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Application of response surface methodology for heterogeneous catalytic removal of paracetamol by OMS-2/persulfate

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ABSTRACT

In this study, paracetamol removal by OMS-2 (manganese oxide octahedral molecular sieves) as a novel catalyst and persulfate (PS) was investigated. The response surface methodology was used to model paracetamol removal, optimize operational parameters, and determine the impact of operational parameters. OMS-2 amount, persulfate concentration and paracetamol concentration were chosen as operational parameters in central composite design technique. The level of OMS-2 was between 0.025 and 0.50 g/L, while persulfate and paracetamol levels were 0.50–10.00 g/L and 5.00–250.00 mg/L, respectively. The influence of these three independent variables on paracetamol removal was evaluated using ANOVA. According to the results of variance analysis (ANOVA), the quadratic model was statistically significant ($P < 0.0001$), and the determination coefficient value (R^2: 0.9662) was high. The high coefficient of determination of the quadratic model showed that the experimental results fit well with the predicted results, that is, the model was valid for predicting the experimental results. Each independent variable was effective. The desirability function demonstrated that optimum conditions were OMS-2 amount of 0.40 g/L, persulfate concentration of 5.93 g/L, and paracetamol concentration of 54.66 mg/L for maximum paracetamol removal. The OMS-2/PS system exhibited excellent catalytic performance for paracetamol removal.

Keywords: OMS-2; Optimization; Paracetamol; Persulfate; Response surface methodology

1. Introduction

Pharmaceutically active compounds are frequently detected in environmental media such as surface waters, groundwater and soil. The contamination of natural resources with such compounds has brought environmental research to the fore. Thousands of tons of pharmaceutically active compounds are excreted without being metabolized or as active metabolites and are discharged into the sewer every year. These compounds can eventually reach surface water and even drinking water. Paracetamol (acetaminophen or N-acetyl-p-aminophenol) is the most widely used pain medication and is available on prescription and over-the-counter in the United States. For example, between 2001 and 2005, 24–29 million doses of paracetamol were sold. In parallel with these data, paracetamol is one of the most frequently identified anthropogenic compounds in rivers and groundwater at levels up to μg/L [1]. Concentrations of 10–65 μg/L have been reported in drinking waters in some cities in the United States. Also it was detected in surface waters (1.38–15.7 μg/L) and groundwater (0.38 μg/L) [2]. On the other hand, in studies on paracetamol metabolism in humans, it has been suggested that paracetamol-induced hepatoxicity is the most important cause of acute liver failure (ALF) in the USA and reactive metabolites of paracetamol can contribute to the development of drug-induced toxicity [1]. It is toxic to organisms living in water and land, even at very low concentrations and has an endocrine-disrupting effect

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on some fish and crustacean species. This leads to disruption in offspring production, developmental abnormalities, sex hormone alteration, and increased mortality in some cases [3]. Like other popular pharmaceuticals, paracetamol and its metabolites are discharged into wastewater via feces and possibly due to improper disposal. Paracetamol is degraded quite effectively by biological processes, but still, noticeable concentrations are found in wastewater treatment plant effluents or surface waters. Despite its degradation in wastewater treatment plants, the widespread use of paracetamol enables very high loads to reach natural environments. The biodegradation of paracetamol takes days or even months [4]. In addition, it can turn into toxic compounds with chlorination processes used in wastewater treatment plants. Therefore, it is necessary to develop effective treatment processes to limit the presence of paracetamol in aquatic environments [5]. It was detected in the influent at a 14.0–67.5 μg/L concentration in Gyeongsang public wastewater treatment plants in South Korea. The concentration of paracetamol in the influent and effluent of a conventional wastewater treatment plant in Jordan (USA), were 36.7 μg/L and 0.041 μg/L, respectively [2].

Various treatment methods such as ozonation, H_2O_2/UV, TiO_2 /UV, electrochemical and photo-Fenton are recommended for paracetamol removal in the literature [6]. However, with ozonation and H_2O_2/UV, only partial mineralization up to 30% and 40% respectively in the pH range of 2.0–5.5 is achieved. Therefore, more appropriate methods should be applied to ensure complete mineralization. As the techniques used for paracetamol removal are both expensive and inadequate and cause the formation of some highly toxic by-products, it makes it necessary to explore other potential solutions [7]. For this purpose, it is seen that some modifications have been made to the existing techniques for the effective removal of pollutants from aqueous environments and different studies have been carried out to develop new techniques. It cannot be underestimated that catalytic processes take an important place among the techniques studied. An effective process that will completely degrade organic compounds in an aqueous environment is the advanced oxidation process. The advanced oxidation processes are based on the formation of reactive species such as hydroxyl radicals that have a strong oxidizing potential in the mineralization of organic pollutants to simple compounds, CO_2 and H_2O [8]. Various types of oxidizing agents such as permanganate, ozone, H_2O_2, persulfate alone or in combination with other oxidants are used for the degradation of organic compounds [9]. Persulfate and sulfate radicals are applied in wastewater treatment and degradation of organic compounds and are recommended as an alternative to HO· radicals due to their high redox potential (2.5–3.1 V). Sulfate radicals (3.4×10^{-5} s) have a longer lifespan than HO radicals (2×10^{-8} s), so these radicals are more likely to react with organic pollutants [9,10]. In general, peroxymonosulfate (PMS) and peroxydisulfate (PDS) are used as oxidants in persulfate-based chemical oxidation processes and are strong oxidizing agents with a standard redox potential of 1.82 and 2.01 V, respectively. PMS and PDS can break down organic pollutants at different degradation rates, leading to differences in their structure and properties. Although H_2O_2 and persulfate are thermodynamically strong oxidizers and can degrade organic pollutants, the direct reaction of H_2O_2 or persulfate with most organic pollutants is slow [9]. Therefore, H_2O_2 and $S_2O_8^{2-}$ systems are activated mostly by alkali, activated carbon, heat, UV, transition metals (Fe^{2+}, Mn^{2+}, Ce^{3+}, Ni^{2+}, V^{3+}, Ru^{3+}, and Co^{2+}), and natural minerals [7,11]. All these activation processes involve different mechanisms for generating free radicals [9].

Manganese oxides are common metal oxides found in soil and have low toxicity to the environment. As promising alternative catalysts to iron-based materials, a wide variety of manganese oxides have been applied in Fenton and Fenton-like reactions for the generation of hydroxyl radicals [12]. Tang et al. [13] in their studies investigating the activation potential of peroxymonosulfate using manganese oxide nanoparticles, found that tetragonal structured Mn_3O_4 nanoparticles exhibit high catalytic activity for dye degradation and can be used in a wide pH range. In the literature, cryptolelane type manganese oxide OMS-2 has been used in the heterogeneous activation of peroxymonosulfate for the removal of Acid Orange 7 dye from aqueous solution. It has been found that the catalyst is highly active in the degradation of dyes [14].

Response surface methodology or RSM is a collection of mathematical and statistical techniques useful for modeling and analyzing problems. This method can optimize several responses affected by more than one factor to obtain the optimum value. RSM consists of 3 stages including design and experiments, response surface modeling, and optimization of the process or product [15–17]. Most of the package programs produced for the application of the response surface method use a quadratic polynomial model.

In the literature, there are very few studies on the use of the OMS-2/persulfate system for the removal of various pollutants. In our previous study, the OMS-2/persulfate process was used for paracetamol removal and it was determined that the amount of OMS-2, persulfate and paracetamol concentrations were important factors affecting the paracetamol removal by OMS-2/persulfate [3]. However, to our knowledge, there is no research on the optimization of paracetamol removal from aqueous solution by OMS-2/persulfate using RSM as a statistical analysis method. For this purpose, in this study, the interactive effects of more than one parameter (OMS-2 amount, persulfate concentration, and paracetamol concentration) for paracetamol removal from aqueous solution using the RSM with central composite design (CCD) were investigated and the optimum conditions were determined. Statistical analysis of the model was performed by using ANOVA. The interaction among the process variables and their contribution were assessed.

2. Materials and methods

2.1. Chemicals and reagents

Paracetamol (4-acetamidophenol, $C_8H_9NO_2$, 98%) used for this study was purchased from Alfa Aesar (France). Its molecular weight, density and solubility (20°C) are 151.17 g/mol, 1.293 g/cm^3 and 14 mg/mL, respectively [18]. Potassium persulfate ($K_2S_2O_8$) was obtained from Merck (Germany). HPLC-grade methanol was purchased from Chem-Lab (Belgium). Other chemicals used for this experimental research are of analytical purity.

2.2. Catalytic degradation experiments

OMS-2 production was reported in detail in our previous study [19]. The experimental runs were performed in flasks of 250 mL at working volume of 100 mL. Each experimental run was initiated by adding the required amount of OMS-2 and persulfate to 100 mL of paracetamol solution at a specific concentration. Each experimental run was performed on an orbital shaker at 30 °C and 150 rpm.

2.3. Determination of paracetamol

The molecular formula of paracetamol is presented in Fig. 1. Periodically, a 5 mL sample was drawn, centrifuged (Nuve NF 200), and filtered through a 0.22 μm PTFE filter. The measurement was made using high-performance liquid chromatography (HPLC) (Shimadzu) equipped with a C18 column (5 μm, 4.6 mm × 150 mm). As the mobile phase, a mixture of methanol, ultrapure water and acetic acid (35/65/0.1; v/v/v) was used at a flow rate of 0.4 mL/min. Detection was performed with a diode array detector at 243 nm.

2.4. Experimental design

Response surface methodology was employed to determine the optimum conditions for maximum paracetamol removal and to understand the roles of the variables affecting each other.

In the preliminary trials performed in our study [3], OMS-2 amount, persulfate concentration and paracetamol concentration were found to be important factors affecting paracetamol removal by the OMS-2/PS system. These were chosen as independent variables and their ranges are given in Table 1. Experimental runs were determined according to the experimental plan of CCD. Experimental runs were completed with 20 experiments. Second-order polynomial coefficients were calculated and analyzed using the Design-Expert Software (version 7.0) statistical package. Statistical analysis of the model was performed by using ANOVA. OMS-2 amount (*A*), persulfate amount (*B*) and paracetamol concentration (*C*) as independent variables were studied at five different levels (–α, –1, 0, 1, +α) in the design. Paracetamol removals (%) obtained at 5th, 10th, and 15th minutes were taken as the responses of the design experiments, and the experimental and predicted paracetamol removals (%) are presented in Table 2. ANOVA results are given in Tables 3 and 4.

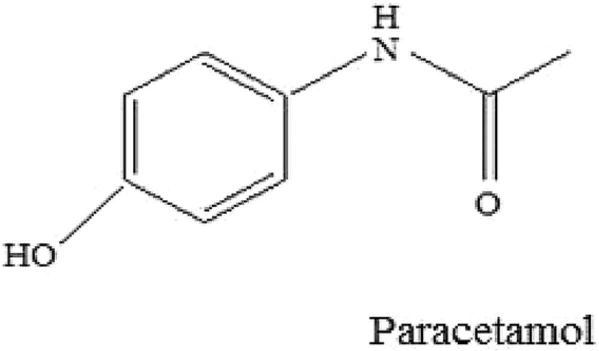

Fig. 1. The molecular formula of the paracetamol.

3. Results and discussion

3.1. Model fitting and statistical analysis

Based on the results of experimental studies and after data analysis, the quadratic polynomial equation given below was obtained as empirical relationships between the paracetamol removal (after 5 min) and OMS-2 amount (*A*), persulfate concentration (*B*), and paracetamol concentration (*C*) (Eq. 1):

$$\text{Paracetamol removal}\left(\%\right): R1: +67.54 + 17.54A + 6.55B - 11.35C - 1.90AB + 1.15AC + 3.63BC - 4.13A^2 - 2.15B^2 + 2.30C^2 \quad (1)$$

The direction (positive or negative) and intensity of the effect of OMS-2 amount (*A*), persulfate concentration (*B*) and paracetamol concentration (*C*) on the paracetamol removal can be understood by looking at the factors in front of the *A*, *B* and *C* terms [20]. According to the developed model, the increasing order of the effect of independent variables on paracetamol removal was persulfate concentration (*B*) < paracetamol concentration (*C*) < OMS-2 amount (*A*). Eq. (1) shows that the paracetamol concentration has a negative effect (β_3: –11.35), whereas OMS-2 amount (*A*) and persulfate concentration (*B*) have positive effects on the paracetamol removal efficiency. The adequacy of the model equation was determined using an analysis of variance (ANOVA). The model *F*-value of 31.74 and the *p*-value of <0.0001 indicate that the model was significant. The coefficient of determination (R^2) revealed that 96.62% of the variability in the response can be explained by the regression model of paracetamol removal [20]. It also revealed that 3.38% of the total variation could not be explained by the model. The adjusted determination coefficient of 93.57%

Table 1
Levels of the parameters in CCD

Independent variables (concentration)	Symbol code	Range and levels				
		–1,682(–α)	–1	0	+1	+1,682(+α)
OMS-2 amount (g/L)	*A*	0.025	0.121	0.260	0.400	0.500
Persulfate conc. (g/L)	*B*	0.50	2.43	5.25	8.07	10.00
Paracetamol conc. (mg/L)	*C*	5.00	54.66	127.50	200.34	250.00

Table 2
CCD matrix, response results

Runs	Variables			Responses						
				Paracetamol removal (%), t: 5 min		Paracetamol removal (%), t: 10 min		Paracetamol removal (%), t: 15 min		Paracetamol removal (%), t: 180 min
	A	B	C	Exp.	Predic.	Exp.	Predic.	Exp.	Predic.	Exp.
1	0.12	8.07	54.66	63.6	63.3	65.4	63.8	73.5	71.3	80.5
2	0.40	2.43	54.66	92.8	90.3	96.4	92.7	97.0	92.0	97.8
3	0.26	5.25	127.50	71.4	67.5	80.9	77.0	86.4	82.7	99.4
4	0.40	8.07	54.66	85.3	92.3	96.3	99.8	87.8	95.8	92.3
5	0.03	5.25	127.50	23.7	26.4	23.2	29.4	27.9	35.5	63.5
6	0.40	8.07	200.34	76.5	79.2	85.4	88.0	92.3	94.1	95.2
7	0.26	5.25	127.50	66.1	67.5	75.5	77.0	82.2	82.7	99.4
8	0.12	2.43	54.66	55.0	53.7	62.9	57.4	69.0	64.6	97.1
9	0.26	5.25	127.50	66.9	67.5	74.6	77.0	82.3	82.7	99.4
10	0.12	2.43	200.34	27.1	21.4	38.0	31.6	47.1	36.5	96.1
11	0.26	5.25	127.50	66.3	67.5	76.0	77.0	80.1	82.7	99.4
12	0.26	5.25	5.00	94.2	93.1	90.9	93.8	95.7	96.7	90.7
13	0.26	5.25	250.00	55.8	55.0	61.0	62.2	68.9	71.7	98.9
14	0.12	8.07	200.34	41.7	45.6	49.0	49.8	52.3	54.7	85.8
15	0.26	0.50	127.50	45.1	50.4	50.7	59.4	54.1	65.0	97.0
16	0.40	2.43	200.34	61.0	62.6	70.5	69.2	79.2	78.8	97.0
17	0.26	5.25	127.50	68.6	67.5	77.7	77.0	84.9	82.7	99.4
18	0.26	10.00	127.50	79.7	72.5	85.3	80.7	90.6	83.5	90.1
19	0.26	5.25	127.50	65.6	67.5	77.7	77.0	81.2	82.7	99.4
20	0.50	5.25	127.50	89.9	85.3	93.4	91.3	95.5	91.7	98.2

Table 3
ANOVA results for paracetamol removal by OMS-2/PS

Source	Sum of squares	DF	Mean square	F-value	Probability (P) > F
Model	7,101.06	9	789.01	31.74	<0.0001 significant
Residual	248.56	10	24.86		
Lack of fit	224.77	5	44.95	9.45	0.0138
Pure error	23.79	5	4.76		
Corrected total	7,349.63	19			

R^2: 0.9662, Adj. R^2: 0.9357, Pred. R^2: 0.7553, Adeq. Precision: 20.335, CV: 7.69

(Adj. R^2) corrects the determination coefficient for the sample size and the number of terms in the model [21]. The Adj. R^2-value was very close to R^2-value. So the model was confirmed to be very important. The adequate precision and coefficient of variance (CV) values for the paracetamol removal were 20.335 and 7.69, respectively. Adequate precision value was greater than 4 as desired for the model. The model cannot be considered reproducible if the CV value is greater than 10% [22]. The importance of each parameter was evaluated according to the p-value. A p-value <0.05 indicates statistical significance for the response. Table 4 shows the factors that have a significant effect on paracetamol removal. OMS-2 amount (A) ($p < 0.0001$), persulfate concentration (B) (p:0.0007) and paracetamol concentration (C) ($p < 0.0001$) and quadratic OMS-2 amount (A^2) (p:0.0104) were significant terms. It was found that OMS-2 amount and paracetamol concentration were highly significant for paracetamol removal with a p-value < 0.0001. The following was the order of significance for paracetamol removal with regard to the F-value: OMS-2 amount (169.03) > paracetamol concentration (70.76) > persulfate concentration (23.54). These results are also verified by the perturbation plot given in Fig. 2. This shows high steepness with coded factor A (OMS-2 amount) that describes the principal factor for paracetamol removal.

To avoid misleading results, it is also necessary to check the level of competence of the model. This can be accomplished by the residual graphs being examined to approach the model [23]. In the normal probability and studentized residual plot (Fig. 3), the residuals were spread out in an almost straight line. Furthermore, it shows that a response transformation was not required, there was no apparent problem with normality and a good correlation between the experimental and predicted values, while the variables followed a normal distribution [24]. Therefore, the model could be used to predict the paracetamol removal from experimental conditions given. The residual vs. run plots for the response are displayed in Fig. 4a and b. In the plot, the points were randomly dispersed around the horizontal line, indicating that the model fitted the data, and the response was systematically affected by the variables. There was no such alarm because all the points were within the red limits. Fig. 5 represents the predicted vs. actual value plot of paracetamol removal. It can be interpreted from the graph that all the points deviate less than the straight line. This shows that the data obtained from the experiments quite agree with the predicted values obtained from the development of the model.

Table 4
Estimates of the model regression for paracetamol removal by OMS-2/PS

Source	Parameter estimate	*F*-value	Probability (P) > *F*
Intercept	67.54	31.74	<0.0001
A	17.54	169.03	<0.0001
B	6.55	23.54	0.0007
C	–11.35	70.76	<0.0001
AB	–1.90	1.16	0.3064
AC	1.15	0.43	0.5288
BC	3.63	4.23	0.0668
A^2	–4.13	9.91	0.0104
B^2	–2.15	2.69	0.1320
C^2	2.30	3.07	0.1104

3.2. Response surface and counter plots for OMS-2/PS

To assess the interactive relationships between the operational variables and treatment outputs for paracetamol removal, response surface and contour plots (Figs. 6–8) were used based on the quadratic polynomial model.

Fig. 6 demonstrates the effects of OMS-2 amount and persulfate concentration on paracetamol removal at a constant paracetamol concentration of 127.50 mg/L and a reaction time of 5 min. The paracetamol removal efficiency increased with increasing OMS-2 amount. Paracetamol removal efficiencies were 23.7, 67.5 and 89.9% for OMS-2 amounts of 0.02, 0.26 and 0.50 g/L at persulfate concentration of 5.25 g/L and paracetamol concentration of 127.50 mg/L. This result indicates that with an additional OMS-2 amount, more active sites become available for persulfate activation, which produces more radicals and results in a higher paracetamol removal efficiency. When the OMS-2 amount is low (e.g., 0.02 g/L), the paracetamol removal efficiency was 23.7%. Since the persulfate amount was the same, lower removal efficiency indicates a reduced amount of active site in OMS-2. Fan et al. [25] synthesized manganese oxide-loaded sludge-derived biochar (Mn-SDBC) and used it to activate persulfate for Orange G (OG) removal. At 0.5 g/L, a 75.28% removal rate can be achieved in 720 min. When catalyst dosage was amount to 1.0, 1.5, and 2.0 g/L, the OG

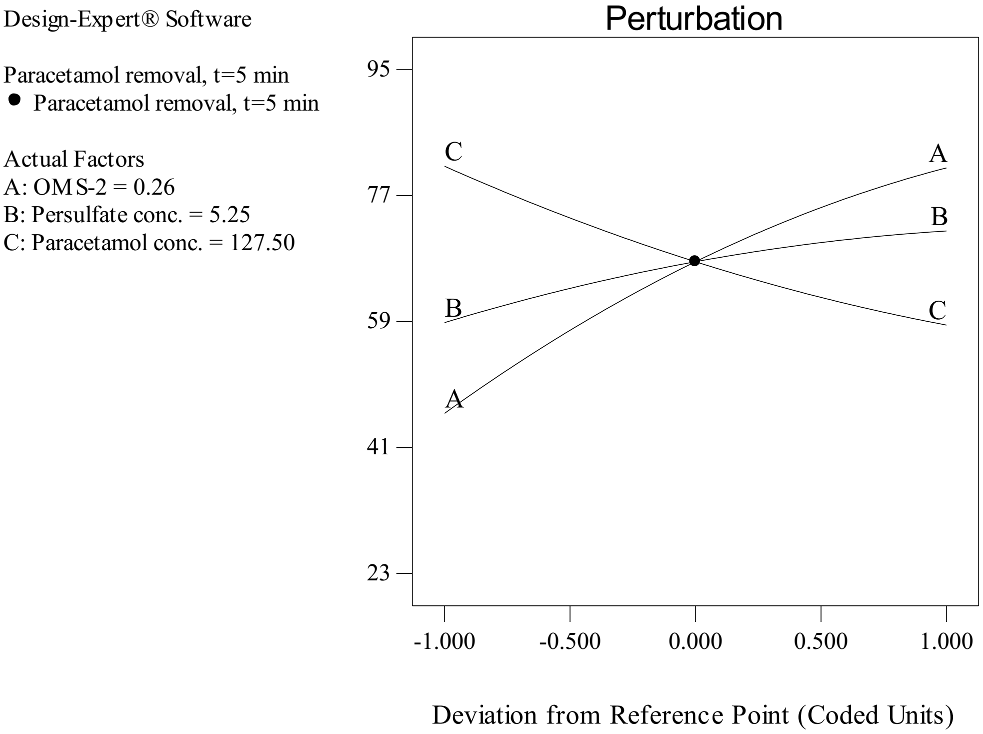

Fig. 2. Perturbation plot comparing effect of parameters including OMS-2 amount (A), persulfate amount (B) and paracetamol concentration (C) on paracetamol removal by OMS-2/PS system.

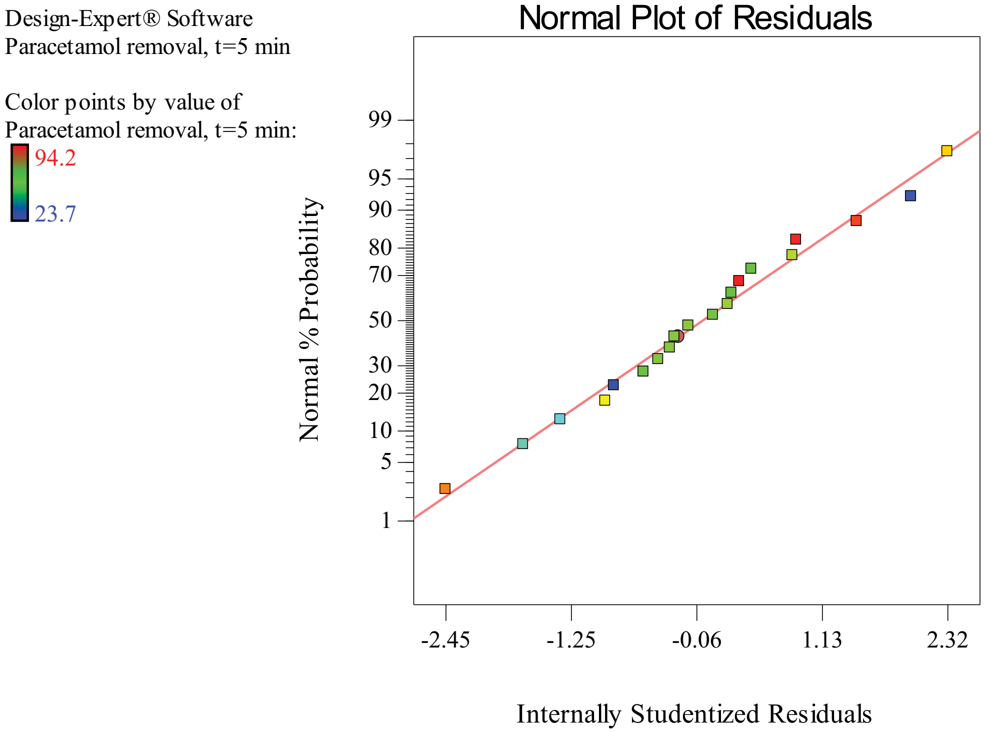

Fig. 3. Normal plot of residuals of paracetamol removal.

removal efficiency increased notably to 90.28%, 94.22%, and 95.94%, respectively.

Enhancing the persulfate concentration could also improve paracetamol removal efficiency. Paracetamol removal efficiencies were 45.1%, 67.5% and 79.7% for persulfate concentrations of 0.50, 5.25 and 10.00 g/L at OMS-2 amount of 0.26 g/L and paracetamol concentration of 127.50 mg/L. The persulfate concentration is known to be directly related to the number of radicals generated leading to paracetamol removal [26]. Since persulfate was the source of high oxidative radicals in the OMS-2/persulfate process, an increase in persulfate concentration consequently enhanced the paracetamol removal efficiency. As more persulfate was added into the solution, a quicker reaction was observed, which indicates that more active species were produced and higher catalytic efficiency has resulted. Tunç [17] examined the removal of Everdirect Supra Red BWS dye with a heat-activated persulfate process, stated that the dye removal efficiency increased with the increase in persulfate concentration, and this could be attributed to the formation of more radicals.

Fig. 7 demonstrates the effects of OMS-2 amount and paracetamol concentration on paracetamol removal at a constant persulfate concentration of 5.25 g/L and a reaction time of 5 min. As can be seen, the paracetamol removal efficiency decreased with increasing paracetamol concentration. Paracetamol removal efficiencies were 94.2%, 67.5% and 55.8% for paracetamol concentrations of 5.0, 127.5 and 250.0 mg/L at OMS-2 amount of 0.26 g/L and persulfate concentration of 5.25 g/L. Due to the same concentrations of produced reactive radicals under the same concentrations of OMS-2 and persulfate, a high concentration of paracetamol in solution will require more time to achieve the same removal efficiency, thus lowering the removal efficiency. The presumed reason was that excess paracetamol molecules occupied a greater number of OMS-2 active sites. This occurrence resulted in decreasing radical production [22].

Duan et al. [27] studied the photodegradation of Acid Orange 7 (AO7) with peroxymonosulfate (PMS) with OMS-2 as a catalyst. At a concentration of 20 mg/L AO7, nearly complete removal was achieved in about 10 min, while at a concentration of 200 mg/L AO7, the removal was 85% within 10 min. At a concentration of 400 mg/L, 75% of AO7 was removed within 20 min.

Fig. 8 demonstrates the effects of persulfate amount and paracetamol concentration on paracetamol removal at a constant OMS-2 amount of 0.26 g/L and a reaction time of 5 min. As can be seen, the paracetamol removal efficiency increased with increasing persulfate amount and decreased with increasing paracetamol concentration.

The effect of initial pH on the paracetamol removal by the OMS-2/PS has not been studied. Many studies have shown that the acidic condition is more suitable for the treatment of organic compounds with activated PS than alkaline conditions [28]. But pH adjustment was not made in our study. As seen in Table 5, in all experimental runs, the pH fell during the reaction due to the decomposition of the persulfate [19]. This shows that, in general, this technology has the advantage of wide pH adaptability and may be applied to real wastewater treatment without adjusting the pH. The structure of OMS-2 may be destroyed by acidic conditions, resulting in Mn leaching. The manganese concentration after the reaction increased (Table 5). This indicated that Mn was leached from OMS-2.

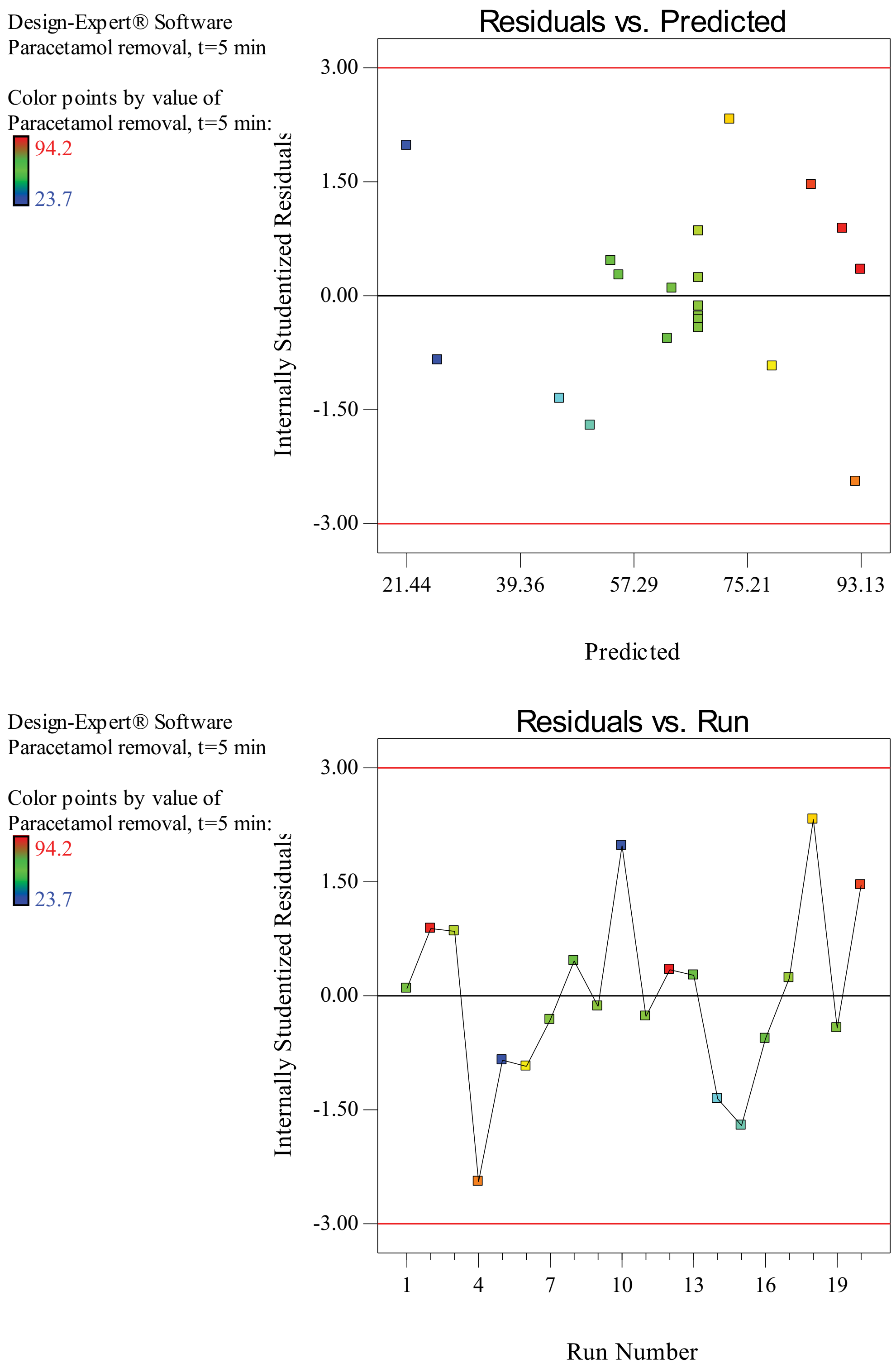

Fig. 4. Residuals vs. predicted plot and residuals vs. run plot of paracetamol removal.

According to the above results, the mechanism of activation of PS by OMS-2 catalyst was proposed as Eqs. (2)–(6). The metal ions on the surfaces of OMS-2 could act as active sites for the reduction of PS to generate sulfate and hydroxyl radicals. First, $S_2O_8^{2-}$ was adsorbed on the surface of OMS-2. Then, Mn ions in OMS-2 serve as active sites to provide redox electrons for the reduction of PS, and the oxidation of Mn occurred [29].

$$S_2O_8^{2-} + Mn(III) \rightarrow SO_4^{-\bullet} + SO_4^{2-} + Mn(IV) \quad (2)$$

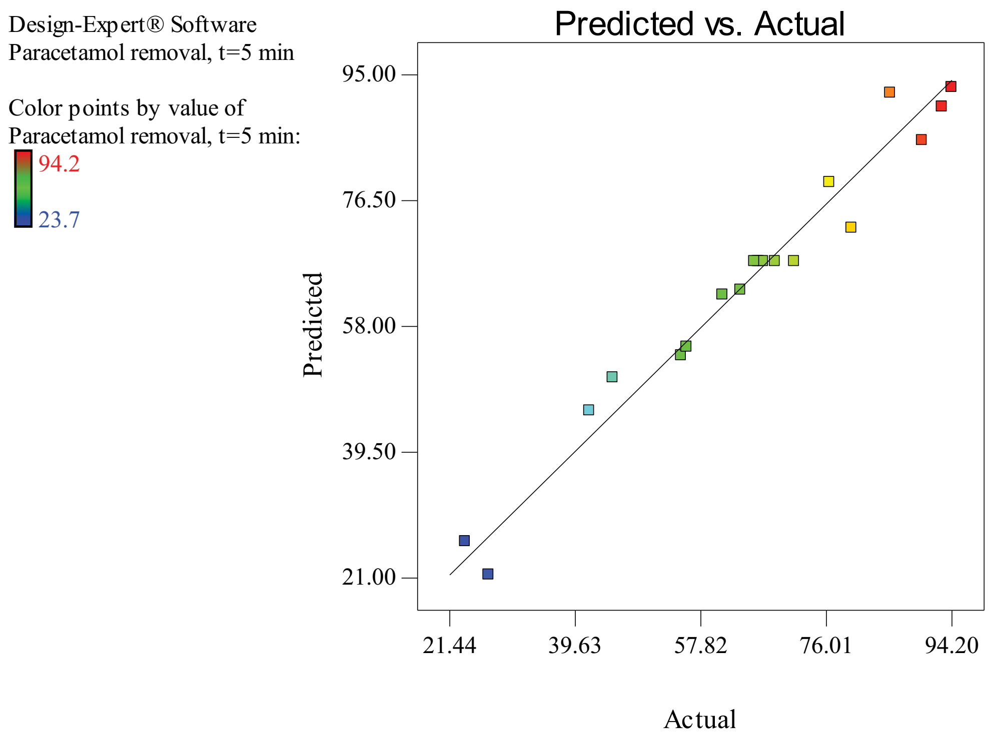

Fig. 5. Plot signifying agreement between actual and predicted values for paracetamol removal.

Table 5
pH variations and Mn concentration leached at the end of runs

Runs	Effluent pH	Leached Mn (mg/L)
1	3.53	16.9
2	2.86	8.0
3	2.75	20.8
4	2.78	4.6
5	3.53	16.9
6	2.65	31.9
7	2.68	14.8
8	3.14	12.5
9	2.82	23.7
10	3.53	45.8
11	2.83	19.2
12	3.05	4.5
13	2.90	52.2
14	3.14	28.7
15	3.74	32.8
16	2.90	43.6
17	2.94	17.8
18	2.73	18.0
19	2.88	15.6
20	2.67	12.2

$$S_2O_8^{2-} + \mathrm{Mn}(\mathrm{II}) \rightarrow + SO_4^{-\bullet} + SO_4^{2-} + \mathrm{Mn}(\mathrm{III}) \tag{3}$$

$$S_2O_8^{2-} + \mathrm{Mn}(\mathrm{IV}) \rightarrow S_2O_8^{-\bullet} + \mathrm{Mn}(\mathrm{III}) \tag{4}$$

$$SO_4^{-\bullet} + H_2O \rightarrow HO^{\bullet} + H^{+} + SO_4^{2-} \tag{5}$$

$$SO_4^{-\bullet} + OH^{-} \rightarrow HO^{\bullet} + SO_4^{2-} \tag{6}$$

Subsequently, Mn with high valence states would convert into Mn(III) via PS. Ultimately, these reactions constructed the Mn transformation cycle [30].

In our previous study, it was revealed that sulfate radicals are the dominant reactive species in the OMS-2/PS system [3]. However, the sulfate radical is very short-lived (30–40 μs) and therefore does not accumulate in the reaction medium [31]. Based on this, we can state that the concentration of sulfate radicals is stable during the reaction. This explains the higher rate of removal in the early stages of the reaction. For example, paracetamol removal efficiencies after 5, 10, 15 and 180 min in run 1 are 63.6%, 65.4%, 73.5% and 80%, respectively. As the reaction time was prolonged, the removal efficiency did not increase much. However, the reaction time was prolonged when very high paracetamol concentrations were used. The longer reaction time increases the process costs. To determine the reaction rate constants in run 1, the first-order kinetic model given in Eq. (7) was applied. Here, k is the first-order rate constant and C is the concentration of paracetamol at various times (t). C_o is the initial concentration of paracetamol.

$$\ln\left(\frac{C}{C_o}\right) = -kt \tag{7}$$

where Time vs. $\ln(C/C_o)$ was plotted, and it can be concluded that data fitted to the first-order kinetic model with

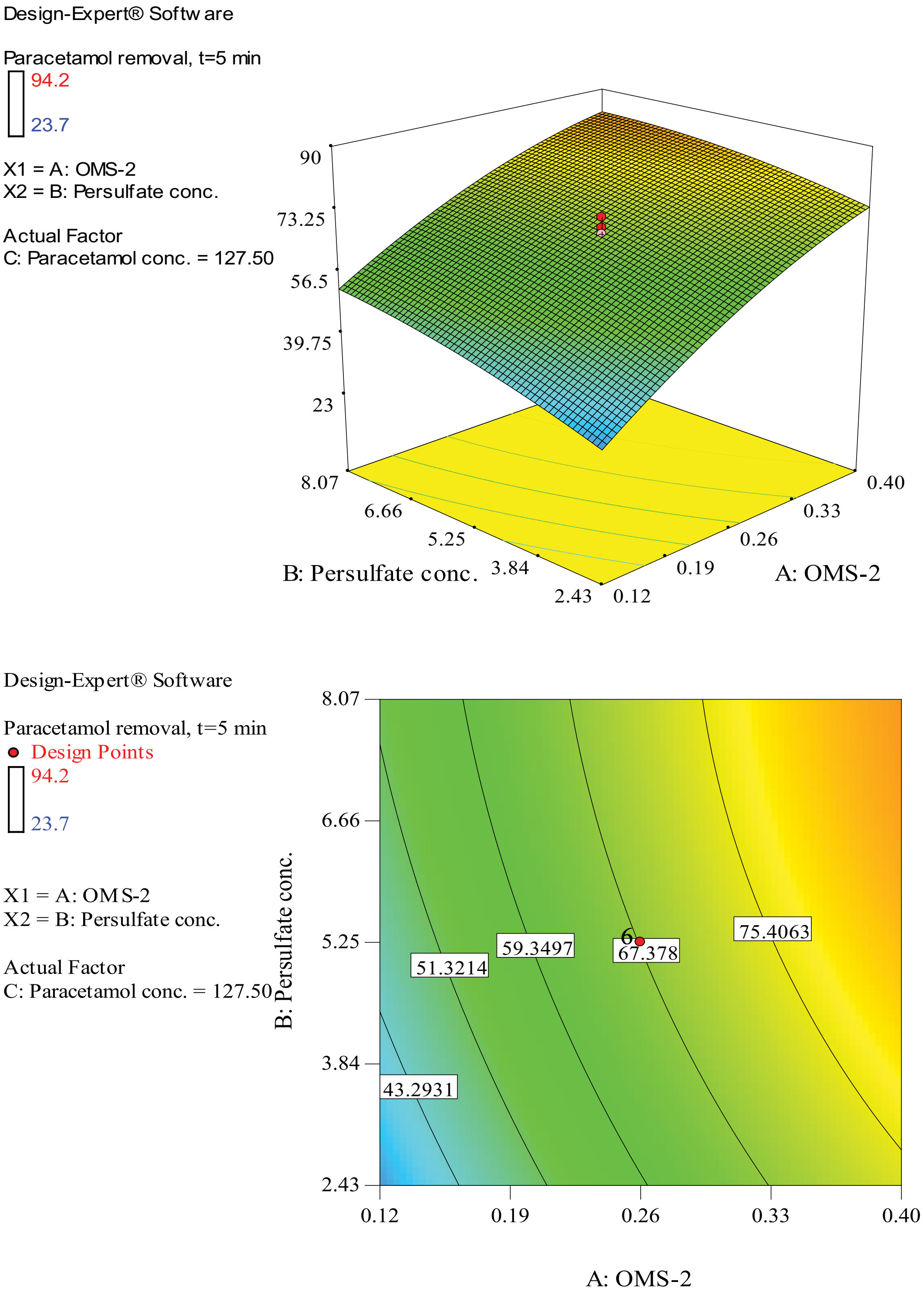

Fig. 6. 3-D surface and contour plots presenting the effect of OMS-2 amount and persulfate concentration on paracetamol removal by OMS-2/PS.

high regression coefficients (R^2, 0.79–1.00). First-order rate constants were 0.2021, 0.1061, and 0.0807 min^{-1} at 5, 10 and 15 min, respectively. It can easily be seen that the reaction time has a negative effect on the reaction rate constants. The highest rate constant was obtained at 5 min. In our previous study, the reusability of OMS-2 was tested and after a reaction time of 180 min in the first cycle, the paracetamol removal efficiency of 99.0% decreased to 52.9% in the fifth cycle.

RSM was applied for reaction times of 5, 10, 15 and 180 min. The determination coefficients (R^2) of the model

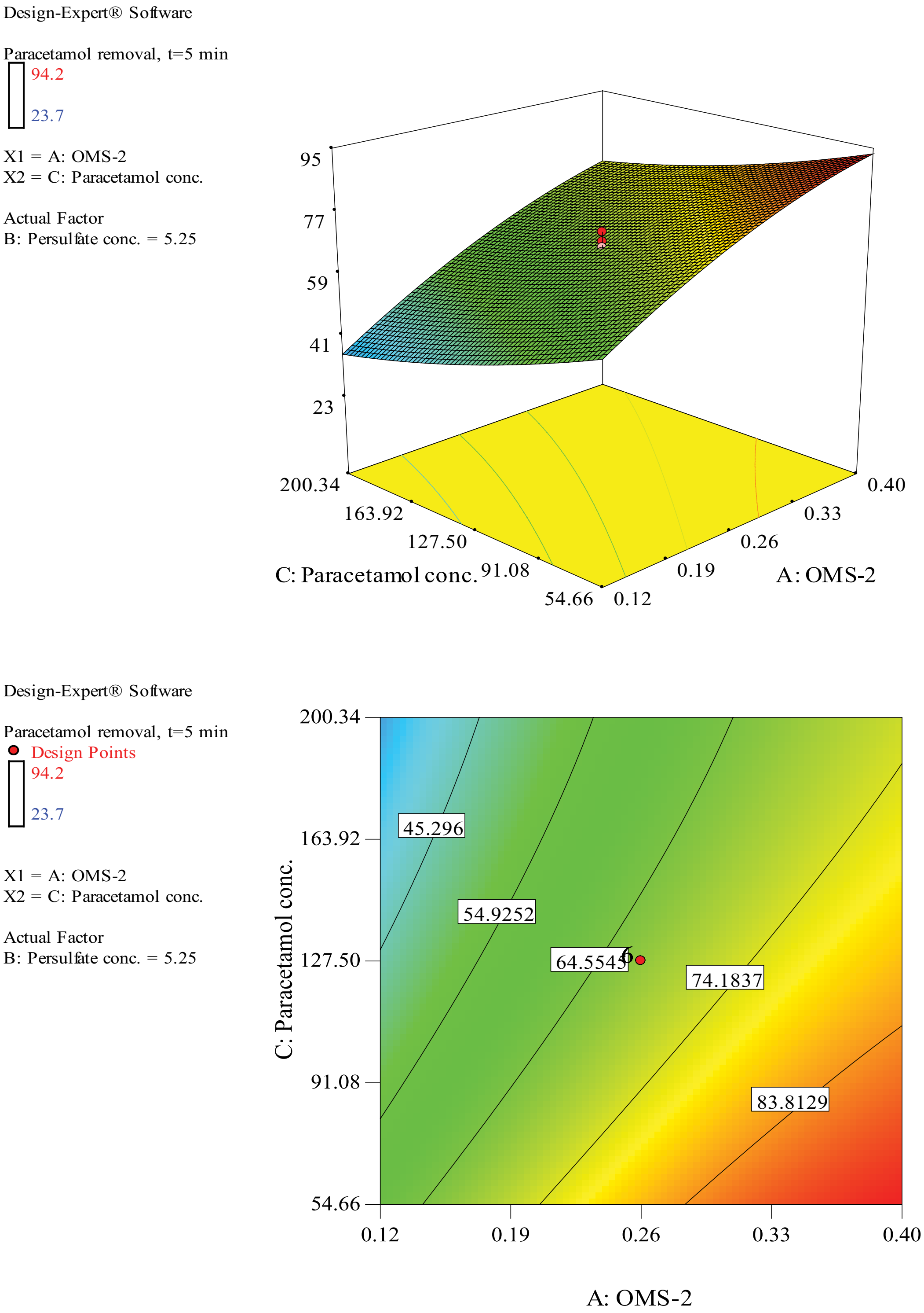

Fig. 7. 3-D surface and contour plots presenting the effect of OMS-2 amount and paracetamol concentration on paracetamol removal by OMS-2/PS.

were 96.62%, 96.09%, 92.04% and 82.91% while the Adj. R^2-values of the model were 93.57%, 92.58%, 84.87% and 65.52% for reaction times of 5, 10, 15 and 180 min, respectively. However, according to the ANOVA results, the highest determination coefficient was obtained in a reaction time of 5 min. Therefore, ANOVA results of reaction time of 5 min were given.

The desirability function can be used for the prediction of determining the most suitable experimental conditions. The desirable ranges as a numerical can change from zero to

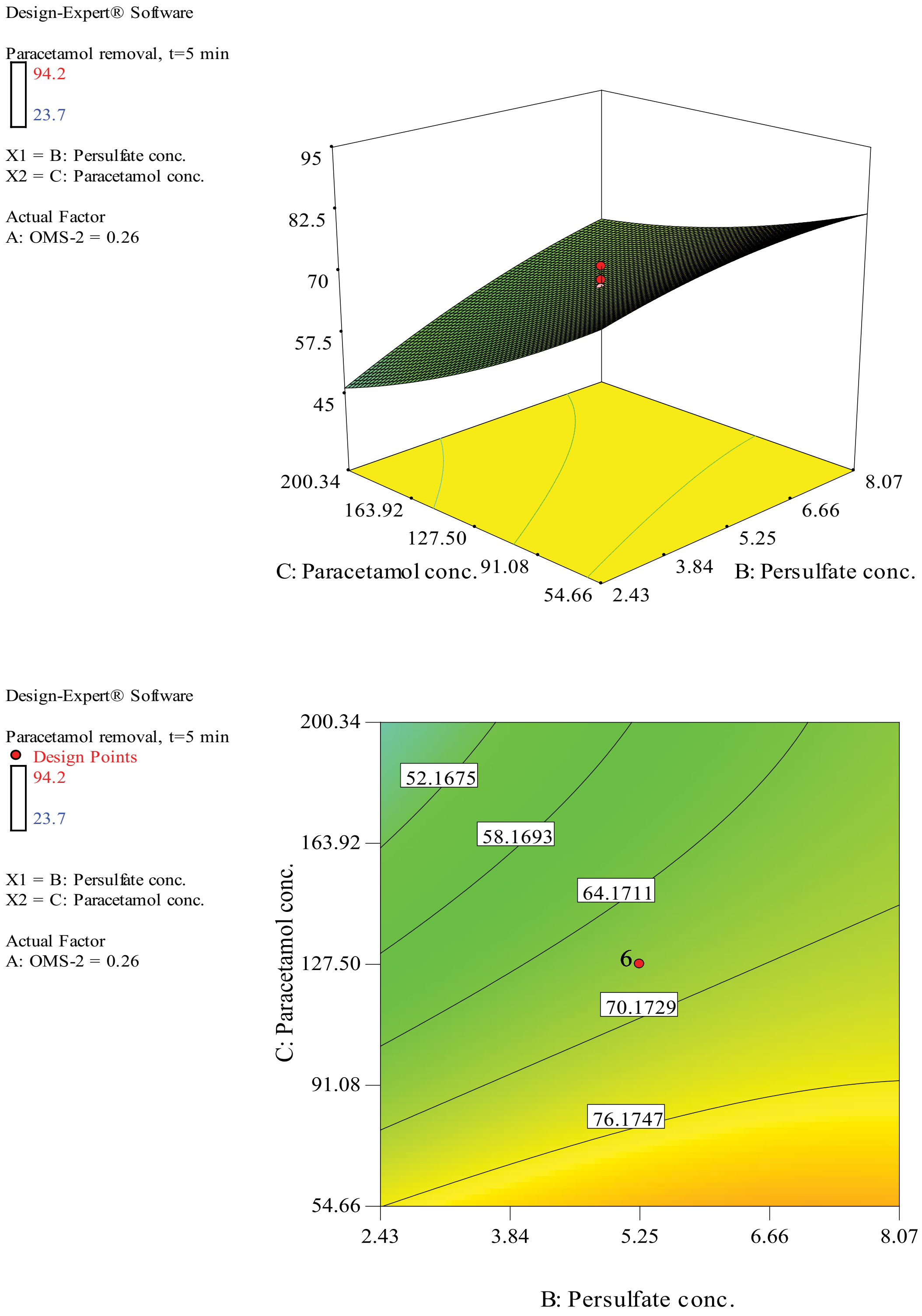

Fig. 8. 3-D surface and contour plots presenting the effect of persulfate concentration and paracetamol concentration on paracetamol removal by OMS-2/PS.

one or the desired goal [32]. In the present study, the target was maximum paracetamol removal. Optimum conditions for maximum paracetamol removal were found as OMS-2 amount of 0.40 g/L, persulfate concentration of 5.93 g/L and paracetamol concentration of 54.66 mg/L by using desirability function (Fig. 9). Under these conditions, the paracetamol removal efficiency was 93.6%.

Various process variables and optimization results of several studies in which RSM was applied to remove pollutants using persulfate activated with different activators are

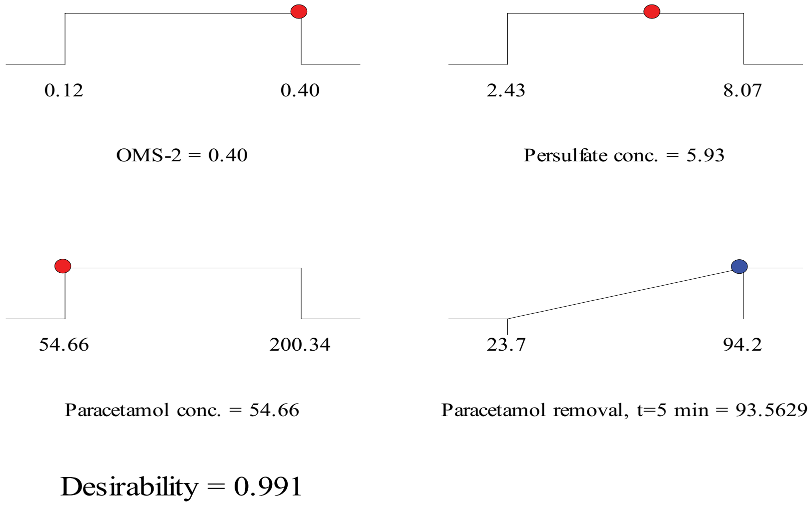

Fig. 9. Desirability ramps for maximum paracetamol removal by OMS-2/PS system.

Table 6
Several process variables and optimization results of few studies that RSM was applied in removal of pollutant

Process	Pollutant	RSM		Optimization		References
		Method	Process variables	Optimum conditions	Efficiency	
Heat-activated peroxydisulfate (PDS)	Paracetamol	CCD	Temperature PDS concentration Initial pH Paracetamol concentration	68 °C 5 mM pH 6 0.33 mM	94.2%	[33]
Persulfate ($S_2O_8^{-2}$) in the presence of biochar modified by lanthanum chloride and ultrasonic waves (US)	Phenol	CCD	Phenol concentration pH Catalyst dose Persulfate concentration Temperature Contact time	86 mg/L pH of 4 43 mg/L 86 mg/L 41°C 63 min	97.68%	[34]
Electrochemically activated persulfate	Sulfamethoxazole	CCD	pH Current (mA) Persulfate concentration (mM) Electrolysis time (min)	4 18.5 mA 3.83 mM 56 min	83.21%	[35]
Nano zero-valent iron-modified Degussa P25-TiO_2/ZnO photocatalyst with persulfate	p-nitrophenol	CCD	pH Fe^0 wt.% $K_2S_2O_8$	pH 7.5 25/1.5 wt.% Fe^0/ZnO 3 mg/L	86.9%	[36]
Ferrous (Fe^{2+})-activated potassium persulfate (PS)	Reactive Black 5	CCD	pH PS Fe^{2+}	3.72 0.39 mM 0.29 mM	93.28%	[37]
Biochar-supported zero-valent iron (ZVI/BS) catalysed persulfate (PS)	Atrazine	CCD	ZVI/BC PS pH	175 mg/L 2 mM pH 3	83.77%	[38]
OMS-2/persulfate	Paracetamol	CCD	OMS-2 amount Persulfate concentration Paracetamol concentration	0.40 g/L 5.93 g/L 54.66 mg/L	93.6%	Present study

presented in Table 6. In comparison with given processes, the OMS-2/persulfate process almost exhibited similar performance for removing the pollutants. The results of this study showed that this process is an effective process for the removal of pollutants.

4. Conclusion

In this study, the OMS-2/persulfate process was used for paracetamol removal. RSM was employed to evaluate, model, and optimize paracetamol removal by the OMS-2/persulfate process. According to the results of variance analysis (ANOVA), the second-order polynomial model was statistically significant. RSM showed that increasing OMS-2 amount (*A*) and persulfate concentration (*B*) had a positive effect while increasing paracetamol concentration (*C*) had an adverse effect on paracetamol removal. *A*, *B*, *C*, and A^2 on the paracetamol removal were important model variables. The experimental design methodology was considered to determine the optimal values of the operating parameters, leading to 93.6% paracetamol removal under the optimal conditions, namely the OMS-2 amount of 0.40 g/L, the persulfate concentration of 5.93 g/L, and the paracetamol concentration of 54.66 mg/L. As a result, it can be said that the OMS-2/persulfate process is effective in the removal of paracetamol from aqueous solutions; moreover, CCD and RSM are eligible tools in the optimization of paracetamol removal from aqueous solutions through the OMS-2/persulfate process.

Declarations

Conflict of interest

The authors declare no conflict of interest associated with this manuscript.

Ethical approval

We state that this material has not been published and is not under active consideration by another journal.

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