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ORIGINAL PAPER

Photocatalytic degradation of vancomycin using titanium dioxide and optimization by central composite design

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Abstract

Conventional wastewater treatment processes are not completely effective in removing vancomycin. In this study, affecting parameters on vancomycin degradation, such as pH, catalyst, initial vancomycin concentration, temperature, and reaction time were investigated simultaneously during a removal process based on titanium dioxide with ultraviolet irradiation in an aqueous solution. Titanium dioxide was synthesized and characterized using X-ray diffraction and scanning electron microscopy. The average size of the synthesized crystals was 4.7 ($\pm$0.2) nm. Design of experiments was done by a central composite design based on the response surface methodology and multiple linear regression was implemented to construct the final model and evaluate the design. The total sum square values of the model were compared with the total sum squares of the error (residual) using Analysis of Variance. R^2 in the final model was 0.92, which was close to R^2_{adj} (0.88). The optimal values of vancomycin degradation (pH = 5.1, initial concentration of vancomycin = 58.2 mg l^{-1}, titanium dioxide = 54.9 mg in 250 ml reactor, temperature = 39.6 °C, time = 36.3 min) were obtained. Vancomycin degradation efficiency with the ultraviolet application was 89.5% which reached 93% with aeration and 25% without ultraviolet. After twice catalyst reuse, it was decreased from 89.5 to 80% and 78%. According to the results, obtained optimal conditions during treatment by titanium dioxide is an acceptable way to eliminate vancomycin in pharmaceutical industries wastewater, in high concentrations and mild-acidic pH, which does not require high temperatures and much time.

Keywords Antibiotic · Advanced oxidation process · Aqueous solution · Photocatalysis · Removal efficiency · Response surface methodology

Introduction

According to the Centers for Disease Control and prevention (CDC) in the United States, 28,000 deaths from antibiotic resistance occur annually, and 2 million Americans are infected with these bacteria annually (Martens and Demain 2017). In European Union Countries, Vancomycin resistance has been reported from 0.0 to 59.1% during 2014–2018 (Piezzi et al. 2020). In the United States, at least 23,000 people die each year due to hospital infections (Nishiyama et al. 2017) moreover, Fifty-five thousand cases of Vancomycin-resistant enterococci (VRE) infections were reported in the United States in 2017 (Abutaleb et al. 2021). There are known subdivisions of Antibiotics such as Quinolones, β-lactams, Tetracyclines, Macrolides and Glycopeptides that, Vancomycin represents a group of glycopeptides which has a high molecular chain (Antunes et al. 2017). Excessive application of Vancomycin, which has no significant effect on gram-negative species, will lead to VRE with serious concern for *Enterococcus*

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faecalis and *Enterococcus faecium* (Herrero et al. 2002; Varela et al. 2013). Currently Vancomycin is the last line of defense against infections caused by gram-positive pathogenic bacteria (Dinu et al. 2020; Melese et al. 2020), that it is used mainly in infections caused by Staphylococcus aureus and Enterococcus spp., where the microorganism is completely resistant to treatment or when the patient is allergic to penicillin. However, there is not much knowledge about the presence and effects of Vancomycin in the environment (Antunes et al. 2017). Reported studies have not specifically focused on Vancomycin degradation. Various concentrations of Vancomycin have been found in the aquatic environment and long-term shelf life in natural water has also been reported (Lofrano et al. 2014). Wastewater treatment processes are not completely effective in removing Vancomycin, so municipal wastewater can be a way for Vancomycin to enter surface water. Vancomycin and its degradation products in aquatic environments may lead to destructive effects on the environment and human health. Vancomycin, as an antibiotic, may also cause acute or chronic toxic poisoning of bacteria, algae, invertebrates, and fish in the aquatic environment (Cao et al. 2018). The highest Vancomycin concentrations in the wastewater entering the treatment plant and the sludge were 54.90 ± 5.97 and 46.32 ± 3.60 mg l^{-1}, respectively (Qiu et al. 2016). Hospitals play an important role in the spread of antibiotic-resistant bacteria which enter the sewer system and spread to the environment (Hocquet et al. 2016; Sib et al. 2019; Wei et al. 2020). The level of antibiotics in surface waters is ng l^{-1} and mg l^{-1} in the hospital wastewater and the concentration of many antibiotics in the soil ranges from ng kg^{-1} soil to hundreds of μg kg^{-1} soil (Cycoń et al. 2016). One of the ways to remove antibiotics in aquatic environments is Advanced Oxidation Processes (AOP_s). The AOP_s processes are UV, UV/O_3, UV/H_2O_2, TiO_2/H_2O_2, Fe^{2+}/H_2O_2, UV/TiO_2 which are used individually or in combination together (Kurt et al. 2017). The main mechanism of advanced oxidation processes is based on the production of hydroxyl radicals that are almost capable of oxidizing many organic compounds (Fazilati 2019). The Titanium dioxide (TiO_2) photocatalyst is a semiconductor photocatalyst with a broad band gap (3.2 eV) and has been successfully utilized for the treatment of organic environmental pollutants. The clear reaction mechanism of the TiO_2/UV process is shown in the following reactions (Kurt et al. 2017).

$$TiO_2 + h\nu \rightarrow e^{-}CB + h + VB \tag{1}$$

$$H_2O + h + VB \rightarrow OH^{\cdot} + H^{+} \tag{2}$$

$$O_2 + e^{-}CB \rightarrow O_2^{\cdot-} \tag{3}$$

$$O_2^{\cdot-} + H_2O \rightarrow OH^{\cdot} + OH^{-} + O_2 + HO_2^{-} \tag{4}$$

TiO_2 has been widely used among various inhomogeneous semiconductor photocatalysts due to its special properties such as mechanical and chemical stability, Eco-friendly, non-toxicity, low-cost synthesis and easy recovery (Madani et al. 2013).

Ambrosetti et al. showed the removal efficiency of Amoxicillin, Erythromycin, Streptomycin, Ciprofloxacin by photocatalysis with TiO_2 and ZnO. Amoxicillin, Erythromycin, Streptomycin, Ciprofloxacin was decomposed under UV and sunlight for 15 min. In each solution, 0.01 g of zinc oxide or 0.01 g of titanium dioxide was added. In comparison, Zinc oxide required much more time to degrade antibiotics than titanium dioxide (Ambrosetti et al. 2015). The maximum removal rate of alachlor was estimated 98.44% from aqueous media using TiO_2 nanoparticles (NPs) under UV (Jamshidi et al. 2019). A study by Shokri et al. showed, 90% mineralization and 100% of degradation of chloramphenicol were obtained after 18 min of UV-C irradiation when (1 wt%) TiO_2/Ag NPs were used (Shokri et al. 2013). Furthermore, Under optimal operating conditions (pH 7; temperature 25 °C), complete degradation (approximately 100%) of oxytetracycline was achieved in 180 min (Calcio Gaudino et al. 2021). Also, more than 95% of the Tetracycline (TC) antibiotic was removed within 40 min, 40 ppm of TC, and 1 g l^{-1} of TiO_2 under UV irradiation (Daghrir et al. 2013). According to the mentioned studies, the degradation of antibiotics can change depending on the conditions such as pH, temperature, reaction time, catalyst, and pollutant concentration. Therefore, in this study, for the first time, different effective parameters of Vancomycin removal efficiency such as concentration of Vancomycin, TiO_2 amount, pH, temperature and reaction time were investigated simultaneously using a multivariate approach based on Central Composite Design (CCD). Also, the optimum conditions were studied by considering the interaction effect of the parameters. Moreover, the Vancomycin degradation efficiency with and without UV radiation was considered and the effects of aeration and catalyst recovery under optimal conditions were investigated as well. This study was conducted at the school of health, Shiraz University of Medical Sciences, Shiraz, Iran, 2019–2021.

Materials and methods

Chemicals and equipment

Titanium tetrachloride ($TiCl_4$) and hydrochloric acid (HCL) which were used for synthesizing TiO_2 obtained from Merck Company (Germany). Vancomycin was prepared from Sigma Aldrich Company (USA) with purity greater than 80% HPLC grade (High Performance Liquid Chromatography). All standard samples and batch experiments were prepared using deionized distilled water. Methanol and water used in chromatography analysis had “Chromatographic grade” from Merck Company (Germany).

To identify and detect Vancomycin in the samples, High-Performance Liquid Chromatography (HPLC) was used. KNAUER HPLC (AZURA model, Germany) was equipped by PDA UV–Vis Detector with a C18 column (Eurospher 100-5, 250 × 4 mm—KNAUER) in reverse phase mode and using a mobile phase containing 30% ultrapure water and 70% methanol (70:30 V/V). The flow rate of the mobile phase was 1.2 ml min^{-1}, and the UV detector was set at 229 nm wavelength for detection. A sample injection loop of 20 µl was used in the experiments and this loop was full during each injection. Before the injection, the samples were filtered by syringe filter cellulose acetate membrane with a pore size of 0.22 µm. The retention time of Vancomycin in the photocatalytic reaction was 2.36 min and the detection range of Vancomycin was in the concentration range of 0.01–100 mg l^{-1}.

Synthesis of TiO_2

TiO_2 white powder was obtained based on the method previously reported by Yener et al. (2017). Briefly, 13.7 ml of $TiCl_4$ (0.5 M) was added to a 250 ml flask containing 62.18 ml of HCL (3 M), to control the hydrolysis reaction. Reactions were carried under the hood because the reaction was highly thermogenic and caused a dense white cloud during the preparation of the $TiCl_4$ solution. The reaction vessel was placed in a cool water container. Then, the solution was stirred at 95 °C with 500 rpm for 3 h at room temperature. After completing the reaction, the yellow supernatants were separated and white precipitates were passed through the filter paper, and the remaining precipitates were washed several times by distilled water until neutralizing the acid suspension. The remaining white precipitant on the paper filter was placed in the oven at 60 °C for 1 day to be dried.

Characterization

To determine the crystal structure and the crystalline size of the prepared nanocatalyst, the X-ray diffraction (XRD) was used with the XRD Bruker D_8 Advance powder diffractometer (Bruker, Germany) by applying the refection mode with Cu-K_α radiation ($\lambda = 1.5406$ Å). ZEISS (SIGMA VP model, Germany) Field Emission Scanning Electron Microscope (FE-SEM) was used to analyze the morphology of nanostructures, and the energy-dispersive X-ray spectroscopy (EDX) was applied to identify the chemical compounds.

Reactor

Vancomycin degradation and removal reactions were performed in an aqueous medium in a 250 ml glass reactor. The set-up of the temperature in the reaction was done by a hot water circulation in the reactor jacket to the desired temperature. During the test, a UV-C lamp (6 watts-230 v-254 nm) was placed in a quartz tube at the center of the reactor. Before starting the tests, temperature and pH were adjusted for different samples. HCl and NaOH were used to adjust the pH values whenever required. A magnetic stirrer was used during the tests. The reactor was placed in Aluminum foil to prevent visible light and ultraviolet light interference. The centrifuging of samples was done in the test tubes to separate the utilized nanocatalyst. Figure 1 shows the reactor used in the study. The Vancomycin removal efficiency ($E\%$) was calculated from the following equation:

$$E\ (\%) = \left(C_0 - C\right)/C_0 \times 100 \tag{5}$$

where C_0 and C represent Vancomycin concentration before and after the TiO_2/UV process, respectively.

The experimental parameters

In this study, five experimental parameters were studied and optimized in removal of Vancomycin which is represented as follows. Initial concentration of Vancomycin was 15, 30, 45, 60, 75 (mg l^{-1}), TiO_2 dosage: 25, 50, 75, 100, 125 (mg), temperature: 25, 30, 35, 40, 45 (°C), pH: 3, 5, 7, 9, 11, and reaction time: 15, 30, 45, 60, 75 (min).

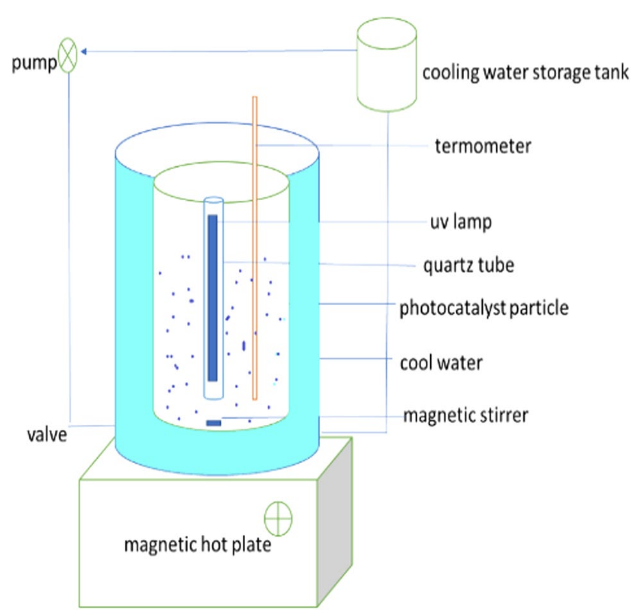


Fig. 1 Photochemical reactor used for removal of vancomycin

Experimental design

Because of the limitations of one-at-a-time approaches (Jamshidi et al. 2019) several multivariate experimental design methods for optimizing the effective parameters in the chemical processes have been proposed, among which Response Surface Methodology (RSM) is a well-known one. RSM is a set of mathematical and statistical methods for modeling and analyzing the problem. This method is used simultaneously to respond the problem (objective) by affecting several input independence variables and to optimize this response. In this method, the relationships between multiple or irrelevant variables are measured using the effect of independent variables. One of the most commonly used Response surface methods is the Central Composite Design (CCD), which is implemented at 5 levels (Aggarwal et al. 2008). Therefore, a central composite design was used to optimize and evaluate the effect of different performance parameters on the degradation process of Vancomycin by TiO_2/UV. Here, a total of 42 experiments were designed using CCD to optimize the five experimental variables (initial Vancomycin concentration, TiO_2 concentration, temperature, time, pH). In this design, five levels were assumed for each variable which is presented in Table 1. The design of the experiments and analysis of variance and Multiple Linear Regression (MLR) was conducted using Design-Expert software (Stat-Ease Inc.) run on a PC with Windows 7 operating system.

Results and discussion

Characterization using XRD

Based on Fig. 2, characteristics diffraction peaks were at 2θ equal to 69.9, 54.2, 43.9, 41.2, 36.1, and 27.4 were obtained which were in agreement with the pattern of the rutile form

Table 1 The parameters and levels used for the experimental design in removal of vancomycin

	Unit	−1	+1	0	−alpha	+alpha
pH (*A*)		5	9	7	3	11
Initial concentration of vancomycin (*B*)	mg l^{-1}	30	60	45	15	75
TiO_2 amount (*C*)	mg	50	100	50	25	125
Temperature (*D*)	°C	30	40	35	25	45
Time (*E*)	min	30	60	45	15	75

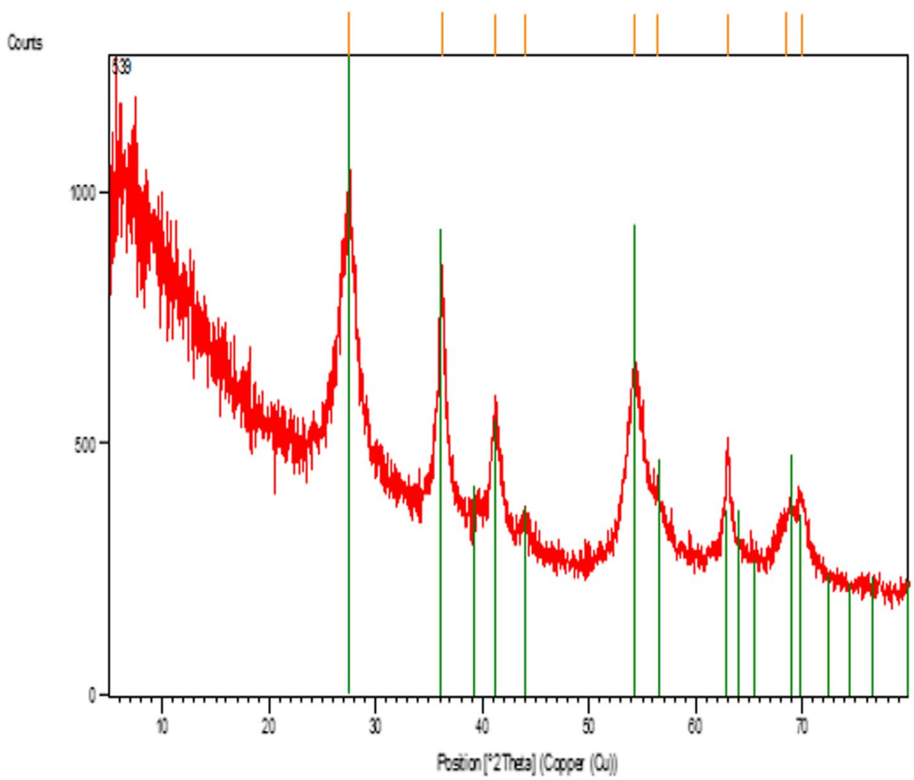


Fig. 2 The XRD pattern of synthesized TiO_2

of TiO_2. The characteristics peaks of other crystalline forms of TiO_2 NPs (Anatase and Brookite) were not observed in the obtained NPs. Based on the Scherrer equation, the average crystalline size of the prepared nanocatalyst was also calculated from the four sharpest peaks of the XRD pattern which was equal to 4.7 ($\pm$0.2) nm.

SEM imaging

The shape of TiO_2 NPs was investigated by field emission scanning electron microscopy (FE-SEM). Accordingly, TiO_2 NPs had spherical and granular shapes, as displayed in Fig. 3a. The size of the nanoparticles ranged from 20 to 69 nm. Elemental analysis by EDX of TiO_2 nanoparticles is shown in Fig. 3b as well. EDX showed that Ti content was 74.9% and the percentage of O and Cl were 24.3% and 0.8%, respectively.

CCD model

Experimental parameters for Vancomycin degradation from aqueous solutions were optimized using the synthesized nanocomposites after their characterization and using the CCD experimental design. The utilized 42 runs suggested by CCD are shown in Table S1 (Supporting information). Table 2 shows the Analysis of Variance (ANOVA) results of the model made based on the CCD method.

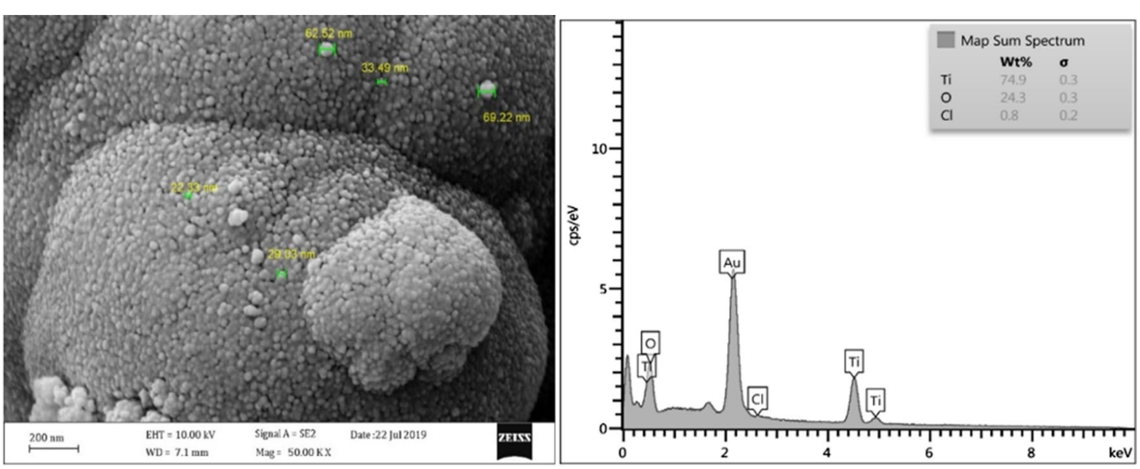
According to Table 2, the parameters entered in the obtained equation based on the designed runs for Vancomycin degradation with TiO_2 catalyst are pH (*A*), initial concentration of Vancomycin (*B*), TiO_2 amount (*C*), temperature (*D*), time (*E*). Also, pH and initial Vancomycin concentration interaction (*AB*), pH and temperature interaction (*AD*), initial concentration of Vancomycin and temperature interaction (*BD*), temperature and time interaction (*DE*), pH self-interaction (A^2), initial concentration of Vancomycin self-interaction (B^2), and time self-interaction (D^2).

Based on these results, the obtained linear model after MLR regression analysis is shown in Eqs. (6) and (7) which shows the model based on the coded and original values of experimental parameters:

$$\begin{aligned}\text{Peak area} = {} & 237.15 - 9.467A + 76.43B - 14.27C \\ & + 36.4D - 28.59E - 38.06AB - 16.55AD \\ & + 37.84BD + 18.49DE - 13.48A^2 \\ & - 21.4B^2 - 28.7D^2 - 26.57E^2\end{aligned} \tag{6}$$

$$\begin{aligned}\text{Peak area} = {} & -1674.5 + 157.5A + 4.87B - 0.57C \\ & + 65.42D + 0.09E - 1.27AB - 1.65AD \\ & + 0.5BD + 0.24DE - 3.37A^2 \\ & - 0.09B^2 - 1.14D2 - 0.11E^2\end{aligned} \tag{7}$$

In Eqs. (6) and (7), the negative or positive signs or coefficients in the equation, indicate the negative (reverse) or positive (direct) effects of the parameters or the interaction terms on the Vancomycin peak area as an index for its removal efficiency. Due to the reverse relationship of Vancomycin and degradation efficiency, the parameters with a negative sign have a positive effect on the removal efficiency and so on. For an acceptable model, R^2 should not be less than 0.75 (Moriasi et al. 2015) and the R^2 of the suggested model was 0.92 and it was close to $R^2_{adj} = 0.88$. R^2_{adj} indicates the correlation between the value predicted by the model and the actual values under experimental conditions (Golbraikh and Tropsha 2000). Also, the correlation coefficient of prediction (R^2_{pred}) was 0.81, which is more than 0.75, and indicates a significant relationship between the effective parameters and



(a) (b)

Fig. 3 SEM image (**a**) and EDX elemental analysis (**b**) for the synthesized TiO_2

Table 2 Analysis of variance of different parameters using CCD method in vancomycin removal

Source	Sum of squares	*Df*	Mean Square	*F*-value	*p* value Prob > *F*	
Model	391,481.4	13	30,113.96	25.18	< 0.0001	Significant
pH (*A*)	2869.71	1	2869.71	2.40	0.1325	
Initial concentration of vancomycin (*B*)	186,910.2	1	186,910.2	156.33	< 0.0001	
TiO_2 amount (*C*)	6514.14	1	6514.14	5.44	0.0270	
Temp (*D*)	42,377.76	1	42,377.76	35.44	< 0.0001	
Time (*E*)	26,139.95	1	26,139.95	21.86	< 0.0001	
AB	23,177.93	1	23,177.93	19.38	0.0001	
AD	4384.42	1	4384.42	3.66	0.0658	
BD	22,912.88	1	22,912.88	19.16	0.0002	
DE	5473.04	1	5473.04	4.57	0.0412	
A^2	9127.60	1	9127.60	7.63	0.0100	
B^2	22,979.38	1	22,979.38	19.22	0.0001	
D^2	41,348.59	1	41,348.59	34.58	< 0.0001	
E^2	35,434.72	1	35,434.72	29.63	< 0.0001	
Residual	33,476.48	28	1195.58			
Lack of fit	22,363.37	13	1720.25	2.321932	0.0605	Not significant

C.V. %	PRESS	R^2	R^2_{adj}	R^2_{pred}	Adeq precision
16.91	80,659.57	0.92	0.88	0.81	18.62

responses (peak area) (Nikaeen et al. 2020). The signal-to-noise ratio of the Adequate Precision rate was 18.62, which indicates that the model has an appropriate signal. According to the literature, an adequate precision higher than four, indicates a precise and acceptable model (Variyana et al. 2019).

F-value is the ratio of the mean squares of the model or each parameter to the mean squares of the not fitted data. The *p* value indicates the probability of error in accepting the validity of the observed results. The lower the *p* value, the higher the accuracy. The smaller the *p* value and the larger the *F*-value shows more significant coefficients in the MLR model. Defined simply, a *p* value is a data-based measure that helps to show a departure from a specified null hypothesis (Jamshidi et al. 2019). The total *F*-value in this analysis was 25.18, which indicates the significance of the model. In this analysis, *B*, *C*, *D*, *E BD*, *AD DE*, *AB*, A^2, B^2, D^2, and E^2 were significant parameters (affecting the removal reaction) (p value < 0.1).

One of the methods used to identify the errors in the design of experiments is to plot the residual normal curve. Residual is the difference between the observation and the values of the prediction model of the dependent variable. For a statistically correct model, this value must be small and its distribution must be normal (Bruce and Bruce 2017). Figure 4a shows the normal plot of the Vancomycin removal process, indicating that about 98% of the experiments data have an error of less than 2.9 and only about 2% have an error of more than − 2.5. These are random errors and the appropriate distribution confirms the model developed for Vancomycin removal, using TiO_2 catalyst. The distribution of residual values in different peak areas (as the indicator of removal of Vancomycin from aqueous media using a TiO_2 catalyst) versus the actual value is shown in Fig. 4b. The distribution of the residual values on both sides of the axial line does not show a pattern on one side of the zero lines. It is clear that the residual values in these diagrams have no special or unusual pattern and thus no systematic error can be detected and the model is valid. Figure 4c also shows the random distribution of the residual value, similar to Fig. 4b, but here the residuals are represented in different runs. As it was denoted previously, distribution in both sides of the zero line confirms the absence of systematic errors in removal experiments (Nekoeinia et al. 2015). Also, as it is represented in Fig. 4d, there is a good consistency between the actual peak area and the predicted value of the model in the removal process of Vancomycin.

Response surface of interaction factors

To investigate the effect of various interaction factors (independent variables) on the degradation of Vancomycin (dependent variable), three-dimensional (3D) surface representations of the interaction terms are illustrated in Fig. 5. Figure 5a shows the 3D plot of the interaction between pH and the initial concentration of Vancomycin. As observed in

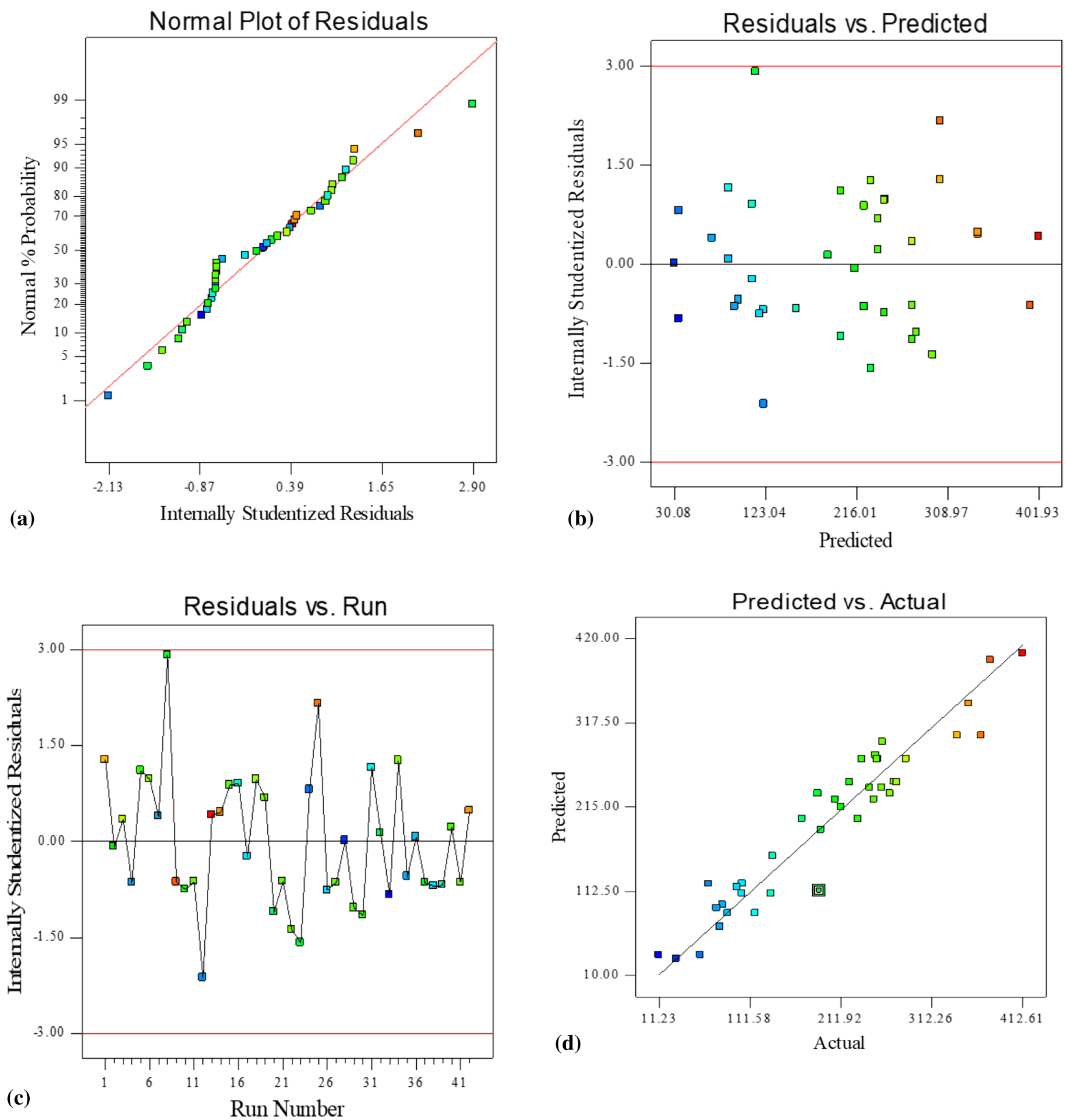


Fig. 4 Normal probability plot of the studentised residual (**a**), the residual plot versus predicted response (**b**), the residual plot versus different runs (**c**), predicted response values versus their actual values (**d**)

Fig. 5a, as the initial concentration of Vancomycin increases, the peak area of chromatograms also increases and the amount of antibiotic elimination decreases.

The 3D surface of the effect of pH and temperature on the Vancomycin peak is shown in Fig. 5b. As can be observed, with increasing temperature, the amount of peak area increased and the removal of Vancomycin using TiO_2 decreased. As the pH increases from 5 to 9, the peak area also is slightly increases. This means that the Vancomycin removal efficiency was done better at acidic pH around 5 in comparison with higher and alkaline pH. Malakootian showed that the removal of ciprofloxacin was inversely related to pH (Malakootian et al. 2020). Also, Peterson showed that the TiO_2 catalyst removed penicillin from the

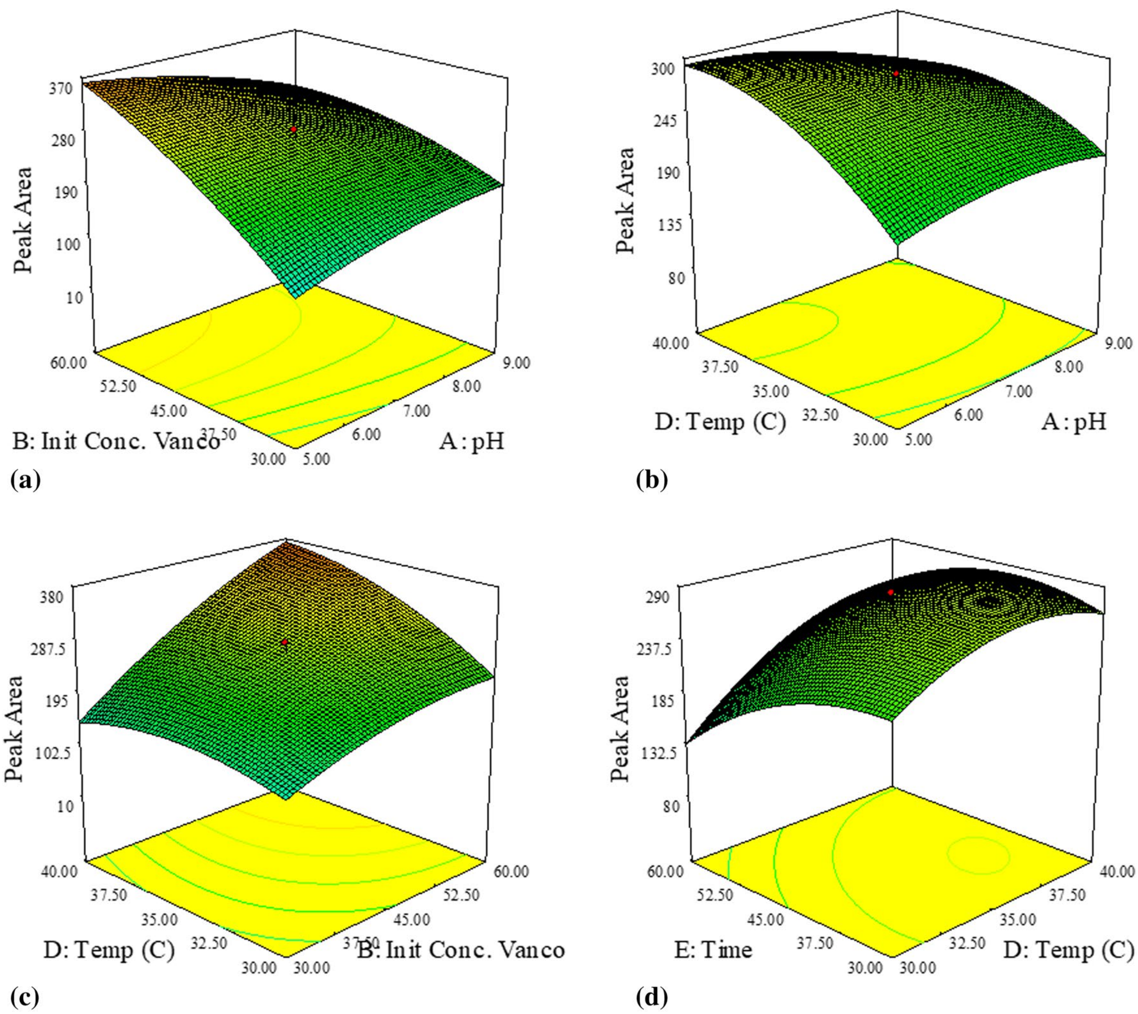


Fig. 5 Three-dimensional response surface plots of interaction: interaction between pH and initial concentration of vancomycin (**a**), interaction of pH and temperature (**b**), interaction of initial concentration of vancomycin and temperature (**c**), interaction of temperature and time (**d**)

aqueous solutions and the highest removal rate were at pH values 4 to 6 (Peterson et al. 2012).

It was observed that the removal of antibiotics was strongly dependent on pH (Kebede et al. 2019). Because it has a great effect on the production of hydroxyl radicals, the solubility of contaminants and catalyst surface charge play an important role in the decomposition and removal of antibiotics (Bagal and Gogate 2012; Daghrir et al. 2013). The surface charge properties of TiO_2 change with pH. Surface charge TiO_2 at pH = 6.5 was zero and was positive in acidic solution and negative in alkaline solution (Liu et al. 2007).

It has been reported that Vancomycin has 6 pKa values: 7.75, 8.89 (basic), 2.18, 9.59, 10.4, and 12.0 (acidic) (Jia et al. 2013). Thus, in pH values between 2.2 and 7.7, the Vancomycin has not intensive positive or negative charge; thus, it has a little repulsive effect with TiO_2 surface which can increase the interaction of drug with nano-catalyst and increase the removal efficiency.

Muruganandham et al. showed that the reaction rates of phorate decomposition were relatively independent of solution temperature and pH values (Muruganandham et al. 2014) Degradation of β-lactam antibiotics (Penicillin and Cephalosporins) increases with increasing temperature (Roca et al. 2011). Figure 5c shows the trend of change in the peak area, as a function of the initial concentration of Vancomycin and temperature. The interaction between the initial concentration of Vancomycin and temperature is effective on the removal of Vancomycin (p value < 0.1). As shown in Fig. 5a, high concentrations of contaminants can form intermediates. These compounds can capture OH radicals in side reactions and also can be adsorbed by the catalyst surface which can lead to a decrease in the active surface of the catalyst. In the situation of surface, the catalyst was not able to absorb the active form OH^0, H_2O, O_2 sufficiently. This condition reduces the reaction with capacitance holes and conduction band electrons produced by the catalyst.

In addition, in an environment with high concentrations of pollutants, fewer photons reach the catalyst surface, which reduces the optical activity (Farzadkia et al. 2014).

Figure 5d shows the effect of reaction time and temperature on the peak area of Vancomycin as the indicator of the removal process which was obtained at a concentration of 45 mg l^{-1} Vancomycin and pH = 7 using TiO_2 dose equal to 75 mg. As observed in this fig, with increasing temperature, the peak area increases, and the antibiotic removal rate is decreased. With increasing the reaction time, the peak area decreases and the removal efficiency increases. It should be emphasized that the above discussion is used to show that the total trends and optimum value of all parameters cannot be reached solely by considering these plots. In better words, the optimum value will be obtained by considering all the parameters simultaneously and using a multivariate approach.

Vancomycin removal efficiency under optimal conditions

After analyzing the model and obtaining the optimum values of experimental parameters of Vancomycin removal using simplex approach, the optimum conditions was calculated as: pH = 5.1, initial concentration of Vancomycin = 58.2 mg l^{-1}, TiO_2 dosage = 54.9 mg in 250 ml reactor, temperature = 39.6 °C, and reaction time = 36.3 min. In these conditions, the removal efficiency was evaluated in the presence of TiO_2 nanocatalyst so that the removal efficiency with UV radiation and without it, was 89.5% and 25%, respectively. In the same vein, Safari et al. stated that the removal of tetracycline was 83.2% by TiO_2/UV and 23.8% by presence of UV alone. With TiO_2/UV, more hydroxyl ions are formed in solution and antibiotic decomposition occurs faster. (Safari et al. 2015). Kim and Tanaka also found that two UV lamps were more effective at removing pharmaceuticals and personal care products than one UV lamp. Two UV lamps Photolyze more water molecules and produce more hydroxyl (Kim and Tanaka 2009). Increasing the initial concentration of the pollutant may reduce the performance of the UV rays to reach the TiO_2 level because the ultraviolet light is reduced or scattered by fine solid particles (Chong et al. 2009; Jamshidi et al. 2019). Jamshidi et al. also showed that under the optimum conditions (alachlor concentration of 30 mg l^{-1}, TiO_2 concentration of 100 mg l^{-1}, temperature of 35 °C, reaction time of 60 min), removal of alachlor was 98.44% (Jamshidi et al. 2019). Lofrano et al. showed the degradation of Vancomycin in the presence of TiO_2 (0.1 and 0.2 g) was obtained 95–85% for 120 min. (Lofrano et al. 2014). In addition, Lofrano et al. investigated the degradation of Vancomycin in the presence of TiO_2 and ZnO with initial concentrations; 20–50 mg l^{-1} for Vancomycin and 0.1 and 0.5 g l^{-1} for TiO_2 and ZnO at normal pH. Therefore the Vancomycin removal came to 70–85% in 10 min by ZnO and 73–59% in 90 min by TiO_2 (Lofrano et al. 2018). In comparison, this study revealed that more degradation efficiency (89.5%) was achieved by optimizing the conditions in a lower amount of catalyst (54.9 mg) and lower time (36.3 min) in the presence of TiO_2/UV. Thus, Vancomycin removal efficiency for real wastewater sample under optimal conditions was 84%.

Vancomycin removal efficiency under optimal conditions in the presence or absence of aeration

As a fact, stirring of liquids increases the photocatalytic reaction by increasing the rate of aeration and oxygenation of the solution, in addition, increasing the aeration rate can lead to a decrease in the resistance of external mass transfer and performing light degradation (Chong et al. 2009). To show the role of aeration in the suggested process, airing was done in the mentioned optimized conditions, so the removal efficiency of Vancomycin was increased by aeration (93%).

Catalyst recovery and reuse

To investigate the catalyst recycling, the experiments was performed based on the optimal conditions for this purpose, the catalyst was checked at the end of the run by centrifuging, and washing several times with distilled water; then, it was dried at 60 °C and reused in another similar cycle, i.e., Vancomycin removal. After performing two cycles, the degradation efficiency was decreased from 89.5 to 80% in the former step and to 78% in the latter. Accumulation of pollutants on the surface of the catalyst can cause a partial blocking on active sites of the catalyst and reducing the absorption of light by the catalyst and decreasing the hydroxyl radicals production (Argyle and Bartholomew 2015). As the result, the catalyst potential for removing vancomycin was slightly changed during the two runs.

Conclusion

The results showed the efficiency of the application of TiO_2/UV on the degradation of vancomycin in the aqueous media. In this study for the first time, the various affecting parameters on the photocatalytic degradation of vancomycin were explored simultaneously using a multivariate approach based on CCD. ANOVA results of the model made based on the CCD method showed, R^2 of the final model was 0.92, which was close to R^2_{adj} (0.88). This showed a correlation between the predicted and the actual response values. The results showed, various parameters such as, initial concentration of vancomycin, TiO_2 amount, pH, temperature and reaction time can significantly influence the photocatalytic degradation of vancomycin. Optimization is important for photocatalytic degradation process for large scale application. Overall, the optimal conditions for vancomycin removal (89.5%) were as follows: pH = 5.1, initial concentration of vancomycin = 58.2 mg l^{-1}, TiO_2 dosage = 54.9 mg, temperature = 39.6 °C, and time = 36.3 min. According to the results, vancomycin degradation was decreased with increasing temperature and initial vancomycin concentration. Also, the degradation efficiency was increased with decreasing pH and increasing reaction time. Furthermore, under optimal conditions, vancomycin efficiency can be increased by aeration and the use of ultraviolet radiation with a catalyst. The results obtained from the optimal conditions help to eliminate vancomycin in real conditions especially the wastewater of the pharmaceutical industries. It could be suggested that such multivariate optimization is a good way to obtain acceptable efficiency for vancomycin elimination in the aqueous media.

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Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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