

Granular Activated Carbon assisted Ozonation of Cephalexin Antibiotic

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Summary: This study investigates removal of cephalexin using ozonation in the presence of granular activated carbon. Initial experiments were carried out about adsorption of cephalexin onto granular activated carbon, effect of catalytic ozonation, and biodegradability of cephalexin solution. The effect of ozonation on pH, ozone utilization efficiency and decomposition byproducts, was observed. Response surface methodology was adopted to optimize three operating parameters pH of solution, ozone supply and cephalexin concentration. GAC assisted ozonation, was found to be effective in decomposing COD (chemical oxygen demand) and cephalexin from solution. Optimum values of variables were pH from 7-8, ozone supply 30 mg/L and 100 mg/L of cephalexin solution. The complete removal of cephalexin and 60% COD removal was achieved at these optimum input values.

Keywords: Ozonation, Activated Carbon, Optimization, Cephalexin, COD, Water Treatment, Response Surface Methodology

Introduction

Presence of pharmaceuticals and other micro-pollutants in effluents of water treatment plants has increased the risk for distribution of these pollutants into aquatic environment. Persistence of such micro-pollutants is linked to adverse effects for aquatic ecosystem and surrounding population [1-5]. Endocrine disrupting compounds require special attention as these can disrupt the hormonal metabolism of endocrine system and endogenous hormones. A vast variety of synthetic hormones, pharmaceuticals compounds, personal care products, pesticides are suspected in endocrine disrupting category [6, 7]. Cephalexin is sold commercially with names Novolexin or Ceporex etc and is used to treat urinary and skin diseases [8]. It is administered in liquid suspensions, capsules, and Tablets. The adsorption studies for removal of aqueous solutions of cephalexin were followed in [9, 10]. Liu *et al.* [9] compared adsorption capacity of Fe⁺³/Cu⁺² loaded activated carbons and activated carbon for adsorption of cephalexin and found better performance of metal loaded activated carbon. Guo, *et al.* [10], investigated removal of cephalexin using ultrasonic radiations. The authors found 71% reduction in COD level and 50% increase in biodegradability of cephalexin solution at 200 W of radiation dose for 2 hs of radiations. Akhtar, *et al.* [11], reported a study on removal of COD from aqueous solution of cephalexin by ozonation in presence of granular activated carbon catalyst and found 60% removal of COD at optimized conditions.

Adjoining activated carbon as catalyst in ozonation process offsets the limitations in each technology. Activated carbon initiates decomposition of dissolved ozone into oxidant radicals thereby enhancing ozone utilization efficiency. Combining activated carbon and ozone may be helpful for in situ regeneration of activated carbon. It is because; adsorption capacity of activated carbon shrinks quickly on reaching saturation in absence of ozonation. The shutdown absorber column is frequent for replenishing exhausted active carbon. Ozone activated carbon combination may solve the problem. Use of activated carbon might be useful in total demineralization of water solution. Active sites in activated carbon induce decomposition of ozone there by producing oxygen atom and hydroxyl radicals (OH) [12, 13].

RSM is used to optimize operating responses in minimal number of experiments unlike classic methods that are based on sequential optimization of parameters. Statistical methods can design experiments, build models, evaluate effectiveness of operating parameters, and optimize operating conditions for desired responses [14]. Central composite design is normally applied to second order models. This contains axial points, cubic points and centre points. Cubic points rotate around a centre point to optimize assessment of various points. Centre composite design can effectively optimize operating variables in different lab scale problems.

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In this study, aqueous solution cephalixin was ozonated in the presence of granular activated carbon. The performance was measured in their capacity to remove CEX and COD from solution. The ozone utilization efficiency and products of decomposition were determined. The response was optimized using response surface methodology for input parameters CEX concentration, pH and ozone concentration.

Experimental

The batch reactor was a 250 ml three-neck flask and temperature was controlled through a water bath. The solution mixture was stirred with a magnetic stirrer continuously to improve gas liquid contact. Ozone was generated through a commercial reactor Ozonia Lab 2B generator using oxygen as gas feed with maximum ozone generation capacity of 10 g/h. The ozone generator was capable of producing up to 50 mg/L ozone supply at gas flow rate of 0.5 l/min. Reactor exhaust gas was washed with KI solution. Oxygen/ozone gas dosage and temperature were fixed at 50 mg/L and $26 \pm 1^\circ\text{C}$, respectively, in all experiments.

In a typical experimental run, 200 ml of cephalixin solution was added to three-neck flask. The solution was stirred at constant rate of 300 rpm/min using magnetic stirrer. The GAC dose was added just before start of experiment and ozone-laden gas was passed through solution via metallic diffuser subsequently. The 5 ml aliquot of samples were drawn from solution at different time intervals and were quenched by adding several drops of 0.05 M sodium thiosulfate solution.

Samples were passed through 0.45 μm nylon filter papers before HPLC or COD analysis. Synergi Hydro-RP (250 mm \times 4.6 mm, 5 μm) column was used to determine concentration of CEX in samples after the experiment at 254nm using mobile phase acetonitrile and in (25:75 v/v) ratio. The pH of mobile phase was maintained at 4.3 using dil. CH_3COOH and its flow rate was 1.5 ml/min. The pH of mobile phase was maintained for $\text{CH}_3\text{COONH}_4$ solution after filtration from 0.45 μm membranes. Further details can be found in [15]. GC-MS analysis was carried out using a Perkin Elmer autosystem gas chromatograph analysis fitted with a flame ionization detector (FID), on column injector and fused silica capillary column (BP5 25 m \times 0.32 mm i.d). Helium gas flow was set at 0.9 ml/min. COD was analyzed by HACH DR 5000. Dissolved ozone concentration was measured according to Rakness method [16]. Amount of ozone consumption (mg) was measured using BMT 964 BT analyzer (Germany) according to

Eq. (1) using modified method as described in [17, 18].

$$\text{O}_3 \text{ consumption} = \Delta\text{O}_3 \times Q \times \Delta t \quad (1)$$

where ΔO_3 is change in gas phase concentration of O_3 across reactor (mg/L), Q is gas flow rate (l/min), and Δt is time interval between sampling. The central composite rotatable design (CCRD) was applied for optimization of three operating parameters i.e. inlet ozone dose (mg/L), concentration of cephalixin (mg/L) and pH. The desired responses were % removal of cephalixin and COD. The quadratic model was developed after performing analysis of variance (ANOVA) on significant terms. The contour plots measured the effect of interacting variables.

Results and Discussion

GAC as Ozonation Catalyst

The BET surface area of GAC was 944.31 m^2/g shown in Table 1 showing its significance as porous material. The microporous character seems dominant as compared to mesoporus, suggesting the presence of deep pores in bottle neck style. It is assumable that physical sorption will dominate since there may be little chance for interaction between CEX and GAC. GAC seems to contain sufficient pore volume and BET surface area to act as adsorbent for pollutant in solution and to provide a base for catalytic ozonation. The hysteresis loop for N_2 -desorption deviated from N_2 -adsorption curve at P/P_0 values of 0.5 - 1.0 shown in [15]. Such sort of adsorption-desorption curves resemble with type I of IUPAC classification for low relative pressure and type IV for high relative pressure [19].

Fig. 1 shows the adsorption of CEX on activated carbon and is an indication that absorptive catalysts may be helpful in concentrating substrate mass. CEX removal increased from 10% to 70 % as GAC dose increased from 1-4 g/L. This region can be regarded as sharp increase in removal of CEX concentration. However, excessive GAC amount did not reflected proportional effect on CEX removal. As dose increased that extended, saturation limit of GAC dose and adsorbed more of CEX. However, for high GAC dose, CEX concentration was not enough to saturate adsorbent completely. As a result, rate of adsorption of CEX onto adsorbent decreased. The rate of adsorption depends upon relative concentration of adsorbate and saturation level of adsorbent. The decrease in concentration of CEX in aqueous solution may be plausible reason for decrease in adsorption rate. Liu *et al.* [9] reported decrease in amount of CEX adsorbed onto GAC for

longer times that 90% of CEX was adsorbed in 2 hr and remaining was adsorbed in several hs.

Table-1: BET surface area and pore volume of GAC used in experiments

Sample	T _c (°C)	BET (m ² /g)	V _{mes} (cm ³ /g)	V _{mic} (cm ³ /g)	V _{Total} (cm ³ /g)
GAC	126	944.31	0.1654	0.3217	0.4871

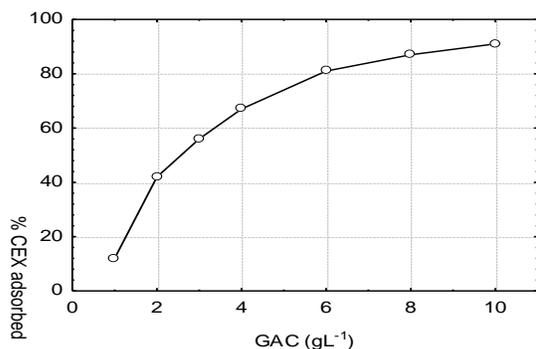


Fig. 1: Effect of GAC dose on adsorption of CEX Conditions: Time 1 h; Temperature 26 ± 1 °C, CEX concentration, 200 mg/L.

Fig. 2 shows that complete removal of CEX was achieved for > 3 g/L of GAC dose. Removal of COD increased from < 20 % in the absence of GAC catalyst to > 40% for GAC dose of 5 g/L. The ozonation may require extended time duration to achieve significant degree of mineralization i.e. COD removal. That because, secondary products of ozonation are relatively stable to ozone treatment and hydroxyl radicals may be alternative solution to these stable byproducts [20]. Overall, GAC dose was found effective in mineralizing cephalixin from solution compared to in absence of any GAC.

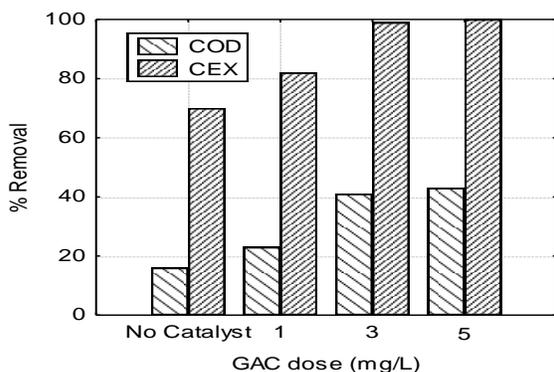


Fig. 2: Effect of GAC dose on removal of CEX and COD during ozonation Condition: CEX conc. 200 mg/L, pH 7-7.5, O₃ dose 21 mg/L, Time CEX 5 min, COD 15 min, Temperature 26 ± 1°C.

Fig. 3 shows variations in pH during ozonation of cephalixin solution. The ozonation of

cephalexin tends to produce smaller molecules that are acidic in nature such as carboxylic acid [21] leads to decrease in overall pH. The rate of decrease in pH was higher at initial stages of ozonation and stabilized towards end. The stability of pH at end stage is attributed to i) decrease in rate of reaction as concentration of cephalixin goes down and ii) carboxylic acidic groups act as weak acids. The accumulation of weak acids in acidic pH regime does not influence change in pH to significant extent. Fig. 3 also describes removal of COD from cephalixin solution per unit amount of ozone consumed. The removal of COD was about 9 mg/mg O₃ for initial 100 seconds and gradually decreased to below 6 mg/mg O₃ for longer time duration. The consumption efficiency of ozone seems better at initial stages of ozonation. The plausible reason may be fresh solution of COD when decomposition of COD was at faster rates comparatively. The ozone consumption efficiency at later stages decreased gradually corresponding to decrease in COD concentration. In dilute solution, ozone may act as an excess reagent meaning ozone may leave the reactor without decomposing COD. Due to similar reason, concentration of O₃ at exhaust of reactor went up. It is true that decomposition of COD decreases gradually, ozonation process needs to operate for longer times to achieve significant mineralization.

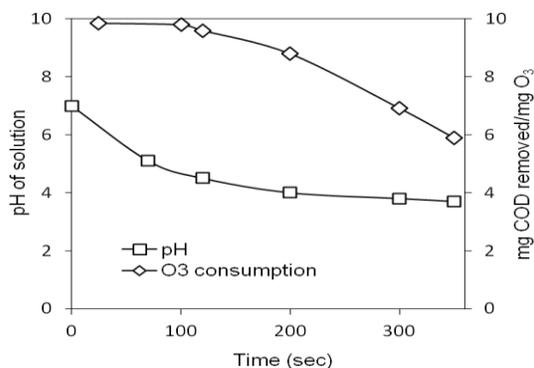


Fig. 3: The effect of time on i) change in pH during ozonation and ii) on amount of COD removed per unit gram of O₃ consumed. (Initial pH = 7, initial COD 290 mg/L).

Fig. 4 shows increase in biodegradability of cephalixin solution during ozonation. There was 30% increase in biodegradability for 15 min of ozonation.. However, as ozonation time was increased beyond 15 min little effect of further ozonation was found on biodegradability. That may indicate refractory nature of secondary by-products produced during ozonation. The biodegradability was enhanced by 58% after 45 min of ozonation. Organic compounds having

BOD₅/COD value more than 0.3 are biodegradable in natural environment [22]. Therefore, short time exposure of cephalixin solution is enough to eliminate its refractory nature of cephalixin.

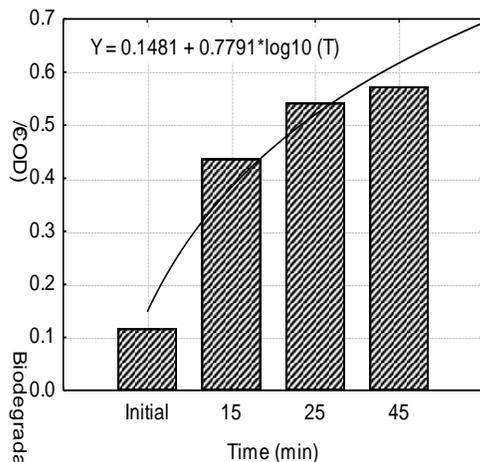


Fig. 4: Increase in biodegradability of CEX solution during ozonation in presence of GAC.

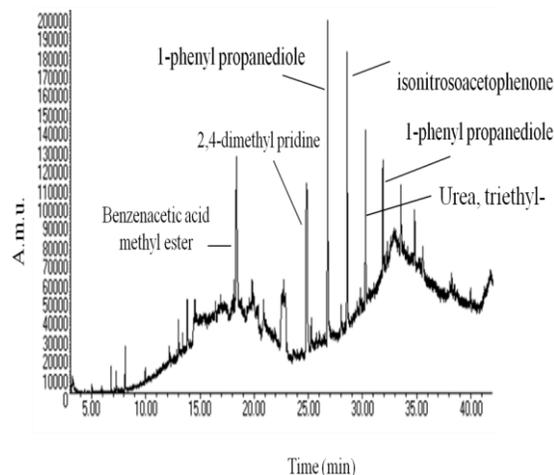


Fig. 5: Decomposition byproducts of CEX ozonation in presence of GAC.

The generation of decomposition byproducts during ozonation of CEX in presence of GAC catalyst is described in Fig. 5. The absence of any peak for CEX indicates its complete removal during 15 min of ozonation. The resulting by-products were mainly alcohols (1-phenyl propane-diol), ketenes (iso-nitroso-acetophenone), and esters (urea, triethyl ester, benzenacetic acid) etc. These decomposition byproducts indicate that mainly products were of

intermediate molecular sizes. This demonstrated that these byproducts were stable to applied ozone dose

Response Surface Optimization

Design of experiments consisted of 16 experimental runs out of which 2 centre points, 6 star points and 8 were full factorial design points. Under given experimental conditions, experiments were performed to obtain two responses. Table 2 gives information about input and response parameters. The removal of CEX was 100% in most of experimental runs while maximum of 56% COD was removed. The regression analysis of two responses can be presented in the form of following quadratic models as given in Eqs. (2) and (3), respectively.

$$\begin{aligned} \% \text{ CEX removal} = & -20.428 + 10.378 * X_1 - 0.527 * X_1^2 + 5.876 * X_2 \\ & - 0.083 * X_2^2 - 0.068 * X_3 - 0.0001 * X_3^2 - 0.0761 * X_1 * X_2 \\ & - 0.0008 * X_1 * X_3 \end{aligned} \quad (2)$$

$$\begin{aligned} \% \text{ COD removal} = & 30.939 + 2.161 * X_1 + 0.2163 * X_1^2 + 0.01296 * X_2 \\ & + 0.02478 * X_2^2 - 0.1959 * X_3 - 0.00034 * X_3^2 - 0.07413 * X_1 * X_2 \\ & - 0.00858 * X_1 * X_3 + 0.00234 * X_2 * X_3 \end{aligned} \quad (3)$$

where X₁ is pH, X₂ is ozone dose (mg/L) and X₃ is concentration of CEX (mg/L). Positive terms cause increase in COD removal negative terms cast negative impact [23].

The values of r² were 0.9521 indicating offset of 4.5% between actual and predicted CEX response values. The values of adjusted r² (0.9340) also indicate reliability of model. This may highlight adequacy of model to predict removal of cephalixin within acceptable error limit. The predicted model was tested with analysis of variance (ANOVA) for F-value and p-value (Table 3). Predicted model for CEX was significant (p-value 0.03008). Five terms (X₁, X₂, X₁², X₂² and X₁₂) were significant with p-value < 0.05. The order of significance according to F-value was X₂² > X₂ > X₁² > X₁₂ > X₁. The improved model for % CEX removal was obtained Eq. (4) after eliminating insignificant terms from Eq. (2).

$$\begin{aligned} \% \text{ CEX removal} = & -20.428 + 10.378 * X_1 - 0.527 * X_1^2 \\ & + 5.876 * X_2 - 0.083 * X_2^2 - 0.0761 * X_1 * X_2 \end{aligned} \quad (4)$$

Table-2: Complete experimental design of uncoded values and experimental response variables.

Runs	Input variables matrix (Uncoded experimental design)			Response variables	
	pH(X_1)	O ₃ (mg/L)(X_2)	CEX (mg/L)(X_3)	% COD removal	% CEX removal
1	4	16	100	30	75
2	4	16	300	18.4	55
3	4	35	100	56.2	100
4	4	35	300	49.5	94
5	10	16	100	45.1	90
6	10	16	300	19.5	85
7	10	35	100	64	100
8	10	35	300	53.4	90
9	7	21	200	32	93
10	2	21	200	24.6	60
11	12	21	200	48.2	84
12	7	4	200	28	18
13	7	38	200	48.1	98
14	7	21	24	54.0	100
15	7	21	376	29.0	75
16	7	21	200	34.6	93

Table-3: ANOVA table for removal of CEX from solution.

Source	Sum of Squares (SS)	Degree of freedom	Mean Square	F-value	p-value
Model					0.03008
X ₁	296.89	1	296.895	9.4258	0.00377
X ₁ ²	406.32	1	406.321	12.8998	0.01148
X ₂	1779.96	1	1779.962	56.5103	0.00015
X ₂ ²	1645.39	1	1645.392	52.2379	0.00035
X ₃	431.27	1	431.276	13.6921	0.43214
X ₃ ²	14.43	1	14.430	0.45812	0.52372
X ₁₂	312.19	1	312.192	9.91147	0.01985
X ₁₃	15.125	1	15.125	0.48019	0.51425
X ₂₃	17.141	1	17.141	0.54419	0.48853
Error	188.98	6	31.498		
Total-SS	7161.75	15			
R ²	0.9736		Adjusted R ²	0.9340	

Similarly, value of r^2 (0.9724) and adjusted r^2 (0.932) described accuracy and significance of predicted response for COD removal in Eq. (3). ANOVA analysis was also performed for COD quadratic model (Table 4). The p-value of model was 0.00676, i.e., model was significant for prediction of COD response. The order of significance of significant terms (p-value < 0.05) was $X_2 > X_1 > X_3 > X_3^2 > X_2^2$. Improved model after elimination of insignificant terms was obtained as follows Eq. 5.

$$\% \text{ COD removal} = 30.939 + 2.161 * X_1 + 0.01296 * X_2 + 0.02478 * X_2^2 - 0.1959 * X_3 - 0.00034 * X_3^2 \quad (5)$$

Table-4: ANOVA table for removal of COD from solution.

Source	Sum of Squares	Degree of freedom	Mean Square	F-value	p-value
Model					0.00676
X ₁	434.78	1	434.78	46.13	0.00049
X ₁ ²	27.93	1	27.93	2.964	0.13589
X ₂	976.35	1	976.36	103.61	0.00005
X ₂ ²	71.82	1	71.82	7.621	0.03282
X ₃	392.11	1	392.11	41.61	0.00065
X ₃ ²	142.10	1	142.10	15.07	0.00814
X ₁₂	0.028	1	0.0285	0.003	0.95793
X ₁₃	0.36	1	0.3613	0.0383	0.85123
X ₂₃	9.42	1	9.4263	1.0003	0.35585
Error	56.51	6	9.4234		
Total SS	2073.81	15			
R ²	0.97274		Adjusted R ²	0.93184	

Contour Plots for CEX Removal

The removal of CEX observed sharp increase as a function of inlet ozone concentration over dose range 4 mg/L to 40 mg/L (Fig. 6a). Removal of CEX virtually achieved maximum for about 30 mg/L of inlet ozone dose. On the other hand, concentration of CEX did not influence much of removal pattern. For a given concentration of CEX, rate of reaction will depend upon inlet ozone dose, only. When sufficient ozone dose is available to react with CEX, rate of removal will be fast irrespective of initial CEX concentration. However, time for complete removal of CEX may slightly increase at low O₃/CEX ratio. This is true for concentrated CEX solution. The interaction effect of pH and O₃ supply is shown in Fig. 6b. By varying pH of solution from 4-10, O₃ supply varied from 15-25 mg/L for complete removal of CEX. Since lower concentration of O₃ supply is preferred, inlet O₃ supply of 15-20 mg/L would be sufficient at pH ~7-8. The interacting role of pH and CEX concentration is shown in Fig. 6c. CEX removal depended more on pH than CEX concentration. CEX was possible to remove completely from solution at pH 8 virtually all concentrations of CEX up to 350 mg/L. The pH 8 was considered an optimum value for effective

ozonation. The dependence of CEX removal on initial concentration of CEX in solution was agonistic and less significant.

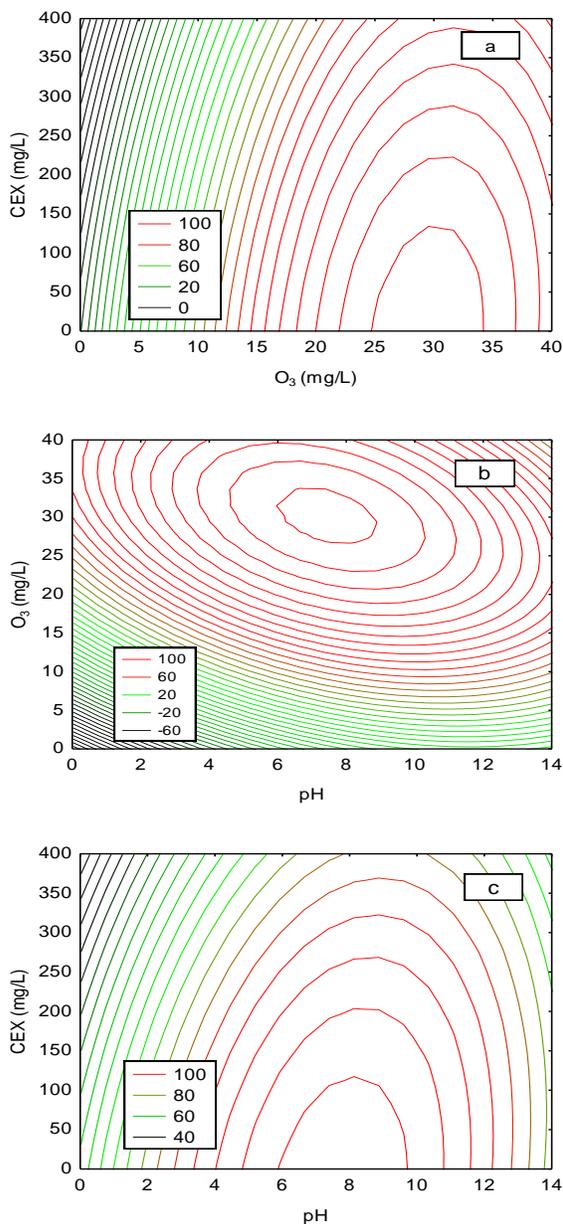
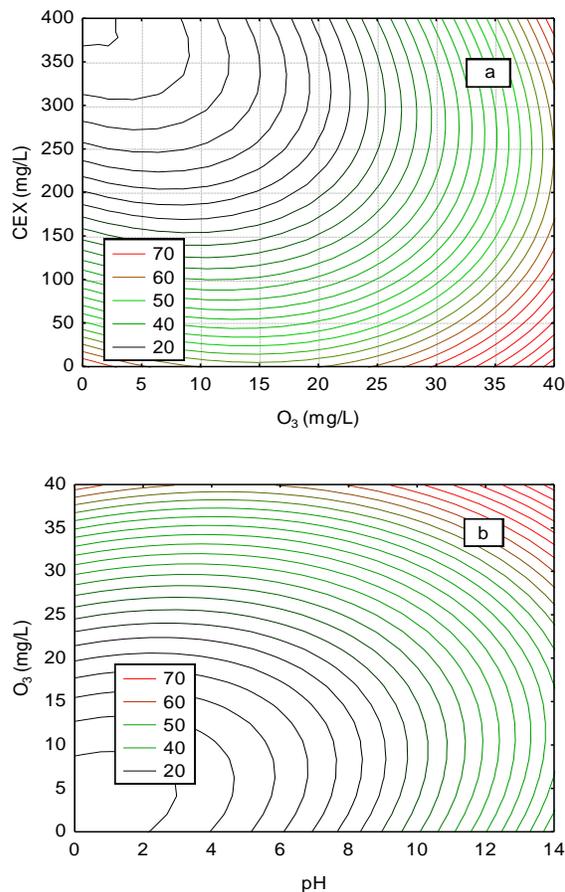


Fig. 6: Contour plots for effect of interaction variables on CEX removal. Centre point value was selected for constant input variable.

Contour Plots for COD Removal

Contour plots representing effect of input variables on COD removal are shown in Fig. 7. Concentrated solutions of CEX imparted agonistic effect on removal of COD (Fig. 7a). More than 60 %

removal of COD was achieved for ozone dose (30 mg/L) at intermediate concentration of CEX (100 mg/L). The concentration of CEX was less influencing compared to ozone concentration. For O₃ dose, on other hand, removal of COD increased from 20-60 mg/L for O₃ supply of 10-40 mg/L. However, effect of change in O₃ dose was minimal for dose range of 30-40 mg/L. The O₃ dose of 30 mg/L can be regarded as optimum for removal of COD. To extended increase in removal of COD above 60 %, extended duration of ozonation may be a better option. Extending time to beyond 20 min will encourage higher efficiency. The interaction effect of pH and O₃ supply is shown in Fig. 7b. To achieve more than 70 mg/L of COD removal, pH required to be 10-12 pH and O₃ supply beyond 40 mg/L. It represented refractory nature of COD degradations. Both input variables exerted positive influence on removal. To achieve complete removal of COD from solution, concentrated O₃ supply at high pH may be associated with large ozonation times. Similar conclusion is deducible from Fig. 7c that beyond 90% of COD removal was achievable only for CEX concentrations of 50 mg/L. For concentrated solutions, efficiency of ozonation process reduced sharply.



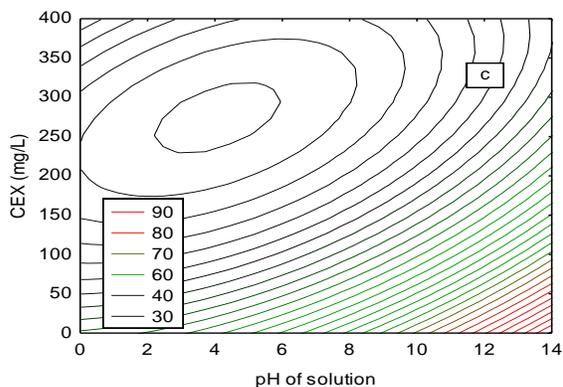


Fig. 7: Contour plots for effect of interaction variables on COD removal. Centre point value was selected for constant input variable

Conclusions

The removal of cephalexin and COD was studied by ozonation in presence of granular activated carbon in a batch stirred reactor. GAC with BET surface area $944.31 \text{ m}^2/\text{g}$ adsorbed 80% of CEX from solution 6 g/L and 90% at 10 g/L in 1 hr. GAC catalyst removed 22% extra COD and helped in removing CEX completely compared to without GAC catalyst run. Optimum dosage of GAC catalyst was selected as 3 g/L since it gave complete removal of CEX from solution and nearly same COD removal as 5 g/L. Ozone consumption decreased from 10 mg of COD removed per mg of O_3 to 6 mg of COD per mg of O_3 at 350 seconds of ozonation. Biodegradability of solution greatly increased beyond COD/BOD₅ of 0.3 for short exposure of ozonation. The decomposition products indicated various compounds produced during ozonation of cephalexin might be easily biodegradable. Optimization studies found that removal of CEX required relatively lower amount of ozone dosage compared to COD. Removal of CEX was completely virtually for 15-20 mg/L of ozone supply at pH 7-8. The optimum value of removal of COD was 60%. Ozone supply and pH were positively influencing variables and cephalexin concentration was agonistic influencing variable.

NOMENCLATURE

ANOVA	Analysis of variance
CCRD	Central composite rotatable design
CEX	Cephalexin antibiotic
COD	Chemical oxygen demand
GAC	Granular activated carbon
HPLC	High performance liquid chromatography
RSM	Response surface methodology

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