Experimental and numerical study on the degradation of mefenamic acid in a synthetic wastewater

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Abstract. The present work aims to study the degradation of mefenamic acid (MFA) in synthetic wastewater experimentally and numerically. The experiments were carried out using utilizing homemade Cu doped TiO$_2$ in a solar irradiated falling film reactor. Two operating variables are investigated; pH of the wastewater in the range of (3-10) and synthesis wastewater flow rate (1-3 L/min). The numerical study involves the optimization of the variables. The multifactorial design method, Design of Experiments (DOE), and Response Surface Methodology (RSM) were used to evaluate the interaction effect of the two variables on the degradation of mefenamic acid. The significance of the results was evaluated by statistical analysis of variance (ANOVA). The results show that the removal efficiency increasing with increasing pH and decreases with wastewater flow rate. The results have shown that the interaction effects between mentioned factors were highly significant in influencing MFA degradation by analyzing statistics and ANOVA.

Keywords: Pharmaceuticals; Response Surface Methodology; wastewater; Cu doped TiO$_2$

1. Introduction
Mefenamic acid is a non-steroidal anti-inflammatory drug (NSAID), indicated for relief of mild to moderate pain and primary dysmenorrhea treatment [1]. The presence of mefenamic acid is noticed in many resources of water residue in many countries. Wastewater effluent from some Iraqi hospitals contains unacceptable pharmaceuticals that threaten the aquatic environment if they are not removed [2]. Research on toxicity reported that exposure to MFA could highly motivate untoward influences on aqueous living creatures like luminescence suppression, swim performance change, and doom [3, 4]. The Advanced Oxidation Processes (AOP) is considered an effective method for degrading this pharmaceutical complex. Colombo et al. [5] studied experimentally the degradation of MFA using the Fenton and Photofenton processes for the degradation of MFA. The authors combined the factorial design method, Design of Experiments (DOE), and Response Surface Methodology (RSM) to investigate the interaction effect of the two variables on the degradation of mefenamic acid. The authors revealed that pH was the most effective factor while liquid flow rate gave a reverse image.

Recently, the Design of Experiment DOE is one of the methods used to investigate the multi-levelled fractional design's performance and optimize the desired factors (to obtain either a minimized or maximized response). Gunaraj [7] performed Central Composite Design CCD and Response Surface Methodology RSM methods to optimize the interaction effect of the open-circuit voltages, welding speed nozzle-to-plate distance in the submerged arc welding of pipes. The optimization of the operating variables versus coagulant dosage and pH value was investigated by Ghafari [8] using CCD and RSM techniques. Furthermore, Zabeti [9] also made optimized CaO catalyst activity for biodiesel production.
using CCD and RSM, and they investigated the maximizing of yield production with the interaction effects of precursor dosage and calcination

The present work aims to study experimentally and numerically the degradation of mefenamic acid (MFA) in synthetic wastewater utilizing a homemade Cu doped TiO$_2$ in a solar irradiated falling film reactor.

2. Optimization Technique

To understand the interaction effect between the two factors, experiments were done according to the Experimental Design method. The process was followed by an optimization technique to detect the optimum condition at which a maximum removal efficiency can gain.

The optimization technique is started with the identification of the independent factors and the desired product. The pH of the wastewater and the flow-rates were the factors, while the removal efficiency is the desired product. After it is necessary to determine these factors' effect, many experiments should be done to cover these factors' effect and their interactions on the desired product. The (Experimental Design) is considered the best method used for this purpose. In this method, The Central Composite Design CCD is used, as it is the proper technique. In this method, the number of experiments is calculated according to the following equation [10] [11].

\[ n = 2^k + 2k + nc \]

where k is the number of studied experimental factors. Each experimental factor is tested at five levels: maximum (+1), middle (0), minimum (-1), and two in-between (+2).

After designing the experiments, the regression analysis for the specified set of runs is done. The analysis of variance (ANOVA) was used to evaluate the capability of the models. This method determines the factors that significantly affect the responses by using some statistical tests like Fisher's statistical test (F-test). The calculated effects by ANOVA that fall below a confidence level of 95% were rejected to improve the regression model.

3. Experimental Work

The experiments were done in a photocatalytic reactor type and solar reactor with 50L volume. PVC tank and pump (type, KSP). The photocatalytic reactor was used as a batch mode process. More details of the rig setup are mentioned in the work of Zainb [6]. A test skid unit is arranged as shown in Figure 1.

![Figure 1: The experimental rig](image)

The reactor consists of transparent flat glass with dimensions 1100*800*4 mm. It was built upon a chrome-coated steel plate, reflecting the light that enters the liquid film. The unit consists of sunlight collectors, a synthetic wastewater preparation tank, a circulation pump, and a control valve. The unit is equipped with several flow meters and a control valve that facilitates evaluating the various operating parameters. The tanks were used to prepare feed water and to store rejected or permeated water. The solar collector was installed in an inclined platform with an inclination of 37° concerning the horizontal...
plane and facing south with ultraviolet UV 1.2kJ/L. A circulating pump was used to feed synthetic wastewater from the tank to the solar collectors via a calibrated flow meter and control valve. Two sets of experiments were done. The first is set to study the effect of both pH and volumetric flow rate of wastewater on removal efficiency of MFA by changing pH values from 3 to 10 at a constant flow rate of 1 L/min and changing the volumetric flow rate from 1 to 3 L/min at constant pH=10. The Experiment of Design sets the second to study the interaction effect of both pH and volumetric flow rate.

4. Results and Discussion

4.1. Experimental Results

4.1.1. Effect of pH. A set of experiments was done by varying the wastewater's pH values from 3-10 pH at a constant flow rate (10L/min). The results are shown in figure 2. The figure indicates that removal efficiency increases as the pH values increase. This result can be due to that increasing the pH and turning the solution into an alkaline solution. The TiO$_2$ group gains a negative charge according to the following equation

\[
\text{TiO}_2 + \text{OH}^- \leftrightarrow \text{TiO}^- + \text{H}_2\text{O}
\]

Hence, the surface of Cu-doped TiO$_2$ will be a negative charge and weakens the attractive electro force on the Cu-doped TiO$_2$ surface, leading to an increase in the cation's adsorption molecules of MFA onto the solar irradiation surface of Cu-doped TiO$_2$. According to this reason, the degradation of MFA increases as the pH value increases. Similar results were obtained by the work of Colombo [5].

![Figure 2: The removal efficiency of MFA against pH values at a volumetric flow rate = 10L/min](image)

4.1.2. Effect of Flow Rate. Figure 3 shows the effect of increasing flow rate from 1L/min to 3 L/min on the removal efficiency at a constant pH value of 10. The figure indicates that increasing the wastewater flow causes a decrease in MFA removal efficiency. This behaviour is similar to that obtained by the work of Lou [12]. This behaviour can be due to two reasons, and the first is that increasing flow rate reduces the contact time incident solar energy and the catalyst. The second reason is that increasing the suspension flow causes an increase in the liquid thickness, resulting in restriction of solar light breakthrough and limiting the photooxidation performance.
4.2. Optimization Results

According to the central composite rotatable design (CCRD) method, thirty experiments were planned to examine the effect of the two operating variables (pH and wastewater flow rate) and their interaction effects. Table 1 shows the variable and the value associated with each level.

Table 1: Variables and values associated with levels

| Variable          | Unit     | Level |
|-------------------|----------|-------|
|                   |          | -2    | -1   | 0    | +1   | +2   |
| pH                |          | 3     | 4    | 6.5  | 8    | 10   |
| Volumetric flow rate | L/min    | 1     | 1.5  | 2    | 2.5  | 3    |

The experimental results of the removal efficiency depending on runs are shown in Table 2. The statistical analysis of the experimental results was done using Expert Design Software. A least-squares method was used by fitting a response surface and the measured values to derive a mathematical correlation of removal efficiency. Various models have been used, as shown in Table 3.

Table 2: Experimental results according to CCRD

| No of experiment | X₁  | X₂  | Removal Efficiency (%) |
|------------------|-----|-----|------------------------|
| 1                | -1  | -1  | 0.5                    |
| 2                | 1   | -1  | 0.8                    |
| 3                | -1  | 1   | 0.4                    |
| 4                | 1   | 1   | 0.4                    |
Table 3: Summary of the model used to fit the removal percentage

| Source      | Sequential p-value | St.dev | R²    | Adjusted R² | Predicted R² |
|-------------|--------------------|--------|-------|-------------|--------------|
| Linear      | 0.101              | 0.113  | 0.36  | 0.24        | -0.962       |
| 2FI         | 0.163              | 0.103  | 0.49  | 0.32        | -4.02        |
| Quadratic   | 0.0012             | 0.046  | 0.92  | 0.87        | -4.17        |
| Cubic       | 0.0000             | 1.000  | 1.00  | 1.00        |              |

The above table reveals that the p-value of the quadratic function is lower than 0.05, while other models are not. Both linear and Sequential sum of squares for the two-factor interaction (2FI) give a lower value of $R^2$, while the quadratic function is good enough to fit the data. Hence, the quadratic model was the best model to fit the data, so it was adopted.

According to the experimental removal efficiency results and the mathematical model regression analysis of the quadratic model in CCD with the best $R^2$ value, the mathematical presentation is

$$RE\% = a + b \times A + c \times B + d \times AB + e \times A^2 + f \times B^2$$

(3)

This model considers linear effects, quadratic effects, and two-way interactions of two studied factors. The variance analysis (ANOVA) was used to indicate the generated model's accuracy and determine the statistically significant factors. Tables 4 and 5 show the performance of the ANOVA test. The table shows that some have a higher p-value (>0.05, terms that were not statistically significant).

Table 4: The ANOVA of regression analysis results of equation 2

| Factor       | Coefficient Estimate | df | Standard Error | 95% CI Low | 95% CI High | VIF |
|--------------|----------------------|----|----------------|------------|-------------|-----|
| Intercept    | 0.6883               | 1  | 0.0172         | 0.6476     | 0.7289      |     |
| A-pH         | 0.0836               | 1  | 0.0225         | 0.0305     | 0.1368      | 1.10|
| B-Flow Rate  | 0.0255               | 1  | 0.0453         | -0.0816    | 0.1327      | 2.81|
| AB           | -0.0960              | 1  | 0.0279         | -0.1619    | -0.0301     | 1.05|
| A²           | 0.2134               | 1  | 0.0836         | 0.0158     | 0.4111      | 8.41|
| B²           | -0.5246              | 1  | 0.1188         | -0.8056    | -0.2437     | 10.74|

The estimated coefficient characterizes the expected variation in response per unit factor value change when all other factors are held constant. The VIF detects the variance increasing capacity of the estimated regression coefficient when the predictors are interrelated. When the factors are orthogonal, the VIFs values are equal to one; VIFs values more than one value indicates multi-collinearity, i.e. more difficulty correlating the factors. The VIFs values of less than ten are tolerable.

Table 5: Results for ANOVA for the model

| Source | Sum of Squares | df | Mean Square | F-value | p-value |
|--------|----------------|----|-------------|---------|---------|


The summary of ANOVA is shown in Table 7. The model F-value compares the variance of the model to residual's variance, while the P-value measures the probability of obtaining the null hypothesis. The result reveals that the suggested model is best to fit the simulation data. The Model F-value of 17.36 indicates the suggested model is significant.

The low values of P-values (less than 0.0500) indicate that the model terms are significant. In this case, the linear form of pH, the interaction between the two variables and the square root of both pH and volumetric flow rate are significant model terms. This result means that these terms have a high influence on removal efficiency. Suppose the values are more significant than 0.1000, which indicates that the model terms are insignificant. The low values of Lack of Fit of F-value indicate that the Lack of Fit is insignificant relative to the pure error. The Non-significant lack of fit is best; it indicates that the model is fit. The higher regression coefficient ($R^2 = 0.92$) supported the model's significance from the statistical point of view. These values validate that the model is significant.

4.3. Model validity
The normal probability plot and the residual test were examined to ascertain the model's accuracy and validity, formed by the Design-Expert software version 12. Figure 4 displays the normality plot of removal efficiency. The figures also reveal the residuals were adjacent to the straight line and were scattered randomly around it with no particular pattern, showing no abnormal behaviour against noise.

The plot of the predicted values of removal efficiency against the actual values is shown in figure 5. The data points are evenly scattered around the line, showing that the model gave a good prediction. The predicted against actual values plot is shown in figure 6. The figure indicates the good fitness of the experimental model to the actual values.
Figure 4: Normal plots of residuals for MFA removal efficiency

Figure 5: Predicted values of MFA removal efficiency
Figure 6: The actual and predicted values of MFA removal efficiency

The experimental design model’s behaviour is expressed by the 3-dimensional surface plot and the contour plot. Those plots give dynamic information about the system. Figure 7 reviles the pH effect and volumetric flow rate on the percentage removal. An increase in both pH and volumetric flow rate increased the removal percentage of MFA to 1.8 L/mi after it decreases. This behaviour is different from that shown in figures 2 and 3. This behaviour is because this figure shows the combined effect between both flow rate and pH on removal efficiency, while both figures 2 and 3 show the individual effect of these parameters.

Figure 7: The model plot (a) 3D plot (b) contour plot
4.4. Optimization Results

The optimization is used to investigate the optimum operating conditions. In this process, the optimum desirability was determined depending on the goals set for each factor and responses. In this work, the goal for pH and the volumetric flow rate was set to "in range". Indeed, the removal efficiency is set at goals of "maximize", respectively. RSM in Expert Design Software was used to get the optimum conditions. The results are illustrated in table 6 and shown in figure 8. The maximum value of removal efficiency is 84.5% gained with pH = 8.8 and Q= 1.73

| Name          | Goal      | Lower Limit | Upper Limit | Predicted value | Experimental values |
|---------------|-----------|-------------|-------------|-----------------|---------------------|
| A:pH          | is in     | 3           | 10          | 8.86            | 10                  |
| B:Flow Rate   | is in     | 0.6         | 3           | 1.73            | 1                   |
| Removal       | maximize  | 0.4         | 0.82        | 0.84            | 0.82                |
| Efficiency    |           |             |             |                 |                     |

Figure 8: The optimization results plot

5. Conclusions

- The use of solar irradiated falling film was successfully degraded the mefenamic acid (MFA) in synthetic wastewater.
- The degradation process decreases with increasing flow rate while it increases with increasing the pH value of the solution.
- The interaction effect between flow rate and pH, utilized by ANOVA, was highly significant in influencing the removal efficiency. Therefore, the interaction effects between parameters should not be neglected.
- Through optimization, the optimum desired operating condition in this range of study in accordance with the desired goals set was found at a flow rate of 1.73L/min and pH equals 8.86.
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