The degradation product of ciprofloxacin with  $TiO_2$  nanoparticles has low toxicity as indicated by the stable growth of *E. coli*. The resulting clear zone is influenced by the amount of ciprofloxacin residue remaining and the resistance of *E. coli* to ciprofloxacin. The residual amount of ciprofloxacin was indicated by the value of % degradation, where the higher the % degradation, the less residue is left, so that the resulting clear zone is smaller. The degradation pathway of ciprofloxacin begins with the adsorption of ciprofloxacin molecules onto the surface of  $TiO_2$  nanoparticles which then in the presence of light produces several radicals. These radicals react by destroying the piperazine ring through several reactions including oxidation reactions, substitution, deformylation and several others. The simplest identified degradation product compound of ciprofloxacin was p-floroaniline (compound **K**) with an  $m/z$  value of 111. The results indicated the ability of  $TiO_2$  nanoparticles to degrade ciprofloxacin at high concentrations. This can be used as a reference for several industries, especially the pharmaceutical industry in the treatment of ciprofloxacin waste. It is suggested that further research should be focused on the selection of  $TiO_2$  nanoparticle powder separation methods, separation and analysis of the toxicity of each degradation product.

#### References

- [1] Hassani, A., Khataee, A., Karaca, S., Fathinia, M. (2016). Heterogeneous Photocatalytic Ozonation of Ciprofloxacin using Synthesized Titanium Dioxide Nanoparticles on a Montmorillonite Support: Parametric Studies, Mechanistic Analysis and Intermediates Identification. *RSC Advances*, 6(90), 87569-87583. DOI: 10.1039/c6ra19191f
- [2] Yogita, S.P., Hendrayana, M.A., Sukrama, I.D.M. (2018). Pola Kepekaan Bakteri *Salmonella typhi* Terisolasi dari Darah terhadap Siprofloksasin dan Seftriakson di RSUP Sanglah Periode Januari 2015 - Maret 2017. *Jurnal Medika*, 7(12), 1-6.
- [3] Musdalipah, M. (2018). Identifikasi Drug Related Problem (DRP) pada Pasien Infeksi Saluran Kemih di Rumah Sakit Bhayangkara Kendari. *Jurnal Kesehatan*, 11(1), 39-50. DOI: 10.24252/jkesehatan.v11i1.4908
- [4] Restyana, A., Admaja, W. (2019). Analisa Biaya Penggunaan Seftriakson dan Siprofloksasin Pasien Infeksi Saluran Kemih di Rumah Sakit X Kabupaten Jombang Tahun 2017. *Pharmacy*, 16(2), 347-355. DOI: 10.30595/pharmacy.v16i2.5847
- [5] Pratiwi, I., Azis, S., Kusumastuti, E. (2018). Rasionalitas Penggunaan Antibiotik Ciprofloxacin pada Penderita Demam Tifoid. *Biomedical Journal of Indonesia*, 4(2), 46-51. DOI: 10.32539/BJI.V4I2.7959
- [6] Raini, M. (2016). Antibiotik Golongan Fluorokuinolon: Manfaat dan Kerugian. *Media Litbangkes*, 26(3), 163-174. DOI: 10.22435/mpk.v26i3.4449.163-174
- [7] Ghanbari, F., Zirrahi, F., Olfati, D., Gohari, F., Hassani, A. (2020).  $TiO_2$  Nanoparticles Removal by Electrocoagulation using Iron Electrodes: Catalytic Activity of Electrochemical Sludge for the Degradation of Emerging Pollutant. *Journal of Molecular Liquids*, 310, 113217. DOI: 10.1016/j.molliq.2020.113217
- [8] Lima, V.B., Goulart, L.A., Rocha, R.S., Steter, J.R., Lanza, M.R.V. (2020). Degradation of Antibiotic Ciprofloxacin by Different AOP Systems using Electrochemically Generated Hydrogen Peroxide. *Chemosphere*, 247, 1 2 5 8 0 7 . D O I : 10.1016/j.chemosphere.2019.125807
- [9] Rusch, M., Spielmeier, A., Zorn, H., Hamscher, G. (2018). Biotransformation of Ciprofloxacin by *Xylaria longipes*: Structure Elucidation and Residual Antibacterial Activity of Metabolites. *Appl. Microbiol. Biotechnol.*, 102(19), 8573-8584. DOI: 10.1007/s00253-018-9231-y

- [10] Giri, A.S., Golder, A.K. (2014). Ciprofloxacin Degradation from Aqueous Solution by Fenton Oxidation: Reaction Kinetics and Degradation Mechanisms. *RSC Advances*, 4(13), 6738-6745. DOI: 10.1039/c3ra45709e
- [11] Deng, J., Wu, G., Yuan, S., Zhan, X., Wang, W., Hu, Z.-H. (2019). Ciprofloxacin Degradation in UV/Chlorine Advanced Oxidation Process: Influencing Factors, Mechanisms and Degradation Pathways. *Journal of Photochemistry and Photobiology A: Chemistry*, 371, 151-158. DOI: 10.1016/j.jphotochem.2018.10.043
- [12] Ansori, S., Sriatun, S., Pardoyo, P. (2016). Modifikasi Zeolit Alam Menggunakan TiO<sub>2</sub> Pewarna Indigo Carmine. *Jurnal Kimia Sains dan Aplikasi*, 19(2), 68-71. DOI: 10.14710/jksa.19.2.68-71
- [13] Khataee, A., Alidokht, L., Hassani, A., Karaca, S. (2013). Response Surface Analysis of Removal of a Textile Dye by a Turkish Coal Powder. *Advances in Environmental Research*, 2(4), 291-308. DOI: 10.12989/AER.2013.2.4.291
- [14] Usman, M.R., Noviyanti, A.R., Eddy, D.R. (2017). Photocatalytic Degradation of Diazinon Using Titanium Oxide Synthesized by Alkaline Solvent. *Indonesian Journal of Chemistry*, 17(1), 22-29. DOI: 10.22146/ijc.23548
- [15] Hassani, A., Eghbali, P., Kakavandi, B., Lin, K.-Y.A., Ghanbari, F. (2020). Acetaminophen Removal from Aqueous Solutions through Peroxymonosulfate Activation by CoFe<sub>2</sub>O<sub>4</sub>/mpg-C<sub>3</sub>N<sub>4</sub> Nanocomposite: Insight into the Performance and Degradation kinetics. *Environmental Technology & Innovation*, 20, 101127. DOI: 10.1016/j.eti.2020.101127
- [16] Anggraini, D.I., Pujilestari, I. (2017). Efektivitas Fotodegradasi Amoksisilin yang Dikatalisis dengan TiO<sub>2</sub> dengan Keberadaan Ion Ag(I). *Jurnal Kimia Sains dan Aplikasi*, 20(3), 105-109. DOI: 10.14710/jksa.20.3.105-109
- [17] Türkay, G.K., Kumbur, H. (2019). Investigation of Amoxicillin Removal from Aqueous Solution by Fenton and Photocatalytic Oxidation Processes. *Kuwait Journal of Science*, 46(2), 85-93.
- [18] Eckert, H., Bobeth, M., Teixeira, S., Kühn, K., Cuniberti, G. (2015). Modeling of Photocatalytic Degradation of Organic Components in Water by Nanoparticle Suspension. *Chemical Engineering Journal*, 261, 67-75. DOI: 10.1016/j.cej.2014.05.147
- [19] Silva, A.R., Martins, P.M., Teixeira, S., Carabineiro, S.A.C., Kuehn, K., Cuniberti, G., Alves, M.M., Lanceros-Mendez, S., Pereira, L. (2016). Ciprofloxacin Wastewater Treated by UVA Photocatalysis: Contribution of Irradiated TiO<sub>2</sub> and ZnO Nanoparticles on the Final Toxicity as Assessed by *Vibrio fischeri*. *RSC Advances*, 6(98), 95494-95503. DOI: 10.1039/C6RA19202E
- [20] Salma, A., Thoröe-Boveleth, S., Schmidt, T.C., Tuerk, J. (2016). Dependence of Transformation Product Formation on pH During Photolytic and Photocatalytic Degradation of Ciprofloxacin. *Journal of Hazardous Materials*, 313, 49-59. DOI: 10.1016/j.jhazmat.2016.03.010
- [21] Diao, Z.-H., Xu, X.-R., Jiang, D., Liu, J.-J., Kong, L.-J., Li, G., Zuo, L.-Z., Wu, Q.-H. (2017). Simultaneous Photocatalytic Cr(VI) Reduction and Ciprofloxacin Oxidation Over TiO<sub>2</sub>/Fe<sup>0</sup> Composite Under Aerobic Conditions: Performance, Durability, Pathway and Mechanism. *Chemical Engineering Journal*, 315, 167-176. DOI: 10.1016/j.cej.2017.01.006
- [22] Gan, Y., Zhang, M., Xiong, J., Zhu, J., Li, W., Zhang, C., Cheng, G. (2019). Impact of Cu Particles on Adsorption and Photocatalytic Capability of Mesoporous Cu@TiO<sub>2</sub> Hybrid Towards Ciprofloxacin Antibiotic Removal. *Journal of the Taiwan Institute of Chemical Engineers*, 96, 229-242. DOI: 10.1016/j.jtice.2018.11.015
- [23] Kutuzova, A., Dontsova, T., Kwapinski, W. (2021). Application of TiO<sub>2</sub>-Based Photocatalysts to Antibiotics Degradation: Cases of Sulfamethoxazole, Trimethoprim and Ciprofloxacin. *Catalysts*, 11(6), 728. DOI: 10.3390/catal11060728
- [24] Usman, M.R., Prasasti, A., Islamiah, S., Firdaus, A.N., Marita, A.W., Fajriyah, S., Yanti, E.F. (2020). Ceftriaxone Degradation by Titanium Dioxide (TiO<sub>2</sub>) Nanoparticles: Toxicity and Degradation Mechanism. *Jurnal Kimia Valensi*, 6(1), 82-89. DOI: 10.15408/jkv.v6i1.12475
- [25] Eddy, D.R., Ishmah, S.N., Permana, M.D., Firdaus, M.L. (2020). Synthesis of Titanium Dioxide/Silicon Dioxide from Beach Sand as Photocatalyst for Cr and Pb Remediation. *Catalysts*, 10(11), 1248. DOI: 10.3390/catal10111248
- [26] Sanjay, S.S., Kavalapure, R., Palled, M.S., Alegaon, S.G. (2020). Development and Validation of UV-Spectrophotometric Method for Determination of Ciprofloxacin and Curcumin in Bulk Powder. *IJPSR*, 11(3), 1161-1166. DOI: 10.13040/ijpsr.0975-8232.11(3).1161-66
- [27] Mortazavian, S., Saber, A., James, D.E. (2019). Optimization of Photocatalytic Degradation of Acid Blue 113 and Acid Red 88 Textile Dyes in a UV-C/TiO<sub>2</sub> Suspension System: Application of Response Surface Methodology (RSM). *Catalysts*, 9(4), 360-379. DOI: 10.3390/catal9040360

- [28] Hu, X., Hu, X., Peng, Q., Zhou, L., Tan, X., Jiang, L., Tang, C., Wang, H., Liu, S., Wang, Y., Ning, Z. (2020). Mechanisms Underlying the Photocatalytic Degradation Pathway of Ciprofloxacin with Heterogeneous TiO<sub>2</sub>. *Chemical Engineering Journal*, 380, 122366. DOI: 10.1016/j.cej.2019.122366
- [29] Valdes, L., Perez, I., de Menorval, L.C., Altshuler, E., Fossum, J.O., Rivera, A. (2017). A Simple Way for Targeted Delivery of an Antibiotic: In Vitro Evaluation of a Nanoclay-Based Composite. *PLoS One*, 12(11), e0187879. DOI: 10.1371/journal.pone.0187879
- [30] Viet, P.V., Tran, H.N. (2019). Adsorption and Photocatalytic Degradation of Methylene Blue by Titanium Dioxide Nanotubes at Different pH Conditions. *Advances in Natural Sciences: Nanoscience and Nanotechnology*, 10(4), 1-6. DOI: 10.1088/2043-6254/ab5100
- [31] Ratnawati, R., Enjarlis, E., Husnil, Y.A., Christwardana, M., Slamet, S. (2020). Degradation of Phenol in Pharmaceutical Wastewater using TiO<sub>2</sub>/Pumice and O<sub>3</sub>/Active Carbon. *Bulletin of Chemical Reaction Engineering & Catalysis*, 15(1), 146-154. DOI: 10.9767/brec.15.1.4432.146-154
- [32] Saudi, H.A., 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
- [33] Malakootian, M., Nasiri, A., Amiri Gharaghani, M. (2019). Photocatalytic Degradation of Ciprofloxacin Antibiotic by TiO<sub>2</sub> Nanoparticles Immobilized on a Glass Plate. *Chemical Engineering Communications*, 207(1), 56-72. DOI: 10.1080/00986445.2019.1573168
- [34] Chudlori, B., Kuswandi, M., Indrayudha, P. (2012). Microbial Patterns and Antibiotic Resistance of Isolates Collected from Specimen Pus in Dr. Moewardi Hospital Period 2012. *Pharmakon*, 13(2), 70-76.
- [35] Badal, S., Her, Y.F., Maher, L.J. (2015). Nonantibiotic Effects of Fluoroquinolones in Mammalian Cells. *Journal of Biological Chemistry*, 290(36), 22287-22297. DOI: 10.1074/jbc.M115.671222
- [36] Ukpo, G.E., Owolabi, M.A., Imaga, N.O.A., Oribayo, O.O., Ejiroghene, A.J. (2017). Effect of *Carica papaya* (Linn) Aqueous Leaf Extract on Pharmacokinetic Profile of Ciprofloxacin in Rabbits. *Tropical Journal of Pharmaceutical Research*, 16(1), 127. DOI: 10.4314/tjpr.v16i1.16
- [37] Aggelopoulos, C.A., Hatzisymeon, M., Tataraki, D., Rassias, G. (2020). Remediation of Ciprofloxacin-Contaminated Soil by Nanosecond Pulsed Dielectric Barrier Discharge Plasma: Influencing Factors and Degradation Mechanisms. *Chemical Engineering Journal*, 393, 124768. DOI: 10.1016/j.cej.2020.124768
- [38] Guo, H.G., Gao, N.Y., Chu, W.H., Li, L., Zhang, Y.J., Gu, J.S., Gu, Y.L. (2013). Photochemical Degradation of Ciprofloxacin in UV and UV/H<sub>2</sub>O<sub>2</sub> Process: Kinetics, Parameters, and Products. *Environmental Science and Pollution Research*, 20(5), 3202-3213. DOI: 10.1007/s11356-012-1229-x
- [39] Karl, W., Schneider, J., Wetzstein, H.G. (2006). Outlines of an "Exploding" Network of Metabolites Generated from The Fluoroquinolone Enrofloxacin by The Brown Rot Fungus *Gloeophyllum striatum*. *Appl. Microbiol. Biotechnol.*, 71(1), 101-113. DOI: 10.1007/s00253-005-0177-5
- [40] Pietruszka, J., Hohn, E., Solduga, G. (2006). Synthesis of Enantiomerically Pure Cyclopropyl Trifluoroborates. *Synlett*, 2006(10), 1531-1534. DOI: 10.1055/s-2006-944185
- [41] Ervens, B. (2004). A Modeling Study of Aqueous Production of Dicarboxylic Acids: 1. Chemical Pathways and Speciated Organic Mass Production. *Journal of Geophysical Research*, 109(D15), 1-20. DOI: 10.1029/2003jd004387
- [42] Antonin, V.S., Santos, M.C., Garcia-Segura, S., Brillas, E. (2015). Electrochemical Incineration of The Antibiotic Ciprofloxacin in Sulfate Medium and Synthetic Urine Matrix. *Water Res.*, 83, 31-41. DOI: 10.1016/j.watres.2015.05.066
- [43] Amorim, C.L., Moreira, I.S., Maia, A.S., Tiritan, M.E., Castro, P.M. (2014). Biodegradation of Ofloxacin, Norfloxacin, and Ciprofloxacin as Single and Mixed Substrates by *Labrys portucalensis* F11. *Appl. Microbiol. Biotechnol.*, 98(7), 3181-3190. DOI: 10.1007/s00253-013-5333-8