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Central Composite Design-Based Optimization of Heterogeneous Fenton-Like Catalytic Oxidation of Real Pharmaceutical Wastewater Using Cu-Fe/SiO_2

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Key Words	Pharmaceutical wastewater, COD removal, Catalytic oxidation, Cu-Fe/SiO_2, Process optimization
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Abstract: This research explores heterogeneous Fenton-like catalytic oxidation for the treatment of actual pharmaceutical wastewater with Cu–Fe supported on SiO_2 as an active catalyst. Catalyst preparation and characterization via X-ray diffraction (XRD), scanning electron microscopy (SEM), Fourier-transform infrared (FTIR) spectroscopy and BET analysis for poros1ity, crystallinity and active site distribution were completed. To optimize treatment parameters, response surface methodology using central composite design (CCD) investigated catalyst dosage, H_2O_2 concentration, initial pH and reaction time for the maximum chemical oxygen demand (COD) removal. The CCD determinant generated a quadratic model ($R^2 = 0.9881$) to predict experimental results which, when confirmed via successful achievement of proposed conditions, resulted in 76.07% COD removal. This work indicates the efficiency, reproducibility and feasibility of scaling the Cu–Fe/SiO_2 catalyst for pharmaceutical wastewater treatment and is a step toward sustainability.

Keywords: Pharmaceutical wastewater, Chemical oxygen demand (COD) removal, Catalytic oxidation, Cu–Fe/SiO_2, Process optimization

1. INTRODUCTION

The global rise of pharmaceutical production and consumption has led to billions of gallons of pharmaceutical wastewater (PWW) each year from industrial effluent release, making PWW one of the most complex industrial-by-product issues to plague the discipline of environmental engineering and wastewater treatment. PWW is characterized by an extraordinarily high chemical oxygen demand (COD) often greater than 5,000mg/L and a notorious brew of xenobiotics, recalcitrant and toxic organic pollutants. Specifically, PWW contains active pharmaceutical ingredients (APIs), antibiotics, solvents, EDCs, and sustainable agents such as surfactants and complexing agents. All of these are released into the environment at concentrations that cause acute and chronic toxicity to aquatic organisms, reduce microbial consortium operability, contribute to the presence of antibiotic-resistant genes (ARGs), and endanger public health and ecosystem stability. Unlike general municipal wastewater or the wastewater generated from other industries, PWW is defined by an unregulated profile and low biodegradability similar to how drugs meant for human use are processed by the human body and excreted in a non-degraded state. Thus, this convoluted composite presents a severe problem for simple discharge into receiving waters that must now deal with such effluents and poses issues for agricultural systems that might apply non-treated water for irrigation and treatment and the resultant particles that become prolific transformation products (Fu et al. 2019, Luo et al. 2019, Ahidjo et al. 2024). Biological treatment options such as activated sludge, anaerobic digestion constitute the traditional relative means to extract organic pollutants from municipal and some industrial waste streams in ideal environments. Yet, this is not always the case, and without fail, biological treatment options require an emphasis on biodegradability. Therefore, such treatment options for pharmaceutical wastewater (PWW) are largely ineffectual. This occurs for two reasons: 1) toxic constituents within pharmaceutical wastewater inhibit biological activity and 2) recalcitrant molecules preclude proper chemical oxygen demand (COD) removal leading to more toxic, recalcitrant intermediates. Enhanced systems ranging from membrane bioreactors (MBRs) or hybrid solutions integrating biological stimulus and physicochemical phenomena yield superior effluent quality and favorable outcomes. Yet again, membrane bioreactors experience membrane fouling due to excess retained solids, or treatment enhancements fail in the face of antibiotics, pharmaceuticals and endocrine disrupting compounds (EDCs) constituting the real-life PWW (Nebot et al. 2015). The largest unresolved component is the failure to remove pharmaceuticals from the NGO flow post-treatment, as evidenced by WWTP analysis that determined many pharmaceutical compounds existed in both influent and effluent despite average populations and more rural settings judging such results implausible within their community confines. Unfortunately, WWTPs have become considered an active avenue of pharmaceuticals entering the greater aqueous environment. Using sensitive detection variables, the same pharmaceutical remnants that entered the WWTP stream ended up in the effluent discharge. Therefore, new treatment methods for PWW need to be more efficient, reliable and cost efficient (Dai et al. 2023, Alfarsi et al. 2025). Thus, Advanced Oxidation Processes (AOPs)—homogenous Fenton and Fenton-like processes present a feasible option for treatment alternatives under generating conditions. AOPs create a wealth of reactive hydroxyl radicals (-OH) which irreversibly degrade complex organic components into much smaller byproducts like H2O and CO2. However, homogenous Fenton reaction and its derivatives are limited beyond practical application to large scale high strength pharmaceutical waste streams. Fenton's reaction occurs at a strictly acidic pH (~pH 3) with an abundance of iron salts producing non-manageable sludges and a rapid deactivation/catalyst leaching phenomena. These operational limitations increase overall treatment costs while generating residual management issues that negatively impact overall efficiency when neutral pH or cost efficacy is required for high temperature industrial operations (Xu et al. 2022). To address these issues, the recent emergence of heterogeneously operating Fenton-like catalysts—largely due to bimetallic systems supported on high surface area substrates such as silica (SiO_2) has expanded the research and development behind advanced PWW treatment. One of the most promising of such new materials includes Cu–Fe/SiO_2 catalysts which utilize the bimetallic, synergistic redox cycling potential between copper and iron (i.e., Cu^{2+}/Cu^{+} and Fe^{3+}/Fe^{2+} transformations) to generate hydroxyl radicals over a milder range of conditions including near-neutral pH. Furthermore, SiO_2 as a catalytic support aid in site dispersion, thermal and chemical stabilization of the catalytic structure, and porosity control all necessary factors to promote effective contact with intended non-target species and efficient contaminant breakdown. In proof-of-concept studies, researchers note that the Cu–Fe/SiO_2 catalysts achieve rapid reaction rates and extents of organic and pharmaceutical contaminant removal, outperforming degradation efficiencies of traditional homogeneous endpoints and single metal heterogeneous options. Central Composite Design (CCD) under Response Surface Methodology (RSM) provides a powerful solution to much of the optimization needs generated by complex systems. CCD allows for the exploration and modelling of independent operating variables and their interactions and attempts to find the optimal response conditions for pollutant removal (Sandhwar & Prasad 2017, Sandhwar & Prasad 2018, Luo et al. 2019, Kumar et al. 2021, Thomas et al. 2021, Xu et al. 2022, Dai et al. 2023, Yang & Xue 2024).

Quantitative performance comparison highlights limitations of existing benchmarks relative to real pharmaceutical wastewater treatment challenges. Fe/Cu composites achieved only 36% COD removal in real antibiotic wastewater under unspecified H_2O_2 and catalyst dosing conditions, demonstrating limited efficacy for complex pharmaceutical matrices. Homogeneous Fe^{2+}/H_2O_2 systems report 78.4% COD removal in real pharmaceutical wastewater using 1 mg/L Fe^{2+} but generate problematic iron sludge and lack catalyst recyclability (Omar et al. 2024, Wang et al. 2025). FeCr-SBA-15/AC on SBA-15/activated carbon support delivers impressive 97% removal but targets synthetic methyl orange dye (single compound, easily degradable chromophore) rather than multi-component pharmaceutical effluents, with 0.75 g/L dosing and no H_2O_2 consumption reported. CuFe/SBA-15 catalysts show promise for model pollutants but provide no quantified COD removal data, H_2O_2 doses, or operational conditions, limiting benchmarking utility (Hamieh et al., 2025). CuO/Fe_3O_4/SiO_2 composites report qualitatively "high removal" for dyes without specific COD percentages, H_2O_2 consumption metrics, or catalyst loadings, precluding rigorous performance evaluation (Ngoc & Vu 2022). While many studies have reported on Cu-Fe catalysts, the present work is novel in terms of its actual application, support and parameter optimization. First, many studies use prepared solutions of single pharmaceuticals, while this study tests an effective solution using real pharmaceutical wastewater, which includes many recalcitrant organic compounds and poses a much more difficult solution for Fenton-like oxidation (Chen et al. 2013, Nguyen et al. 2020, Thomas et al 2021, Nam et al. 2025, Wang et al. 2025). Second, the catalyst is supported on SiO_2, which is a much less used support than Al_2O_3, activated carbon or magnetic ferrites. SiO_2 has increased surface dispersion characteristics and a structurally neutral disposition which offer effective dispersive and Cu-Fe redox properties. Third, the parameters were optimized using central composite design (CCD) for real wastewater purposes and not synthetic pollutants to create greater observed relevancy and applicability to actual industrial demand.

The present work envisages the synthesis of Cu–Fe/SiO_2 composite catalyst using wet impregnation method and examine its efficiency for the treatment of real pharmaceutical wastewater via catalytic activation of hydrogen peroxide. The developed catalyst was characterized using different characterization techniques such as XRD, SEM, FTIR and BET to understand its properties. To evaluate the effect of key operational parameters on COD removal efficiency, batch experiments were carried out based on the CCD framework. The developed statistical models inform prediction and adjustment of reaction conditions for best performance. Ultimately, the aim of this study is to facilitate an efficient catalytic reaction for the treatment of pharmaceutical wastewater with sustainability in mind to foster an effective new course of action for subsequent projects to improve environmental sustainability measures and safeguard public health. These findings show the advantages of a heterogeneous Fenton-like approach to safety and environmental quality with a more efficient, cost-effective and sustainable approach to treating pharmaceutical wastewater.

2. MATERIALS AND METHODS

2.1. Chemicals

All chemicals such as Copper (II) Nitrate Trihydrate ($Cu(NO_3)_2 \cdot 3H_2O$, Iron(III) Nitrate Nonahydrate ($Fe(NO_3)_3 \cdot 9H_2O$), Tetraethyl Orthosilicate (TEOS, $Si(OC_2H_5)_4$), Ethanol (C_2H_5OH) etc. used in this study were of analytical grade and used without further purification. The following chemicals were procured from Neelkanth Hari Chemical, Vadodara, Gujarat, India. All glassware and instruments used in the synthesis and analysis were thoroughly cleaned with chromic acid and rinsed with deionized water to prevent any contamination.

2.2. Characteristics of pharmaceutical industry wastewater

The wastewater, which was treated in the catalytic oxidation processes was supplied from a pharmaceutical plant placed in Vadodara. The initial total dissolved solid, chemical oxygen demand, pH, biological oxygen demand, and turbidity of the wastewater were assessed and are detailed in Table 1. The samples were stored in refrigerator at 4 °C until use.

Table 1: Characterization of real pharmaceutical wastewater

Sr. no	Parameters	Unit (SI)	Measured Value
1	pH		8.2
2	Turbidity	NTU	28.40
3	COD	mg/L	6112
4	BOD (3 days at 27 degree Celsius)	mg/L	2987
5	Total dissolved Solid	mg/L	2780

2.3. Catalyst preparation

The Cu–Fe/SiO_2 heterogeneous catalyst was synthesized via the wet impregnation method (Kumar et al. 2021), utilizing commercially available SiO_2 powder as a support. This method allows for facile preparation and effective dispersion of active metal species onto the support. Copper(II) nitrate trihydrate ($Cu(NO_3)_2 \cdot 3H_2O$) and iron (III) nitrate nonahydrate ($Fe(NO_3)_3 \cdot 9H_2O$) were obtained at stoichiometric amounts.

After accurate weighing, the weighed portions were dissolved in a minimal amount of deionized water to afford a mixed metal nitrate solution in aqueous form. The loading ratio of Cu:Fe was maintained at 1:1 and the total metal loading was calculated at 10 wt% of the total mass of the catalyst. To the metal nitrate solution obtained, commercial amporphous SiO_2 powder was added gradually with continuous stirring conducted at room temperature to ensure proper impregnation. After 4 hours of stirring, the slurry was transferred to a petri dish and dried in a hot air oven set at 110°C for 12 hours. Upon drying, the resultant solid precursor was calcined in a muffle furnace at 500°C for 4 hours in air to decompose the nitrates and yield the metals oxides (CuO and Fe_2O_3 or Fe_3O_4) with enhanced stability and strong adhesion to the surface of SiO_2. The resulting calcined catalyst was cooled to room temperature, ground into a fine powder and stored in airtight containers for further experimentation in catalytic studies. The resultant catalyst is an active and stable Cu–Fe/SiO_2 for heterogeneous Fenton-like reactions of pharmaceutical wastewater treatment (Liu et al. 2024, Li et al. 2025).

The selected 1:1 Cu:Fe molar ratio was not arbitrary; it is widely reported to enhance Fenton-like activity due to the synergistic redox cycling between Cu^{2+}/Cu^{+} and Fe^{3+}/Fe^{2+}, which accelerates the generation of hydroxyl radicals (Chen et al. 2024, Wang et al. 2024, Hu et al. 2025). Several studies have shown that equimolar Cu–Fe compositions yield higher catalytic activity and stability compared to non-equimolar ratios because both metals participate simultaneously in electron transfer cycles (Vainoris et al. 2022, Kongkoed et al. 2024, Wang et al. 2024, Nam et al. 2025). Similarly, the 10 wt% total metal loading was selected based on literature indicating that loadings in the range of 8–12 wt% provide optimal dispersion of mixed metal oxides on oxide supports without causing pore blockage, crystallite overgrowth, or agglomeration (Munnik et al. 2015, Peralta-Ladino et al. 2025, Tajoli et al. 2025). Higher loadings (>15 wt%) often lead to particle sintering during calcination, while lower loadings (<5 wt%) can result in insufficient active sites (Bellouard et al., 2024, Khan et al. 2025). The molar concentration of the precursor solution was maintained at 0.5 M for both Cu and Fe salts to enable homogeneous impregnation while preventing oversaturation of the support surface. The impregnation step was conducted at the native solution pH, governed by the nitrate precursors; this pH range is appropriate for maintaining metal ions in soluble form and ensuring uniform distribution over SiO_2 without premature precipitation (Tricoli et al. 2010, Bravo-Suarez et al. 2025).

2.4. Catalyst characterization

The structural, morphology and surface properties of Cu–Fe/SiO_2 were extensively examined and characterized via various instruments in order to understand the nature of the catalyst for in situ reaction. X-Ray Diffraction

(XRD) was employed for crystallite structure and phase determination where a D6 PHASER X-Ray Diffractometer (Bruker India Scientific Pvt. Ltd.) with Cu Kα radiation (λ = 1.5406 Å) in the 2θ range of 10°–80° was utilized for analysis. Figure 1 represents the XRD spectrum of synthesized catalyst. The XRD pattern for the synthesized Cu–Fe/SiO_2 catalyst indicates the presence of both amorphous and crystalline phases. The broad halo between 20–25° (2θ) is attributed to the formation of amorphous SiO_2, which corroborates the selection of silica as the support material for the catalyst. Superimposed crystalline features on the SiO_2 halo relate to the characteristic crystalline phases presumed from the presence of copper and iron oxides. The peaks corresponding to CuO (tenorite, monoclinic) are noted at 35.5°, 38.7°, and 48.7°, while the peaks appearing at about 30.2°, 35.6°, 43.3°, 57.3°, and 62.9° are attributed to Fe_2O_3 (hematite). Additionally, the overlapping peaks at 30.3°, 33.1°, and 51.4° indicate the presence of a $CuFe_2O_4$ spinel phase formed, which is a mixed Cu–Fe oxide phase that is commonplace in bimetallic systems. Thus, the presence of crystalline phases over the amorphous SiO_2 support indicates that the Cu and Fe species have been loaded successfully onto silica to provide many redox active sites and maintain structural stability for effective heterogeneous Fenton-like catalysis (Ning et al. 2018, Ren et al. 2020, Pratiwi et al. 2021). Scanning Electron Microscopy (SEM) on an SU3800 Hi-SEM system (Hitachi High-Tech India Pvt. Ltd.) discerned particle morphology and distribution. Figure 2 indicates SEM micrograph. According to the SEM provided, the surface morphology of the catalyst is non-uniform as it appears to be comprised of irregular shaped/agglomerated particles. They appear to be somewhat loosely packed, forming clusters/areas of rough and porous characteristics—ideal for enhancing surface area and possessing necessary active sites. The microstructure of Cu–Fe/SiO_2 is heterogeneous as there are small fragmented like structures and large plate-like formations which suggests that the metal oxides dispersed nicely on the silica support. These are structures are in line with what would be beneficial for mass transfer and catalytic activity because the roughness/pore openings allow easy access and engagement of the species with the catalyst surface. Thus, the SEM suggests that the catalysts are appropriately structured for heterogeneous Fenton-like catalytic activity for wastewater treatment (Martínez et al 2017, Ning et al. 2021,Thomas et al. 2021). Fourier Transform Infrared Spectroscopy (FTIR) from a Bruker Alpha II FTIR spectrometer compiled via KBr pellet technique in the wavenumber range of 400–4000 cm^{-1} determined surface functionality. Figure 3 shows FTIR spectrum. The FTIR spectrum of the Cu–Fe/SiO_2 catalyst (Figure) shows specific absorption bands, which indicate the formation of the silica support and metal oxides. The presence of silica is confirmed by a strong and broad band at 1080–1100

cm^{-1} with shoulders at 800 cm^{-1}, which relate to the asymmetric and symmetric stretching vibrations of Si–O–Si linkages. In addition, a weak band appears at 950–970 cm^{-1}, relating to Si–OH stretching vibrations, corresponding to surface silanol groups. Moreover, absorptions in the lower wavenumber region pertain to the generation of metal oxides as Cu and Fe were integrated onto the silicon matrix; thus, the absorption between 580–680 cm^{-1} correspond to Fe–O and Cu–O stretching vibrations. Finally, a broad band between 3400–3450 cm^{-1} and a weak peak at 1630 cm^{-1} relate to O–H stretching and bending vibrations of water and/or surface hydroxyl groups. Therefore, the FTIR suggests that a Cu–Fe/SiO_2 composite was formed and that silica and silica functional groups were absorbed and created (Ning et al. 2018, Ren et al. 2020). The textural property surface area was assessed via BET surface area on a Micromeritics ASAP 2020 where nitrogen adsorption–desorption isotherms after degassing the sample at 150°C under vacuum was used to calculate specific surface area via Brunauer–Emmett–Teller method. Such information provides an initial overview of the solid properties of the catalyst which enhance the effectiveness of the catalyst during reaction, particularly for degradation of pharmaceutical wastewater. BET surface area measurement of the synthesized Cu–Fe/SiO_2 catalyst revealed a surface area of 111.1 m^2/g. This indicates a porous structure of the catalyst which is advantageous because this relatively large surface area possesses a high number of active sites. Better active dispersion of Cu and Fe during the heterogeneous Fenton-like oxidation reaction enhances the efficiency of pharmaceutical wastewater degradation (Guerreiro et al. 1997, Martínez et al. 2017, Sandhwar and Prasad 2017, Krupińska 2024, González-Castaño et al. 2021, Jia et al. 2022, Mekki et al. 2023, Salehzadeh et al. 2023).

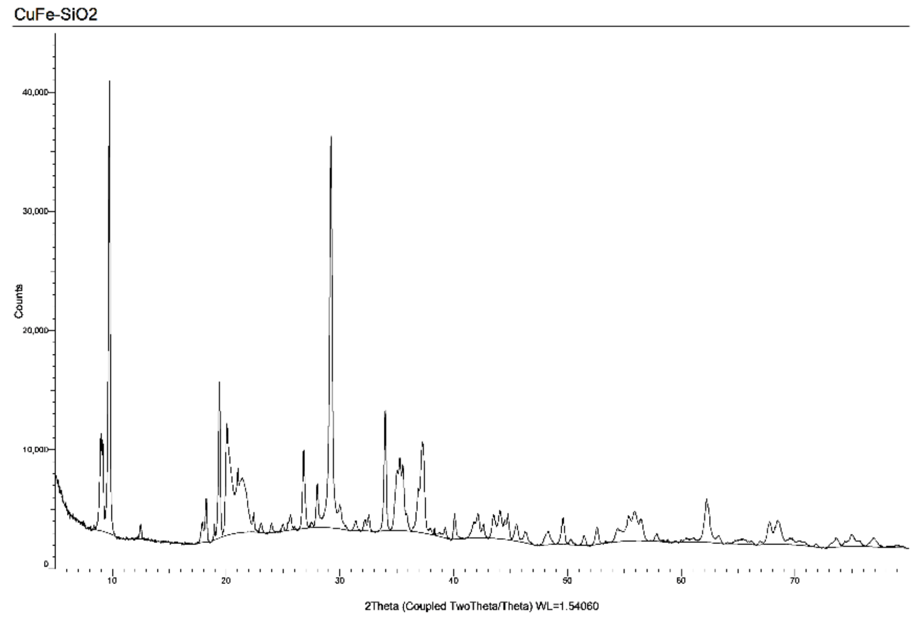

Fig 1: XRD Spectrum of synthesized catalyst

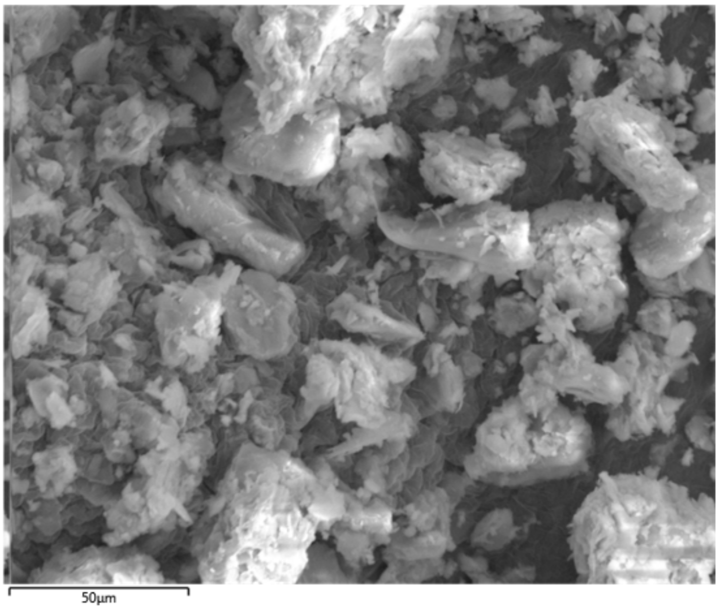

Fig 2: SEM micrograph of synthesized catalyst

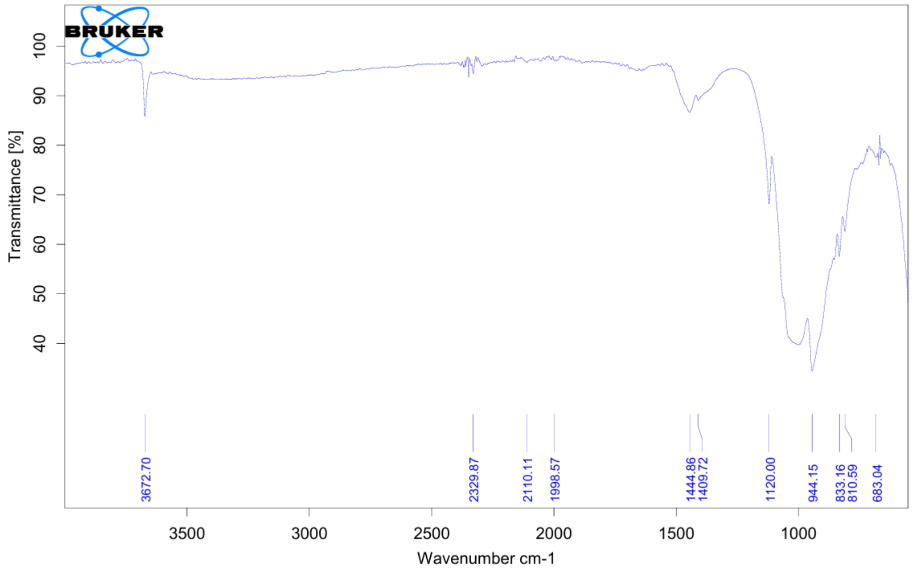

Fig 3: FITR spectrum of synthesized catalyst

2.5. Experimental set-up and procedure

The current investigation was conducted within a 250 mL round bottom three-necked glass reactor, wherein the central neck was sealed with a complete reflux system. During each trial, 100 mL of wastewater was introduced into the reactor along with the necessary amount of catalyst and H_2O_2, and then placed on a hot plate equipped with a magnetic stirrer. Various pH levels were tested; therefore, the initial pH of the mixture was adjusted using 1 M NaOH or 1 M H_2SO_4 prior to the addition of the catalyst and oxidant. Following the 3-hour reaction period, 2 mL of supernatant was periodically extracted from the reactor and promptly filtered through a 0.22 µm Millex syringe filter. The resulting samples obtained were subsequently subjected to COD analysis using APHA standard method. All procedures were repeated in duplicate, and the mean values were calculated with error bars indicating the standard deviation. Figure 4 shows the experimental setup.

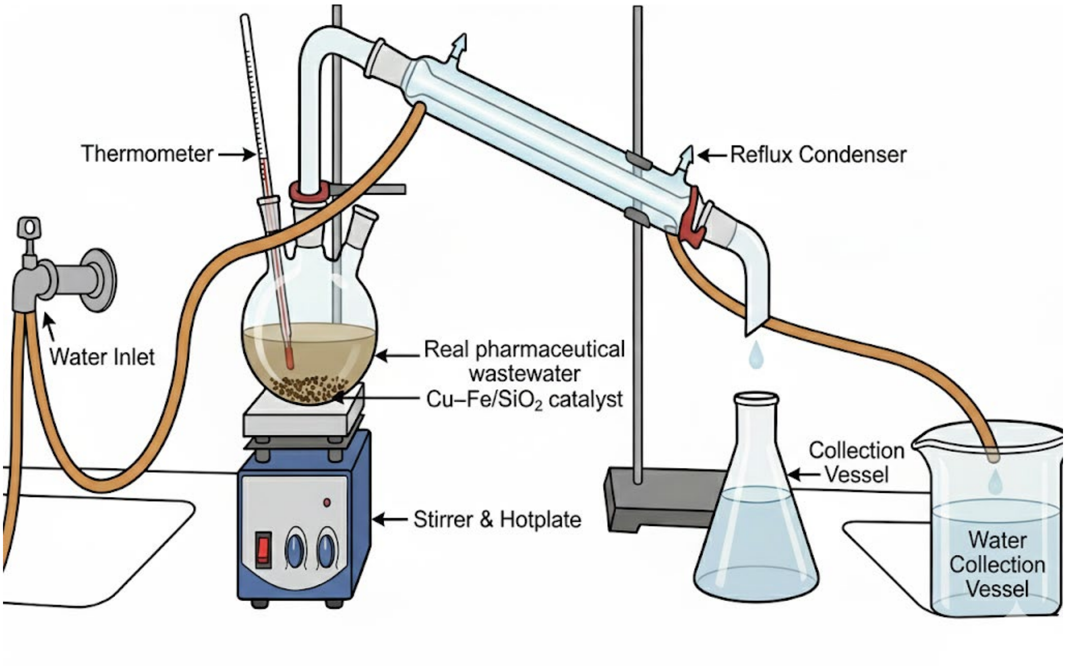

Fig 4: Experimental setup

Preliminary trial experiments were carried out to determine appropriate operating ranges for key variables, namely catalyst dosage, H_2O_2 concentration, initial pH, and reaction time. These exploratory tests were essential to establish the upper and lower bounds for the subsequent optimization study. The finalized ranges of the independent variables are presented in Table 2. To systematically investigate the effects and interactions of these parameters on COD removal efficiency, Response Surface Methodology (RSM) was employed using a Central Composite Design (CCD). The experimental runs were arranged according to the CCD matrix, also summarized in Table 3, which incorporated various combinations of the independent variables (pH, catalyst dosage, and treatment time). This design framework enabled efficient modelling of the degradation efficiency and identification of optimal operating conditions.

Table 2: Variables and their levels obtained from the statistical software

Central Composite Design characteristics				
Levels	**Parameters (Range)**			
	A	B	C	D
	Catalyst dosage (g/L)	**H_2O_2 concentration (mM)**	**Initial pH**	**Reaction time (min)**
-2α	0.2	5	3	15
-α	0.4	30	4	45
0	0.6	55	5	75
+α	0.8	80	6	105
+2α	1	105	7	135

Table 3: CCD predicted set of experiments

Run No.	A	B	C	D
1	0.4	30	4	45
2	0.8	30	4	45
3	0.4	80	4	45
4	0.8	80	4	45
5	0.4	30	6	45
6	0.8	30	6	45
7	0.4	80	6	45
8	0.8	80	6	45
9	0.4	30	4	105
10	0.8	30	4	105
11	0.4	80	4	105
12	0.8	80	4	105
13	0.4	30	6	105
14	0.8	30	6	105
15	0.4	80	6	105
16	0.8	80	6	105
17	0.2	55	5	75
18	1	55	5	75
19	0.6	5	5	75
20	0.6	105	5	75
21	0.6	55	3	75
22	0.6	55	7	75
23	0.6	55	5	15
24	0.6	55	5	135
25	0.6	55	5	75
26	0.6	55	5	75
27	0.6	55	5	75
28	0.6	55	5	75
29	0.6	55	5	75
30	0.6	55	5	75

3. RESULTS AND DISCUSSIONS

3.1 Effect of catalyst dosage, H_2O_2 concentration, pH, and reaction time on COD removal efficiency

The effect of significant operating variables on COD removal efficiency via RSM is displayed in the three-dimensional surface plots seen in Figures 5 (a–e). For instance, catalyst dosage is shown a significantly positive contribution to COD removal but to an extent; observing the contour plots, higher increases in catalyst loading from 0.4 g/L to 0.8 g/L increase degradation efficiency as more active Cu–Fe redox sites are available for subsequent H_2O_2 decomposition and •OH radical formation. However, anything beyond that can lead to radical scavenging means or serious aggregation of catalyst particles which can reduce efficiency (Kumar et al. 2011, Yuan et al. 2022). Furthermore, the concentration of H_2O_2 has a significant concern of COD removal; raising increases in dosage from 30 to 80 mg/L increases efficiencies as it opens up more reagent for •OH formation. However, just like with the catalyst loading, excess loading of H_2O_2 can lead to a radical scavenging effect as HO_2• occurs. Since HO_2• has a lower oxidation potential, productivity also reduces. The pH has an adjusted impact on COD removal efficiency as the lowest pH (pH 4–5) provides the highest efficiency. At low pH, iron and copper remain in a soluble form as redox-active, thus having a high activity in the Fenton-like reactions (Singh et al. 2013). However, neutral pH conducts a ferric hydroxide precipitation which reduces active sites available and diminishes catalytic activations.

The fact that both Fe^{3+}/Fe^{2+} and Cu^{2+}/Cu^{+} cycles operate well in the acidic pH domain (pH 3–4) means activated H_2O_2 and - OH maximization occurs. This is because at a low pH, Fe^{2+} stays soluble and can effectively engage H_2O_2 while the Cu sites regenerate $Fe^{3+} \rightarrow Fe^{2+}$ relatively easily. Thus, this sustains the dual redox cycle; however, as pH increases, Fe^{3+} precipitation occurs and Cu speciation becomes more complex meaning that electron transfer becomes more difficult and - OH is reduced. This explains why the COD removal is most effective in the mildly acidic window and less effective outside of it—discuss this mechanistic relationship (Fischbacher et al. 2017, Liu et al. 2018, Maekawa et al. 2014, Walling et al. 2021). Additionally, SiO_2 is a high-surface area support that is chemically inert this means that it stabilizes Cu and Fe oxide species and provides dispersed surface redox sites that are not aggregated. Silica coating or dispersion increases particle stability in aqueous environments, minimizes metal leaching and SiO_2 can tune surface charge which will both impact pollutants adsorption and H_2O_2 approach to active sites. Thus, relate the activity and low leaching to improved dispersion and stabilization of Cu–Fe sites on SiO_2 but do not relate it to any Fenton activity of the support itself (Martínez et al. 2017, Ning et al. 2018, Ren et al. 2020). Furthermore, the time factor has a slight impact on COD removal as efficiencies gradually change during 45–105 min. A longer reaction time allows for the effective blend between the catalyst and oxidant to ensure proper mineralization of the organics (Aghazadeh et al. 2017, Zhang et al. 2017, Ruziwa et al. 2023, Huilin et al. 2025). Yet, after 90 minutes, the reduction begins to plateau which signifies saturation of active sites and reduced transferable biogenic organic matter. The reasons for the plateau in COD removal after ~90 min can be attributed to these aspects because (i) radical/oxidant depletion: bulk H_2O_2 concentration decreases and the effective steadystate •OH flux decreases; (ii) formation of recalcitrant intermediates: partially oxidized species that are less reactive with •OH can grow in concentration to prevent further mineralization; and (iii) mass-transfer limitations: general slower diffusion of remaining organics to active surface sites or blocked pores/sites from oxidation by-product adsorption. From an operational perspective, these can be countered by staged H_2O_2 dosing (maintaining available oxidants), improved hydrodynamics (external mass-transfer resistance minimized), periodic catalyst regeneration (surface fouling removed) (Kwan & Voelker 2002, Ban et al. 2020, Fischbacher et al. 2017, Krupińska 2024). Thus, all interactions better suggest that optimal COD removal (~76%) occurs at optimal catalyst loading (0.68 g/L), H_2O_2 concentration (≈65 mg/L), weakly-acidic pH (≈5.0) and reaction time of ≈86 min. This also suggests that properly balanced operations yield effective efficiencies without excessive reagents.

Table 4: Comparison of reported Fenton and heterogeneous Fenton-like catalysts for wastewater treatment

Catalyst/ system	**Metal type**	**Support/ configuration**	**Wastewater/ pollutant**	**pH**	**COD (or target) removal (%)**	**Time (min)**	**Ref.**
Fe/SnO_2 heterogeneous Fenton	Fe	SnO_2	Textile wastewater	2	86	90	Kaya & Asci 2022
Fe_2O_3/SiO_2 heterogeneous Fenton	Fe	SiO_2	Phenol solution	3	64.6	60	Zhao et al. 2017
Fe–Ce/Al_2O_3 photo-Fenton	Fe–Ce	Al_2O_3	p-Nitrophenol wastewater	4	72.9	120	Ban et al. 2020
rGO/nZVI heterogeneous Fenton	Fe^0	rGO (nanocomposite)	Textile wastewater	3	81.5 (Batch process)	110	Phong & Loc 2025
NZVI@ACF/H_2O_2	Fe^0	Activated carbon fiber	Cutting-fluid waste	5	99.8	120	Su et al. 2018
Homogeneous Fe^{2+}/H_2O_2	Fe^{2+}	– (homogeneous)	Hospital wastewater	3.1	95	93	Ghjair & Abbar 2023
Homogeneous Fe^{2+}/H_2O_2	Fe^{2+}	– (homogeneous)	Industrial effluent (edible oil industry)	3	93.5	50	Ayoub 2022

Table 4 shows that the comparative performances of the Fenton and Fenton-like systems are closely related to the composition of the catalysts, support materials, and operational conditions. Kaya and Asci (2022) observed 86%

COD removal from textile wastewater with an Fe/SnO_2 heterogeneous Fenton catalyst at pH 2 within 90 min and emphasized that iron-based systems can exhibit extremely high efficiency under strongly acidic conditions. Zhao et al. (2017) explored the efficiency of the Fe_2O_3/SiO_2 catalyst in phenol degradation and showed a moderate COD removal of 64.6% at pH 3 in 60 min; thus, silica support stabilizes the iron sites with relatively lower activity. Ban et al. (2020) applied a photo-Fenton system (Fe–Ce/Al_2O_3) on p-nitrophenol wastewater and achieved 72.9% COD removal at pH 4; this process took a longer reaction time of 120 min. Phong and Loc (2025) demonstrated increased efficiency with an rGO/nZVI heterogeneous Fenton catalyst, achieving 81.5% COD removal from textile wastewater at pH 3 within 110 min, benefitting from enhanced electron transfers and surface area. Su et al. (2018) attained an exceptionally high COD removal of 99.8% using NZVI@ACF for cutting fluid wastewater at pH 5; such nanostructured systems may involve higher cost and recovery challenge. Conversely, above 93% COD removals were attained within relatively short times by homogeneous Fe^{2+}/H_2O_2 systems reported by Ghjair and Abbar (2023) and Ayoub (2022). Overall, the comparison underlines the trade-off of efficiency versus operational sustainability, and it becomes increasingly relevant to apply heterogeneous supported Fenton catalysts for wastewater treatment.

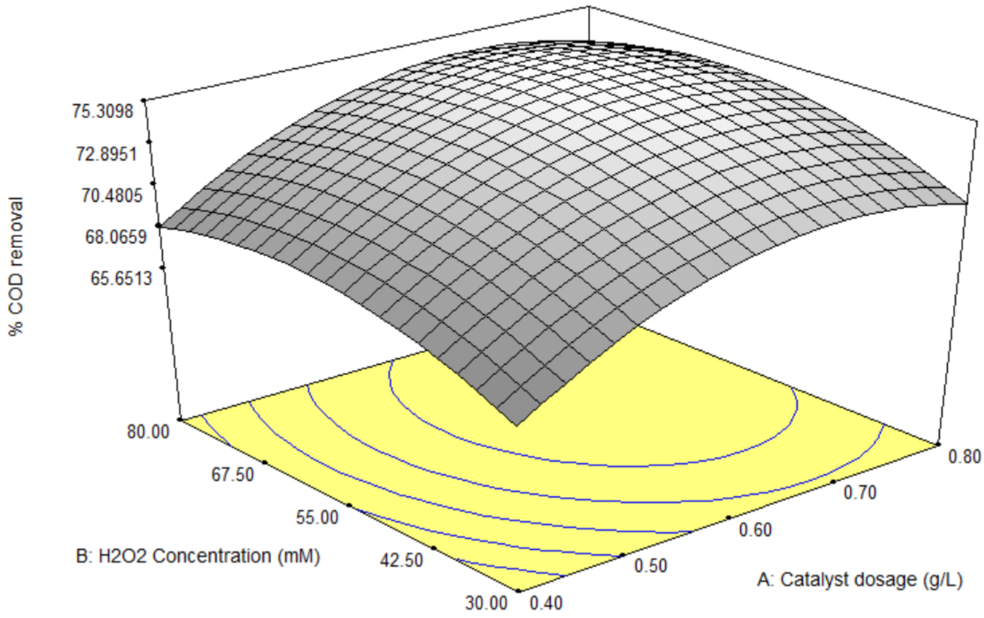

Fig. 5(a)

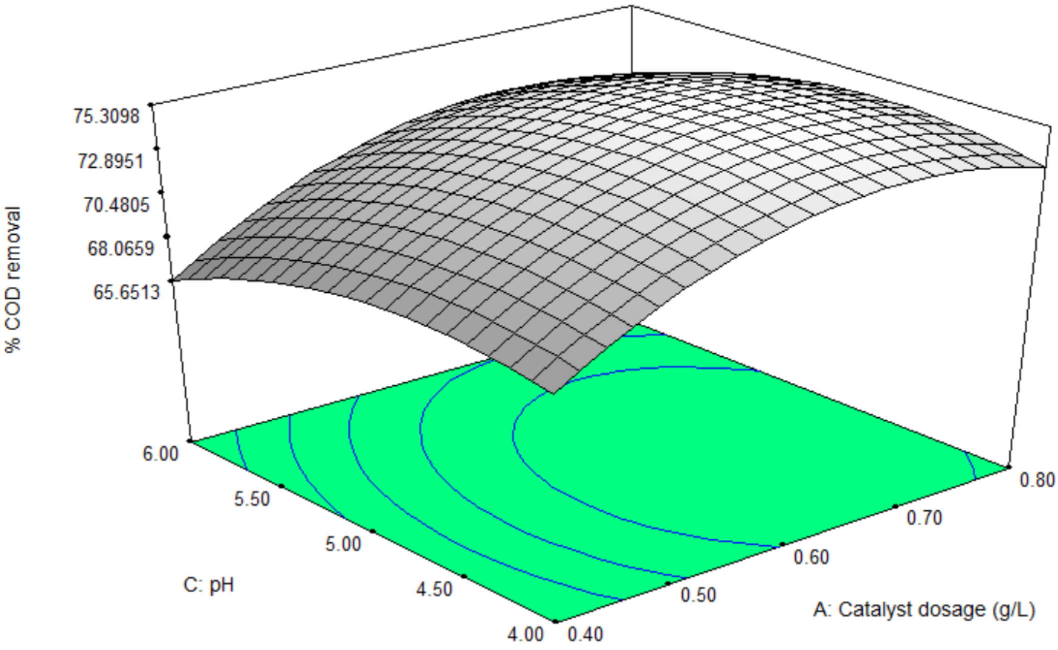
75.3098
72.8951
70.4805
68.0659
65.6513
% COD removal
6.00
5.50
5.00
4.50
4.00
C: pH
0.40
0.50
0.60
0.70
0.80
A: Catalyst dosage (g/L)

Fig. 5(b)

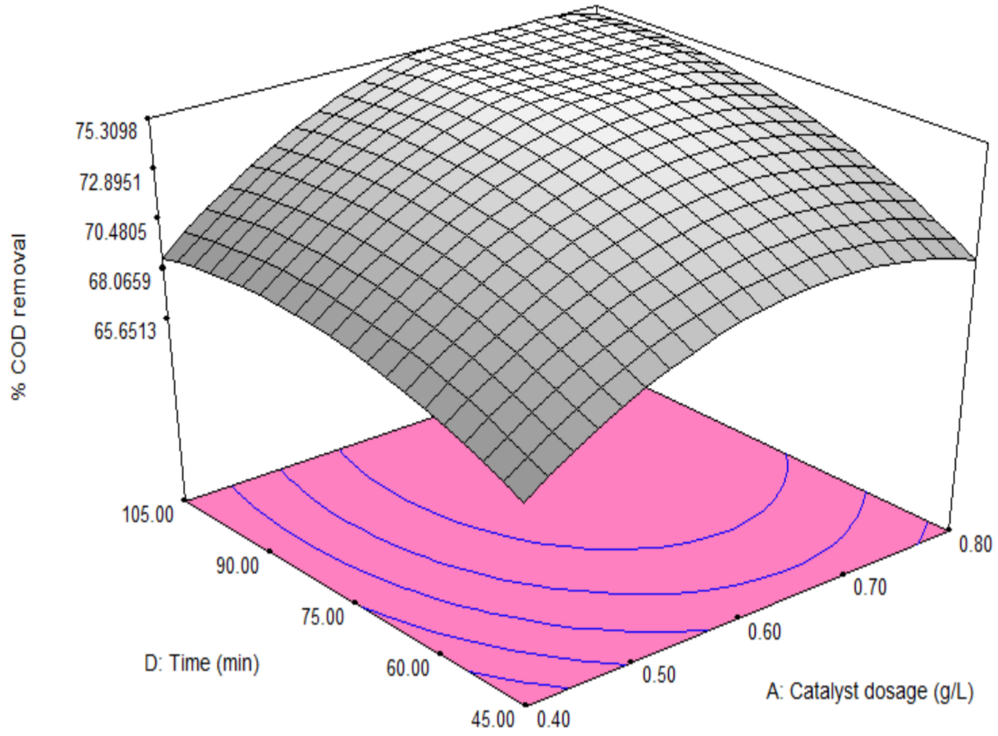
75.3098
72.8951
70.4805
68.0659
65.6513
% COD removal
105.00
90.00
75.00
60.00
45.00
D: Time (min)
0.40
0.50
0.60
0.70
0.80
A: Catalyst dosage (g/L)

Fig. 5(c)

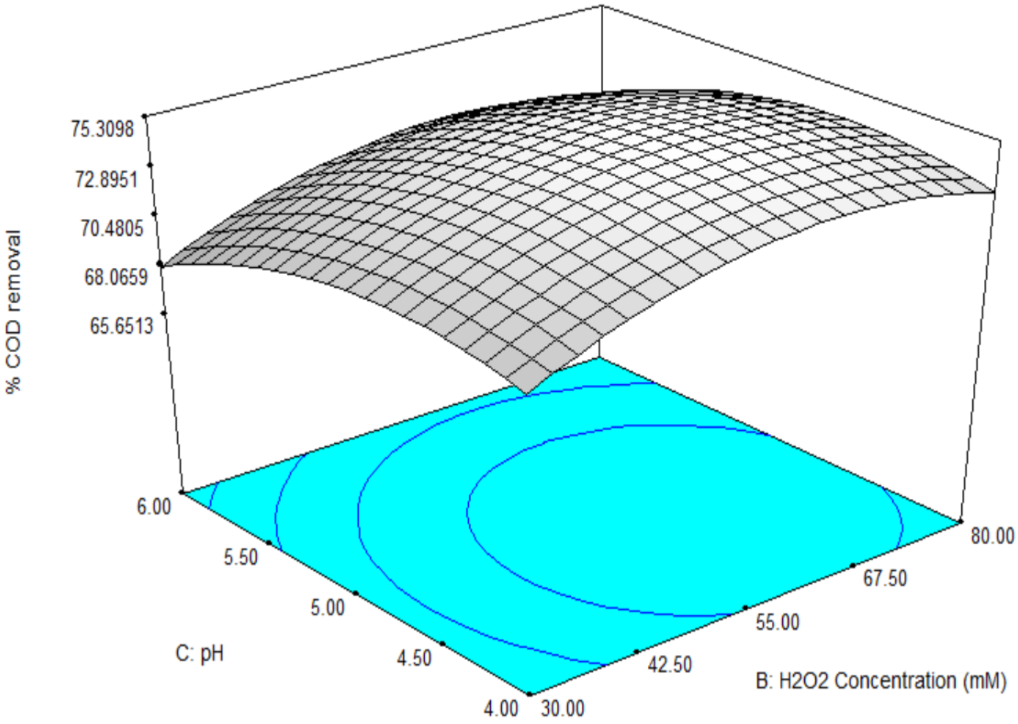
% COD removal
75.3098
72.8951
70.4805
68.0659
65.6513
6.00
5.50
5.00
4.50
4.00
C: pH
30.00
42.50
55.00
67.50
80.00
B: H2O2 Concentration (mM)

Fig. 5(d)

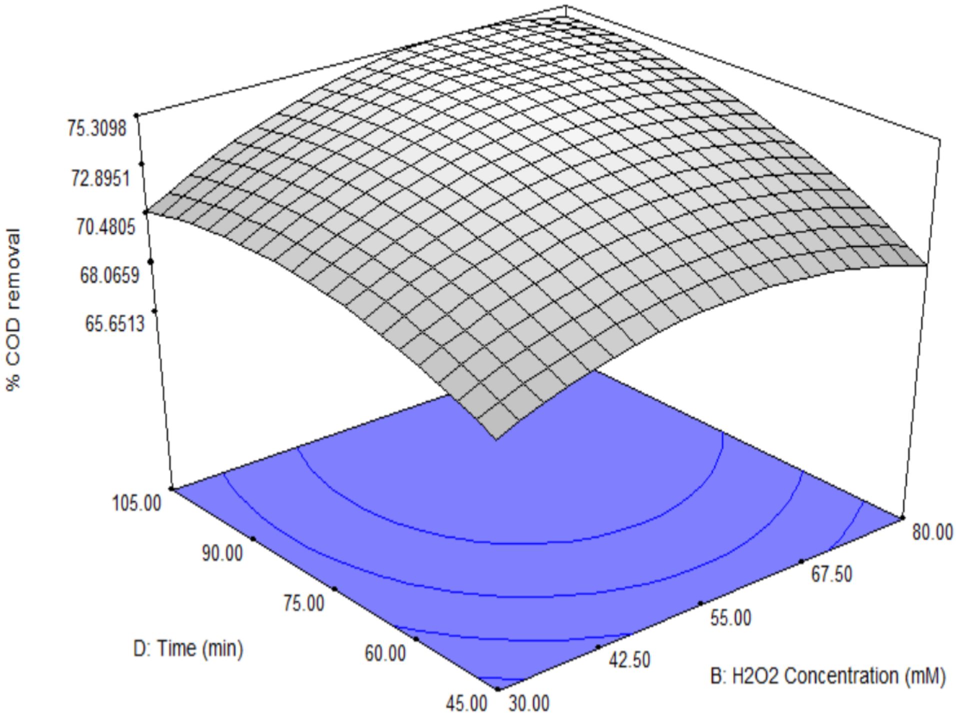
% COD removal
75.3098
72.8951
70.4805
68.0659
65.6513
105.00
90.00
75.00
60.00
45.00
D: Time (min)
30.00
42.50
55.00
67.50
80.00
B: H2O2 Concentration (mM)

Fig. 5(e)

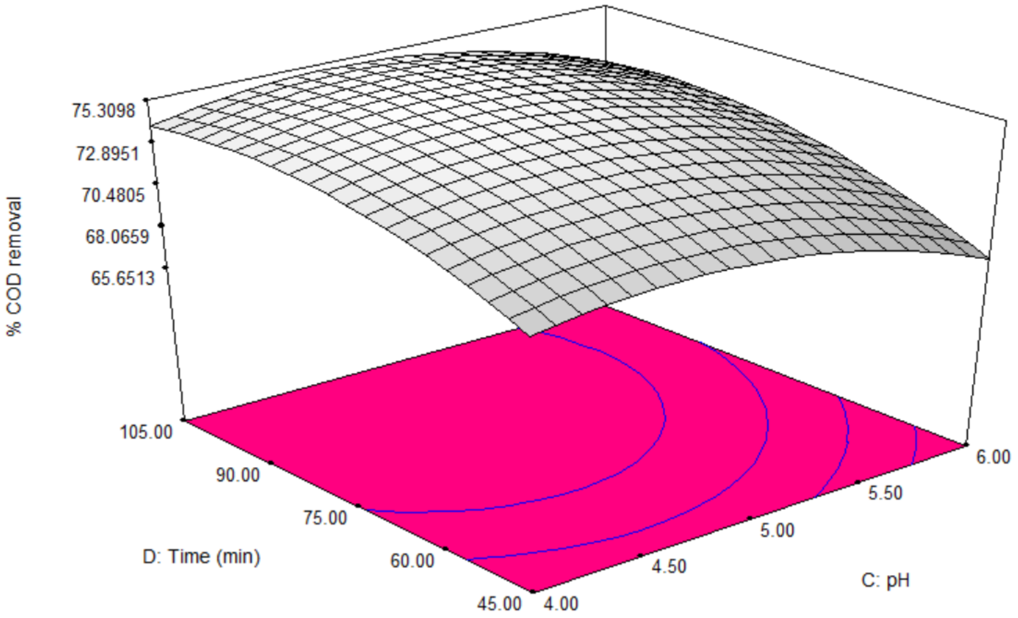

Fig. 5(f)

Fig 5: Effect of (a)catalyst dosage and H_2O_2 concentration (b) catalyst dosage and pH (c) catalyst dosage and time (d) H_2O_2 concentration and pH (e) pH and time on % COD removal

3.2 Catalyst reusability study

To investigate the economic practicality of the heterogeneous Fenton-like process, the stability of $CuFe/SiO_2$ was assessed under optimized conditions (catalyst dosage 0.68 g/L; pH 4.9; H_2O_2 concentration 65.28 mM; reaction time 86.81 min). During the first cycle, the catalyst operated with maximum functionality (74.11% COD removal) since all active surface sites and Cu-Fe redox centers were open for reaction. The catalyst was separated via centrifugation after each run, washed with distilled water, dried, and reused without reactivation. It should be noted that the activity decreased slowly upon reusing it over four cycles, resulting in 69.78% in cycle 2, 60.21% in cycle 3, and 52.23% in cycle 4. The deactivated activity is in line with the expected trend for a heterogeneous Fenton catalyst. This includes partial leaching of active metal species during use as well as the gradual accumulation of recalcitrant carbonaceous residues on the catalyst, which limited the availability of active sites for reaction, as well as decreased effective hydroxyl radical formation. Such behaviour has been widely documented for Cu-Fe-based mixed oxide systems under sequential oxidative use.

3.3 Radical quenching, reaction mechanism and control experiment studies

To validate Cu-Fe/SiO_2 and heterogeneous Fenton-like mechanisms, radical quenching experiments were performed, which unambiguously identified hydroxyl radicals (- OH) as the main ROS contributing to pharmaceutical wastewater degradation at the optimal CCD experimental parameters. In radical quenching tests, tert-butanol (t-BuOH, 1- OH scavenger) and potassium iodide (KI, a scavenger for other non-radicals and bulk -OH) were added to solutions at 10 mM. In the Cu-Fe/SiO_2/H_2O_2 system, radical quenching was highly inhibited with COD removal decreasing from 74.11% (based on the tested run) to 33.9%, equating to ~54% inhibition. Thus, it can be concluded that -OH radicals were the dominant oxidizing agents. On the other hand, quenching by KI resulted in a smaller inhibition of 11.6%, with efficiency reducing from 74.11% to about 62.51%. Thus, limited inhibition suggests that the Cu-Fe/SiO_2/H_2O_2 system occurs predominantly by •OH radicals confined to the surface at catalyst-active sites. Since KI acts predominantly on surface oxidative species and fails to effectively quench freely diffusing radicals (or homogenous Fe-based) pathways, the absence of significant inhibition indicates that leached-Fe Fenton reactions, superoxide or singlet oxygen do not significantly contribute as active species for the tested conditions (Li, et al. 2018, Nath et al. 2022, Shao et al. 2022, Li et al. 2023).

The resulting mechanism occurs through three main steps.

(1) H_2O_2 activation via iron redox cycle (Wang et al., 2024, Hu et al. 2025):

Surface Fe^{3+} is first reduced by H_2O_2 to generate Fe^{2+} and the formation of hydroperoxyl species (•OOH) follows Fenton activation as an occurrence of Fe^{2+} and H_2O_2 generating -OH radicals (•OH) and regenerating Fe^{3+} as shown in equations [1] and [2].

$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + \cdot OOH + H^+ \quad [1]$$

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + \cdot OH + OH^- \quad [2]$$

(2) Synergistic Cu-Fe redox shuttle (Faheem et al. 2018, Wang et al., 2024, Hu et al. 2025):

Cu^{2+}/Cu^+ couples with Fe^{3+}/Fe^{2+} on the catalyst surface, making electron transfer easier and thus accelerating the Fe^{2+} re-generation step where Cu^+ facilitates faster approach and even activates H_2O_2 as well to create more •OH than inherently produced as shown in equations [3] and [4].

$$Cu^{2+} + Fe^{2+} \leftrightarrow Cu^+ + Fe^{3+} \quad [3]$$

$$Cu^+ + H_2O_2 \rightarrow Cu^{2+} + \cdot OH + OH^- \quad [4]$$

(3) Pharmaceutical pollutant degradation (Thomas et al. 2021, Jiang et al. 2026):

The lattice-confined •OH produced at the Cu-Fe sites oxidize the adsorbed pharmaceutical organics. Successive radical reactions create ring-opening, fragmentation and finally mineralization to CO_2 and other inorganic residues. Control experiments validated the heterogeneous reaction of the Cu-Fe/SiO_2/H_2O_2 system. Conducting the reaction in the presence of H_2O_2 only resulted in a low COD removal value (usually 7.6 %), demonstrating that self-decomposition of H_2O_2 minimally contributed to the oxidation. Similarly, applying the catalyst alone without H_2O_2 indicated a COD decrease of 5.8%, suggesting that adsorption or non-radical catalysis played a limited role (Ksibi, 2006, Erasmus et al. 2016, Aljuboury et al. 2017, Kwan & Voelker 2002). For example, to further determine the effect of soluble metal species, the reaction filtrate was tested under similar conditions after centrifugation to remove the catalyst; the obtained filtrate indicated that only 6.1% COD removal occurred, demonstrating that leached Fe or Cu ions played a negligible role in the oxidation (Ksibi 2006, Thomas et al. 2021, Jiang et al. 2026). Thus, collectively these findings support that the catalytic activity of Cu and Fe primarily arises from surface-confined Cu-Fe redox active sites, and thus, Cu-Fe/SiO_2/H_2O_2 operates via a genuine heterogeneous Fenton-like process instead of a homogeneous one (Li et al. 2015, Jiang et al. 2026).

3.3 Optimization study and ANOVA analysis

Table 5 represents the CCD predicated and experimental results (% COD removal) at optimum operating conditions. RSM optimization of COD removal efficiency and subsequent ANOVA statistics confirm the validity and predictability of the resultant quadratic model. The model possesses a fairly high coefficient of determination ($R^2 = 0.9881$), meaning the model accounts for over 98% of the variances of COD removal; the adjusted R^2 (0.9769) is very close to R^2 and implies that very little accuracy is lost with adjustments due to the number of predictors. Furthermore, the predicted R^2 (0.9572) has a substantial correlation with adjusted R^2, where similarly predicted values will hold similar reliability. Moreover, the standard deviation (0.78) and coefficient of variation (C.V. = 1.15%) reflect phenomenal levels of accuracy and repeatability of the experimental endeavours. The Adeq Precision (31.677), a signal-to-noise ratio, exceeds the threshold of 4, suggesting that the model has an adequate signal. Lastly, the low PRESS value (32.34) confirms the model's predictability as well (Sarrai et al. 2016, Deepa et al. 2021, Pasciucco et al. 2025). The model F-value of 88.74 with a corresponding $p < 0.0001$ confirms that the quadratic model is highly significant. Final results of the quadratic equation [5] based on coded factors reveal that catalyst dosage (A), H_2O_2 concentration (B) and reaction time (D) have positive effects on COD removal while pH (C) has a marginally negative one. Furthermore, all squared components (A^2, B^2, C^2, D^2) generated negative coefficients as well, suggesting that a curvature effect occurs and there is a point of optimization instead of a linear relationship for all variables. Lastly, the interaction terms AD and BD are significantly impactful in determining COD removal efficiency, implying that these variables work in conjunction to enhance removal capabilities. The positive linear coefficients of A, B and D suggest that maximum COD removal will occur from increases then levels off. The negative quadratic terms of all four factors (A^2, B^2, C^2, D^2) suggests that this is not the case to extremes as excessive catalyst, excessive oxidant or excessive increases in reaction time do not yield greater proportional removal percentage radical saturation and scavenging prevail. In addition, the highest interaction coefficient is for B and D (0.77 BD) suggesting H_2O_2 dosage and reaction time are the most interacting collaborative parameters. In addition, the interaction terms AB, AC, BC are all relatively small in value suggesting these parameters are not as collaboratively interactive as increasing the other two together meaning they're more independently. Thus, this CCD is effective to determine optimum operating conditions for highest COD removal. Ultimately, these optimization findings suggest that the resultant quadratic model is statistically valid for it is clear that the optimized conditions yield maximum COD removal (~76%) with only moderately adjusted conditions. In conclusion, findings from these optimization steps indicate that the established quadratic model is statistically significant and optimized conditions result in maximum COD removal (~76%) with balanced operating conditions.

Table 5: CCD predicted optimum operating conditions and their experimental and CCD results

Catalyst dosage (g/L)	**H_2O_2 concentration (mM)**	**pH**	**Time (min)**	**% COD removal**	
				CCD (Pre.)	Test Run
0.68	65.28	4.9	86.81	76.07	74.11

Final equation in terms of coded factors:

$$\textbf{\%COD removal} = 74.62 + 2.54\,A + 1.23\,B - 1.22\,C + 1.94\,D - 3.07\,A^2 - 2.15\,B^2 - 1.95\,C^2 - 1.70\,D^2 - 0.00125\,(A*B) + 0.19\,(A*C) + 0.57\,(A*D) + 0.043\,(B*C) + 0.77\,(B*D) + 0.29\,(C*D) \quad [5]$$

Where: A = Catalyst dosage (g L^{-1}), B = H_2O_2 concentration (mM), C = pH, D = Reaction time (min)

4. CONCLUSIONS

This work substantiates a Cu–Fe/SiO_2 heterogeneous Fenton-like catalyst for real pharmaceutical wastewater treatment effectively. According to CCD-based response surface optimization, COD removal is mainly affected by catalyst dosage, H_2O_2 concentration, pH, and reaction time. The removal efficiency of 76% COD with the optimized conditions (0.68 g/L as catalyst dosage; 65.28 mM as H_2O_2 concentration; pH of 4.9; 86.81 min as reaction time) and the significance between experimental and predicted values within the range of $P<0.0001$ confirming that the quadratic model fits well the experimental data ($R^2 = 0.9881$). Compared with conventional single-metal (e.g., Cu/Fe) or unsupported catalysts reported in the literature, Cu–Fe/SiO_2 can better provide active-site dispersion, lower metal leaching, and improved surface-mediated •OH generation to satisfy complex pharmaceutical effluents. However, some shortcomings are inevitable. Catalyst deactivation in multiple cycles indicates that metal may be leached out or catalysts may be fouled on the surface, indicating the need for catalyst regeneration and long-term stability under continuous working conditions will be further evaluated. Besides, cost evaluation, life cycle analysis for spent catalysts' environmental safety and control, and pilot-scale treatment proposal are required for subsequent developments before implementing this catalyst into practice. Therefore, these findings confirm that Cu–Fe/SiO_2 is an effective and stable heterogeneous Fenton-like catalyst for sustainable pharmaceutical wastewater treatment while paving the way for subsequent efforts in real-world applications.

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