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The effect of Antibiotic on Patients Diagnosed by Corona Pandemic and Ways for Removing them: Azithromycin as a Case Study

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ABSTRACT

Pharmaceutical materials are defined as chemical compounds used in the treatment, prevention and diagnosis of diseases, thus maintaining the physical and mental health of humans and animals alike. These pharmaceuticals, especially antibiotics, pose a threat to humans and the environment at the present time, as their increased use led to an increase in their concentrations in wastewater, which led to the emergence of a new environmental problem. Due to the conversion of Corona disease into a pandemic suffered by the whole world, the use of antibiotics has increased significantly, including the drug azithromycin. For this reason, it is certain that azithromycin concentrations have increased dramatically in domestic or hospital wastewater, which must be treated with maximum efficiency, to maintain public health and safety on the one hand, and to avoid the occurrence of more serious complications on the other hand. The current review article highlights treatment methods for one of the most important types of antibiotics used in the last two years, which is azithromycin.

1. Introduction

One of the common problems threatening water resources today is the problem of pollution caused by all kinds of industrial activity, especially the textile industry and its toxic dyes, the food industry (such as olive presses), the chemical industry (the use of heavy metals, modern polycyclic hydrocarbons) and others [23]. But the pharmaceutical industry remains the most dangerous, and among these contaminated residues we find antibiotics [29]. Antibiotics are one of the most important human discoveries in the field of medicine and scientific progress in the pharmaceutical industry, as they play an important role in treating many diseases in humans and animals [13]. Just as these antibiotics are used in the treatment of some diseases in the fields of human and veterinary medicine, they are also used to accelerate the growth process in feed used for marine and wild animal production, as they resist many infections caused by bacteria or germs [4]. However, as many researchers and organizations have emphasized, this type of medicine, which is frequently used in most countries of the world, and often without a prescription, is considered the fourth cause of death due to its high share of side effects and the degree of toxicity that affects various body systems, the most dangerous of which is raising liver and kidney enzymes [30]. The annual global use of these substances is 40.2 billion DDD in 2018, an increase of 46% since the beginning of the new millennium, due to domestic, hospital or manufacturing use [9]. This large amount takes its way into domestic or industrial waterways to pollute most of the water environments associated with it after passing through sewage treatment plants [15]. Previous studies proved the inefficiency of these stations in removing many antibiotics, which sometimes do not exceed 10%, depending on the physical and chemical properties of these substances. Added to this is the treatment technology, as many studies have proven the presence of these antibiotics in various aquatic environments (surface and ground water, sea, drinking water, etc.) [11]. In the past few years, it has become clear that the discharge of sewage water directly to natural water sources is the basis of environmental pollution that can affect not only surface water, but also groundwater as well [15]. On the other hand, marine and fresh waters have recently become attracting an increasing number of pollutants associated with drug residues for human and animal use and industrial activities [26]. The presence of these antibiotics in the water of sewage treatment plants and in the waste of hospitals, private clinics and pharmaceutical factories [19], as well as in the waters of fish farming activities in the sea is a real environmental problem that is no less important than pollution by any other substances such as heavy metals, dyes, organic materials, toxic and carcinogenic wastes, since these antibiotics show a high resistance to biodegradation in aqueous media [8]. Antibiotics are thrown into sewage with urine and feces, as well as industrial waste from pharmaceutical laboratories, and their polluting effect on the environment increases when there is a mixture of these substances with their metabolites [28].

The increase in the presence of these pharmaceutical substances in wastewater, even at concentrations as low as one part per million (ppm), as a result of the increase in their production resulting from excessive consumption of them, especially when they are thrown without any treatment, constitutes a problem that must be addressed and treated as soon as possible, to avoid the negative effects that may occur as a result of biological accumulation and its transmission to humans through the food chain [7]. Other studies have proven that the direct danger posed by the combined antibiotics causes, through their accumulation, a great danger to human health and safety. Many researchers from all over the world have noticed in recent years the presence of increasing cases of antibiotic-resistant bacteria, which are bacteria that are not affected by treatment with known antibiotics, that is, they do not become infected as a result of the use of familiar antibiotics [2]. These resistant bacteria may lead to difficult-to-treat human diseases, at other times, to his death. Within this vision, researchers and specialists in environmental and medical affairs worked hard on two main aspects: The first is a biomedical one, which consists in conducting new research to develop and produce advanced types of antibiotics capable of destroying antibiotics while at the same time being harmless to humans. The second is environmental, by studying ways to remove these antibiotics with the largest possible concentration of waste water and to clean waterways from what they can contain [31]. Determining the efficient and economical treatment method requires first identifying the types of antibiotics presented to the watercourse and studying their behavior, properties and effects [17]. What increased the effects of this problem in the last two years is the Corona pandemic, which led to a very large increase in the use of antibiotics in general and azithromycin in particular, due to its influential and vital role in reducing the effects of this deadly disease on humans [1]. Azithromycin is considered one of the medical antibiotics used to treat the coronavirus, due to its anti-inflammatory properties that coincide with the infection with corona. This, of course, led to an unprecedented increase in the concentrations of this type of antibiotic in domestic or hospital wastewater, which requires a careful study to find out the latest and most recent medical data on these pharmaceutical substances [24], [12]. The current paper aims at a comprehensive review of the methods used in the last two years 2020-2021 to determine the methods used to dispose of azithromycin lysine residues in water, to maintain public health and safety on the one hand,

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and to avoid the occurrence of more serious complications on the other hand. As it is known, the Corona virus is subject to mutation through the occurrence of mutations that lead to an increase in its pathogenicity and the speed of its spread.

2. Azithromycin

It is a macrolide antibiotic used to treat a number of bacterial infections. It can also be used for a number of sexually transmitted diseases as well as used to combat malaria, along with other medications. Azithromycin can be taken orally or intravenously as a single daily dose. Azithromycin was first produced in 1980. Figure 1 shows the chemical structure of this antibiotic. Azithromycin is on the World Health Organization's List of Essential Medicines, a list of the most important medicines needed by a major health care system. It is available as a drug equivalent, and is sold under many brand names around the world such as ZEROX, ZITHROMAX, ZOCIN, AZOMYCIN, AZI-ONCE, AZIMAC, ZIMAX, ZETRON, AZOMAX, AZALIDE, AZATRIBACT, AZINDAMON, AZIROWA, AZITHROGLOB, AZITHROMIN, AZIWOK, AZOMAX, AZALIDE, AZATRIBACT, AZINDAMON, AZIROWA, AZITHROGLOB, AZITHROMIN, AZIWOK, AZOMAX, AZROYZIAZIN, AZIROWC, I.D. ZITHROPHATE, ZITHROMAX, ZITHROKAN, ZITHRODOSE, ZISROCIN, XITHRONE, XEREXOMAIR, XEREXOMAIR, UNIZITHROCURE, UNIZITHRIN, SYSTYMYCIN, RAME-ZITHRO, and others. In 2013, the US Food and Drug Administration (FDA) issued a medical warning about its use because it showed potential risk to the heart muscle, and because of its direct effect on the heartbeat that could cause fatal problems for patients. The scientists noted that it can cause abnormal changes in the electrical activity of the heart that may prolong the QT interval, causing a rare arrhythmia (www.drugs.com).

3. Action

Azithromycin works to reduce and inhibit the synthesis of proteins not in humans but in bacteria and germs, which limits their growth and reproduction. It is a widely used as antibiotic, and is effective against a wide range of bacteria such as *Haemophilus influenza*, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, and others. The effectiveness of the drug begins within 2-3 hours and a few days may pass until the full effect of the drug is felt, while the period of its effectiveness ranges between 3-5 days. Azithromycin antibiotic is used to treat a variety of infections including otitis media, pharyngitis, streptococcal pharyngitis, bronchitis, rhinitis, acute bacterial sinusitis, tonsillitis, chronic obstructive pulmonary disease, travelers' diarrhea, and some other intestinal infections. In addition to its use in the treatment of some types of pneumonia, skin infections, pelvic inflammatory disease, and sexually transmitted diseases such as urethritis and cervicitis. In some cases, it may be used as an alternative to penicillin, for patients with penicillin allergy.

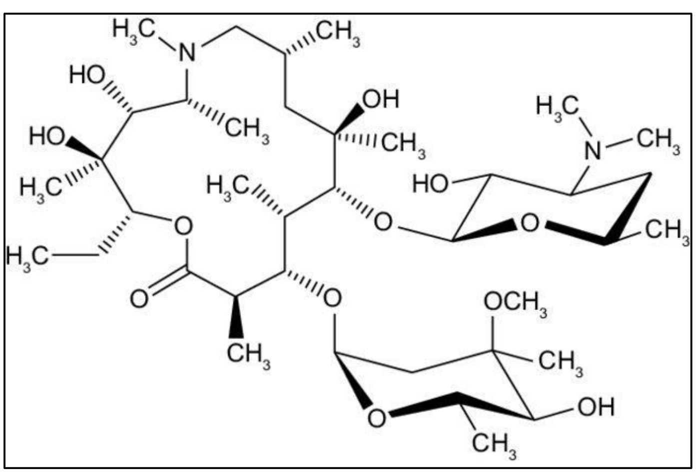

Figure 1 Chemical structure of azithromycin (www.drugs.com)

4. Side effects

Many common, possible and rare side effects have been reported for the use of the antibiotic Azithromycin. Common side effects include nausea, vomiting, diarrhea and upset stomach. An allergic reaction or some type of diarrhea caused by dysmenorrhoea may occur, as well as congestion, coughing, and dizziness. Among the side effects indicated for the use of this drug are ulceration, irritation, or itching of the skin, cracking and dryness of the skin, fever, swelling, the appearance of blood in the stool, pain throughout the body, chest pain. No harm has been shown during pregnancy in pregnant women. The safety of its use during breastfeeding has not been established, but it is likely that it is safe to use.

5. Removal of azithromycin residues from wastewater

Through a comprehensive literature review regarding the methods of removing medical substances and pharmaceuticals, including antibiotics, an increasing interest has been observed in removing azithromycin from wastewater or contaminated solutions in the last two years, i.e. 2020 and 2021. The reason for this - as mentioned above - is due to the spread of COVID-19 disease on a large scale in the whole world, which increased the consumption of antibiotics in general and azithromycin in particular, due to its effective therapeutic ability in reducing the effects of this disease. In this section, most of the research that studied the removal of this drug from polluted water during the pandemic period will be reviewed.

Early in 2020, Natalie Pinon, through her doctoral thesis at the University of Nevada, Las Vegas UNLV, studied the use of a new and promising technique, the Sonication technique, to determine the factors affecting the process of removing antibiotics from water. The study included sulfamethoxazole, clarithromycin, tetracycline, lincomycin, trimethoprim, beside azithromycin. The treatment experiments were carried out using the QSonica Sonicator, Q500 batch system, while the studied factors were the concentration of H_2O_2, amplitude, irradiation method and at a constant temperature 30±5°C. The sample checking process to determine the processing efficiency was carried out using high-precision LC-MS, and the detection limits reached 1ppb. Produce as few hydroxyl radicals as possible during the sonication process. The best capacity used to remove most of the antibiotics was 75%, or about 85 W, while the treatment efficiency decreased when the capacity was raised to 100%, or about 120 W. But azithromycin and clarithromycin had different behavior, as the best removal efficiency was achieved at 100% capacity, higher than it was at 75%, reaching 43.88% after it was 43.61%, respectively, for azithromycin, while the difference was clear for Clarithromycin, where it rose from 57.01% at to 68.56 % at 75% and 100%, respectively. The most important feature of this study is that the antibiotics used were in a mixture form, not to mention that their concentrations were very low, approximately 20 parts per billion, which makes them actually mimic the concentrations often found in wastewater of these medicinal substances. On the other hand, the technology used is environmentally friendly and does not lead to the production of any kind of harmful residues. On the other hand, this method is considered somewhat expensive when compared to other commonly used traditional methods [22].

[5] conducted a comparative study to determine the ability of biological treatment, activated carbon and ozone to remove different types of antibiotics, including azithromycin. The studied drugs were divided into 3 classes (sulfonamides, macrolides, quinolones) and antidepressants which include serotonin–norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), norepinephrine–dopamine reuptake inhibitors (NDRIs), and anti-psychotics were analyzed in the WWTP samples. The studied pharmaceutical substances included Acetaminophen, Acetylsulfamethoxazole, Amitriptyline, Anhydro erythromycin, Azithromycin, Bupropion, Caffeine, Carbamazepine, Ciprofloxacin,

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Citalopram, Clarithromycin, Diclofenac, Haloperidol, Lamotrigine, Trimetholine, Primetholine, Primethinox. The field of study was 7 wastewater treatment plants (WWTPs) in the eastern United States and the polluted water used in the research was real water, which was appropriately collected over a 24 hour period. The time for collecting samples was on two meals, the first between August and December of 2017, and the second between June and July of 2018. The collected sample bottles were kept in ice or refrigerated during the collection period and the samples were analyzed at various points of the treatment process using (LC-MS) liquid chromatography-mass spectrometry while the detection limit for anti-azithromycin was 0.81 ng per liter. The results for 14 out of 15 and 9 out of 11 compounds that were identified in the uptake of the studied treatment plants showed that the total removal efficiency of the biological treatment was lower than the efficiency of using activated carbon and ozone, reaching 50% and 95%, respectively. While the total treatment efficiency of azithromycin was 100%, 96%, 100%, 60% and 45% for each of WWPT1, WWPT2, WWPT3, WWPT6 and WWPT7, respectively, while azithromycin could not be measured in the inflow of the remaining treatment plants. The methods used in the study area stations showed that they are effective in removing antibiotics, including azithromycin, due to the lack of a specific effect on zebrafish in the short term.

Three conventional methods were investigated to study their susceptibility to remove azithromycin from contaminated Synthetic Aquatic Solution Contaminated with Azithromycin (ASCA) by [25]. The studied methods are ultraviolet radiation (UV) and oxidation process using Fe(VI) in addition to adsorption with zinc oxide nanoparticles. The percentage of removal using different methods was determined by measuring the concentration of azithromycin in the aqueous solutions produced after treatment, which was done by measuring COD based on the APHA standard method. Several variables were tested to determine the optimum conditions for removing the antibiotic from the ASCA manufactured solutions, which are temperature, acidity, hydraulic retention time (HRT) in addition to the amount of nanoparticles for the adsorption process and iron concentration in the oxidation process. The laboratory results showed that the removal efficiency reached 73% by using the ultraviolet radiation (UV) technology at the optimum conditions, which was the pH function, HRT, the temperature and the UV radiation power in the amount of 7, 1 hour, 65 ° C, 163 mW/cm^2, respectively. While the optimum conditions were 2, 15 min., 25 °C, 0.05 mg/L for each of the pH, HRT, temperature, and the amount of zinc oxide nanoparticles using the adsorption technology, which achieved an optimal removal that reached 100%, while the results matched isothermal adsorption with a Langmuir model with a correlation coefficient of R^2 = 0.99. As for the last method, which is oxidation using Fe(VI), azithromycin was completely eliminated with an acid function of 2, and a hydraulic retention time of 20 min., a temperature not exceeding 50 °C, the ratio of the concentration of Fe(VI) to the initial concentration of azithromycin ranging was between 0.011 - 0.012.

The separation method by membrane was used to study the removal of azithromycin from different real samples, where [6] was prepared ZnO/Si as a thin film by plasma-enhanced chemical vapor deposition (PECVD) method. The treatment process was carried out in a batch-type unit (thermostatic shaker) at different operating conditions, which included the acidity function, the amount of ZnO/Si thin film, the processing time and three values for the initial concentration of the antibiotic, which ranged between 2-12, 0.007-0.05 g, 0-120 min., (15, 30 and 50) mg/L, respectively, while the shaking speed was fixed at 150 revolutions per minute, and the experiments were conducted at laboratory temperature. HPLC was used to measure azithromycin concentrations in the treated solutions via a C18 column with a length of 25 cm and at a wavelength of 210 nm. The prepared membrane was characterized using XRD, XPS and SEM tests, and the obtained results showed that azithromycin molecules were adsorbed on the surface of the prepared membrane with a capacity of 213.32 mg/g and that the percentage removal reached less than 100% at acidity function, adsorption dose, initial concentration and contact time. Its amounts are 7, 0.025 g, 15 mg/L, 45 min., respectively. The equilibrium results showed that adsorption is subject to Redlich-Peterson (R-P) isotherm models with correlation coefficient R^2 = 0.9881. The regeneration process of the prepared ZnO/Si membrane was studied with several chemicals, namely hydrochloric acid, nitric acid, and sodium hydroxide at a concentration of 0.1 molar, in addition to ethanol. Nitric acid (HNO_3) showed the highest desorption efficiency, as the removal efficiency of azithromycin decreased by using it to 70% after eight successive cycles, while sodium hydroxide (NaOH) was the lowest, as the reverse adsorption efficiency of the membrane decreased to less than 40% from the first session.

[21] tested on a lab scale the removal of the azithromycin antibiotic using one of the advanced oxidation methods, which is ultrasound technique. Laboratory experiments were conducted using an ultrasonic transducer (Meinhardt Ultrasonics) with a maximum capacity of half a liter, and with different ranges of operating conditions, namely the acidity function 3, 7 and 9, the power of ultrasound 16.5, 25, 41.5 and 50 watts, and the processing time 0-60 min, iron ion concentration 0, 0.5, 2.5 and 5 mg/L, and hydrogen peroxide 0, 2.4, 4.8 and 7.2 mg/L and UV irradiation at low frequency 40 kHz, while the studied azithromycin concentration was constant throughout all experiments, which is 1.0 mg/L. Azithromycin concentrations were determined using Ultra-High-Performance Liquid Chromatography (UHPLC) and three times to reduce error. The results showed that the optimal conditions were at an acid function of 9, a time of 1 hour, a power of sound waves of 50 W, and in the presence of irradiation, and the removal efficiency was close to 50%. As for using iron ions and hydrogen peroxide (H_2O_2), the efficiency was reduced to 30% or less, while the decrease in efficiency was slight in the absence of ultraviolet irradiation.

The advanced oxidation technique was studied again to remove the antibiotic azithromycin, but in another way, which is the photo-fenton catalyzed technique using a Suntest CPS+(Atlas) photosimulator and using iron sulfate ($FeSO_4$) as a source of divalent iron ions in the presence of light radiation and hydrogen peroxide (H_2O_2), which is the main source for the generation of free hydroxyl radicals (OH^*). The flasks used were of the glass type made of borosilicate, and the distance between the light source and the surface of the solution was 15 cm, while the height of the solution in the flask was not more than 5 cm. The operational parameters studied were the initial concentration of H_2O_2, iron sulfate $FeSO_4$ and azithromycin, whose values ranged between 5.0 - 35.0 mg/L, with a difference of 7.5, 2.5 - 7.5 mg/L, with a difference of 1.25, 1-3 mg/L, respectively, while the value of pH, the amount of irradiation and the reaction time are fixed at 3 and 500 W/m^2, and half an hour, respectively. Examination of the processed samples was done using the Acquity UPLC system (Waters Corporation) via the Acquity UPLC BEH C18 column and using the Masslynx 4.1 program. The mineralization of organic matter and nitrate concentration in the treated samples were measured using standard methods 4129D and 526D. The obtained results showed that the efficiency of antibiotic removal was directly related to the concentration of divalent iron ions and the concentration of hydrogen peroxide, while it was inversely with the concentration of azithromycin. The maximum efficiency achieved reached approximately 92.0% under the optimal conditions of 27.5, 7.5, 1.0 mg/L of hydrogen peroxide, ferrous sulfate, azithromycin respectively. This study included the use of additional processing techniques and methods and their comparison with the photo-fenton advanced oxidation process. The results of the comparison showed that according to the studied methods for removing azithromycin, the following sequence was taken: photo-fenton advanced oxidation technology, Fe(II)+light, Fenton method, photo-fenton + isopropanol, H_2O_2+light, H_2O_2 alone, Photolysis and Hydrolysis. The removals for the studied methods were 91.9%, 60.5%, 57.2%, 51.1%, 25.9%, 20.6%, 2.1% and 1.8%, respectively [16].

[10] studied the ability of simulated sunlight radiation and hydrogen peroxide to remove azithromycin from aqueous solutions in the laboratory using a Suntest CPS+(Atlas) photosimulator, which has an irradiance of

0.5 kW/m^2. The concentration of azithromycin ranged between 0.5-3.0 mg/L, while the acidity function was variable with three values: 3, 6, and 9, while the concentration of hydrogen peroxide was 240, 480, and 720 mg/L. The samples were analyzed based on the Acquity UPLC system (Waters Corporation) via the Acquity UPLC BEH C18 column and using the Masslynx 4.1 program. The obtained results indicated that free hydroxyl radicals generated from hydrogen peroxide are the main factor responsible for removing pollutants by the advanced oxidation method, but the increase in acidity and hydrogen peroxide concentration had an opposite effect on the generation of free radicals. Therefore, the removal efficiency was 33.5% at pH = 3 and [H_2O_2] = 270 mg/L, while at pH = 9 and [H_2O_2] = 240 mg/L, the removal efficiency was 80.5%. While the effect of increasing the concentration of the antibiotic was inversely with the efficiency of the treatment within a time period of two hours.

[18] benefit from the photocatalyst Ag@$Bi_4O_5I_2$/SPION@calcium alginate (ABSA) prepared by hydrothermal impregnation, in addition to a group of other catalysts to study the removal of azithromycin from aqueous solutions in the presence of visible light, UV rays, NIR, sunlight. The change in the pH function was studied within a range between 3-11, while the antibiotic concentration was 10 mg/L, the amount of the catalyst used was 0.3 g and the temperature was 30 ºC. The results showed that the performance of the used catalysts was in the following sequence: ABSA (98.4%) > BSA (81.6%) > Fe_3O_4@$Bi_4O_5I_2$ (67.9%) > $Bi_4O_5I_2$ (51.5%). This means that the photocatalytic factor ABSA was the most efficient among the rest of the other catalysts. In this study, the rate constant for the prepared catalyst was calculated, as its value was 0.08321 min^{-1} and its value was eight times bare $Bi_4O_5I_2$.

Sawdust of North Indian rosewood (scientific name *Dalbergia sissoo*) was used as raw material to prepare two types of activated carbon; ordinary (AC) and magnetic (MAC). AC was prepared by drying the raw material *Dalbergia sissoo* sawdust at 70 °C after treating it with 0.1 M hydrochloric acid and washing it with distilled water twice. As for the magnetic activated carbon, it was prepared by mixing it with a mixture of iron tri-chloride ($FeCl_3.7H_2O$) and iron sulfate ($FeSO_4.7H_2O$) in a ratio of 1:2 and then treating it with sodium hydroxide (NaOH) of a similar molarity to hydrochloric acid, and finally thermally treating it until charred in an electric oven. The two types of activated carbon were characterized by several tests: EDSX, SEM, FTIR, TG/DTA and XRD, as well as the surface area values of 18.63 and 49.53 m^2/g for MAC and AC, respectively. The ability of the prepared materials for adsorption of azithromycin from the prepared solutions was tested with concentrations, acidity function, adsorbent quantity, temperature, temperature and contact time ranged between 10-160 mg/L, 2-12, 0.01-0.15 g, 298-333 K and 5-240 minutes for time. Consecutively, the experiments were conducted in a batch unit and at a constant agitation speed of 170 rpm. The obtained results showed that the optimal conditions for adsorption were achieved at an initial concentration of 80 mg/L, acid function of 6 and 7 for AC and MAC, respectively, 0.1 g, for 120 minutes, while the isothermal, kinetic and thermodynamic calculations showed that the adsorption follows the Langmuir model and the degree model. The second is false and that the reaction is endothermic, positive random and spontaneous at all temperatures [27].

[20] used a nanocomposite consisting of activated carbon loaded with iron, silicon and zinc (PAC/Fe/Si/Zn) prepared by co-precipitation as an adsorbent for two types of antibiotics, azithromycin and cefixime from aqueous solutions by UV-assisted. PAC/Fe/Si/Zn adsorption medium was prepared in three stages, the first stage included loading iron on activated carbon (PAC) powder by co-precipitation method, and iron sulfate ($FeSO_4.7H_2O$) was used as a source of iron ions and a sodium hydroxide solution was added with it in addition to $NaBH_4$ solution. In the next stage, the silicon (Si) was loaded onto the resulting material from the first stage by simultaneous dropping of Tetraethyl ortho-silicate (TEOS) with tri-sodium citrate dehydrate on PAC/Fe suspension with stirring for 3 hours in a Stirrer device at a temperature of 40°C. As

for zinc, it was loaded in the last stage by adding 50 ml of aqueous zinc nitrate $Zn(NO_3)_2.6H_2O$ to PAC/Fe/Si while stirring for half an hour. PAC/Fe/Si/Zn was obtained by collecting it using a magnet with strength of 1.2 Tesla and then washing it with ethanol before being dried overnight at 120°C. The ability of the prepared adsorption medium to remove azithromycin and cefixime in a batch system and in the presence of ultraviolet rays was tested by using a UV lamp (UV-C lamp, 254 nm and 6W PHILIPS). Four different operating conditions were investigated for their effect on treatment efficiency, which were the acidity function (3, 7, 9 and 11), contact time (0-140) min., the amount of adsorbent (0.01-0.04) g, and the initial concentration of the azithromycin (10- 40) ppm. The results showed that the best acidity function for removing azithromycin and cefixime is 9 and 11, respectively, and the adsorption reached the equilibrium state after two hours of treatment, and the highest removal efficiency was achieved at 0.04 g of PAC/Fe/Si/Zn, while 10 and 20 ppm were the concentration preferred for azithromycin and cefixime respectively.

Two types of organic clays (montmorillonite K10) and (3-aminopropyltriethoxysilane) were modified to be used as adsorbents for the azithromycin antibiotic from aqueous solutions. The modified clays, called L-methionine modified montmorillonite K10 (LMP clay) and (3-aminopropyltriethoxysilaneized magnesium phyllosilicate; denoted as (AMP clay)), were characterized using multiple assays including FTIR, TEM, PXRD, DLS, EDS and TG and FE-SEM. On the other hand, the BET test was achieved via the N_2 adsorption–desorption isotherm indicated that the surface area of both LMP and AMP were 215 and 325 m^2/g, respectively. Batch adsorption experiments were carried out using pre-prepared solutions. The studied operating conditions were the acidity function, temperature, adsorbent quantity and contact time, the initial concentration of the antibiotic, whose ranges ranged between 2-12, 25-55 ºC, 0.1-2.0 g/L, 10-180 min., 25-500 mg/L, respectively, and it is worth noting that the pH range 2-8 was chosen to simulate hospital wastewater. The obtained experimental results indicated that the two prepared materials were highly efficient, as the removal percentage reached 98% for LMP clay and 93% for AMP clay at the optimum conditions of 8, 25°C, 0.5 g/L, 50 mg/L for pH and temperature, adsorbents dose and initial concentration of azithromycin, respectively. While the isotherm study indicated that the adsorption followed the Freundlich isotherm model, with an adsorption capacity of 286.1 and 298.78 mg/g for both AMP and LMP, respectively. The kinetic study of the process predicted that the adsorption was subject to a pseudo-second-order kinetic model, while the removal process was spontaneous, exothermic, and negative entropy, as confirmed by thermodynamic calculations. [14] also studied in this study the reuse of LMP and AMP adsorption materials, and the materials showed high efficiency, where the efficiency was higher than 92% after four adsorption cycles.

6. Conclusions

It is noted that the number of studies dealing with the removal of azithromycin is constantly increasing due to the increase in the use of this antibiotic in the period extending from the end of 2019 until now. This increasing as a result of the spread of the COVID-19 pandemic, which led to a significant increase in the demand for antibiotics, including azithromycin, and consequently increased the amount of household and hospitals wastewater that contain this antibiotic. The advanced oxidation method topped the other methods used to remove this antibiotic –in this period–, followed by the adsorption method. These two techniques are among the widespread techniques for treating polluted water, especially in the last two decades. The reviewed research indicated that it is possible to reach very high removal rates of more than 95% of the initial concentration, which makes the ways of developing these methods more interested by researchers, engineers and those interested in the affairs of water treatment and waste disposal. From what was indicated on the reviewed papers and other researches, they did not address how to safely, economically and usefully dispose of the residual waste after the end of the process, which makes the treatment technology incomplete

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and includes a clear deficiency in its general concept. Finally, the aim of this review article is to draw attention to an important problem, which is the treatment of wastewater from medical and pharmaceutical contaminants, whether antibiotics or other medicines and medical drugs, given the current health conditions, which require concerted efforts to support the members of health institutions and win this The fierce war that the whole world is experiencing.

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