PHOTOCATALYTIC OXIDATION OF AZITHROMYCIN IN AQUEOUS SOLUTION BY TiO_2-COATED FIBERGLASS MEMBRANE

Giovanina - Iuliana LUPU[1], Liliana BOBIRICĂ[2], Constantin BOBIRICĂ[3], Cristina ORBECI[4]

The objective of the present paper was to investigate the photocatalytic oxidation of azithromycin, which was one of the most used antibiotics during the COVID-19 pandemic, from aqueous solutions by using an UV photocatalytic reactor equipped with three different TiO_2-coated fiberglass photocatalytic membrane. The synthetic aqueous solution of azithromycin was prepared at an initial COD (chemical oxygen demand) equivalent concentration of 500 mg O_2/L and was photocatalyzed for two hours. The photocatalytic oxidation efficiency after two hours of irradiation was in the range of 50 - 90% depending on the type of photocatalytic membrane used.

Keywords: azithromycin, photocatalytic oxidation, fiberglass membrane, titanium dioxide

1. Introduction

Water represents the most important natural and vital resource, safety of water quality being essential for people's health and well-being [1]. Fast growing of industrial development and urbanization, the modernization and advanced of industries and population, all this leads to an important growth of pollution at globally level. Another worrying situation which contributes at increase of pollution is the global demand for water, which are also growing so fast. During the Covid-19 pandemic, has been reported a high consumption of a series of drug such as antibiotics, antivirals, and analgesics [1], [2]. One of the most often used antibiotic

[1] PhD student, Faculty of Chemical Engineering and Biotechnologies, University POLITEHNICA of Bucharest, Romania, giovanina.lupu@upb.ro

[2] Department of Analytical Chemistry and Environmental Engineering, Faculty of Chemical Engineering and Biotechnologies, University POLITEHNICA of Bucharest, Romania, liliana.bobirica@upb.ro

[3] Department of Analytical Chemistry and Environmental Engineering, Faculty of Chemical Engineering and Biotechnologies, University POLITEHNICA of Bucharest, Romania, constantin.bobirica@upb.ro

[4] Department of Analytical Chemistry and Environmental Engineering, Faculty of Chemical Engineering and Biotechnologies, University POLITEHNICA of Bucharest, Romania, cristina.orbeci@upb.ro

in the coronavirus pandemic period and not only was the azithromycin, either in the form of tablets or as a powder in suspension, especially for kids up to 12 years old. Azithromycin is a semisynthetic macrolide antibiotic, widely used in the treatment of respiratory tract infections, such as pharyngitis, pneumonia, chronic bronchitis, and bronchopneumonia. In the last two years, the concentration of the drugs which was used in the treatment of Covid-19 have a big increase in the water and wastewater. This consumption has led to the inevitable appearance of this antibiotic in municipal wastewater, which implies paying more attention to its treatment [2], [3].

The conventional treatment technologies fail to remove these organic compounds from different types of wastewaters, reason for which they are becoming an emerging concern in the environmental protection. Advanced oxidation processes (AOPs) have been proven to be very efficient in removing organic contaminants present in aqueous solutions, including the antibiotics. Many research papers conclude that the advanced oxidation processes can be successfully applied for the removal of drugs, especially antibiotics. Efficiency up to more 80% removal of azithromycin was obtained using these processes [4], [5].

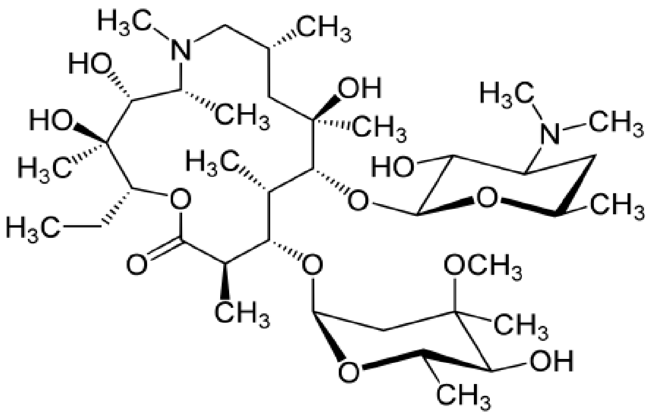

Fig. 1. Chemical structure of Azithromycin

Azithromycin is an antibiotic with broad spectrum, from macrolide group of antibiotics and it is using a large scale for treatment of several respiratory diseases. The chemical and physical properties of azithromycin is shown next, in the Table 1.

Table 1

Chemical and physical properties of azithromycin

Chemical formula	$C_{38}H_{72}N_2O_{12}$
Molecular weight	748.996 $g \cdot mol^{-1}$
Appearance	White crystal powder

Melting point	113 - 115°C
Solubility	Slightly soluble in water. DMSO (dimethyl sulfoxide):100 mg/mL Ethanol:100 mg/mL.

This drug, in addition to its antibacterial activity, has demonstrated to have antiviral and immunomodulatory activities, that are of significant interest in almost all viral infections, including Covid-19. Therefore, big increases of the consumption of this drug in the context of the current Covid-19 pandemic period has been founded in municipal wastewaters [6]. Also, azithromycin was detected in groundwater sources and hospital wastewater in almost all the world. The concentrations detected were two or three times higher compared to the period before Covid-19 pandemic. Given this trend, numerous methods of removing this antibiotic from aqueous solutions have been tested. Table 2 shows some of them with the removal efficiency obtained for each one.

Table 2

Methods for removing azithromycin from aqueous solutions

Removal method	Experimental conditions	Removal efficiency, %	Reference
Adsorption on ZnO nanoparticles	Adsorbent dosage 0.05 mg/L, hydraulic retention time 20 min, temperature 60 °C, pH 2	100	[7]
UV irradiation	Hydraulic retention time 20 min, temperature 60 °C, pH 2	73	
Fe (VI) oxidation	Fe (VI) concentration 2.53 mg/L, hydraulic retention time 20 min, temperature 60 °C pH 2	100	
UV/sodium persulfate	Azithromycin initial concentration 5 mg/L, irradiation time 30 min, pH 7	98.3	[8]
Adsorption onto organoclay adsorbents: L-methionine modified montmorillonite K10 (LMP clay)	Azithromycin initial concentration 50 mg/L, Adsorbent dosage 0.5 g/L, contact time 180 min, pH 8, temperature 25 °C	98	[9]
Adsorption onto organoclay adsorbents: 3-aminopropyltriethoxysilane functionalized magnesium phyllosilicate (AMP clay)		93	
Adsorption onto activated porous carbon prepared from Azolla filiculoides	Azithromycin initial concentration 100 mg/L, Adsorbent dosage 1 g/L contact time 75 min, pH 9, temperature 60 °C	98	[10]

Adsorption onto saponin-modified nano diatomite	Azithromycin initial concentration 100 mg/L, Adsorbent dosage 2.5 g/L contact time 60 min, pH 9, temperature 25 °C	90	[11]
Heterogeneous Fenton with amino/thiol-functionalized MnFe2O4 magnetic nanocatalysts	Azithromycin initial concentration 0.1 mg/L, catalyst dosage 1 g/L, H_2O_2 concentration 29.4 mM/L, temperature 30 °C, pH 3, reaction time 240 min	92.6	[12]
Peroxi-electrocoagulation	Azithromycin initial COD concentration 190 mg/L, current density 20 mA/cm^2, H_2O_2 concentration mM/L, electrolysis time 60 min, pH 3	95.6	[13]
Adsorption onto waste-product-derived graphene oxide	Azithromycin initial concentration 0.1 mg/L, adsorbent dosage 0.25 g/L, contact time 15 min, pH 7	98.8	[14]
Simulated sunlight radiation	Azithromycin initial concentration 0.5 mg/L H_2O_2 concentration 480 mg/L, irradiation time 30 min, pH 6	77	[15]

Therefore, the objective of this work is to test a photocatalytic system composed of an UV photocatalytic reactor and the fiberglass photocatalytic membrane with different content of photocatalyst (TiO_2) to remove azithromycin from aqueous solutions.

2. Material and Methods

2.1 Materials and chemical reagents

Azitrox formulation (200 mg/5 ml powder for oral suspension - antibiotic azithromycin) from Zentiva was purchased from a human pharmacy. It contains the active component (azithromycin dihydrate) and a series of organic and inorganic excipients (sugar, trisodium phosphate anhydrous, hydroxypropyl cellulose, xanthan gum, and banana flavor).

Hydrogen peroxide solution with a concentration of 30% was purchased from Sigma-Aldrich and its role is to be a source of hydroxyl radical species. A solution of 1 N (normality) sulfuric acid (H_2SO_4) purchased from Sigma- Aldrich was used for adjusting the value of pH of the working solutions to the default values. Chemical oxygen demand (COD) analysis was performed by using potassium dichromate ($K_2Cr_2O_7$), mercuric sulphate ($HgSO_4$), silver sulphate (Ag_2SO_4), potassium acid phthalate ($C_8H_5KO_4$), as well as sulfuric acid 95 - 97% by mass, all of them of analytical grade purchased from Sigma-Aldrich. Distilled water was used to prepare all reagents and working solutions. The photocatalytic membranes are made on an inert fiber glass support with photocatalyst (TiO_2) deposited on its surface. In this respect, the fiberglass membranes were immersed in a suspension of sodium silicate and titanium dioxide at a mass ratio of sodium silicate:titanium dioxide of 10:1. Next, the membranes were oven dried at 105°C for an one hour, followed by calcination in a furnace at 180°C for two hours.

In the next part of this paper, the acronym AZT will be used for the antibiotic (azithromycin).

2.2 Photocatalytic degradation experiments

The photocatalytic degradation experiments were carried out according to the conditions presented in Table 3. The synthetic aqueous solution of azithromycin was prepared at an initial COD (chemical oxygen demand) equivalent concentration of 500 mg O_2/L. However, the concentration of the initial solution obtained from the calculation based on the stoichiometry of the oxidation reaction was checked each time by COD analysis. After the preparation of the working solution, its pH was adjusted to the default value and the volume of H_2O_2 was added to reach the H_2O_2/AZT molar ratio of 1. UV photocatalytic reactor equipped with photocatalytic membrane was used and the working solution was continuously recirculated at room temperature by a recirculation vessel via an external centrifugal pump.

Tabel 3

Photocatalytic conditions for experimental tests

reactor volume, L	1.5
recirculation flow rate, L/min	2.0
volume of AZT working solution, L	2.0
UV lamp	High-pressure mercury lamp; power = 120 W
pH of AZT working solution	3
H_2O_2/AZT molar ratio	1
Reaction time, minutes	120
TiO_2-coated fiberglass photocatalytic membrane	0.5, 1, 2% TiO_2 (by mass)

The photocatalytic degradation progress was checked by a continuous monitoring of the evolution of the organic substrate of the working solution as a function of irradiation time. Samples of 10 mL were taken from the reactor at predefined irradiation times (5, 15, 30, 60, 90, 120 minutes). Next, the samples were prepared and analyzed for the organic content by COD analysis according to the

APHA 5220 D standard method [16]. LT 200 digestion unit and DR 3800 spectrophotometer (Hach Lange GmbH) were used in COD analysis.

3. Results and discussion

The results obtained after testing the three photocatalytic membranes are presented in Figs. 1 - 4. For all the three membranes were calculated the photocatalytic oxidation rate constant and the AZT degradation efficiency. The results obtained for the first photocatalytic membrane (0.5%TiO_2-coated fiberglass photocatalytic membrane) are shown in Fig. 1.

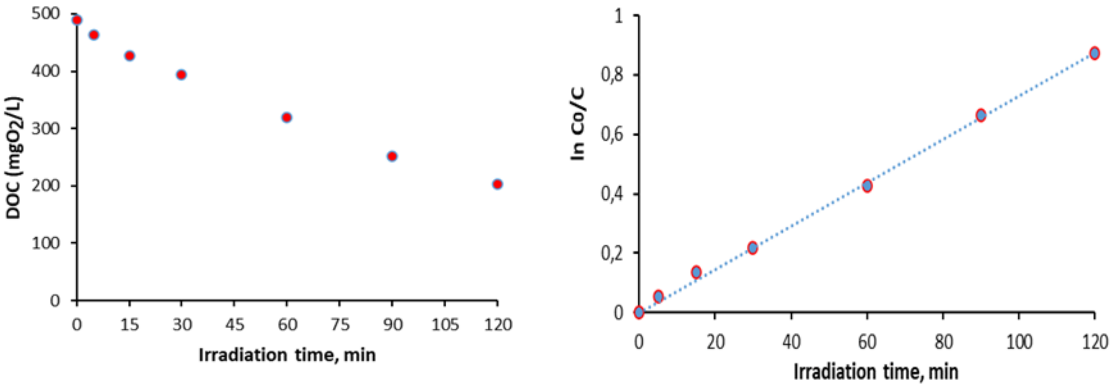

Fig. 1. Kinetics of the photocatalytic degradation of the organic content of the Azitrox using the 0.5%TiO_2-coated fiberglass photocatalytic membrane

As it can be seen, the concentration of the organic substrate decreases with the increase of the irradiation time. The content in the organic substrate of the aqueous solution decreases constantly during the two hours of irradiation from an initial concentration of approximately 500 mg O_2/L to a final concentration of approximately 200 mg O_2/L. From Fig. 1 it could be remarked that the evolution of photocatalytic degradation in time its matches on a pseudo-first-order kinetics with the rate constant value of 0.007 min^{-1}.

For the second photocatalytic membrane (1%TiO_2-coated fiberglass photocatalytic membrane) the results are presented in Fig. 2. It could be observed (Fig. 2) that the concentration of organic substrate is decreasing constantly with the irradiation time, the final concentration at 120 minutes reaching the value of approximately 136 mg O_2/L, a concentration approximately 3.4 times lower than the initial concentration. Again, a pseudo-first-order kinetics fits the experimental data, and the rate constant has a value of 0.01 min^{-1}.

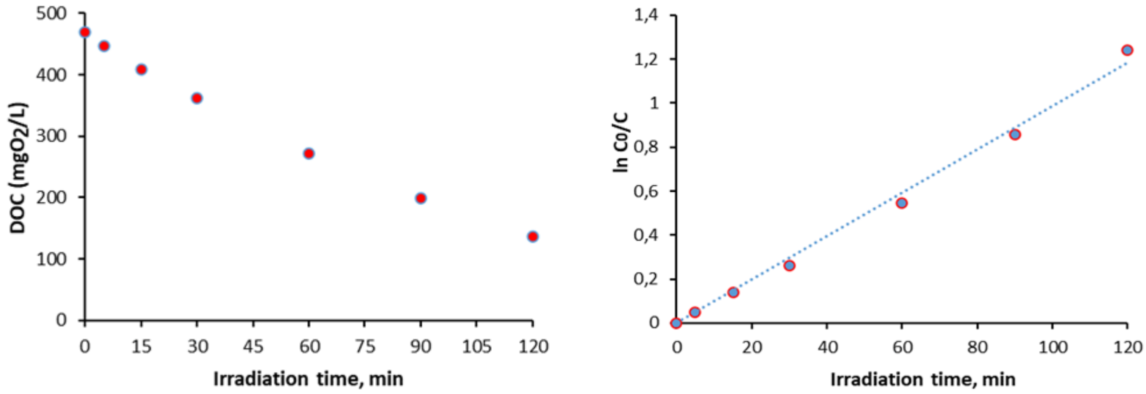

Fig. 2. Kinetics of the photocatalytic degradation of the organic substrate of the Azitrox using the 1%TiO_2-coated fiberglass photocatalytic membrane.

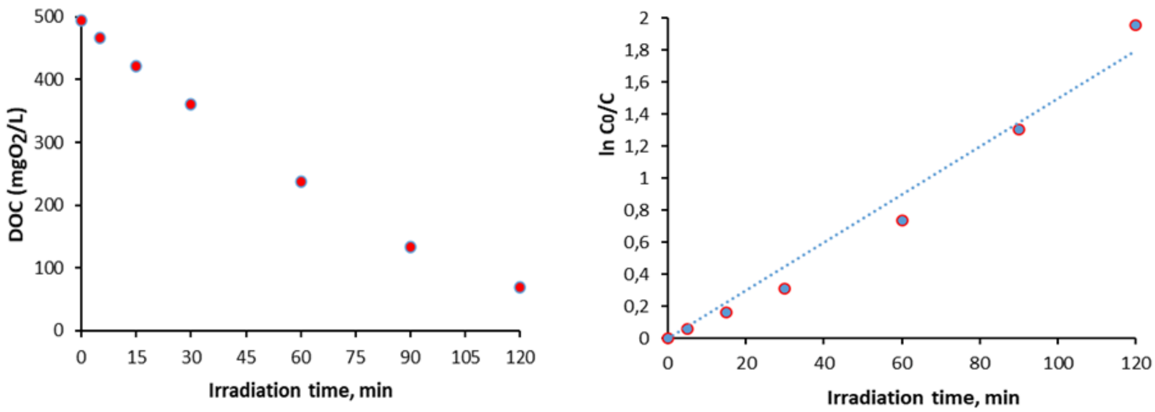

Fig. 3. Kinetics of the photocatalytic degradation of the organic substrate of the Azitrox using the 2%TiO_2-coated fiberglass photocatalytic membrane.

For the third photocatalytic membrane (2%TiO_2-coated fiberglass photocatalytic membrane) the results are shown in Fig. 3. Regarding this membrane, it has a good capability to degrade the organic substrate in the photocatalytic conditions in which the photocatalytic reactor was operated. At the end of the two hours of irradiation, the organic substrate content of the aqueous solution was approximately seven times lower compared to that at the beginning of the photocatalytic oxidation process. This result corresponds to an organic substrate degradation efficiency of almost 90%. Although the experimental results follow quite well a pseudo-first-order kinetics with a rate constant of 0.015 min^{-1}, it seems that the degradation rate in the first 30 minutes is somewhat lower than afterwards. This evolution could be attributed to the slow degradation of azithromycin in the first minutes of photocatalysis, followed by a faster degradation of both the intermediates formed and the excipients present in the Azitrox formulations.

The degradation efficiency obtained for all three photocatalytic membranes tested is presented in Fig. 4. As it can be seen, the efficiency increases with the increase of the TiO_2 content deposited on the fiberglass membrane. Thus, the membrane with a 2% TiO_2 content has an efficiency approximately 1.5 times higher than the one with 0.5% TiO_2 content and approximately 1.2 times higher than the one with 1% TiO_2 content.

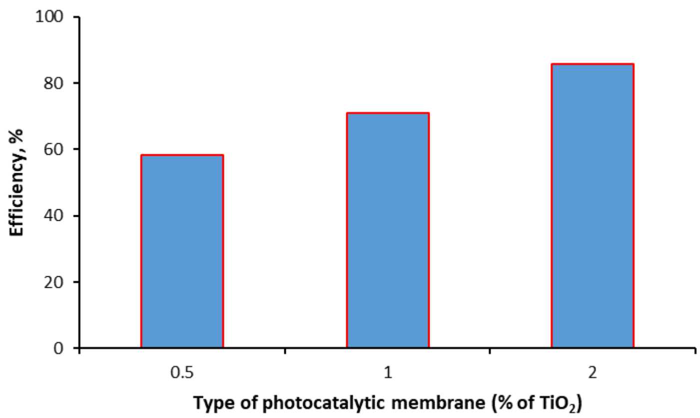

Fig. 4. Degradation efficiency of photocatalytic membranes

4. Conclusions

The experimental results obtained showed a good photocatalytic oxidation efficiency of the organic substrate present in the Azitrox formulations of the tested photocatalytic membranes. The photocatalytic degradation efficiency of the organic substrate is between 50 – 90% depending on the type of photocatalytic membrane used. It seems that increasing the content of TiO_2 deposited on the fiberglass membrane leads to an increase in the photocatalytic degradation efficiency, the best results being recorded for the membrane with 2% TiO_2 of approximately 90%. This result is also supported by the kinetic parameters of the photocatalytic oxidation process, the rate of degradation of the organic substrate increasing with the TiO_2 content of the fiberglass membranes.

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REFERENCES

[1]. *Carlos Augusto Morales-Paredes, Joan Manuel Rodríguez-Díaz, Nuria Boluda-Botella*, Pharmaceutical compounds used in the COVID-19 pandemic: A review of their presence in water and treatment techniques for their elimination, Science of The Total Environment, **vol. 814**, Mar. 2022, 152691

[2]. *Hugues Kamdem Paumo, Sadou Dalhatou, Lebogang Maureen Katata-Seru, Boniface Pone Kamdem, Jimoh Oladejo Tijani, Venkataraman Vishwanathan, Abdoulaye Kane, Indra Bahadur*, TiO_2 assisted photocatalysts for degradation of emerging organic pollutants in water and wastewater, Journal of Molecular Liquids, **vol. 331**, June 2021, 115458

[3]. *J. Arun, N. Nirmala, P. Priyadharsini, S.S. Dawn, A. Santhosh, K.P. Gopinath, M. Govarthanan*, A mini-review on bioderived carbon and its nanocomposites for removal of organic pollutants from wastewater, Materials Letters, **vol. 310**, Mar. 2022, 131476

[4]. *Nazanin Nasrollahi, Vahid Vatanpour, Alireza Khataee*, Removal of antibiotics from wastewaters by membrane technology: Limitations, successes, and future improvements, Science of The Total Environment, **vol. 838**, Part 1, Sept. 2022, 156010

[5]. *Jianlong Wang, Shizong Wang*, Toxicity changes of wastewater during various advanced oxidation processes treatment: An overview, Journal of Cleaner Production, **vol. 315**, Sept. 2021, 128202

[6]. *Marcela Jaramillo-Baquero, Henry Zúñiga-Benítez, Gustavo A. Peñuela*, Use of Photo-Fenton for macrolide antibiotic azithromycin removal, Acta Periodica Technologica, no. 51, 2020, pp. 29-37

[7]. *Amirreza Talaiekhozani, Sahar Joudaki, Farhad Banisharif, Zeinab Eskandari, Jinwoo Cho, Ghasem Moghadam, Shahabaldin Rezania*, Comparison of Azithromycin Removal from Water Using UV Radiation, Fe (VI) Oxidation Process and ZnO Nanoparticles, International Journal of Environmental Research and Public Health, **vol. 17**, no.5, Mar. 2020, 1758

[8]. *Sadeghi M, Sadeghi R, Ghasemi B, Mardani G, Ahmadi A.* Removal of Azithromycin from Aqueous Solution Using UV- Light Alone and UV Plus Persulfate ($UV/Na_2S_2O_8$) Processes, Iranian Journal of Pharmaceutical Research, **vol. 17** (Special Issue 2), May 2018, pp. 54-64

[9]. *Javad Imanipoor, Mohsen Mohammadi, Mohammad Dinari*, Evaluating the performance of L-methionine modified montmorillonite K10 and 3-aminopropyltriethoxysilane functionalized magnesium phyllosilicate organoclays for adsorptive removal of azithromycin from water, Separation and Purification Technology, **vol. 275**, Nov. 2021, 119256

[10]. *Davoud Balarak, Amir Hossein Mahvi, Saeideh Shahbaksh, Md A Wahab, Ahmed Abdala*, Adsorptive Removal of Azithromycin Antibiotic from Aqueous Solution by Azolla Filiculoides-Based Activated Porous Carbon, Nanomaterials (Basel), **vol. 11**, no. 12, Dec. 2021, 114248

[11]. *Siavash Davoodi, Behnaz Dahrazma, Nasser Goudarzi, Hajar Ghasemian Gorji*, Adsorptive removal of azithromycin from aqueous solutions using raw and saponin-modified nano diatomite, Water Science & Technology, **vol. 80**, no.5, Sept. 2019, pp. 939-949

[12]. *Hangdao Qin, Yingchang Yang, Wei Shi, Yuanbin She, Sizhan Wu*, Heterogeneous Fenton degradation of azithromycin antibiotic in water catalyzed by amino/thiol-functionalized $MnFe_2O_4$ magnetic nanocatalysts, Journal of Environmental Chemical Engineering, **vol. 9**, no. 5, Oct. 2021, 106184

[13]. *Ahmad Reza Yazdanbakhsh, Mohammad Reza Massoudinegad, Sima Eliasi, Amir Sheikh Mohammadi*, The influence of operational parameters on reduce of azithromycin COD from

wastewater using the peroxi electrocoagulation process, Journal of Water Process Engineering, **vol. 6**, June 2015, pp. 51-57

[14]. *Bushra Parvin Upoma, Sabina Yasmin, Md. Aftab Ali Shaikh, Tajnin Jahan, Md. Anamul Haque, Mohammad Moniruzzaman, and Md Humayun Kabir*, A Fast Adsorption of Azithromycin on Waste-Product-Derived Graphene Oxide Induced by H-Bonding and Electrostatic Interactions, ACS Omega, **vol. 7,** no.34, Aug. 2022, pp. 29655-29665

[15]. *Pablo Andrés Cano, Marcela Jaramillo-Baquero, Henry Zúñiga-Benítez, Yudy A.Londoño, Gustavo A.Peñuela*, Use of simulated sunlight radiation and hydrogen peroxide in azithromycin removal from aqueous solutions: Optimization & mineralization analysis, Emerging Contaminants, **vol. 6**, Dec.2020, pp. 53-61

[16]. *Greenberg, A.E., Clesceri, L.S., Eaton, A.D.*, Standard Methods for the Examination of Water and Wastewater, 18rd edition, American Public Health Association, American Water Works Association, Water Environment Federation: Washington, DC, USA, 1992, pp. 5-9