

Empirical modeling and Validation of Classical Fenton Technology for complete removal of anticonvulsant from high dosed simulated wastewater.

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Abstract

The increasing worldwide contamination of water bodies with thousands of pharmaceutical recalcitrant compounds is one of the key environmental problems facing the Earth. Therefore, there is need to develop a model to combat this situation. Classical Fenton reaction is used in this study to generate HO· in-situ for the mineralization of one of the major recalcitrant (primidone) from wastewater. Influences of major operating parameters on the removal efficiency were investigated using Center Composite Design (CCD) of Response Surface Methodology (RSM). 22µl H₂O₂ and 8.8mg Fe²⁺ at pH 3 was found to be the optimum with 98.84% removal within 50 minutes. Meanwhile, as the initial primidone dose decreases to 100 mg/L, 99.77% removal was achieved and at 50 & 75 mg/L, 100% achieved within 20 minutes. Both statistical and experimental validations of the Model were verified and found to be in good agreement. Pseudo-first order kinetics reaction rate and half life were obtained to be 0.039 min⁻¹ and 17.77mins Respectively.

Keyword: Primidone, anticonvulsant, wastewater, degradation. Empirical modeling, Classical Fenton.

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I. Introduction

The critical aspect of the sustainability of the Earth is the cases arising from the environmental issues. With the increase in demands of high standard of living and subsequent exploitation of natural resources has lead to the inability of natural cleaning processes to harness the environmental loads cause by industrial waste. Over the years past, pharmaceuticals of different kind have been manufactured and consumed in response to uphold the life of human and its livestock. The situation poses chronic chemical risk by lack of adequate water treatment. Incomplete removal of drug residues during passage through sewage treatment plants (STP's) has continued to be of concern to the environmental researchers of resent [1].

Primidone (5-ethyl-5-phenylhexahydropyrimidine-4,6-dione) a heterocyclic nitrogen compound synthesized by reacting ethylphenylmaloric acid diamide with formamide. Is a water-insoluble desoxybarbiturate [2] which was formulated in 1949 [3] but was first reported to be clinically effective as an anticonvulsant by Handley and Stewart [4]. The compound is essentially non-polar, and structurally different from phenobarbitone by the absence of carbonyl group at the position two of the pyrimidine ring [5]. Some of the active metabolites of primidone includes 2-ethyl-2-phenylpropanediamide and 5-ethyl-5-phenyl-1,3-diazinane-2,4,6-tione which are also prescribed as an anticonvulsant drugs [6]. Meanwhile, 5-ethyl-2-hydroxyl-5-phenyl-1,3-diazinane-4,6-dione (2-hydroxyprimidone) was found to be the intermediate of both compound [7]. Primidone is partly eliminated in an unchanged form via Urinary excretion, while the part is converted into its metabolites by the liver [8]. This drug is designed to treat movement disorders including convulsion, Parkinson tremors etc as well as migrains among other diseases. Though there various harmful effects of primidone on human organism like; sedation, nausea, vertigo, diplopia loss of libido and feeling of intoxication [9]. Perucca and Gilliam [10], reported some side effects; unsteadiness, imbalance, dizziness, nystamus and disturbances in coordination.

Till date, the promising occurrence of primidone in the environment has been studied by several authors. Bourgin *et al.*, [11] disclosed primidone as one of the most recalcitrant compounds to conventional biological treatment among 43 pharmaceuticals studied in urban wastewater treatment plants. Henzler *et al.*, [12], has proved from their research that primidone was neither degraded nor absorbed during river bank filtration process. Reh *et al.*, [13] stated that primidone had low potential input, with relatively high detection frequency of 10%. Aminat *et al.*, [14] studied about the degradation and sorption of 53 pharmaceuticals present

in Urban wastewater treatment plant effluents discharged into simulated estuarine waters and identified primidone as one of the most stable with a persistence index of 100. Many other researchers, has also disclosed the occurrences and fate of primidone in the water bodies [15-17]. Removal of this anticonvulsant drug from water bodies has less frequently studied. Although, attempts has been made by many authors using AOP(s) at very low initial dose (< 50mg/L). Degradation of the emergent contaminants by UV-C, UV-C/H₂O₂ and neutral Photo-Fenton was carried out by De la Cruz *et al.*, [18]. The result obtained in their work shows that direct UV-C photodegradation process is less effective for the removal of the pharmaceuticals while photo-Fenton gives 54% within 10 minutes reaction time (H₂O₂:Fe(II) – 50:5mg/L).

Dong *et al.*, [19], discussed direct sunlight photodegradation of primidone in ultrapure water (0.5µg/L) and in two urban wastewater treatment plant secondary effluents (DOC 6.2 and 8mg/L; primidone initial concentration of 0.119-0.226µg/L). Following the researcher, after five days, the amount of primidone degraded by direct photolysis was low (5%), whereas 35-88% of primidone was oxidized by the HO[•] generated from the photolysis of some organic/inorganic compound present in the secondary effluents. Some other authors has attempted the removal of primidone using Ozone-based Advanced oxidation processes including homogeneous and heterogeneous phases [20-23]. Nevertheless, the data obtain from the literature were insufficient to develop statistical model for predicting primidone removal for industrial application at the point of discharge. The need to generate intensive data for computation and empirical modeling become the aim of the present work.

This work is focused on the mineralization of primidone at high initial dose (≤ 200mg/L) using Center Composite Design (CCD) in Response Surface Methodology (RSM) to model an equation for sequential removal by Classical Fenton. The main objectives are to determine the effect of operating parameters (H₂O₂ & Fe²⁺), the combining effect, optimize the variable factors and the validation of the compatibility of the empirical model within the design space.

II. Material and Methods

2.1 Classical Fenton process (Fe²⁺/H₂O₂)

Classical Fenton process is the simplest of all AOPs where H₂O₂ (reactant) and Fe²⁺ (catalyst) are used. Oxidation usually performed at room temperature, the three parameters which affect the process being pH, H₂O₂ dosage and Fe²⁺ dosage. The optimum pH for the Classical Fenton process has been reported as 2.8 – 3.0 in the literature and it was confirmed by the preliminary experiments conducted in this study. Hence the pH of the solution was adjusted 3 while conducting the experiment with 0.1N sulphuric acid and 0.1N sodium hydroxide. Then the required amount of Ferrous Sulphate (FeSO₄.7H₂O) was added to the solution and mixed well following the addition of the required amount of hydrogen peroxide (50%). The system was kept under constant stirring at 120rpm throughout the experiment. However, the reaction time started upon the addition of hydrogen peroxide and hence time is noted from that moment onward. The initial concentration of primidone under study was measured 200mgL⁻¹.

2.2 Response Surface Methodology (RSM)

In this work, Center Composite Design (CCD) of RSM has been used for modeling. RSM consists of a collection of statistical and mathematical tools which are useful in modeling and analysis of problems by which response of interest are influenced by several variables. Two variable factors are considered for this design, namely H₂O₂ and Fe²⁺ doses at constant pH and initial primidone dose. The ranging concentrations of the variables were determined in the preliminary study which was used for the design (Table 1).

2.3 Analytical Procedures

Changes in primidone concentration in aqueous solution were determined by reversed phase high performance liquid chromatography, HPLC (Agilent 1200 series) equipped with visual wavelength detector (VWD). A mixture of acetonitrile and water (50:50, v/v) was used as the mobile phase. The samples were eluted through the C₁₈ column (Zorbax Eclipse XDB C₁₈ 150 x 4.6mm 5µm) at a flow rate of 0.6mL/min. The signal was detected at elution time of 2.7 ±0.1 minute with a detector wavelength of 221nm and injection volume of 20µL. A Linear relationship between area of the peak and concentration of the primidone was established by preparing a calibration curve which is used to ascertain the percentage removal efficiency.

| Table 1: Operating Parameters and Ranges selected for the Experiments | | | | | | |
|---|----------------|--------------|-----|------|------|------|
| Independent variable | Symbols used | Coded Levels | | | | |
| | | - α | -1 | 0 | +1 | + α |
| Fe ²⁺ (mg/100mL) | X ₁ | 0.0 | 0.8 | 4.8 | 8.8 | 9.6 |
| H ₂ O ₂ (µL/100mL) | X ₂ | 6.6 | 8.0 | 15.0 | 22.0 | 23.4 |

III. Results and Discussion

3.1 Effect of Operating Parameters:

pH, concentrations of H₂O₂ and Fe²⁺ are the major variables affecting the process. Consequently all further experiments were carried out at pH 3. Experimental responses for fifty minutes (50mins) of reaction time are presented in Figure 1 as depicted from the design of the experiment corresponding to the variable combination ratios.

The mechanism of reaction is initiated by the generation of hydroxyl radicals ·OH in acidic medium, which present a number of cyclic reactions that utilizes the ferrous or ferric ions as a catalyst to decompose the H₂O₂ (eqn. 1 & 2).



Figure 1; indicate the dependence of primidone removal in the reaction mixture of the variable factors. An increase in the removal of primidone (%) from 24.48 to 68.48% was observed when Fe²⁺ concentration increased from 0.8 to 8.8 mg/100mL at H₂O₂ concentration of 8.0μL/100mL (runs 1 and 2). Also, increase in reduction of primidone concentration was noticed with increase in H₂O₂ concentration (run: 1 and 3; 2 and 4). This is as a result of increased hydroxyl radical formation accompanying the increase in variable's concentration (equation 1) [24]. ·OH generated principally decomposes the organic pollutants (RH) via hydrogen abstraction (eqn. 3) [25].

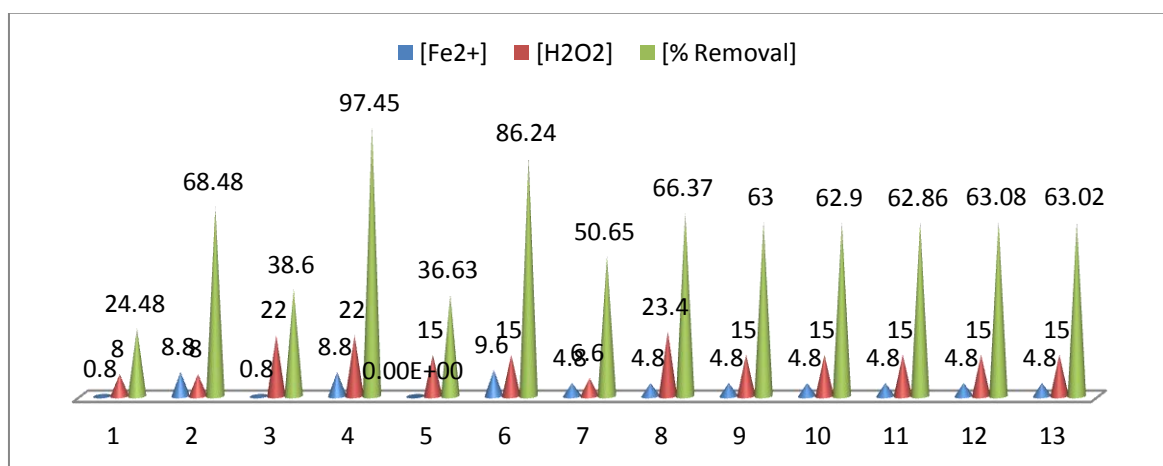
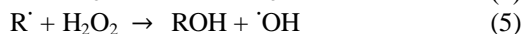
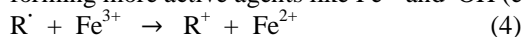


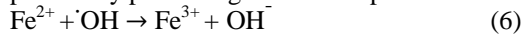
Figure 1: Combined effect of Variables [Fe²⁺], [H₂O₂], and Response [% Removal]



This gives organic radical (R') intermediate that engaged in competitive reaction between Fe³⁺ and H₂O₂, forming more active agents like Fe²⁺ and ·OH (eqn 4 & 5).



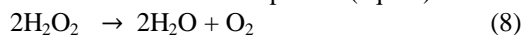
Obviously, a number of competitive reactions also do occur (eqn. 6 and 7), which negatively affect the oxidation process by promoting the consumption of ·OH.



Experimental runs, nos. 6 and 8, do indeed demonstrate quite clearly that the use of excess Fe²⁺ (run no. 6), or excess H₂O₂ (run no. 8) have indeed resulted in lower percent primidone removal.

3.2 Combined Effect of Variable

Considering the conditions of H₂O₂ and Fe²⁺ that gave 97.45% removal in run 4; in run no: 6 the value of Fe²⁺ is 9.6 which is above its counterpace in run no. 4 and in run no: 8 the value of H₂O₂ were 23.40μL also high than the value in run no. 4 also, yet their responses (86.24% and 66.37% respectively) were lower to compare to the response in run no. 4. Increasing H₂O₂ and Fe²⁺ beyond this values decreases the removal slightly because of the scavenging effect of H₂O₂ and Fe²⁺. Auto decomposition of H₂O₂ also contribute to the reduction in removal responses (eqn. 8).



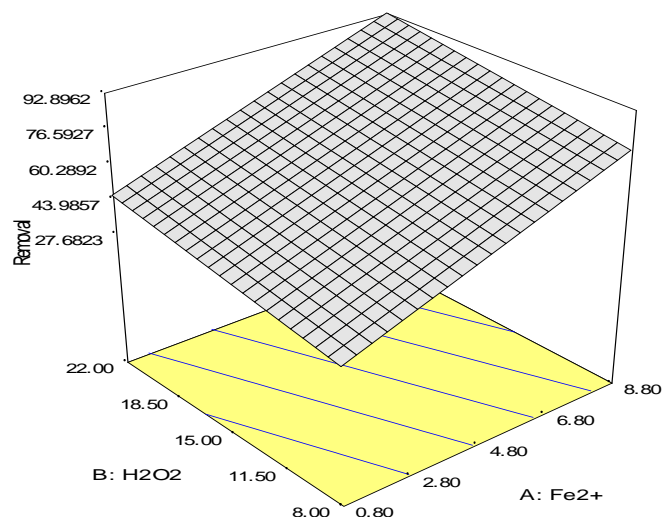


Figure 2: Combined effects (3-D visual display) of $[Fe^{2+}]$ and $[H_2O_2]$

The highest removal efficiency of primidone was obtained for initial H_2O_2 and Fe^{2+} concentrations of $22.0\mu L$ and $8.8mg$ respectively. Figure 3 is a contour plot of figure 2. From this plot, the combined ratio of the variables on the removal efficiency can be predicted as shown at the point of interception.

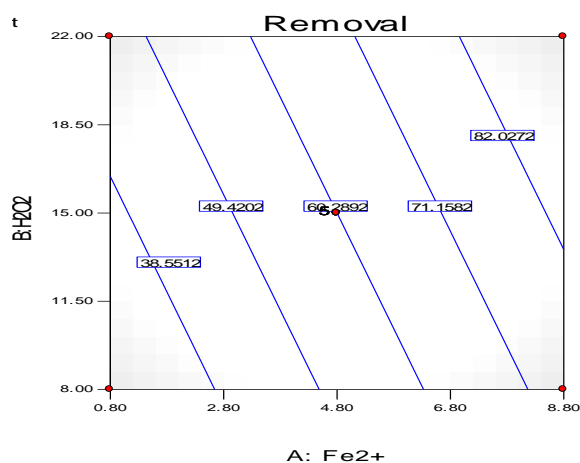


Figure 3: Contour plot of the combined effect of the operating parameters.

The interaction plot (figure 4) predicts no significant direct interaction of the two variables $[H_2O_2]$ ($22.00\mu L$) and $[Fe^{2+}]$ ($8.00mg$) at the selected ratio towards the substrate. This however, show that the interaction is more of the intermediate generated during the reaction and the targeted organic compound of interest. Denoting the predominancy of equation 3. The outcome of the reactivity of both increases percentage removal of primidone as the individual concentrations increase up to their optimal values. The removal efficiency of the combined variables can thus be interpreted as dependent on the catalytic activities of Fe^{2+} and the consequent amount of hydroxyl radical produced at any step of the reaction. The one factor plot (figure 5) at $15.00\mu L$ as the center point for $[H_2O_2]$ indicates that increase in the concentration of Fe^{2+} increases the % removal within the designed space. This also is evident in figure 6 at center position of Fe^{2+} ($4.8 mg$) and variable $[H_2O_2]$ concentration. These center points at the relevant H_2O_2 and Fe^{2+} concentrations may thus be referred for relevance to equation one (1) which describes the reaction step in which H_2O_2 and Fe^{2+} interact to yield the hydroxyl radical and the hydroxyl group, the former being the actual oxidizing agent.

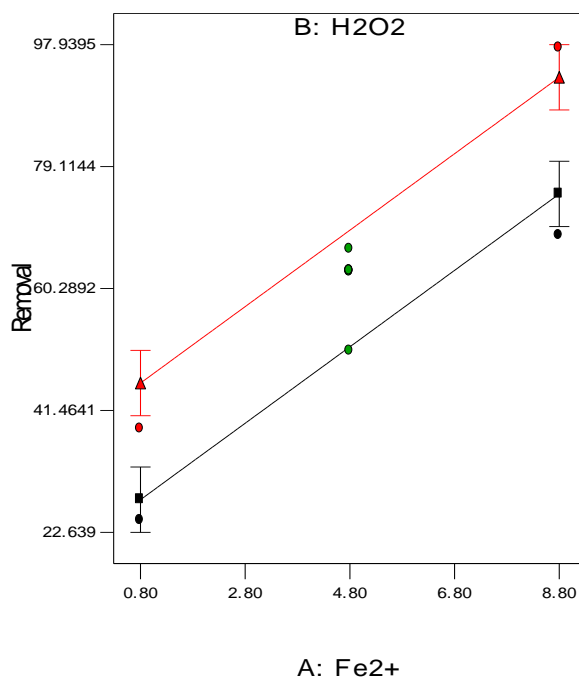


Figure 4: The interaction plot at design points, $[H_2O_2] = 22.0$ and $[Fe^{2+}] = 8.0$

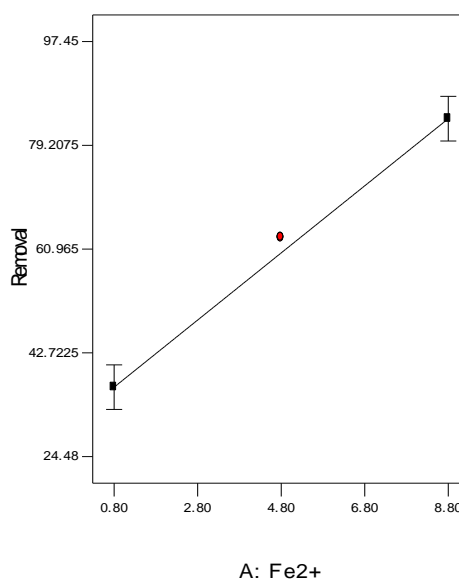
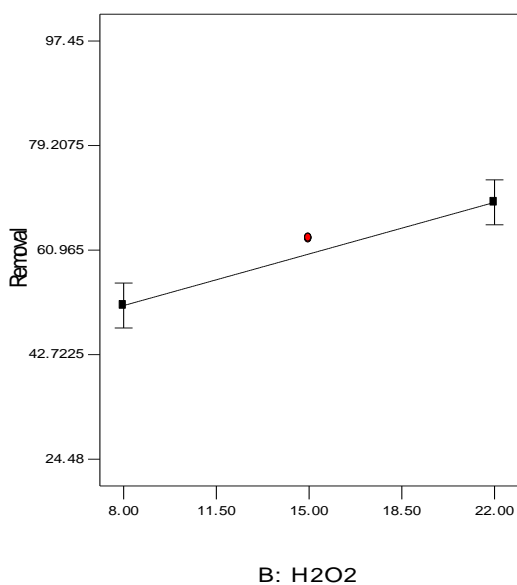


Figure 5: One factor plot for %Removal against $[Fe^{2+}]$ at $[H_2O_2]$ at actual factor $[Fe^{2+}] = 4.80$

Figure 6: One factor plot for %Removal against actual factor $[H_2O_2] = 15.00$

3.4 Empirical Modeling and Statistical Analysis

The response surface methodology helps in identifying the significant parameters used in this study. The model developed for Classical Fenton reaction can generally be represented in truncated form as:

$$Y = A_0 + A_1X_1 + A_2X_2 \quad (9)$$

Y is the response variable of primidone removal (%) in coded units, A_0 is the intercept, A_1 and A_2 are regression coefficients for linear effect. The estimated regression coefficients are presented in Table 2 in coded terms. It is possible to use the model in un-coded terms to predict the primidone removal (%) for any combination of two variables within the experimental domain. The prob. > F values for all the terms are less than 0.05 (95% confidence level (CL)). Under these conditions, it can be concluded that all the terms are significantly affecting the response of the system.

| Factor | Coefficient estimate | DF | Standard | 95%CL Low | 95% CL High |
|--|----------------------|----|----------|--------------|----------------|
| Intercept | 60.29 | 1 | 1.27 | 57.46 | 63.12 |
| X ₁ : Fe ²⁺ | 23.60 | 1 | 1.74 | 19.71 | 27.49 |
| X ₂ : H ₂ O ₂ | 9.00 | 1 | 1.74 | 5.12 | 12.29 |

The final equation in term of coded factors (Table 2) is:

$$Y = 60.29 + 23.60X_1 + 9.00X_2 \tag{10}$$

Thus,

$$\% \text{Removal} = 60.29 + 23.60[\text{Fe}^{2+}] + 9.00[\text{H}_2\text{O}_2] \tag{11}$$

Final Equation in terms of Actual factors:

$$\% \text{Removal} = 12.67 + 5.9[\text{Fe}^{2+}] + 1.286[\text{H}_2\text{O}_2] \tag{12}$$

| Source | Sum of Squares | DF | Mean Square | F Value | Prob> F | |
|----------------|-------------------|----|----------------|------------|----------|-------------|
| Model | 4390.438 | 2 | 2195.219 | 104.8296 | < 0.0001 | significant |
| X ₁ | 3832.546 | 1 | 3832.546 | 183.0179 | < 0.0001 | |
| X ₂ | 557.8922 | 1 | 557.8922 | 26.64136 | < 0.0004 | |
| Residual | 209.4083 | 10 | 20.94083 | | | |
| Pure Error | 0.03248 | 4 | 0.00812 | | | |
| Cor Total | 4599.846 | 12 | | | | |

Values from the Analysis of Variance (ANOVA) of the model are given in Table 3. The Model F-value of 104.83 implies that the model is significant. In this study, the model parameters X₁[Fe²⁺] and X₂[H₂O₂] are significant model terms.

| Statistics | Std. Dev. | Mean | C.V. | PRESS | R-Squared | Adj R-Squared | Pred Squared | R- Precision | Adeq Precision |
|------------|-----------|----------|---------|----------|-----------|---------------|--------------|-----------------|----------------|
| Responses | 4.576115 | 60.28923 | 7.59027 | 448.3914 | 0.954475 | 0.94537 | 0.90252 | | 29.6657 |

The predictability of the model is quantified by calculating the standard statistical parameters, namely, the standard deviation (Std. Dev.), mean, coefficient of variation (CV), Predicted residual error sum of square statistic (PRESS), R-Squared, Adjusted R-Square, Predicted R-Squared and Adeq. Precision. The values are presented in Table (4) and show that the model is able to predict the responses with adequate accuracy and as expressed in eqn. 12.

From the results, the “Pred. R-Squared” of 0.9025 is in reasonable agreement with the “Adj. R-Square” of 0.9454. “Adeq. Precision” measures the signal to noise ratio. A ratio greater than 4 is desirable. That is to say that the ratio of 29.666 from the experiment indicates an adequate signal response. It is evident that this model can be used to navigate the design space.

3.5 Validation of the Model

Model validation explains the degree of agreement between computer base modeling and the real world application. In this study, two methods have been used to validate the authenticity of the developed model: Diagnostics case statistics and experimental method.

3.5.1 Diagnostic Case Statistics

The statistical data in Figure 7 and 8 compare the actual experimental values obtained in a thirteen (13) experimental run order from the combining effect of variables (X₁: [Fe²⁺] and X₂: [H₂O₂]) and the predicted values which were calculated from the developed mathematical model (equation 12).

The low residual value of the rang $0 \leq X \leq 0.5$ are clear evidence that both the Actual and the predicted values are in perfect harmony at all point.

This is clearly ascertained in Figure (9) indicating that there is actually no outlier since all the experimental points fall within $-3.5 \leq X \leq 3.5$.

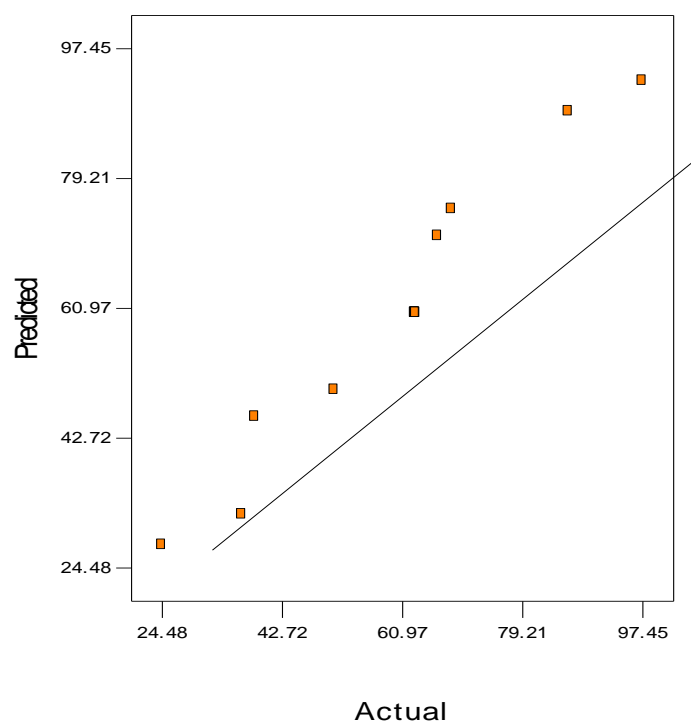


Figure 7: Plot of Predicted values against Actual values

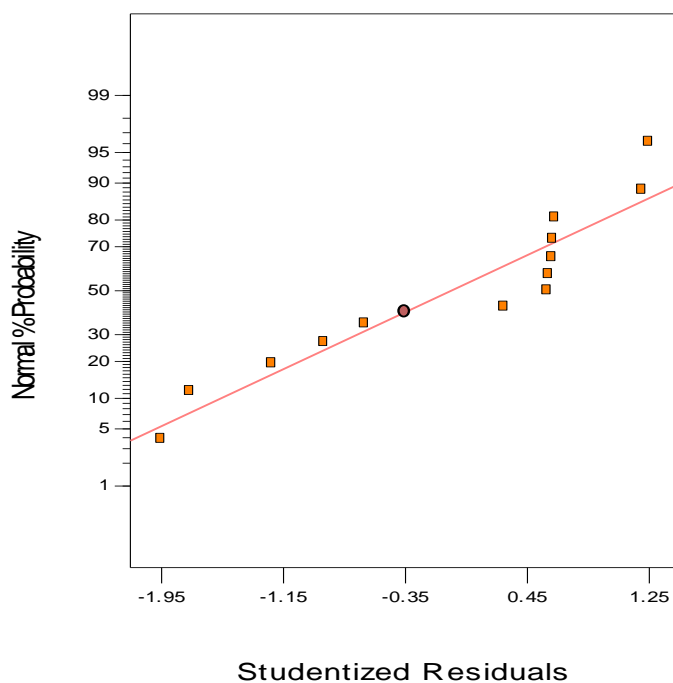


Figure 8: Plot of Normal % Probability against studentized Residuals

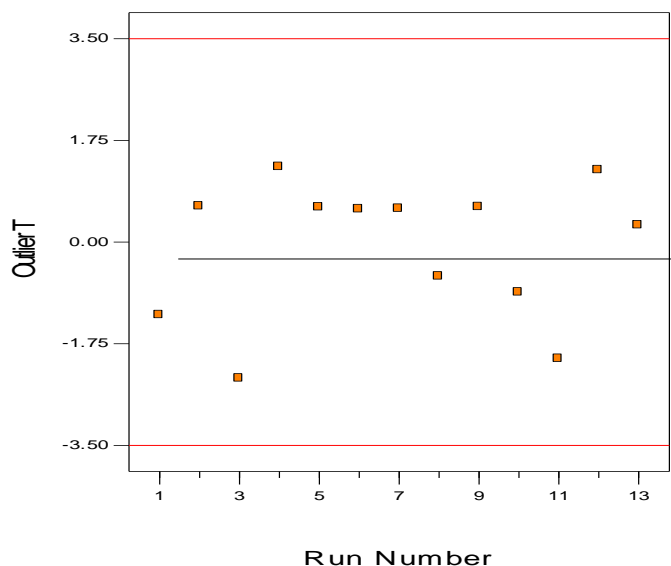


Figure 9: Plot of Outlier t against Run Number

3.5.2 Experimental Validation

Experimental verification were conducted at different combinations of independent variables which were not used to formulate the model, but were within the experimental range were used to test the adopted model. The primidone removal percent obtained from the model predictions compared favourably with the experimental values thus obtained (Table 5). These validations confirm the suitability of the model for prediction of the performance of Classical Fenton Process for the degradation of primidone within the experimental range.

| Run Order | [Fe ²⁺] (mg/100mL) | [H ₂ O ₂] (μL/100mL) | Predicted value | Observed Value |
|-----------|-----------------------------------|--|-----------------|----------------|
| 1 | 3.5 | 16.00 | 55.6751 | 60.1245 |
| 2 | 8.0 | 20.00 | 85.6030 | 80.7687 |
| 3 | 7.0 | 9.00 | 65.5518 | 62.5678 |

3.6 Optimization of Operating Parameters:

This helps in identifying the combination of independent variables that optimizes the responses. Optimization gives a maximum primidone removal value of 92.8962% at optimum initial H₂O₂ and Fe²⁺ concentrations of 22.00 μL and 8.80 mg respectively. Optimization values are listed in column 4 of Table 6, and are quite close to the experimentally observed optimum response value of 98.84%.

| S/N | [Fe ²⁺] | [H ₂ O ₂] | Removal | Desirable | |
|-----|---------------------|----------------------------------|---------|-----------|----------|
| 1 | 8.80 | 22.00 | 92.8962 | 0.938 | Selected |
| 2 | 8.76 | 22.00 | 92.6754 | 0.935 | |
| 3 | 8.80 | 21.69 | 92.5031 | 0.932 | |

IV. Kinetic Study

The Kinetic study is an indispensable part of chemical reactions which is important for better understanding of chemical processes. This phase is carried out on the bases of the optimum conditions obtained as stated above.

The change in the concentration of primidone with time, for varying amounts of H₂O₂ and Fe²⁺ is shown in Figure 11 and 12.

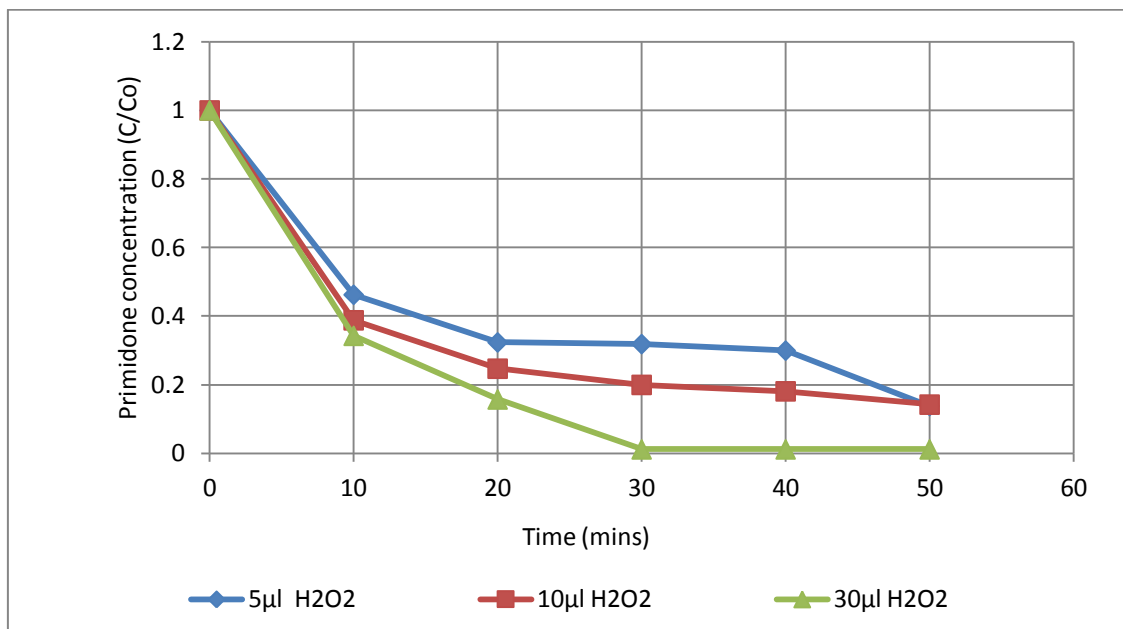


Figure 11: Effect of initial H₂O₂ concentration on primidone removal at Fe²⁺ concentration of 8.8 mg

An increase in removal from 54.26 % to 99.77± 0.28 % was observed when the H₂O₂ concentration increased from 5 μL to 30 μL for a Fe²⁺ concentration of 8.8 mg/100mL (Figure 11). A very slight decrease in removal of primidone was observed when H₂O₂ concentration increased from 5 μL to 10 μL at 50 minutes reaction time. 30μL H₂O₂ at 50mins reaction time, complete removal was observed.

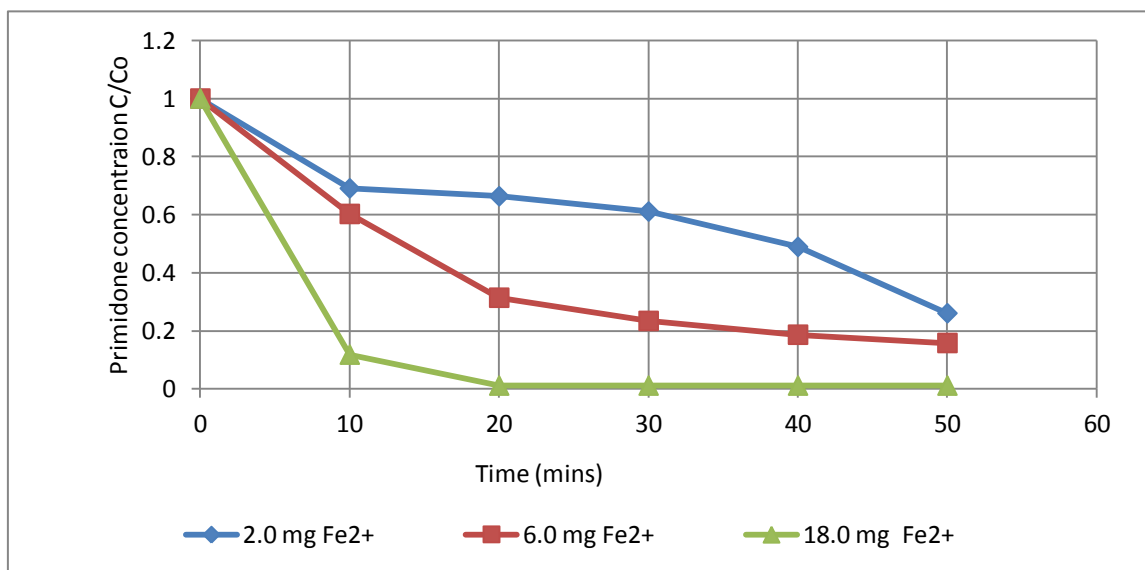


Figure 12: Effect of initial Fe²⁺ concentration on Primidone removal at H₂O₂ concentration of 22 μl.

The effect of Fe²⁺ concentration on primidone removal is shown in Figure 12. An increase in percent removal of this organic compound from 31.2 % to 99.77± 0.28 % was observed when the Fe²⁺ concentration increased from 2 to 18 mg/100mL. Complete removal of primidone was achieved when the concentration of Fe²⁺ was 18 mg/100mL for reaction time of 20min. The use of minimum amount of Fe²⁺ is recommended to reduce sludge formation and scavenging effect of reagents [26]. This also reduces cost.

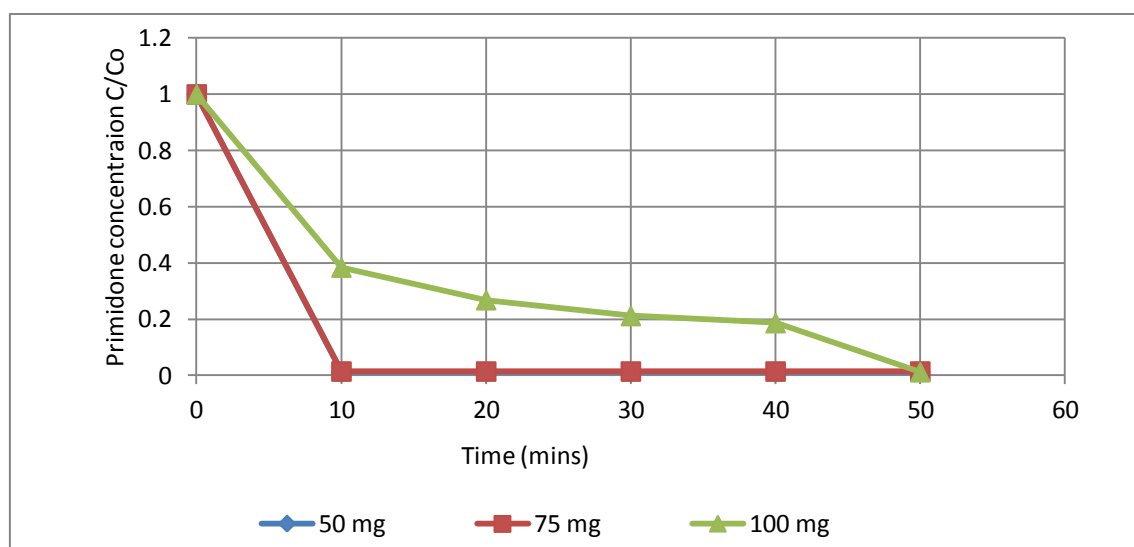


Figure 13: Effect of initial concentration of primidone on the degradation of primidone by Classical Fenton process.

The effect of initial concentration of primidone was also studied by varying the concentration of primidone at initial Fe^{2+} concentration of $8.8\text{ mg}/100\text{ mL}$ and H_2O_2 concentration of $22\ \mu\text{L}/100\text{ mL}$. The relevant data are shown graphically in Figure 13. At low concentrations of 50 and 75 mg/L, the primidone disappeared very fast (within 10 minutes reaction time), whereas at the higher concentration of 100 mg/L, 99.77% removal was achieved at 50 minutes.

Further experiment were conducted to obtain pseudo-first order rate constant, k' , and half life period ($t_{1/2}$).

The pseudo first order rate constant (k)

$$K = \ln(C/C_0)/t \quad (13)$$

$$K = 3.9 \times 10^{-2} \text{ mins}^{-1}$$

$$\text{And Half-life, } t_{1/2} = \ln(2)/K = \ln(2)/(3.9 \times 10^{-2} \text{ mins}^{-1}) = 17.77 \text{ mins.}$$

V. Conclusion

The conclusions derived from the research are:

- Classical Fenton is a viable option for degradation of primidone.
- The rate of removal efficiency increases with an increase in initial H_2O_2 and Fe^{2+} dose.
- The adopted model can be use to navigate the design space
- Optimization is important since excess use of reagents will result in scavenging of reactive radicals and increase cost of operating.
- The pseudo-first order reaction constants obtained for the processes at optimized condition is $0.039\ \text{min}^{-1}$, and the half life at optimal condition is 17.77mins.

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