Research Article

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Optimization for Removal of COD and BOD through RSM-CCD by Activated Sludge Treatment Process for Pharmaceutical Wastewater

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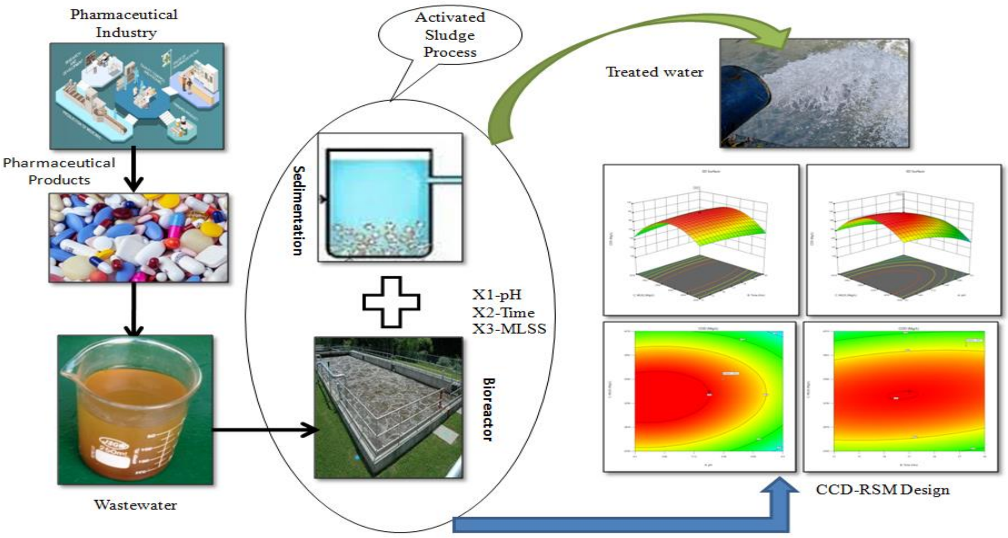
ABSTRACT

Wastewater generated from home and commercial operations is a polluting component of water. One of the main contributors for the production of wastewater by various manufacturing processes is the pharmaceutical industry. The commercial operations of industry are causing an increase in the amount of organic and inorganic contaminants, such as total suspended solids, chemical oxygen demand (COD) and biological oxygen demand (BOD). Activated sludge process reduces COD, BOD and Total Suspended Solids (TSS), with three input variables: pH, time and Mixed Liquor Suspended Solids (MLSS). The Central Composite Design-Response Surface Methodology (CCD-RSM) is used to optimize responses for COD and BOD removal efficiency. To achieve optimization results, numerous sets of trials were conducted for the input variables - pH (4.2–6.5), time (12–30 h) and MLSS (2520–4310 mg/l). The analyzed models were shown to be quadratic and highly significant by the F-value and P-value. The regression coefficients (R2) for the quadratic models developed for removal efficiency, COD, and BOD5 are 0.9996, 0.9995 and 0.9996, respectively. According to CCD-RSM, the optimal matching input factors for the greatest removal efficiency of BOD and COD were: MLLS = 3415 mg/l, time = 21 h and pH = 5.35. Using the traditional method, the maximum removal (95%) of BOD and COD was seen at pH = 6.5, time = 12 h and MLLS = 4310 mg/l.

Keywords: Pharmaceutical wastewater; Activated Sludge Process; CCD-RSM.

GRAPHICAL ABSTRACT



An overview of the generation of pharmaceutical wastewater from the pharmaceutical industry and an activated sludge treatment process with optimization of the removal percentage of COD and BOD supported with response surface methodology-centered composite design is graphically shown above.

1. INTRODUCTION

Drug manufacture is the primary activity of the pharmaceutical industry. Research, development and discovery are all incorporated in the pharmaceutical industry. As a result of active pharmaceutical substances, herbal preparations and allopathic roots, the pharmaceutical sector is very diverse. Only a small percentage of the pharmaceutical industries are administered by state or federal governments, with the majority being run by private entities. Although the nature of the pharmaceutical industry differs depending on the product line, the production method is largely the same. Pharmaceutical medications have a direct relationship to the nature of diseases and how they are treated. There is little evidence from studies to suggest that neighboring sources of water bodies, such as lakes, ponds and rivers, contain pharmaceutical compounds including ibuprofen, erythromycin, naproxen and ketoprofen (Balakrishna *et al.* 2017). Active pharmaceutical ingredients (API) from the pharmaceutical industries are produced and consumed at a high pace, providing effluent treatment (Khan *et al.* 2013; Mutiyar and Mittal, 2014). The sewage system flushes drugs that human metabolism cannot completely metabolize (Jones *et al.* 2005). The quantity of medication released is highly hazardous to aquatic life and could lead to antibiotic resistance in pathogenic microorganisms (Barnes *et al.* 2002; Behera *et al*, 2001). For the treatment of domestic/industrial wastewater, a suspended growth system employs bacteria and microorganisms that remain in suspended form (Horan, 2003). Using biological treatment, the Activated Sludge (AS) Process is a traditional way of eliminating organic and biodegradable material from wastewater (Hauduc *et al.* 2013). AS treatment is a frequently used method for the exclusion of organic contaminants such as chemical oxygen demand (COD) and biochemical oxygen demand (BOD) and is preferred for its ease of use, operational facilities and high effectiveness, along with its efficacy in eliminating organic matter and nutrients, including nitrogen, from wastewater and activated sludge process (Nikpour, *et al.* 2010). Different organic wastes, such as nitrogen, phosphorus, chlorides, and heavy metals, may also be removed with the help of the activated sludge method (Seviour and Lindrea, 1998). During 1912–1914, Arden and Lockett discovered the AS method (Ardern and Lockett, 1914). The AS Process is made up of three parts: a bioreactor, a settling tank that serves as the final clarifier, and partially returned active sludge. The application of activated sludge treatment has been successful in various industries, including confectionery, paper mill, textile, and pharmaceutical wastewater treatment (El-Gohary *et al.* 1999; Nasir *et al.* 2010; Ortiz-Alvarez, Gélvez *et al.* 2017; Abdelfattah *et al.* 2023). The bioreactor's microbial population breaks down complex organic chemicals into simpler and more stable ones. These treatment methods result in the breakdown of dissolved and suspended organic components in wastewater (Ahansazan *et al.* 2014). Numerous microorganisms in the form of bacteria, fungi, protozoa, viruses, E-coli and algae are used to achieve the appropriate percentage of removal of organic compounds like BOD and COD (Gerardi, 2003). For their microbiological growth, these bacteria need a sufficient amount of oxygen in the form of air. Any biological treatment method's success depends on the F:M (food supplied to microorganisms) ratio, which must be kept within ideal limits throughout the cycle. Research shows that industrial wastewater can be remedied using activated sludge (Alleman, 1997). CCD-RSM was developed to improve wastewater and conventional treatment techniques to optimize wastewater and conventional treatment processes (Bashir *et al.* 2015; Jasni *et al.* 2020). Wastewater treatment for the dairy industry was examined and optimized using a multi-stage flexible bio-film reactor (MFBR) in conjunction with the response surface methodology (Abdulgader *et al.* 2020). Few studies have been completed to optimize the reaction surface technology for treating different types of industrial wastewater. RSM, in combination with reaction surface technology, was utilized to clean up sugar industrial waste utilizing chitosan (Pambi and Musonge, 2016). An Up-flow anaerobic sludge blanket (UASB) reactor was used to treat wastewater from the slaughterhouses (Chollom *et al.* 2020). An anaerobic co-digestion modeling and optimization for potato waste were carried out and a neural-network-linked genetic algorithm was also devised (Jacob and Banerjee, 2016). Wastewater from printing and packing has also been studied as a candidate for electrocoagulation-flotation treatment. Significant improvements in the removal percentage of color, COD, turbidity, and alkalinity were obtained by optimizing the electrocoagulation process through the application of response surface methodology (RSM) and central composite design (CCD) (Emamjomeh *et al.* 2020). Numerous wastewater treatment systems have been optimized by the application of response surface methodology (RSM). For instance, RSM was utilized to improve the coagulation-flocculation process for the effluent from palm oil mills, leading to increased COD and BOD removal efficiency (Ahmad *et al.* 2005). Additionally, RSM was applied to enhance the removal efficiencies of the potassium ferrate electrocoagulation method used to treat textile effluent (Moradnia *et al.* 2016). These studies demonstrate the effectiveness of RSM in optimizing treatment procedures for treating wastewater to remove organic contaminants. For wastewater treatment, other optimization techniques have been used in addition to RSM. Utilizing Taguchi's experimental design method, the elimination of COD and Acid Red 18 dye by electrochemical oxidation was optimized (Yousefi *et al.* 2018). The investigation was successful in maximizing removal efficiency by optimizing the process parameters. In a similar vein, Taguchi's experimental design strategy was effective in maximizing the hydrothermal carbonization process's ability to remove pesticides and medicinal compounds from sewage sludge (Miserli *et al.* 2022; Miserli, Nastopoulou *et al.* 2022). These studies highlight the potential of optimization methods in advancing the efficiency of effluent treatment processes. Furthermore, different treatment processes combination has been explored for the elimination of organic compounds from wastewater. For instance, it has been demonstrated that the breakdown and biodegradability of textile wastewater can be improved by combining electron beam irradiation with the AS process (Nasir *et al.* 2010). The AS process achieved COD removal efficiencies between 70% and 79% (Nasir *et al.* 2010). This demonstrates the potential of combining different treatment processes to achieve higher removal efficiencies. Response surface methodology along with coagulation-flocculation strategy was adopted for wastewater from paste manufacturing (Khannous *et al.* 2011; Birjandi *et al.* 2013) and wastewater from the paper recycling paste sector (Wang *et al.* 2007). An overview of Response Surface Methodology's wastewater treatment process is provided (Jasni *et al.* 2020). RSM performed coagulation flotation and optimization to treat the mineral oil-related wastewater (Tetteh *et al.* 2017). Finally, the various parameters, such as isotherm and kinetics, which influence how botanical plant waste adsorbs phenol amalgam, were investigated using CCD-RSM statistical modeling (Dargahi *et al.* 2023).

1.1 OBJECTIVES

The goal of the study is to improve BOD and COD removal conditions and treatment process efficiency. The best circumstances for the withdrawal of organic biodegradable loads from pharmaceutical wastewater can be found by analyzing potential components and their interactions with the use of RSM-CCD. The goal is to obtain high removal rates of BOD and COD through process optimization with the help of RSM-CCD, which will lessen the environmental impact of pharmaceutical wastewater. The process of optimization could entail modifying a number of variables, including pH, MLSS and hydraulic retention time. The ultimate objectives are to treat pharmaceutical wastewater effectively and economically, to guarantee that environmental laws are followed and to safeguard both the environment and public health.

2. MATERIAL AND METHOD

The investigation was conducted on the effluent from an API manufacturing facility that was treated using a full-mixed activated sludge method. By keeping variables within specific ranges, pharmaceutical wastewater is treated using the activated sludge technique. The three variables taken into account in this study are pH, time, and MLSS. The pH spans from 4.2 to 6.5, the time period is between 12 and 30 h and the MLSS concentration is between 2520 and 4310 mg/l. The sample was taken from the pharmaceutical company in Jammu, India, which makes APIs and brings the samples to a regulated temperature in less than 48 h. The study was conducted from October to December (winter). The laboratory was equipped with the three essential components of the AS process, *viz*, the bioreactor, settling tank and a means for the partial return of an appropriate amount of the activated sludge. For the bioreactor's growing microorganisms to have enough oxygen, air has been supplied by an external blower. The elimination percentages of COD, BOD_5 and MLSS were computed using the APHA procedure.

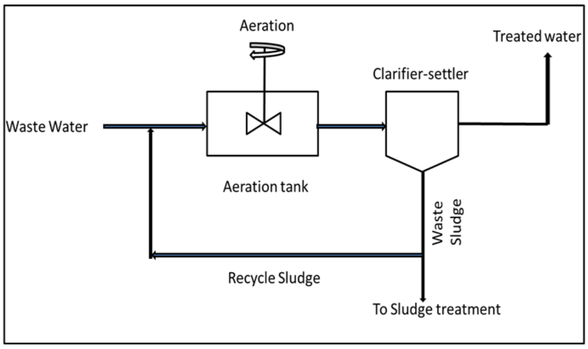
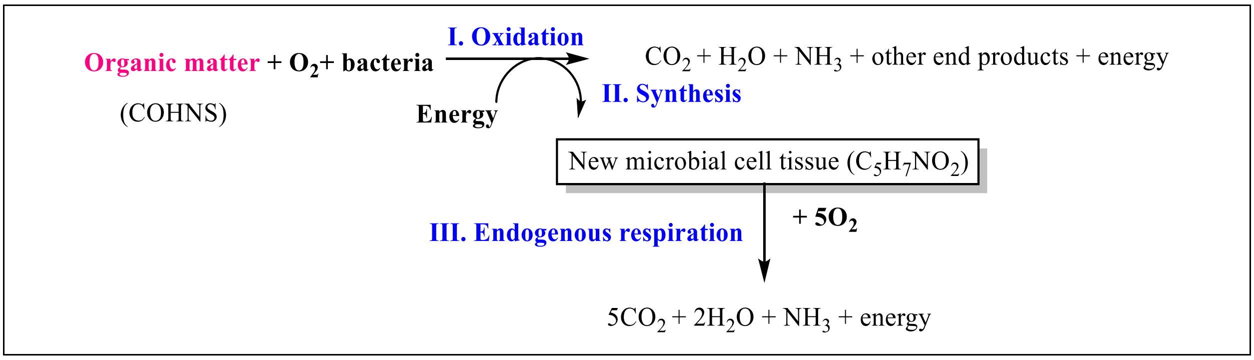


Fig. 1: Flow diagram for Activated Sludge Process (ASP)

2.1 ACTIVATED SLUDGE PROCESS

Biological wastewater treatment is the most commonly used process and ASP is one of the important approaches (Hauduc *et al.* 2013). This method helps in the removal of various types of organic waste like nitrogen and phosphorous (Seviour and Lindrea, 1998). The process was developed in 1912-1914 by Arden and Lockett. Generally, three components were included in ASP. In ASP, microbes break down complex organic molecules into biodegradable compounds in quest for nourishment. As a result, soluble and suspended organic materials are removed from wastewater (Ahansazan *et al.* 2014). In this method (Fig. 1), an aeration tank acts as a bioreactor, a settling tank acts as a fine clarifier, separating wastewater and activated sludge solid from treated water, and a return activated sludge is used to transport settled AS from the clarifier to the aeration tank's influent. To generate a biological floc, the bacteria used in the activated sludge process are generally *Achromobacter, Escherichia Coli, Aerobacter, Flavobacterium, Alcaligens, Nocardia, Arzthrobacter, Sphaerotilus, Bacillus, Pseudomonas* and *Citromonas, Zoogloea*. (Gerardi, 2003). The atmospheric air or, in rare situations, pure oxygen is added to a combination of primary processed or filtered sewage (or industrial effluent) coupled with organisms. Biological activities in the aeration tank lower the concentration of biodegradable components in the influent in activated sludge plants. The efficiency of biodegradable components depends on factors like BOD, temperature, COD, food to micro-organisms and O_2. Mixed liquor is dumped into settling tanks at the effluent of the aeration tank, and treated wastewater is drained off to be discharged to a natural water source or to be allowed to be treated further before being discharged. The settling AS is returned to the aeration tank's head (RAS) to re-seed the incoming sewage (or industrial wastewater) into the tank. The excess sludge is withdrawn from the treatment process to maintain a well-defined F:M ratio (IWA).

In this process, microorganisms oxidize the organic material present in influent wastewater (biomass, activated sludge) in the aerator for endogenous respiration and the formation of new cells within the activated sludge process. The oxygen essential for microbial activity is provided. The microbial agglomerates inside the aerator effluent are settled in the final settler, purifying the effluent. In the initial process, the oxidation of organic matter in the wastewater by micro-organisms is converted to CO_2 and H_2O. Energy released during this oxidation process is used to convert some parts of organic matter into new microbial cell tissue. In the final stage, the new microbial cell tissue formed consumes their cell tissue to utilize energy for the cell maintenance. The process can be represented as:



*COHNS= Carbon, Oxygen, Hydrogen, Nitrogen, Sulphur in organic matter (Modi, 2017).

To maintain a sufficient level of microorganisms in the process, a partial portion of the concentrated settling sludge is returned to the aeration tank. A portion of the extra sludge is withdrawn regularly. Per unit, mass of partially activated sludge and the rate of further processing bio-activated sludge are the two key factors for this goal (Cakici and Bayramoglu, 1995). To reduce the settling of sludge, different activated sludge plants were designed with different parameters. The plug flow process includes tampered aeration (for uniform oxygen distribution), step-aeration (to distribute two-thirds of air towards the front half and one-third to the latter half of the plant), and a completely mixed system (complete mixing of biomass with the return activated sludge) (Seviour and Lindrea, 1998). It is, in general, more environment-friendly than harsh chemical methods such as chlorination (New *et al.* 2000). However, the production of large amounts of sludge, high energy consumption (Sreekanth *et al.* 2009), and operational problems such as foaming, coloring, and bulking in secondary clarifiers are associated with activated sludge plants. The microbial species selection depends on the temperature of the activated sludge. Several studies show the relationship between the impact of pharmaceuticals and the activated sludge process. A study shows that when the concentration of pharmaceuticals is small its impact is negligible (Stamatelatou *et al.* 2003). At high concentrations, its effects cannot be neglected.

2.2 EXPERIMENTAL DESIGN AND MODEL

One of the most cutting-edge strategies for improving results above traditional methods (Tetteh *et al.* 2017). For the analysis of 3-level complete factorial designs, Box-Behnken designs, CCD and Doehlert designs, RSM is typically utilized. RSM is a method for response optimization when more than two visible elements are involved. Two parameters in RSM are significant: one independent variable (predicted) and one dependent variable (response).

There is a logical connection between the experimental variables and the response, and this relationship may be explained visually (Azila *et al.* 2008; Özer *et al.* 2009).

For factorial design, statistical data analysis, regression model building and method scenario optimization, the Design-Expert (12.0.11.0) version was used. The study looked at independent variables including pH (X_1), Time (X_2) and MLSS (X_3). The most significant link between the recommended reaction and treatment effectiveness for COD and BOD removal is shown in Table 1, which presents the coded independent variables as -1, 0 and +1 (Three levels).

The removal efficiency for COD and BOD was assessed using,

$$\text{Removal (\%)} = \frac{(c_i - c_e)}{m} \times 100 \quad \ldots\ldots.1$$

Equation (1) was used to compute the eradication of COD and BOD in percentage. The COD and BOD elimination rates are the outcomes of the variables, and Table 2 displays the experimental settings and levels of coding.

Table 1. Independent variables (Three levels) with codes as -1, 0, and +1

Factor	Name	Minimum	Maximum	Coded Low	Coded High	Mean	Std. Dev.
X_1 (A)	pH	3.42	7.28	-1 ↔ 4.2	+1 ↔ 6.5	5.3	1.2
X_2 (B)	Time (Hr)	5.86	36.14	-1 ↔ 12.0	+1 ↔ 30.0	21.0	9.6
X_3 (C)	MLSS (Mg/l)	2520.00	4310.00	-1 ↔ 2520.0	+1 ↔ 4310.0	3415.0	730.7

Table 2. Experimental factors and levels of coding

		Experimental factors			Level of coding		
Std	Run	pH	Time (h)	MLSS (mg/l)	pH	Time (Hr)	MLSS (mg/l)
1	1	4.20	12	2520	-1	-1	-1
2	2	6.50	12	2520	+1	-1	-1
17	3	5.35	21	3415	0	0	0
8	4	6.50	30	4310	+1	+1	+1
4	5	6.50	30	2520	+1	+1	-1
9	6	3.42	21	3415	-1	0	0
6	7	6.50	12	4310	+1	-1	+1
5	8	4.20	12	4310	-1	-1	+1
11	9	5.35	6	3415	0	-1	0
3	10	4.20	30	2520	-1	+1	-1
12	11	5.35	36	3415	0	+1	0
10	12	7.28	21	3415	+1	0	0
7	13	4.20	30	4310	-1	+1	+1

Three variables were used in the CCD model analysis of the response behavior. The CCD model was used to analyze the response behavior with three variables. The COD and BOD removal yields served as the response variables. Typically, a CCD model is constructed to allow for the execution of $2^k + 2k + k_o$ investigations, where k stands for the quantity of replicates and k_o for the quantity of attributes to be evaluated. The quadratic response surface model's estimation of the yield of COD's % recovery was made using:

$$Y=\beta_0 + \sum_{i=1}^{k}(\beta_i X_i)+\sum_{i=1}^{k}\beta_{ii}X_{ii}^{2}+\sum_{i=1}^{k-1}\sum_{j=2}^{k}\beta_{ij}X_iX_j+\varepsilon \quad i\neq j \ldots\ldots\ldots2$$

In Equation (2), Y represents the anticipated outcome for X_i, X_j,…X_k. The input variables' coded values indicate the intercept terms, which are linear, quadratic, and interaction, X_k (Maddipati *et al.* 2001; Kumar *et al.* 2013) and, X_i^2, X_j^2,…. X_k^2 are the square effect; the interaction effects are represented by, X_jX_k , X_iX_k and, X_iX_k, where, β_o , β_i *(i=1,2,….k)* β_{ii} *(i=1,2,….k)* and, β_{ij} *(i=1,2,….k*; j=1,2,…*k*) represent the regression coefficients (R^2). The 95% (p-value) confidence level serves as the criterion for accepting or rejecting the model terms. The margin between observed and predicted values is a random error (ε).

Three quadratic coefficients comprise the regression coefficients (β), random error (ε) and the number of components that need to be examined or adjusted in the experiment (k).

For variables that are thought of as independent and have coded values, the quadratic response surface model equation can alternatively be written as a final response (Y):

$$Y=\beta_0+\beta_1X_1+\beta_2X_2+\beta_3X_3+\beta_{12}X_1X_2+\beta_{13}X_1X_3+\beta_{23}X_2X_3+\beta_{11}X_1^2+\beta_{22}X_2^2+\beta_{33}X_3^2 \ldots\ldots3$$

The second-order polynomial equation, as represented above, is the ultimate expression for removal efficiency, COD and BOD.

2.3 MODEL ASSESSMENT FOR REMOVAL EFFICIENCY

To show the dependability of the different models, including linear, 2FI, quadratic and cubic, the merit produced from the sequential model sum of squares for removal percentage was evaluated (Table 3). Similar to the COD and BOD responses, just one model, *i.e.*, Quadratic vs. 2FI, was proposed. The highest polynomial model that is significant and not aliased was selected to get the best results from CCD-RSM. The F-value (767.50) was better, and the quadratic model's p-value (<0.0001) was very significant.

Table 3. Sequential model sum of squares models for all three major parameters - Removal efficiency, COD and BOD

Sequential Model Sum of Squares for Removal Efficiency Response						
Source	**Sum of Squares**	**df**	**Mean Square**	**F-value**	**p-value**	
Mean vs. Total	85942.23	1	85942.23			
Linear vs. Mean	**526.19**	**3**	**175.40**	**8.55**	**0.0053**	**Suggested**
2FI vs. Linear	25.37	3	8.46	0.3188	0.8120	
Quadratic vs. 2FI	**158.89**	**3**	**52.96**	**514.95**	**0.0001**	**Suggested**
Cubic vs. Quadratic	0.3086	3	0.1029			Aliased
Residual	0.0000	0				
Total	86653.00	13	6665.62			
Sequential Model Sum of Squares COD Response						
Mean vs. Total	2.372E+05	1	2.372E+05			
Linear vs. Mean	261.17	3	87.06	2.31	0.1453	
2FI vs. Linear	42.38	3	14.13	0.2850	0.8348	
Quadratic vs. 2FI	**297.05**	**3**	**99.02**	**908.96**	**< 0.0001**	**Suggested**
Cubic vs. Quadratic	0.3268	3	0.1089			Aliased
Residual	0.0000	0				
Total	2.378E+05	13	18292.00			
Sequential Model Sum of Squares for BOD Response						
Mean vs. Total	17575.69	1	17575.69			
Linear vs. Mean	65.88	3	21.96	0.8886	0.4833	
2FI vs. Linear	96.00	3	32.00	1.52	0.3029	
Quadratic vs. 2FI	**126.31**	**3**	**42.10**	**1064.73**	**< 0.0001**	**Suggested**
Cubic vs. Quadratic	0.1186	3	0.0395			Aliased
Residual	0.0000	0				
Total	17864.00	13	1374.15			

2.2.1 Model Assessment for COD

Only one model, quadratic vs. 2FI, was suggested by CCD for the assessment of COD. The model was chosen based on an elevated F-value (612.61) and a very small p-value (<0.0001), which was considered very significant and positive.

2.2.2 Model Assessment for BOD

Since all of these models were recommended during the optimization, the linear, 2FI, quadratic and cubic models were chosen for the BOD model assessment. The model with the greatest score, quadratic vs. 2FI, was picked. The higher magnitude of F (809.78) and lower p-value (0.0001) in Table 3 both demonstrate the quadratic model's high significance.

3. RESULTS AND DISCUSSION

The results of a qualitative wastewater analysis are displayed in Table 4. The major parameters consider for optimization in CCD-RSM are COD, BOD and Removal efficiency.

Table 4. Characteristics analysis of pharmaceutical wastewater

Parameter	Pre-treatment (Influent)		Post-treatment (Effluent)	
	Average value	Standard Deviation	Average value	Standard Deviation
Color	Dark Brown	----	Pale yellow	----
pH	5.7	±0.51	7.18	±0.19
TDS (mg/l)	1011	±98.50	790.39	±113.99
TSS (mg/l)	252.1	±85.46	61.89	±9.18
Chloride (mg/l)	829.45	±75.39	202.26	±34.96
COD (mg/l)	4532.7	±1650.78	146.78	±5.96
BOD (mg/l)	923.34	±19.37	38.83	±3.55

To achieve the desired outcomes, 13 tests were run twice. Tables 5, 6, and 7 provide summaries of the outcomes from these thirteen investigations. With varying circumstances of pH 6.5, 12-hour hydraulic retention times, and 4310 mg/l MLSS concentration, removal of COD and BOD by 95% was reported. Table 8 displays the outcome of the analysis of variance (ANOVA) for elimination percentage, COD and BOD. As the table illustrates, almost every variable in the statistical quadratic model is significant ($p<0.0001$).

Table 5. CCD Experimental outcome for Removal Percentage of COD and BOD

Run	No.	pH	Time (h)	MLSS (mg/l)	Percentage Removal of COD and BOD	Actual Value	Predicted Value
1	1	4.2	12	2520	74	74.00	73.81
2	2	6.5	12	2520	82	82.00	82.25
17	3	5.3	21	3415	78	78.00	78.00
8	4	6.5	30	4310	90	90.00	90.19
4	5	6.5	30	2520	84	84.00	83.94
9	6	3.4	21	3415	76	76.00	76.22
6	7	6.5	12	4310	95	95.00	95.00
5	8	4.2	12	4310	84	84.00	84.06
11	9	5.3	5.8	3415	76	76.00	75.94
3	10	4.2	30	2520	74	74.00	74.00
12	11	5.3	36.1	3415	72	72.00	72.06
10	12	7.2	21	3415	94	94.00	93.78
7	13	4.2	30	4310	78	78.00	77.75

Table 6. CCD Experimental COD Arbitrary

Run	No.	pH	Time (h)	MLSS (mg/l)	Removal %	COD before treatment (mg/l)	COD after treatment (mg/l)	Actual Value for COD	Predicted Value of COD
1	1	4.2	12	2520	74	542	141	141	140.99
2	2	6.5	12	2520	82	711	128	128	127.91
17	3	5.3	21	3415	78	659	145	145	145.00
8	4	6.5	30	4310	90	1300	130	130	130.01
4	5	6.5	30	2520	84	794	127	127	127.26
9	6	3.4	21	3415	76	600	144	144	144.21
6	7	6.5	12	4310	95	2480	124	124	124.16
5	8	4.2	12	4310	84	838	134	134	133.74
11	9	5.3	5.8	3415	76	592	142	142	142.12
3	10	4.2	30	2520	74	519	135	135	134.84
12	11	5.3	36.1	3415	72	507	142	142	141.88
10	12	7.2	21	3415	94	2167	130	130	129.79
7	13	4.2	30	4310	78	609	134	134	134.09

Table 7. Capricious CCD Experimental for BOD

Run	No.	pH	Time (h)	MLSS (mg/l)	Removal %	Initial BOD (mg/l)	Final BOD (mg/l)	Actual value of BOD	Predicted value of BOD
1	1	4.2	12	2520	74	162	42	39	39.08
2	2	6.5	12	2520	82	167	30	29	28.92
17	3	5.3	21	3415	78	191	42	42	42
8	4	6.5	30	4310	90	380	38	42	41.92
4	5	6.5	30	2520	84	175	28	29	28.92
9	6	3.4	21	3415	76	167	40	40	39.81
6	7	6.5	12	4310	95	640	32	34	33.92
5	8	4.2	12	4310	84	225	36	36	36.08
11	9	5.3	5.8	3415	76	175	42	42	42
3	10	4.2	30	2520	74	131	34	31	31.08
12	11	5.3	36.1	3415	72	150	42	42	42
10	12	7.2	21	3415	94	600	36	36	36.19
7	13	4.2	30	4310	78	155	34	36	36.08

Table 8. ANOVA for Quadratic models

Response 1: Removal Efficiency						
Source	**Sum of Squares**	**df**	**Mean Square**	**F-value**	**p-value**	
Model	710.46	9	78.94	767.50	< 0.0001	Significant
A-pH	371.96	1	371.96	3616.37	< 0.0001	Significant
B-Time	18.11	1	18.11	176.09	0.0009	Significant
C-MLSS	136.12	1	136.12	1323.49	< 0.0001	Significant
AB	1.13	1	1.13	10.94	0.0455	Significant
AC	3.13	1	3.13	30.38	0.0118	Significant
BC	21.12	1	21.12	205.39	0.0007	Significant
A^2	32.67	1	32.67	317.60	0.0004	Significant
B^2	10.67	1	10.67	103.71	0.0020	Significant
C^2	37.84	1	37.84	367.86	0.0003	Significant
Residual	0.3086	3	0.1029			
Cor Total	710.77	12				
Response 2: COD						
Model	600.60	9	66.73	612.61	< 0.0001	Significant
A-pH	250.97	1	250.97	2303.94	< 0.0001	Significant
B-Time	0.0732	1	0.0732	0.6722	0.4724	**Insignificant**
C-MLSS	10.13	1	10.13	92.95	0.0024	Significant
AB	15.13	1	15.13	138.85	0.0013	Significant
AC	6.13	1	6.13	56.23	0.0049	Significant
BC	21.13	1	21.13	193.93	0.0008	Significant
A^2	42.67	1	42.67	391.68	0.0003	Significant
B^2	6.00	1	6.00	55.08	0.0051	Significant
C^2	267.98	1	267.98	2460.00	< 0.0001	Significant
Residual	0.3268	3	0.1089			
Cor Total	600.92	12				
Response 3: BOD						
Model	288.19	9	32.02	809.78	< 0.0001	Significant
A-pH	15.88	1	15.88	401.62	0.0003	Significant
B-Time	0.0000	1	0.0000	0.0000	1.0000	**Insignificant**
C-MLSS	50.00	1	50.00	1264.45	< 0.0001	Significant
AB	32.00	1	32.00	809.25	< 0.0001	Significant
AC	32.00	1	32.00	809.25	< 0.0001	Significant
BC	32.00	1	32.00	809.25	< 0.0001	Significant
A^2	10.67	1	10.67	269.75	0.0005	Significant
B^2	0.0000	1	0.0000	0.0000	1.0000	**Insignificant**
C^2	110.30	1	110.30	2789.35	< 0.0001	Significant
Residual	0.1186	3	0.0395			
Cor Total	288.31	12				

The analysis of variance (ANOVA) findings for the COD, BOD and elimination percentage are shown in Table 8. Removal efficiency, COD and BOD each have an F-value of 767.50, 612.61 and 809.78, respectively, highlighting the significance of the model created for these metrics.

There is less than 0.01% chance that noise would result in an F-value this high. A P-value of less than 0.0500 indicates that the model terms are important (Wahab and Ahmed, 2018). When evaluating removal effectiveness, we discovered that the simulation variables A, B, C, AB, AC, BC, A^2, B^2 and C^2 are significant because they have a value less than 0.0500. Only one model term, B, is insignificant in the case of COD because of its greater value of 0.0500. In the context of BOD, the terms A, C, AB, AC, BC, A^2 and C^2 are important. However, due to the greater numerical value of 0.0500, terms B and B^2 are insignificant. Table 9 contains exhibits for fit statistics for removal efficiency, COD and BOD. The regression coefficients (R^2) for the quadratic models developed for removal efficiency, COD and BOD are, respectively, 0.9996, 0.9995 and 0.9996. There are relatively negligible changes in R^2 and adjusted R^2 for the quadratic models built for removal efficiency, COD and BOD, with respective values of 0.9983, 0.9978 and 0.9984. The models entirely satisfied the ANOVA coefficients the closer the determination value (R^2) came to 1.

It is advised that the Adeq Precision quantity, which demonstrates the measurement of signal-to-noise level, should be higher than 4 when designing a CCD; the Adeq Precision values in the current CCD optimization are 81.5281, 71.9882 and 74.9879. The coefficient of variance (C.V.), which can be computed as the ratio of the standard error of the estimate to the mean value of the response, demonstrated the repeatability of the model. The current study's measurements of the C.V. are 0.3944, 0.2443 and 0.5408 - extremely low when compared to the 10% stipulated upper limit. The equation of the actual and coded response that CCD provided is summarized in Table 10.

Table 9. Fit Statistics for the Removal efficiency, COD and BOD

Removal Efficiency	Std. Dev.	0.3207	R^2	0.9996
	Mean	81.31	Adjusted R^2	0.9983
	C.V. %	0.3944	Adeq. Precision	81.5281
COD	Std. Dev.	0.3301	R^2	0.9995
	Mean	135.08	Adjusted R^2	0.9978
	C.V. %	0.2443	Adeq. Precision	71.9882
BOD	Std. Dev.	0.1989	R^2	0.9996
	Mean	36.77	Adjusted R^2	0.9984
	C.V. %	0.5408	Adeq Precision	74.9879

Table 10. Equation for all Responses in tabulated form with coded and actual factors

S. No.	**Parameters**	**Removal Efficiency**		**COD**		**BOD**	
		Coded Factors	**Actual Factors**	**Coded Factors**	**Actual Factors**	**Coded Factors**	**Actual Factors**
		+78.00	+139.12328	+145.00	+9.23604	+42.00	-6.71496
1	pH (X_1)	+5.22	-18.32006	-4.29	+13.46329	-1.08	-0.189556
2	Time (X_2)	-1.15	+1.10044	-0.0732	-0.857848	+0.0000	-1.88174
3	MLSS (X_3)	+4.12	-0.024795	-1.13	+0.070841	+2.50	+0.039074
4	pH * Time ($X_1.X_2$)	+0.3750	+0.036232	+1.38	+0.132850	+2.00	+0.193237
5	pH * MLSS ($X_1.X_3$)	+0.6250	+0.000607	+0.8750	+0.000850	+2.00	+0.001943
6	Time * MLSS ($X_2.X_3$)	-1.62	-0.000202	+1.63	+0.000202	+2.00	+0.000248
7	pH² ($X^2{}_1$)	+2.47	+1.87136	-2.83	-2.13870	-1.41	-1.06935
8	Time² ($X^2{}_2$)	-1.41	-0.017459	-1.06	-0.013095	+0.0000	+0.000000
9	MLSS² ($X^2{}_3$)	+3.56	+4.44972E-06	-9.49	-0.000012	-6.09	-7.59750E-06

The final form of the coded equation for removal efficiency, COD and BOD is presented after the response model suggests eliminating non-significant variables, specifically B (X_2) from the COD response, and B (X_2) and B^2 (X_2^2) from the BOD response.

$$Y_{R.E.} = 78.00 + 5.22X_1 - 1.15X_2 + 4.12X_3 + 0.3750X_1X_2 + 0.6250X_1X_3 - 1.62X_2X_3 + 2.47X_1^2 - 1.41X_2^2 + 3.56X_3^2 \quad \ldots\ldots 4$$

$$Y_{COD} = 145.00 - 4.29X_1 - 1.13X_3 + 1.38X_1X_2 + 0.875X_1X_3 + 1.63X_2X_3 - 2.483X_1^2 - 1.06X_2^2 - 9.49X_3^2 \quad \ldots\ldots 5$$

$$Y_{BOD} = 42.00 - 1.08X_1 + 0.000X_2 + 2.50_3 + 2.00X_1X_2 + 2.00X_1X_3 + 2.00X_2X_3 - 1.41X_1^2 - 0.000X_2^2 - 6.09X_3^2 \quad \ldots\ldots 6$$

After eliminating irrelevant factors provided by the design, the true equation for removal efficiency, COD and BOD is now written in the following form.

$Y_{R.E.}$=139.12–18.32X_1+1.10X_2 –0.024X_3+0.0362X_1X_2+0.0006X_1X_3 – 0.0002X_2X_3+1.87X_1^2 − 0.0174X_2^2+0.000004X_3^2 ……………...…………7

Y_{COD} = 9.236 +13.463X_1 – 0.857 X_2+0.070X_3+0.132X_1X_2+ 0.0008X_1X_3 +0.0002X_2X_3 - 2.13X_1^2 − 0.013X_2^2 – 0.00002X_3^2 ..……..8

Y_{BOD}=-6.71–0.189X_1+ 0.039X_3+0.193X_1X_2+0.019X_1X_3 +0.0002X_2X_3–1.06X_1^2 +0.000007X_3^2 ………………...........................9

The optimization of the removal of COD and BOD in pharmaceutical wastewater with the assistance of RSM-CCD through the activated sludge treatment process is a crucial aspect of wastewater management. Numerous investigations into various approaches and procedures for the efficient treatment of pharmaceutical wastewater and the elimination of BOD and COD have been carried out. One study (Nasr *et al.* 2022) examined the use of industrial wastewater treatment for confectionery, utilizing UASB and AS systems. The study found that the AS system achieved removed 87% and 86% of the BOD and COD, respectively. This study demonstrates the effectiveness of the AS treatment practice in eliminating COD and BOD from wastewater. Fenton oxidation was the method utilized in another investigation by (Abdelfattah, Abuarab, *et al.* 2022) to treat highly loaded pharmaceutical effluent. A higher BOD/COD ratio of 0.6 and a COD elimination rate of 80.4% were recorded by the study. This suggests that Fenton oxidation may be a useful technique for pharmaceutical wastewater BOD/COD ratio improvement and COD removal. (Amirian *et al.* 2018) carried out research on the application of photo-nanocatalysis for the treatment of wastewater from textiles. In order to maximize the removal of COD and color from wastewater, the study employed RSM in conjunction with CCD. This work illustrates how RSM-CCD can be used to optimize the removal of BOD and COD from the treatment process. (Castiglioni *et al.* 2006) investigated the elimination of drugs from Italian sewage treatment plants (STPs). The study showed that the nature of the drug, the type of treatment used and the features of the influent can all have an impact on the removal rate of pharmaceuticals in STPs. This study emphasizes the significance of taking into account several variables to optimize the removal of COD and BOD in pharmaceutical wastewater. (Emamjomeh *et al.* 2020) carried out research on the application of electrocoagulation-flotation for the treatment of wastewater from printing and packaging. The study utilized RSM-CCD to optimize the operational conditions for the removal of color and COD. The outcome exhibits the finest conditions resulted in 97.8 and 92.1 percentage removal efficiencies for color and COD, correspondingly. This study demonstrates the effectiveness of electrocoagulation-flotation and RSM-CCD in attaining high COD and color removal efficiency in wastewater. In conclusion, it is a difficult and varied task to optimize the removal of BOD and COD from pharmaceutical wastewater using the RSM-CCD by activated sludge treatment process. Various methods and techniques, such as Fenton oxidation, electrocoagulation-flotation and photo-nanocatalytic processes, have been explored to accomplish higher exclusion percentages of COD and BOD. The efficacy of the treatment process is greatly influenced by variables like the type of medication, the method of treatment used and the operational conditions. Pharmaceutical wastewater can be treated more effectively and under ideal conditions for the removal of BOD and COD by using RSM-CCD.

3.1 EFFECTS OF REMOVAL EFFICIENCY

By varying the variables of pH, time and MLSS in the experimental design of thirteen numbers, the removal effectiveness for the organic parameters, *viz,* COD and BOD were determined. Equation (1)'s formula was used to calculate the elimination efficiency for both pollutants that were taken into consideration. With a variety of factors, such as pH, time and MLSS, removal efficiency with the activated sludge process was seen to range from 74 to 95 percent by a conventional method. By using RSM's multiple regression analysis of the central composite design, the matrix points - 16 factorial, 8 axial and 6 centers - were determined. To investigate the meaningful effects of the model, the ANOVA for the removal efficiency (presented in Table 8) was developed. 95 percent removal efficiency was reported at 6.5 pH, 12 h and 4310 mg/l MLSS. As can be seen from Equation (7), all of the factors have impacts on removal efficiency that are more or less substantial; although X_2 (time) has the highest positive coefficient. As a result, the influence of the time variable is crucial to the effectiveness of the removal procedure. The equation also takes into account the interaction between time (X_2) and MLSS (X_3), which has a negative influence, as well as the positive interactions between pH (X_1) and time (X_2), pH (X_1), and MLSS (X_3). The highest positive numerical value in the equation was assigned to the interaction between pH (X_1) and MLSS (X_3). The model's significant effect is only seen in one quadratic term, pH (1.87X_1^2). Fig. 2 shows the CCD-RSM (A) Contouring and (B) 3D plot for Removal efficiency between two variables (Time vs. MLSS).

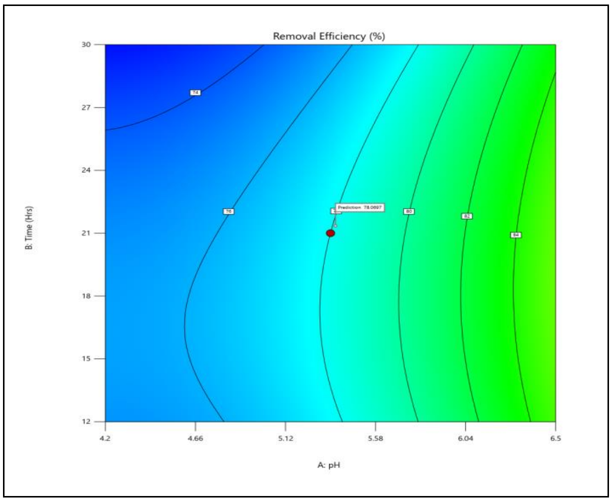


Fig. 2 (A): CCD-RSM for Contouring for Removal Efficiency between two variables (Time *vs.* pH)

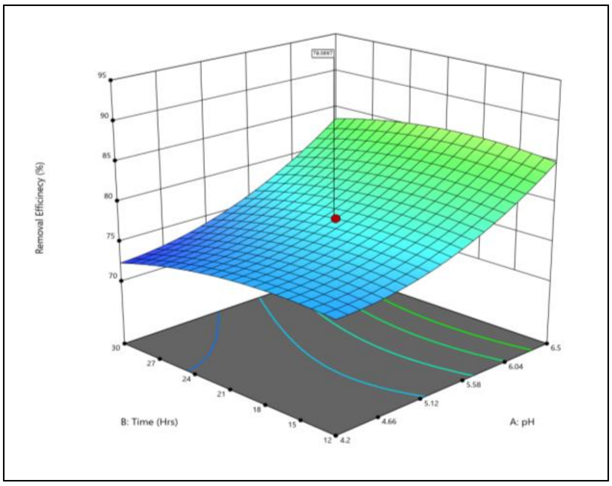


Fig. 2 (B): CCD-RSM 3D for Removal Efficiency between two variables (Time *vs.* pH)

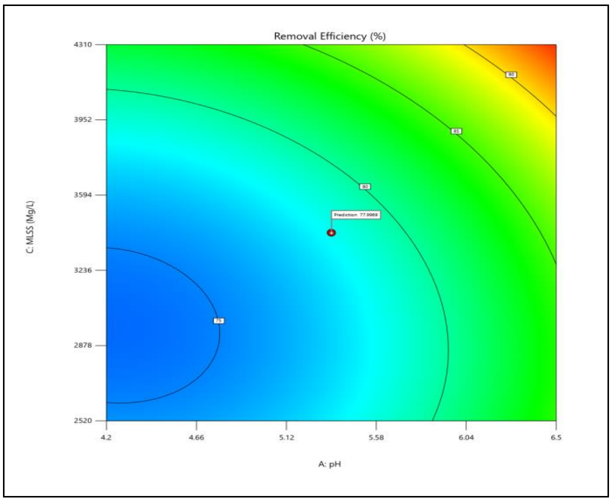


Fig. 3 (A): CCD-RSM Contouring for Removal Efficiency between two variables (pH *vs.* MLSS)

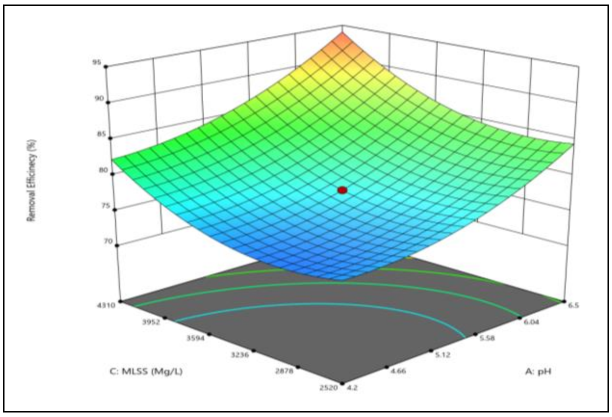


Fig. 3 (B): CCD-RSM-3D plot for Removal Efficiency between two variables (pH *vs.* MLSS)

Fig. 3 shows the CCD-RSM (A) Contouring and (B) 3D plot for removal efficiency between two the variables - pH *vs.* MLSS.

Fig. 4 shows the CCD-RSM (A) Contouring and (B) 3D plot for Removal Efficiency between two variables - Time *vs.* MLSS.

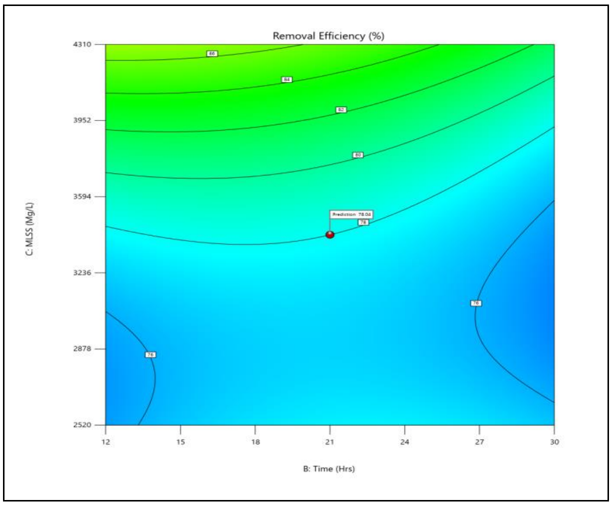


Fig. 4 (A): CCD-RSM Contouring for Removal Efficiency between two variables (Time *vs.* MLSS)

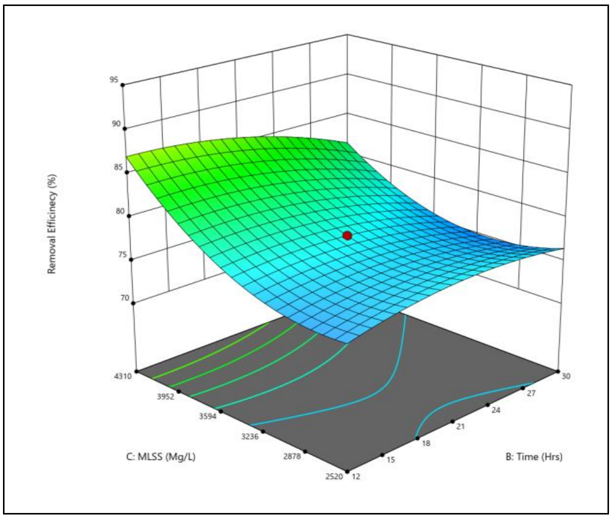


Fig. 4 (B): CCD-RSM-3D plot for Removal Efficiency between two variables (Time *vs.* MLSS)

Due to their lower numerical values, all of the interaction parameters in the quadratic equation (7), such as pH, Time and MLSS, are significant model terms. The perturbation curve and cubic diagram for removal efficiency which represent in Fig. 5 (A) and Fig 5 (B) assist to draw a correlation between pH, time and MLSS with their input variable range.

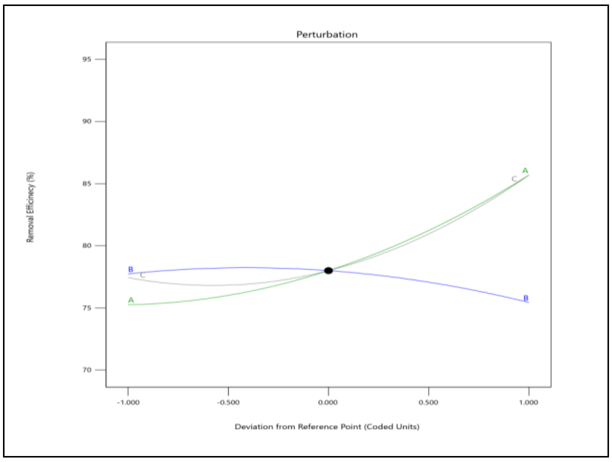


Fig. 5 (A): Perturbation curve between all three variables - pH, Time and MLSS, for removal efficiency

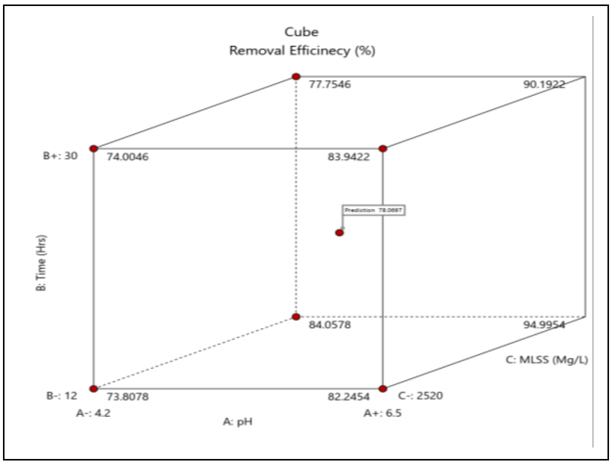


Fig. 5 (B): Cubic diagram for all three variables - pH, Time, and MLSS, for removal efficiency

3.2 EFFECTS OF COD

According to the series of trials recommended by the CCD model, COD was estimated. The amount of oxygen needed by the microorganisms in the bioreactor to decompose the organic load is measured by the COD. The ultimate value of COD has been attained with the aid of the CCD model and factors such as pH, time and MLSS that changed throughout the series of trials. Following optimization using the CCD model displayed in Table 6, the elimination of COD and the actual as well as the projected values are displayed. We estimated values both initially and ultimately using the procedures described in APHA (APHA). To investigate how the model and various variables interact, the ANOVA about COD is given in Table 7. F-value (612.61) for the constructed model is noticeable. As seen, only the variable X_2 is insignificant because of the higher value from 0.005. Significant interactions exist between all the variables, including pH, time, MLSS and the quadratic model components (X_1^2, X_2^2, X_3^2). Fig. 6 (A) shows the CCD-RSM for contouring for COD between the two variables (Time *vs.* pH) and Fig. 6 (B) exhibits the CCD-RSM for 3D plot for COD between the two variables (Time *vs.* pH).

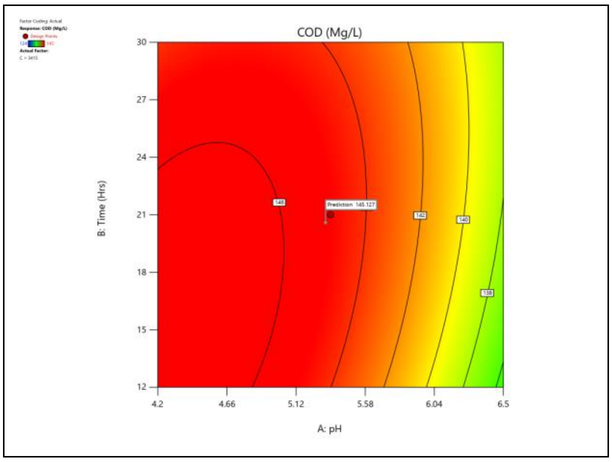


Fig. 6 (A): Contouring for COD between two variables (Time *vs.* pH)

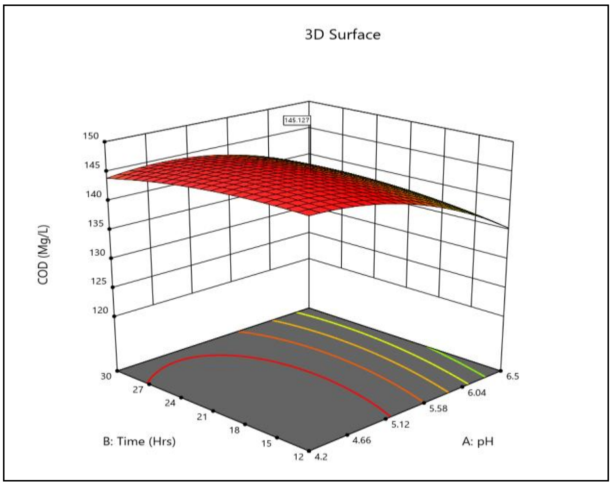


Fig. 6 (B): Exhibits the CCD-RSM for 3D plot for COD between two variables (Time *vs.* pH)

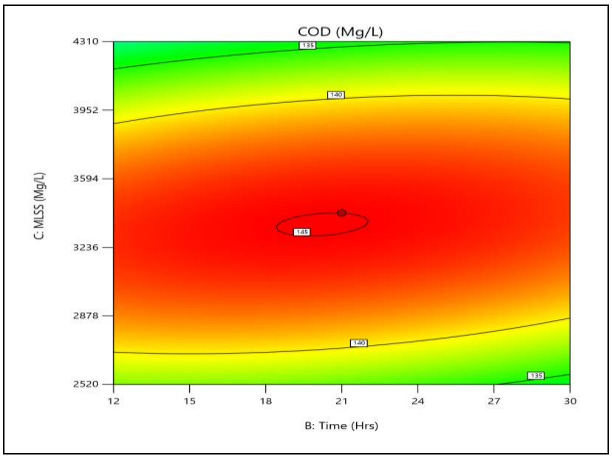


Fig. 7 (A): provides the CCD-RSM Contouring plot for COD between Time vs. MLSS

The model's predictions for the optimal COD value (145 mg/l) and the interactions of the variables at pH (5.35), time (21 h) and MLLS (3415 mg/l) were made. Fig. 7 (A) provides the CCD-RSM Contouring plot for COD between Time and MLSS and Fig. 7 (B) demonstrates the CCD-RSM of 3D plot for COD between Time and MLSS.

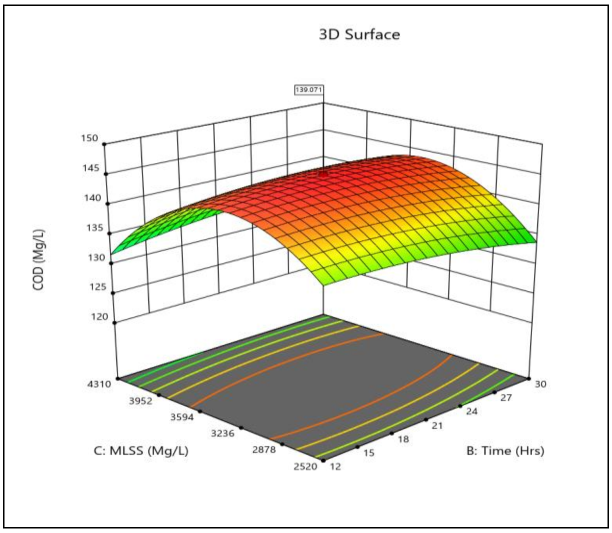


Fig. 7 (B): demonstrates the CCD-RSM of 3D plot for COD between Time vs. MLSS

Another graphical representation exhibits the correlation between Ph vs. MLSS. Fig. 8 (A) and Fig. 8 (B) represent the CCD-RSM for contouring and 3D plot for COD between the two variables - pH *vs.* MLSS respectively.

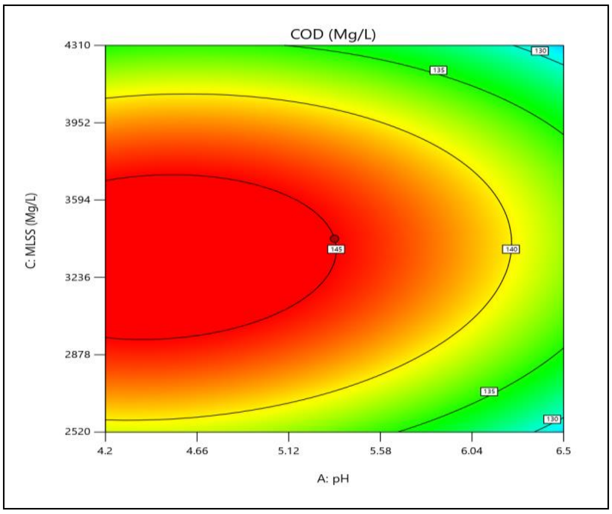


Fig. 8 (A): CCD-RSM for contouring plot for COD between two variables pH vs. MLSS

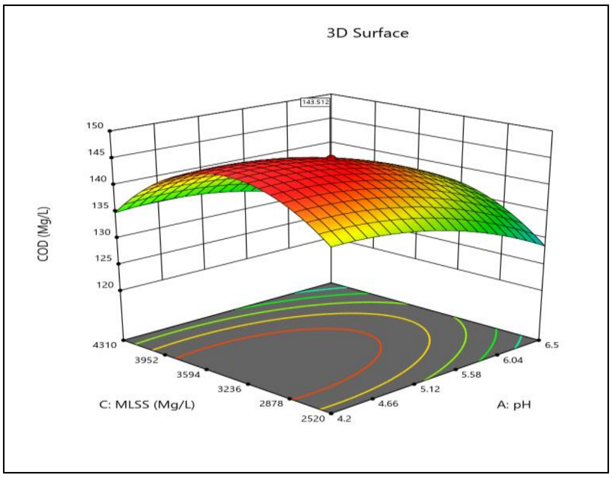


Fig. 8 (B): CCD-RSM for 3D plot for COD between two variables pH vs. MLSS

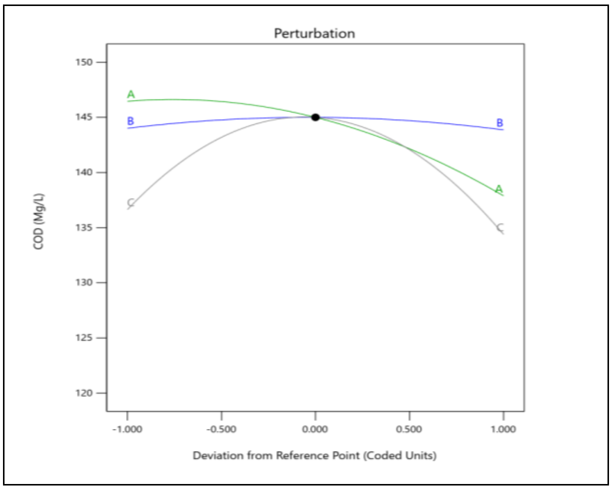


Fig. 9 (A): Perturbation curve between MLSS, Time and pH for COD

Since each interaction parameter in the quadratic Equation (7) has a numerical value less than 0.005, such as pH, Time, and MLSS, they are all considered significant model terms. Equation (8) makes clear that while the output response of the Time variable is negative, that of the pH and MLSS variables is positive for the elimination of COD. The Perturbation curve between MLSS, Time, and pH for COD has shown in Fig 9 (A) which exhibits the deviation from reference points for the removal of COD.

However, the relationship responses of all the variables - pH, Time and MLSS, are positive. All of the individual terms' quadratic responses are negative. Due to the larger positive values among the variables taken into consideration, pH's individual effect on the elimination of COD is at its peak. The Cubic diagram between MLSS, Time and pH for COD shown in Fig. 9 (B) provides the relationship between all three variables with their extremist's range for the output of COD.

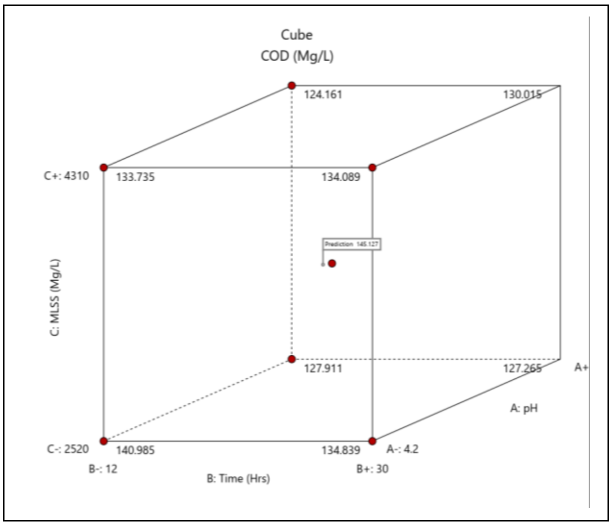


Fig. 9 (B): Cubic diagram between MLSS, Time and pH for COD

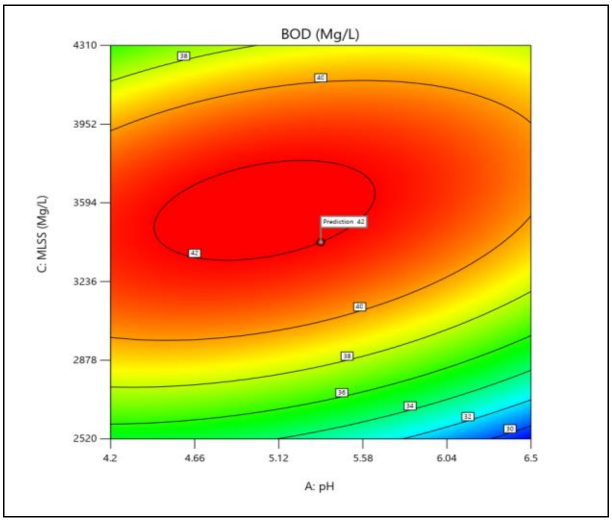


Fig. 10 (A): contour plot for BOD between two variables (pH *vs.* MLSS)

3.3 EFFECTS OF BOD

The CCD recommended thirteen different experiment numbers for the BOD and COD calculations. The biological oxygen demand, or BOD, is what microorganisms in the bioreactor need to decompose the organic load. By adjusting the variables in the CCD model namely, Time, pH and MLSS, with a series of trials, the final value of BOD was obtained. The approach described was followed to estimate the starting and final values. The approach outlined in APHA was followed in order to estimate the starting and final values. The CCD-RSM's ANOVA model was displayed in (Table 7) with a significant F-value of 809.78. The ANOVA model demonstrates that the variables X_2 and the quadratic model terms are insignificant since their higher values of 0.005 indicate that they are. In Fig. 10 (A) and (B), the contour and 3D plots are displayed.

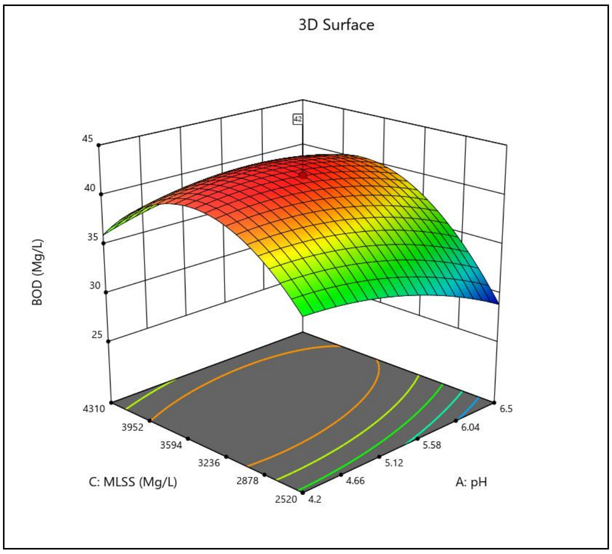


Fig. 10 (B): 3D plot for BOD between two variables (pH *vs.* MLSS)

The influence of the MLSS term is very significant due to only having positive value, as is clear from the final Equation No. 9 after the inconsequential terms have been eliminated, and the interaction between all terms is important and has a positive impact. There are only two major quadratic model terms (X_1^2, X_3^2). In Fig. 11 (A and B) displayed the contour and 3D plots between Time and pH.

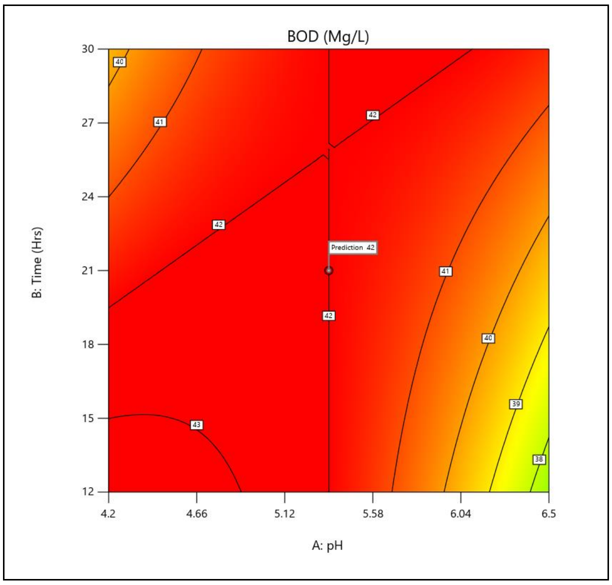


Fig. 11 (A): CCD-RSM for contouring for BOD between two variables (Time *vs.* pH)

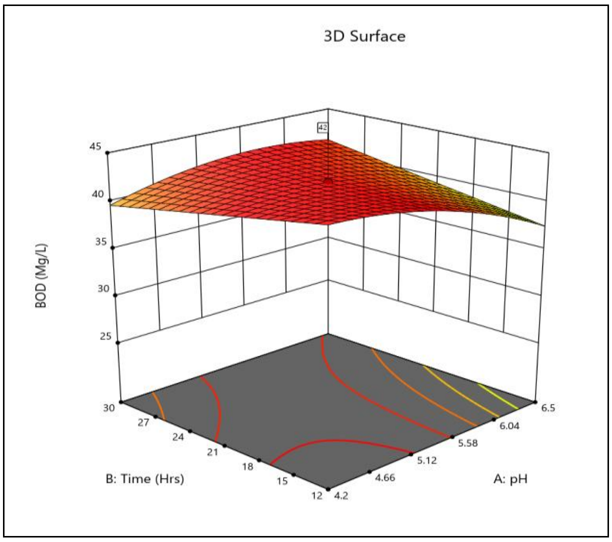


Fig. 11 (B): CCD-RSM 3D plot for BOD between two variables (Time *vs.* pH)

Similarly, Fig.12 (A) and (B) provides the correlation between MLSS and TIME for contouring and 3D plot, respectively.

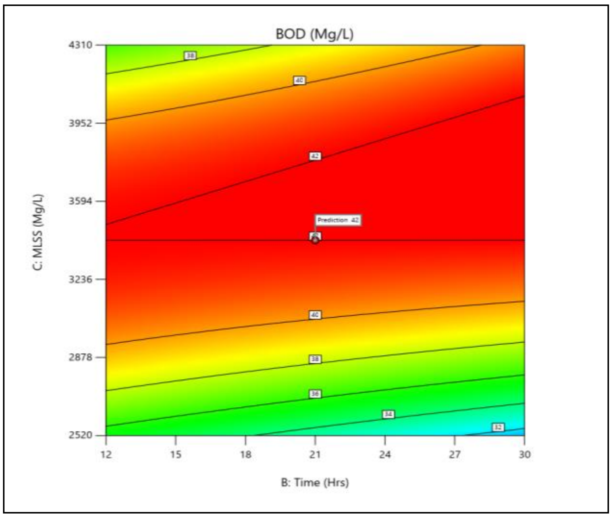


Fig. 12 (A): CCD-RSM for contouring for BOD between two variables (MLSS *vs.* Time)

For removal of BOD from wastewater, the Perturbation curve between MLSS, Time and pH, shown in Fig. 13 (A), exhibits the deviation from reference points for the removal of COD and Cubic diagram between MLSS, Time, and pH for COD shown in Fig. 13 (B) provides the relationship between all three variables with their extreme range for the output of COD.

The optimal value of BOD (42 mg/l) using the CCD model is provided by the variables - pH (5.35), Time (21 h) and MLLS (3415 mg/l).

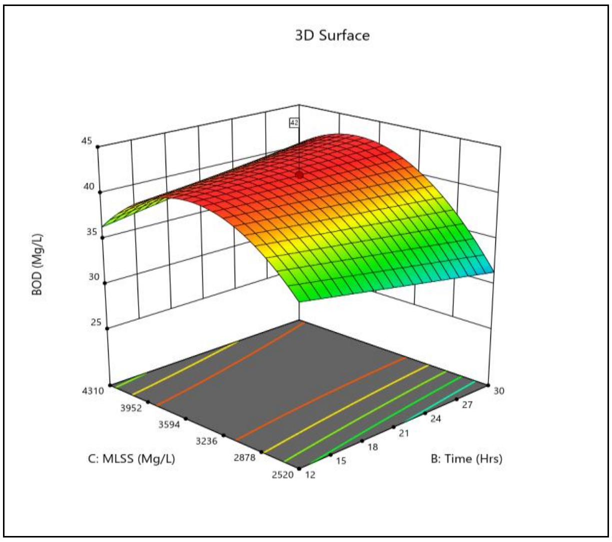


Fig. 12 (B): CCD-RSM 3D plot for BOD between two variables (MLSS *vs.* Time)

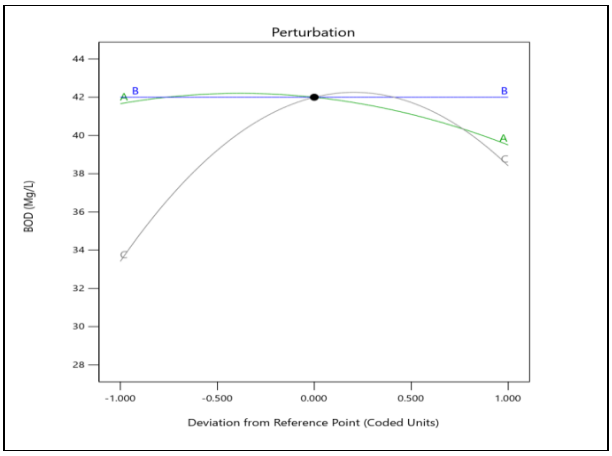


Fig. 13 (A): Perturbation curve between MLSS, Time and pH, for removal of BOD

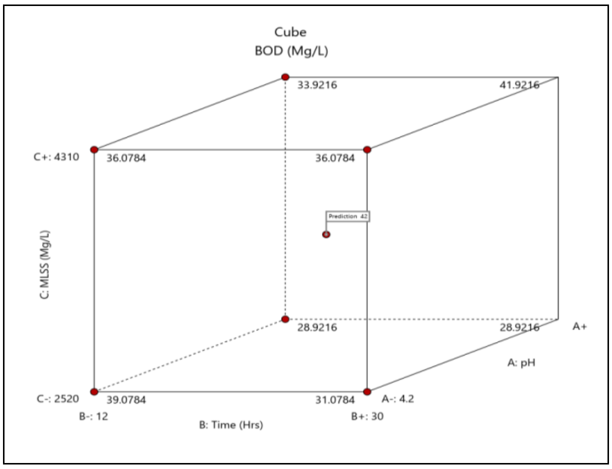


Fig. 13 (B): Cubic diagram between MLSS, Time and pH, for BOD

Equation (9) makes it clear that the output reaction of the MLSS variable is exclusively positive for the elimination of BOD, whereas the output response of the other individual variables is negative. However, all of the variables, including pH, Time, and MLSS, have positive interactions. Individual terms like pH have a negative quadratic reaction, while MLSS has a positive quadratic response. According to the CCD model, the quadratic term's (Time) response is negligible.

4. CONCLUSION

The activated sludge treatment process has been extensively studied for the removal of COD and BOD from pharmaceutical wastewater. Numerous studies have investigated the efficiency and performance of this process in treating various types of wastewaters, including pharmaceutical wastewater. One study by (Paraskeva and Diamadopoulos, 2006) reviewed different technologies for olive mill wastewater treatment and reported more than 40% COD removal and approximately 95% oil and grease removal using the activated sludge process. Another study by (Machdar *et al.* 2000) (Machdar, Sekiguchi et al. 2000) evaluated a combined system of a UASB reactor and a curtain type DHS reactor for sewage treatment. The system achieved 94-97% unfiltered BOD removal, 81-84% unfiltered COD removal, and 63-79% SS removal. (Nasr *et al.* 2022) of confectionery industrial wastewater and reported satisfactory results with average COD and BOD removal rates of 92%.

Pharmaceutical wastewater must be treated with input factors including pH, Time, and MLSS in order to remove COD and BOD. The CCD-RSM model was used to optimize output variables, including COD, BOD, and their removal efficiency, in this study's attempt to treat wastewater with these characteristics. The data from CCD were best fit by the second-order polynomial equation (2). The removal efficiency model F-value (767.50), COD model F-value (612.61), and BOD model F-value (809.78) all show that the model is significant. In quadratic models created for removal efficiency, COD, and BOD, the regression coefficients (R^2), are 0.9996, 0.9995 and 0.9996, respectively. Table 10 displays an overview of all the p-values for removal efficiency, COD and BOD.

The most favorable result has been demonstrated by time ($1.10X_2$), as seen from the data for removal efficiency. The relationship between time MLSS ($0.0002X_2X_3$) and pH time ($0.0362\ X_1X_2$) is likewise regarded as good. The model's significant effect is only seen in one quadratic term, pH ($1.87\ \mathbf{X_1^2}$). The output responses of the variables - pH ($13.463\ X_1$) and MLSS ($0.070\ X_3$) are favorable for the elimination of COD shown; however, the output response of the other individual variable, Time ($0.857\ X_2$), is unfavorable. However, all of the variables, including pH, Time and MLSS, have positive interactive responses ($0.132\ X_1X_2$, $0.0008\ X_1X_3$ and $0.0002\ X_2X_3$). All of the individual terms' quadratic responses are negative ($2.13\ X_1^2, 0.013\ X_2^2, 0.00002\ X_3^2$). The right combination of pH (5.35), time (21 h) and MLLS (3415 mg/l) will effectively remove COD and BOD.

Only the MLSS variable's output reaction for the BOD is positive ($0.039X_3$) and significant, but the responses for the other individual variables (pH) are both negative ($-0.189X_1$) and significant. The interaction responses of pH, Time and MLSS are all positive ($0.189\ X_1X_2$, $0.019X_1X_3$ and $0.0002X_2X_3$). The pH ($-1.06\mathbf{X_1^2}$) quadratic response for individual terms is negative. According to the CCD model, the quadratic term's (time) response is negligible. The significant and insignificant responses of the variables are presented in (Table 11) with color coding.

Table 11. p– values for all the variables (p < 0.05   0.05 ≤ p < 0.1   p ≥ 0.1)

	Intercept	X_1	X_2	X_3	$X_1 X_2$	$X_1 X_3$	$X_2 X_3$	X_1^2	X_2^2	X_3^2
Removal Efficiency	78	5.21879	-1.1516	4.125	0.375	0.625	-1.625	2.47487	-1.41421	3.56434
p-values		< 0.0001	0.0009	< 0.0001	0.0455	0.0118	0.0007	0.0004	0.0020	0.0003
COD	145	-4.28687	-0.0732233	-1.125	1.375	0.875	1.625	-2.82843	-1.06066	-9.48591
p-values		< 0.0001	0.4724	0.0024	0.0013	0.0049	0.0008	0.0003	0.0051	< 0.0001
BOD	42	-1.07837	-4.12067E-15	2.5	2	2	2	-1.41421	1.81299E-16	-6.08579
p-values		0.0003	1.0000	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.0005	1.0000	< 0.0001

These studies demonstrate that the activated sludge treatment is efficient in eradicating COD and BOD from pharmaceutical wastewater. The CCD-RSM helps the researchers to create 3D graphs between the variables and visualize the model's petrophysical behavior which is the novelty of the work for the optimization and treatment of pharmaceutical wastewater. The process of AS can achieve significant removal efficiencies along with removal of COD and BOD; it can be integrated with other treatment technologies to improve the performance. However, the specific removal efficiencies could change based on the wastewater's properties and the treatment system's operating settings.

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CONFLICT OF INTEREST

The authors have no competing interests that would prevent them from publishing this research work as is.

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