

## Optimization of Acetaminophen and Methylparaben Removal within Subsurface Batch Constructed Wetland Systems

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### ABSTRACT

The response surface methodology accompanied by Central Composite Design (CCD) was employed in this study to optimize the *Alternanthera spp*-based phytoremediation process for the individual removal of acetaminophen and methylparaben. Two operational variables, including concentration (A) (20, 60,100 mg/L) and sampling time (B) (7, 14, 21, and 35 days) were involved in the study for removal efficiency (Y) as response. CCD had required a total of 18 experiments for each compound. Analysis of variance (ANOVA) was conducted to verify the adequacy of the proposed mathematical models and revealed good agreement with the experimental data. The observed  $R^2$  values (0.9732 and 0.9870), adjusted  $R^2$  (0.9620 and 0.9816) and predicted  $R^2$  (0.9383 and 0.9721) for AC and MP, respectively, indicated that the developed models were significant at the 95% probability level. Concentration factor was found to be insignificant in the mathematical models; in contrast, sampling time was found to be of a crucial role. The removal of AC and MP were 89.23% and 64.48% under optimum conditions of A = 100 mg/L and B = 35 days respectively. The validation test confirmed the predicted results obtained by Central Composite Design, as the removals achieved under optimum conditions were 91.04% and 59.17% for AC and MP, respectively, which were in good agreement with the results proposed by the theoretical design.

**Keywords:** phytoremediation, ornamental plant, constructed wetlands, PPCPs, central composite design.

### INTRODUCTION

Recently, emerging organic contaminants (EOCs) including pharmaceuticals and personal care products (PPCPs) and pesticides have attracted the most attention, after conventional pollutants (such as heavy metals and persistent organic pollutants) were the most threatening to the aquatic environment (Xu et al., 2019). PPCPs are widely consumed substances which are frequently detected in surface and ground waters (Hijosa-Valsero et al., 2010). PPCPs have been monitored with concentrations in the range of ng/L to mg/L at different regions around the world, such as Brazil (Couto et al., 2020), China (Junaid et al., 2019), Czech Republic (Vymazal et al., 2017), India (Williams et al., 2019), Portugal

(Gaffney et al., 2015) and South Africa (Archer et al., 2017). However, there are several practices that would raise the concentrations of PPCPs in the aquatic environment dramatically. For example, Petrie et al. (2016) noted the possibility of intentional or accidental release of high loads of pharmaceuticals (often surplus or expired) into wastewater, and emphasized that the associated facilities (such as pharmacies) may have directly disposed of large quantities of fluoxetine in the aquatic environment.

The growing concern about PPCPs results from their recalcitrant behavior in the receiving ecosystems and the unknown consequences of their continual release (Hijosa-Valsero et al., 2010). PPCPs represent a potential threat, as the presence of such substances in the ecosystems

may cause antibiotic resistance and endocrine disruptions on humans, livestock and aquatic life (Liu et al., 2019).

Constructed wetlands (CWs) are an affordable choice for wastewater treatment, which are efficiently eliminated or attenuate various contaminants, including PPCPs. Nevertheless, the large area requirements needed to meet the water quality parameters make the application of CWs restricted to wastewater treatment in small urban communities or as tertiary treatments units dealing with the effluents of conventional WWTP (Hijosa-Valsero et al., 2016).

The overall removal or transformation of nutrients and organic contaminants in CWs involve a set of simultaneous physical, chemical and biological processes; where biodegradation, plant uptake and adsorption have the paramount contributions. However, the removal efficiency of CWs is crucially affected by several factors, including wetland type, vegetation type, substrate media, climatic conditions, pollutants concentration and the hydraulic properties of the design (hydraulic retention time and hydraulic loading rate) (Weerakoon et al., 2020).

The optimization step is conducted to seek the best solution for specific conditions, which improves the efficiency of the any process or system (Titah et al., 2018). Several optimization methods have been created for research and industrial projects, and each has its own benefits and weaknesses. One-factor-at-a-time method (OFAT) is a classical optimization methodology which suffers from many weaknesses, including being time-consuming and costly (Sanusi et al., 2016; Ntakiyiruta et al., 2020); further, this method is ineffective in several situations, including predictive studies and evaluation of the interactions between parameters (Darajeh et al., 2016; Sanusi et al., 2016; Ntakiyiruta et al., 2020). Therefore, researchers resorted to statistical and mathematical experimental designs (such as response surface methodology, artificial neural networks and genetic algorithms) as an alternative to the classical approaches (Sanusi et al., 2016).

Response surface methodology (RSM) is an analytical approach which can be applied to identify the optimized operation conditions for a multi-variable structure such as wastewater treatment systems. RSM can be established to evaluate the relationship between the independent and response variables depending on certain criteria. Implementing the RSM approach requires the

fewest number of experimental trials, making the optimized processes less time-consuming (Darajeh et al., 2016).

RSM is frequently applied in the wastewater treatment process in order to reach the required aims, particularly for improvement of the pollutant removal efficiency and reduction of operating cost (Ting et al. 2020). However, understanding of the design variables under investigation is essential to achieve an adequate model (Darajeh et al., 2016).

Optimizing the significant parameters is a key step in the phytoremediation process (Sanusi et al., 2016). Several studies have reported the successful application of the RSM models in optimizing phytoremediation process. Central composite design (CCD) was the widely adopted model in most of these studies; for example, Darajeh et al. (2016) used CCD for optimizing the treatment process of palm oil mill effluent (POMSE) via floating CW by *Chrysopogon zizanioides* L. The researchers choose the removal of chemical oxygen demand (COD) and biological oxygen demand (BOD) as dependent variables, while the concentration of POMSE and the density of the plant represented the influence factors. Optimizing the removal of ammoniacal nitrogen (AN) by *Eichhornia crassipes* was carried out by CCD, as reported by Ting et al. (2020) with four influence factors (pH, retention time, plant density and salinity) and five responses (AN removal efficiency, biomass growth, COD, BOD and total suspended solids). Thani et al. (2020) employed CCD for optimizing the removal of nickel by *Alocasia puber*, with nickel concentration and exposure time as independent variables and the removal efficiency as a response. Mojiri et al. (2017) as well, utilized the same model for optimizing the removal of chromium and cadmium from aqueous solutions in constructed wetlands. CCD was also used by Sanusi et al. (2016) for optimizing the degradation of total petroleum hydrocarbon in constructed wetland planted by *Paspalum scrobiculatum*, where diesel concentration, time and aeration rate represented the independent variables. Besides, another design has been employed, which is Box–Behnken Design (BBD), to optimize the factors that influence the removal of the different contaminants such as diesel (Al-Baldawi et al., 2014) and triclosan (Lam et al., 2020).

In certain circumstances, researchers may have to reduce the number of trials, as in the case of expensive and time consuming experiments.

In such situations, researchers need to rely on fewer points in the design and this is what the D-optimal design provides (Khan et al., 2016). Khan et al. (2016) confirmed that adopting the D-optimal design reduced the number of experiments by 40.38–50% compared with the CCD (Khan et al., 2016).

Thus, the objective of this study was to apply RSM accompanied by central composite design to acquire the optimal conditions for the removal of two PPCPs (AC and MP), individually, in subsurface horizontal-flow constructed wetlands using *Alternanthera spp.* The optimization study would be beneficial for the design of the phytoremediation process to remove AC and MP effectively from the wastewater.

## MATERIALS AND METHODS

### Chemicals and plant materials

High purity Acetaminophen (AC) was obtained from Middle East Laboratories Co. Ltd. (Iraq). Methylparaben (MP) (purity >99%) was purchased from VWR Chemicals (UK). An ornamental plant species (*Alternanthera spp.*) was purchased from Al-Zawraa Park, Baghdad. The plants were rinsed gently, and then acclimatized in tap water for two weeks to favor the growth of roots. Homogenous plants were selected for the experiments.

### Set up of the subsurface batch systems

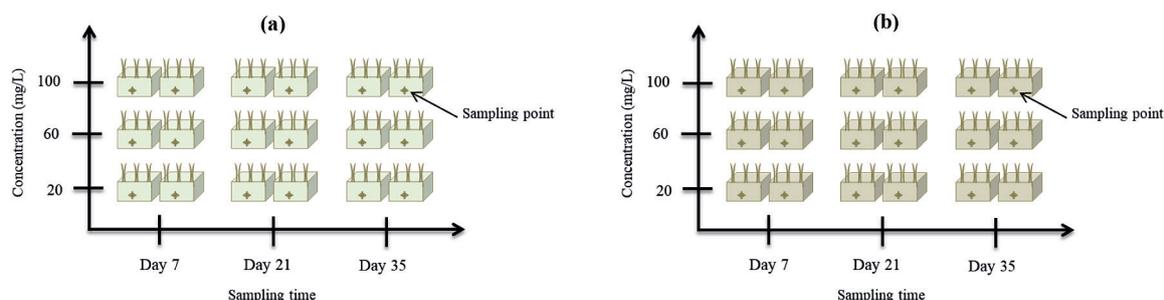
Two sets of experiments were conducted: one for AC and another for MP. For each set, a glass mesocosms-scale phytoremediation tanks were constructed with the dimensions of 0.3×0.3×0.3 m and water capacity of 20 L. A

schematic description for AC and MP sets are given in Figure 1. Homogenous *Alternanthera spp.* plants were washed gently and acclimated in tap water for two weeks prior to the experiments, then planted at mesocosms with density of 10 plants/mesocosm. Gravel was used as a substrate to a depth of 20 cm (5 cm of coarse gravel (9.5–13.5 mm) in the bottom, 10 cm of fine gravel (ø 6.5–9.5 mm) and 5 cm of fine gravel (ø 2.5–6.5 mm) in the top). All mesocosms were placed under the outdoor condition and operated in batch mode. Stock solutions of 1000 mg/L for both AC and MP were prepared, individually. Then, 5 L of diluted solution with different concentrations (20, 60 and 100 mg/L) were fed to each CWL, so that the water level was controlled within the gravel surface to simulate a horizontal subsurface constructed wetlands (SSB-CWL). Tap water was added to the tanks regularly to compensate the loss of water and maintain a constant water level. Finally, the effluent from each CWL was collected throughout the 35-day exposure and analyzed for AC and MP.

### Analysis of AC and MP

The water samples were first filtered through a 0.45 µm syringe filter, then directly analyzed via UV-visible spectrophotometer (UV-1800, Shimadzu, Japan) to quantify the concentrations of AC (based on USP 29 assay) and MP (based on Piovesan et al. (2018)), as described in supplementary materials. The absorbance values were qualified at maximum wavelength of 242 and 255 nm for AC and MP, respectively, then the concentration of both compounds was calculated.

The removal efficiency for the target compounds were calculated based on the initial and final concentrations in the synthetic wastewater, according to equation (1):



**Figure 1.** Schematic diagram of the mesocosm-scale CWLs: (a) AC and (b) MP

$$RE\% = \frac{C_i - C_t}{C_i} \times 100 \quad (1)$$

where:  $RE$  is the removal efficiency (%);  
 $C_i$  and  $C_t$  (mg/L) are the pollutant concentration initially and through time.

### Optimizing the removal of AC and MP with the central composite design

RSM was performed to estimate the relations existing between two of experimental variables namely concentration of the contaminant in wastewater (A) and sampling time (B), with the measured responses, namely the removal efficiency by *Alternanthera spp* (Y).

Central composite design (CCD) was applied as the Design of Expert (Version 6.0.1, Stat-Ease Inc., Minneapolis, MN, USA) for data interpretation and regression modeling, in which a total of 18 runs were conducted for each AC and MP, separately, with 2 center points, 16 axial points and  $\alpha = 1$ . The experiments included a duplicate for each run to evaluate the magnitude of the random error. The experimental design was performed with the relevant factors at three levels (+1, 0, -1): concentration (20, 60, and 100 mg/L) and sampling time (7, 21, and 35 days) as indicated in Table 1. The relation between the independent parameters and the responses was mathematically described by the quadratic model, as shown in Eq. (2) (Al-Baldawi et al., 2014):

$$Y = \beta_0 + \beta_1 A + \beta_2 B + \beta_{11} A^2 + \beta_{22} B^2 + \beta_{12} AB + \varepsilon \quad (2)$$

where:  $Y$  is the predicted response (removal efficiency for AC or MP);  
 $A$  and  $B$  are the independent variables,  
 $A^2$  and  $B^2$  are the square effects and  $AB$  s the interaction effects;  
 $\beta_0$  is the regression constant,  
 $\beta_1$  and  $\beta_2$  are the linear coefficients,

$\beta_{11}$  and  $\beta_{22}$  are quadratic coefficients and  $\beta_{12}$  is the interaction coefficient;  $\varepsilon$  is the random error.

The fitness of the proposed models was assessed by conducting analysis of variance (ANOVA), where a valid model must achieve a significant F-value and P-value, while the value with lack of fit must be insignificant (Al-Baldawi et al., 2014; Titah et al., 2018). Diagnostics plots were also assessed to verify the validity of the models. Further evaluation of the proposed models was conducted by testing the coefficient of determination ( $R^2$ ), adjusted coefficient of determination ( $R^2_{\text{adjust}}$ ) and predicted coefficient of determination ( $R^2_{\text{predict}}$ ), where the correlations close to 1.0 indicate a good relationship between the expected and the actual values of the response (Al-Baldawi et al., 2014; titah et al., 2018). Moreover, the effects of involved parameters were also compared using 3D response surface plots.

Optimization was performed to identify the optimum conditions for achieving the highest removal efficiency for AC and MP.

### Validation of the models

In order to verify the optimized results, two additional mesocosms, planted with *Alternanthera spp*, were used, in which the predicted optimum conditions of the independent parameters (concentration and sampling time) proposed by CCD were simulated. Then, the actual results attained in this step were compared with the predicted optimal values.

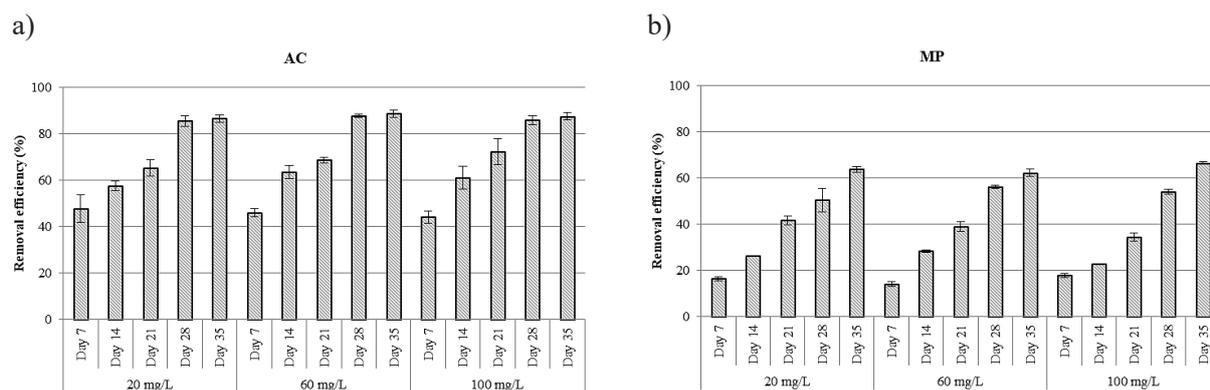
## RESULTS AND DISCUSSION

### Developing the quadratic models by central composite design

CCD was performed to model and optimize the removal of AC and MP, individually, by *Alternanthera spp* from synthetically prepared wastewater. The analysis was carried out at a significance level of 5%. The actual results obtained from the experimental design (represented in Figure 2) were fitted to a quadratic model through multiple regression analysis, where the positive coefficient values represented a synergistic effect, while the negative coefficient values represented an antagonistic effect. The quadratic models that

**Table 1.** Parameters involved in the experimental design.

Parameters	Factors	Range and levels		
		-1	0	+1
Concentration (mg/L)	A	20	60	100
Sampling time (day)	B	7	21	35



**Figure 2.** Removal of AC and MP from the synthetically prepared wastewater throughout a 35-days experiment

relate the removal rates (response) and the independent variables were developed by CCD and described in terms of the coded parameters as given in Equation 2 and 3.

$$Y_{AC} = 69.10 + 0.74A + 20.81B - 0.58A^2 - 1.97B^2 + 1.13AB \quad (3)$$

$$Y_{MP} = 37.31 - 0.51A + 24.03B + 1.59A^2 + 1.71B^2 + 0.35AB \quad (4)$$

where:  $Y_{AC}$  and  $Y_{MP}$  – removal efficiency (%) for AC and MP, respectively,  
 $A$  – concentration (mg/L) of AC or MP,  
 $B$  – sampling time (day).

The actual removal rates, in addition to the predicted response values for AC and MP sets, are presented in Table 2. The highest and lowest AC removal rates achieved during the experiments were 89.69% and 42.21%, respectively; while the maximum and minimum removal rates predicted by CCD were 89.23% and 45.34%, respectively. As for MP, the highest and lowest removal rates were 66.91% and 13.33%, respectively; while the maximum and minimum removal rates predicted by CCD were 64.80% and 14.99%, respectively. The agreement of the actual data with the responses predicted by RSM raises the reliability and applicability of the proposed model (Ozturk et al., 2021). In this study, there is a satisfactory correlation between the predicted output values

**Table 2.** Central composite design matrix for actual and predicted responses of AC and MP

Run	Concentration (mg/L)	Sampling time (Day)	Removal (%)			
			Acetaminophen		Methylparaben	
			Actual	Predicted	Actual	Predicted
1	20.00	7.00	43.45	46.13	37.58	37.31
2	60.00	35.00	87.52	87.95	64.50	64.80
3	20.00	21.00	62.77	67.78	13.33	14.99
4	60.00	21.00	69.53	69.10	66.05	64.49
5	20.00	35.00	87.56	85.49	66.91	64.49
6	20.00	35.00	85.51	85.49	15.80	17.44
7	100.00	21.00	68.23	69.26	33.06	38.39
8	100.00	21.00	76.16	69.26	16.86	17.44
9	60.00	7.00	44.78	46.32	14.86	14.99
10	100.00	7.00	42.21	45.34	40.16	39.41
11	60.00	35.00	89.69	87.95	61.06	63.06
12	60.00	21.00	67.90	69.10	40.59	37.31
13	60.00	7.00	47.32	46.32	17.10	15.72
14	100.00	35.00	86.46	89.23	62.85	64.80
15	20.00	21.00	67.69	67.78	35.73	38.39
16	20.00	7.00	51.83	46.13	63.30	63.06
17	100.00	7.00	46.00	45.34	18.36	15.72
18	100.00	35.00	88.60	89.23	43.12	39.41

calculated using the suggested quadratic models and the actual experimental values, which indicated the accuracy of these models. Thus, the proposed models showed good prediction ability under the considered conditions.

### Fitting and analysis of variance for response surface quadratic models

A “good fit” model is necessary to avoid unclear or inadequate results in the optimization process (Al-Baldawi et al., 2014; Ozturk et al., 2021). Regression analysis, in addition to the diagnostics plot, were adopted to assess the fitness of the developed models. ANOVA was conducted to test the significance and adequacy of the suggested mathematical models as a whole, in addition to the individual terms in the models.

The ANOVA results for the proposed models (AC-removal model and MP-removal model) are listed in Table 3. F-test was considered to assess the significance of the proposed models. The criterion that must be met for the acceptability and reliability of the model is an increase in the F-value of the proposed model in conjunction with a decrease in P-value (Bajpai et al., 2020).

The F-value for AC and MP removal models were 87.00 and 182.45, respectively, indicating that the models are significant and can effectively explain most of the variation in the response (Al-Baldawi et al., 2014). This refers to only 0.01% chance for “Model F-Value” this large to occur due to noise. Besides, the associated P-value was considered to decide whether the F-value was large enough to confirm the statistical significance (Al-Baldawi et al., 2014; Ewadh et al., 2019). The P-values for the AC and MP removal models were found to be lower than 0.05 (particularly, < 0.0001 for both AC and MP), indicating that both models were statistically significant at the 95% probability level.

The lack of fit F-value of 1.46 for the AC model revealed that the lack of fit is not significant, thus the variations of the data around the fitted model were not significant, compared to the pure error. Nonsignificant lack of fit is good, as the model approaches perfect fitness referred to the significance of the model (Bayuo et al., 2020). Moreover, there was a 29.02% chance that a “Lack of Fit F-value” this large could have occurred due to noise. In contrast, the lack of fit F-value for MP model was 11.27, implying that the lack of fit was

**Table 3.** ANOVA analysis of the proposed quadratic models for AC and MP removal from wastewater

Source	Sum of squares	DF	Mean square	F value	Prob > F	
Acetaminophen						
Model	5231.55	5	1046.31	87.00	<0.0001	significant
A	6.54	1	6.54	0.54	0.4749	
B	5197.84	1	5197.84	432.20	<0.0001	
A <sup>2</sup>	1.37	1	1.37	0.11	0.7417	
B <sup>2</sup>	15.52	1	15.52	1.29	0.2781	
AB	10.28	1	10.28	0.85	0.3735	
Residual	144.32	12	12.03			
Lack of Fit	47.18	3	15.73	1.46	0.2902	not significant
Pure error	97.14	9	10.79			
Cor Total	5375.87	17				
Methylparaben						
Model	6955.45	5	1391.09	182.45	<0.0001	significant
A	3.09	1	3.09	0.40	0.5365	
B	6929.60	1	6929.60	908.88	<0.0001	
A <sup>2</sup>	10.07	1	10.07	1.32	0.2729	
B <sup>2</sup>	11.71	1	11.71	1.54	0.2389	
AB	0.99	1	0.99	0.13	0.7254	
Residual	91.49	12	7.62			
Lack of fit	72.26	3	24.09	11.27	0.0021	significant
Pure error	19.23	9	2.14			
Cor total	7046.94	17				

significant, which is unacceptable. There was only a 0.21% chance that a “Lack of Fit F-value” this large could occur due to noise.

Further statistical measures, including the coefficients of determination ( $R^2$ ) and adjusted  $R^2$ , had to be evaluated to ensure the adequacy of the suggested models (Table 4). ANOVA results confirmed the significance of the models with good  $R^2$  (0.973 and 0.987) and adjusted  $R^2$  (0.962 and 0.981) values for AC and MP, respectively, which indicates that the proposed models could explain 97.3% and 98.7% of the response variability for AC and MP, respectively (Ting et al., 2020). Further, the predicted  $R^2$  values of 0.938 and 0.972 for AC and MP, respectively, showed good agreement with the adjusted  $R^2$  of both models. The obtained values of  $R^2$ , adjusted  $R^2$  and predicted  $R^2$  were close to 1, demonstrating a good fitness of the models in the experimental data (Hamad, 2020). “Adeq Precision” quantifies the signal to noise ratio, a ratio greater than 4 is preferred (Al-Baldawi et al., 2014; Bajpai et al., 2020; Wang et al., 2020). The signal to noise ratio achieved in the present study was 21.92 for AC and 31.24 MP, indicating an adequate signal.

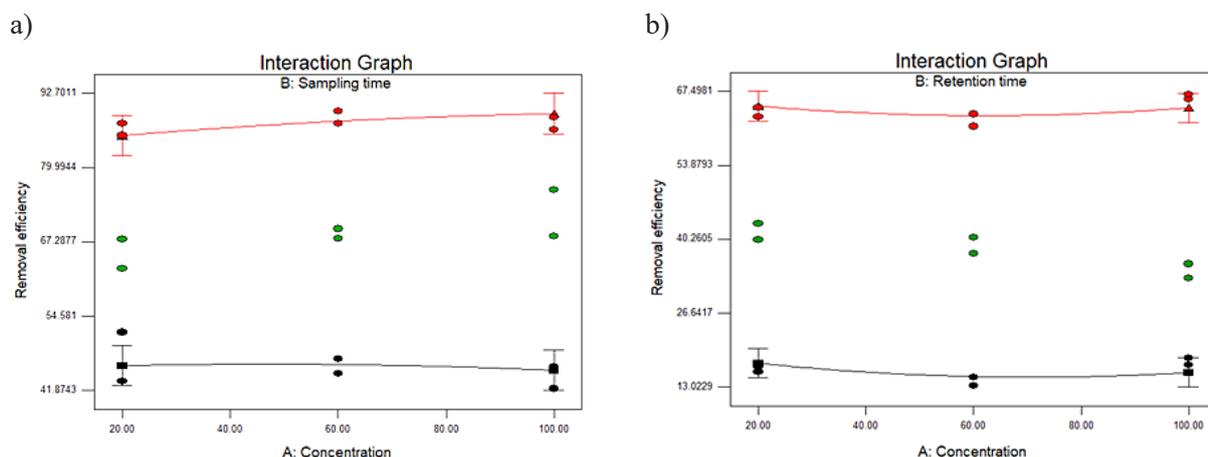
Regarding the concentration factor represented by term A, the low F-value of 0.54 and 0.40 for AC and MP models, respectively, along with the high P-value ( $> 0.1$ ) for both models indicated

that this factor was not significant for both AC and MP removal models. In contrast, the sampling time (term B) was found to be significant for both models and had a substantial impact on the responses. Further, the quadratic effects ( $A^2$  and  $B^2$ ), in addition to the interaction effects (AB) were not significant in both models. Figure 3 represents the contour plots for the interactive effect of terms A and B on the response (Y) for the AC and MP models.

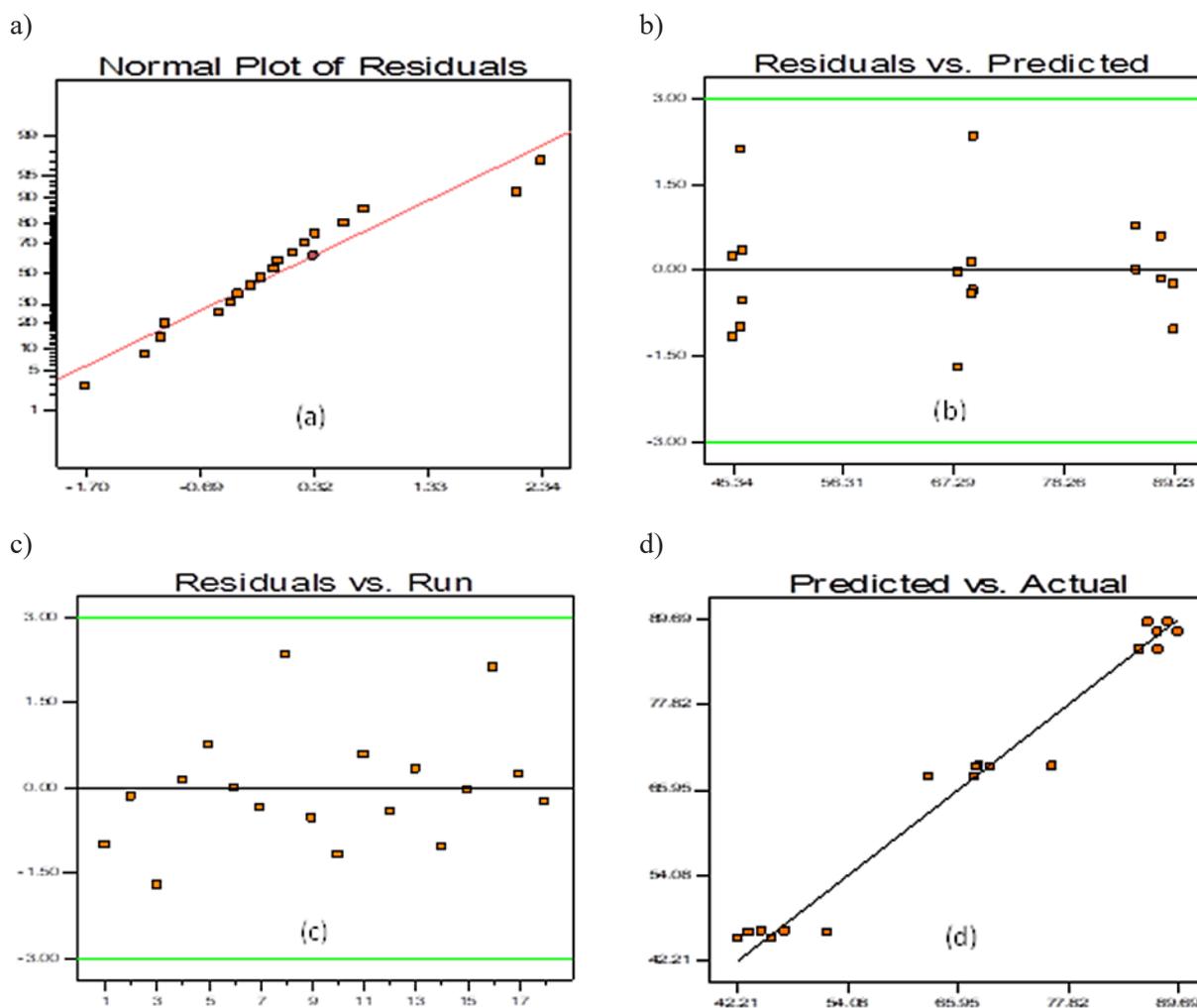
The diagnostics plots of the models statistical properties are illustrated in Figures 4 and 5. Analyzing normal plot of residuals is of particular importance, as it contributes to verifying the normality assumption needed to verify statistical modeling (Al-Baldawi et al., 2014). The diagnostic of normal residuals (Figures 4a and 5a) confirms that the probability for both AC and MP removal models follows an acceptable linear trend. The linearity of studentized residuals graph points out to the normality of the error distribution. In turn, the points with nonlinear path refer to abnormal error distribution, thus correction of the original data might be recommended (Teiri et al., 2020). As shown in Figures 4b and 5b, representing the plot of the studentized residuals versus the predicted response values, the error values were within the specified standard range (indicated by the green lines) which were calculated based on the normal distribution of the error and the standard deviation. Checking the diagnostic of the number of studentized residuals per run provides a close assessment for the number of trials with high errors (Teiri et al., 2020). Figures 4c and 5c, representing the number of studentized residuals per run demonstrated that the error for all points is also within the specified standard range. The plot of the actual versus the predicted responses

**Table 4.** Statistics of the proposed quadratic models

Statistical parameters	Values of developed models	
	AC	MP
R-squared	0.973	0.987
Adjusted R-squared	0.962	0.981
Predicted R-squared	0.938	0.972
Adeq precision	21.92	31.24



**Figure 3.** Interactive effects of concentration and sampling time (AB) on removal efficiency (Y): (a) AC (b) MP



**Figure 4.** Diagnostic plots for AC removal representing (a) studentized residuals versus the normal probability, (b) studentized residuals versus predicted response values, (c) run versus studentized residuals, (d) actual responses values versus the predicted response values

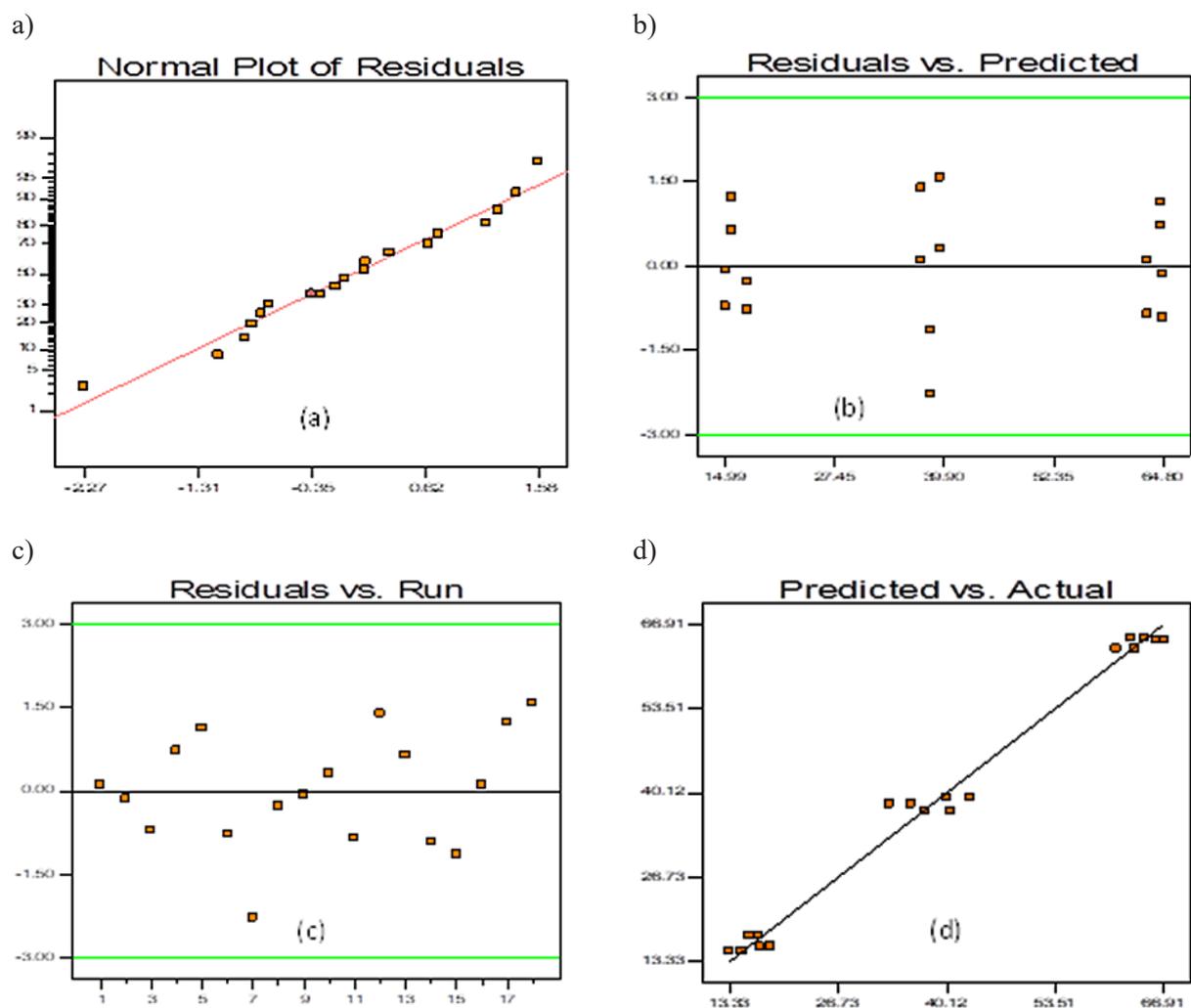
(Figures 4d and 5d) reveals that the predicted values fitted well with the actual values.

### Optimization of operational conditions

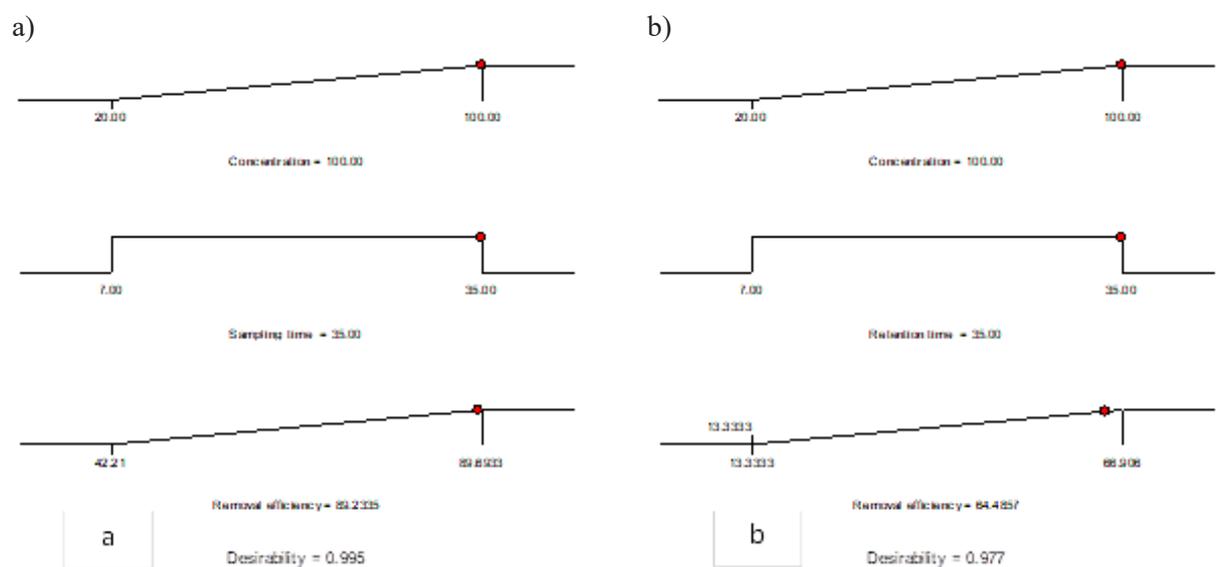
The impact of parameters, namely, concentration and sampling time on the removal of AC and MP were analyzed to achieve maximum efficiency of phytoremediation by using *Alternanthera spp.* The optimization process aims to specify the optimum operation conditions needed for maximizing removal for both AC and MP from wastewater. The desirability function methodology was adopted for this purpose. The variables of AC and MP concentrations were set at the maximum (100 mg/L) while sampling time was set in range of the experiment. By conducting the function of numerical optimization in the Design Expert software, desirability of 0.995 and 0.977% was found for the maximum AC and MP

removal, respectively, as shown in Figure 6. The maximum AC and MP removals from wastewater were 89.23% and 64.48%, respectively, under the optimized conditions of: concentration ( $A = 100$  mg/L) and sampling time ( $B = 35$  days).

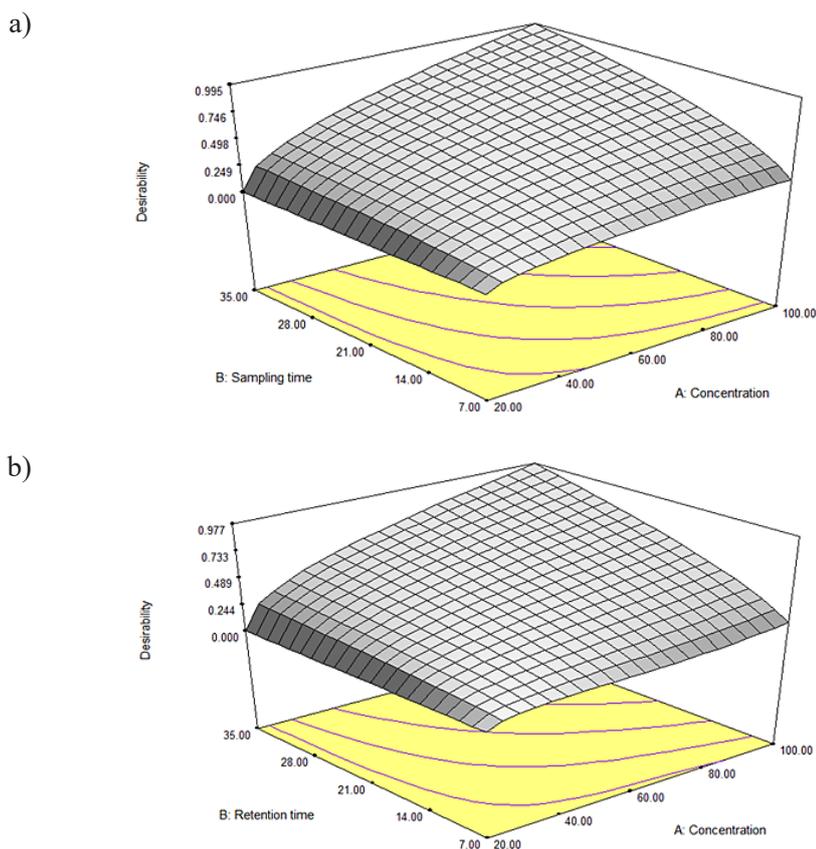
In Figure 7, the influence of the investigated parameters on AC and MP removal are illustrated as 3D response surface plots. It was observed that concentration ranging between 20 to 100 mg/L led to a steady removal from wastewater for both AC and MP. This might be attributed to the relatively high levels of concentrations. The effect of sampling time ( $B$ ) was an increase in the response within 7 to 35 days. This confirmed that longer sampling time of phytoremediation reduces more AC and MP concentration in wastewater and indicates that the equations effectively represent the relationship between the response (AC and MP removal from wastewater) and the significant input variables.



**Figure 5.** Diagnostic plots for MP removal representing (a) studentized residuals versus the normal probability, (b) predicted versus studentized residuals, (c) run versus studentized residuals, (d) actual responses values versus the predicted response values



**Figure 6.** Desirability slope for numerically-optimized conditions: (a) AC and (b) MP



**Figure 7.** Optimum conditions for: (a) AC removal (b) MP removal

## Validation

Further experiments were conducted in order to validate the obtained optimum conditions created by RSM. This run validated the accuracy of the model and reported 91.04% and 59.17% of AC and MP removal, respectively, which closely agreed with the predicted results attained by CCD with the error of 5% and 7%, respectively. The high agreement between the experimental and theoretical response indicates the precision of the response surface models (Kumari and Gupta, 2019).

## CONCLUSIONS

Central Composite Design was employed to build response surface models and optimize the removal of AC and MP from wastewater via phytoremediation by *Alternanthera spp* at mesocosm-scale constructed wetlands. The coefficients of determination ( $R^2$ ) and adjusted  $R^2$  for the proposed models were close to 1 which

confirms the significance of the regression models to predict the responses. The predicted values obtained by the models exhibited good agreement with the experimental results. Sampling time had a significant influence on the removal process for both AC and MP, whereas the concentration of target compounds did not show any significant influence. According to the results of this study, phytoremediation represents a feasible treatment technology for the removal of PPCPs from contaminated wastewater that can be successfully improved and optimized via the response surface methodology approaches.

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